Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Structure Elucidation of Host–Guest Complexes of Tartaric and Malic Acids by Quasi-Racemic Crystallography**

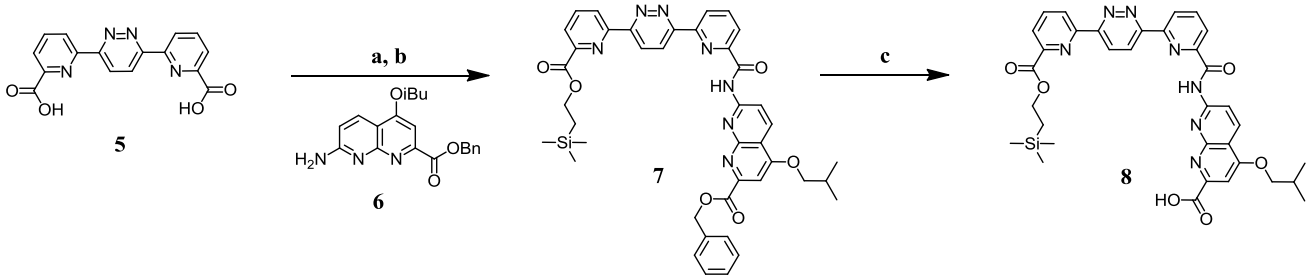
*Guillaume Lautrette, Brice Kauffmann, Yann Ferrand, Christophe Aube, Nagula Chandramouli, Didier Dubreuil, and Ivan Huc**

anie_201305364_sm_miscellaneous_information.pdf

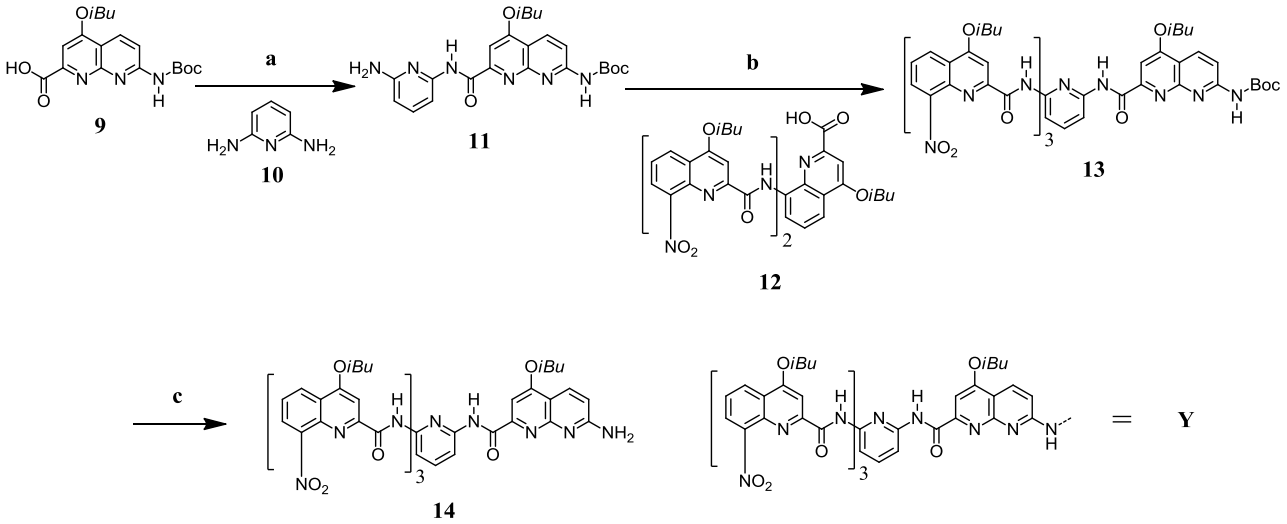
Table of contents

Page S2	Synthetic schemes
Page S4	Material and methods
Page S5	^{1}H NMR titrations and structural studies
Page S10	Crystallography
Page S16	Experimental section
Page S22	References
Page S23	NMR spectra

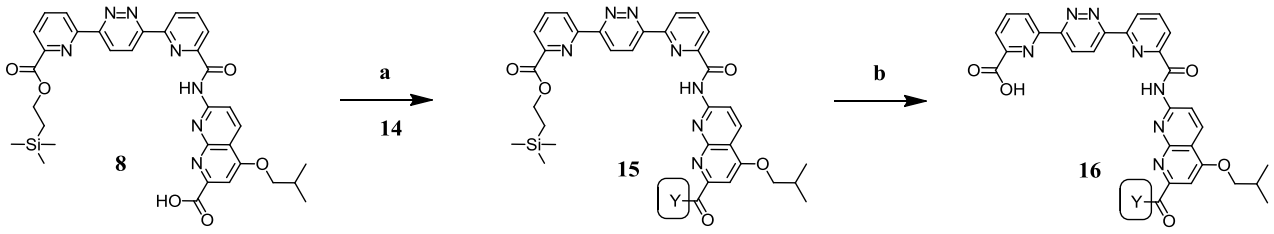
Synthetic schemes



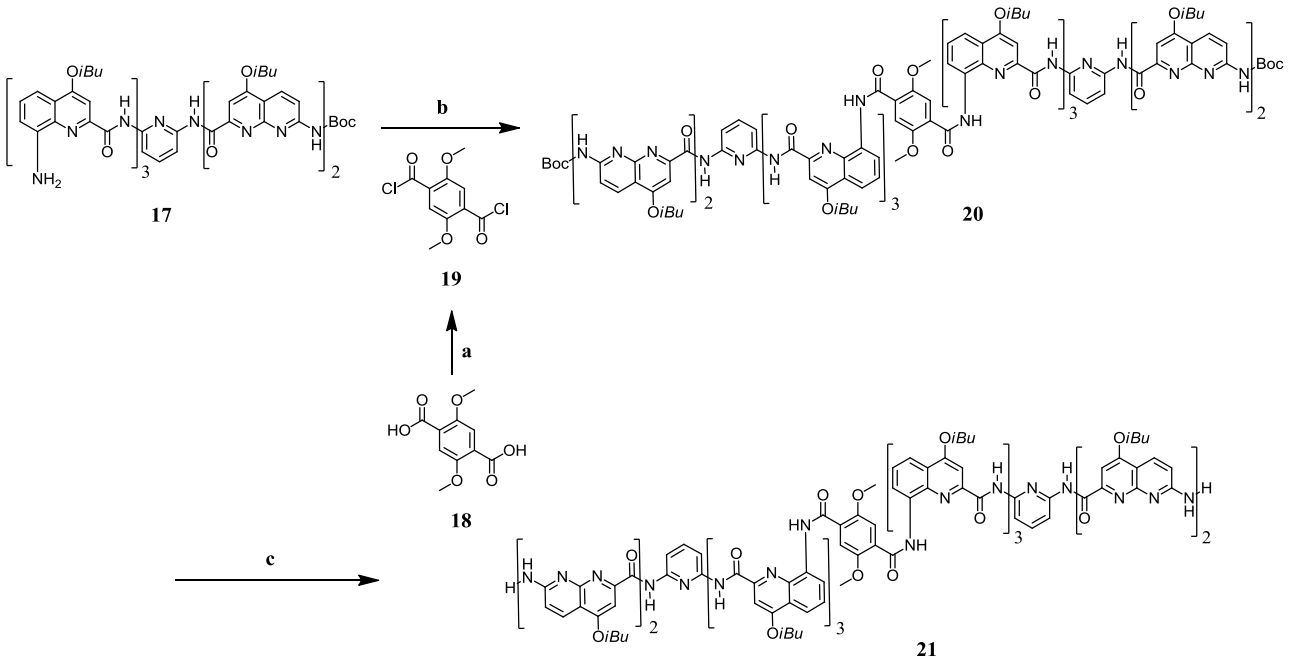
Scheme S1. Desymmetrization of the central diacid **5** : (a) 2-(Trimethylsilyl)ethanol, PyBOP, DIPEA, $CHCl_3$, RT then 45°C, and one pot (b) **6**, PyBOP, 45°C; (c) 10% Pd/C, H_2, DMF, RT.



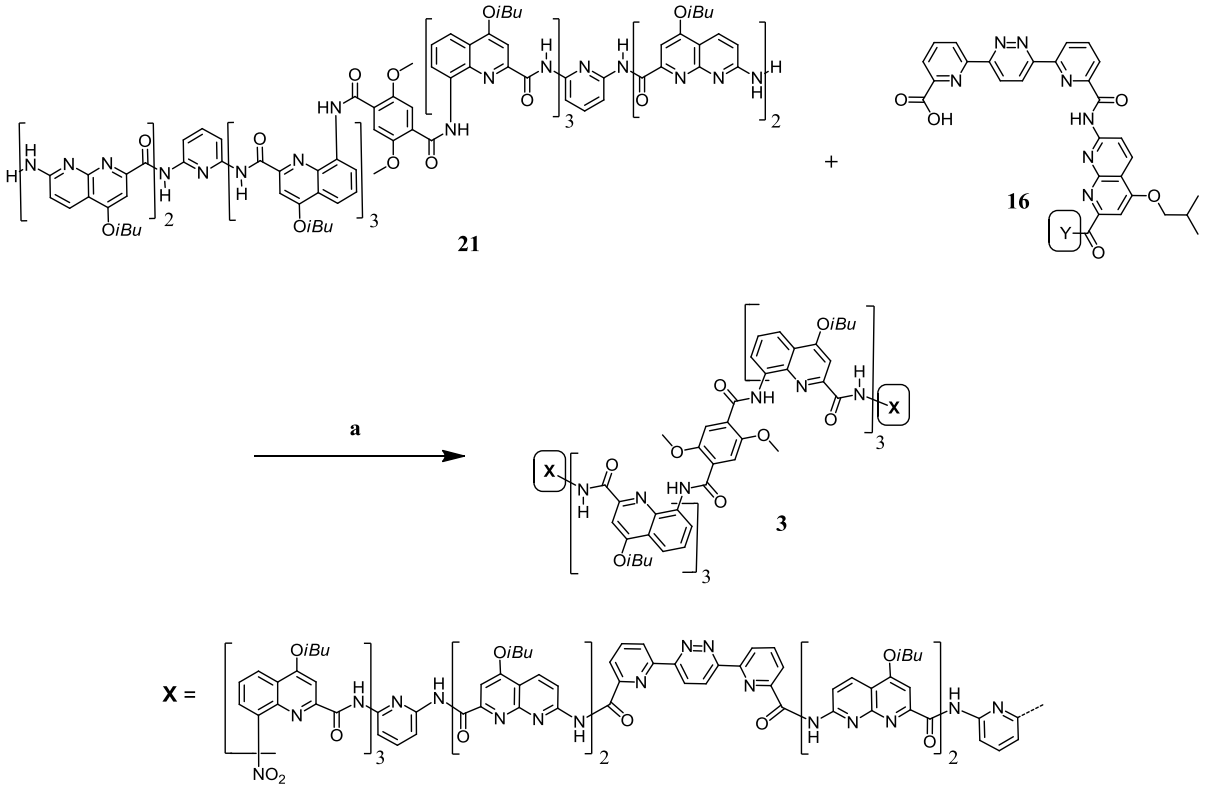
Scheme S2. Synthesis of pentamer **14**: (a) PyBOP, DIPEA, $CHCl_3$, RT then 45°C; (b) PyBOP, DIPEA, $CHCl_3$, RT then 45°C; (c) TFA, $CHCl_3$, RT.



Scheme S3. Synthesis of heptamer **16**: (a) PyBOP, DIPEA, $CHCl_3$, RT then 45°C; (b) TBAF, THF, RT.



Scheme S4. Synthesis of tridecamer **21**: (a) 1-chloro-*N*,*N*,2-trimethylpropenylamine, $CHCl_3$, RT; (b) DIPEA, CHCl3, 0°C then RT; (c) TFA, $CHCl_3$, RT.



Scheme S5. Synthesis of capsule **3**: (a) PyBOP, DIPEA, $CHCl_3$, RT then 45°C.

