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Supporting Information

Homochiral versus Heterochiral Dimeric Helical Foldamer Bundles: Chlorinated-Solvent-Dependent Self-Sorting

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1 List of Abbreviations

CD → circular dichroism

DCM → dichloromethane

DCE → dichloroethane

DIPEA→ *N*,*N*-diisopropylethylamine

DMF→ *N*,*N*-dimethylformamide

DMSO → dimethyl sulfoxide

DOSY → diffusion ordered spectroscopy

HR-ESI → high resolution electrospray ionization

EtOAc → ethylacetate

eq → equivalent

Fmoc → fluorenylmethoxycarbonyl

HBTU → hexafluorophosphate benzotriazole tetramethyl uronium

HFIP → hexafluoroisopropanol

HSQC → heteronuclear single quantum correlation

Me → methyl

MeOH → methanol

Min → minutes

MPLC → Medium pressure liquid chromatography

MS → mass spectrometry

MW → microwave

hex → hexane

NMP → N-Methyl-2-pyrrolidone

NMR → nuclear magnetic resonance

Pd/C → palladium on carbon

r. t. → room temperature

SPS → solid phase synthesis

***t*Bu** → *tert*-butyl

TFA → trifluoroacetic acid

THF → tetrahydrofuran

TLC → thin layer chromatography

UV/Vis → ultraviolet–visible

2 Supplementary figures

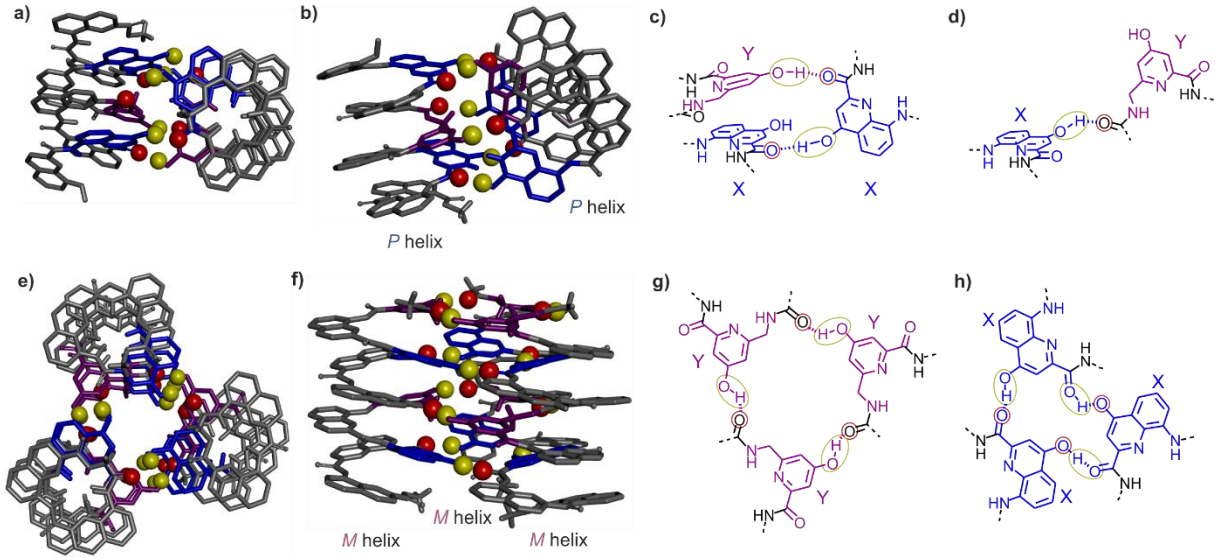


Figure S1. Previously described aggregates and corresponding hydrogen bonding motifs. Top (a) and side view (b) of a crystal structure of a tilted dimer of **1**.[1] Top- (e) and side view (f) of a crystal structure of a trimer of **2**.[1] The hydroxy protons and carbonyl oxygen atoms of the arrays of hydrogen bonds are shown as yellow and red balls, respectively. The X units are shown in blue and the P units in red tubes. Included solvent molecules, nonpolar hydrogen atoms and side-chains are omitted for clarity. The patterns of hydrogen bonds in the tilted dimer of **1** are shown in (c) and (d) and those in the trimer of **2** are shown in (g) and (h).

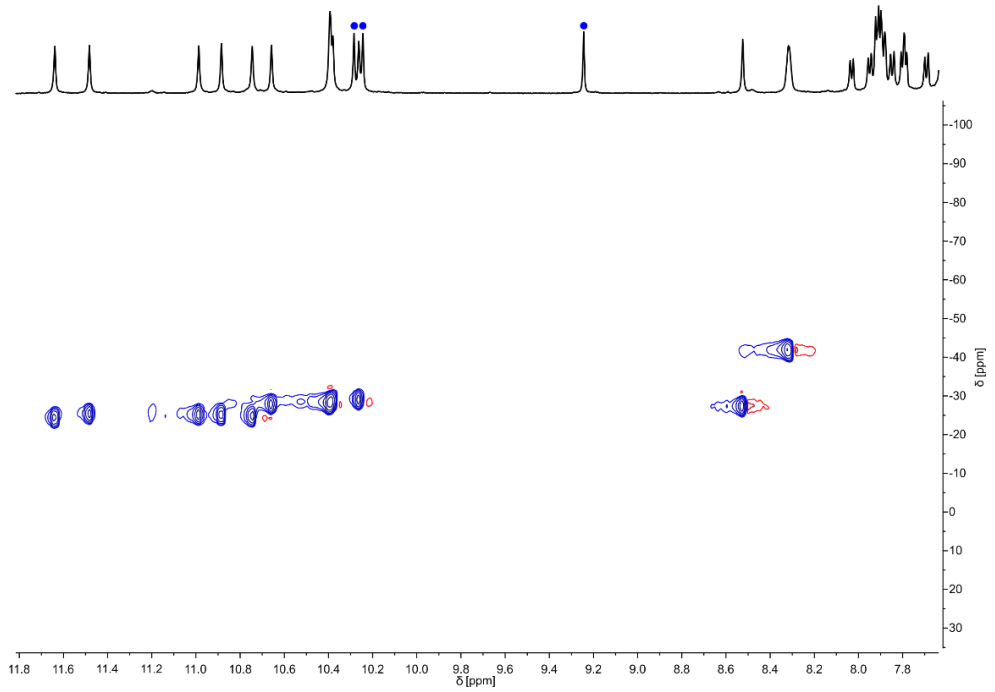


Figure S2. **Identification of hydrogen bonded OH signals of 3 in $CDCl_3$.** Part of the $^{15}N,^{1}H$ HSQC NMR spectrum of **3** (500 MHz, 8 mM in $CDCl_3$) at 25 °C showing the amide and hydroxy proton resonances. Only NH resonances correlate, blue dots indicate the signals of OH protons. The spectrum was measured after 2 h equilibration.

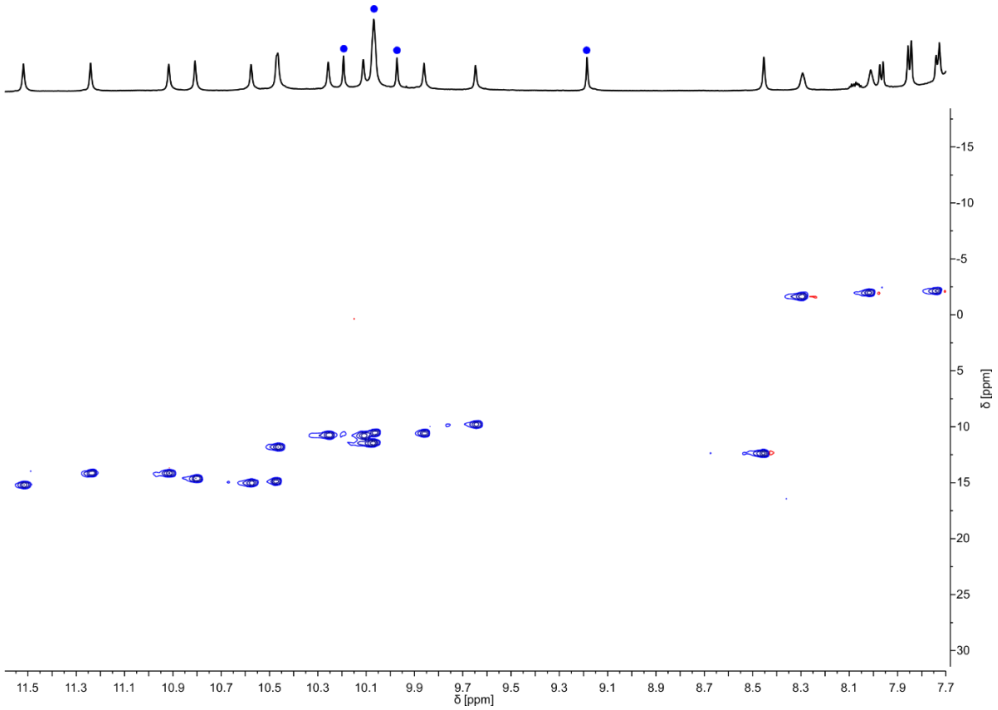


Figure S3. Identification of hydrogen bonded OH signals of 4 in $CDCl_3$. Part of the 500 MHz $^{15}N,^{1}H$ HSQC NMR spectrum of **4** (6.9 mM in $CDCl_3$) at 25 °C showing the amide and hydroxy proton resonances. Only NH resonances correlate, blue dots indicate the signals of OH protons. A pyridine solution of **4** was evaporated, dried and the solid was dissolved in $CDCl_3$ and incubated for four weeks prior to measuring the spectrum.

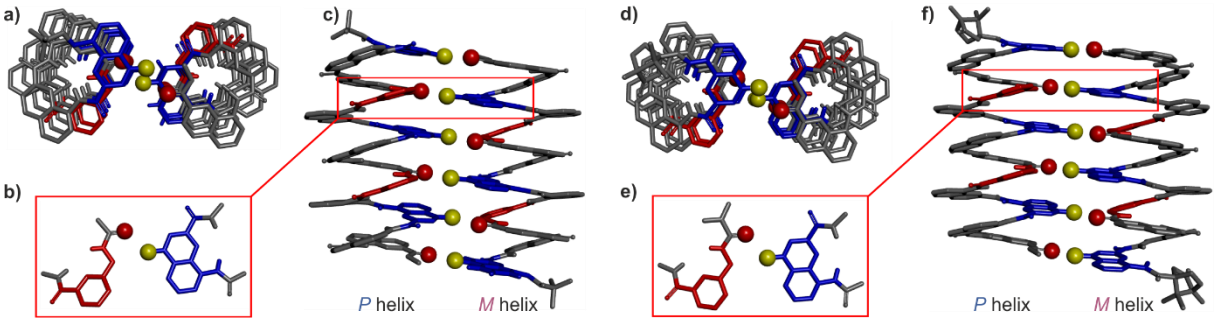


Figure S4. Crystal structures of 3 and 5 from chloroform. Top view (a) and side view (c) of the solid state structure of **3** obtained from crystals grown from $CHCl_3$. The prevalent hydrogen-bonding pattern is shown in (b). Top view (d) and side view (f) of the pseudo-racemic solid state structure of **5** obtained from crystals grown from $CHCl_3$ (a pseudo center of inversion applies to the helices but not to the camphanyl groups). The prevalent hydrogen-bonding pattern is shown in (e). Both structures show a *PM* shifted dimer. The hydrogen-bonding donor and acceptors are shown as yellow and red balls, respectively. The X units are shown in blue and the P Units in red tubes. Included solvent molecules, hydrogen atoms and side-chains are omitted for clarity.

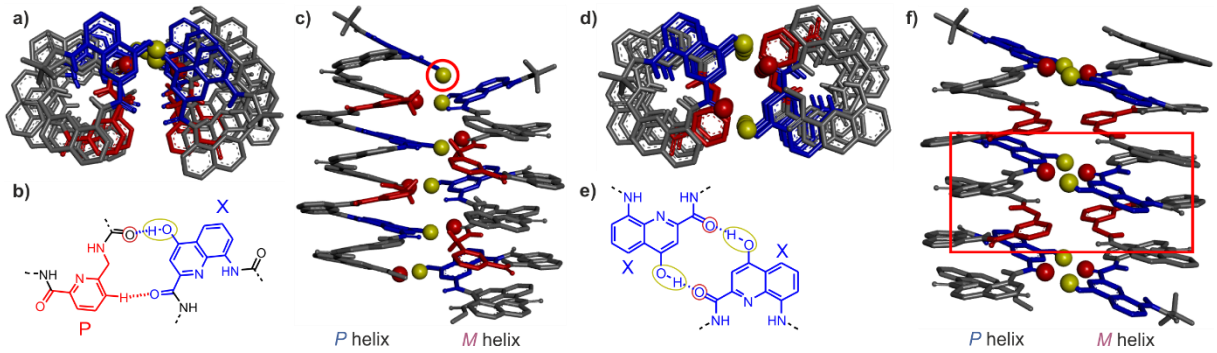


Figure S5. Energy minimized models of alternate, not experimentally observed hydrogen-bonded *PM* dimers. Top view (a) and side view (c) of an energy-minimized computational model[2] of **3** in a head-to-head *PM* shifted dimer arrangement (as opposed to the head-to-tail observed in the crystal). The prevalent hydrogen-bonding pattern is shown in (b). Here, one hydroxy group is not involved in hydrogen-bonding (encircled in red in c). Top view (d), side view (f) and hydrogen-bonding pattern (e) of an energy-minimized computational model[2] of a *PM* head-to-tail (not shifted) parallel arrangement of **3** as observed in a helix-turn-helix tertiary structure.[3] Here, two hydrogen bonds form every other helix turn, instead of one every helix turn in the shifted dimer. The hydrogen-bonding donors and acceptors are shown as yellow and red balls, respectively. The X units are shown in blue and the P Units in red tubes. Included solvent molecules, hydrogen atoms and side-chains are omitted for clarity.

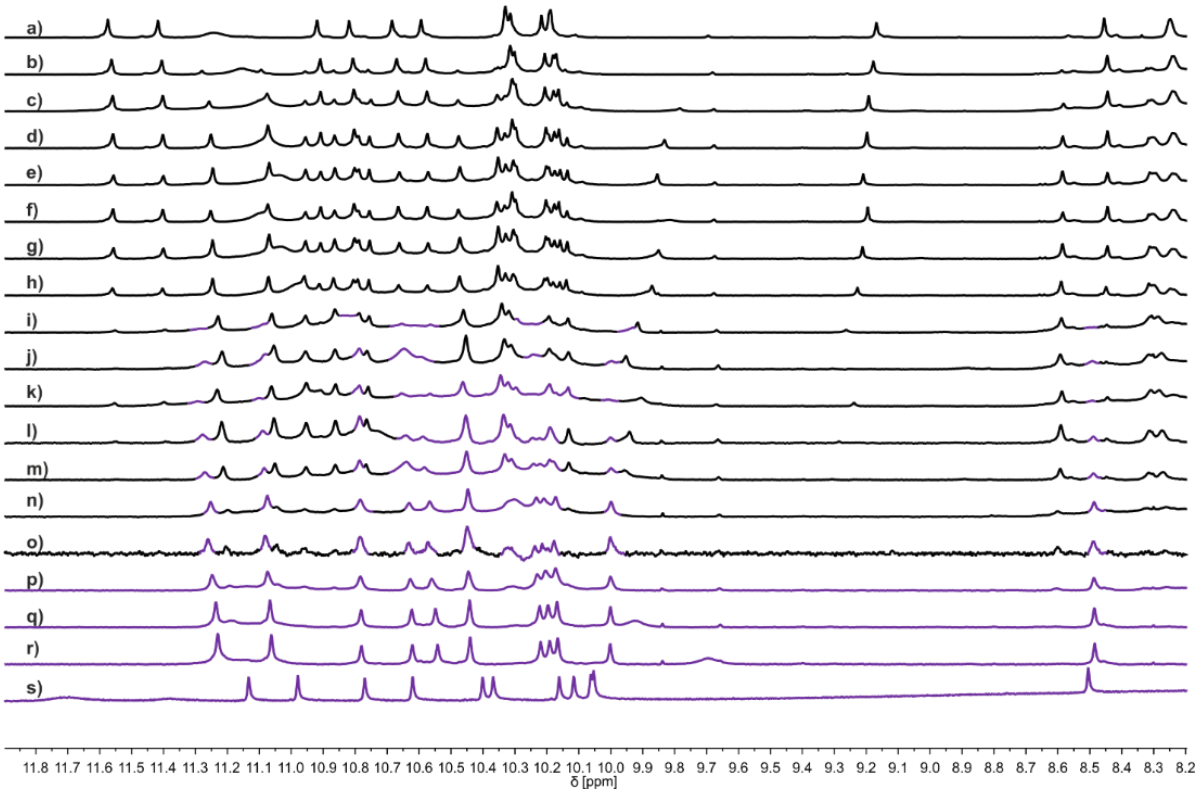


Figure S6. Solution NMR observation of the DMSO-induced dissocation of 3_2. Part of the 500 MHz ^{1}H NMR spectra of **3** (2.4 mM in $CDCl_3$/DMSO-d_6) at 25 °C showing the amide and hydroxy proton resonances. The volume percentages of DMSO-d_6 are 2 (a), 4 (b), 6 (c), 8 (d), 10(e), 12 (f), 14 (g), 16 (h), 18 (i), 20 (j), 22 (k), 24 (l), 26 (m), 28 (n), 30 (o), 32 (p), 34 (q), 36 (r) and 100 (s), respectively. Signals marked in violet color indicate the monomer. All spectra were measured after a 2h incubation time to reach equilibrium.

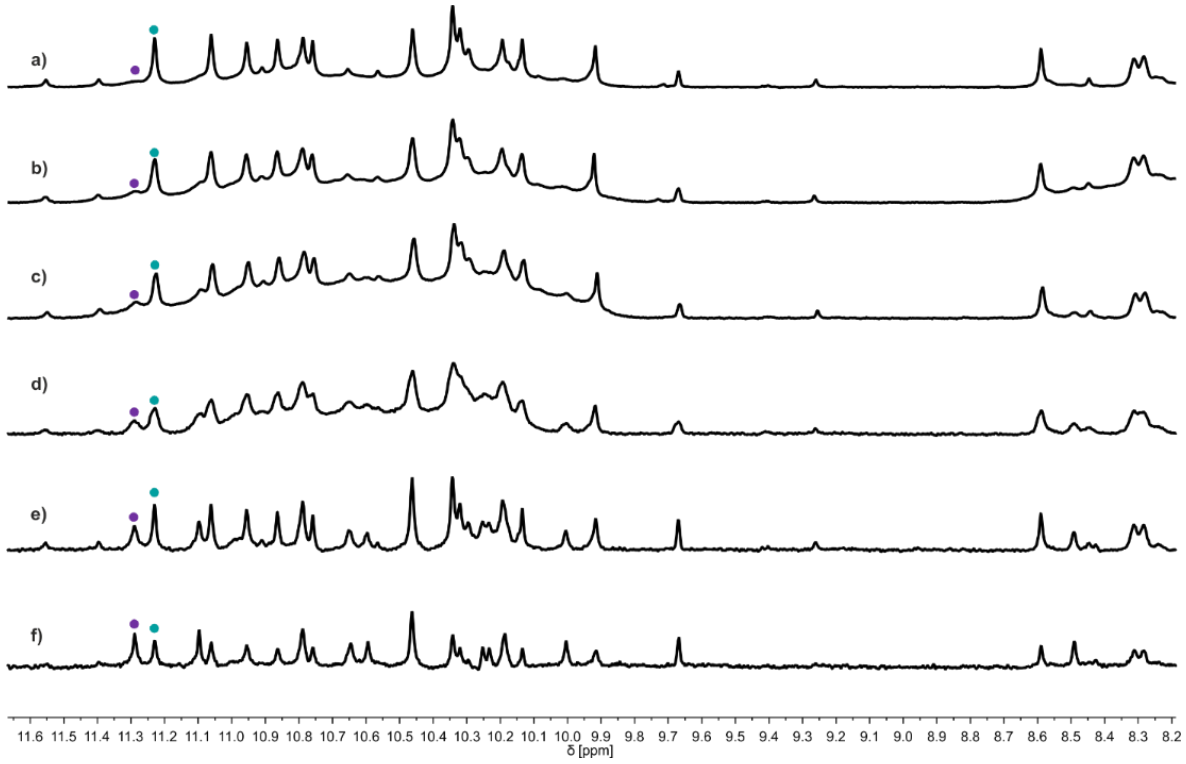


Figure S7. Solution NMR estimation of the dissociation contant of 3_2. Part of the 500 MHz ^{1}H NMR spectra of **3** (in 10:90 DMSO-d_6/$CDCl_3$) at 25 °C showing the amide and hydroxy proton resonances. The total concentration of the sample was 2.44 mM (a), 1.22 mM (b), 0.61 mM (c), 0.30 mM (d), 0.15 mM (e), and 0.076 mM (f). The signals whose integration was used for the determination of the dissociation constant are marked in turquoise and violet. The ratio of monomer to dimer is 10:100 (a), 22:100 (b), 42:100 (c), 92:100 (d), 140:100 (e), 260:100 (f). Thus, the concentration of monomer in solution is 0.12 mM (a), 0.12 mM (b), 0.11 mM (c), 0.095 mM (d), 0.062 mM (e) and 0.043 mM (f). The concentration of dimer in solution is 1.16 mM (a), 0.55 mM (b), 0.25 mM (c), 0.103 mM (d), 0.044 mM (e), 0.017 mM (f). The dissociation constant was calculated using the following equation: $K = \frac{[Monomer]^2}{[Dimer]}$. The value of the dissociation constant equals 1.24 x 10^{-5} (a), 2.62 x 10^{-5} (b), 4.84 x 10^{-5} (c), 8.76 x 10^{-5} (d), 8.73 x 10^{-5} (e) and 1.09 x 10^{-4} M (f) leading to an average dissociation constant K_d of 62 µM. All spectra were measured after a two-week incubation time to reach equilibrium.

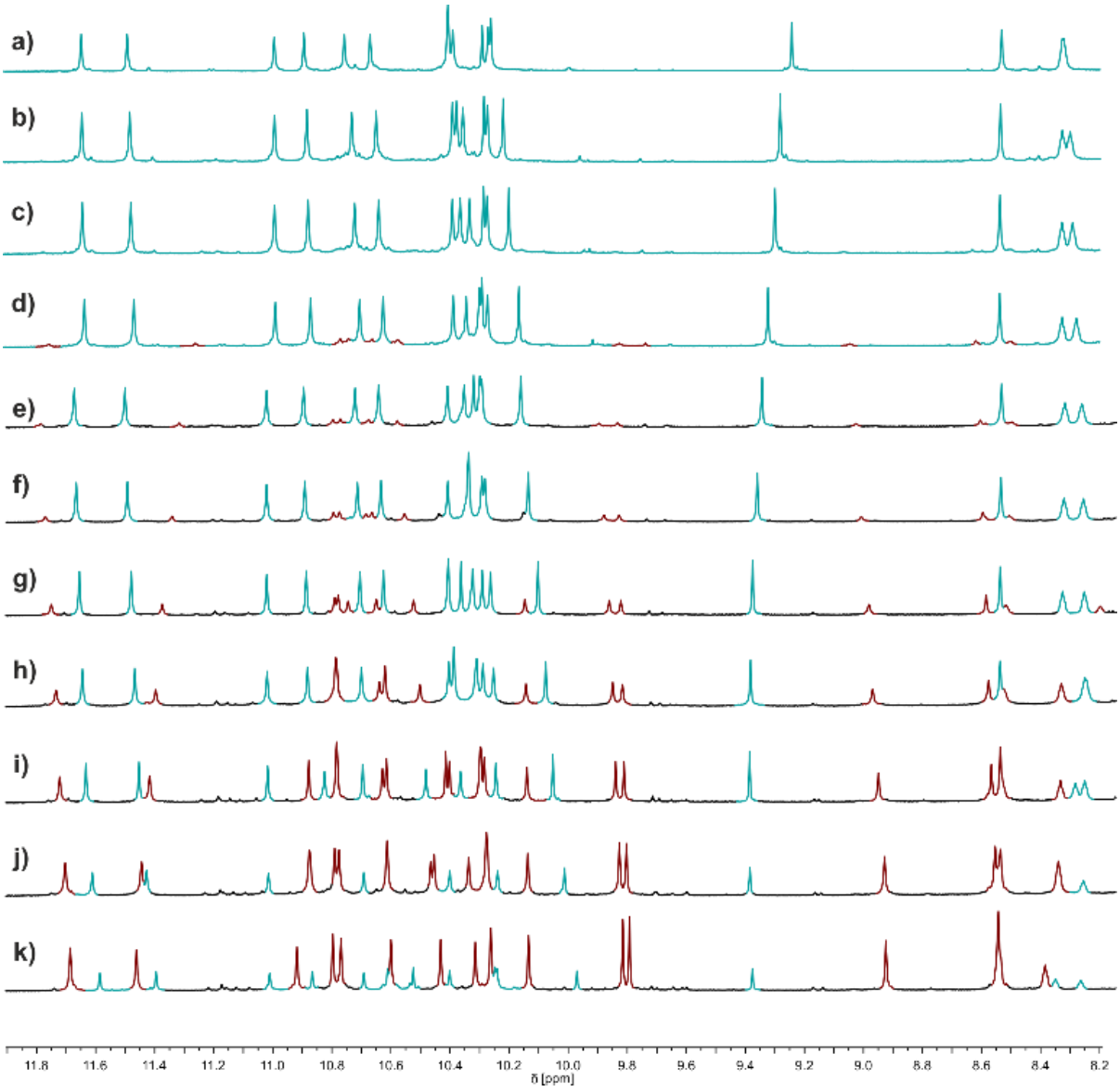


Figure S8. Conversion of the *PM* into the *PP/MM* shifted dimer of 3 upon increasing the proportion of CD_2Cl_2 in $CDCl_3$. Part of the 500 MHz ^{1}H NMR spectra of **3** (2.4 mM in $CDCl_3/CD_2Cl_2$) at 25 °C showing the amide and hydroxy proton resonances. The volume percentages of CD_2Cl_2 are 0 (a), 10 (b), 20 (c), 30 (d), 40 (e), 50 (f), 60 (g), 70 (h), 80 (i), 90 (j) and 100 (k). The signals of two different species are marked with different colors. Signals of the species dominant in $CHCl_3$ (*PM* shifted dimer) are marked in turquoise, those of the species dominant in CH_2Cl_2 (*PP/MM* shifted dimer) are marked in brown. All spectra were measured after a 2h incubation time to reach equilibrium.

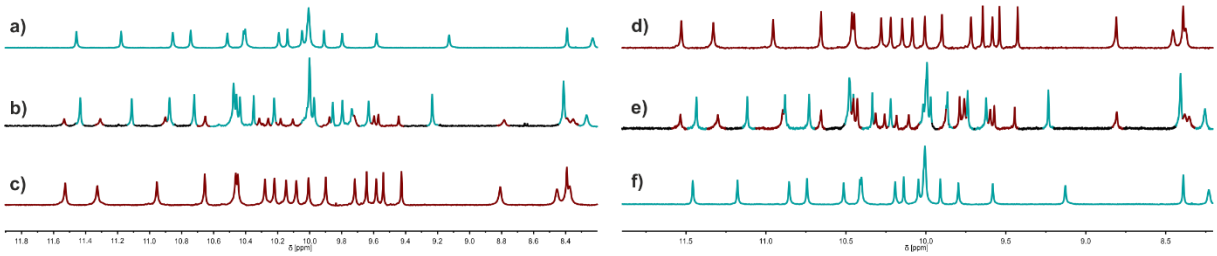


Figure S9. Interconversion of the *PM* and *PP/MM* shifted dimers of 4 upon changing $CDCl_3/CD_2Cl_2$ solvent mixtures. Part of the 500 MHz ^{1}H NMR spectra of **4** (2.4 mM in various solvents) at 25 °C showing the amide and hydroxy proton resonances. a) In $CDCl_3$. b) In 1:1 $CDCl_3/CD_2Cl_2$ after evaporating and re-dissolving sample a). c) In CD_2Cl_2 after evaporating and re-dissolving sample b). d) same as c). e) In 1:1 $CDCl_3/CD_2Cl_2$ after evaporating and re-dissolving sample e). f) In $CDCl_3$ after evaporating and re-dissolving sample e). The slight differences between b) and e) suggest that one sample (probably b) had not fully reached equilibrium. The signals of two different species are marked with different colors. Signals of the species dominant in $CHCl_3$ (*PM* shifted dimer) are marked in turquoise, those of the species dominant in CH_2Cl_2 (*PP/MM* shifted dimer) are marked in brown. Samples were incubated at least three weak prior to measurement.

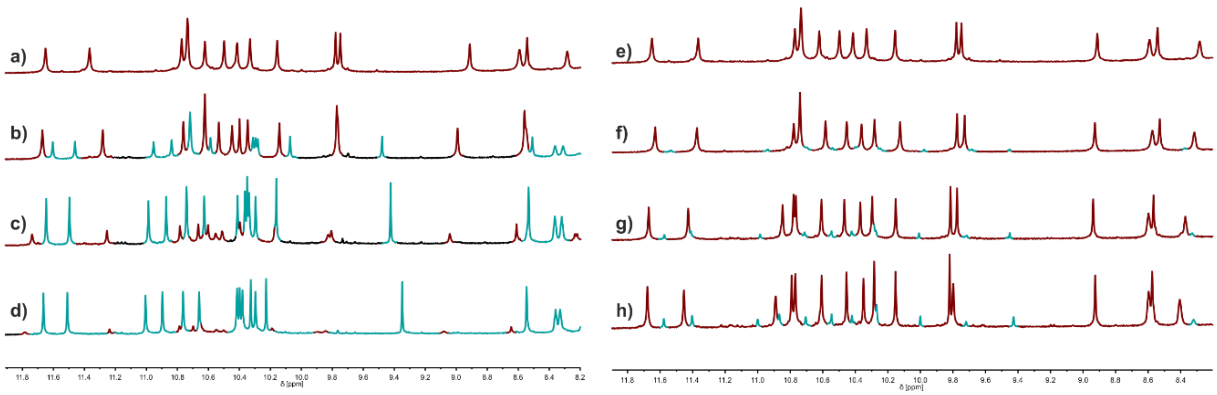


Figure S10. Interconversion of the *PM* and *PP/MM* shifted dimers of 3 upon changing $CDCl_3/(CD_2Cl)_2/CD_2Cl_2$ solvent mixtures. a)-d) Part of the 500 MHz ^{1}H NMR spectra of **3** (2.4 mM in $CDCl_3/(CD_2Cl)_2$ mixtures) at 25 °C showing the amide and hydroxy proton resonances. The volume percentages of $(CD_2Cl)_2$ are 100 (a), 75 (b), 50 (c), 25 (d). e)-f) Part of the ^{1}H NMR spectra (500 MHz, 25 °C) showing the amide and hydroxy proton resonances of **3**, 2.4 mM in $CD_2Cl_2/(CD_2Cl)_2$. The volume percentages of $(CD_2Cl)_2$ are 100 (e), 75 (f), 50 (g), and 25 (h). The signals of two different species are marked with different colors. Signals of the species dominant in $CHCl_3$ (*PM* shifted dimer) are marked in turquoise, those of the species dominant in CH_2Cl_2 (*PP/MM* shifted dimer) are marked in brown. All spectra were measured after a 2h incubation time to reach equilibrium.

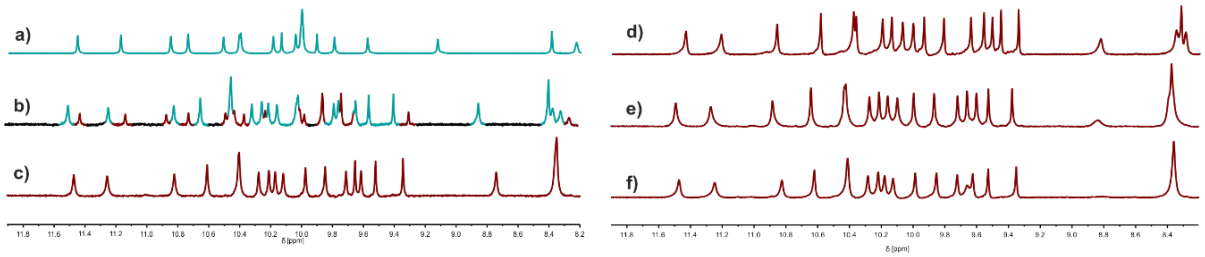


Figure S11. Interconversion of the *PM* and *PP/MM* shifted dimers of 4 upon changing $CDCl_3$/$(CD_2Cl)_2$/CD_2Cl_2 solvent mixtures. Part of the 500 ^{1}H NMR spectra of **4** (2.4 mM in various solvent mixtures) at 25 °C showing the amide and hydroxy proton resonances. a) In $CDCl_3$. b) In 1:1 $CDCl_3$/$(CD_2Cl)_2$. c) In $(CDCl_2)_2$ (sample from b)). d) In CD_2Cl_2. e) In 1:1 CD_2Cl_2/$(CD_2Cl)_2$. f) In in $(CD_2Cl)_2$ (sample from e)). The signals of two different species are marked with different colors. Signals of the species dominant in $CHCl_3$ (*PM* shifted dimer) are marked in turquoise, those of the species dominant in CH_2Cl_2 (*PP/MM* shifted dimer) are marked in brown. Samples were incubated at least three weak prior to measurement.

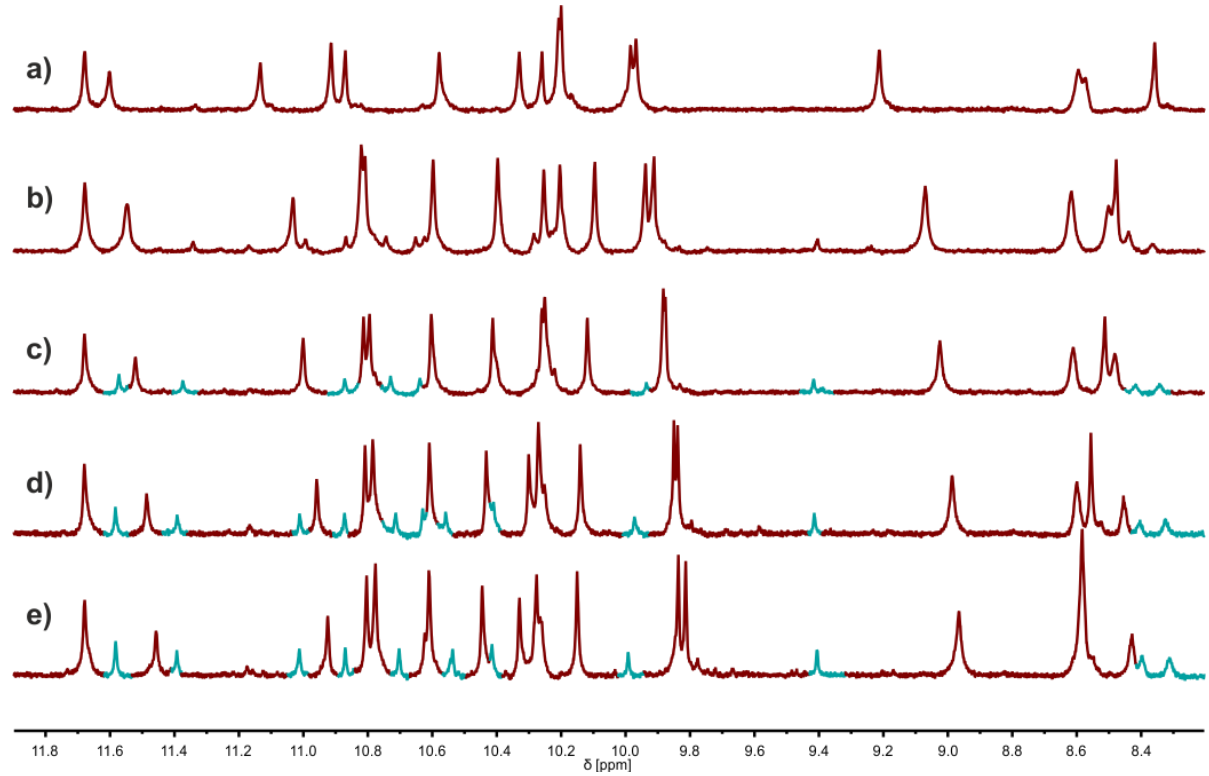


Figure S12. Interconversion of the *PM* and *PP/MM* shifted dimers of 3 upon changing toluene-d_8/CD_2Cl_2 solvent mixtures. Part of the 500 MHz ^{1}H NMR spectra of **3** (2.4 mM in CD_2Cl_2/toluene-d_8 mixtures) at 25 °C showing the amide and hydroxy proton resonances. The volume percentages of CD_2Cl_2 are 0 (a), 25 (b), 50 (c), 75 (d) and 100 (e). The signals of two different species are marked with different colors. The signals of two different species are marked with different colors. Signals of the species dominant in $CHCl_3$ (*PM* shifted dimer) are marked in turquoise, those of the species dominant in CH_2Cl_2 (*PP/MM* shifted dimer) are marked in brown. All spectra were measured after a 12h incubation time to reach equilibrium.