Materials and methods

Nuclear Magnetic Resonance

NMR experiments on capsule **3** were recorded on two different NMR spectrometers: (1) an Avance III NMR spectrometer (Bruker Biospin) with a vertical 16.45T narrow-bore/ultrashield magnet operating at 700 MHz for ^{1}H observation by means of a 5-mm TXI $^{1}H/^{13}C/^{15}N$ probe with Z gradient capabilities; (2) an Avance III NMR spectrometer (Bruker Biospin) with a Standard Bore Cryo Probe operating at 800 MHz for ^{1}H observation by means of a 5-mm TCI $^{1}H/^{13}C/^{15}N$ probe with Z gradient capabilities. Chemical shifts are reported in parts per million (ppm, δ) relative to the ^{1}H residual signal of the deuterated solvent used. ^{1}H NMR splitting patterns with observed first-order coupling are designated as singlet (s), doublet (d), triplet (t), or quartet (q). Coupling constants (*J*) are reported in hertz. Samples were not degassed. Data processing was performed with Topspin 2.1 software.

Crystallography

Data collections were performed at the IECB X-ray facility (UMS 3033 CNRS) on a RIGAKU MM07 and a Bruker Microstar rotating anodes at the copper k_{α} wavelength at 213K (capsule **3**) and at the French CRG Beamline FIP at ESRF at the wavelength 0.81 Å (capsule **3**⊃(*L*-**2**)$_2$ and capsule **3**⊃(*L*-**2**; *L*-**4**)) . The crystals were mounted on cryo-loops after quick soaking on Paratone—N oil from Hampton research and flash-frozen. All crystal structures were solved using the charge flipping algorithm implemented in the SUPERFLIP software[1] and refined using SHELXL.[2] Full-matrix least-squares refinement was performed on F^2 for all unique reflections, minimizing $w(Fo^2- Fc^2)^2$, with anisotropic displacement parameters for non-hydrogen atoms. The positions of hydrogen atoms were located on a subsequent differential electron-density map. Hydrogen atoms were included in idealized positions and refined with a riding model, with Uiso constrained to 1.2 Ueq value of the parent atom (1.5 Ueq when CH_3). Data statistics are reported in the tables S1 to S3 and in the cif files with CCDC reference numbers 945577 (**3**⊃(*L*-**2**; *L*-**4**), 945684 (**3**⊃(*L*-**2**)$_2$ and 946079 (empty capsule **3**). The BYPASS[3] procedure was used to take into account the electron density in the potential solvent area for the crystal structure of all capsules which resulted in an electrons count of 242 within a volume of 1770.4 Å^3 in the unit cell for capsule **3**⊃(*L*-**2**)$_2$, 2984 electrons within 10779.3 Å^3 for capsule **3**⊃(*L*-**2**; *L*-**4**) and 407 electrons within 1677.9 Å^3 for the empty capsule; most probably the cavities are partly occupied by disordered solvent molecules. Some atoms showed unrealistic displacement parameters and converged to non-positive definite displacement parameters.

^{1}H NMR titrations

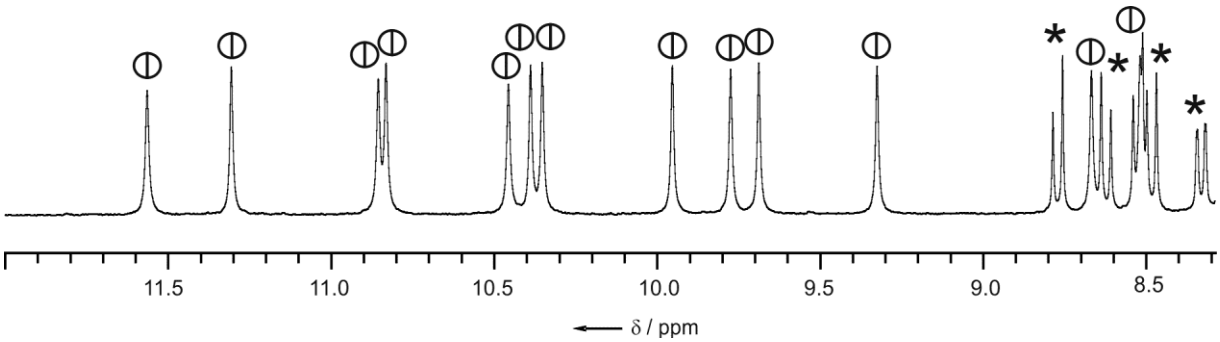


Figure S1. Representative 300 MHz NMR spectrum of the low field resonances of **3** (2 mM) in $CDCl_3$ at 298K showing 13 amides peaks. Stars (*) denote some naphthyridine aromatic resonances.

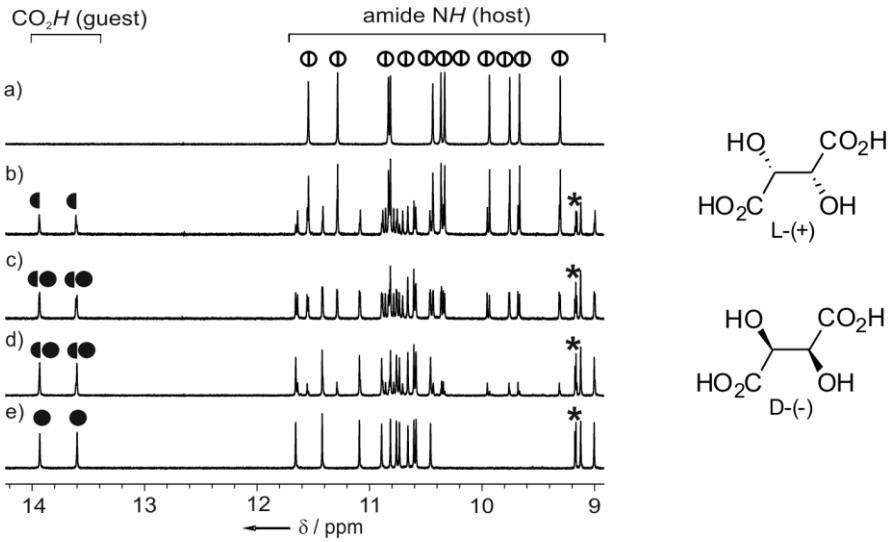
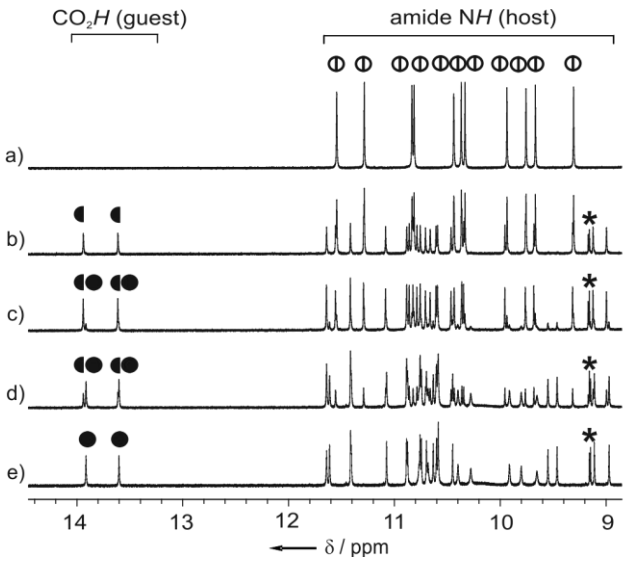


Figure S2. Representative 800 MHz NMR spectra of **3** (0.5 mM) in a $CDCl_3$:DMSO mixture (99:1) at 298K titrated with *D/L*-**2**: a) 0 equiv.; b) 0.5 equiv.; c) 1 equiv.; d) 1.5 equiv. and e) 2 equiv.. Amide signals of the empty host are marked with two merged empty half circles. Signals of the 1:1 complex (matching-empty) are denoted with black half circles whereas those of the 1:2 complex (matching-matching) are denoted with a full black circles. Stars denote some aromatic resonances.



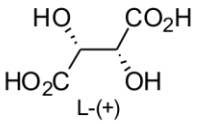


Figure S3. Representative 700 MHz NMR spectra of **3** (0.5 mM) in a $CDCl_3$:DMSO mixture (99:1) at 298K titrated with *L*-**2**: a) 0 equiv.; b) 0.5 equiv.; c) 1 equiv.; d) 1.5 equiv.; e) 2 equiv.. Amide signals of the empty host are marked with two merged empty half circles. Signals of *L*-**2** carboxylic acid protons in the *M*-helix (matching) are denoted with full black half circles for **3**⊃*L*-**2**. Signals of the *L*-**2** carboxylic acid protons in the *M*-helix (matching) are denoted with black circles for **3**⊃(*L*-**2**)$_2$. Signals of the *L*-**2** carboxylic acid protons in *P*-helix (mismatching) have not been assigned here (see Figure S3 for more details). Stars denote some aromatic resonances.

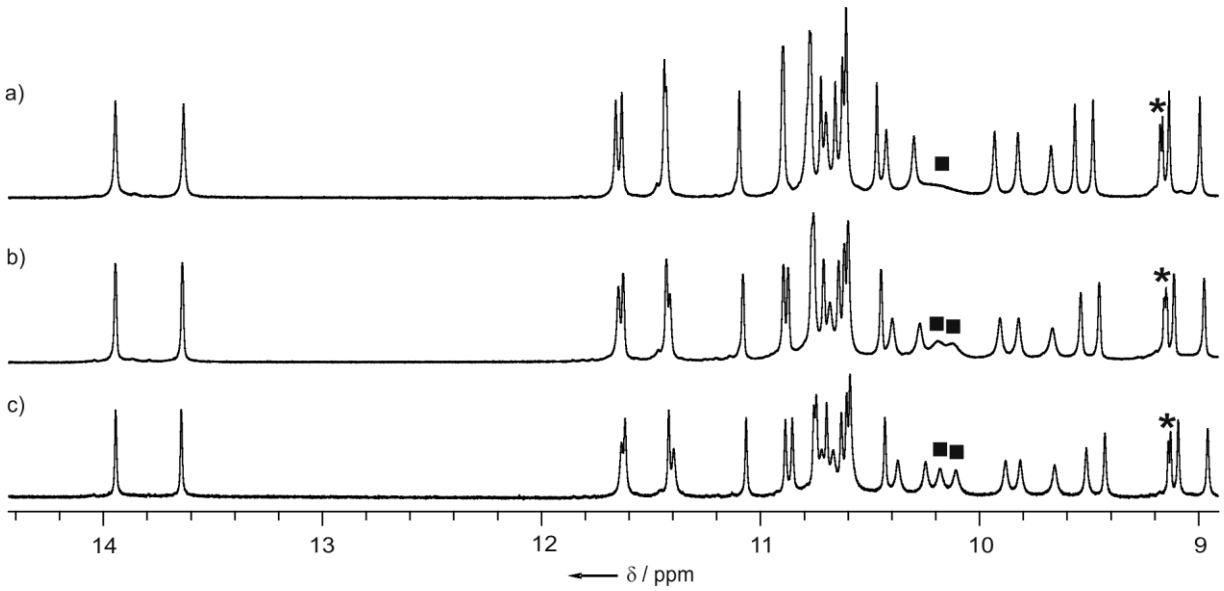


Figure S4. Representative 700 MHz NMR spectra of **3**⊃(*L*-**2**)$_2$ (4 mM) in a $CDCl_3$:DMSO (99:1) mixture at: a) 298K; b) 283K; c) 273K. Signals of *L*-**2** carboxylic acid protons are marked with black squares in the *P*-helix (mismatching). At 298K they are found to be at coalescence whereas upon decreasing the temperature to 273K they split into two well resolved peaks.

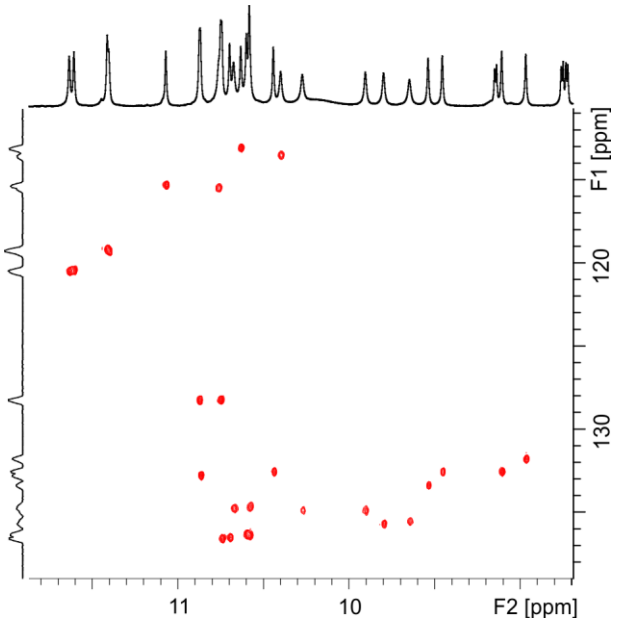


Figure S5. Zoom of 2D HSQC ^{15}N (700MHz) spectrum of **3**⊃(*L*-**2**)$_2$ (4 mM) in a $CDCl_3$:DMSO mixture (99:1) at 298 K showing 26 ^{1}H-^{15}N cross-peaks corresponding to the 26 amide NHs of dissymmetrical capsule **3**. No cross peak can be observed at 10.20 ppm corresponding to the mismatching *L*-**2** resonances. The horizontal scale (F2) is that of ^{1}H resonances and the vertical scale (F1) is that of ^{15}N resonances.

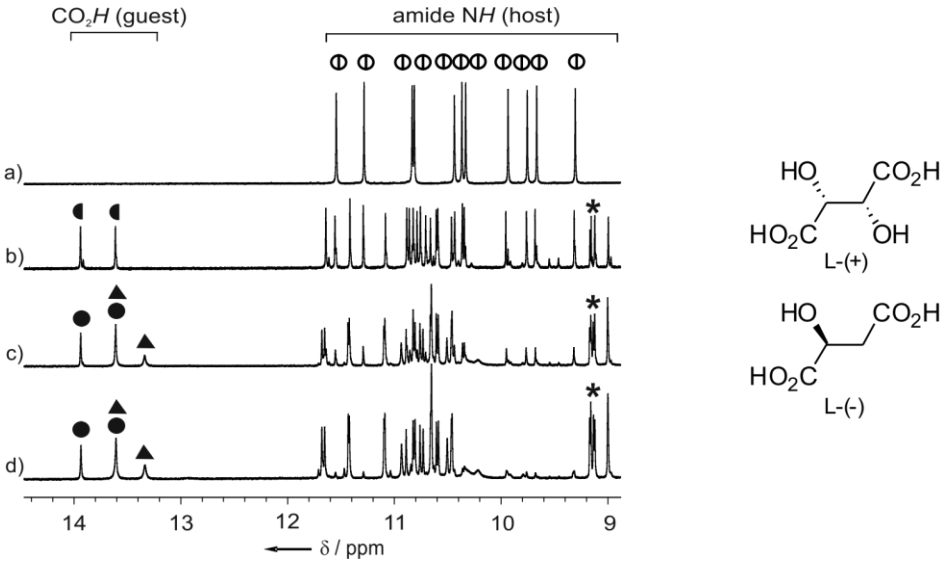
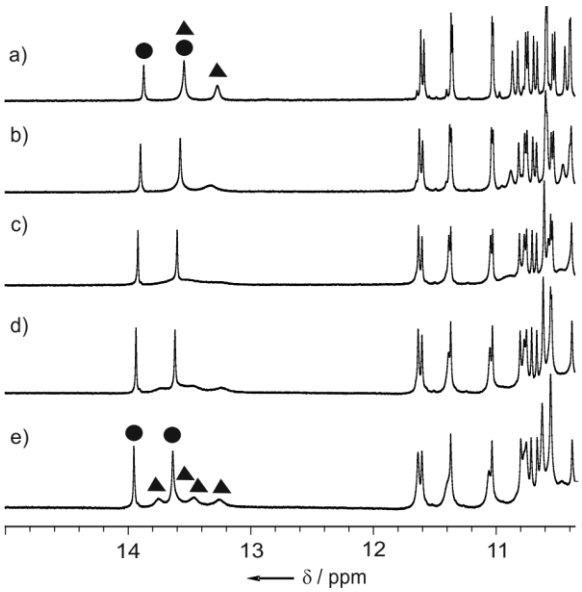


Figure S6. Representative 700 MHz NMR spectra of **3** (0.5 mM) in a $CDCl_3$:DMSO (99:1) mixture at 298K titrated with *L*-**2** and *L*-**4**: a) 0 equiv., b) 1 equiv. of *L*-**2**, c) 1 equiv. of *L*-**2** and 1 equiv. of *L*-**4** , d) 1 equiv. of *L*-**2** and 3 equiv. of *L*-**4**. Amide signals of the empty host are marked with two merged empty half circles. Signals of *L*-**2** carboxylic acid protons in *M*-helix (matching) are denoted with full black half circles for **3**⊃*L*-**2**. Signals of *L*-**2** carboxylic acid protons are marked with black circles in *M*-helix (matching) and *L*-**4** carboxylic acid protons are denoted with black triangles in *P*-helix (matching) for **3**⊃(*L*-**2**; *L*-**4**). Stars denote some aromatic resonances.



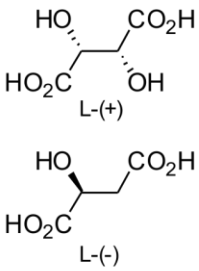


Figure S7. Representative 700 MHz NMR spectra of **3**⊃(*L*-**2**; *L*-**4**) (1 mM) in a $CDCl_3$:DMSO mixture (99:1) at : a) 298K; b) 273K; c) 263K; d) 253K and e) 243K. Signals of the *L*-**2** carboxylic acid protons are marked with black circles in the *M*-helix (matching) and *L*-**4** carboxylic acid protons are denoted with black triangles in the *P*-helix (matching).

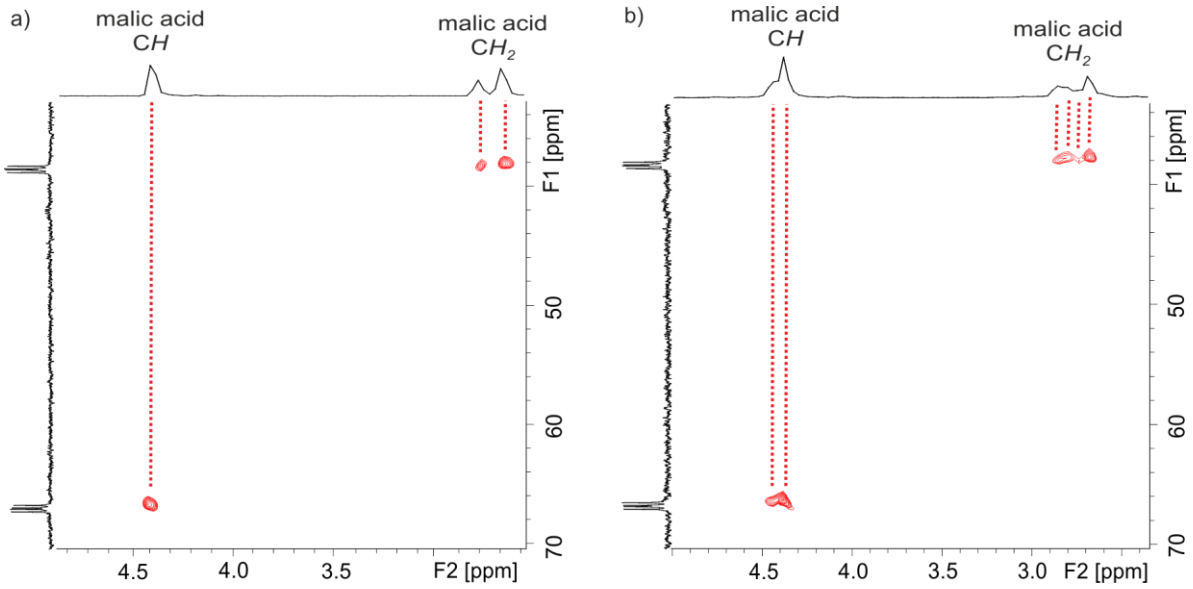
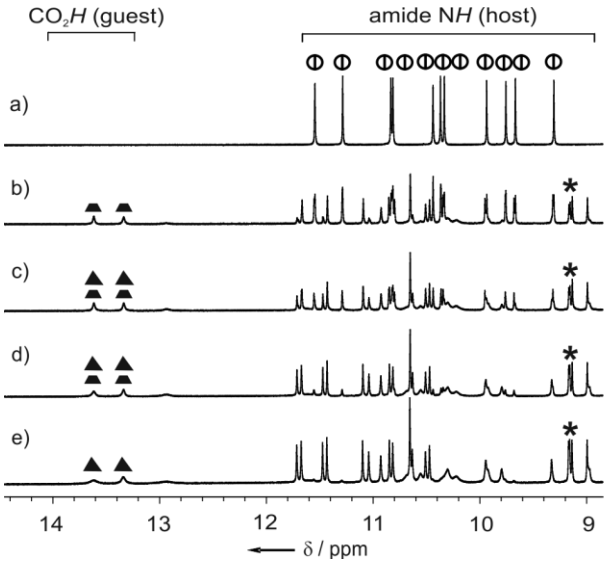


Figure S8. Zoom of 2D HSQC (700MHz) spectrum of **3**⊃(*L*-**2**; *L*-[$^{13}C_4$]-**4**) ([**3**]=1 mM; [*L*-**2**]= 1mM and [*L*-**4**] = 1.5mM) in a $CDCl_3$:DMSO mixture (99:1) at : a) 298K; b) 243K. The horizontal scale (F2) is that of ^{1}H resonances and the vertical scale (F1) is that of ^{13}C resonances.



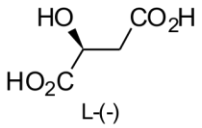
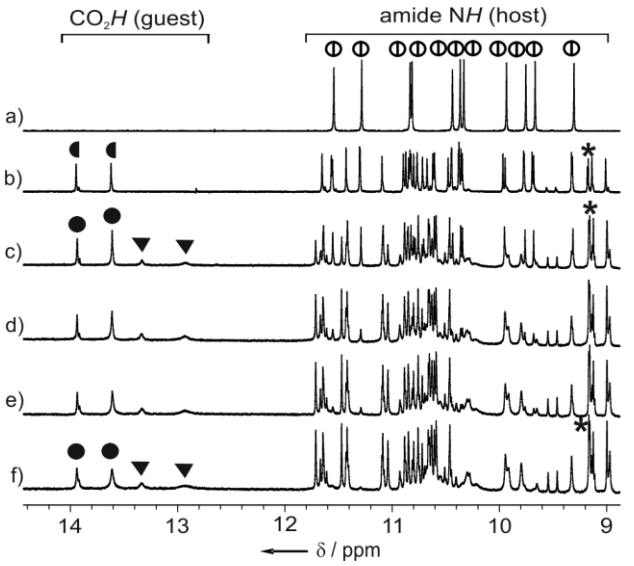


Figure S9. Representative 700 MHz NMR spectra of **3** (0.5 mM) in a mixture of $CDCl_3$:DMSO (99:1) at 298K titrated with *L*-**4**: a) 0 equiv.; b) 1 equiv.; c) 2 equiv.; d) 5 equiv. and e) 12 equiv.. Amide signals of the empty host are marked with two merged empty half circles. Signals of *L*-**4** acid carboxylic acid protons in the *P*-helix (matching) are denoted with black trapezoid for **3**⊃*L*-**4** (1:1 complex). Signals of the *L*-**4** carboxylic acid protons in the *P*-helix (matching) are denoted with black triangles for **3**⊃(*L*-**4**)$_2$. Signals of the *L*-**4** in *M*-helix (mismatching) have not been assigned. Stars denote some aromatic resonances.