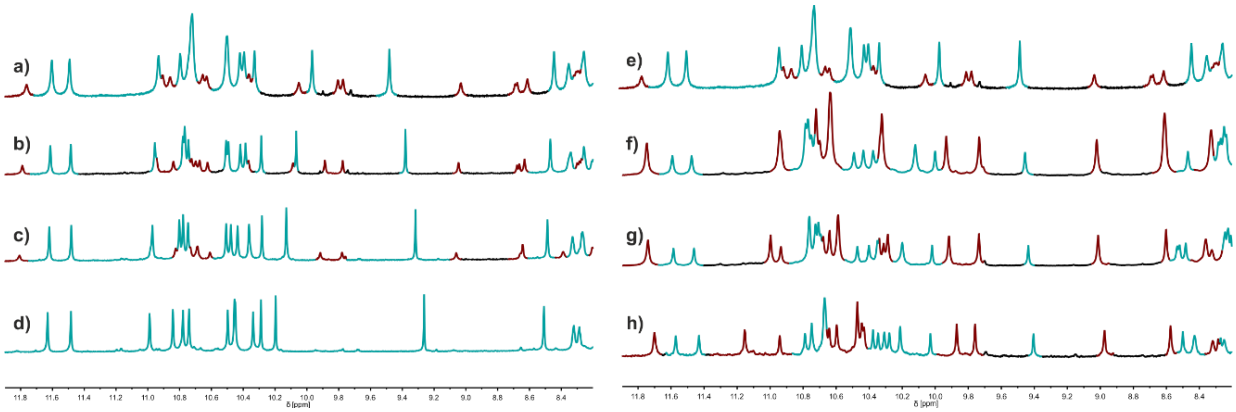


Figure S13. Interconversion of the *PM* and *PP/MM* shifted dimers of 4 upon changing $CDCl_3/(CDCl_2)_2/CD_2Cl_2$ solvent mixtures. a)-d) Part of the 500 MHz ^{1}H NMR spectra of **3** (2.4 mM in $CDCl_3/(CDCl_2)_2$ mixtures) at 25 °C showing the amide and hydroxy proton resonances. The volume percentages of $/(CDCl_2)_2$ are 100 (a), 75 (b), 50 (c), and 25 (d). e)-f) Part of the ^{1}H NMR spectra (500 MHz, 25 °C) showing the amide and hydroxy proton resonances of **3** at 2.4 mM in $CD_2Cl_2/(CDCl_2)_2$ mixtures. The volume percentages of $(CDCl_2)_2$ are 100 (e), 75 (f), 50 (g), and 25 (h). The signals of two different species are marked with different colors. Signals of the species dominant in $CHCl_3$ (*PM* shifted dimer) are marked in turquoise, those of the species dominant in CH_2Cl_2 (*PP*/*MM* shifted dimer) are marked in brown. All spectra were measured after a 2h incubation time to reach equilibrium.

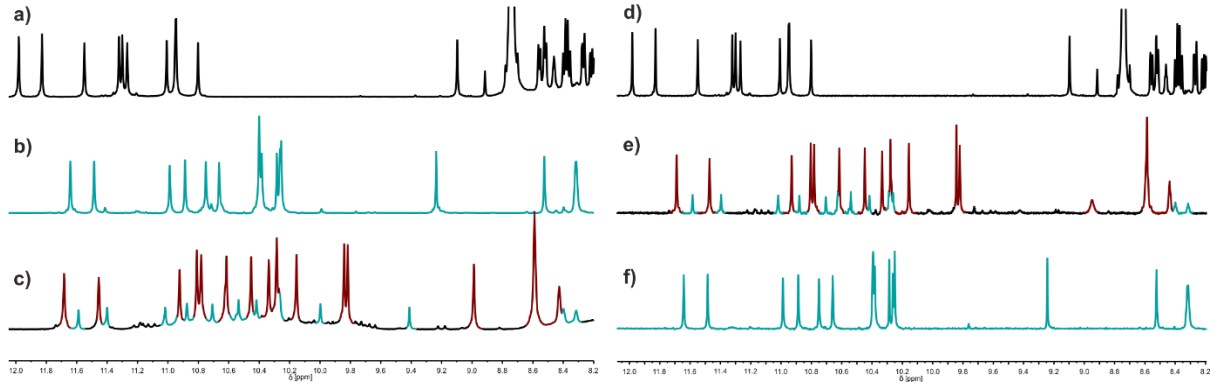


Figure S14. Control experiment to verify thermodynamic equilibrium is reached between the *PM* and *PP/MM* shifted dimers of 3. Part of the 500 ^{1}H NMR spectra of **3** (2.4 mM in various solvents) at 25 °C showing the amide and hydroxy proton resonances. a) in pyridine-*d*5. b) in $CDCl_3$ after evaporating and re-dissolving the pyridine-d_5 sample. c) in CD_2Cl_2 after evaporating and re-dissolving the $CDCl_3$ sample. d) in pyridine-*d*5. e) in CD_2Cl_2 after evaporating and re-dissolving the pyridine-d_5 sample. f) in $CDCl_3$ after evaporating and re-dissolving the CD_2Cl_2 sample. The signals of two different species are marked with different colors. Signals of the species dominant in $CHCl_3$ are marked in turquoise, those of the species dominant in CH_2Cl_2 are marked in brown. The spectrum in pyridine-d_5 in black shows the monomer. All spectra were measured after a 2h incubation time to reach equilibrium.

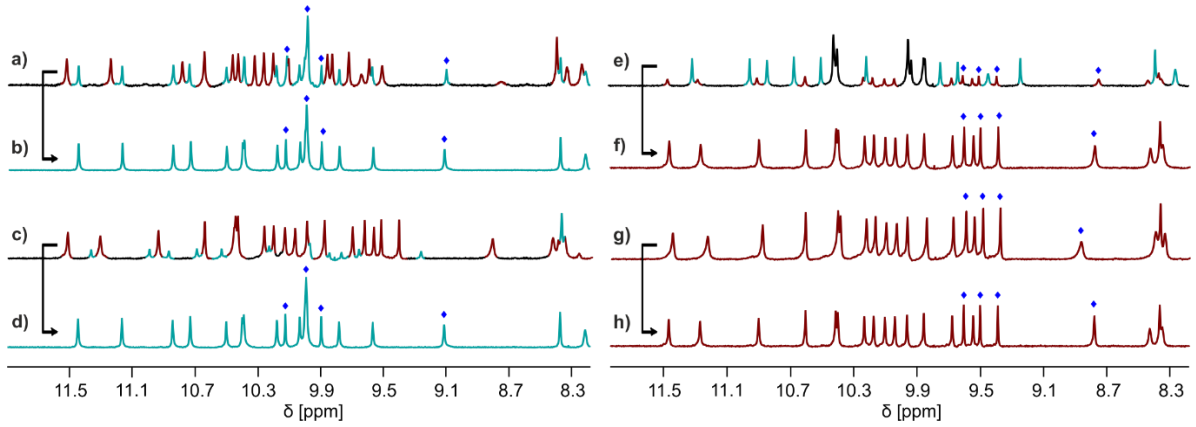


Figure S15. Control experiment to verify thermodynamic equilibrium is reached between the *PM* and *PP/MM* shifted dimers of 4. Extracts of 500 MHz ^{1}H NMR-spectra of **4** (2.4 mM) at 25 °C in various solvents and after various equilibration times. a) Sample evaporated from an equilibrated CD_2Cl_2 solution, re-dissolved in $CDCl_3$, and incubated for 2 days. b) Same sample after a three-week incubation. c) Sample evaporated from an equilibrated pyridine solution, re-dissolved in $CDCl_3$, and incubated for 2 days. d) Same sample after a three-week incubation. e) Sample evaporated from an equilibrated $CDCl_3$ solution, re-dissolved in CD_2Cl_2, and incubated for 1 day. f) same sample after a six-week incubation. g) sample evaporated from an equilibrated pyridine solution, re-dissolved in CD_2Cl_2, and incubated for 2h. h) Same sample after a three-week incubation. The signals of two different species are marked with different colors.

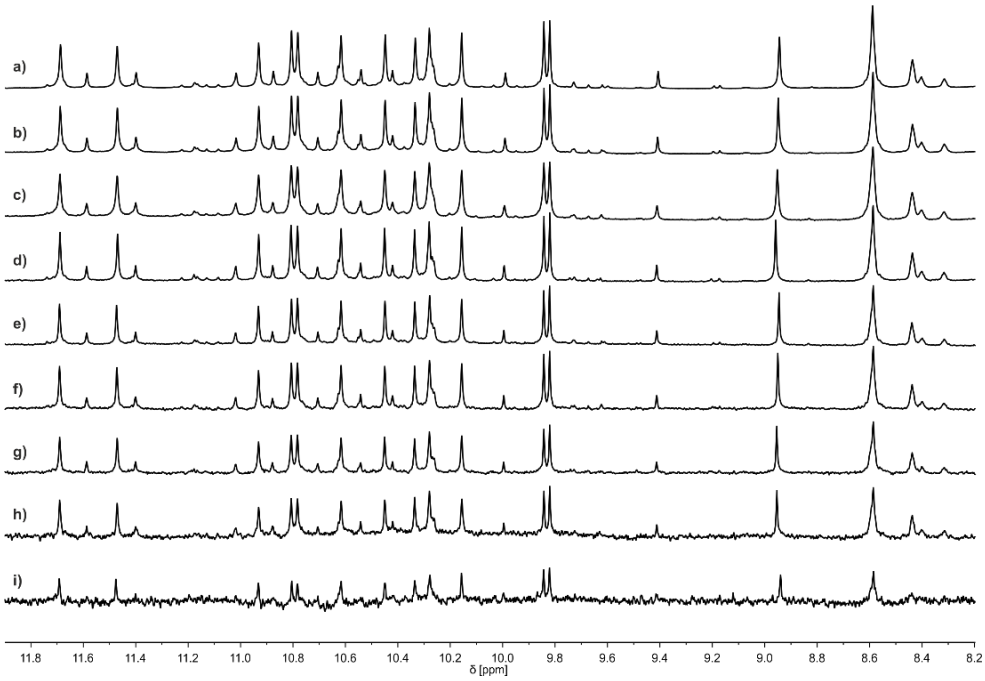


Figure S16. The proportions of the *PM* and *PP/MM* shifted dimers of 3 do not depend on concentration. Part of the 500 MHz ^{1}H NMR spectra of **3** (CD_2Cl_2, 25 °C) showing the amide and hydroxy proton resonances at 2.2 mM (a), 1.1 mM (b), 0.55 mM (c), 0.28 mM (d), 0.14 mM (e), 0.7 mM (f), 0.035 mM (g), 0.017 mM (h) and 0.009 mM (i). All spectra were measured after a two-week incubation time to reach equilibrium.

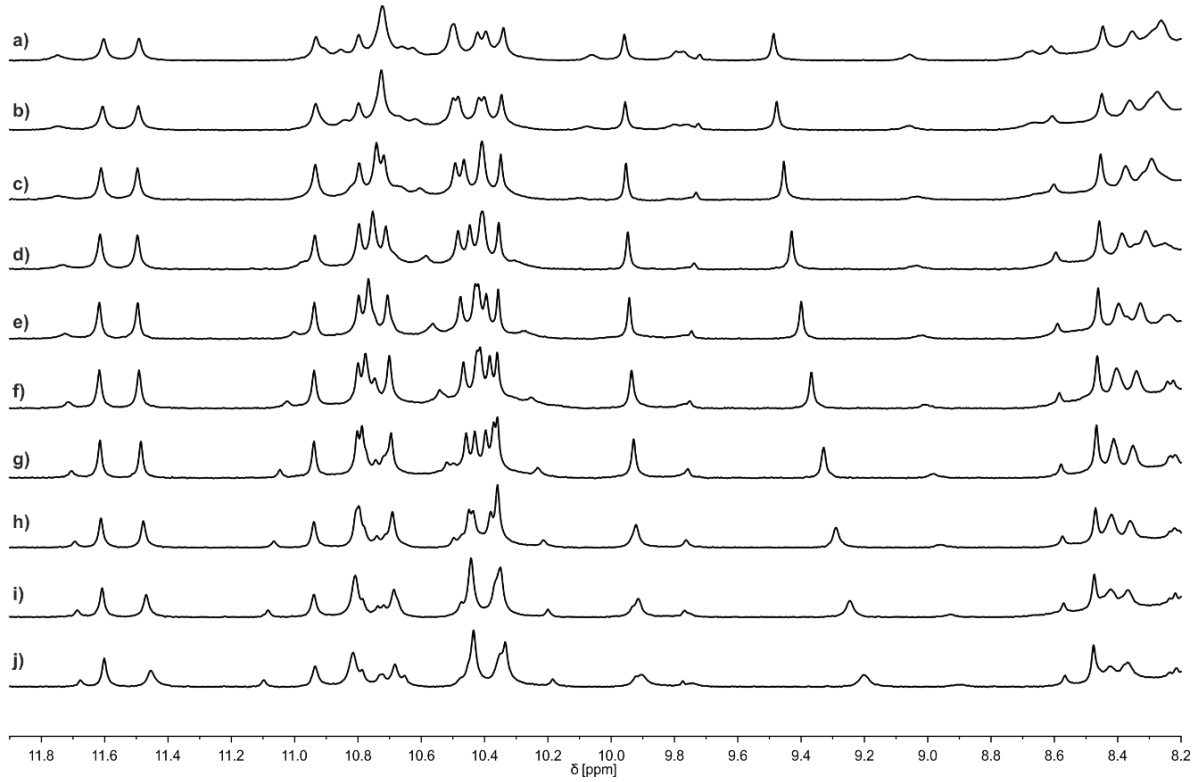


Figure S17. The proportions of the *PM* and *PP/MM* shifted dimers of 3 do not depend on temperature. Part of the 400 MHz ^{1}H NMR spectra of **3** (2.5 mM in $(CDCl_2)_2$) showing the amide and hydroxy proton resonances at 25 °C (a), 30 °C (b), 40 °C (c), 50 °C (d), 60 °C (e), 70 °C (f), 80 °C (g), 90 °C (h), 100 °C (i), and 110 °C (j). The initial spectrum was measured after a two-week incubation time to reach equilibrium. Between each other measurement the sample was equilibrated for 15 min.

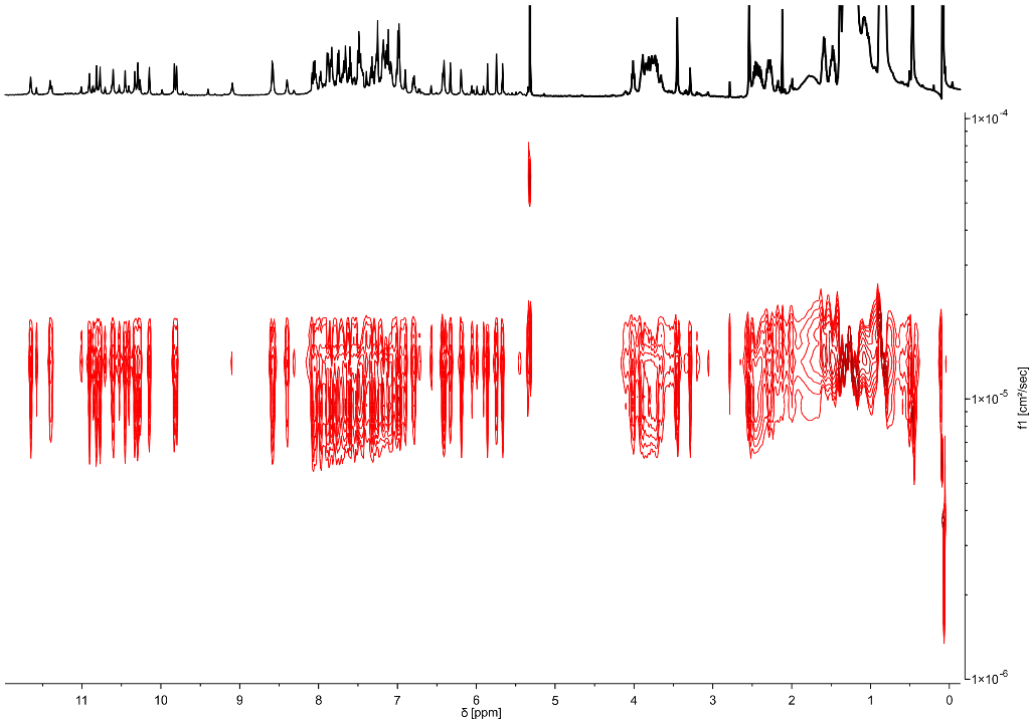


Figure S18. The *PM* and *PP*/*MM* shifted dimers of 3 have the same hydrodynamic radius. 500 MHz ^{1}H DOSY spectrum of **3** (5 mM in CD_2Cl_2) at 25 °C. The spectrum was measured after a two-hour incubation time to reach equilibrium.

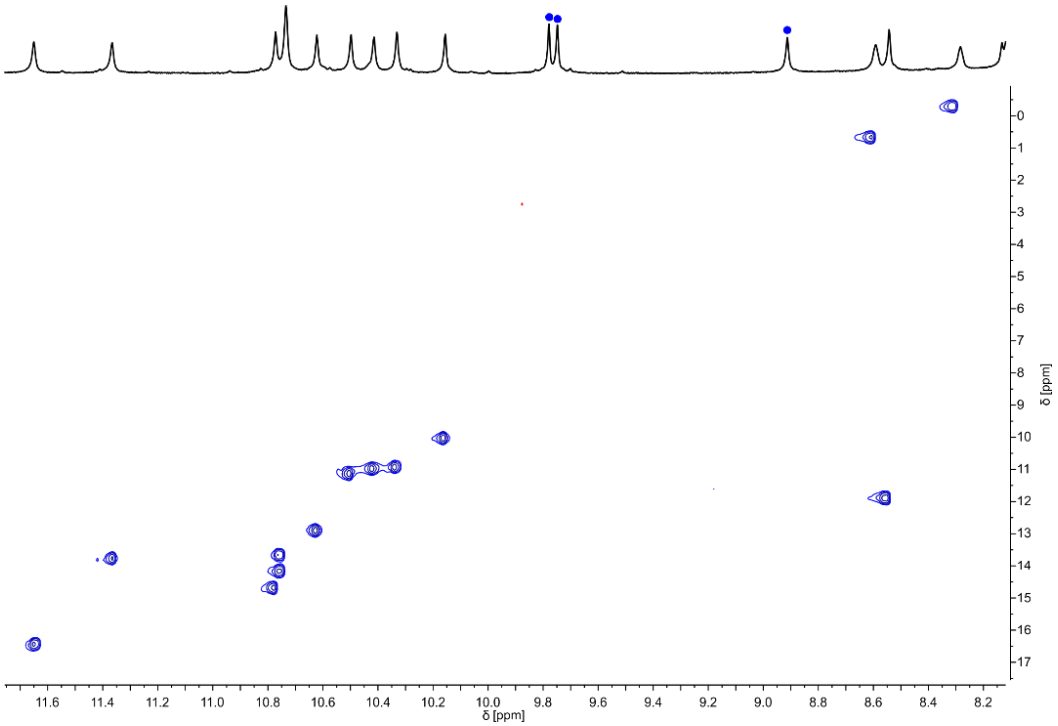


Figure S19. Identification of hydrogen bonded OH signals of 3 in $(CD_2Cl)_2$. Part of the 500 MHz ^{15}N,^{1}H HSQC NMR spectrum of **3** (4.4 mM in $(CD_2Cl)_2$ at 25 °C showing the amide and hydroxy proton resonances. Only NH resonances correlate, blue dots indicate the signals of OH protons. The spectrum was measured after a two-hour incubation time to reach equilibrium.

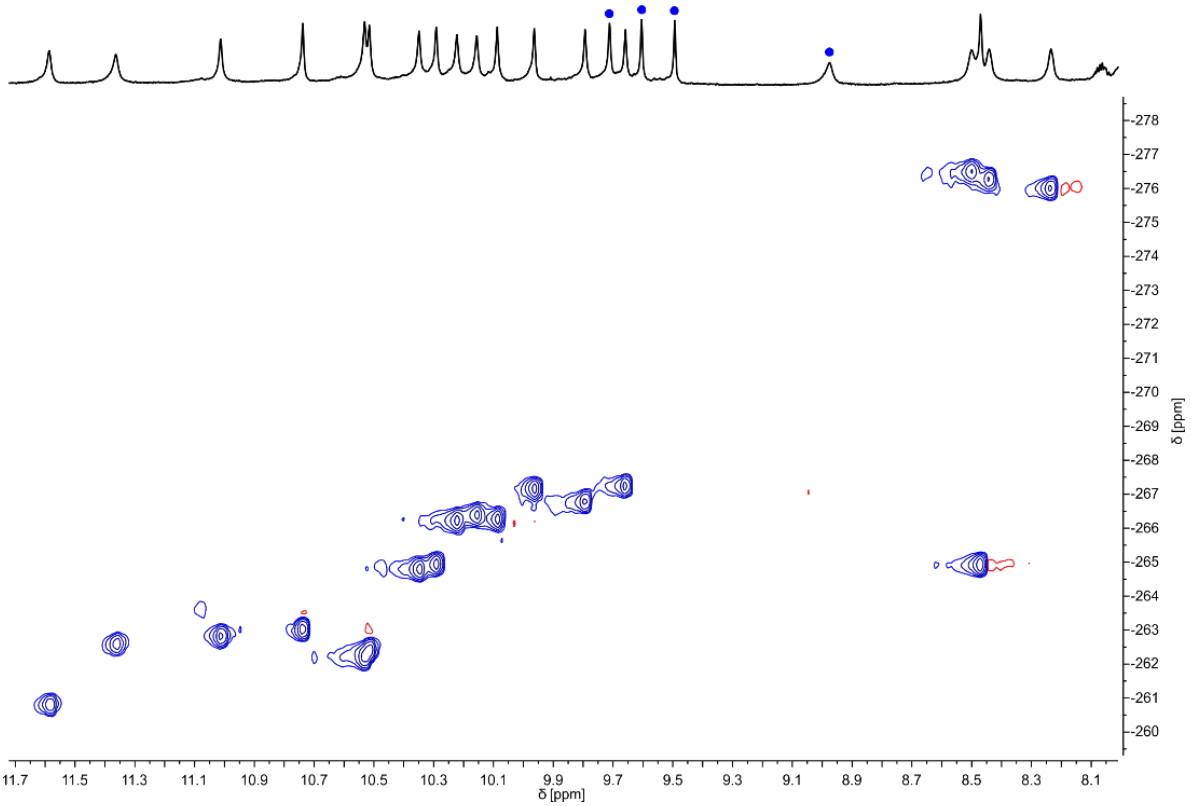


Figure S20. Identification of hydrogen bonded OH signals of 4 in CD_2Cl_2. Part of the 500 MHz $^{15}N,^{1}H$ HSQC NMR spectrum of **4** (7.02 mM in CD_2Cl_2) 25 °C showing the amide and hydroxy proton resonances. Only NH resonances correlate, blue dots indicate the signals of OH protons. A pyridine solution of **4** was evaporated, dried and the solid was dissolved in CD_2Cl_2 and incubated for four weeks prior to measuring the spectrum.

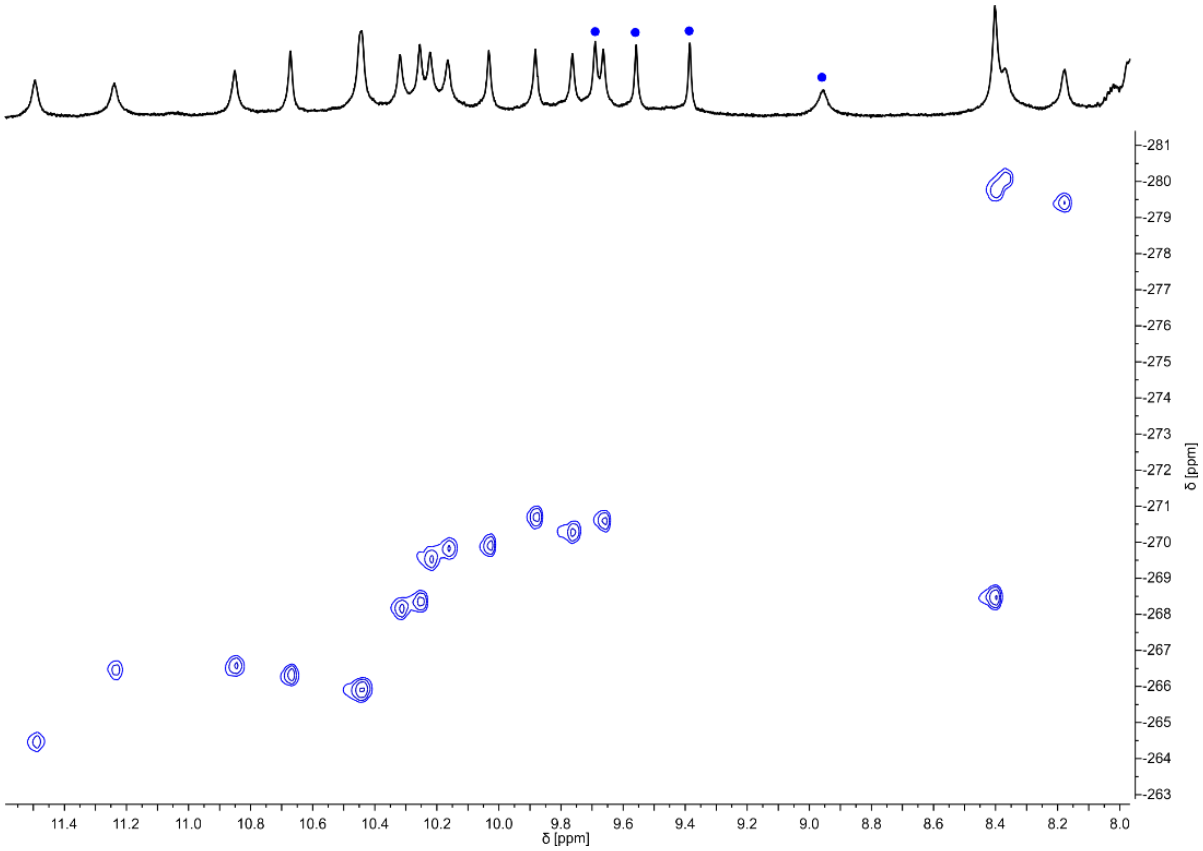


Figure S21. Identification of hydrogen bonded OH signals of 4 in $(CD_2Cl)_2$. Part of the 500 MHz ^{15}N,^{1}H HSQC NMR spectrum of **4** (6.92 mM in $(CD_2Cl)_2$) at 25 °C showing the amide and hydroxy proton resonances. Only NH resonances correlate, blue dots indicate the signals of OH protons. A pyridine solution of **4** was evaporated, dried and the solid was dissolved in $(CDCl_2)_2$ and incubated for four weeks prior to measuring the spectrum.

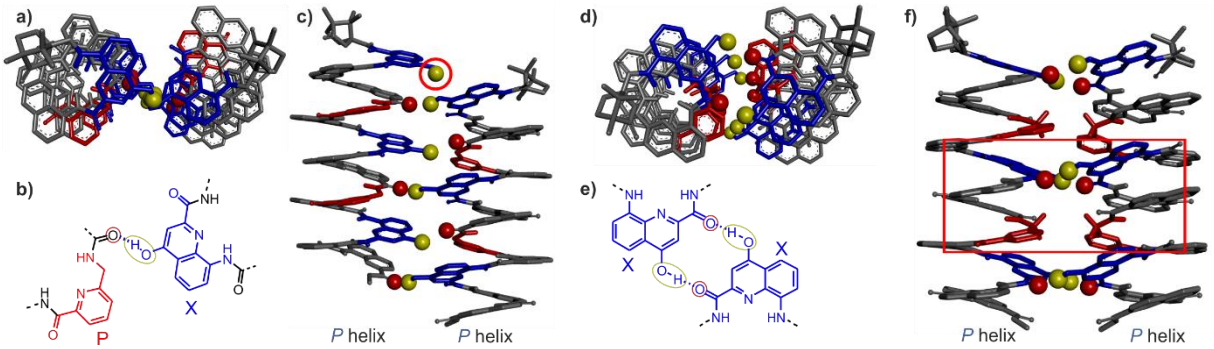


Figure S22. Energy minimized models of alternate, not experimentally observed hydrogen-bonded *PP* dimers. Top view (a) and side view (c) of an energy-minimized computational model[2] of **5** in a head-to-head *PP* shifted dimer arrangement (as opposed to the head-to-tail observed in the crystal). The prevalent hydrogen-bonding pattern is shown in (b). Here, one hydroxy group is not involved in hydrogen-bonding (encircled in red in c). Top view (d), side view (f) and hydrogen-bonding pattern (e) of an energy-minimized computational model[2] of a *PP* head-to-head (not shifted) parallel arrangement of **5** as observed in a helix-turn-helix tertiary structure.[1,3,4] Here, two hydrogen bonds form every other helix turn, instead of one every helix turn in the shifted dimer. The hydrogen-bonding donors and acceptors are shown as yellow and red balls, respectively. The X units are shown in blue and the P Units in red tubes. Included solvent molecules, hydrogen atoms and side-chains are omitted for clarity.

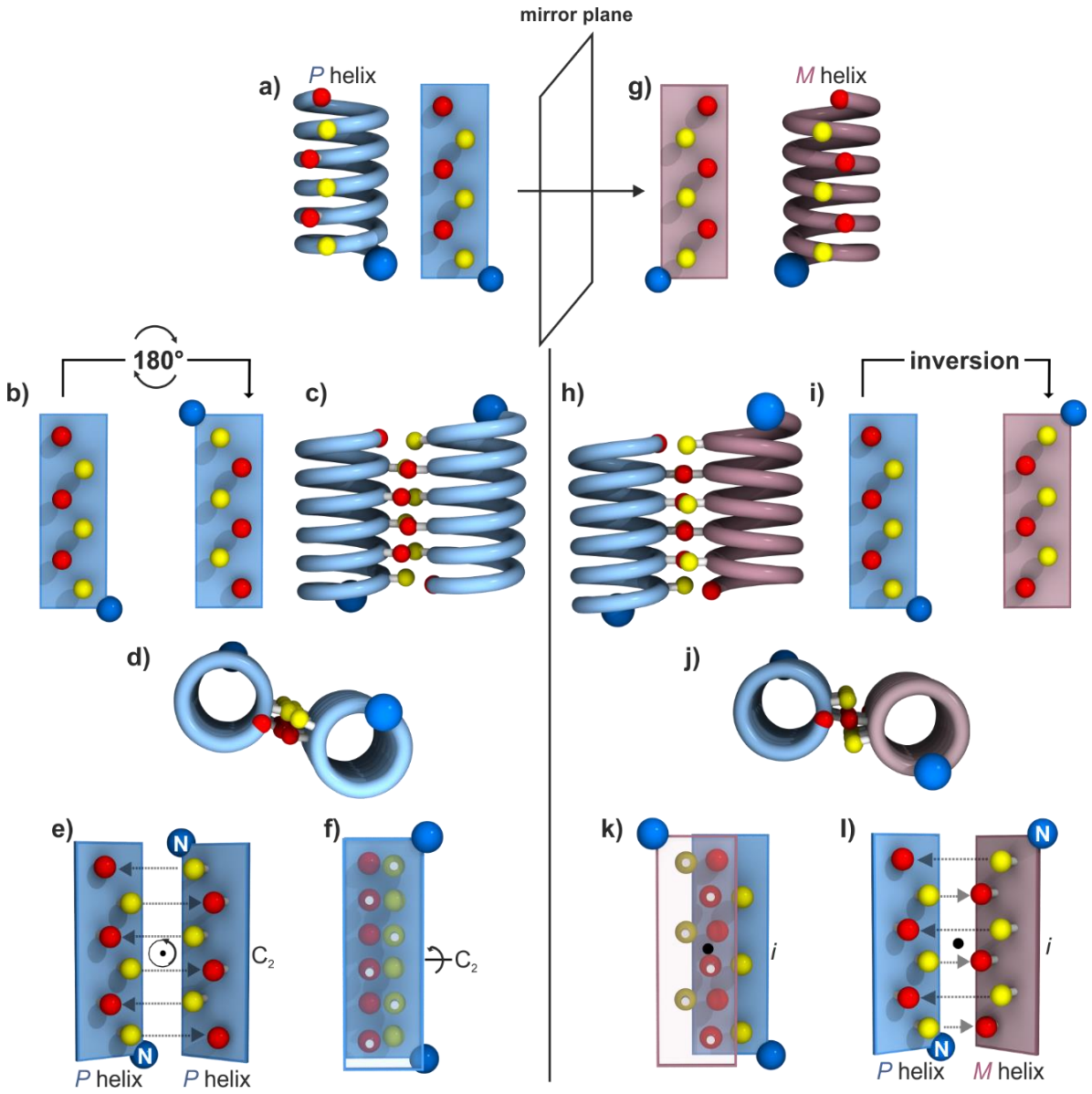


Figure S23. Schematic representation of foldamer helix assembly into shifted dimers. a) Front view of the hydrogen array of hydrogen bond donors and acceptors on a *P* helix (in blue) and its simplified representation on a plane. Hydroxy hydrogen bond donors are shown as yellow spheres. Amide carbonyl oxygen atoms that act as hydrogen bond acceptors (and only those) are shown as red spheres. Blue spheres indicate the N-terminus of the helix. b)-f) Views of the formation of a head-to-tail chiral (*PP*) shifted dimer, including the 180° rotation of the array of hydrogen bond donors and acceptors (b); a side-view (c) and a top-view (d) of the chiral dimer; an "open-book" view with arrows linking each hydrogen bond donor to the corresponding acceptor (e); and a transparent view showing the two hydrogen-bonding array above each other (f). g) Mirror image of the views in a) showing the enantiomeric *M* helix (in purple). h)-l) Views of the formation of a head-to-tail *PM* (*meso*) shifted dimer, including the inversion of the array of hydrogen bond donors and acceptors (i); a side-view (g) and a top-view (j) of the *PM* dimer; an "open-book" view with arrows linking each hydrogen bond donor to the corresponding acceptor (l); and a transparent view showing the two hydrogen-bonding array above each other (k).

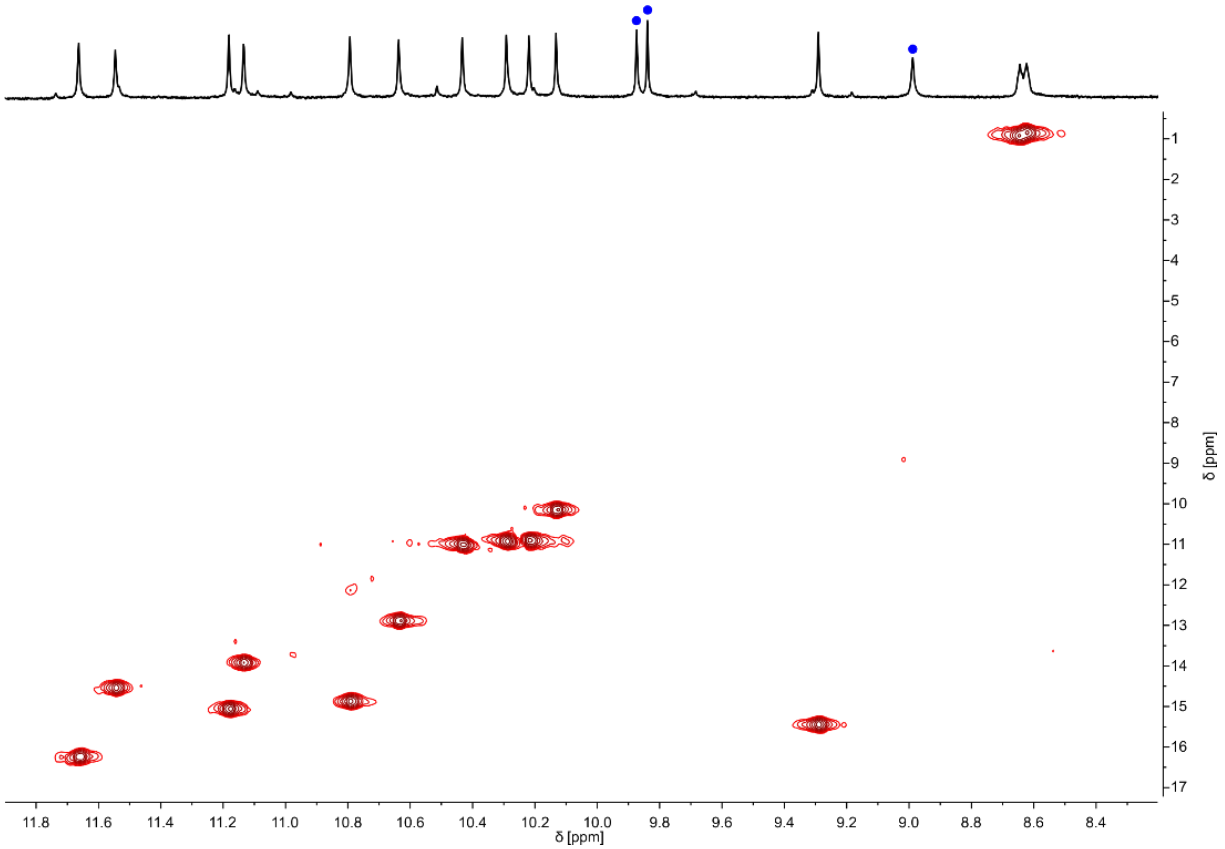


Figure S24. Identification of hydrogen bonded OH signals of 5 in CD_2Cl_2. Part of the 500 MHz ^{15}N,^{1}H HSQC NMR spectrum of **5** (8.0 mM in CD_2Cl_2) at 25 °C showing the amide and hydroxy proton resonances. Only NH resonances correlate, blue dots indicate the signals of OH protons. The spectrum was measured after a two-hour incubation time to reach equilibrium.