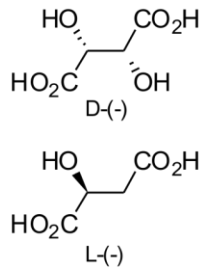


Figure S10. Representative 800 MHz NMR spectra of **3** (0.5 mM) in a $CDCl_3$:DMSO mixture (99:1) at 298K titrated with *D*-**2** and *L*-**4**: a) 0 equiv.; b) 1 equiv. *D*-**2**, c) 1 equiv. *D*-**2** and 1 equiv. *L*-**4**; d) 1 equiv. *D*-**2** and 3 equiv. *L*-**4**; e) 1 equiv. *D*-**2** and 5 equiv. *L*-**4**, d) 1 equiv. *D*-**2** and 10 equiv. *L*-**4**. Amide signals of the empty host are marked with two merged empty half circles. Signals of the *D*-tartaric acid carboxylic acid protons in the *P*-helix (matching) are denoted with full black half circles for **3**⊃*D*-**2** (1:1 complex). Signals of the *D*-**2** carboxylic acid protons are marked with black circles in the *P*-helix (matching) and *L*-**4** carboxylic acid protons are denoted with black triangles in the *M*-helix (mismatching) for **3**⊃(*D*-**2**; *L*-**4**). Stars denote some aromatic resonances.

Crystallography

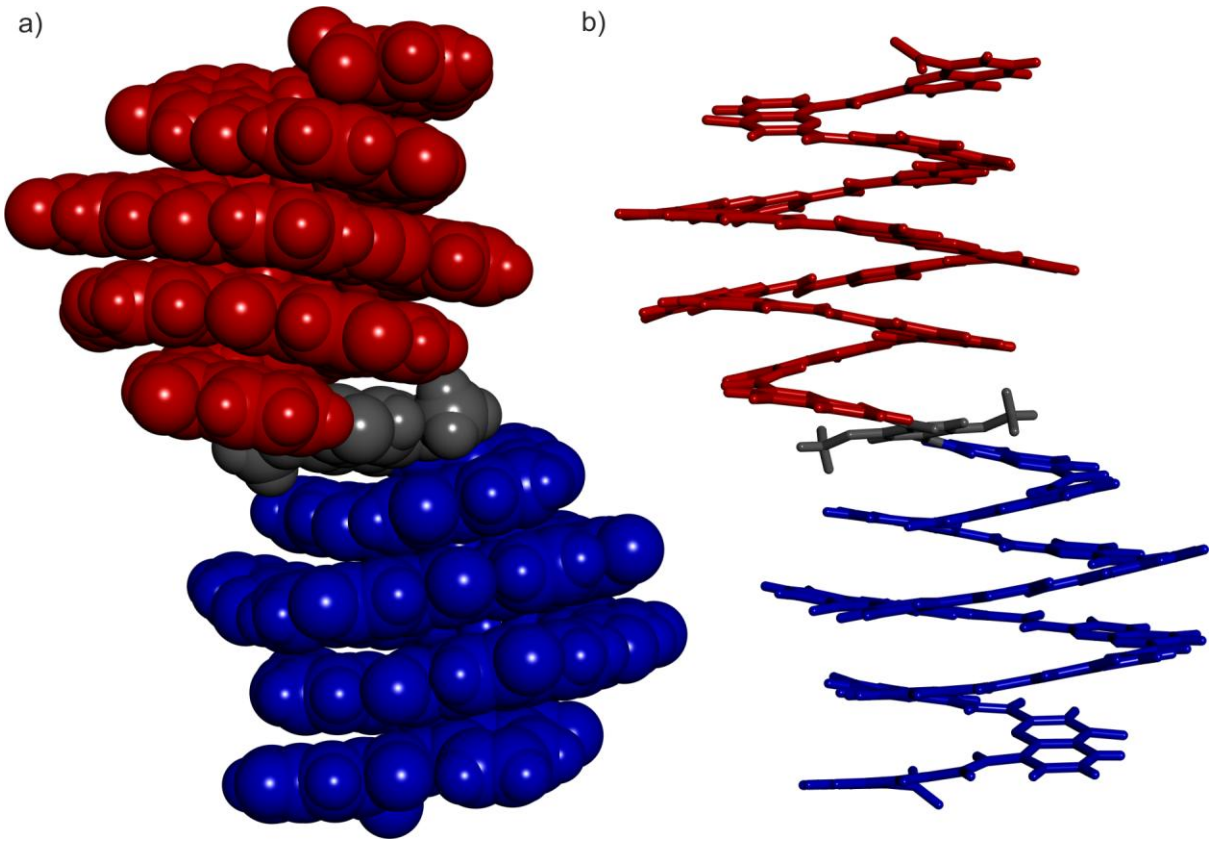


Figure S11. Side view of the crystal structure of **3**: a) in CPK representation; b) in tube representation. Red color denotes an M handedness whereas P handedness is colored in blue. Isobutyl side chains and included solvent molecules have been removed for clarity.

Table S1: Crystal data and structure refinement for capsule **3**

Formula	C177 H175 Cl12 N34 O27
M	3635.90
Crystal system	triclinic
Space group	P-1
a/Å	19.328(4)
b/Å	23.191(5)
c/Å	24.336(5)
α/°	111.96(3)
β/°	101.16(3)
γ/°	90.59(3)
U/Å^3	9884(4)
T /K	100(2)
Z	2
ρ/g cm^{-1}	1.222
Shape and color	Colorless needle
size (mm)	0.1x0.01x0.01
λ/ Å	0.810
μ/mm^{-1}	0.336
Total reflections	101234
Unique data	26244
R_{int}	0.0288
parameters/restraints	2247
*R*1, *wR*2	0.0874/0.2308
goodness of fit	1.066

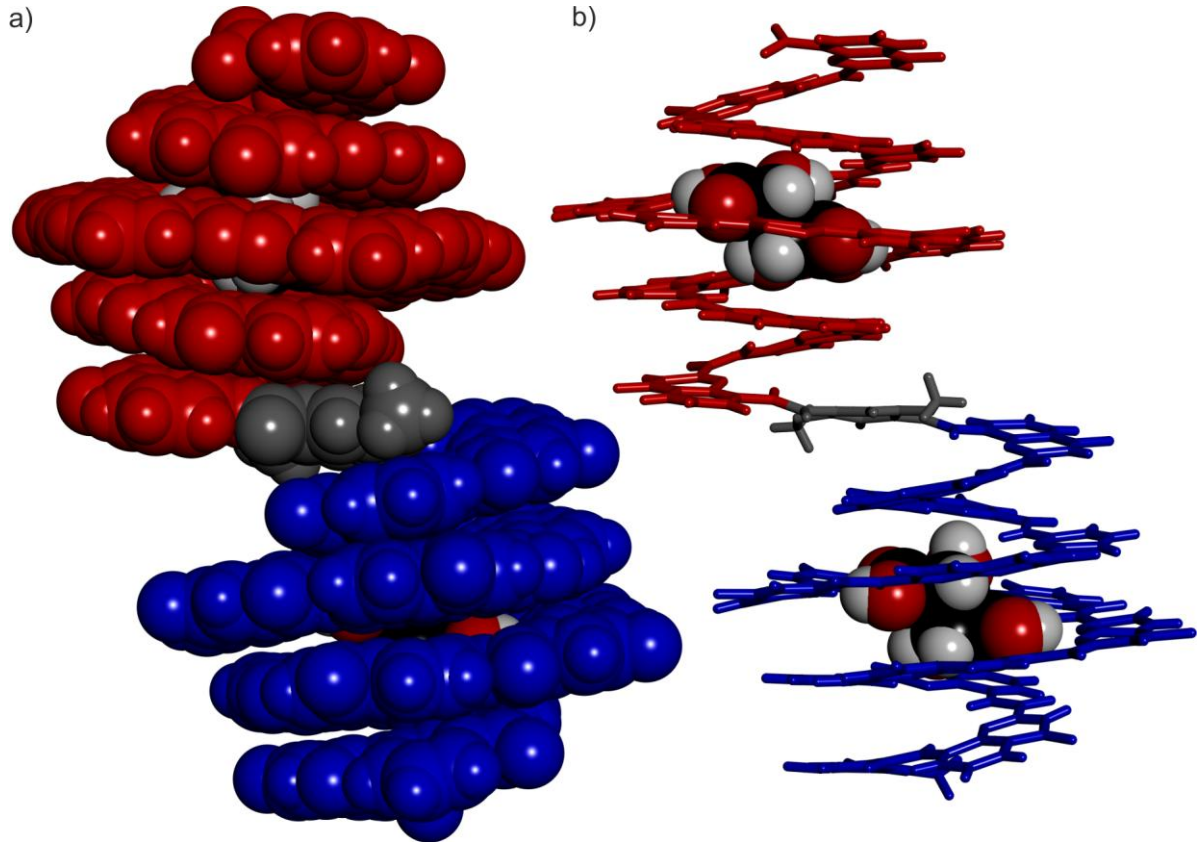


Figure S12. Side view of the crystal structure of **3**⊃(*L*-**2**)$_2$: a) in CPK representation; b) in tube representation (host) and CPK representation (guests). Red color denotes an M handedness whereas P handedness is colored in blue. Isobutyl side chains and included solvent molecules have been removed for clarity.

Table S2: Crystal data and structure refinement for capsule **3**⊃(*L*-**2**)$_2$

Formula	C351 H331 Cl27 N68 O64
M	7482.97
Crystal system	triclinic
Space group	P1
a/Å	19.2020(7)
b/Å	23.5256(9)
c/Å	24.3865(17)
α/°	68.902(8)
β/°	80.410(7)
γ/°	89.959(6)
U/Å^3	10113.2(10)
T /K	213(2)
Z	1
ρ/g cm^{-1}	1.229
Shape and color	Colorless prism
size (mm)	0.2x0.2x0.2
λ/ Å	1.54178
μ/mm^{-1}	2.289
Total reflections	148263
Unique data	59784
R_{int}	0.0681
parameters/restraints	4592/14
*R*1, *wR*2	0.1053/ 0.2287
goodness of fit	0.773

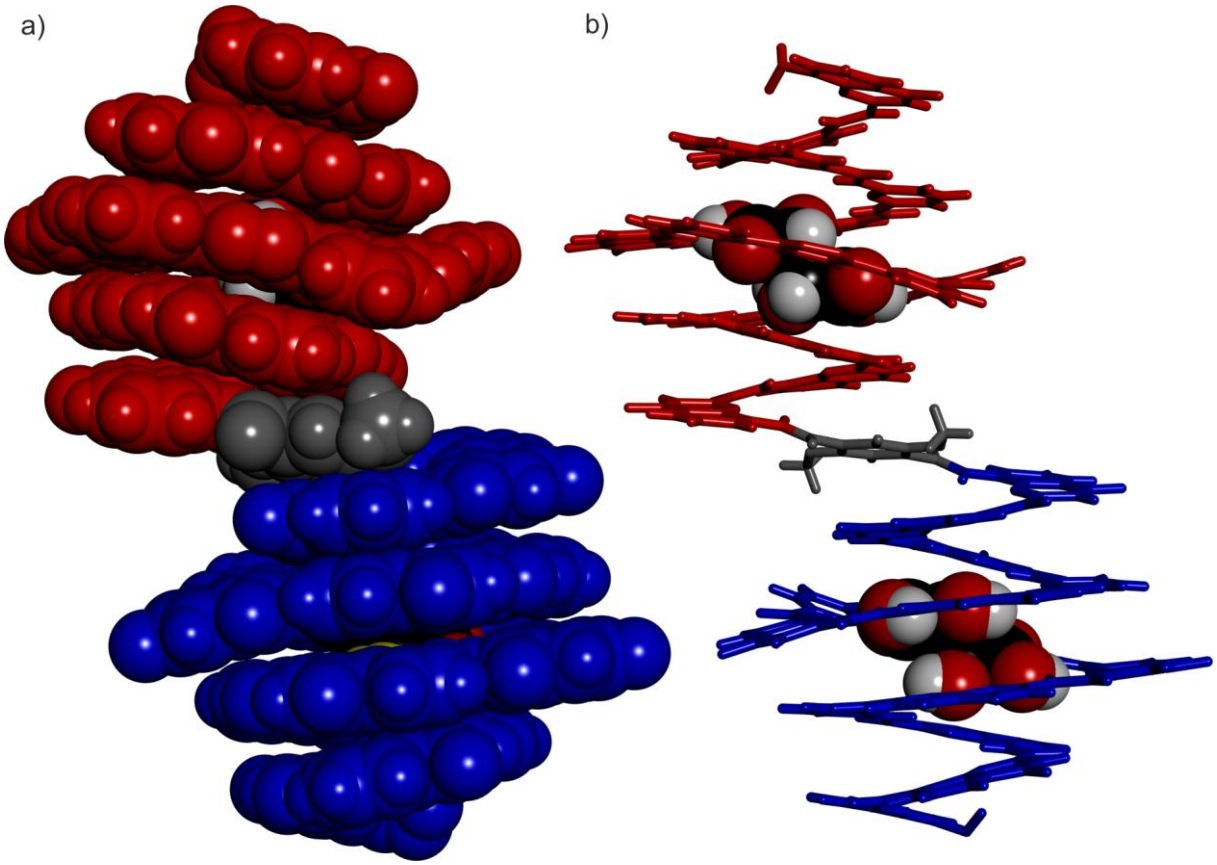


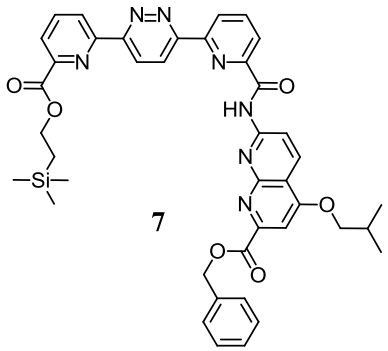
Figure S13. Side view of the crystal structure of **3**⊃(*L*-**2**; *L*-**4**): a) in CPK representation; b) in tube representation (host) and CPK representation (guests). Red color denotes an M handedness whereas P handedness is colored in blue. Isobutyl side chains and included solvent molecules have been removed for clarity.

Table S3: Crystal data and structure refinement for capsule **3**⊃(*L*-**2**; *L*-**4**).

Formula	C342 H322 N68 O63
M	6394.67
Crystal system	monoclinic
Space group	P2/c
a/Å	37.152(7)
b/Å	17.322(4)
c/Å	62.533(13)
β/°	104.17(3)
U/Å^3	9884(4)
T /K	100(2)
Z	4
ρ/g cm^{-1}	1.089
Shape and color	Colorless needle
size (mm)	0.1x0.02x0.02
λ/ Å	0.810
μ/mm^{-1}	0.103
Total reflections	307141
Unique data	60427
R_{int}	0.0708
parameters/restraints	4267/23
$R1$, $wR2$	0.1472/ 0.3965
goodness of fit	1.539

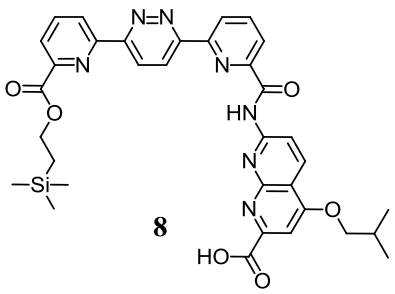
Experimental section.

General. All reactions were carried out under a dry nitrogen atmosphere. Commercial reagents were purchased from Sigma-Aldrich or Alfa-Aesar and were used without further purification unless otherwise specified. Chloroform, diisopropylethylamine (DIPEA) were distilled from 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. Chromatography on silica were carried out on Merck GEDURAN Si60 (40-63 μm). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded in deuterated solvents on 300 and 400 MHz spectrometers. Chemical shifts are reported in parts per million (ppm, δ) relative to the signal of the NMR solvent used. ^{1}H NMR splitting patterns with observed first-order coupling are designated as singlet (s), doublet (d), triplet (t), or quartet (q). Coupling constants (J) are reported in hertz. Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m) or broad (br). ^{13}C NMR spectra were recorded on 300 or 400 MHz spectrometers. Chemical shifts are reported in ppm (δ) relative to carbon resonances of the NMR solvent. Mass spectra (MS) were obtained using electrospray ionization (ESI) or matrix-assisted laser desorption/ionization (MALDI).



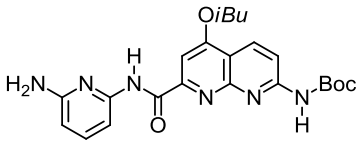
7

Dimer 7. To a solution of diacid **5**[4] (3.1 mmol, 1 g) in dry chloroform (100 mL) under nitrogen was added DIPEA (12.4 mmol, 1.6 mL) and PyBOP (3.1 mmol, 1.6 g). Then 2-(Trimethylsilyl)ethanol (2.8 mmol, 0.32 mL) was added in 30 minutes. After 48 hours at 45°C, amine **6**[5] (3.1 mmol, 1.1 g) and PyBOP (4.65 mmol, 2.4 g) was added to do the second reaction one pot. The resultant mixture was stirred at 45°C for 72 hours. Then, the solvents were removed under reduced pressure and the residue was purified by flash chromatography (SiO_2) eluting with EtOAc: dichloromethane (15:85 vol/vol) and by precipitation from minimum amount of MeOH to obtain **7** as a white solid (29 %, 0.610 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm = 10.89 (s, 1H); 9.06 (d, ^3J = 7.1, 1H); 8.96 (m, 3H); 8.86 (d, ^3J = 9.1, 1H); 8.70 (d, ^3J = 9.0, 1H); 8.50 (d, ^3J = 7.7, 1H); 8.27 (d, ^3J = 8.6, 1H); 8.20 (t, ^3J = 7.8, 1H); 8.09 (t, ^3J = 7.8, 1H); 7.57 (m, 3H); 7.36 (m,3H); 5.53 (s, 2H); 4.59 (m, 2H); 4.07 (d, ^3J = 6.5, 2H); 2.30 (m, 1H); 1.29 (m, 2H); 1.15 (d, ^3J = 6.7, 6H); 0.14 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm = 165.6; 165.4; 163.6; 163.0; 158.3; 157.2; 155.6; 154.3; 153.6; 152.8; 152.4; 149.0; 148.6; 139.2; 138.3; 135.8; 134.4; 128.9; 128.6; 128.5; 126.2; 126.1; 125.7; 125.4; 124.9; 124.2; 115.5; 115.1; 101.5; 75.8; 67.9; 64.5; 28.2; 19.3; 17.5; -1.2. HRMS (ES^+): *m/z* calcd for $C_{41}H_{41}N_7O_6Si$ $[M+H]^+$ 756.2981 found 756.2983.



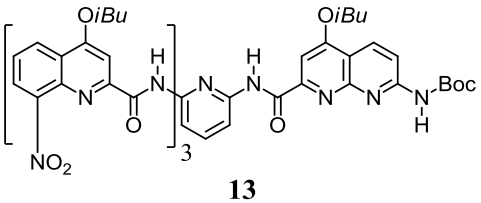
8

Dimer 8. To a solution of dimer **7** (0.607 mmol, 0.45 g) in DMF (30 mL) was added Pd/C (45 mg) under nitrogen. Then the reaction mixture was vigorously stirred under hydrogen atmosphere at room temperature for 12 h. The mixture was filtered through a pad of Celite with dichloromethane and concentrated under vacuum to give product **8** as a white solid (98 %, 0.395 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm = 10.84 (s, 1H); 9.07 (d, ^{3}J = 7.8, 1H); 8.93 (m, 3H); 8.77 (d, ^{3}J = 9.0, 1H); 8.51 (d, ^{3}J = 7.6, 1H); 8.24 (m, 3H); 8.10 (t, ^{3}J = 7.8, 1H); 7.72 (s, 1H); 4.58 (t, ^{3}J = 8.3, 2H); 4.14 (d, ^{3}J = 6.4, 2H); 2.33 (m, 1H); 1.27 (t, ^{3}J = 8.6, 2H); 1.16 (d, ^{3}J = 6.7, 6H); 0.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 165.1; 164.6; 162.9; 158.0; 156.9; 154.5; 153.9; 153.4; 152.7; 148.6; 148.4; 139.2; 138.2; 134.8; 126.1; 126.0; 125.7; 125.4; 124.6; 124.2; 115.7; 115.2; 100.2; 76.2; 64.4; 28.2; 19.3; 17.4; -1.4. HRMS (ES^+): *m/z* calcd for $C_{34}H_{35}N_7O_6Si$ $[M+H]^+$: 666.2491 found 666.2490.



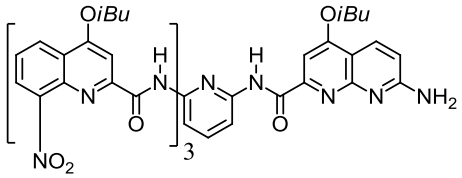
11

Dimer 11. Acid **9**[5] (0.690 mmol, 0.250 g) and 2,6-diaminopyridine **10** (6.9 mmol, 0.750 g) were dissolved in dry chloroform (30 mL). Then, DIPEA (2.76 mmol, 0.5 mL) and PyBOP (1.38 mmol, 0.720 g) were added at RT and the reaction mixture was heated at 45°C for 24 hours. The solvent was evaporated and the residue was dissolved in CH_2Cl_2, washed with a citric acid solution (5% aq), water (3 times), dried over Na_2SO_4, filtered and then concentrated. The residue was purified by precipitation from minimum amount of MeOH to obtain **11** as a white solid (74 %, 0.230 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm = 10.43 (s, 1H); 8.56 (d, ^{3}J = 9.1, 1H); 8.32 (d, ^{3}J = 9.1, 1H); 8.11 (d, ^{3}J = 9.3, 1H); 7.65 (s, 1H); 6.30 (d, ^{3}J = 8.5, 1H); 7.53 (dd, ^{3}J = 8.1, 2H); 4.33 (s, 2H); 4.09 (d, ^{3}J = 6.6, 2H); 2.29 (m, 1H); 1.57 (s, 9H); 1.13 (d, ^{3}J = 6.7, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm = 164.0; 162.4; 157.5; 155.1; 154.8; 153.9; 152.2; 149.7; 140.0; 134.2; 114.1; 113.7; 104.7; 103.7; 98.8; 82.1; 75.6; 28.3; 28.2; 19.3. MS (ES^+): *m/z* calcd for $C_{23}H_{28}N_6O_4$ $[M+H]^+$: 453.2245 found 453.2240.



13

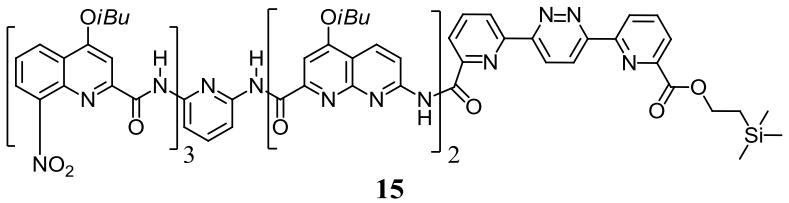
Hexamer 13. Acid **12**[6] (0.550 mmol, 0.426 g) and trimer amine **11** (0.500 mmol, 0.230 g) were dissolved in dry chloroform (15 mL). Then, DIPEA (2 mmol, 0.35 mL) and PyBOP (1 mmol, 0.520 g) were added at RT and the reaction mixture was heated at 45°C for 24 hours. Then, the solvents were removed under reduced pressure and the residue was purified by flash chromatography (SiO_2) eluting with EtOAc:dichloromethane (10:90 vol/vol) and by precipitation from minimum amount of MeOH to obtain **13** as a yellow solid (64 %, 0.386 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 11.99 (s, 1H); 11.89 (s, 1H); 9.82 (s, 1H); 9.51 (s, 1H); 9.14 (d, ^3J = 8.9, 1H); 8.66 (d, ^3J = 9.0, 1H); 8.59 (d, ^3J = 8.9, 1H); 8.52 (d, ^3J = 9.8, 1H); 8.39 (d, ^3J = 9.1, 1H); 8.05 (m, 2H); 7.94 (s, 1H); 7.76 (m, 3H); 7.62 (d, ^3J = 8.0, 1H); 7.55 (d, ^3J = 9.0, 1H); 7.51 (s, 1H); 7.38 (t, ^3J = 8.3, 1H); 7.32 (s, 1H); 7.00 (s, 1H); 6.84 (t, ^3J = 9.6, 1H); 6.49 (t, ^3J = 8.0, 1H); 4.21 (d, ^3J = 6.3, 2H); 4.07 (m, 4H); 3.94 (d, ^3J = 6.5, 2H); 2.37 (m, 3H); 2.10 (m, 1H); 1.59 (s, 9H); 1.22 (m, 20H); 1.04 (d, ^3J = 6.7, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 164.0; 163.5; 163.4; 163.2; 163.1; 162.5; 161.5; 161.0; 154.7; 154.6; 154.4; 153.9; 152.2; 150.9; 149.7; 148.7; 147.8; 145.3; 139.9; 139.4; 139.2; 139.0; 135.0; 134.5; 134.1; 128.4; 128.1; 126.5; 126.0; 124.4; 123.7; 122.4; 122.3; 119.3; 117.8; 116.4; 115.5; 114.2; 113.5; 110.6; 108.7; 99.9; 99.8; 97.8; 82.3; 75.9; 75.8; 75.5; 75.4; 28.4; 28.3; 28.2; 28.1; 19.5; 19.4; 19.4; 19.3. MS (ES^+): *m/z* calcd for $C_{65}H_{68}N_{12}O_{12}$ $[M+H]^+$: 1209.5152 found 1209.5148.