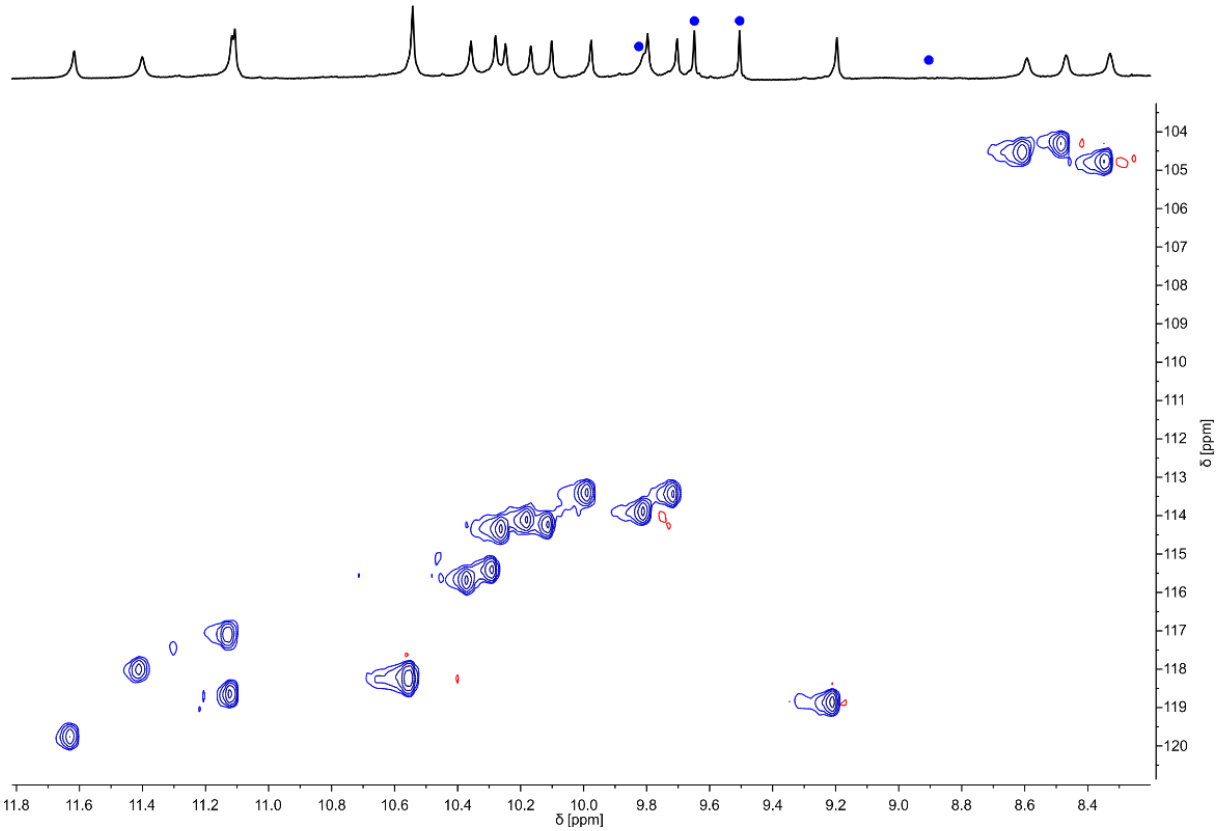


Figure S25. Identification of hydrogen bonded OH signals of 6 in CD_2Cl_2. Part of the 500 MHz $^{15}N,^{1}H$ HSQC NMR spectra (11.1 mM in CD_2Cl_2) at 25 °C showing the amide and hydroxy proton resonances of **6** after 2 h after pyridine-treatment. A pyridine solution of **6** was evaporated, dried and the solid was dissolved in CD_2Cl_2 and incubated for 2h prior to measuring the spectrum. Only NH resonances correlate, blue dots indicate the signals of OH protons.

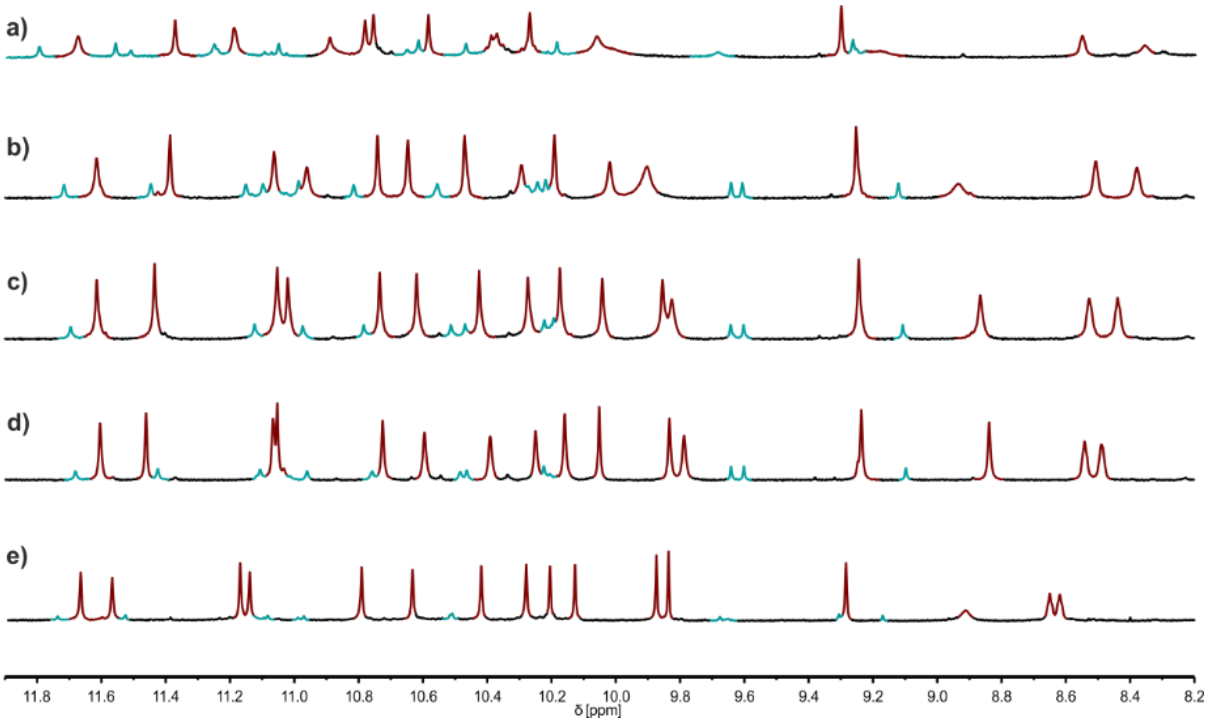


Figure S26. Interconversion of the *PM* and *PP/MM* shifted dimers of 5 upon changing $CDCl_3/CD_2Cl_2$ solvent mixtures. Part of the 500 MHz ^1H NMR spectra of **5** (2.4 mM in $CDCl_3/CD_2Cl_2$ mixtures) at 25 °C showing the amide and hydroxy proton resonances. The volume percentages of CD_2Cl_2 are 0 (a), 25 (b), 50 (c), 75 (d), and 100 (e). The signals of two different species are marked with different colors. Signals of the *PP/MM* shifted dimer are marked in turquoise, those of the *PP* shifted dimer dominant in CH_2Cl_2 are marked in brown. The spectra were measured after a two-hour incubation time to reach equilibrium.

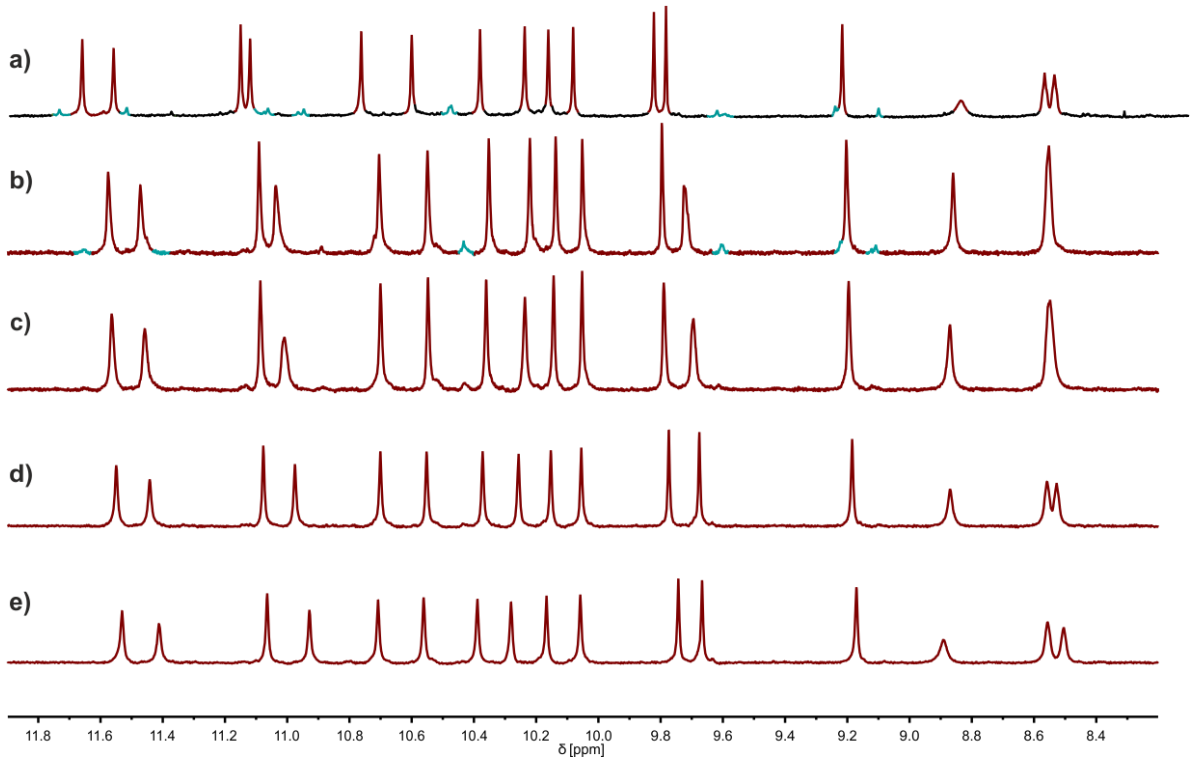


Figure S27. The *PP* shifted dimer of 5 prevails in CD_2Cl_2/$(CD_2Cl)_2$ solvent mixtures. Part of the 500 MHz ^{1}H NMR spectra of **5** (2.4 mM in CD_2Cl_2/$(CD_2Cl)_2$ mixtures) at 25 °C showing the amide and hydroxy proton resonances. The volume percentages of $(CD_2Cl)_2$ are 0 (a),25 (b), 50 (c), 75 (d) and 100 (e). The signals of two different species are marked with different colors. Signals of *PM* shifted dimer are marked in turquoise, those of the *PP* shifted dimer are marked in brown. The spectra were measured after a two-hour incubation time to reach equilibrium.

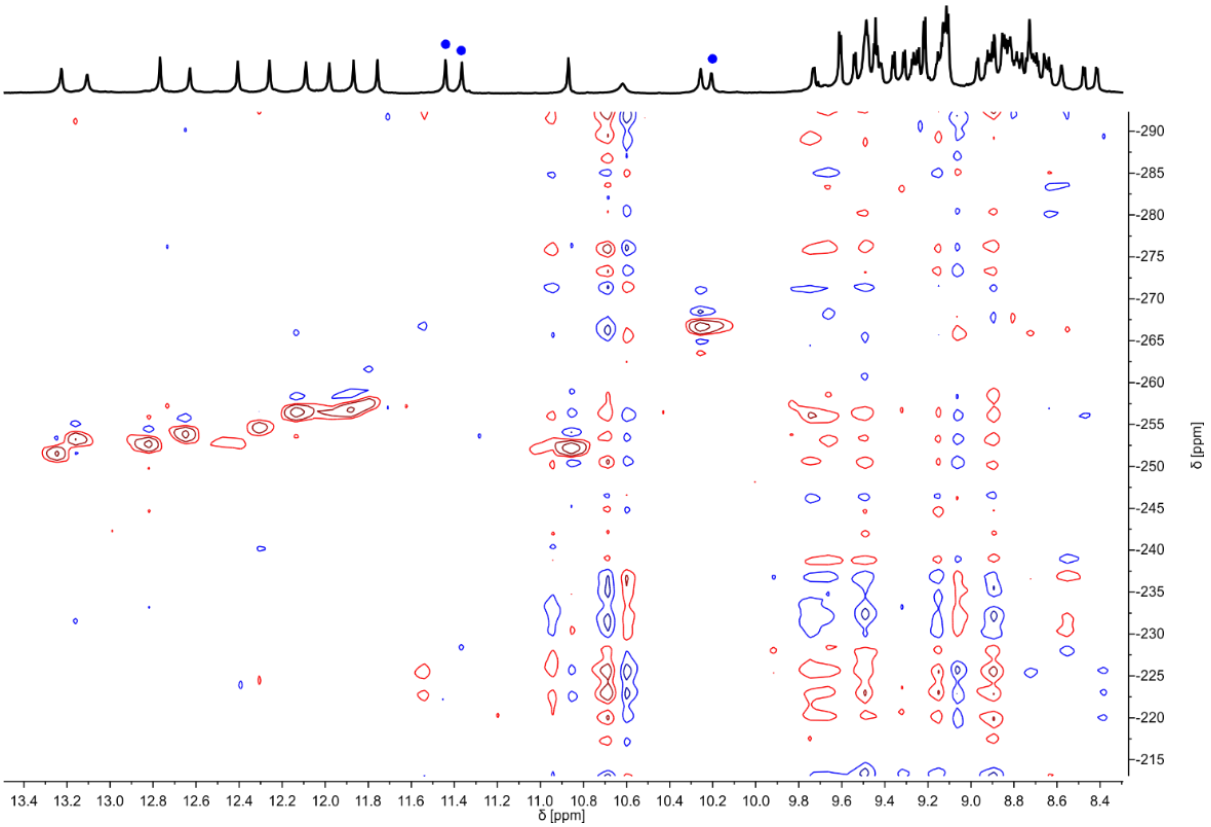


Figure S28. Identification of hydrogen bonded OH signals of 5 in $(CD_2Cl)_2$. Part of the 500 MHz $^{15}N,^{1}H$ HSQC NMR spectrum of **5** (2.31 mM in $(CD_2Cl)_2$ at 25 °C showing the amide and hydroxy proton resonances. Only NH resonances correlate, blue dots indicate the signals of OH protons. The spectrum was measured after a two-hour incubation time to reach equilibrium.

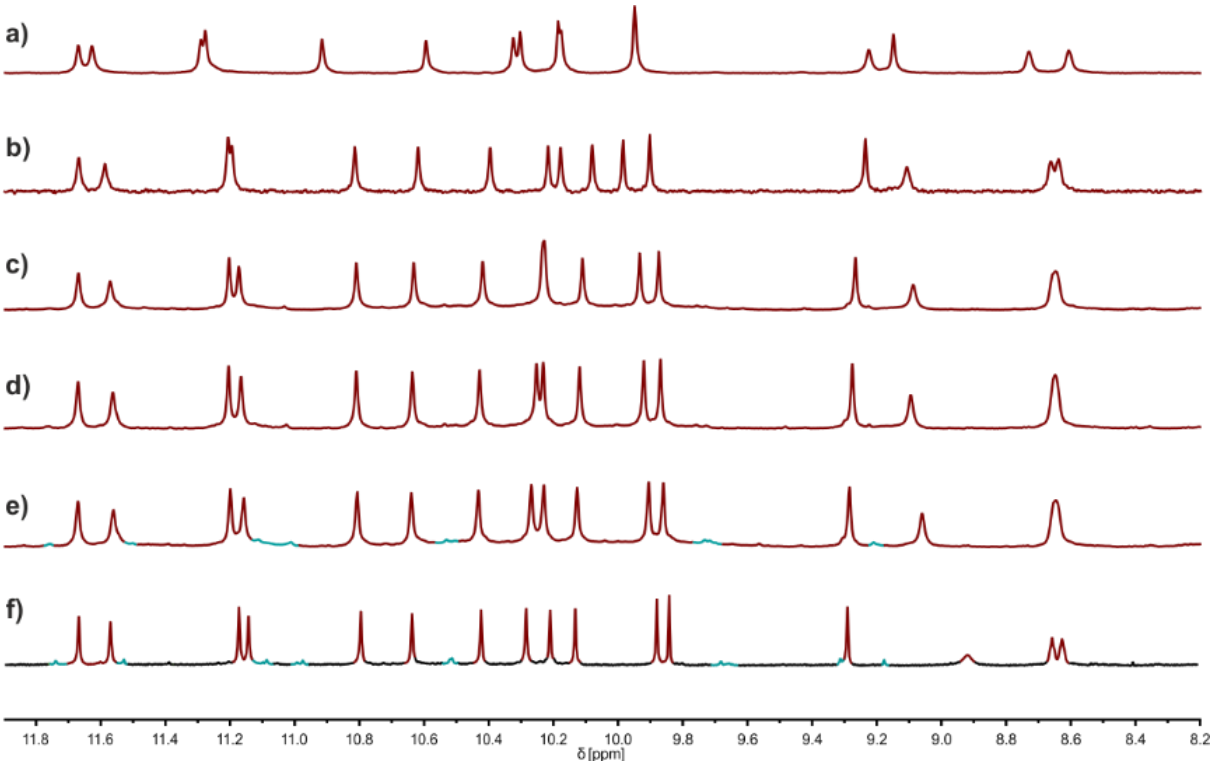


Figure S29. The *PP* shifted dimer of 5 prevails in CD_2Cl_2/ toluene-d_8 solvent mixtures. Part of the 500 MHz ^{1}H NMR spectra of **5** (2.4 mM in CD_2Cl_2/toluene-d_8 mixtures) at 25 °C showing the amide and hydroxy proton resonances. The volume percentages of CD_2Cl_2 are 0 (a), 25 (b), 50 (c), 75 (d) and 100 (e). The signals of two different species are marked with different colors. Signals of the species dominant in $CHCl_3$ are marked in turquoise, those of the species dominant in CH_2Cl_2 are marked in brown. The spectra were measured after a two-hour incubation time to reach equilibrium.

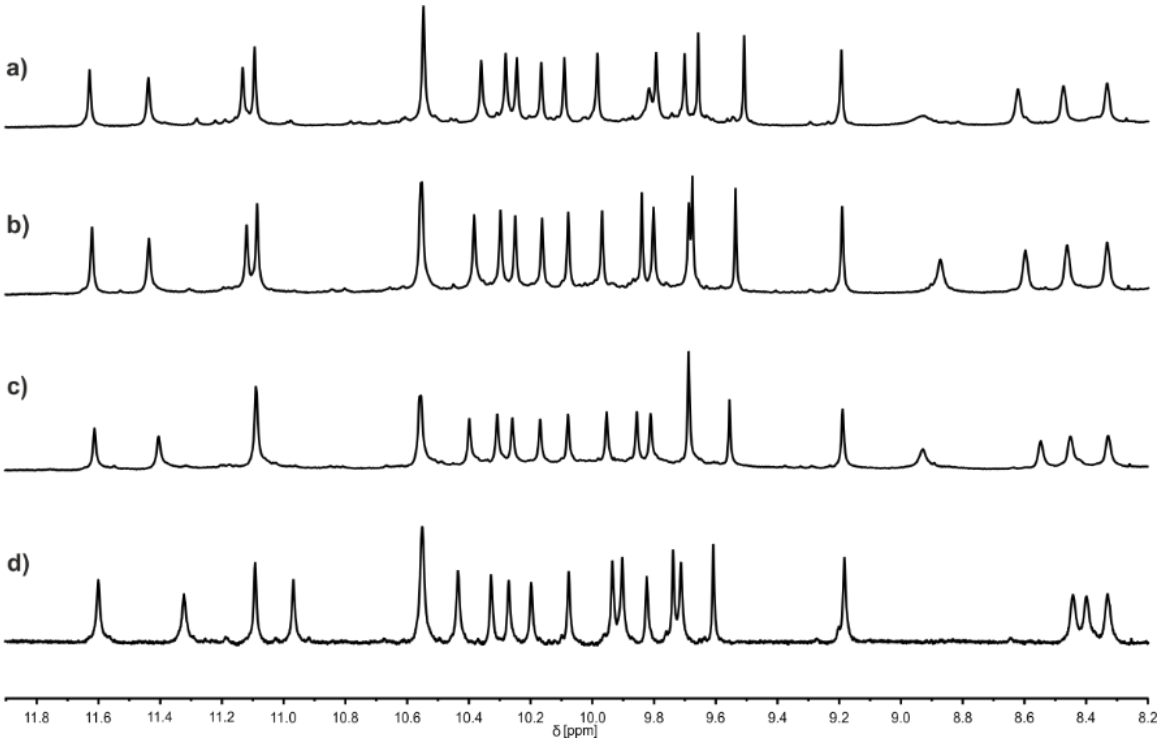


Figure S30. The *PP* shifted dimer of 6 prevails in various solvents Part of the 500 MHz ^{1}H NMR spectra of **6** (2.4 mM in various solvents) at 25 °C showing the amide and hydroxy proton resonances. A pyridine solution of **6** was evaporated, dried and the solid was dissolved in CD_2Cl_2 and incubated for six weeks prior to measuring the spectrum in (a). The sample in a) was evaporated, dried and the solid was dissolved in 1:1 $CDCl_3$/CD_2Cl_2 and incubated for one week (b) and six weeks (c) prior to measuring the spectra. The sample in c) was evaporated, dried and the solid was dissolved in $CDCl_3$ and incubated for six weeks prior to measuring the spectrum (d).

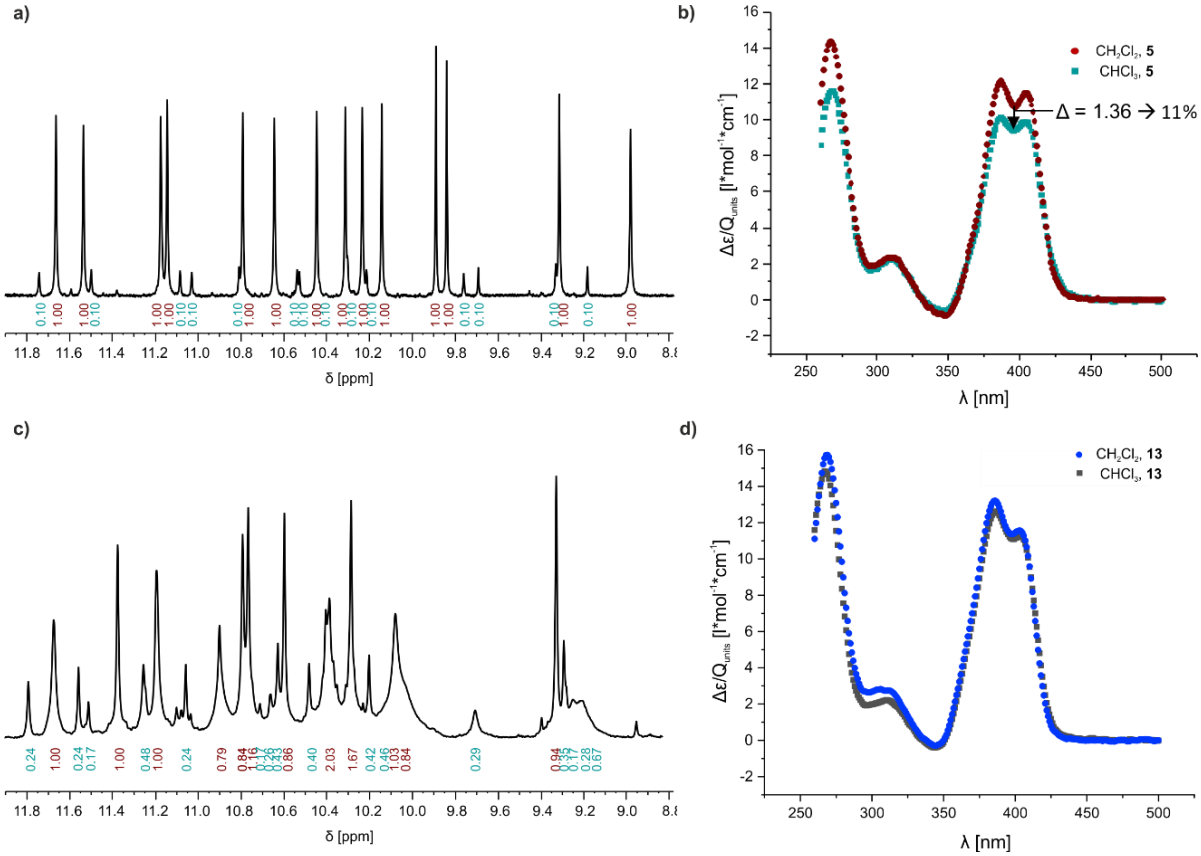


Figure S31. Assignment of the *PM* and *PP/MM* shifted dimers of 5 in $CDCl_3$ and CD_2Cl_2. Part of the 500 MHz ^{1}H NMR spectra of **5** in CD_2Cl_2 (a) and $CDCl_3$ (c) at 25 °C and 2.4 mM showing the integration of amide and hydroxy proton resonances. CD spectra of **5** in CD_2Cl_2 and $CDCl_3$ at 25 °C (b). CD spectra of **13** (protected precursor of **5**, see Scheme S5 for its formula) in CD_2Cl_2 and $CDCl_3$ at 25 °C (d). At these wavelengths, CD bands are mostly due to quinoline rings. The molar extinction (Δε) is thus normalized to the number of Q units for better comparability.

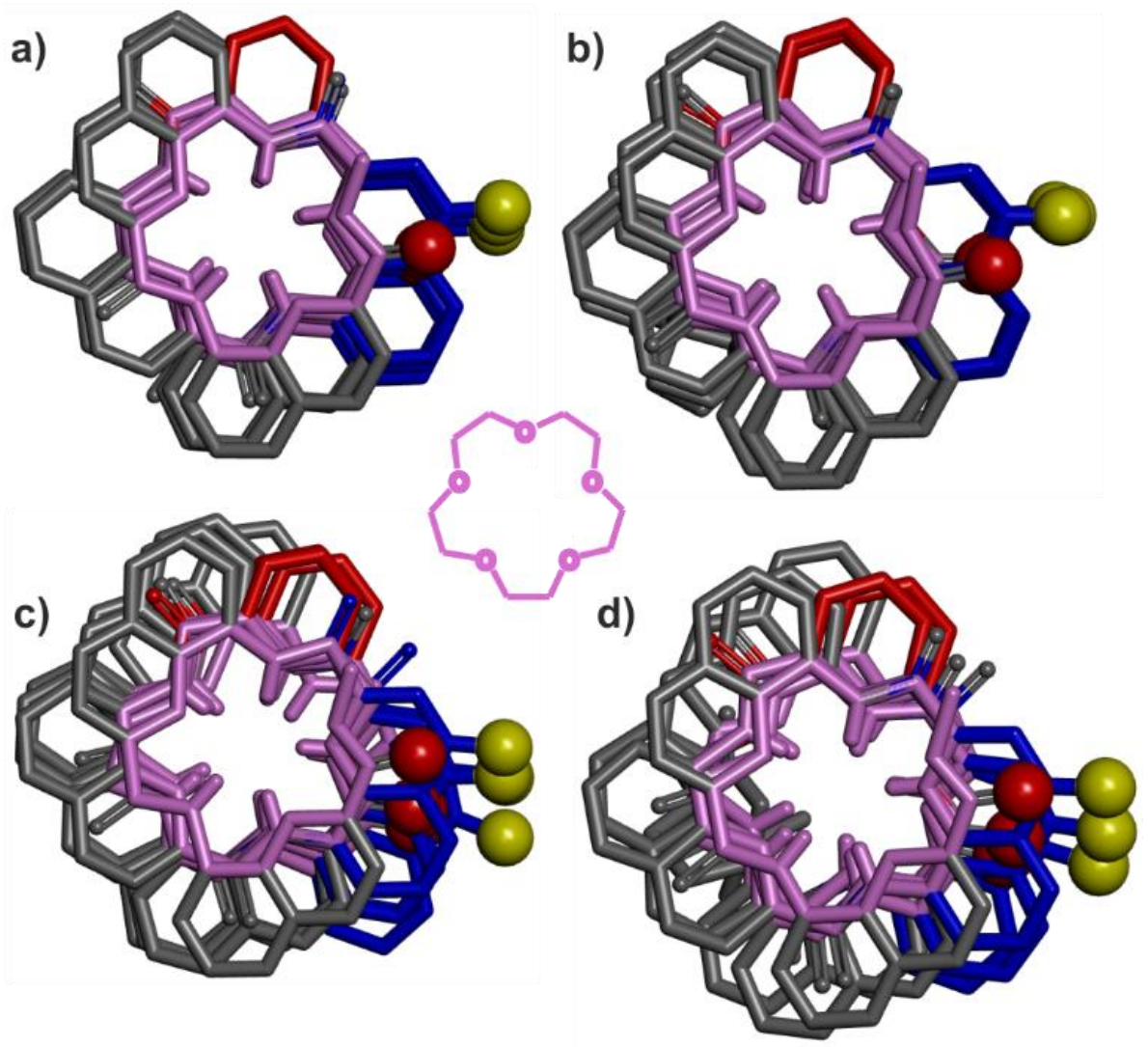


Figure S32. The shapes of the helix inner rims suggest there is no helix torsional strain. Top views of one helix of the crystal structures of the *PM* shifted dimers of **3** (a), **5** (b) and **7** (c) and of the *PP* shifted dimer of **5** (d). The inner rim of the helix is highlighted in pink. The preferred curvature of Q_n oligomers typically shows a 15-crown-5 shape of the inner rim (a 15-crown-5 is shown in the middle of the Figure for comparison). There is little (c, d) or no (a, b) deviation from this pattern in the four cases. The X units are shown in blue, the Y units in violet and the P units in red tubes. Carbonyl and hydroxy oxygen atoms involved in intermolecular hydrogen bonds are shown as red and yellow spheres, respectively. Included solvent molecules, hydrogen atoms and side-chains are omitted for clarity.

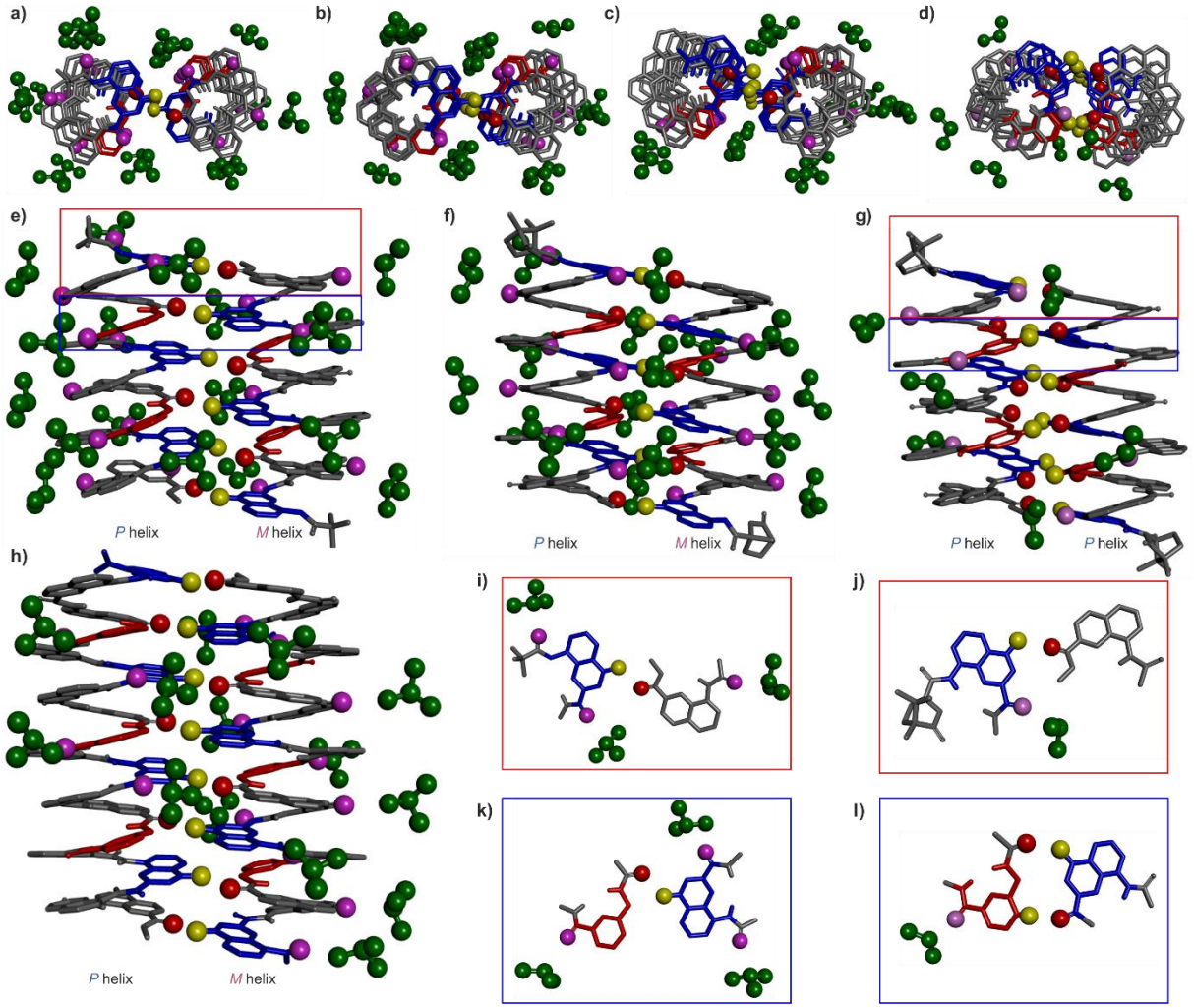
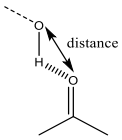


Figure S33. Almost all chloroform molecules hydrogen bond to amide carbonyl groups in solid state structures. Views of various solid state structures showing $CHCl_3$ or CH_2Cl_2 solvent molecules in the crystal lattice. Top views of the *PM* shifted dimers of **3** (a), **5** (b) and **7** (c) with $CHCl_3$ molecules, and top view of the chiral shifted dimer of **5** (d) with CH_2Cl_2 molecules. Side views of the *PM* shifted dimers of **3** (e), **5** (f) and **7** (h) with $CHCl_3$ molecules, and side view of the chiral shifted dimer of **5** (g) with CH_2Cl_2 molecules. Slices of the dimers showing the solvent molecules surrounding the X, P or Q units are shown in i)-k). i) and k) are from the structure of **3** with $CHCl_3$ molecules (red and blue boxes in e). j) and l) are from the structure of **5** with CH_2Cl_2 molecules (red and blue boxes in g). The hydrogen-bonding donor and acceptor sites are shown as yellow and red balls, respectively. Carbonyl groups binding to $CHCl_3$ or CH_2Cl_2 molecules are shown as pink balls. $CHCl_3$ and CH_2Cl_2 molecules are shown as green balls. The X units are shown in blue and the P Units in red tubes. Hydrogen atoms and side-chains are omitted for clarity.

3 Supplementary tables

Table S1. Distances between hydrogen-bonded carbonyl and hydroxy oxygen atoms in the solid state structures of **3** and **5**. Entries are numbered from 1 to 6, as in the structures below. Remarkable values are shown in red.

Entry	Distance 	*PM* dimer of **3**	PP dimer of **5**
1		2.782 Å	2.766 Å
2		2.646 Å	2.680 Å
3		2.710 Å	2.610 Å
4		2.710 Å	2.608 Å
5		2.646 Å	2.645 Å
6		2.782 Å	2.699 Å

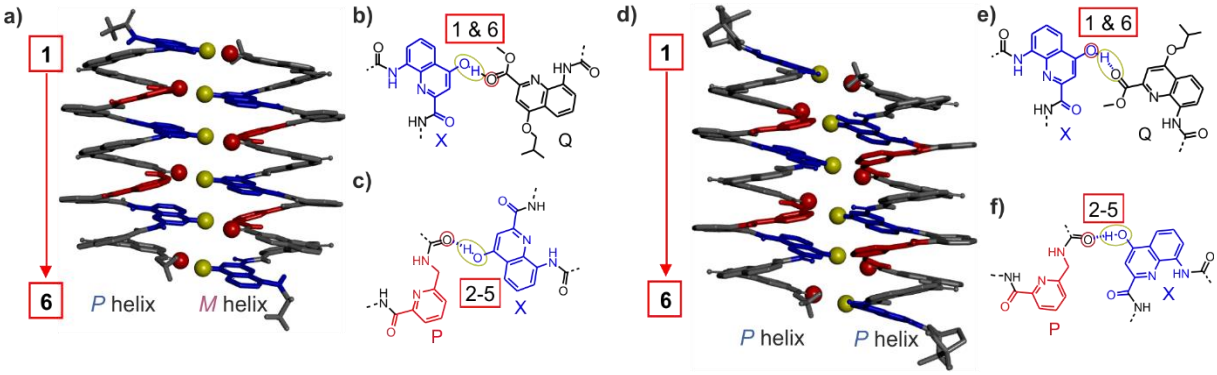


Table S2. C=O···H angles within the hydrogen-bonded carbonyl and hydroxy groups in the solid state structures of **3** and **5**. Entries are numbered as in Table 1. Remarkable values are shown in red.