14

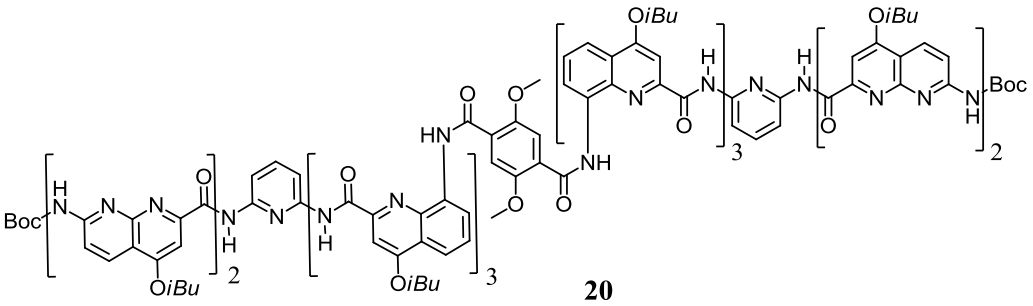
Hexamer 14. Trifluoroacetic acid (0.4 mL) was added drop wise to a solution of **13** (0.064 mmol, 0.078 g) in 2 mL of chloroform under nitrogen at RT. Then, the resultant mixture was stirred at RT for 5 hours. The volatiles were removed under reduced pressure to give a solid which was dissolved in dichloromethane and washed with a saturated solution of $NaHCO_3$, distilled water and then with brine. The organic layers were dry over Na_2SO_4 then the volatiles were removed under reduce pressure to give the amine derivative **14** as yellow solid (99%, 0.070 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm = 12.00 (s, 1H); 11.83 (s, 1H); 9.75 (s, 1H); 9.68 (s, 1H); 9.15 (d, ^3J = 6.9, 1H); 8.54 (m, 2H); 8.34 (d, ^3J = 8.9, 1H); 8.07 (m, 2H); 7.84 (s, 1H); 7.75 (dd, ^3J = 7.9, 2H); 7.66 (s, 1H); 7.62 (d, ^3J = 8.3, 1H); 7.56 (d, ^3J = 6.3, 1H); 7.39 (t, ^3J = 8.0, 1H); 7.30 (s, 1H); 7.06 (m, 2H); 6.77 (d, ^3J = 8.8, 1H); 6.53 (t, ^3J = 8.0, 1H); 5.05 (s, 2H); 4.17 (d, ^3J = 6.4, 2H); 4.06 (m, 4H); 3.96 (d, ^3J = 6.5, 2H); 2.37 (m, 3H); 2.10 (m, 1H); 1.22 (m, 16H); 1.06 (d, ^3J = 6.5, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 163.9; 163.5; 163.4; 163.1; 162.9; 162.8; 161.4; 161.2; 160.1; 155.9; 154.4; 152.3; 150.7; 150.0; 148.8; 147.9; 145.3; 140.0; 139.4; 139.3; 122.5; 122.4; 119.4; 117.6; 116.3; 115.9; 112.3;

110.9; 110.3; 108.6; 99.8; 99.6; 98.0; 97.3; 75.6; 75.5; 75.2; 28.4; 28.3; 28.2; 19.5; 19.4; 19.2. MS (ES^+): *m/z* calcd for $C_{60}H_{60}N_{12}O_{10}$ $[M+H]^+$: 1109.4628 found 1109.4617.



15

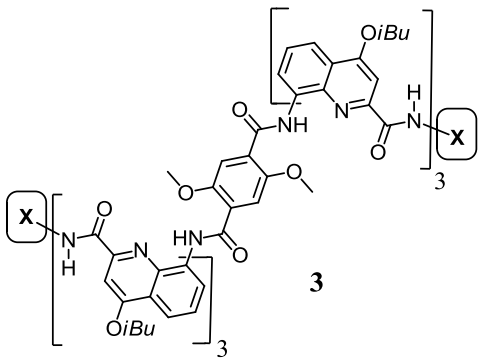
Heptamer 15. Acid **8** (0.230 mmol, 0.167 g) and pentamer amine **14** (0.210 mmol, 0.231 g) were dissolved in dry chloroform (5 mL). Then, DIPEA (0.920 mmol, 0.16 mL) and PyBOP (0.690 mmol, 0.359 g) were added at RT and the reaction mixture was heated at 45°C for 24 hours. Then, the solvents were removed under reduced pressure and the residue was purified by flash chromatography (SiO_2) eluting with EtOAc:dichloromethane (20:80 vol/vol) and by precipitation from minimum amount of MeOH to obtain **15** as a yellow solid (83 %, 0.308 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm = 11.81 (s, 1H); 11.31 (m, 2H); 10.90 (s, 1H); 10.30 (s, 1H); 9.34 (s, 1H); 9.08 (d, ^3J = 9.1, 1H); 8.96 (d, ^3J = 9.0, 1H); 8.79 (m, 4H); 8.61 (d, ^3J = 8.9, 1H); 8.56 (d, ^3J = 8.6, 1H); 8.48 (d, ^3J = 7.7, 1H); 8.38 (m, 3H); 8.15 (m, 2H); 8.00 (d, ^3J = 6.8, 1H); 7.95 (s, 1H); 7.84 (m, 4H); 7.67 (t, ^3J = 8.0, 1H); 7.36 (d, ^3J = 9.1, 1H); 7.29 (d, ^3J = 8.0, 1H); 7.11 (d, ^3J = 7.9, 1H); 7.97 (m, 3H); 6.67 (s, 1H); 6.26 (t, ^3J = 8.0, 1H); 4.10 (m, 9H); 3.60 (m, 1H); 3.27 (m, 2H); 2.39 (m, 5H); 1.26 (m, 26H); 0.76 (m, 3H); 0.47 (m, 3H); -0.31 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm = 164.7; 164.5; 164.0; 163.8; 163.5; 163.1; 163.0; 162.9; 162.3; 161.6; 159.7; 156.8; 155.9; 155.3; 154.9; 154.6; 154.3; 153.9; 152.6; 152.5; 152.4; 150.9; 149.6; 148.9; 148.2; 148.1; 146.9; 144.8; 140.1; 139.0; 138.4; 138.2; 137.6; 134.7; 134.6; 134.2; 128.2; 127.7; 125.9; 125.2; 125.1; 124.3; 124.1; 123.8; 123.5; 122.7; 122.0; 119.0; 117.0; 116.5; 116.0; 115.4; 115.3; 115.0; 114.7; 109.6; 108.0; 101.6; 99.1; 98.7; 98.5; 97.8; 76.1; 76.0; 75.6; 75.5; 63.8; 28.4; 28.3; 28.2; 28.1; 28.0; 19.4; 19.3; -1.8. MS (ES^+): *m/z* calcd for $C_{94}H_{93}N_{19}O_{15}Si$ $[M+H]^+$: 1756.6941 found 1756.6933.



20

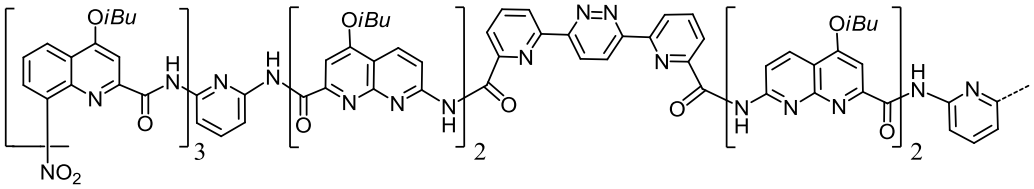
Tridecamer 20. Diacid **18**[7] (0.096 mmol, 0.024 g) was suspended in anhydrous $CHCl_3$ (2 mL). 1-chloro-N,N,2-trimethylpropenylamine (0.041 mL, 0.457 mmol) was added and the reaction was allowed to stir at RT for 2 h. The reaction mixture becomes a solution after 30 min, so the activation does work under these conditions. The solvent and excess reagents were removed under vacuum and the residue was dried under vacuum for at least 1 h to yield diacid chloride **19** as a white solid. To a solution of hexamer amine **17** (0.183 mmol, 0.260 g) and distilled DIPEA (0.457 mmol, 0.079 mL) in dry $CHCl_3$ (3 mL) was added dropwise at

RT a solution of the freshly prepared diacid chloride **19** in dry $CHCl_3$ (3 mL). The reaction was allowed to proceed at RT overnight. The solution was evaporated and the product was purified by precipitation from minimum amount of MeOH to obtain **20** as a white solid (83 %, 0.245 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm = 12.20 (s, 2H); 11.74 (s, 2H); 11.66 (s, 2H); 10.98 (s, 2H); 9.79 (s, 2H); 9.75 (s, 2H); 8.79 (m, 6H); 8.70 (d, ^3J = 8.6, 2H); 8.44 (d, ^3J = 7.0, 2H); 8.31 (d, ^3J = 9.0, 2H); 8.14 (m, 4H); 8.04 (d, ^3J = 7.9, 2H); 7.82 (m, 12H); 7.69 (m, 4H); 7.20 (t, ^3J = 8.0, 2H); 7.05 (m, 2H); 6.94 (m, 4H); 6.78 (s, 2H); 6.60 (t, ^3J = 8.0, 2H); 4.18 (m, 16H); 3.85 (m, 4H); 3.15 (s, 6H); 2.43 (m, 5H); 2.27 (m, 5H); 1.26 (m, 44H); 1.14 (m, 24H); 0.87 (d, ^3J = 6.6, 5H); 0.53 (d, ^3J = 6.7, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 164.1; 164.0; 163.9; 163.8; 163.4; 163.1; 162.7; 162.2; 161.9; 160.8; 160.6; 156.1; 154.8; 154.6; 154.0; 153.6; 152.6; 152.1; 151.0; 150.8; 150.5; 149.5; 148.8; 147.7; 140.0; 138.5; 138.4; 138.2; 135.2; 134.4; 134.3; 133.8; 133.0; 127.1; 127.0; 126.3; 124.8; 122.7; 122.2; 122.1; 118.9; 117.1; 116.8; 115.9; 115.8; 115.3; 114.9; 114.6; 113.9; 109.7; 108.7; 98.9; 98.7; 98.0; 81.4; 75.9; 75.7; 75.4; 75.3; 75.2; 56.2; 28.5; 28.4; 28.3; 28.2; 28.1; 28.0; 19.6; 19.5; 19.4; 19.3; 18.7. MS (ES$^+$): *m/z* calcd for $C_{166}H_{172}N_{30}O_{28}$ $[M+H]^+$: 3034.3030 found 3034.3057.