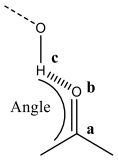
Entry	Angle 	*PM* dimer of **3**	*PP* dimer of **5**
1		137.57°	165.07°
2		135.88°	145.86°
3		135.24°	143.79°
4		135.24°	148.79°
5		135.88°	139.18°
6		137.57°	167.38°

Table S3. O-H···O angles within the hydrogen-bonded carbonyl and hydroxy groups in the solid state structures of **3** and **5**. Entries are numbered as in Table 1. Remarkable values are shown in red.

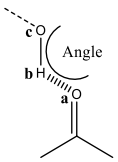
Entry	Angle 	*PM* dimer of **3**	*PP* dimer of **5**
1		162.19°	163.07°
2		146.92°	149.97°
3		152.62°	154.05°
4		152.62°	148.29°
5		146.92°	138.32°
6		162.19°	165.04°

Table S4. Hydrogen bonds geometry in the crystal structures. Atom numbers are those of the cif file.

D—H···A	D—H	H···A	D···A	D—H···A
7				
O1D-H1D···O3E	0.84	1.81	2.63 (2)	163
O6H-H6H···O3C	0.84	2.06	2.70 (2)	133
O2D-H2D···O13G	0.84	1.98	2.77 (2)	155
O4H-H4H···O21	0.84	1.89	2.59 (3)	139
O3D-H3D···O8G	0.84	1.99	2.79 (2)	159
O2H-H2H···O13C	0.84	1.92	2.65 (2)	145
O5D-H5D···O3G	0.84	1.90	2.56 (3)	134
O1H-H1H···O3A	0.84	2.12	2.84 (3)	143
3				
O1C-H1C···O2A^{i}	0.84	1.97	2.77 (2)	159
O3C-H3C···O3B^{i}	0.84	1.88	2.64 (2)	150
O2C-H2C···O8B^{i}	0.84	1.97	2.74 (1)	153
O1H-H1H···O2G^{ii}	0.84	1.98	2.80 (2)	165
O3H-H3H···O3F^{ii}	0.84	1.93	2.65 (2)	144
O2H-H2H···O8F^{ii}	0.84	1.91	2.68 (2)	152
5 (chiral aggregate)				
O1C-H1C···O1	0.84	1.88	2.70 (2)	165
O3F-H3F···O3B	0.84	1.96	2.65 (2)	139
O2C-H2C···O8E	0.84	1.86	2.60 (2)	148
O2F-H2F···O8B	0.84	1.83	2.61 (2)	154
O3C-H3C···O3E	0.84	1.92	2.68 (3)	150
O1F-H1F···O2A	0.84	1.95	2.76 (2)	163
5 (pseudo-racemic aggregate)				
O1C-H1C···O16B	0.84	1.94	2.40 (3)	114
O3A-H3A···O6D	0.84	1.93	2.72 (3)	158
O2C-H2C···O11B	0.84	1.90	2.58 (2)	138
O2A-H2A···O11D	0.84	1.80	2.59 (2)	155
O3C-H3C···O6B	0.84	1.89	2.61 (2)	143
O1A-H1A···O16D	0.84	1.97	2.75 (3)	154

Symmetry codes: (i)-x, -1-y, 1-z, (ii) 1-x, -y, 1-z

See the section on crystallography below for Tables S5 and S6.

4 Supplementary methods

4.1 MS analyses

HR-MS spectra were recorded on a Bruker microTOF II by direct infusion from acetonitrile in positive ionization mode. The instrument was calibrated in positive mode by direct infusion of a calibration solution (Agilent Technologies ESI-L Low Concentration Tuning Mix). The mass sample was prepared by adding 10 µL of a solution of the sample in DCM (0.1 mg/mL) to 1 mL of a solution of 0.1% formic acid in acetonitrile.

4.2 Molecular modeling

Models were simulated by using Maestro version 11.5 (Schrödinger Inc.). Energy minimized structures were obtained using MacroModel energy minimization with the following parameters: force field: MMFFs; solvent: none; electrostatic treatment: constant dielectric; dielectric constant: 1.0; charges from: force field; cutoff: normal; Van der Waals: 7.0; electrostatic: 12.0; H-bond: 4.0; mini method: TNCG; maximum iterations: 2500; converge on: gradient; convergence threshold: 0.05; constraints: distances. As a starting point, the coordinates of the crystal structure of **3** (CCDC entry # 2209189) and **5** (CCDC entry # 2209187) were used. A single helix was first energy-minimized. In a second round, two helices were placed in a plausible arrangement, and distance constraints between plausible hydrogen-bonding partners were set on purpose to 2.5. While setting the constraints, it was important to match the hydroxy group to their correct hydrogen-bonding carbonyl partner. The energy-minimized model was fixed was possible unlikely conformations and energy-minimized again. Then all constraints were removed, and energy minimization was repeated. Typically, only minimal changes occurred at this stage, and the structure was exported as a mol2 file.

4.3 Nuclear magnetic resonance spectroscopy

NMR spectra were recorded on different NMR spectrometers: (I) an Avance III HD NMR spectrometer 400 MHz (Bruker BioSpin) for ^{1}H NMR and ^{13}C NMR spectra of small units. (II) an Avance III HD NMR spectrometer 500 MHz (Bruker BioSpin) with CryoProbe™ Prodigy for ^{1}H NMR, ^{1}H,^{15}N-HSQC, and DOSY spectra of foldamers. (III) a Bruker HD NMR spectrometer 400 MHz (Bruker BioSpin) for variable temperature measurements. Chemical shifts are described in part per million (ppm, δ) relative to the ^{1}H residual signal of the deuterated solvent used. Meaning DMSO-d_6 (δ 2.50 ppm), pyridine-d_5 (δ 8.74 ppm), CD_2Cl_2 (δ 5.32 ppm) and $CDCl_3$ (δ 7.16 ppm). ^{1}H NMR splitting patterns with observed first-order coupling are entitled as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) or broad singlet (bs). Coupling constants (*J*) are ported in Hertz.

Sample preparation and incubation times to reach equilibrium required attention. The required equilibration times of sequences **3**-**6** were estimated by equilibrating each sample in $CDCl_3$ and CD_2Cl_2 after complete disruption of the aggregates. Complete disruption was achieved by dissolving the sample in pyridine and then evaporating the solvent. Spectra were measured at different time intervals from 2h to 9 weeks until no further change was observed. Additionally, samples were dissolved and incubated

in $CDCl_3$ and CD_2Cl_2 after being brought to equilibrium in the other solvent. At equilibrium, the same spectra were obtained regardless of the solvent history of the sample. However, the required incubation times were found to depend on the previous solvent in which the sample was equilibrated. For example, **4** is monomeric in pyridine and forms a *PM* shifted dimer in $CDCl_3$. When these solutions are evaporated and re-dissolved in CD_2Cl_2 the starting species are not the same and the equilibrium to produce the homochiral shifted is reached faster with the sample coming from pyridine than with the sample coming from $CDCl_3$.

In the case of shorter sequences **3** and **5**, equilibration times were generally fast (around 5 min). Samples were typically incubated for 2h which gave a large margin. In the case of **4** and **6**, equilibration times are considerably longer and incubation of three to six weeks is indicated.

Solvent-dependency studies of **3** and **5** were carried out by adding *e.g.* CD_2Cl_2 to a solution in *e.g.* $CDCl_3$ stepwise up to 50:50 and by making the reverse experiment, that is adding $CDCl_3$ to a CD_2Cl_2 solution stepwise up to 50:50. Because of the faster equilibration, the same sample could be used and spectra were measured 2h after every addition. In the case of **4** and **6**, equilibration times are much longer and a minimum of two weeks is recommended between each addition. Alternatively, individual samples for each solvent mixture may be prepared and incubated concomitantly.

$^{1}H,^{15}N$-HSQC spectra were recorded with a phase-sensitive pulse sequence with sensitivity enhancement using trim pulses in inept transfer (hsqcetgpsi2) from the Bruker pulse program library. Data acquisition was performed utilizing non-uniform sampling (NUS; NUS amount: 50% with an automatically created NUSList) yielding 1024 (F2) x 128 (F1) data points in Echo/Antiecho gradient selection mode. The recycling delay was 2.0 s and 64 transients per increment were applied at a sweep width of 2.5 kHz in F2 and 7 kHz in F1 resulting in an acquisition time of 0.1462 s. NUS processing was performed using the fully automated NUS processing tool provided by MestReNova. Zero filling in F1 has been used to yield a final matrix of 1K x 1K real points.

The DOSY spectrum was recorded applying a pulse sequence with stimulated echo using bipolar gradient pulses for diffusion from the Bruker pulse program library (stebpgp1s). The diffusion delay Δ (big delta) was set to 120 ms and the diffusion gradient pulse length δ (little delta) was set to 1.2 ms. The number of gradient steps were set to 32 with linear spacing starting from 2% reaching 95% of the full gradient strength in the final step. For each of the 32 gradient amplitudes, 16 transients of 65k complex data points were acquired. DOSY processing was performed with the DOSY processing tool from MestReNova (v.12.x64) employing the Peak Heights Fit algorithm including the overlapped peaks analysis" with 128 points in diffusion dimension and a window of $1.00*10^{-16}$ to $1.00*10^{+03}$ $cm^2\ s^{-1}$.

4.4 CD studies

All CD spectra were recorded on a Jasco J-810 spectrometer with 10 mm quartz cuvette. The following parameters were used: wavelength range from 500 to 250 nm. Scan speed: 200 nm/min; accumulation: 3; response time: 1.0 s; bandwidth: 2; temperature: 25 °C; sensitivity: standard (100 mdeg); data pitch: 1 nm; nitrogen gas flow rate: 500L/h. The sample solution was prepared in distilled chloroform or DCM

filtered over alumina before use. Δε values (in $cm^2.mmol^{-1}$) were obtained by using the formula: Δε = m°/(C.l.32980) where m°= CD value in millidegrees; l = cuvette pathlength in cm; C = sample concentration in mol/L. The CD spectra of **5** and its protected precursor **13** were carried out at 0.01 mM in chloroform and DCM. Thus, a solution of **5** or **13** in pyridine was prepared and the same volume was taken, respectively. After removal of the solvent, the samples were dissolved and incubated in chloroform or DCM.

4.5 X-ray crystallography

The diffraction data for selected single crystals were collected at the IECB x-ray facility (CNRS UMS 3033 – INSERM US001) with a Rigaku FRX rotating anode (2.9 kW) diffractometer. CuKα radiation monochromated with high flux Osmic Varimax HF mirrors was used for data collection. The x-ray source is equipped with a Dectris Pilatus 200K detector and partial chi goniometer. All crystals were kept at 100(2) K during data collection. The data were processed with the CrysAlis PRO software[5] with a multiscan absorption correction. Structures were solved with the ShelXT[6] structure solution program using a dual-space algorithm. Crystal model refinement was performed with ShelXL[7] package using Least Squares minimization implemented in Olex2.[8]

For some side chains, not all C or O atoms were found. During refinement, anisotropic displacement parameters were used for backbones, some solvent molecules and side chains. The C- and N-bound hydrogen atoms were placed at an idealized position. The positions of hydrogen atoms of O-H groups were found based on possible hydrogen bonds. All H atoms were refined in the riding-model approximation, with $U_{iso}(H)=1.2U_{eq}$ (CH, CH_2, NH) and $U_{iso}(H)=1.5U_{eq}$ (OH). EADP, DELU, SIMU and RIGU instructions were employed to model temperature parameters. The geometry of the molecules was improved with DFIX, FLAT or AFIX commands.

The structure of **7** was refined as a racemic twin in a P1 space group. Attempts to perform refinement in a centrosymmetric space group (P-1) were made, but the model was unstable.

The electron density maps were carefully inspected to localize the position of solvent molecules. The unrecognized residual electron density peaks close to chloroform molecules were introduced to the refinement as dummy Cl atoms, in other areas as dummy O atoms. However, some solvent molecules were severely disordered, and their introduction to the model caused significant deterioration of the refinement parameters. Thus, the solvent masking procedure implemented in Olex2[8] was employed to remove them. The solvent radius was set to 1.2 Å, calculated total potential solvent-accessible void volume and electron counts per unit-cell 2689 $Å^3$ and 791, 802 $Å^3$ and 148, 8894 $Å^3$ and 1914, 5921 $Å^3$ and 1301, for racemic crystal structure of **3** and **7**, as well as homochiral and pseudo-racemic crystal structure of **5**, respectively.

The final cif files were checked using IUCR's checkcif algorithm. Due to the characteristics of the crystals, *i.e.* large volume fractions of disordered solvent molecules, weak diffraction intensity, incompleteness of the data and moderate resolution, and twinning, a number of 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:

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_A, B High R1 Value

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

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

PLAT971_ALERT_2_B Check Calcd Positive Resid. Density

PLAT090_ALERT_3_B Poor Data / Parameter Ratio (Zmax > 18)

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

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)

As mentioned above, not all atoms were refined with ADPs

PLAT315_ALERT_2_B Singly Bonded Carbon Detected (H-atoms Missing)

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

PLAT306_ALERT_2_B Isolated Oxygen Atom (H-atoms Missing ?)

Unrecognized electron density was introduced to the refinement as dummy oxygen atoms.

PLAT430_ALERT_2_A Short Inter D...A Contact

Contacts between dummy O atoms.

Table S5 Crystal data and refinement details for racemic crystal structure of **3** and **7**, as well as homochiral of **5**.

Identification code	**3** (racemic)	**5** (homochiral)	**7** (racemic)
Chemical formula	$2(C_{159}H_{148}N_{26}O_{25}Se)\cdot 23.74(CHCl_3)$ solvent**	$C_{164}H_{152}N_{26}O_{27}Se\cdot 4(CH_2Cl_2)\cdot$solvent**	$2(C_{217}H_{200}N_{36}O_{41}S_7Se_2)\cdot 21(O)^*\cdot 1.7(Cl)^*\cdot 23.6(CHCl_3)$ solvent**
Formula weight	8637.59	3337.77	11918.87
Crystal system	Triclinic	Orthorhombic	Triclinic
Space group	P-1	$P2_12_12$	P1
Unit cell dimensions (Å, °)	a=26.6435 (7), α=87.193 (2)	a=34.7079 (1), α=90	a=19.2663 (6) α=107.926 (2)
	b=27.0228 (7), β=68.158 (2)	b=52.844 (2), β=90	b=27.5957 (6) β=92.018 (3)
	c=30.0865 (7), γ=84.410 (2)	c=20.0658 (4), γ=90	c=29.3722 (10) γ=100.461 (2)
Volume ($Å^3$)	20009.2 (9)	36802 (2)	14541.8 (8)
Z	2	8	1
Density (calculated) ($Mg\ m^{-3}$)	1.434	1.205	1.36
Absorption coefficient (mm^{-1})	5.20	1.92	4.47
Crystal size (mm)	0.10 × 0.07 × 0.03	0.20 × 0.06 × 0.02	0.10 × 0.08 × 0.03
Completeness	98.5 (up to 50.43°)	100 (up to 44.48°)	99.4 (up to 50.43°)
Reflections collected	127174	83736	120984
Reflections observed [I > 2σ(I)]	25187	17095	28821
R_{int}	0.078	0.043	0.058
Data/parameters/restrains	41251/3074/657	28971/2767/2491	49594/1812/2979
Goodness-of-fit on F^2	2.35	1.19	1.70
Final R indices [I > 2σ(I)]	0.2341, 0.5699	0.1130, 0.2959	0.1993, 0.4590
R indices (all data)	0.2765, 0.6040	0.1536, 0.3343	0.2396, 0.4962
Largest diff. peak and hole	3.30, -1.57	0.46, -0.44	1.88, -0.70
CCDC #	2209189	2209187	2209188

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

* Unrecognized electron density was introduced to the refinement as dummy oxygen or as chlorine atoms

** Solvent mask was used to remove severely disordered solvent molecules

Table S6. Crystal data and refinement details for pseudo-racemic crystal structure of **5**.

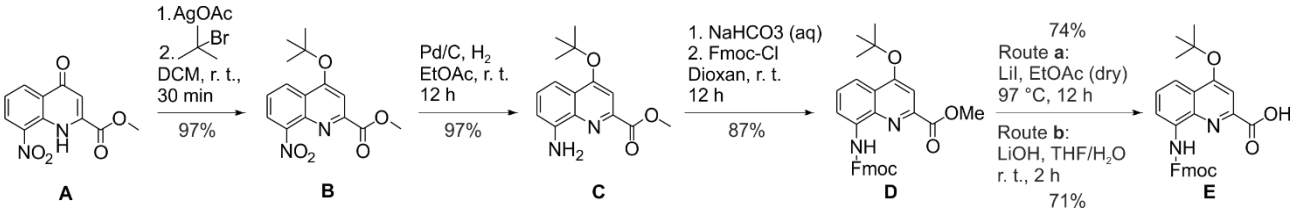
Identification code	**5** (pseudo-racemic)
Chemical formula	$C_{164}H_{152}N_{26}O_{27}Se \cdot 18(CHCl_3) \cdot$solvent**
Formula weight	8144.76
Crystal system	Monoclinic
Space group	P2
Unit cell dimensions (Å, °)	a=26.2355 (5), α=90
	b=20.3023 (6), β=94.254 (2)
	c=41.8226 (8), γ=90
Volume (Å^3)	22215.1 (9)
Z	2
Density (calculated) (Mg m^{-3})	1.218
Absorption coefficient (mm^{-1})	3.73
Crystal size (mm)	0.20 × 0.07 × 0.03
Completeness	91.2 (up to 47.53°)
Reflections collected	76330
Reflections observed [I > 2σ(I)]	22119
R_{int}	0.060
Data/parameters/restrains	37171/2090/3147
Goodness-of-fit on F^2	1.72
Final R indices [I > 2σ(I)]	0.1790, 0.4450
R indices (all data)	0.2162, 0.4794
Largest diff. peak and hole	1.29, -0.56
CCDC #	2209186

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

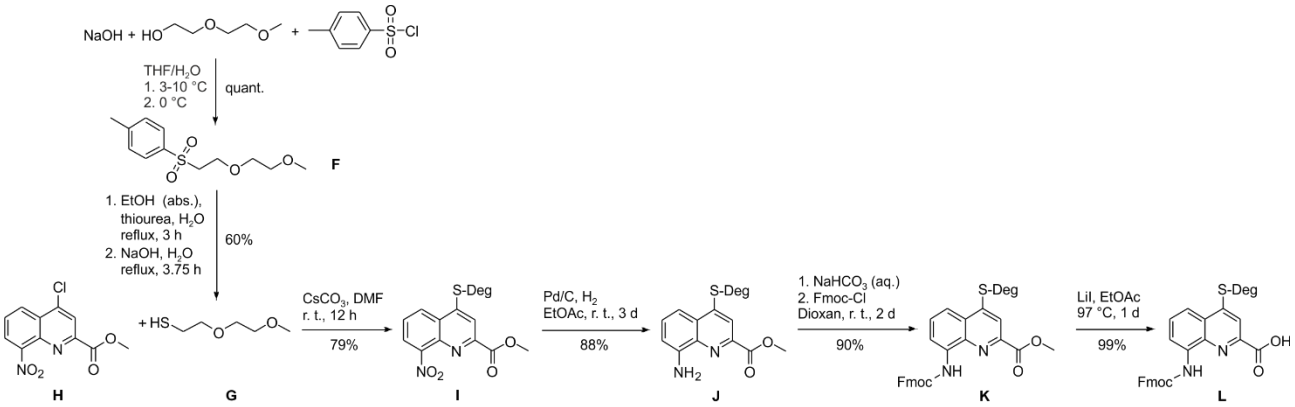
** Solvent mask was used to remove severely disordered solvent molecules

5 Synthetic Schemes

5.1 Synthesis of monomers

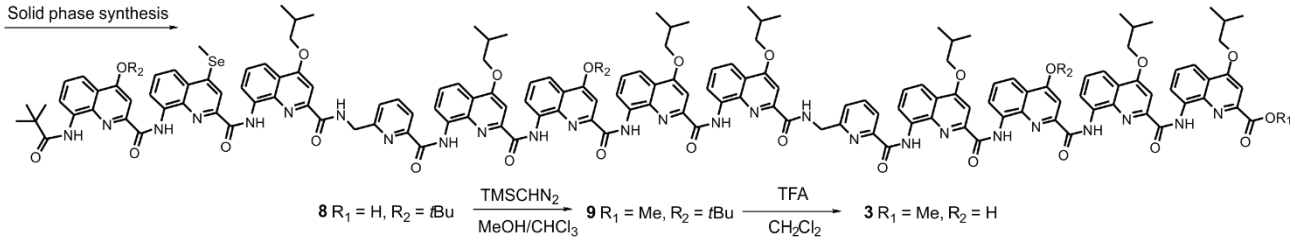


Scheme 1. Synthesis of Fmoc-X-OH **E**. (X denotes *t*Bu-protected X)

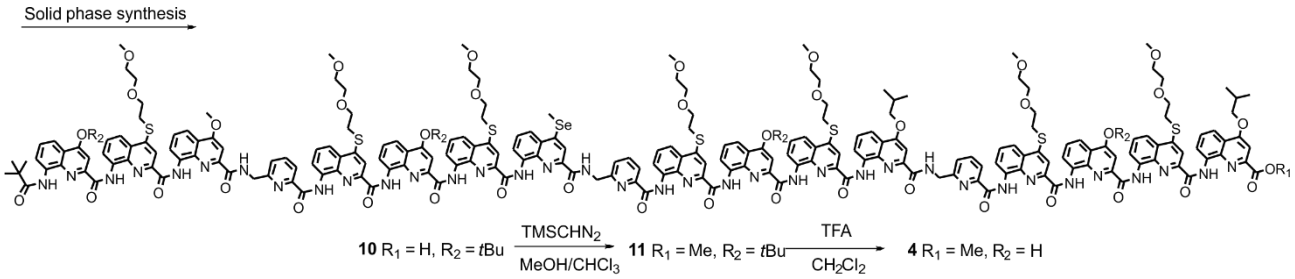


Scheme 2. Synthesis of Fmoc-Q^{D}-OH **L**.

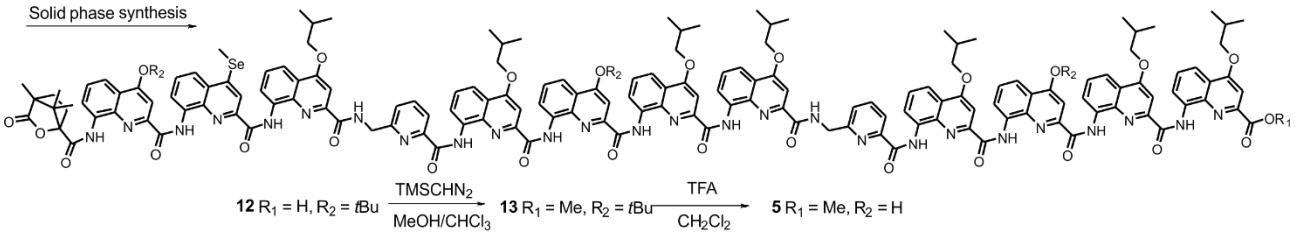
5.2 Synthesis of foldamers



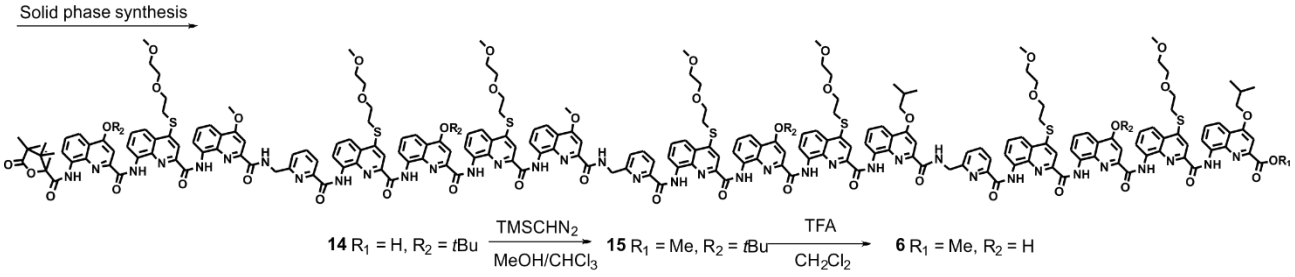
Scheme 3. Synthesis of **3**.



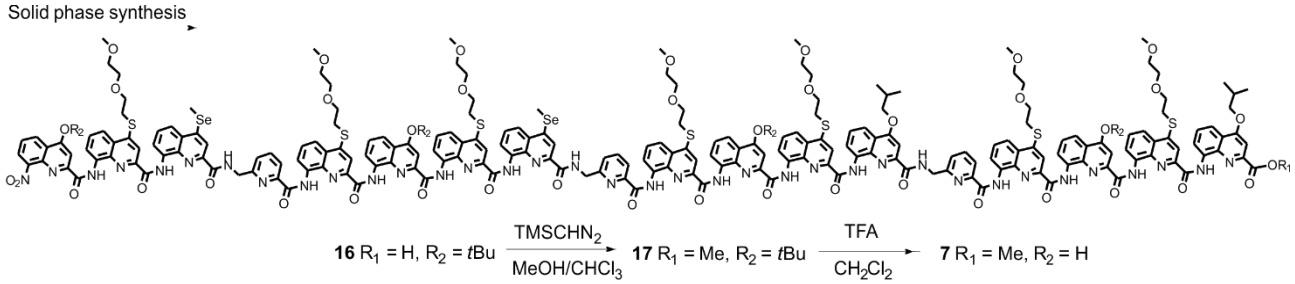
Scheme 4. Synthesis of **4**.



Scheme 5. Synthesis of **5**.



Scheme 6. Synthesis of **6**.



Scheme 7. Synthesis of **7**.

6 Experimental Procedures

6.1 General methods

Commercial available 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. Tetrahydrofuran (THF), dichloromethane (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. 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). MPLC was carried out on puriFlash® XS520Plus (interchim) using a PF-15C18HQ-F0080 column (3.5 x 19 cm, 15µm, 20 bar, interchim. The mobile phase was composed of H_2O (solvent A) and CH_3CN (solvent B). Solid phase synthesis (SPS) was performed manually under MW-irradiation on a CEM Discover (Liberty Bio) microwave oven using an open reaction vessel and an internal fibre optic probe for temperature control. High-resolution electrospray mass spectra were recorded on a Thermo Exactive orbitrap instrument.

6.2 Synthesis of small units

The monomers Fmoc-Q^B-OH,[9] Fmoc-Q^M-OH[10] and Fmoc-P-OH[11] have been synthesized according to the literature. The synthesis of Fmoc-Q^S-OH will be published elsewhere. The syntheses of Fmoc-<u>X</u>-OH (<u>X</u> denotes *t*Bu-protected X) and Fmoc-Q^D-OH were previously reported.[4, 12] Improved/modified protocols are presented below. Final Fmoc-protected amino acid had to have a purity of ≥ 97%.

***Methyl* 4-(*tert*-butoxy)-8-nitroquinoline-2-carboxylate (B).** Methyl 8-nitro-4-oxo-1,4-dihydroquinoline-2-carboxylate (**A**)[9] (88.8 g, 0.36 mol, 1 eq.) and silver acetate (246 g, 1.47 mol, 4.15 eq.) were suspended in DCM (3.8 L) under nitrogen atmosphere and protected from the exposure to light. After stirring for 5 min, *tert*-Butyl bromide (162 mL, 197.6 g, 1.44 mol, 4 eq.) was added dropwise over the course of 5 min. After vigorous stirring of the suspension at r. t for 30 min it was filtered over a pad of celite into a saturated solution of $NaHCO_3$ in water. The residue was washed with DCM until the yellow filtrate remained colorless. The layers of the filtrate were separated, and the DCM phase was washed with water, and then with brine. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue purified via filtration over a pad of silica, the residue was washed with 5% EtOAc in DCM (2 L) until the yellow filtrate remained almost colorless. The filtrate was evaporated in vacuo at 50 °C to give the product as a yellow solid (105.1 g, 0.35 mol, 97%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 25 °C) δ [ppm] 8.44 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.99 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.81 (s, 1H), 7.62 (dd, *J* = 8.5, 7.4 Hz, 1H), 4.03 (s, 3H), 1.69 (s, 9H). **^{13}C NMR** (101 MHz, CD_2Cl_2) δ [ppm] 166.0, 161.1, 151.2, 149.2, 140.6, 127.2, 126.1, 125.9, 124.5, 107.2, 83.2, 28.7. **MS** calcd for $C_{15}H_{16}N_2NaO_2$ $[M+Na]^+$ 327.0951, found (HR-ESI) 327.0952. The data obtained are in agreement with the literature values.[4]

***Methyl* 8-amino-4-(*tert*-butoxy)quinoline-2-carboxylate (C).** Compound **B** (105.1 g, 0.35 mol, 1 eq.) was dissolved in EtOAc (2.21 L) and N_2 was bubbled through for 5 min. After addition of the Pd/C-catalyst (10.5 g, 10*wt*%) vacuum was pulled shortly prior to establishing H_2 atmosphere. The suspension was stirred for 12 h

under H_2 atmosphere at r. t., then the mixture was filtered over a pad of celite, the residue was washed with EtOAc until the yellow filtrate remained colorless. The filtrate was evaporated removed in vacuo at 50 °C water bath to give the product as a yellow solid (93.3 g, 0.34 mol, 99%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 25 °C) δ [ppm] 7.67 (s, 1H). 7.47 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.34 (dd, *J* = 8.4, 7.5 Hz, 1H), 6.91 (dd, *J* = 7.5, 1.3 Hz, 1H), 5.09 (s, 2H), 4.00 (s, 3H), 1.64 (s, 9H), **^{13}C NMR** (101 MHz, CD_2Cl_2) δ [ppm] 166.6, 160.8, 145.9, 145.4, 139.2, 128.7, 126.0, 110.7, 110.7, 107.0, 81.6, 28.8. **MS** calcd for $C_{11}H_{11}N_2O_3$ [M-*t*Bu+H$^+$]$^+$ 219.0764, found (HR-ESI) 219.0763.

***Methyl* 8-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-4-(*tert*-butoxy)quinoline-2-carboxylate (D).** Compound **C** (93.3 g, 0.34 mol, 1 eq.) was dissolved in dioxane (1.0 L), then a solution of $NaHCO_3$ (143.0 g, 1.70 mol, 5 eq.) in water (1.4 L, 10*wt*%-solution) was added and the reaction mixture was cooled down to 0 °C. At this temperature a solution of Fmoc-chloride (114 g, 0.44 mol, 1.3 eq.) in dioxane (357.0 mL) was added dropwise over the course of an hour. After complete addition, the reaction mixture was stirred 1 h at 0 °C, followed by 12 h at r.t.. The reaction mixture was brought to pH 3-4 using a 5% citric acid-solution in water. The precipitate was filtered off, dissolved in DCM, the water-phase separated and the organic layer dried over $MgSO_4$. The solvent was then removed under reduced pressure at 50 °C water bath and precipitated from Et_2O. The product was obtained as white solid (147.4 g, 0.30 mol, 87%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 25 °C) δ [ppm] 9.31 (s, 1 H), 8.41 (s, 1 H), 7.88 (td, *J* = 8.5, 1.2 Hz, 3 H), 7.79 (s, 1 H), 7.77 (dt, *J* = 7.4, 0.9 Hz, 2H), 7.57 (t, *J* = 8.1 Hz, 1 H), 7.50 – 7.45 (m, 2 H), 7.40 (td, *J* = 7.5, 1.2 Hz, 2 H), 4.61 (d, *J* = 7.0 Hz, 2 H), 4.45 (t, *J* = 7.1 Hz, 1 H), 4.09 (s, 3 H), 1.72 (s, 9 H).**^{13}C NMR** (101 MHz, CD_2Cl_2) δ [ppm] 166.3, 161.3, 153.6, 147.0, 144.4, 141.7, 139.2, 135.7, 128.2, 128.2, 127.5, 125.6, 125.0, 120.4, 116.0, 115.7, 107.0, 82.2, 67.6, 47.6, 28.8. **MS** calcd for $C_{30}H_{29}N_2O_5$ [M+H]$^+$ 497.2071, found (HR-ESI) 497.2069.

8-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4-(*tert*-butoxy)quinoline-2-carboxylic acid (E). Synthesis Route a: Compound **D** (79.2 g, 0.16 mol, 1 eq.) was dissolved in EtOAc (1.0 L) and three times degassed with N_2. The mixture was heated to 97 °C and LiI (82.3 g, 0.61 mol, 3.8 eq.) was added in portions. The reaction mixture refluxed for 12 h, then allowed to coold down to r. t. prior to diluting with EtOAc. The solution was washed once with a $Na_2S_2O_3$ solution (5% in water), twice with a solution of citric acid (5% in water), and finally once with water. The organic layer was then dried over Na_2SO_4 and, after filtration, the solvent was removed under reduced pressure at 50 °C water bath. The product was obtained as a yellow solid (57.0 g, 0.12 mol, 74%) with a purity of 97%. **Synthesis Route b:** Compound **D** (2.15 g, 4.33 mmol, 1 eq.) was dissolved in THF (100 mL). A solution of LiOH (waterfree) (104 mg, 4.3 mmol, 1 eq.) in water (10 mL) was added dropwise. The reaction mixture was stirred at r.t. for 2 h, then it was brought to pH 5-6 using a 5% citric acid-solution in water. The mixture was extraced with DCM. The combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was then removed under reduced pressure at 50 °C water bath and the crude purified by MPLC (50-100 CH_3CN in water). The product was obtained as a white solid (1.48 g, 3.07 mmol, 71 %) with a purity of 99 %. **^{1}H NMR** (500 MHz, DMSO-d_6, 25 °C) δ [ppm] 13.52 (s, 1H), 10.42 (s, 1H), 8.33 (s, 1H), 7.93 (d, *J* = 7.5 Hz, 2H), 7.80– 7.77 (m, 3H), 7.71 (s, 1H), 7.63 – 7.55 (m, 1H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 4.61 (d, *J* = 6.4 Hz, 1H), 4.45 (t, *J* = 6.7 Hz, 1H), 1.63 (s, 9H). **MS** calcd for $C_{29}H_{27}N_2O_5$ [M+H]$^+$ 483.1914 found (HR-ESI) 483.1912. The data obtained are in agreement with the literature values.[4]

1-(*p*-Tolylsulfonyl)-3,6-dioxoheptane (F). To a solution of diethylene monomethyl alcohol (150.0 g, 1.25 mol) in dry THF (312.0 mL) was added a solution of NaOH (70.9 g, 1.78 mol) in water (375.0 mL). The mixture was cooled to 0 °C internal temperature, then a solution of *p*-toluenesulfonylchloride (226 g, 0.94 mol) was added dropwise while keeping the internal temperature at 4-10 °C. After complete addition the reaction mixture was stirred at 2°C for 4 h. Before being extracted with with Et_2O (100 mL) five times. The combined organic layers were washed with water until the aqueous phase was neutral. Then the organic layer was dried over Na_2SO_4, filtered and the solvent removed under reduced pressure without heating. The product was obtained as a colorless oil that solidifies over time (280.0 g, quant.). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 7.81 – 7.78 (m, 2H), 7.35 – 7.32 (m, 2H), 4.18 – 4.15 (m, 2H), 3.75 – 3.72 (m, 4H), 3.70 – 3.67 (m, 2H), 3.59 – 3.56 (m, 2H), 3.49 – 3.47 (m, 2H), 3.34 (s, 3H), 2.44 (s, 3H). The data obtained are in agreement with the literature values.[13]

1-Mercapto-3,6-dioxoheptane (G). To a solution of **F** (33.6 g, 0.13 mol) in ethanol (67.0 mL) was added a solution of thiourea (9.2 g, 0.12 mol) in water (4.9 mL). The reaction mixture was refluxed for 3 h, after what a solution of NaOH (6.7 g, 0.17 mol) in water (28.0 mL) was added and the reaction mixture was heated to reflux for 3.75 h. After cooling down to r. t., the crude was acidified with HCl (conc.), extracted with DCM and dried over $MgSO_4$. The residue was purified via distillation at 80 °C oil bath under 20 mbar of pressure to afford the product as a colorless oil (24.5 g, 0.08 mol, 60%). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 3.65 – 3.60 (m, 4H), 3.57 – 3.54 (m, 2H), 3.39 (s, 3H), 2.71 (dt, *J* = 8.2, 6.6 Hz, 2H), 1.59-1.55 (t, *J* = 8.2 Hz, 1H). The data obtained are in agreement with the literature values.[13]

Methyl 4-((2-(2-methoxyethoxy)ethyl)thio)-8-nitroquinoline-2-carboxylate (I). Methyl-4-chloro-8-nitroquinoline-2-carboxylate (**H**) (41.0 g, 0.15 mol, 1.0 eq.) and $CsCO_3$ (75.0 g, 0.23 mol, 1.5 eq.) were dissolved in dry DMF (1.3L) under N_2 atmosphere. Compound **G** (20.0 g, 0.15 mol, 0.94 eq.) was then added and the suspension was stirred overnight at r. t. under N_2 atmosphere. The reaction mixture was then filtered over a small pad of silica and washed with a 1:1 mixture of EtOAc and *n*-hex until the filtrate came of colourless. Some colour remained on the pad, which is assumed to be by-product. The solvent was removed under reduced pressure and the residue was precipitated in DCM/MeOH to obtain a first batch of pure product as a yellow solid (20.063 g). The mother solution was evaporated under reduced pressure and the residue purified via column chromatography on silica gel with cyclohexane/EtOAc (9:1 to 4:6) as eluent. After evaporation at 50 °C water bath the two batches were combined to give the product as a yellow solid (43.6 g, 0.12 mol, 79%). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 8.38 (dd, J = 8.5, 1.4, 1H), 8.12 (1H, s), 8.06 (dd, *J* = 7.5, 1.2, 1H), 7.69 (dd, *J* = 8.5, 7.5, 1H), 4.03 (s, 3H), 3.89 (t, *J* = 6.3, 2H), 3.69 – 3.67 (m, 2H), 3.57 – 3.55 (m, 2H), 3.46 (t, *J* = 6.3, 2H), and 3.37 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ [ppm] 165.6, 150.7, 149.3, 148.9, 138.7, 128.2, 127.7, 126.9, 124.8, 117.1, 72.1, 70.9, 68.9, 59.3, 53.6, 31.7. **MS** calcd for $C_{16}H_{19}N_2O_6S$ $[M+H]^+$ 367.0958, found (HR-ES) 367.1002. The data obtained are in agreement with the literature values.[12]

Methyl 8-amino-4-((2-(2-methoxyethoxy)ethyl)thio)quinoline-2-carboxylate (J). Compound **I** (43.6 g, 0.12 mol, 1 eq.) was suspended in EtOAc (1.0 L) and N_2 was bubbled through for 5 min. After addition of the Pd/C-catalyst (6.5 g, 15*wt*%), vacuum was pulled shortly prior to establishing H_2 atmosphere. The suspension was stirred for 3 d under H_2 atmosphere, then the mixture was filtered over a pad of celite, the residue was washed with EtOAc until the yellow filtrate remained colorless. Some brown color remained on the pad which is assumed to be by-product. The filtrate was evaporated removed in vacuo at 50 °C water bath to give the

product as a yellow solid (35.3 g, 0.105 mol, 88 %). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 7.98 (s, 1H), 7.43 (d, *J* = 2.8 Hz, 1H), 7.39 (s, 1H), 6.96 (dd, *J* = 5.7, 3.0 Hz, 1H), 5.25 (d, *J* = 73.0 Hz, 2H), 4.05 (s, 3H), 3.88 (t, *J* = 6.6 Hz, 2H), 3.74 – 3.68 (m, 2H), 3.62 – 3.57 (m, 2H), 3.39 – 3.41 (m, 5H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ [ppm] 166.2, 148.4, 145.8, 143.6, 136.5, 129.7, 128.1, 115.8, 111.4, 110.8, 72.0, 70.7, 69.1, 60.6, 59.2, 53.0, 31.0. **MS** calcd for $C_{16}H_{20}N_2NaO_4S$ $[M+Na]^+$ 359.1036, found (HR-ESI) 359.1037.

Methyl 8-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4-((2-(2-methoxyethoxy)ethyl)thio)quinoline-2-carboxylate (K). Compound **J** (35.3 g, 0.10 mol, 1 eq.) was dissolved in dioxane (1.0 L), then a solution of $NaHCO_3$ (139.0 g, 1.65 mol, 15 eq.) in water (1.4 L, 10*wt*%-solution) was added and the reaction mixture was cooled down to 0 °C. At this temperature a solution of Fmoc-chloride (35.3 g, 0.14 mol, 1.3 eq.) in dioxane (350.0 mL) was added dropwise over the course of an hour. After complete addition, the reaction mixture was stirred 1 h at 0 °C, followed by 2 d at r.t.. The reaction mixture was brought to pH 3-4 using a 20% HCl-solution in water. The precipitate was filtered off, dissolved in DCM, the water-phase separated and the organic layer dried over $MgSO_4$. The solvent was then removed under reduced pressure at 50 °C water bath to give the product as a brown solid (50.8 g, 0.09 mol, 90%). **^{1}H NMR** (400 MHz, CD_2Cl_2, 25 °C) δ [ppm] 9.30 (s, 1H), 8.40 (s, 1H), 8.05 (s, 1H), 7.96 (d, *J* = 2.0 Hz, 1H), 7.85 – 7.76 (m, 2H), 7.76 – 7.69 (m, 2H), 7.60 (t, *J* = 8.1 Hz, 1H), 7.44 (ddt, *J* = 8.4, 7.5, 1.0 Hz, 2H), 7.39 – 7.30 (m, 2H), 4.58 (d, *J* = 7.0 Hz, 2H), 4.40 (t, *J* = 7.0 Hz, 1H), 4.06 (s, 3H), 3.90 – 3.83 (m, 2H), 3.69 – 3.62 (m, 2H), 3.57 – 3.50 (m, 2H), 3.43 (t, *J* = 6.3 Hz, 2H), 3.34 (s, 3H). **^{13}C NMR** (101 MHz, CD_2Cl_2) δ [ppm] 166.1, 153.8, 150.4, 145.4, 144.5, 141.9, 137.1, 136.6, 129.6, 129.3, 128.3, 127.7, 127.7, 125.7, 121.5, 120.6, 116.9, 116.6, 116.2, 72.4, 71.1, 69.3, 67.9, 59.3, 47.7, 36.9, 31.9, 31.7. **MS** calcd for $C_{31}H_{31}N_2O_6S$ $[M+H]^+$ 559.1897, found (HR-ESI) 559.1896.

8-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4-((2-(2-methoxyethoxy)ethyl)thio)quinoline-2-carboxylic acid (L). Compound **K** (50.8 g, 0.09 mol, 1 eq.) was suspended in EtOAc (0.8 L) and three times degassed with N_2. The mixture was heated to 97 °C and LiI (96.7 g, 0.72 mol, 7.9 eq.) was added in portions. The reaction micture refluxed for 1 d, then allowed to coold down to r. t. prior to recovering the precipitate via filtration. The solid was dissolved in DCM, washed once with a $Na_2S_2O_3$ (5% in water), twice with a solution of citric acid (5% in water), and finally once with water. The organic layer was then dried over Na_2SO_4 and, after filtration, the solvent was removed under reduced pressure at 50 °C water bath. The residue was precipitated in a mixture of EtOAc and Et_2O to give the product as an yellow solid (49.4 g, 0.09 mol, 99%) with a purity of 97%. **^{1}H NMR** (500 MHz, DMSO-d_6, 25 °C) δ [ppm] 13.58 (s, 1H), 10.44 (s, 1H), 8.36 (s, 1H), 8.08 (s, 1H), 7.94 (dt, *J* = 7.6, 1.1 Hz, 2H), 7.78 (dt, *J* = 7.5, 1.1 Hz, 2H), 7.75 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.68 (d, *J* = 7.3 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.37 (td, *J* = 7.5, 1.2 Hz, 2H), 4.62 (d, *J* = 7.0 Hz, 2H), 4.45 (t, *J* = 6.7 Hz, 1H), 3.80 (t, *J* = 6.1 Hz, 2H), 3.62 – 3.58 (m, 2H), 3.50 (t, *J* = 6.1 Hz, 2H), 3.47 – 3.44 (m, 2H), 3.24 (s, 3H). The data obtained are in agreement with the literature values.[12]

6.3 Solid phase synthesis general methods

6.3.1 Loading of the resin via HBTU-coupling

SASRIN resin (800 mg, 100-200 mesh, loading 0.7-1.0 mmol/g) was swollen in DMF for 1 h, transferred to the microwave vessel and washed three times with dry DMF (purchased as 'extra-dry' solvent from Acros Organics). DIPEA (272 µL, 2 eq.) was added to a mixture of Q^B (232 mg; 0.6 eq.) and HBTU (456 mg, 1.5 eq.) in dry DMF (5 mL), then the mixture was added to the resin. The reaction mixture was subjected to treatment

in the microwave (50 °C, 20 min, 25 W), then the resin was washed five times with DMF until the washing solution was colourless, then it was washed ten times with DCM. If the loading was sufficient a capping was performed, otherwise the resin re-loaded. Capping was performed by adding a mixture of DCM/pyridine/benzoyl chloride (v/v/v, 3:1:1) and the resin left for 30 min, then it was rinsed 20x times with DCM.

6.3.2 Estimation of the loading

After drying a small part of the resin under vacuum for 5 h, the loading of the resin was determined. To a small amount of resin (1-2 mg), a freshly prepared of DMF/piperidine (v/v, 8:2, 3 mL) was added. The mixture was shaken and incubated for 5 min. Then the absorption was measured at 290 nm using a NanoDrop One Microvolume UV-Vis Spectrophotometer and a Hellma quartz glass cuvette 104 (path length 10 mm). Three replicates were measured, then the loading was calculated with the following equation:

$$\text{loading}\left(\text{in}\ \frac{\text{mmol}}{\text{g}}\right) = \frac{A_{290\ \text{nm}}}{1.65 * m_{\text{resin}}(\text{in mg})} \qquad (1)$$

6.3.3 Solid Phase Synthesis via in-situ-activation

After swelling of the SASRIN resin (800 mg, 100-200 mesh, loading 0.388 mmol/g, 0.310 µmol) in DMF for 1 h, the resin was transferred into the microwave vessel and washed three times with DMF. For deprotection a 8:2 mixture of DMF/piperidine (6 mL) was added to the resin and nitrogen was bubbled through the suspension for 3 min. The solution was removed, the resin washed five times with DMF and an 8:2 mixture of DMF/piperidine (6 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 (4 mL) and 2,3,5-collidine (5 eq. with regards to the resin-loading) were added to the resin. A mixture of the monomer (2 eq. with regards to the resin-loading) and PPh_3 (4 eq. with regards to the resin-loading) in dest. $CHCl_3$ (4 mL) or dry NMP (4 mL) was prepared. All monomers except for Fmoc-P-OH were dissolved in dest. chloroform. Fmoc-P-OH was dissolved in dry NMP. After the addition of trichloroacetonitrile (4 eq. with regards to the resin-loading), this mixture was added to the resin. Then the reaction mixture was subjected to treatment in the microwave (50 °C, 5 min, 50 W) Then the resin was washed five times with dry THF, then dry THF (4 mL) and 2,3,5-collidine (5 eq. with regards to the resin-loading) were added to the resin. Again, a mixture of monomer (2 eq. with regards to the resin-loading) and PPh_3 (4 eq. with regards to the resin-loading) in dest. $CHCl_3$ (4 mL) or dry NMP (4 mL) with trichloroacetonitrile was prepared and added to the resin. The reaction mixture was again subjected to microwave vessel treatment (50 °C, 5 min, 25 W). After washing with DCM, THF, DMF and DCM, in that order, the resin was kept in a swollen state at 10 °C.

For installation of the pivaloyl- and (1*S*)-camphanic amide the resin (0.030 mmol) was Fmoc deprotected (20% piperidine in DMF, 1 x 3 min and 1 x 7 min), washed with DMF and dry THF, then a solution of DIPEA (31.1 µL, 10 eq.) in dry THF (0.5 mL) was added to the resin. To this suspension a solution of pivaloylchloride or (1*S*)-camphanic acid chloride (3 eq.) in dry THF (0.5 mL) was added and rests on the reaction vessel were rinsed down with dry THF (0.5 mL). The reaction was carried out under MW irradiation (25 W) at 50°C for 5 min. The resin was washed briefly with dry THF, and the process repeated. Successively the resin was washed with DMF and DCM.

6.3.4 Mini Cleavage

To perform a mini cleavage, SASRIN resin (~5 mg) was swelled in DCM for 15 min, then either HFIP [DCM (2.8 mL) and HFIP (1.2 mL)] or TFA [(TFA/DCM 3:7)] were added and the mixture was stirred at r. t. for 1 h (in case of HFIP) or 10 min (in case of TFA). If the mini cleavage was executed with HFIP, the solvent was evaporated. If TFA was used, the reaction mixture was filtered into a saturated sodium carbonate solution. After extraction with DCM, the combined organic layers were dried over magnesium sulfate, and then the solvent was evaporated.

6.3.5 Full Cleavage

To perform the full cleavage, SASRIN resin (~50 mg) was swelled in DCM for 15 min, HFIP [DCM/HFIP, v/v, 1:1 (6 mL in total)] was added, and the mixture was stirred at r. t. for 12 h. Then the solvent was evaporated. The process was repeated until no more foldamer is left on the resin (up to ten times).

6.4 Synthesis of oligomers

Piv-$\underline{X}Q^SQ^BPQ^B\underline{X}Q^BQ^BPQ^B\underline{X}Q^BQ^B$-OH (**8**) Compound **8** was synthesized using the SPS procedures reported in 6.3 on SASRIN resin loaded via HBTU-coupling described in 6.3 (scale: 60.40 µmol). The crude product was obtained after full cleavage and used without further purification (184.5 mg, quant). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 11.18 (s, 1H), 10.81 (s, 1H), 10.80 (s, 1H), 10.74 (s, 1H), 10.68 (s, 1H), 10.60 (s, 1H), 10.51 (s, 1H), 10.28 (s, 1H), 10.21 (s, 1H), 10.12 (s, 1H), 8.52 (s, 1H), 7.96 (d, *J* = 4.3 Hz, 1H), 7.94 – 7.93 (m, 1H), 7.90-7.88 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.82 – 7.73 (m, *J* = 7.78, 4H), 7.72 (d, *J* = 1.2 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.60 (ddt, *J* = 8.7, 7.1, 1.3 Hz, 5H), 7.57 – 7.49 (m, *J* = 7.53, 3H), 7.45 – 7.43 (m, 2H), 7.33 (t, *J* = 7.8 Hz, 3H), 7.23 – 7.19 (m, 5H), 7.13 (d, *J* = 7.5 Hz, 2H), 7.09 – 7.04 (m, 2H), 6.99 – 6.92 (m, 7H), 6.91 – 6.85 (m, 2H), 6.78 – 6.73 (m, 3H), 6.69 (dd, *J* = 7.3, 1.4 Hz, 1H), 6.53 (s, 1H), 6.39 (s, 1H), 6.20 (s, 1H), 6.18 (s, 1H), 5.79 (s, 1H), 5.75 (s, 1H), 5.55 (s, 1H), 2.98 (s, 3H), 2.89 (s, 3H), 2.41 (s, 3H), 2.30 (s, 6H), 1.71 (s, 9H), 1.70 (s, 9H), 1.60 (s, 9H), 1.17 – 1.10 (m, 10H), 1.09 – 1.03 (m, 20H), 0.90 – 0.86 (m, 15H), 0.85 – 0.78 (m, 11H), 0.43 (s, 9H). **MS** calcd for $C_{170}H_{171}N_{26}O_{25}Se$ $[M+H]^+$ 3056.2068, found (HR-ESI) 3056.8976.

Piv-$\underline{X}Q^SQ^BPQ^B\underline{X}Q^BQ^BPQ^B\underline{X}Q^BQ^B$-OMe (**9**) Compound **8** (184.5 mg, 60.40 µmol, 1 eq.) was dissolved in a mixture of dry chloroform/MeOH 3:2 (10 mL) under N_2. $TMSCHN_2$ (2 M in hex, 106.0 µL, 0.17 mmol, 2 eq.) was added dropwise, and the solution was stirred at r.t. for 2 h. A few drops of acetic acid were added, and the solution stirred for 5 min at r.t. Then the solution was diluted with DCM, washed with $NaHCO_3$, dried $MgSO_4$, filtered and concentrated. The crude product was purified via precipitation in DCM/MeOH (90.0 mg, 50% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 11.38 (s, 1H), 11.15 (s, 1H), 10.89 (s, 1H), 10.79 (s, 1H), 10.74 (s, 1H), 10.65 (s, 1H), 10.45 (s, 1H), 10.27 (s, 1H), 10.18 (s, 1H), 10.00 (s, 1H), 8.49 (s, 1H), 7.95 (ddd, *J* = 12.7, 7.4, 1.2 Hz, 1H), 7.91 – 7.89 (m, 1H), 7.85 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.78 (dddd, *J* = 9.8, 7.2, 6.2, 1.3 Hz, 2H), 7.74 – 7.69 (m, 1H), 7.66 (t, *J* = 3.5 Hz, 1H), 7.60 – 7.50 (m, 8H), 7.43 – 7.40 (m, 5H), 7.33 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.30 – 7.27 (m, 1H), 7.24 – 7.19 (m, 4H), 7.17 – 7.13 (m, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 7.07 (d, *J* = 4.3 Hz, 1H), 7.05 (d, *J* = 1.4 Hz, 1H), 7.03 – 6.97 (m, 5H), 6.95 – 6.92 (m, 2H), 6.91 (s, 1H), 6.87 (td, *J* = 7.4, 4.5 Hz, 3H), 6.81 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.70 – 6.66 (m, 2H), 6.50 (s, 1H), 6.34 (s, 2H), 6.33 (s, 1H), 5.73 (s, 1H), 5.69 (s, 1H), 5.50 (s, 1H), 3.96 (s, 1H), 3.94 – 3.90 (m, 2H), 3.87 – 3.83 (m, 2H), 3.74 (t, *J* = 6.0 Hz, 2H), 3.68 (dd, *J* = 8.0, 6.2 Hz, 1H), 3.63 – 3.55 (m, 5H), 3.53 – 3.49 (m, 3H), 3.34 – 3.30 (m, 1H), 3.18 (dd, *J* = 17.0, 3.8 Hz, 1H), 3.08 (s, 3H), 2.43 – 2.36 (m, 6H), 2.32 (dt, *J* =

13.4, 6.7 Hz, 1H), 2.25 – 2.17 (m, 5H), 2.09 (ddd, *J* = 16.7, 10.0, 4.7 Hz, 2H), 1.63 (s, 1H), 1.27 – 1.22 (m, 21H), 1.17 – 1.13 (m, 18H), 1.13 – 1.10 (m, 8H), 1.04 (dd, *J* = 12.8, 6.7 Hz, 8H), 0.90 – 0.78 (m, 9H), 0.44 (s, 9H). **MS** calcd for $C_{171}H_{173}N_{26}O_{25}Se$ $[M+H]^+$ 3070.2225, found (HR-ESI) 3070.9091.

Piv-XQ^{S}Q^{B}PQ^{B}XQ^{B}Q^{B}PQ^{B}XQ^{B}Q^B-OMe (**3**) Compound **9** (13.2 mg, 4.32 µmol) was treated with a 50% solution of TFA in DCM (2 mL) at r.t. for 2 h. Then the solvent was removed under vacuum, obtaining the product as a yellow solid (12.9 mg, quant.). **^{1}H NMR** (500 MHz, DMSO-d_6, 25 °C) δ [ppm] 11.71 (s, 1H), 11.69 (s, 1H), 11.37 (s, 1H), 11.13 (s, 1H), 10.98 (s, 1H), 10.77 (s, 1H), 10.62 (s, 1H), 10.40 (s, 1H), 10.37 (s, 1H), 10.16 (s, 1H), 10.11 (s, 1H), 10.06 (s, 1H), 10.05 (s, 1H), 8.50 (s, 1H), 7.90 – 7.86 (m, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 2H), 7.65 (dt, *J* = 7.3, 1.4 Hz, 4H), 7.59 (td, *J* = 8.2, 2.1 Hz, 3H), 7.55 – 7.44 (m, 5H), 7.44 – 7.38 (m, 4H), 7.37 – 7.30 (m, 3H), 7.24 – 7.17 (m, 3H), 7.11 (dd, *J* = 7.4, 1.4 Hz, 2H), 7.08 – 6.94 (m, 6H), 6.93 – 6.87 (m, 5H), 6.79 (t, *J* = 7.9 Hz, 2H), 6.76 – 6.74 (m, 1H), 6.68 – 6.65 (m, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 6.52 (d, *J* = 7.6 Hz, 1H), 6.40 (s, 1H), 6.24 (s, 1H), 5.85 (s, 1H), 5.84 (s, 1H), 5.63 (s, 1H), 5.51 (s, 1H), 5.38 (s, 1H), 3.95 (t, *J* = 7.5 Hz, 2H), 3.92 – 3.88 (m, 2H), 3.83 (t, *J* = 7.6 Hz, 2H), 3.78 – 3.70 (m, 6H), 3.69 – 3.62 (m, 5H), 3.58 (q, *J* = 8.4 Hz, 3H), 3.50 (t, *J* = 7.7 Hz, 2H), 3.20 (s, 2H), 3.06 (s, 3H), 3.01 (d, *J* = 13.9 Hz, 2H), 2.29 (dq, *J* = 13.7, 6.9 Hz, 2H), 2.25 – 2.16 (m, 2H), 2.14 – 2.06 (m, 2H), 2.03 – 1.96 (m, 3H), 1.68 (t, *J* = 13.9 Hz, 3H), 1.30 – 1.11 (m, 20H), 1.06 (dd, *J* = 14.8, 6.7 Hz, 8H), 0.85 (t, *J* = 6.9 Hz, 4H), 0.36 (s, 9H). **MS** calcd for $C_{159}H_{149}N_{26}O_{25}Se$ $[M+H]^+$ 2902.0347, found (HR-ESI) 2902.9310, calcd for $C_{159}H_{150}N_{26}O_{25}Se$ $[M+2H]^{2+}$ 1451.5210, found (HR-ESI) 1451.9640.

Piv-<u>X</u>Q^{D}Q^{M}PQ^D<u>X</u>Q^{D}Q^{S}PQ^D<u>X</u>Q^{D}Q^{D}PQ^D<u>X</u>Q^{D}Q^D-OH (**10**) Compound **10** was synthesized using the SPS procedures reported in 6.3 on SASRIN resin loaded via HBTU-coupling described in 6.3 (scale: 81.3 µmol). The crude product was obtained after precipitation in EtOAc/*n*-hex, and the product was obtained as a yellow solid (270.0 mg, 73%). **^{1}H NMR** (500 MHz, CD_2Cl_2, 25 °C) δ [ppm] 11.14 (s, 1H), 10.81 (s, 1H), 10.68 (s, 1H), 10.47 (s, 1H), 10.47 (s, 1H), 10.37 (s, 1H), 10.34 (s, 1H), 10.22 (s, 1H), 10.12 (s, 1H), 10.07 (s, 1H), 9.97 (s, 1H), 9.94 (s, 1H), 9.90 (s, 1H), 9.74 (s, 1H), 8.46 (s, 1H), 8.03 – 8.00 (m, 2H), 7.95 (dd, *J* = 14.6, 7.1 Hz, 4H), 7.77 (s, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.68 – 7.61 (m, 4H), 7.55 – 7.44 (m, 6H), 7.44 – 7.28 (m. 7H), 7.23 (d, *J* = 7.3 Hz, 1H), 7.18 – 7.09 (m, 5H), 7.07 – 7.02 (m, 6H), 7.00 (d, *J* = 11.6 Hz, 4H), 6.98 – 6.91 (m, 6H), 6.91 – 6.83 (m, 5H), 6.83 – 6.80 (m, 3H), 6.75 (t, *J* = 8.1 Hz, 2H), 6.68 (dd, *J* = 13.7, 7.3 Hz, 2H), 6.62 (d, *J* = 7.3 Hz, 1H), 6.58 (dd, *J* = 7.4, 3.2 Hz, 2H), 6.37 (t, *J* = 3.5 Hz, 2H), 6.33 (s, 1H), 6.20 (s, 1H), 6.03 (s, 1H), 5.99 (s, 1H), 5.84 (s, 1H), 5.81 (s, 1H), 5.67 (s, 1H), 5.60 (s, 1H), 3.94 – 3.90 (m, 5H), 3.90 – 3.87 (m, 5H), 3.85 (d, *J* = 6.7 Hz, 5H), 3.82 (dd, *J* = 6.1, 3.6 Hz, 10H), 3.80 – 3.76 (m, 9H), 3.74 (d, *J* = 4.7 Hz, 11H), 3.71 (dd, *J* = 9.3, 5.0 Hz, 9H), 3.69 – 3.64 (m, 7H), 3.60 – 3.55 (m, 6H), 3.55 (s, 3H), 3.54 (s, 3H), 3.53 (s, 3H), 3.53 – 3.51 (m, 3H), 3.50 (s, 3H), 3.45 (s, 3H), 3.38 (s, 3H), 3.33 (d, *J* = 7.2 Hz, 1H), 3.31 (s, 3H), 3.26 (q, *J* = 6.3 Hz, 1H), 3.17 – 3.07 (m, 8H), 3.05 – 2.99 (m, 8H), 2.89 – 2.92 (m, 2H), 2.91 (s, 2H), 2.82 (s, 2H), 2.56 (s, 2H), 2.22 (s, 2H), 1.18 – 1.14 (m, 8H), 1.09 – 1.04 (m, 8H), 0.86 – 0.80 (m, 9H), 0.38 (s, 9H). **MS** calcd for $C_{237}H_{240}N_{36}Na_2O_{41}S_7Se$ $[M+2Na]^{2+}$ 2297.73982, found (HR-ESI) 2298.5187.

Piv-<u>X</u>Q^{D}Q^{M}PQ^D<u>X</u>Q^{D}Q^{S}PQ^D<u>X</u>Q^{D}Q^{D}PQ^D<u>X</u>Q^{D}Q^D-OMe (**11**) Compound **10** (175.0 mg, 52 µmol, 1 eq.) was dissolved in a mixture of dry chloroform/MeOH 3:2 (5 mL) under N_2. $TMSCHN_2$ (2 M in hex, 92 µL, 0.10 mmol, 2 eq.) was added dropwise, and the solution was stirred at r.t. for 2 h. A few drops of acetic acid were added, and the solution was stirred for 5 min at r.t. Then the solution was diluted with DCM, washed with $NaHCO_3$, dried $MgSO_4$, filtered and concentrated. The crude product was obtained as a yellow solid (165.0 mg, 94%

yield). **^{1}H NMR** (500 MHz, CD_2Cl_2, 25 °C) δ [ppm] 11.27 (s, 1H), 10.99 (s, 1H), 10.81 (s, 1H), 10.68 (s, 1H), 10.46 (s, 1H), 10.37 (s, 1H), 10.32 (s, 1H), 10.20 (s,1H), 10.12 (s,1H), 10.08 (s, 1H), 9.94 (s,1H), 9.93 (s, 1H), 9.90 (s, 1H), 9.73 (s, 1H),8.45 (s,1H), 8.03 – 8.01 (m, 1H), 7.97 (dd, *J* = 7.3, 1.1 Hz, 1H), 7.93 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.82 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.77 (t, *J* = 3.5 Hz, 1H), 7.67 – 7.59 (m, 5H), 7.59 – 7.43 (m, 12H), 7.43 – 7.38 (m, 3H), 7.36-7.31 (m, 4H), 7.23 (ddd, *J* = 8.1, 4.4, 3.1 Hz, 3H), 7.18 – 7.09 (m, 5H), 7.07 – 7.02 (m, 6H), 7.02 – 6.98 (m, 4H), 6.97 – 6.81 (m, 8H), 6.76 – 6.72 (m, 2H), 6.70 (dd, *J* = 7.3, 1.3 Hz, 1H), 6.65 (d, *J* = 7.3 Hz, 1H), 6.61 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.59 – 6.55 (m, 2H), 6.38 – 6.34 (m, 2H), 6.29 (s, 1H), 6.19 (s, 1H), 6.03 (s, 1H), 5.98 (s, 1H), 5.84 (s, 1H), 5.81 (s, 1H), 5.67 (s, 1H), 5.57 (s, 1H), 3.93 – 3.86 (m, 5H), 3.85 – 3.79 (m, 5H), 3.78 – 3.76 (m, 4H), 3.75 – 3.69 (m, 10H), 3.68 – 3.64 (m, 4H), 3.63 – 3.58 (m, 4H), 3.58 (t, *J* = 1.6 Hz, 2H), 3.57-3.55 (m, 3H), 3.55 (s, 2H), 3.54 (d, *J* = 3.4 Hz, 6H) 3.53 (s, 2H), 3.53 – 3.51 (m, 1H), 3.50 (s, 3H), 3.49 (s, 1H), 3.49 – 3.47 (m, 2H), 3.45 (s, 3H), 3.44 (s, 1H), 3.38 (s, 2H), 3.31 (s, 2H), 3.29 – 3.22 (m, 3H), 3.21 – 3.09 (m, 8H), 3.06 (ddd, *J* = 8.2, 5.6, 2.1 Hz, 4H), 3.03 (s, 4H), 3.03 – 2.95 (m, 5H), 2.95 – 2.92 (m, 1H), 2.91 – 2.82 (m, 2H), 2.72 – 2.67 (m, 1H), 2.22 (s, 2H), 2.12 (s, 3H), 1.69 – 1.67 (m, 2H), 1.65 (s, 6H), 1.61 (s, 12H), 1.58 (s, 6H), 1.25 (s, 4H), 1.16 (q, *J* = 6.9 Hz, 4H), 1.08 (d, *J* = 6.7 Hz, 4H), 1.05 (d, *J* = 6.7 Hz, 4H), 0.90 – 0.81 (m, 9H), 0.39 (s, 9H). **MS** calcd for $C_{238}H_{243}N_{36}NaO_{41}S_7Se$ $[M+H+Na]^{2+}$ 2293.75667, found (HR-ESI) 2294.5324.

Piv-XQ^{D}Q^{M}PQ^{D}XQ^{D}Q^{S}PQ^{D}XQ^{D}Q^{D}PQ^{D}XQ^{D}Q^D-OMe (**4**) Compound **11** (27.1 mg, 5.94 µmol) was treated with a 50% solution of TFA in DCM (2 mL) at r.t. for 2 h. Then the solvent was removed under vacuum, obtaining the product as a yellow solid (23.1 mg, 90%). **^{1}H NMR** (500 MHz, DMSO-d_6, 25 °C) δ [ppm] 11.72 (s, 1H), 11.66 (s, 1H), 11.37 (s, 1H), 11.29 (s, 1H), 11.09 (s, 1H), 10.85 (s, 1H), 10.71 (s, 1H), 10.56 (s, 1H), 10.28 (s, 1H), 10.23 (s, 1H), 10.19 (s, 1H), 10.10 (s, 1H), 9.99 (s, 1H), 9.97 (s, 1H), 9.86 (s, 2H), 9.75 (s, 1H), 9.57 (s, 1H), 8.44 (s, 1H), 7.85 (d, *J* = 6.3 Hz, 1H), 7.79 (d, *J* = 7.3 Hz, 1H), 7.76 – 7.72 (m, 1H), 7.69 (d, *J* = 6.9 Hz, 1H), 7.67 – 7.59 (m, 3H), 7.57 – 7.53 (m, 4H), 7.52 – 7.46 (m, 3H), 7.39 (ddt, *J* = 17.5, 7.5, 4.0 Hz, 4H), 7.34 – 7.22 (m, 3H), 7.19 (q, *J* = 5.8, 3.1 Hz, 6H), 7.13 – 7.06 (m, 10H), 7.01 – 6.92 (m, 5H), 6.91 – 6.75 (m, 12H), 6.69 – 6.62 (m, 3H), 6.58 (d, *J* = 7.0 Hz, 1H), 6.53 – 6.49 (m, 2H), 6.42 (dd, *J* = 13.7, 7.2 Hz, 2H), 6.22 (d, *J* = 9.3 Hz, 3H), 6.08 (s, 1H), 5.98 (s, 1H), 5.83 (s, 1H), 5.62 (s, 1H), 5.60 (s, 1H), 5.59 (s, 1H), 5.46 (s, 1H), 3.85 – 3.63 (m, 24H), 3.62 – 3.56 (m, 6H), 3.54 – 3.52 (m, 2H), 3.48 (s, 1H), 3.51 – 3.44 (m, 15H), 3.42 (s, 3H), 3.39 – 3.38 (m, 8H), 3.37 (s, 3H), 3.31 (s, 3H), 3.25 (s, 3H), 3.12 (tt, *J* = 16.9, 7.9 Hz, 3H), 3.02 (s, 2H), 2.97 (t, *J* = 6.0 Hz, 2H), 2.89 (dt, *J* = 12.2, 6.8 Hz, 2H), 2.10 – 2.03 (m, 2H), 1.60 – 1.41 (m, 3H), 1.40 – 1.35 (m, 2H), 1.30 – 1.24 (m, 7H), 1.19 – 1.15 (m, 2H), 1.12 (dd, *J* = 6.7, 4.6 Hz, 7H), 1.03 (dd, *J* = 13.9, 6.7 Hz, 8H), 0.85 (t, *J* = 6.9 Hz, 2H), 0.32 (s, 9H). **MS** calcd for $C_{222}H_{211}N_{36}NaO_{41}S_7Se$ $[M+H+Na]^{2+}$ 2181.6315, found (HR-ESI) 2182.1131.

(1*S*)-Camph-<u>X</u>Q^{S}Q^{B}PQ^B<u>X</u>Q^{B}Q^{B}PQ^B<u>X</u>Q^{B}Q^B-OH (**12**) Compound **12** was synthesized using the SPS procedures reported in 6.3 on SASRIN resin loaded via HBTU-coupling described in 6.3 (scale: 43.12 µmol). The crude product was obtained after full cleavage and used without further purification (135.9 mg, quant). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 11.20 (s, 1H), 11.18 (s, 1H), 10.95 (s, 1H), 10.71 (s, 1H), 10.69 (s, 1H), 10.58 (s, 1H), 10.42 (s, 1H), 10.26 (s, 1H), 10.19 (s, 1H), 10.05 (s, 1H), 9.20 (s, 1H), 7.98 – 7.94 (m, 3H), 7.84 (d, *J* = 3.5 Hz, 1H), 7.82 – 7.76 (m, 5H), 7.76 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.72 (d, *J* = 1.5 Hz, 1H), 7.70 (t, *J* = 1.5 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.63 – 7.58 (m, signal overlap with signals corresponding to benzoic acid), 7.57 – 7.54 (m, 2H), 7.54 – 7.52 (m, 1H), 7.51 (d, *J* = 2.8 Hz, 1H), 7.50 – 7.45 (m, signal overlap with signals

corresponding to benzoic acid), 7.45 – 7.43 (m, 3H), 7.40 (d, *J* = 7.4 Hz, 1H), 7.34 (s, 1H), 7.30 (s, 2H), 7.25-7.21 (m, 5H), 7.18 – 7.12 (m, 1H), 7.08 (td, *J* = 7.7, 5.3 Hz, 3H), 7.04 – 6.94 (m, 3H), 6.93 (s, 1H), 6.88 (q, *J* = 7.4 Hz, 2H), 6.83 (d, *J* = 7.5 Hz, 1H), 6.81 – 6.76 (m, 2H), 6.75 – 6.70 (m, 2H), 6.55 (s, 1H), 6.39 (s, 1H), 6.27 (s, 1H), 6.23 (s, 1H), 5.72 (s, 1H), 5.71 (s, 1H), 5.58 (s, 1H), 5.49 (s, 1H), 5.35 (t, *J* = 4.7 Hz, 2H), 4.73 (s, 1H), 4.63 (s, 1H), 4.16 – 4.11 (m, 1H), 3.91 – 3.86 (m, 2H), 3.84 – 3.79 (m, 4H), 3.78 – 3.73 (m, 2H), 3.66 – 3.60 (m, 3H), 3.52 – 3.48 (m, 3H), 3.28 – 3.16 (m, 1H), 1.76 – 0.99 (m, signal overlapping with water), 0.91-0.78 (m, signal overlapping with impurities), 0.52 (s, 3H), 0.48 (s, 3H), 0.01 (s, 3H). **MS** calcd for $C_{175}H_{175}N_{26}O_{27}Se$ $[M+H]^+$ 3152.2280, found (HR-ESI) 3152.9801.

(1*S*)-Camph-X$Q^S$$Q^B$PQ^{B}X$Q^B$$Q^B$PQ^{B}X$Q^B$$Q^B$-OMe (**13**) Compound **12** (135.9 mg, 43.12 µmol, 1 eq.) was dissolved in a mixture of dry chloroform/MeOH 3:2 (5 mL) under N_2. $TMSCHN_2$ (2 M in hex, 76 µL, 0.12 mmol, 2 eq.) was added dropwise, and the solution was stirred at r.t. for 2 h. A few drops of acetic acid were added, and the solution was stirred for 5 min at r.t. Then the solution was diluted with DCM, washed with $NaHCO_3$, dried $MgSO_4$, filtered and concentrated. The crude product was purified via precipitation in DCM/MeOH (56.6 mg, 46% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 11.37 (s, 1H), 11.19 (s, 1H), 11.15 (s, 1H), 10.95 (s, 1H), 10.71 (s, 1H), 10.65 (s, 1H), 10.37 (s, 1H), 10.25 (s, 1H), 10.17 (s, 1H), 9.99 (s, 1H), 9.20 (s, 1H), 7.93 (dd, *J* = 7.4, 3.6 Hz, 2H), 7.83 (d, *J* = 7.3 Hz, 1H), 7.77 (dtd, *J* = 14.1, 8.1, 3.6 Hz, 6H), 7.69 (dt, *J* = 8.2, 1.5 Hz, 2H), 7.57 (s, 1H), 7.57 – 7.49 (m, 6H), 7.49 – 7.44 (m, 1H), 7.44 – 7.40 (m, 3H), 7.39 – 7.32 (m, 2H), 7.31 – 7.27 (m, 1H), 7.25 – 7.14 (m, 5H), 7.11 – 7.05 (m, 3H), 7.04 – 6.92 (m, 7H), 6.89 – 6.67 (m, 8H), 6.48 (s, 1H), 6.30 (s, 1H), 6.28 (s, 1H), 6.25 (s, 1H), 5.68 (s, 2H), 5.47 (s, 1H), 3.93 – 3.86 (m, 3H), 3.83 – 3.79 (m, 3H), 3.74 – 3.70 (m, 2H), 3.63-3.53 (m, 9H), 3.29-3.23 (m, 5H), 3.06 (s, 3H), 2.30 (dq, *J* = 13.3, 6.5 Hz, 2H), 2.26 – 2.15 (m, 5H), 2.15 – 2.08 (m, 3H), 2.08 – 1.88 (m, 15H), 1.86 – 1.73 (m, 5H), 1.16 – 1.12 (m, 11H), 1.09 (d, *J* = 6.8 Hz, 9H), 1.02 (dd, *J* = 13.1, 6.7 Hz, 16H), 0.89 – 0.76 (m, 10H), 0.50 (s, 3H), 0.46 (s, 3H), 0.00 (s, 3H). **MS** calcd for $C_{176}H_{176}N_{26}NaO_{27}Se$ $[M+Na]^+$ 3188.2256, found (HR-ESI) 3190.0299.