3

X =



Capsule 3. Oligomer **17** was reacted with tetrabutylammonium fluoride to yield acid **16** and was used in subsequent reaction without purification. Similarly, oligomer **20** was reacted with trifluoroacetic acid to yield diamine **21** and was used in subsequent reaction without reaction. Acid **16** (0.064 mmol, 0.106 g) and diamine **21** (0.032 mmol, 0.090 g) were dissolved in dry chloroform (10 mL). Then, DIPEA (0.128 mmol, 0.02 mL) and PyBOP (0.096 mmol, 0.050 g) were added at RT and the reaction mixture was heated at 45°C for 72 hours. Then, the solvents were removed under reduced pressure and the residue was purified by flash chromatography (SiO_2) eluting with EtOAc:cyclohexane (40:60 vol/vol) and by precipitation from minimum amount of MeOH to obtain **3** as a yellow solid (53 %, 0.103 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm = 11.56 (s, 2H); 11.31 (s, 2H); 10.86 (s, 2H); 10.83 (s, 2H); 10.46 (s, 2H); 10.39 (s, 2H); 10.35 (s, 2H); 9.95 (s, 2H); 9.78 (s, 2H); 9.69 (s, 2H); 9.33 (s, 2H); 8.77 (d, ^3J = 8.9, 2H); 8.67 (s, 2H); 8.62 (d, ^3J = 8.9, 2H); 8.51 (m,

4H); 8.47 (s, 2H); 8.33 (d, ^{3}J = 6.9, 2H); 8.26 (br, 4H); 8.23 (s, 2H); 8.12 (m, 12H); 7.91 (d, ^{3}J = 6.8, 2H); 7.77 (m, 10H); 7.49 (m, 6H); 7.33 (m, 6H); 7.18 (d, ^{3}J = 7.2, 2H); 7.04 (m, 16H); 6.87 (s, 2H); 6.72 (t, ^{3}J = 7.9, 2H); 6.62 (m, 8H); 6.31 (m, 12H); 5.95 (t, ^{3}J = 7.9, 2H); 5.85 (t, ^{3}J = 7.8, 2H); 5.71 (t, ^{3}J = 7.8, 2H); 5.55 (s, 2H); 3.86 (m, 32H); 2.74 (m, 6H); 2.28 (m, 28H); 1.22 (m, 84H); 1.00 (t, ^{3}J = 7.2, 12H); 0.52 (m, 12H); 0.36 (d, ^{3}J = 6.7, 6H); 0.27 (d, ^{3}J = 6.7, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 163.7; 163.5; 163.1; 163.0; 162.9; 162.8; 162.7; 162.6; 162.5; 162.4; 164.2; 162.0; 161.7; 161.5; 161.4; 160.9; 160.7; 160.6; 160.5; 159.8; 159.6; 159.2; 154.8; 154.6; 154.5; 154.0; 153.7; 153.5; 153.4; 153.0; 152.9; 151.8; 151.7; 151.3; 151.0; 150.9; 150.7; 150.6; 150.2; 149.8; 149.6; 148.9; 148.1; 147.8; 147.6; 146.5; 146.4; 144.5; 139.4; 139.2; 138.7; 138.5; 138.1; 137.9; 137.4; 137.0; 136.8; 134.6; 134.5; 134.4; 134.3; 134.2; 134.1; 133.8; 133.5; 133.2; 127.9; 127.1; 126.5; 125.8; 125.3; 125.1; 124.5; 124.0; 123.9; 123.7; 123.5; 123.1; 122.1; 121.8; 121.6; 121.5; 121.0; 117.8; 116.6; 116.2; 115.9; 115.7; 115.4; 115.3; 114.5; 114.4; 114.2; 114.0; 113.9; 113.6; 113.5; 109.1; 108.8; 107.6; 107.2; 100.8; 100.5; 98.8; 98.2; 98.1; 97.5; 96.7; 96.4; 75.9; 75.7; 75.6; 75.2; 75.1; 74.9; 74.8; 74.2; 55.1; 28.5; 28.4; 28.2; 28.1; 28.0; 27.9; 27.6; 27.5; 19.6; 19.5; 19.4; 19.3; 19.2; 19.1; 19.0; 18.5; 18.4. MS (MALDI): *m/z* calcd for $C_{334}H_{314}N_{68}O_{52}$ $[M+H]^{+}$: 6112.41 found 6112.30.

Reference

(1) Palatinus, L.; Chapuis, G. *Appl. Crystallogr.* **2007**, 40, 786.

(2) Sheldrick, G.M. *Acta Cryst.* A64, **2008**, 112.

(3) SQUEEZE, Spek, A. L. *J. Appl. Cryst* **2003**, 36, 7.

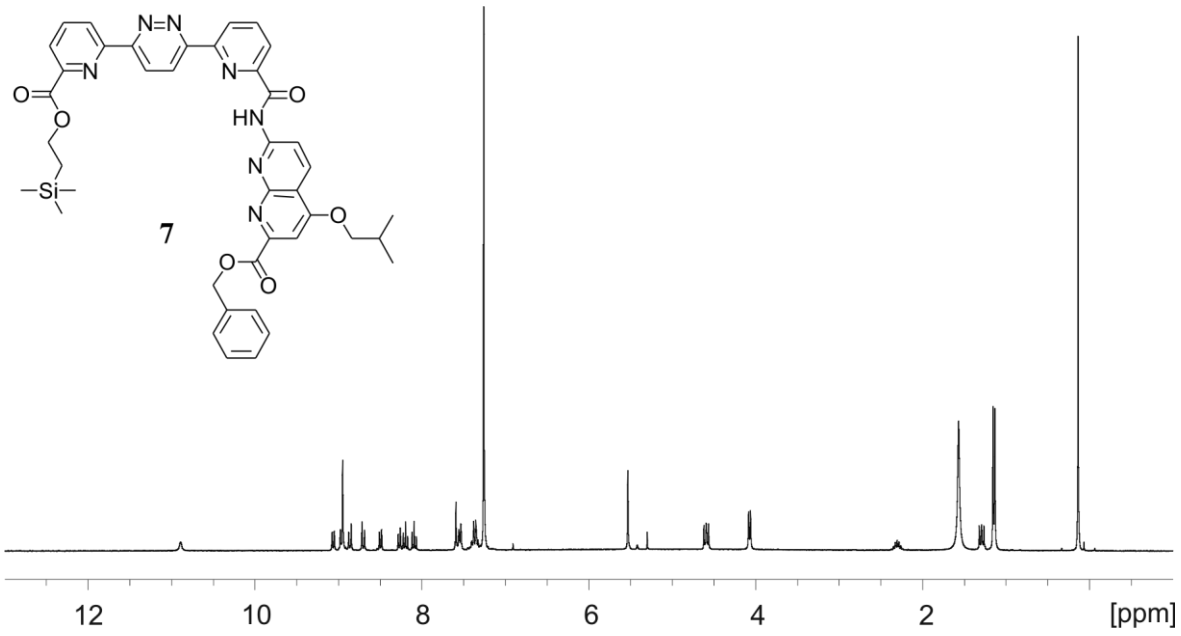
(4) Y. Ferrand, A. M. Kendhale, B. Kauffmann, A. Grélard, C. Marie, V. Blot, M. Pipelier, D. Dubreuil, Ivan Huc, *J. Am. Chem. Soc.* **2010**, 23, 7858.

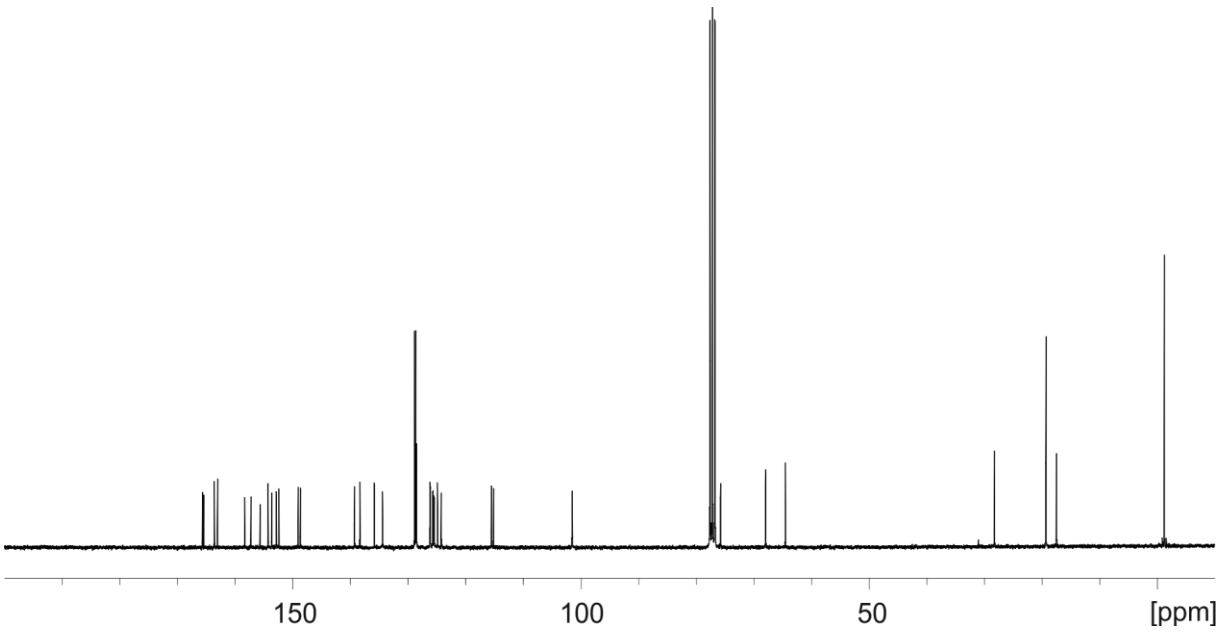
(5) Y. Ferrand, A. M. Kendhale, J. Garric, B. Kauffmann, I. Huc, *Angew. Chem. Int. Ed.* **2010**, 49, 1778.

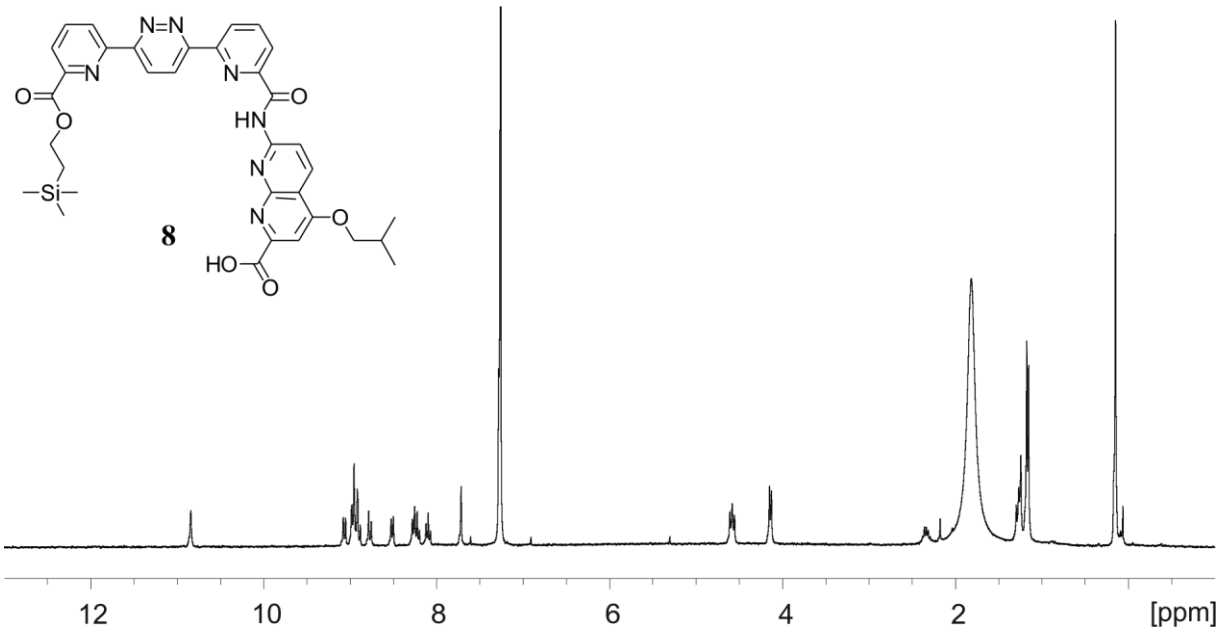
(6) C. Bao, B. Kauffmann, Q. Gan, K. Srinivas, H. Jiang, I. Huc, *Angew. Chem. Int. Ed.* **2008**, 47, 4153.