(1*S*)-Camph-X$Q^S$$Q^B$PQ^{B}X$Q^B$$Q^B$PQ^{B}X$Q^B$$Q^B$-OMe (**5**) Compound **13** (12.4 mg, 3.91 µmol) was treated with a 50% solution of TFA in DCM (2 mL) at r.t. for 2 h. Then the solvent was removed under vacuum, obtaining the product as a yellow solid (11.7 mg, quant.). **^{1}H NMR** (500 MHz, DMSO-d_6, 25 °C) δ [ppm] 11.76 (s, 1H), 11.74 (s, 1H), 11.38 (s, 1H), 11.13 (s, 1H), 10.99 (s, 1H), 10.97 (s, 1H), 10.83 (s, 1H), 10.39 (s, 1H), 10.36 (s, 1H), 10.15 (s, 1H), 10.07 (s, 1H), 10.05 (s, 2H), 9.13 (s, 1H), 7.88 (d, *J* = 7.3 Hz, 1H), 7.74 (d, *J* = 7.3 Hz, 2H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 2H), 7.56 (dt, *J* = 15.4, 7.3 Hz, 4H), 7.49 (d, *J* = 8.1 Hz, 5H), 7.47 – 7.42 (m, 2H), 7.41 – 7.35 (m, 4H), 7.35 – 7.30 (m, 3H), 7.19 – 7.09 (m, 5H), 6.99 (tt, *J* = 18.9, 6.7 Hz, 5H), 6.88 (td, *J* = 14.4, 13.6, 9.2 Hz, 5H), 6.80 (t, *J* = 7.7 Hz, 2H), 6.75 (d, *J* = 7.3 Hz, 1H), 6.71 (d, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 7.3 Hz, 1H), 6.48 (d, *J* = 7.5 Hz, 1H), 6.39 (s, 1H), 6.24 (s, 1H), 5.85 (s, 1H), 5.81 (s, 1H), 5.59 (s, 1H), 5.51 (s, 1H), 5.37 (s, 1H), 3.96 – 3.93 (m, 1H), 3.91 – 3.88 (m, 2H), 3.82 – 3.79 (m, 2H), 3.77 – 3.70 (m, 5H), 3.69 – 3.55 (m, 4H), 3.53-3.44 (m, overlay with water peak), 3.19-3.14 (m, 2H), 3.05 (s, 3H), 3.01 – 2.98 (m, 2H), 2.42 (s, 3H), 2.33 – 2.26 (m, 4H), 2.24 – 2.16 (m, 4H), 2.13 – 2.04 (m, 2H), 2.00 (d, *J* = 7.8 Hz, 1H), 1.72 – 1.66 (m, 4H), 1.56 – 1.43 (m, 4H), 1.42 – 1.32 (m, 4H), 1.28 – 1.21 (m, 4H), 1.21 – 1.13 (m, 4H), 1.13 – 1.09 (m, 4H), 1.07 (d, *J* = 6.7 Hz, 4H), 1.04 (d, *J* = 6.7 Hz, 6H), 0.84 (t, *J* = 6.9 Hz, 8H), 0.47 (s, 3H), 0.40 (s, 3H), -0.07 (s, 3H). **MS** calcd for $C_{164}H_{153}N_{26}O_{27}Se$ $[M+H]^+$ 2998.0558, found (HR-ESI) 2998.8521, calcd for $C_{164}H_{154}N_{26}O_{27}Se$ $[M+2H]^{2+}$ 1499.5316, found (HR-ESI) 1499.9279.

(1*S*)-Camph-<u>X</u>Q^{D}Q^{M}PQ^{D}<u>X</u>Q^{D}Q^{M}PQ^{D}<u>X</u>Q^{D}Q^{B}PQ^{D}<u>X</u>Q^{D}Q^{B}-OH (**14**) Compound **14** was synthesized using the SPS procedures reported in 6.3 on SASRIN resin loaded via HBTU-coupling described in 6.3 (scale: 82 µmol). After full cleavage and precipitation in EtOAc/*n*-hex, the product was obtained as a yellow solid (192.2 mg, 51%). **^{1}H NMR** (500 MHz, CD_2Cl_2, 25 °C) δ [ppm] 11.21 (s, 1H), 11.12 (s, 1H), 10.88 (s, 1H), 10.70 (s, 1H), 10.47 (s, 1H), 10.42 (s, 1H), 10.36 (s, 1H), 10.21 (s, 1H), 10.16 (s, 1H), 10.07 (s, 1H), 9.95 (s, 1H), 9.92 (s, 1H), 9.85 (s, 1H), 9.78 (s, 1H), 9.17 (s, 1H), 8.03 – 8.00 (m, 2H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.84 – 7.81 (m, 2H), 7.75 (ddd, *J* = 7.1, 5.8, 1.2 Hz, 3H), 7.64 – 7.56 (m, 4H), 7.55 – 7.47 (m, 4H), 7.47 – 7.41 (m, 3H), 7.41 – 7.33 (m, 3H), 7.33 – 7.28 (m, 5H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.18 – 7.07 (m, 3H), 7.07 – 7.03 (m, 4H), 7.01 (d, *J* = 2.9 Hz, 3H), 7.00 – 6.90 (m, 6H), 6.90 – 6.84 (m, 5H), 6.84 – 6.73 (m, 7H), 6.69 – 6.63 (m, 3H), 6.60 – 6.55 (m, 2H), 6.35 (s, 1H), 6.33 (d, *J* = 1.7 Hz, 1H), 6.30 (s, 1H), 6.21 (s, 1H), 5.96 (s, 1H), 5.87 (s, 1H), 5.77 (s, 1H), 5.70 (s, 1H), 5.63 (s, 1H), 5.57 (s, 1H), 3.93 – 3.86 (m, 14H), 3.85 – 3.79 (m, 24H), 3.78 – 3.70 (m, 31H), 3.69 – 3.71 (m, 13H), 3.54 (s, 3H), 3.53 (s, 3H), 3.52 (s, 3H), 1.63 (s, 8H), 1.58 (s, 11H), 1.52 (s, 8H), 1.23 – 1.20 (m, 4H), 1.14 (dd, *J* = 14.7, 6.8 Hz, 8H), 1.04 (dd, *J* = 14.6, 6.8 Hz, 8H), 0.88 – 0.79 (m, 10H), 0.46 (s, 3H), 0.42 (s, 3H), -0.04 (s, 3H). **MS** calcd for $C_{242}H_{244}N_{36}Na_2O_{44}S_7$ $[M+2Na]^{2+}$ 2313.7896, found (HR-ESI) 2315.0568.

(1*S*)-Camph-<u>X</u>Q^{D}Q^{M}PQ^{D}<u>X</u>Q^{D}Q^{M}PQ^{D}<u>X</u>Q^{D}Q^{B}PQ^{D}<u>X</u>Q^{D}Q^{B}-OMe (**15**) Compound **14** (192.2 mg, 41.95 µmol, 1 eq.) was dissolved in a mixture of dry chloroform/MeOH 3:2 (5 mL) under N_2. $TMSCHN_2$ (2 M in *n*-hex, 24.8 µL, 0.083 mmol, 2 eq.) was added dropwise, and the solution was stirred at r.t. for 2 h. A few drops of acetic acid were added, and the solution was stirred for 5 min at r.t. Then the solution was diluted with DCM, washed with $NaHCO_3$, dried $MgSO_4$, filtered and concentrated. The product was obtained as a yellow solid (146.7 mg, 76%). **^{1}H NMR** (500 MHz, CD_2Cl_2, 25 °C) δ [ppm] 11.19 (s, 1H), 11.01 (s, 1H), 10.91 (s, 1H), 10.81 (s, 1H), 10.39 (s, 1H), 10.30 (s, 1H), 10.24 (s, 1H), 10.13 (s, 1H), 10.06 (s, 1H), 10.00 (s, 1H), 9.86 (s, 1H), 9.85 (s, 1H), 9.79 (s, 1H), 9.71 (s, 1H), 9.09 (s, 1H), 7.95 – 7.91 (m, 1H), 7.90 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.78 – 7.70 (m, 4H), 7.64 (dd, *J* = 7.4, 1.3 Hz, 2H), 7.60 – 7.52 (m, 4H), 7.52 – 7.38 (m, 12H), 7.38 – 7.29 (m, 6H), 7.24 – 7.21 (m, 3H), 7.17 – 7.14 (m, 1H), 7.07 – 6.90 (m, 12H), 6.88 – 6.60 (m, 13H), 6.57 (d, *J* = 7.4 Hz, 1H), 6.52 – 6.47 (m, 2H), 6.26 – 6.25 (m, 2H), 6.21 (s, 1H), 6.11 (s, 1H), 5.87 (s, 1H), 5.81 (s, 1H), 5.72 (s, 1H), 5.59 (s, 1H), 5.51 (s, 1H), 5.47 (s, 1H), 3.85 – 3.61 (m, 19H), 3.59 – 3.51 (m, 11H), 3.51 – 3.44 (m, 19H), 3.43 (s, 3H), 3.41 – 3.38 (m, 4H), 3.37 (s, 3H), 3.31 (s, 3H), 3.23 (s, 3H), 3.19 – 3.13 (m, 3H), 3.10 – 2.96 (m, 12H), 2.95 (s, 3H), 2.94 – 2.83 (m, 7H), 2.79 – 2.74 (d, *J* = 2.77, 1H), 2.63 – 2.58 (m, 1H), 1.59 (s, 8H), 1.52 (s, 8H), 1.51 (s, 8H), 1.49 (s, 8H), 1.11 (d, *J* = 6.8 Hz, 4H), 1.07 (d, *J* = 6.7 Hz, 4H), 1.00 (dd, *J* = 6.6, 3.5 Hz, 8H), 0.81 – 0.73 (m, 10H), 0.40 (s, 3H), 0.37 (s, 3H), -0.09 (s, 3H). **MS** calcd for $C_{243}H_{246}N_{36}Na_2O_{44}S_7$ $[M+2Na]^{2+}$ 2320.7974 found (HR-ESI) 2321.5576.

(1*S*)-Camph-XQ^{D}Q^{M}PQ^{D}XQ^{D}Q^{M}PQ^{D}XQ^{D}Q^{B}PQ^{D}XQ^{D}Q^{B}-OMe (**6**) Compound **15** (49.5 mg, 10.8 µmol) was treated with a 50% solution of TFA in DCM (3 mL) at r.t. for 2 h. Then the solvent was removed under vacuum, obtaining the product as a yellow solid (47.2 mg, quant.). **^{1}H NMR** (500 MHz, DMSO-d_6, 25 °C) δ [ppm] 11.72 (s, 2H), 11.33 (s, 1H), 11.29 (s, 1H), 11.09 (s, 1H), 10.96 (s, 1H), 10.85 (s, 1H), 10.77 (s, 1H), 10.28 (s, 1H), 10.24 (s, 1H), 10.18 (s, 1H), 10.10 (s, 1H), 10.01 (s, 1H), 9.98 (s, 1H), 9.85 (s, 1H), 9.80 (s, 1H), 9.78 (s, 1H), 9.67 (s, 1H), 9.07 (s, 1H), 7.85 (d, *J* = 7.6 Hz, 2H), 7.74 (d, *J* = 9.8 Hz, 2H), 7.69 (d, *J* = 7.0 Hz, 2H), 7.67 – 7.54 (m, 3H), 7.48 (ddd, *J* = 26.2, 12.7, 8.3 Hz, 6H), 7.42 – 7.27 (m, 11H), 7.27 – 7.16 (m, 7H), 7.16 – 7.02 (m, 6H), 7.01 – 6.72 (m, 15H), 6.69 (dd, *J* = 12.3, 6.6 Hz, 3H), 6.60 (dd, *J* = 7.8, 3.1 Hz, 2H), 6.56 (d, *J* = 6.9 Hz,

1H), 6.51 (d, *J* = 7.9 Hz, 1H), 6.39 (d, *J* = 7.9 Hz, 1H), 6.22 (d, *J* = 8.9 Hz, 2H), 6.16 (d, *J* = 7.2 Hz, 1H), 6.05 (s, 1H), 5.88 (s, 1H), 5.67 (s, 1H), 5.61 (s, 1H), 5.58 (s, 1H), 5.47 (s, 1H), 5.43 (s, 1H), 3.84 – 3.62 (m, 16H), 3.62 – 3.54 (m, 6H), 3.52 – 3.49 (m, 4H), 3.49 – 3.42 (m, 8H), 3.21 – 3.04 (m, 8H), 3.02 (s, 2H), 2.99 – 2.89 (m, 5H), 2.89 – 2.81 (m, 2H), 2.79 – 2.68 (m, 2H), 2.54 (s, 3H), 2.20 – 2.15 (m, 2H), 2.10-2.04 (m, 2H), 1.51 – 1.43 (m, 6H), 1.34 – 1.22 (m, 15H), 1.19-1.11 (m, 14H), 1.03 (dd, *J* = 14.0, 6.7 Hz, 8H), 0.84 (q, *J* = 5.4, 4.0 Hz, 4H), 0.77 (d, *J* = 9.6 Hz, 7H), 0.45 (s, 3H), 0.37 (s, 3H), -0.10 (s, 3H). **MS** calcd for $C_{227}H_{214}N_{36}Na_2O_{44}S_7$ $[M+2Na]^{2+}$ 2208.6722, found (HR-ESI) 2209.1001.

O_2N-$\underline{X}Q^DQ^SPQ^D\underline{X}Q^DQ^SPQ^D\underline{X}Q^DQ^BPQ^D\underline{X}Q^DQ^B$-OH (**16**) Compound **16** was synthesized using the SPS procedures reported in 6.3 on SASRIN resin loaded via HBTU-coupling described in 6.3 (scale: 30.79 µmol). After full cleavage, the crude product was purified via precipitation in DCM/MeOH, and the product was obtained as a yellow solid (71.0 mg, 51%). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 11.14 (s, 1H), 11.08 (s, 1H), 10.83 (s, 1H), 10.54 (s, 1H), 10.53 (s, 1H), 10.44 (s, 1H), 10.40 (s, 1H), 10.16 (s, 1H), 10.10 (s, 1H), 9.96 (s, 1H), 9.94 (s, 1H), 9.91 (s, 1H), 9.78 (s, 1H), 9.48 (s, 1H), 8.08 – 8.04 (m, 4H), 7.93 (d, *J* = 7.2 Hz, 2H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 13.4 Hz, 4H), 7.55 (t, *J* = 6.9 Hz, 4H), 7.44 – 7.41 (m, 4H), 7.40 – 7.36 (m, 4H), 7.35 – 7.30 (m, 11H), 7.14 – 7.12 (m, 2H), 7.08 – 7.04 (m, 4H), 7.04 – 6.98 (m, 5H), 6.97 – 6.94 (m, 2H), 6.92 – 6.88 (m, 4H), 6.87 – 6.85 (m, 2H), 6.81 – 6.74 (m, 2H), 6.70 – 6.67 (m, 3H), 6.66 – 6.61 (m, 4H), 6.57 – 6.54 (m, 2H), 6.46 (d, *J* = 7.0 Hz, 1H), 6.43 (s, 1H), 6.34 (s, 1H), 6.12 (s, 1H), 5.97 (s, 1H), 5.65 (s, 1H), 5.64 (s, 1H), 5.59 (s, 1H), 4.15 – 4.10 (m, 2H), 3.94 – 3.91 (m, 2H), 3.90 – 3.87 (m, 4H), 3.85 – 3.78 (m, 4H), 3.77 – 3.72 (m, 5H), 3.71 – 3.65 (m, 5H), 3.61 – 3.58 (m, 5H), 3.57 (s, 5H), 3.53 (s, 10H), 3.50 (s, 5H) 3.50 – 3.48 (m, 3H), 3.47 (s, 2H), 3.46 (s, 2H), 3.44 – 3.40 (m, 4H), 3.38 (s, 3H), 3.36 (s, 3H), 3.25 – 3.20 (m, 4H), 3.16 – 3.11 (m, 5H), 2.96 (s, 1H), 2.93 (s, 2H), 2.89 (s, 1H), 2.87 – 2.84 (m, 2H), 2.03-0.98 (m, signal overlapping with water). 0.91 – 0.80 (m, 18H). **MS** calcd for $C_{232}H_{232}N_{36}O_{41}S_7Se_2$ $[M+2H]^{2+}$ 2280.6770, found (HR-ESI) 2283.5340, calcd for $C_{232}H_{231}N_{36}NaO_{41}S_7Se_2$ $[M+H+Na]^{2+}$ 2291.6680, found (HR-ESI) 2294.1091.

O_2N-$\underline{X}Q^DQ^SPQ^D\underline{X}Q^DQ^SPQ^D\underline{X}Q^DQ^BPQ^D\underline{X}Q^DQ^B$-OMe (**17**) Compound **16** (67.0 mg, 15 µmol, 1 eq.) was dissolved in a mixture of dry chloroform/MeOH 3:2 (5 mL) under N_2. $TMSCHN_2$ (2 M in hex, 51 µL, 70 µmol, 2 eq.) was added dropwise, and the solution was stirred at r.t. for 2 h. A few drops of acetic acid were added, and the solution was stirred for 5 min at r.t. Then the solution was diluted with DCM, washed with $NaHCO_3$, dried $MgSO_4$, filtered and concentrated. The pure product was a yellow solid (68.0 mg, quant.). **^{1}H NMR** (500 MHz, $CDCl_3$, 25 °C) δ [ppm] 11.32 (s, 1H), 11.08 (s, 1H), 10.99 (s, 1H), 10.83 (s, 1H), 10.52 (s, 2H), 10.45 (s, 1H), 10.16 (s, 1H), 10.11 (s, 1H), 9.96 (s, 1H), 9.94 (s, 1H), 9.89 (s, 1H), 9.77 (s, 1H), 9.46 (s, 1H), 8.07 (dt, *J* = 10.7, 3.9 Hz, 2H), 7.95 – 7.91 (m, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.81 – 7.75 (m, 2H), 7.70 – 7.66 (m, 3H), 7.66 – 7.62 (m, 2H), 7.60 (dt, *J* = 7.9, 1.2 Hz, 3H), 7.57 – 7.51 (m, 3H), 7.51 – 7.42 (m, 4H), 7.42 (d, *J* = 1.1 Hz, 1H), 7.39 (ddd, *J* = 8.0, 5.6, 1.4 Hz, 7H), 7.35 – 7.27 (m, 3H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.14 – 7.09 (m, 1H), 7.09 – 7.03 (m, 5H), 7.03 – 6.97 (m, 5H), 6.97 – 6.91 (m, 3H), 6.90 (q, *J* = 4.7, 3.9 Hz, 4H), 6.86 (q, *J* = 5.4, 4.3 Hz, 4H), 6.79 (d, *J* = 6.1 Hz, 1H), 6.75 (t, *J* = 7.7 Hz, 1H), 6.71 – 6.62 (m, 6H), 6.57 – 6.52 (m, 2H), 6.47 – 6.45 (m, 1H), 6.25 (s, 1H), 6.12 (s, 1H), 5.96 (s, 1H), 5.64 (s, 1H), 5.63 (s, 1H), 5.58 (d, *J* = 3.7 Hz, 1H), 3.90 – 3.86 (m, 3H), 3.86 – 3.80 (m, 4H), 3.80 – 3.68 (m, 8H), 3.67 (s, 4H), 3.61 – 3.56 (m, 9H), 3.55 – 3.51 (m, 14H), 3.50 (s, 8H), 3.42 – 3.40 (m, 3H), 3.38 (s, 4H), 3.36 (s, 4H), 3.16 – 3.08 (m, 5H), 3.03 (s, 3H), 2.96 – 2.82 (m, 2H), 2.80 (s, 2H), 2.35 (t, *J* = 7.5 Hz, 4H), 2.30 (t, *J* = 7.6 Hz, 7H), 2.26 (d, *J* = 8.3 Hz, 4H), 2.17 (s,

3H), 2.15 (s, 3H), 2.09 – 0.99 (m, signal overlapping with water). **MS** calcd for $C_{233}H_{232}N_{36}Na_2O_{41}S_7Se_2$ $[M+2Na]^{2+}$ 2309.6668, found (HR-ESI) 2310.0220.

O_2N-XQ^{D}Q^{S}PQ^{D}XQ^{D}Q^{S}PQ^{D}XQ^{D}Q^{B}PQ^{D}XQ^{D}Q^B-OMe (**7**) Compound **17** (15.0 mg, 3.28 µmol) was treated with a 50% solution of TFA in DCM (4 mL) at r.t. for 2 h. Then the solvent was removed under vacuum, obtaining the product as a yellow solid (14.3 mg, quant.). **^{1}H NMR** (500 MHz, pyridine-d_5, 25 °C) δ [ppm] 11.79 (s, 1H), 11.52 (s, 1H), 11.43 (s, 1H), 11.41 (s, 1H), 11.01 (s, 1H), 10.95 (s, 1H), 10.92 (s, 1H), 10.76 (s, 1H), 10.63 (s, 1H), 10.59 (s, 2H), 10.46 (s, 1H), 10.43 (s, 1H), 10.18 (s, 1H), 8.53 – 8.50 (m, 1H), 8.40 – 8.38 (m, 1H), 8.36 – 8.34 (m, 1H), 8.31 – 8.30 (m, 1H), 8.26 – 8.23 (m, 2H), 8.21 – 8.15 (m, 4H), 8.02 – 7.97 (m, 3H), 7.96 – 7.92 (m, 3H), 7.84 – 7.77 (m, 3H), 7.75 (s, 1H), 7.71 – 7.66 (m, 2H), 7.67 – 7.64 (m, 3H), 7.58 (s, 1H), 7.55 – 7.53 (m, 4H), 7.46 – 7.40 (m, 4H), 7.37 – 7.31 (m, 4H), 7.29 – 7.25 (m, 4H), 7.24 – 7.16 (m, 5H), 7.09 – 6.97 (m, 4H), 6.96 (s, 5H), 6.88 – 6.86 (m, 3H), 6.84 – 6.73 (m, 5H), 6.64 (s, 4H), 6.54 (s, 1H), 6.22 (s, 1H), 6.21 (s, 1H), 6.18 (s, 1H), 3.86 – 3.79 (m, 8H), 3.86 – 3.79 (m, 4H), 3.78 (s, 4H), 3.77 – 3.73 (m, 7H), 3.72 – 3.86 (m, 5H), 3.65 – 3.60 (m, 3H), 3.58 – 3.55 (m, 1H), 3.50 – 3.47 (m, 1H), 3.45 (s, 4H), 3.44 (s, 3H), 3.43 (s, 3H), 3.38 (s, 3H), 3.32 (s, 3H), 3.27 (s, 3H), 3.24 (s, 3H), 3.22 (s, 1H), 2.62 (s, 3H), 2.52 (s, 3H), 2.45 (t, J = 7.4 Hz, 10H), 2.37 – 2.33 (m, 5H), 2.06 – 0.63 (m, signal overlapping with water), 0.52-0.36 (m, 10H). **MS** calcd for $C_{217}H_{201}N_{36}NaO_{41}S_7Se_2$ $[M+H+Na]^{2+}$ 2186.5506, found (HR-ESI) 2186.2298.

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8 NMR spectra of new compounds

8.1 ^{1}H NMR and ^{13}C NMR spectra of new small compounds

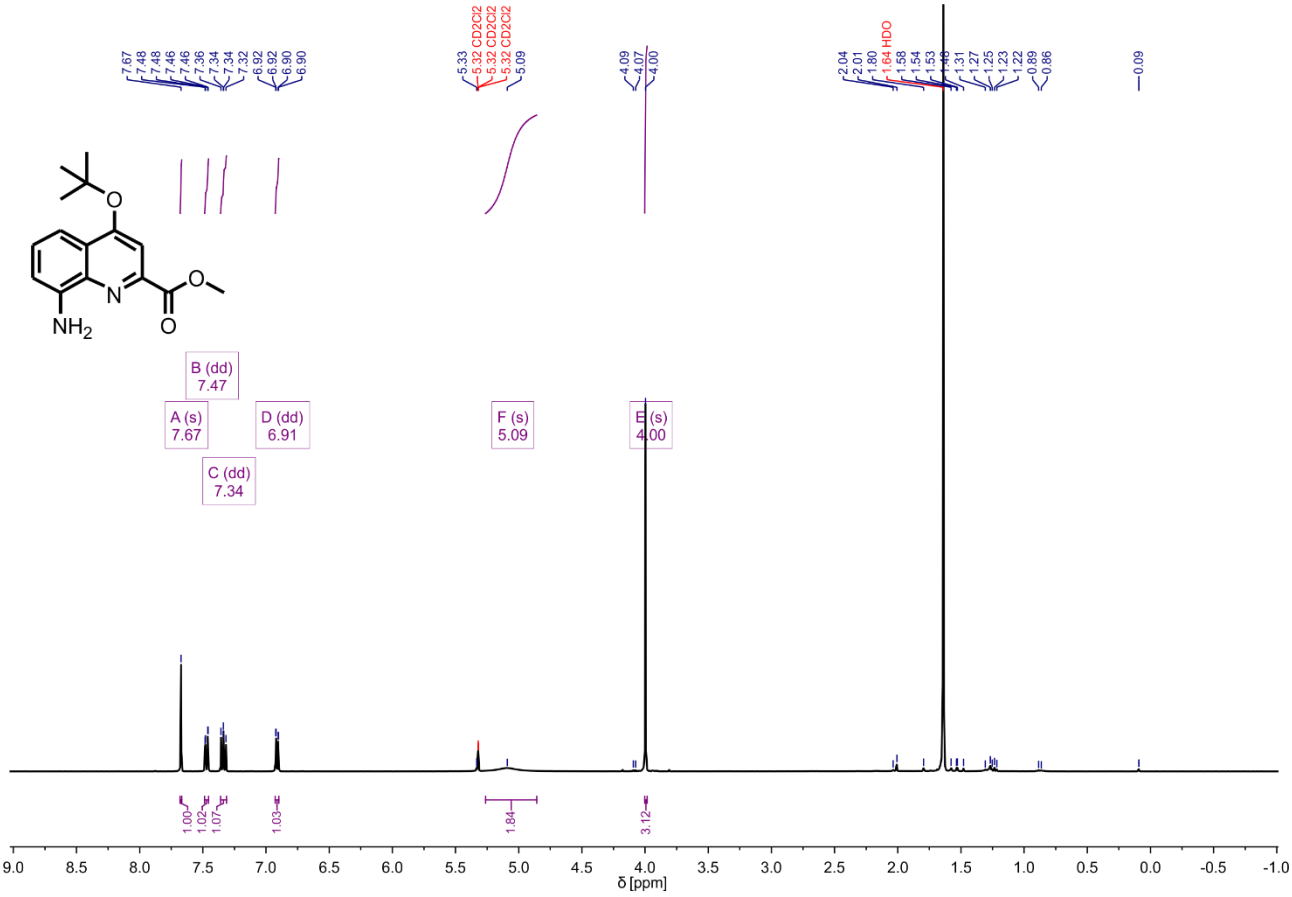

Figure S34. ^{1}H NMR spectrum (400 MHz, CD_2Cl_2) of **C**.

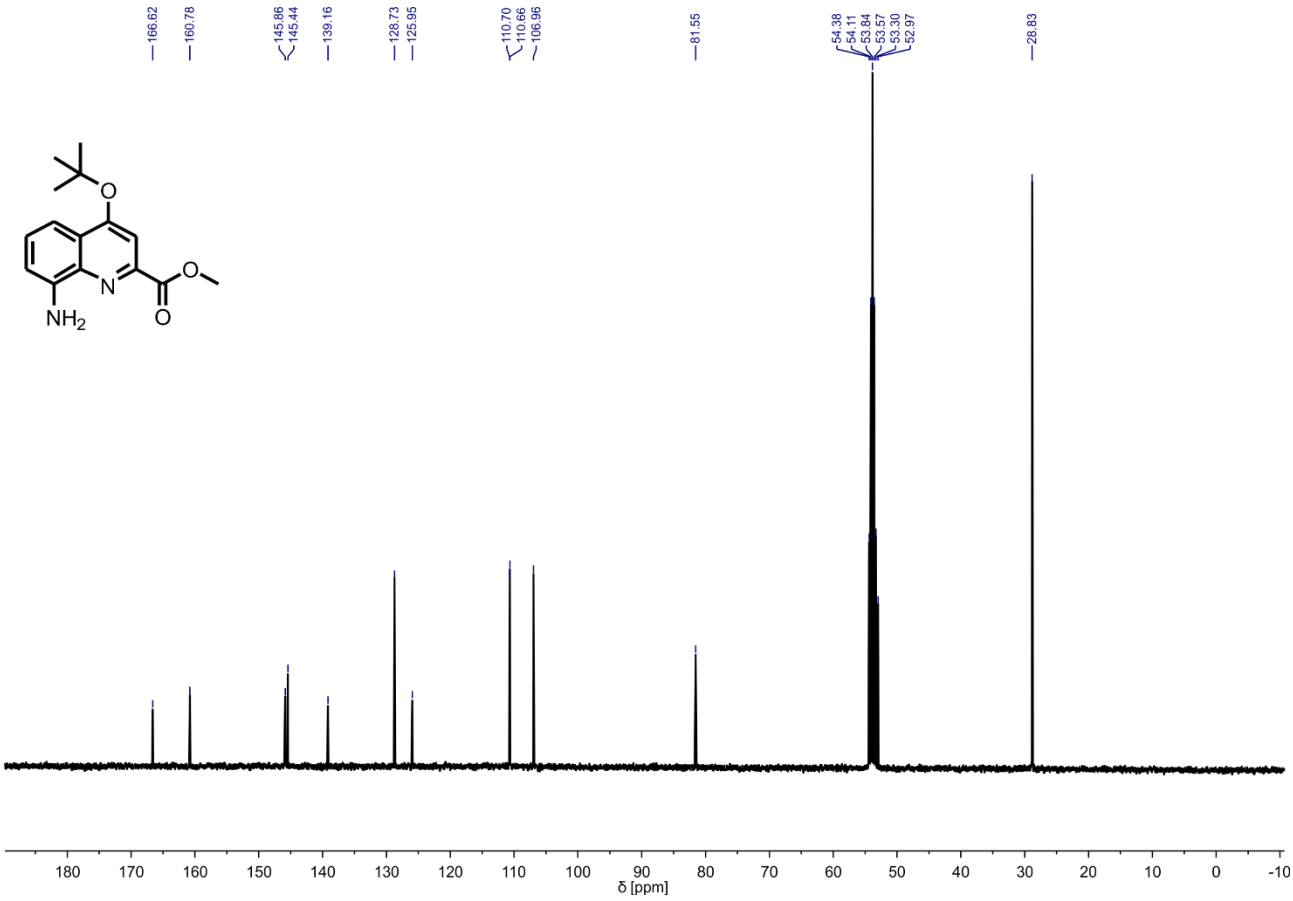

Figure S35. ^{13}C NMR spectrum (101 MHz, CD_2Cl_2) of **C**.

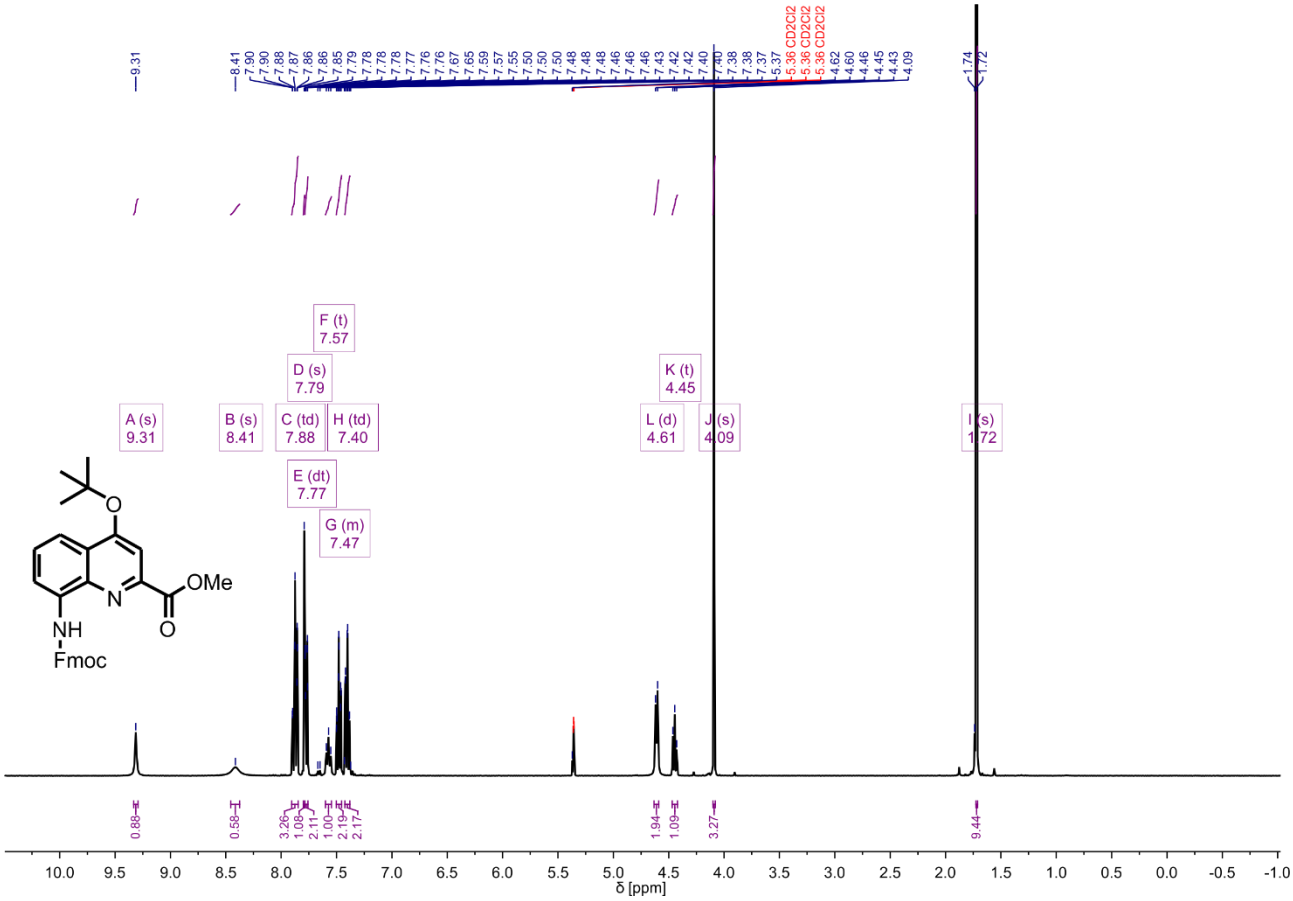

Figure S36. ^{1}H NMR spectrum (400 MHz, CD_2Cl_2) of **D**.

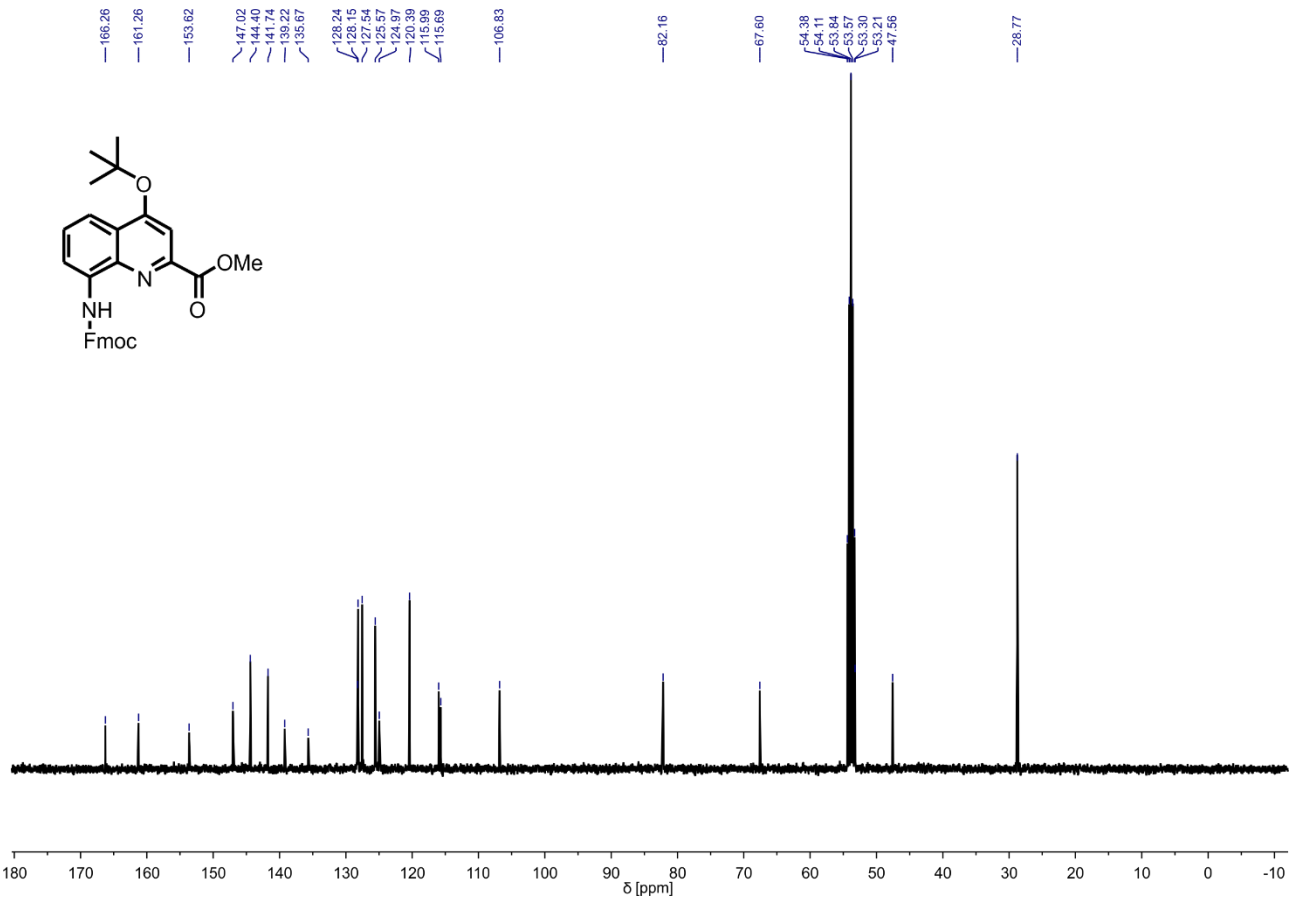

Figure S37. ^{13}C NMR spectrum (101 MHz, CD_2Cl_2) of **D**.

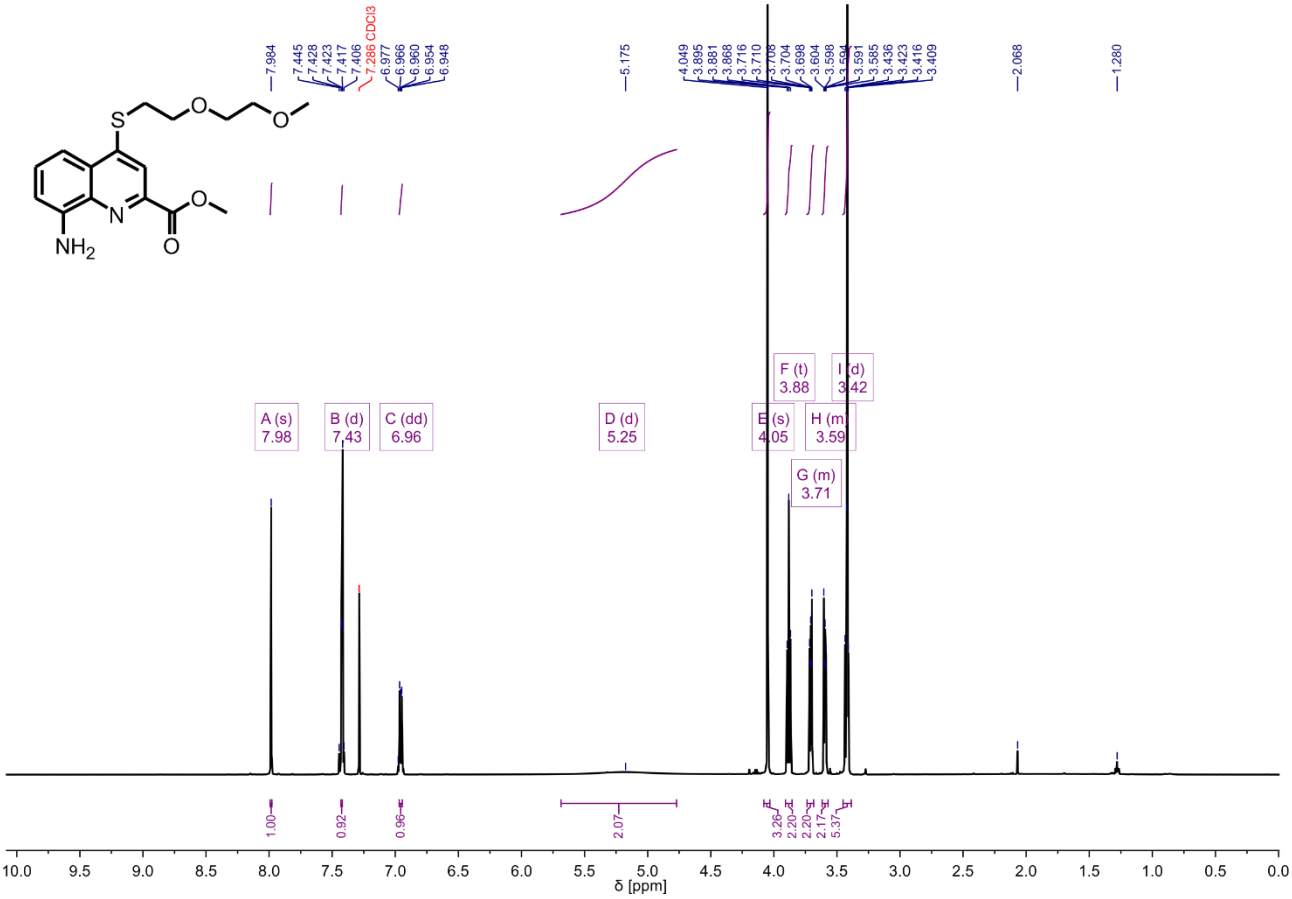

Figure S38. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **J**.

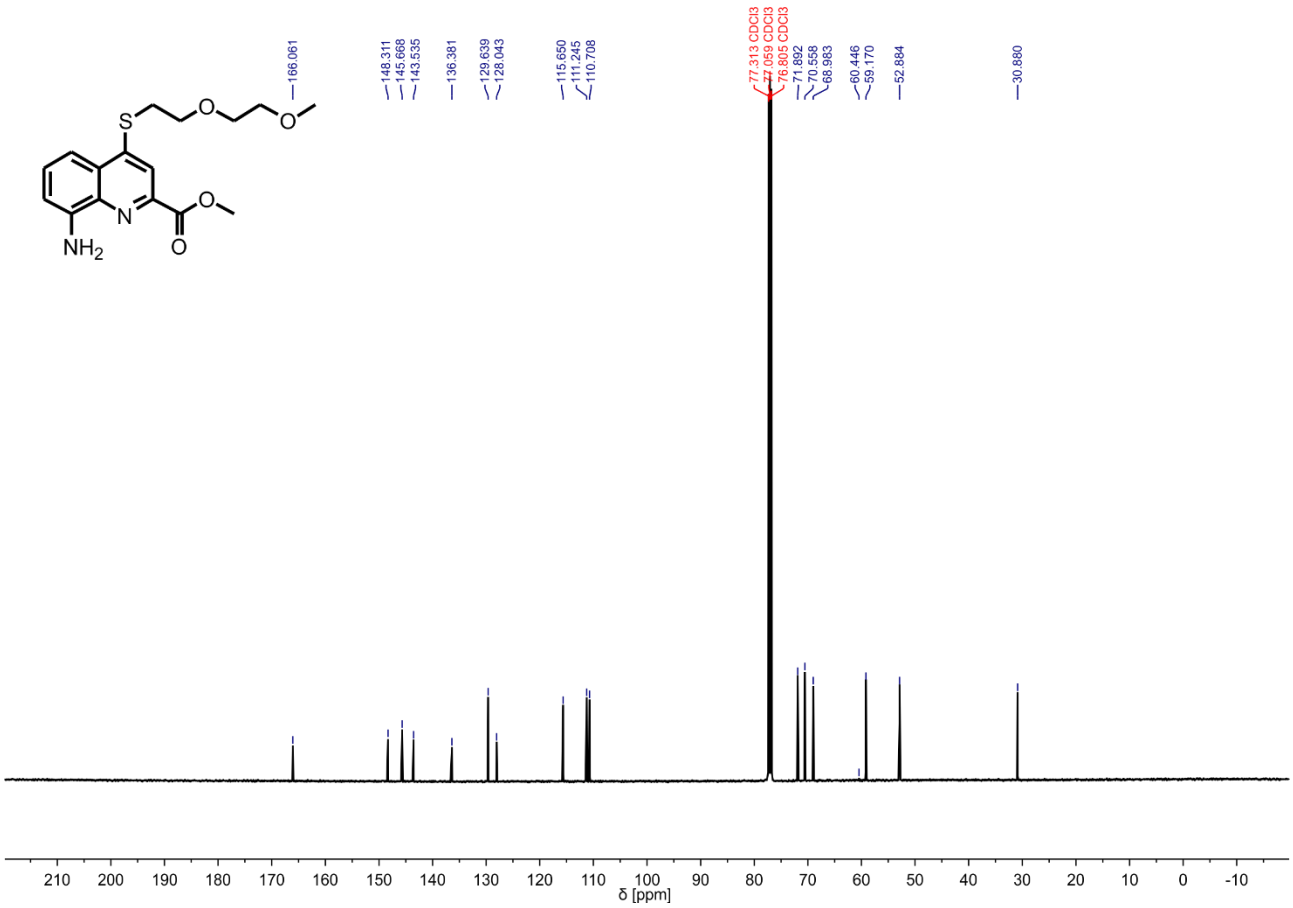

Figure S39. ^{13}C NMR spectrum (126 MHz, $CDCl_3$) of **J**.

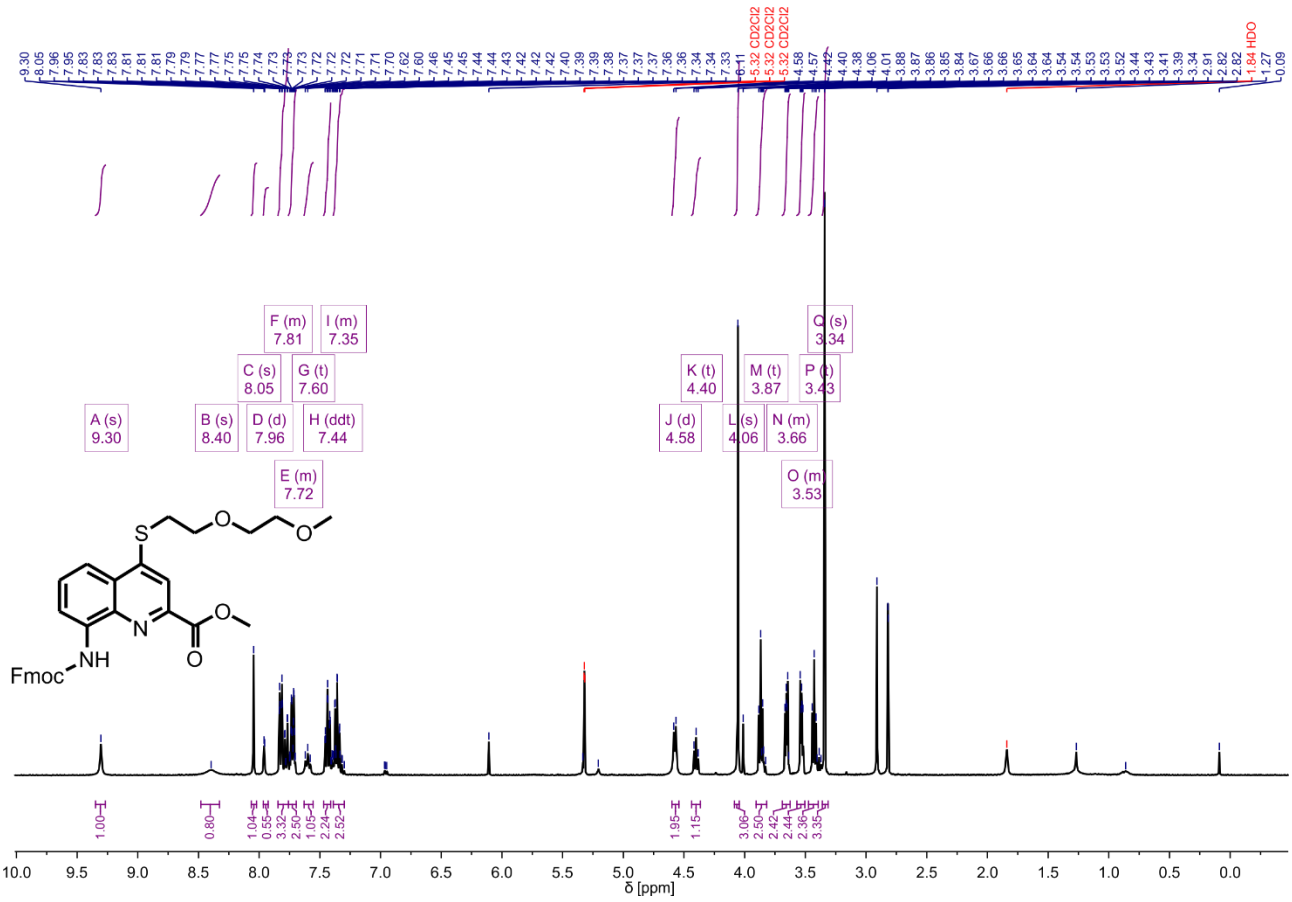

Figure S40. ^{1}H NMR spectrum (400 MHz, CD_2Cl_2) of **K**.

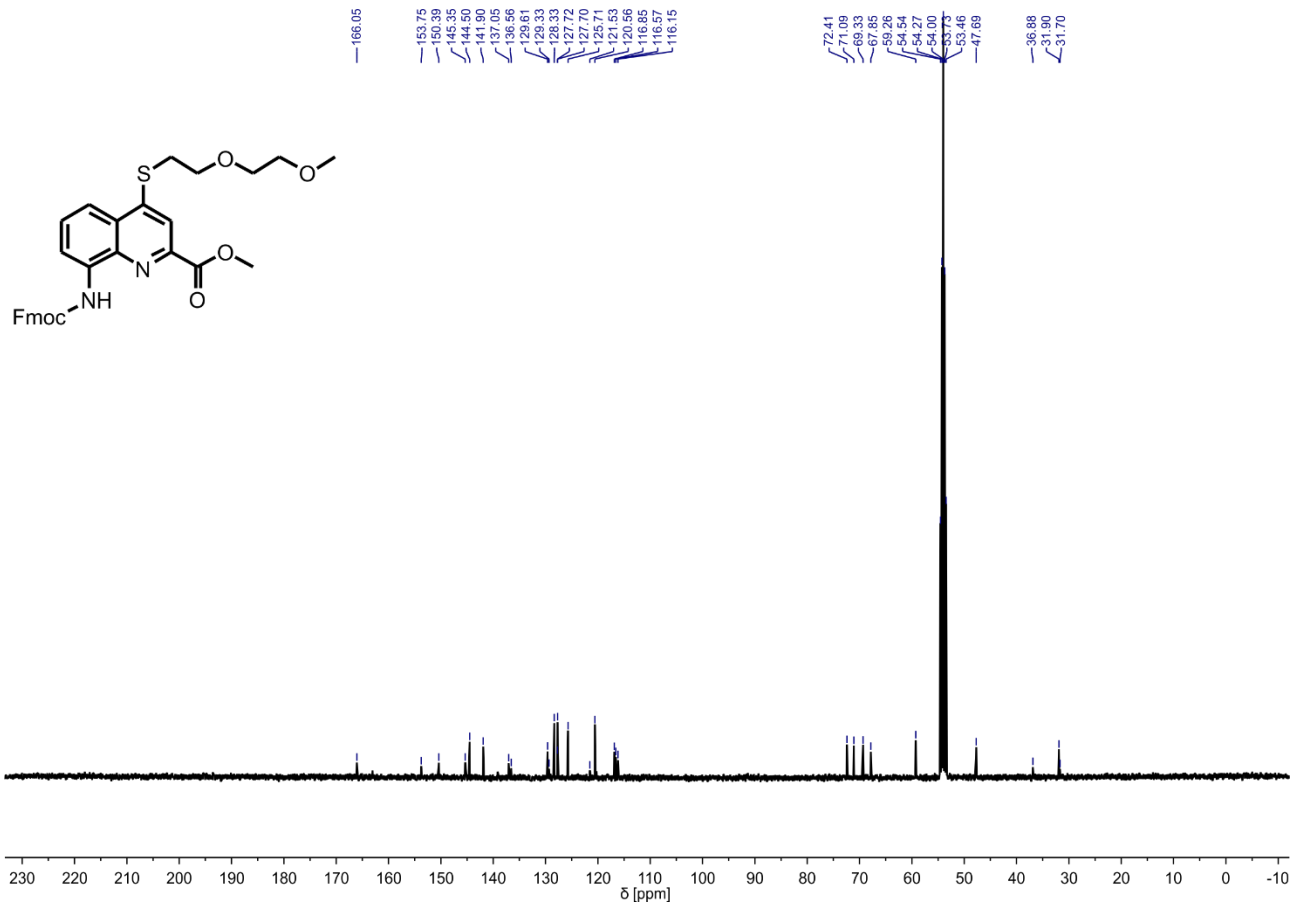

Figure S41. ^{13}C NMR spectrum (101 MHz, CD_2Cl_2) of **K**.

8.2 ^{1}H NMR of new oligomers

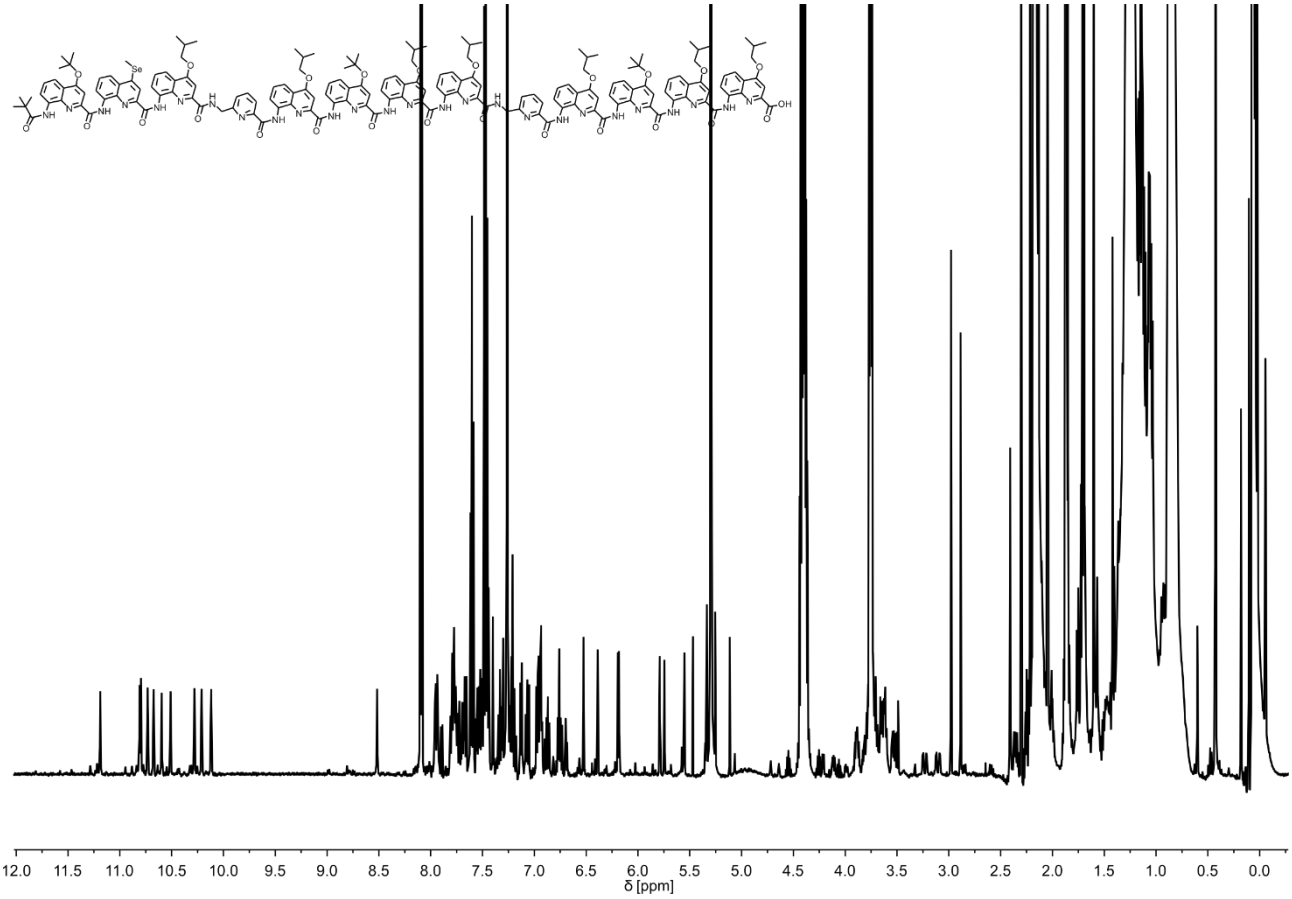

Figure S42. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **8**.

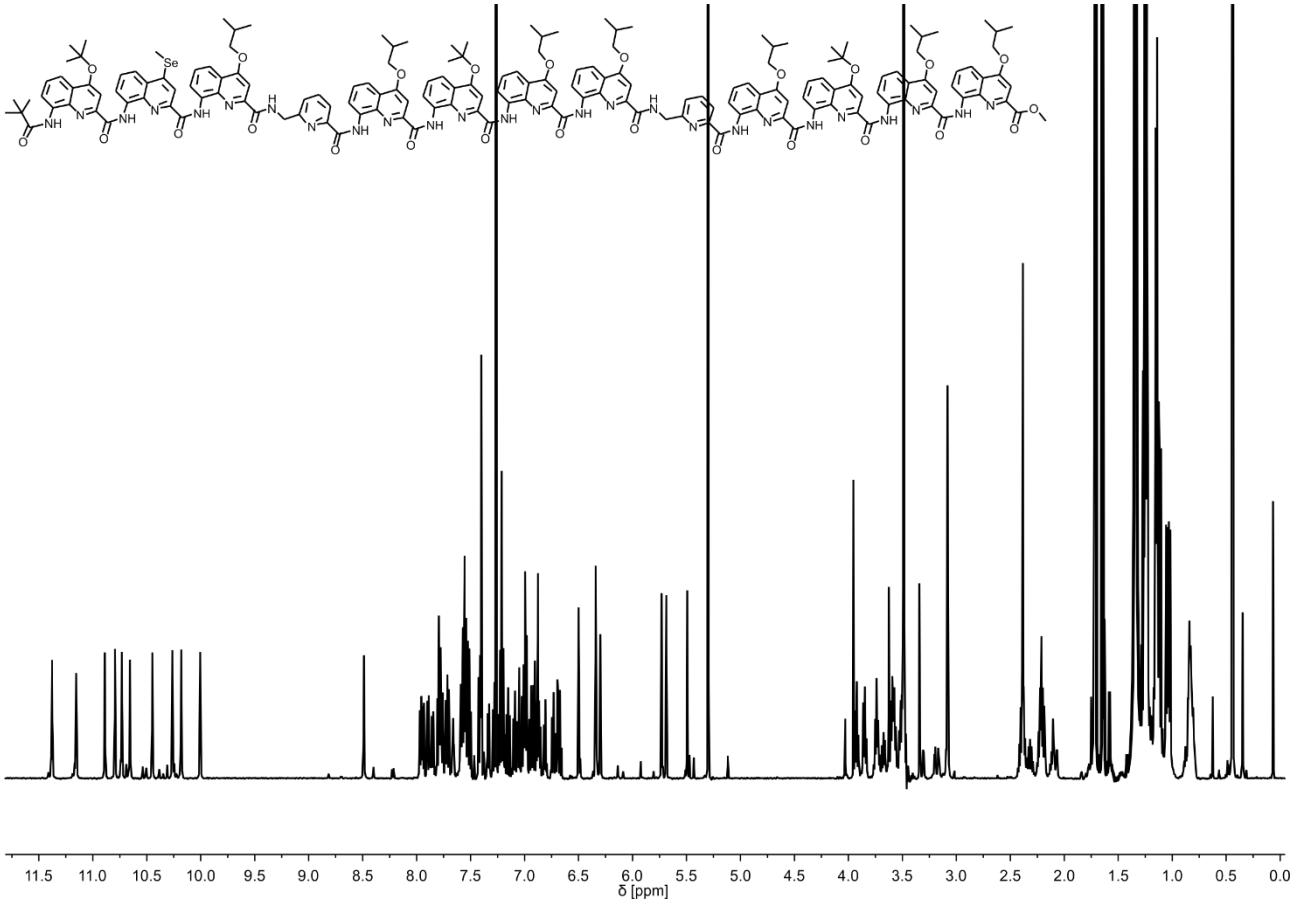

Figure S43. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **9**.

4

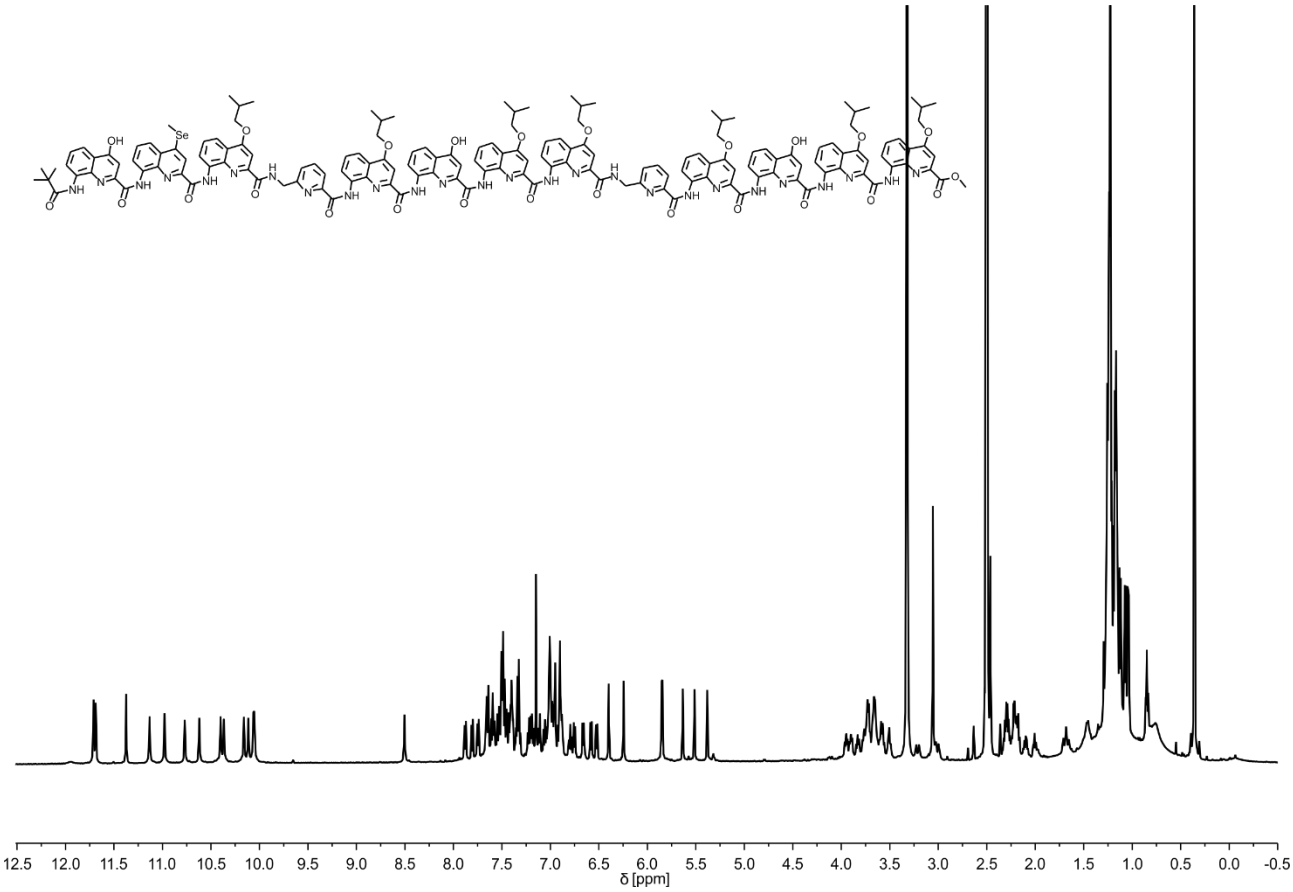

Figure S44. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of **3**.

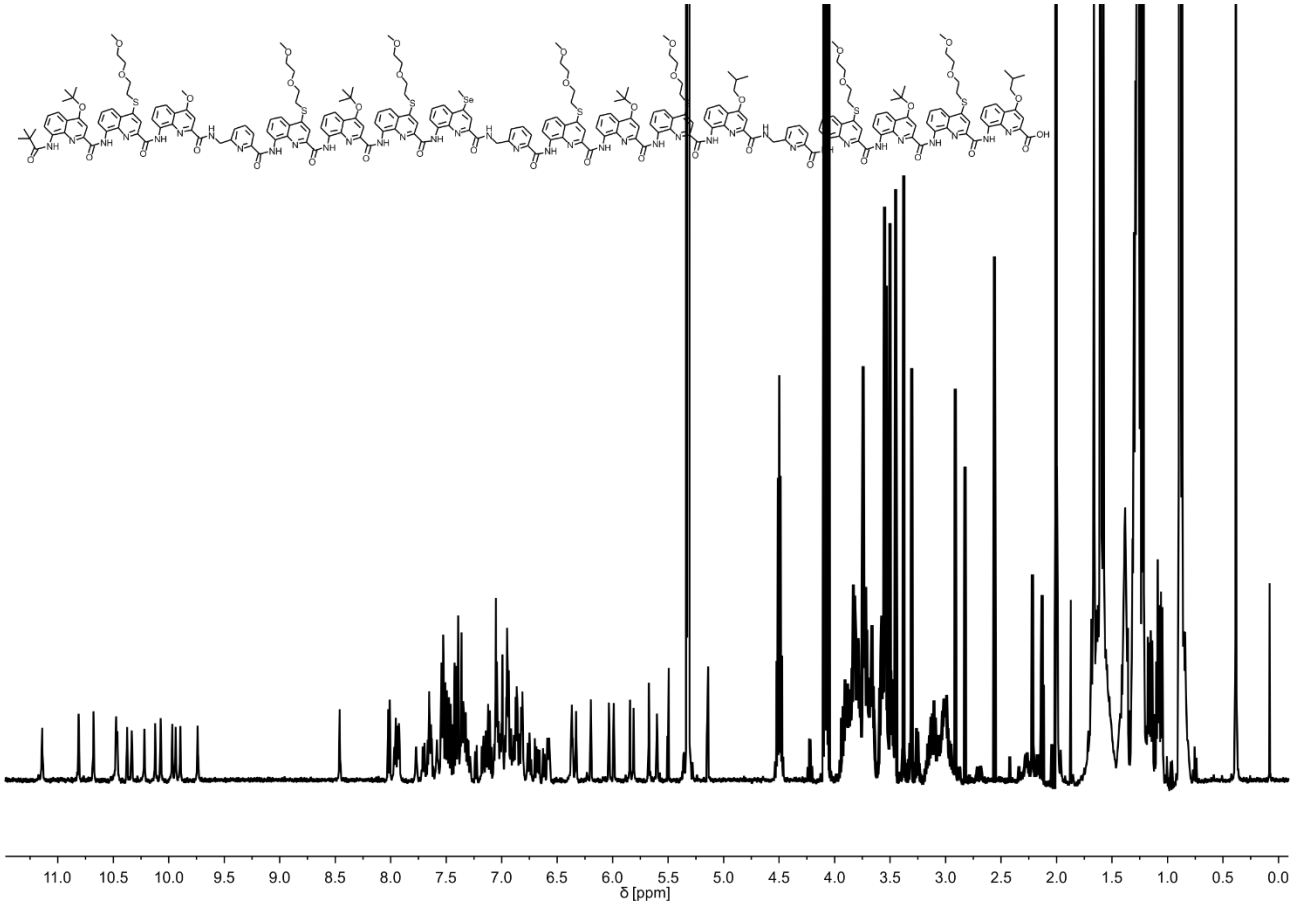

Figure S45. ^{1}H NMR spectrum (500 MHz, CD_2Cl_2) of **10**.

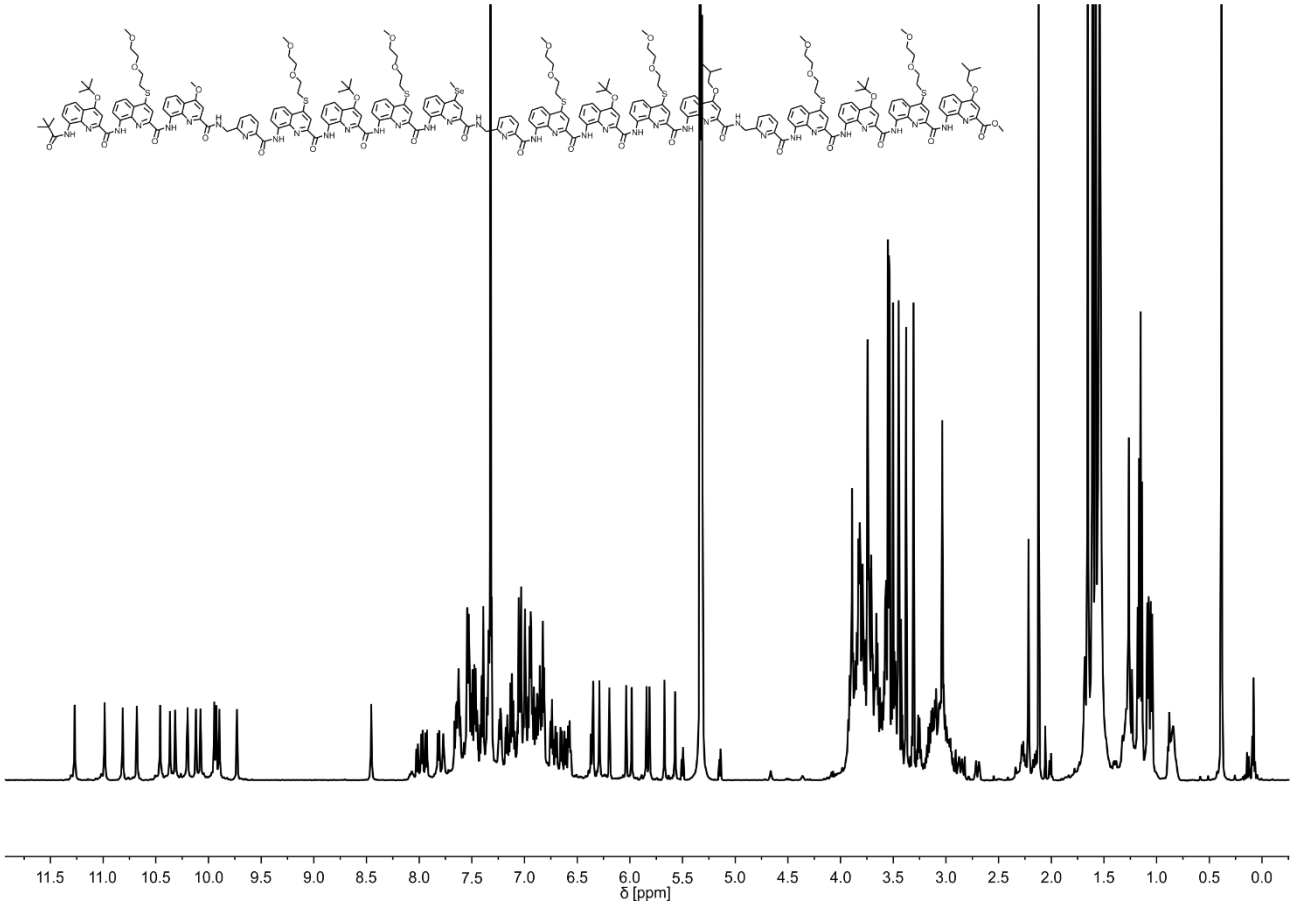

Figure S46. ^{1}H NMR spectrum (500 MHz, CD_2Cl_2) of **11**.

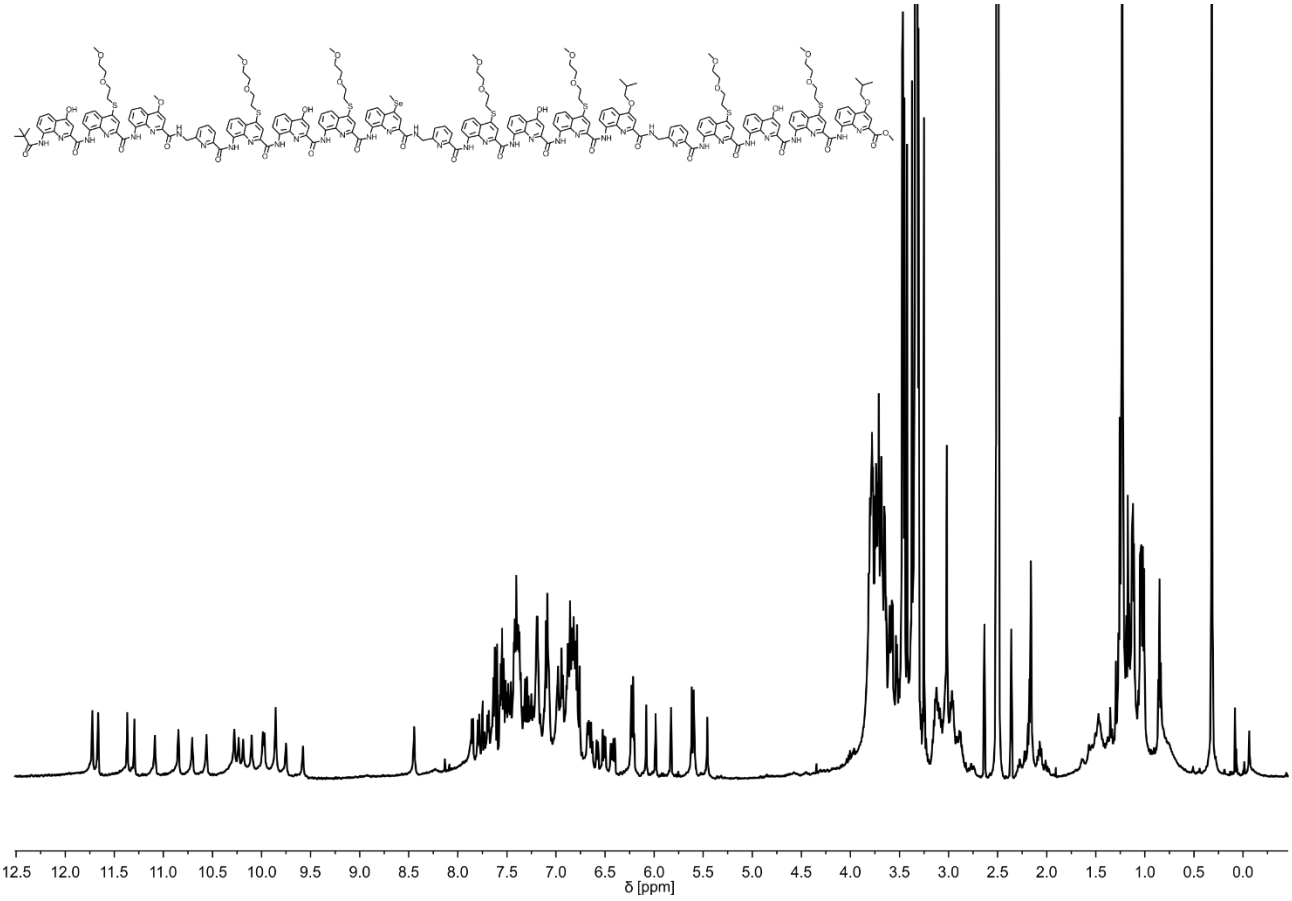

Figure S47. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of **4**.

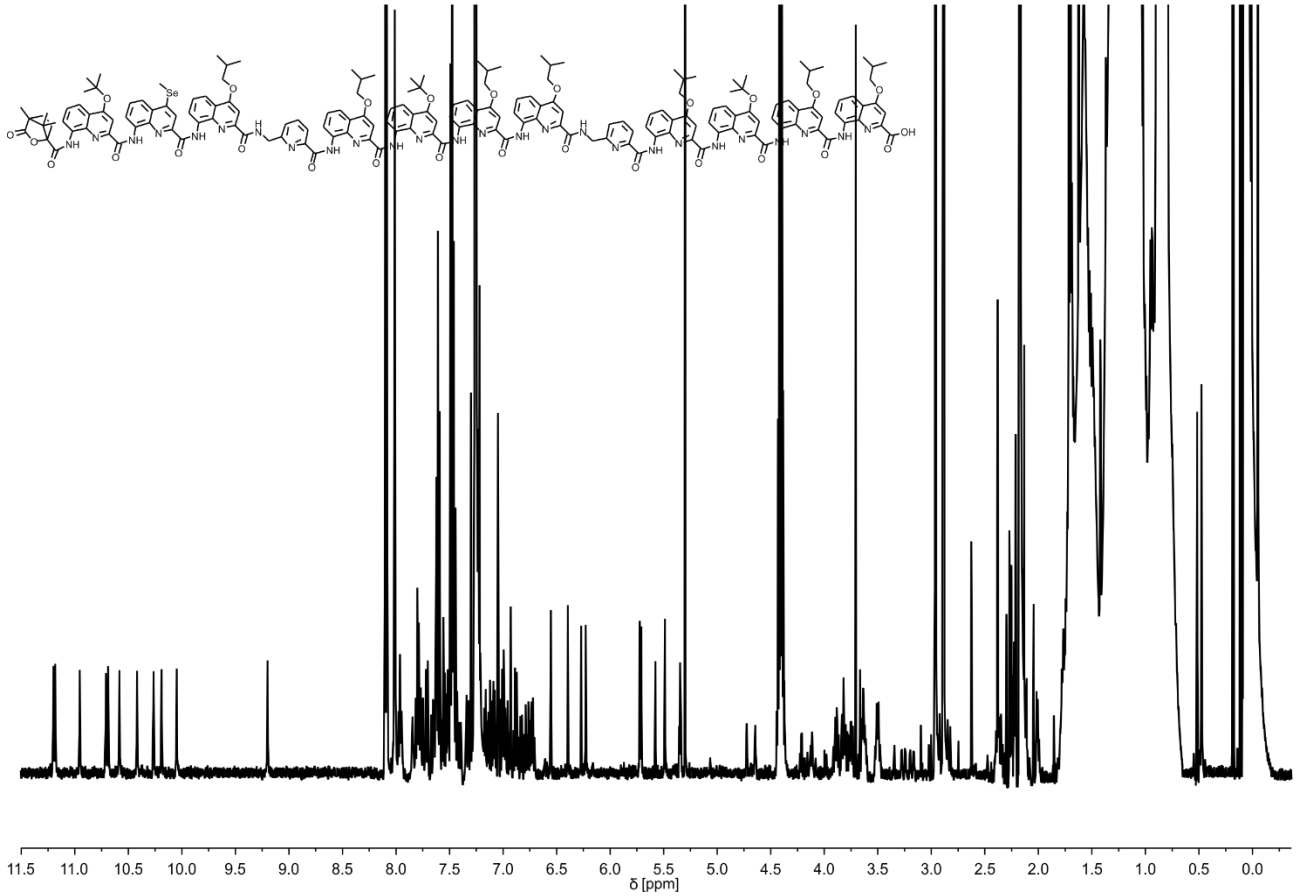

Figure S48. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **12**.

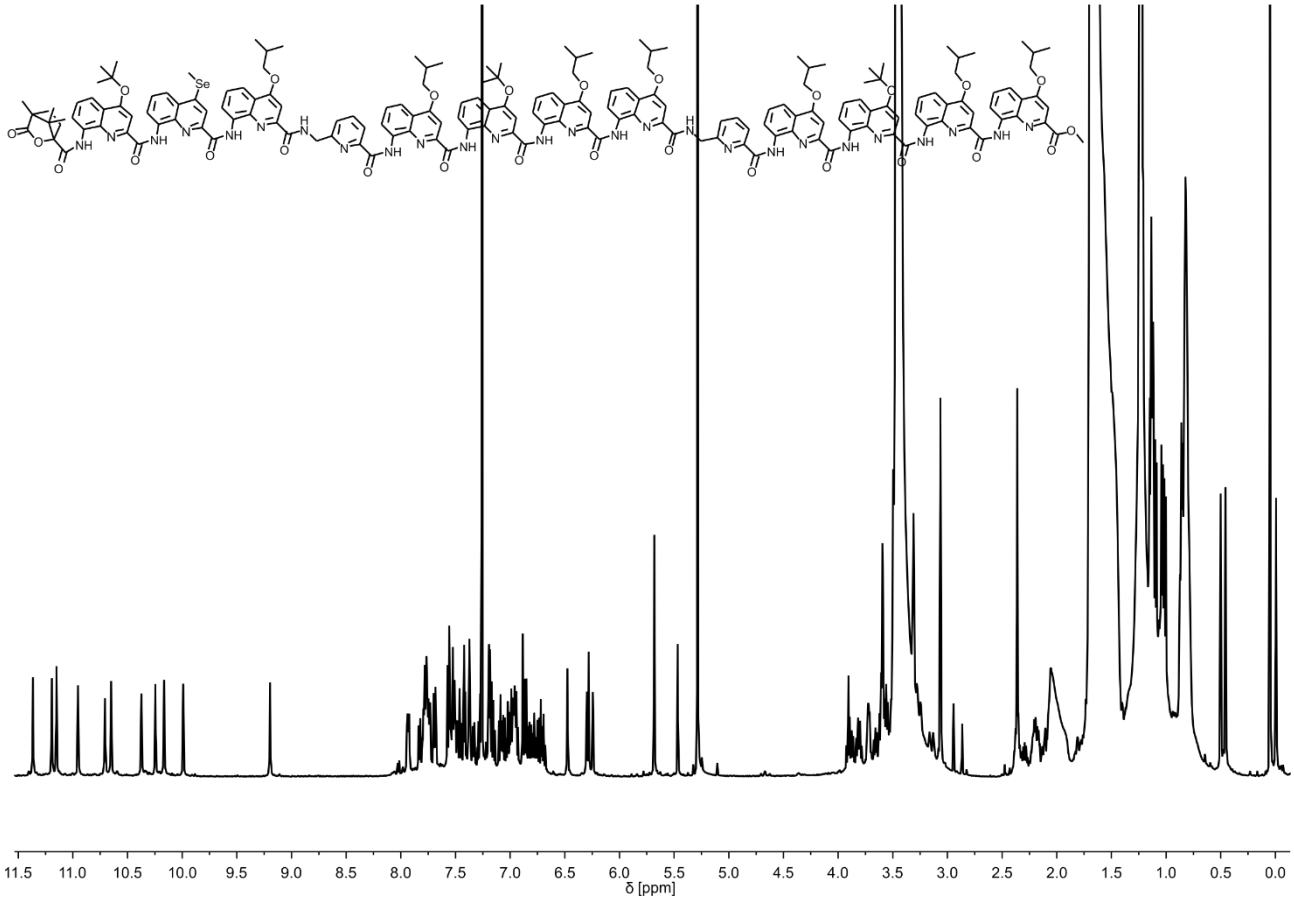

Figure S49. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **13**.

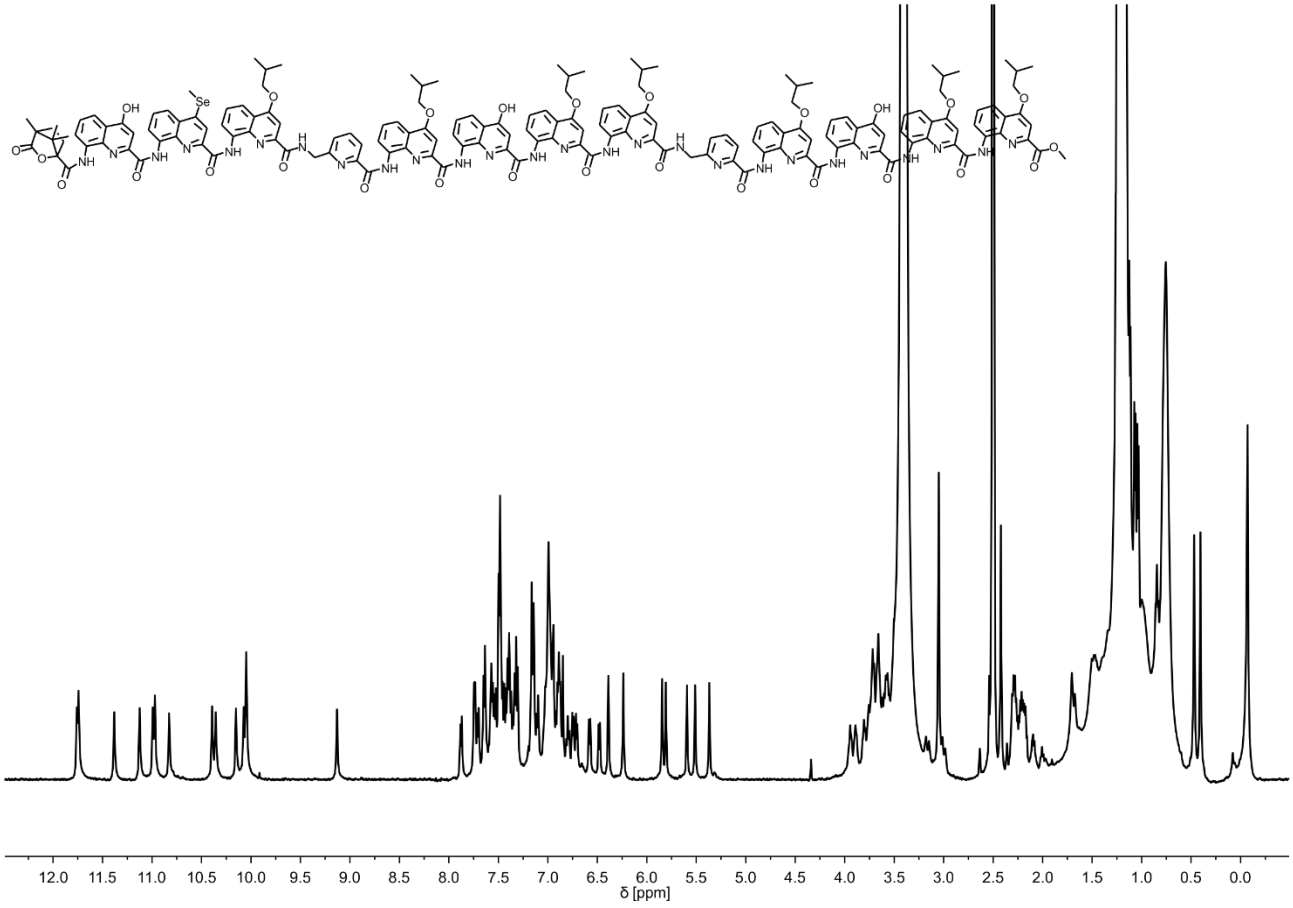

Figure S50. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of **5**.

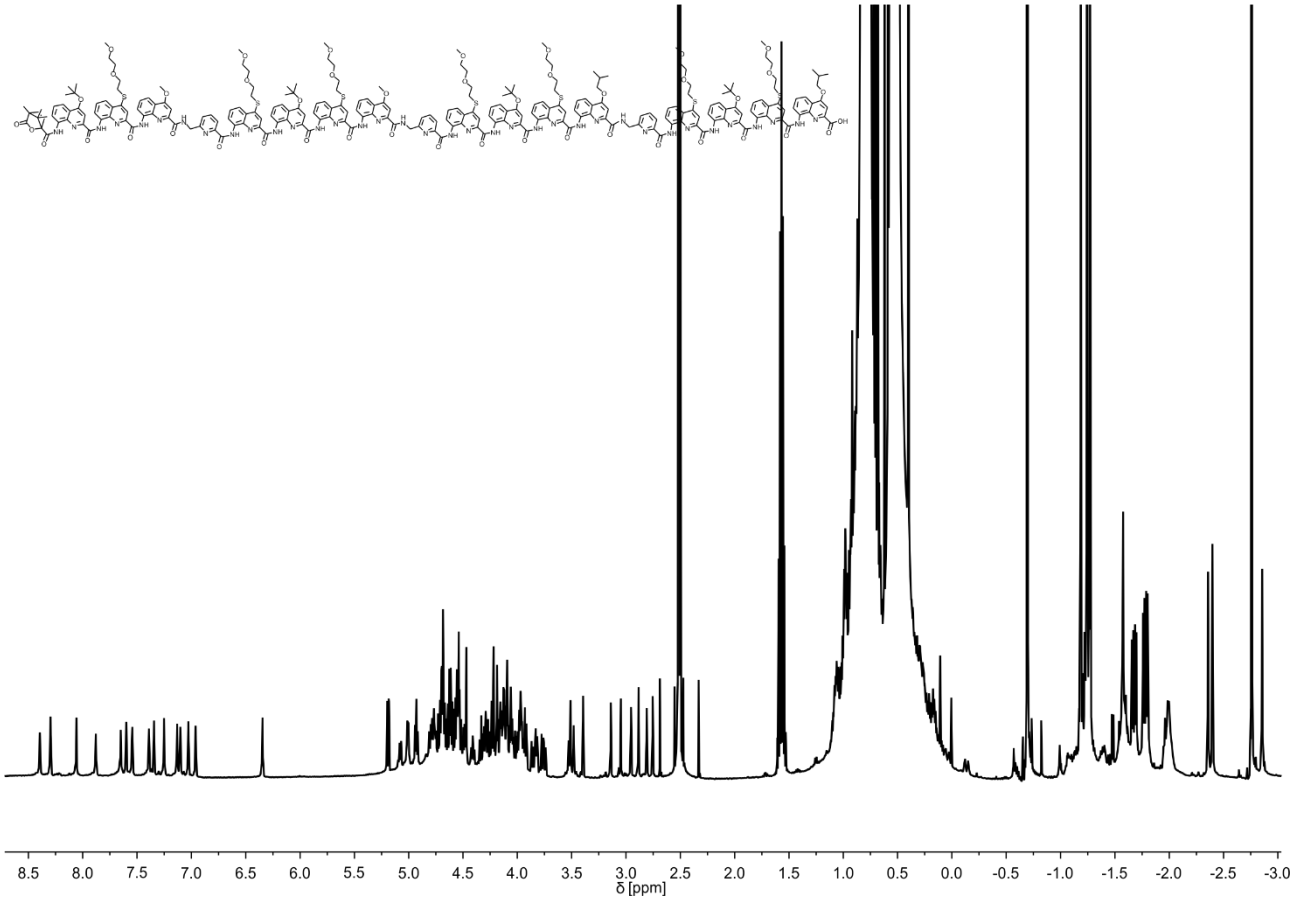

Figure S51. ^{1}H NMR spectrum (500 MHz, CD_2Cl_2) of **14**.

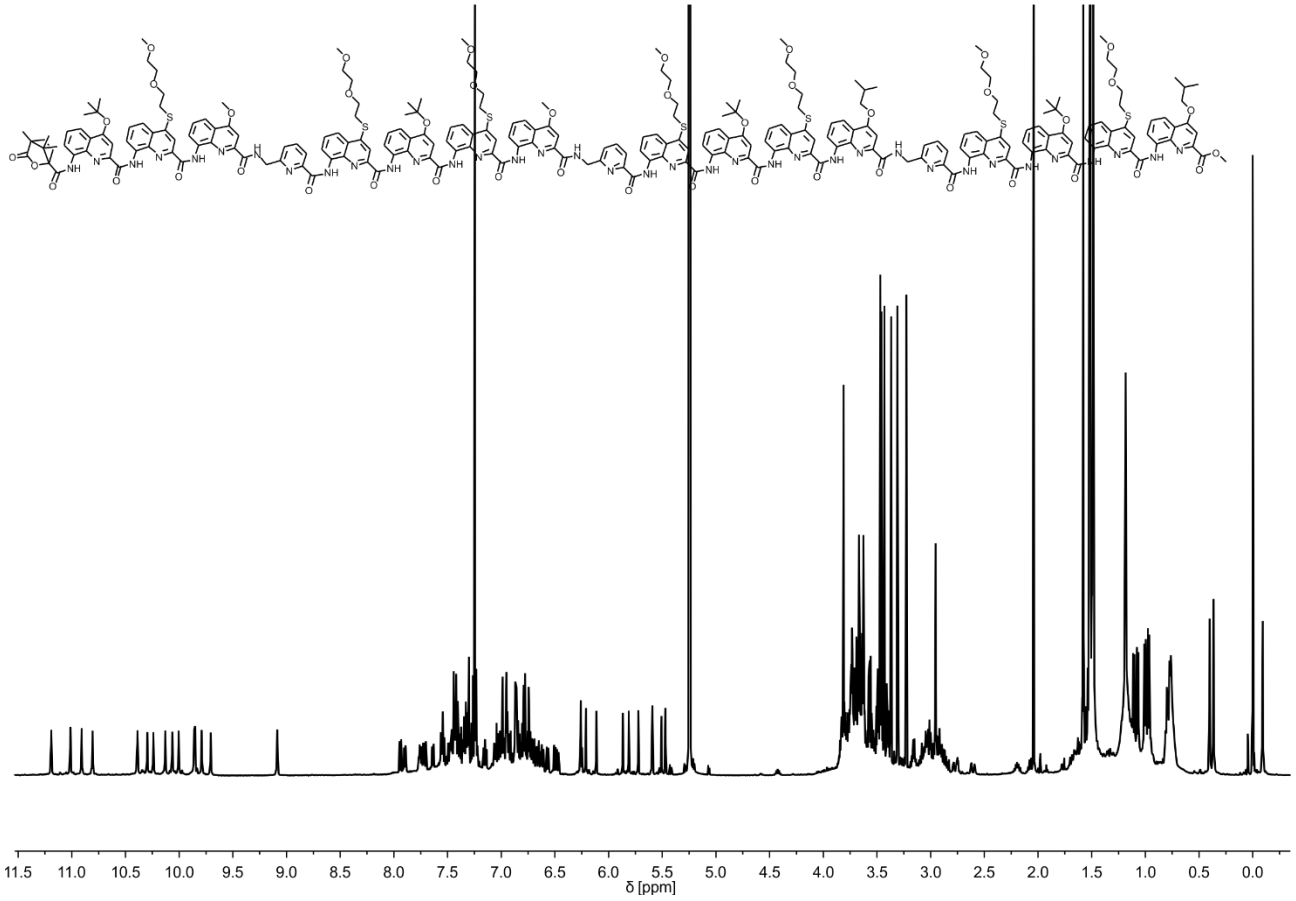

Figure S52. ^{1}H NMR spectrum (500 MHz, CD_2Cl_2) of **15**.

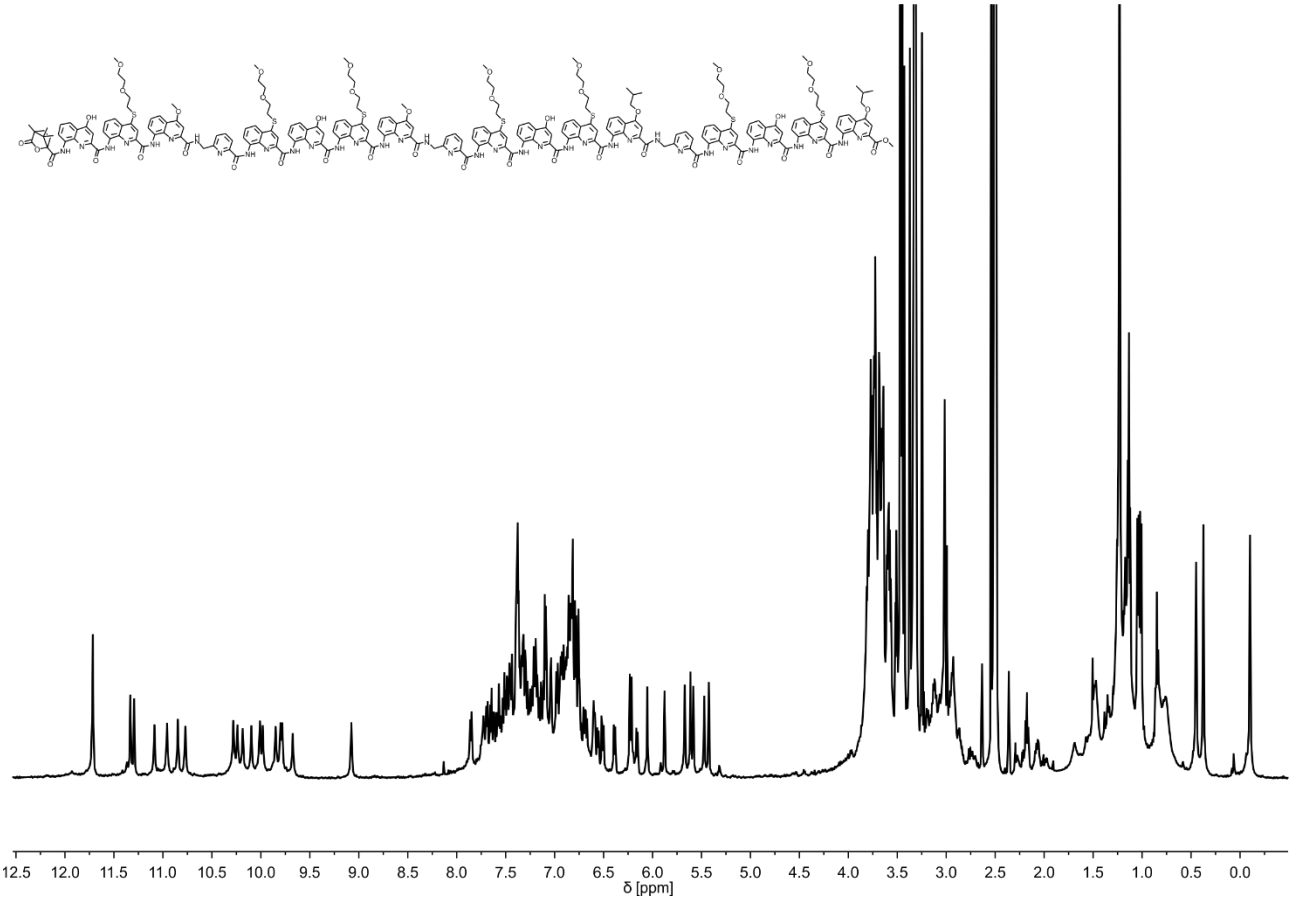

Figure S53. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of **6**.

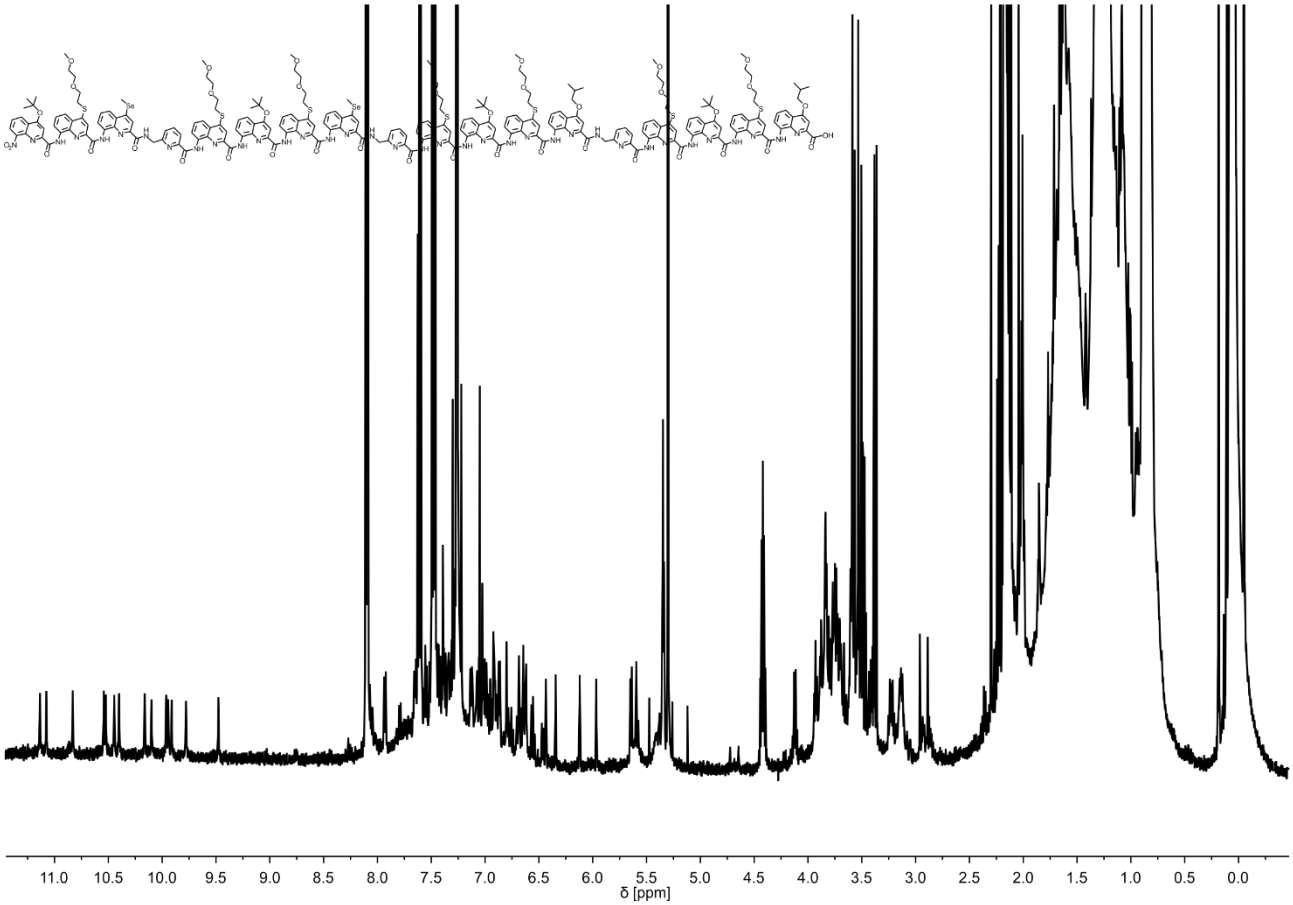

Figure S54. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **16**.

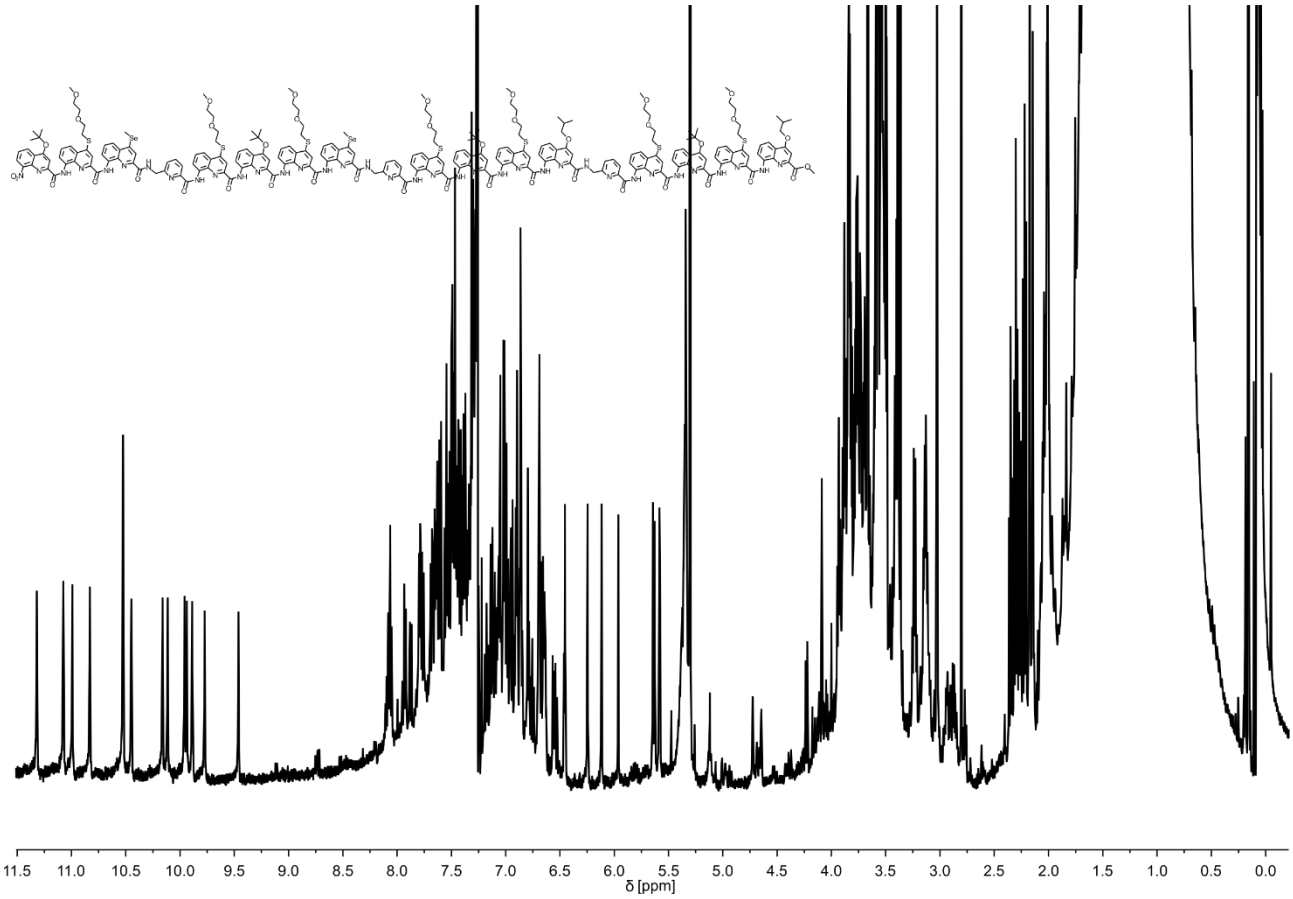

Figure S55. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **17**.

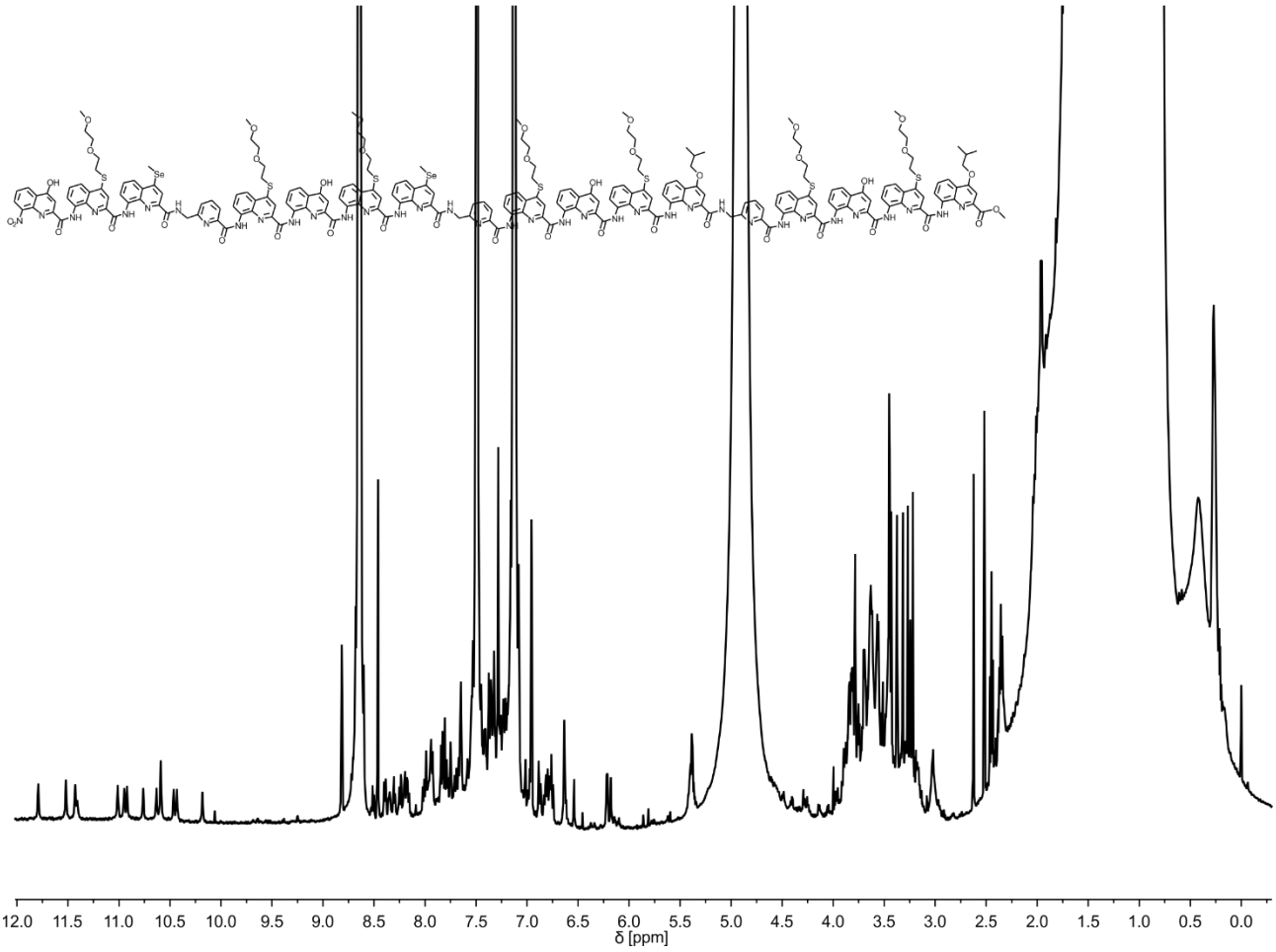

Figure S56. ^{1}H NMR spectrum (500 MHz, pyridine-d_5) of **7**.