(7) V. Maurizot, C. Dolain, Y. Leydet, J-M. Léger, P. Guionneau, I. Huc *J. Am. Chem. Soc.*, **2004**, 32, 10049.

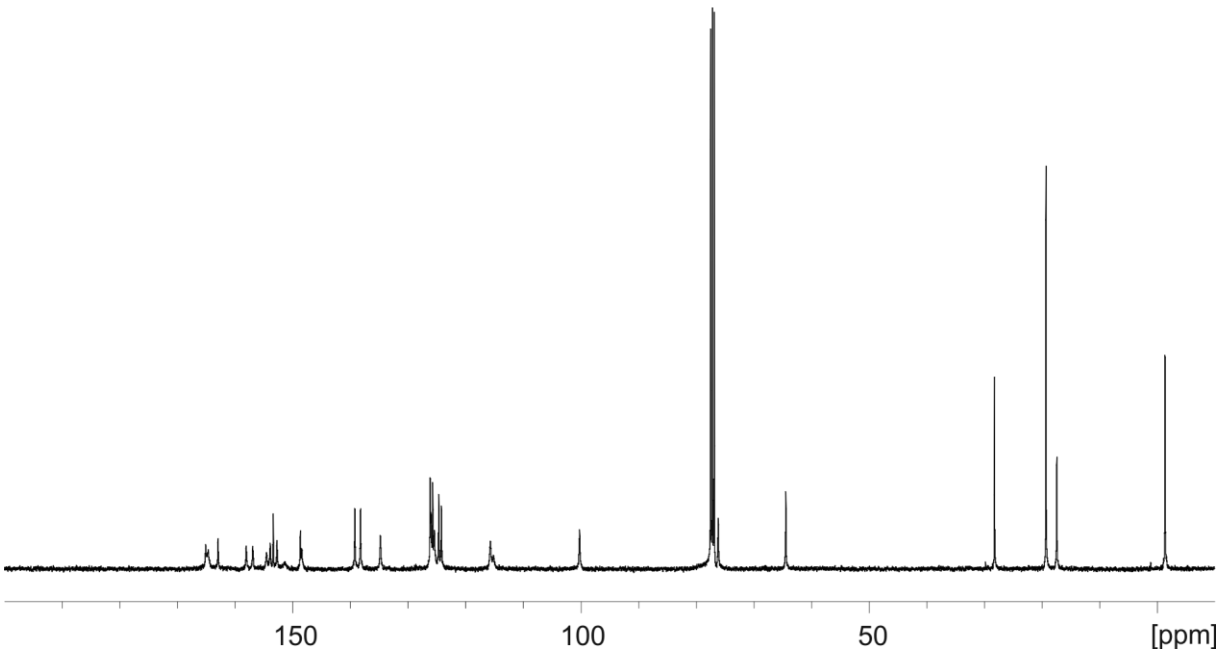
^{1}H NMR and ^{13}C NMR spectra of all relevant synthetic intermediates and title compounds.

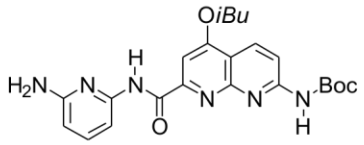




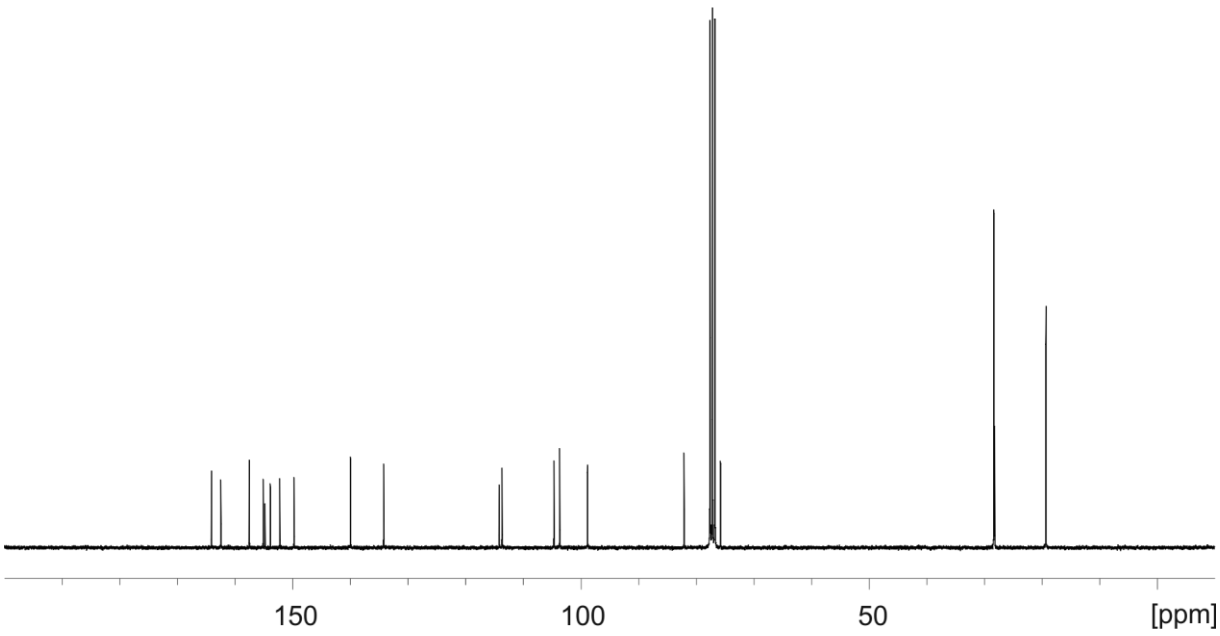


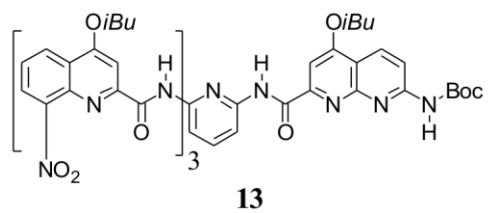
8



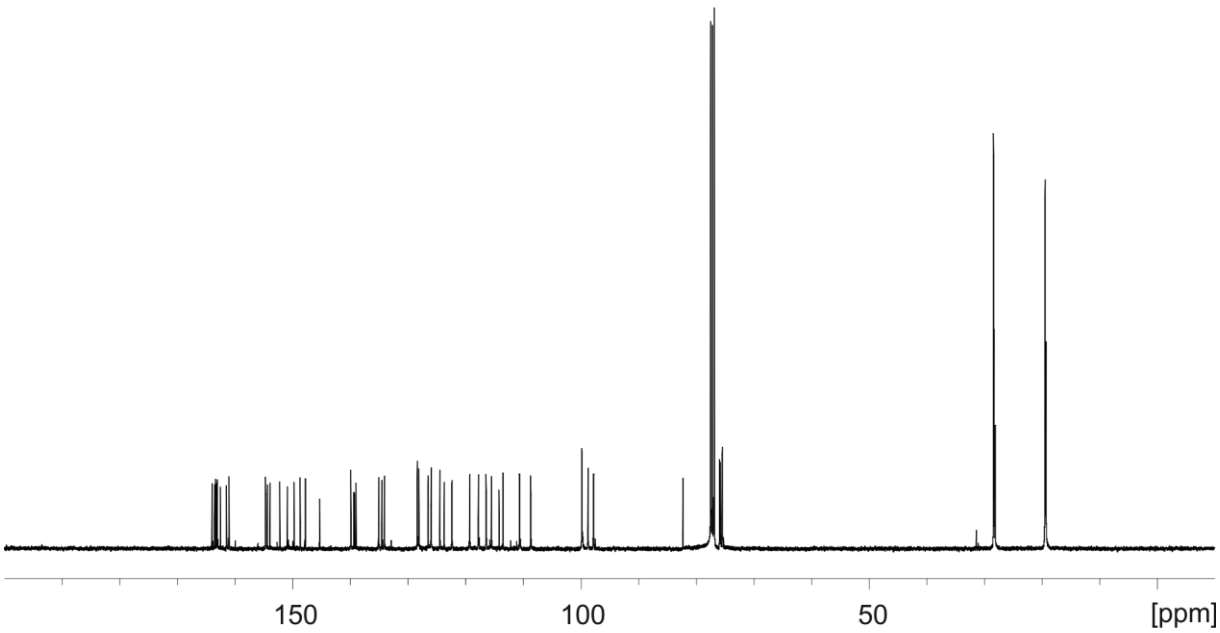


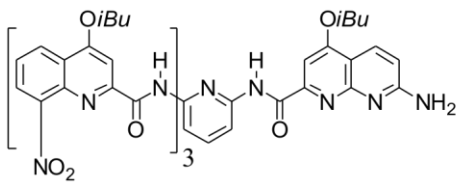
11



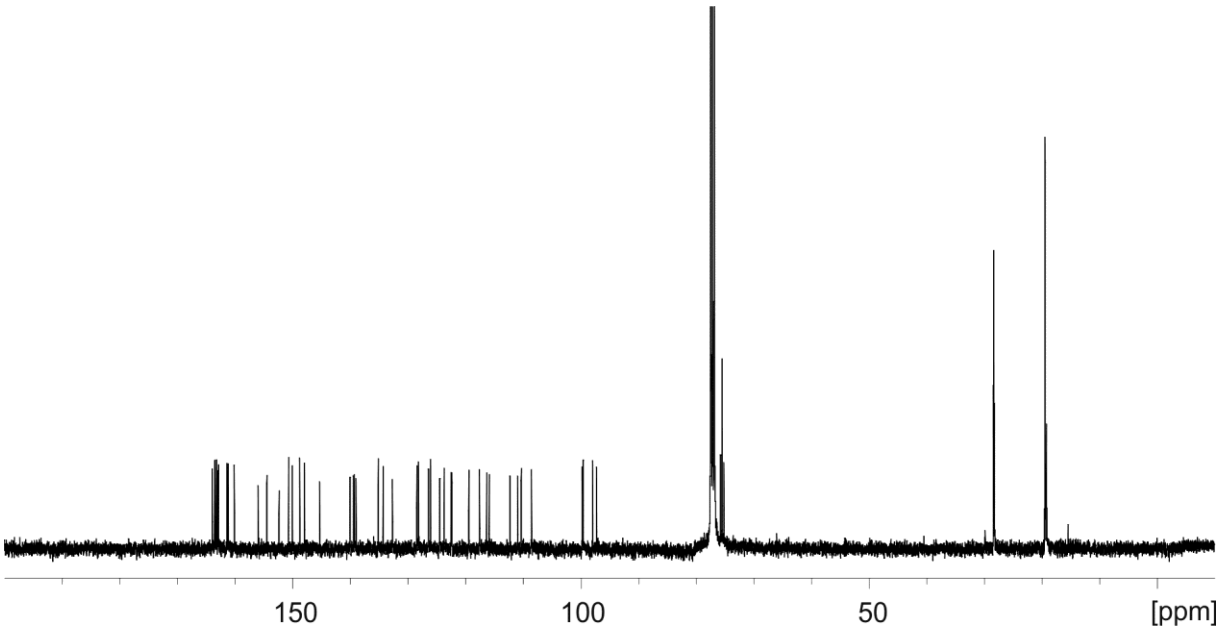


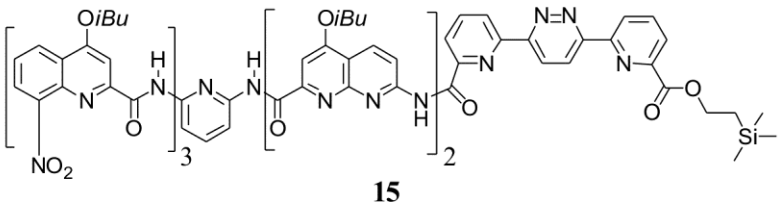
13



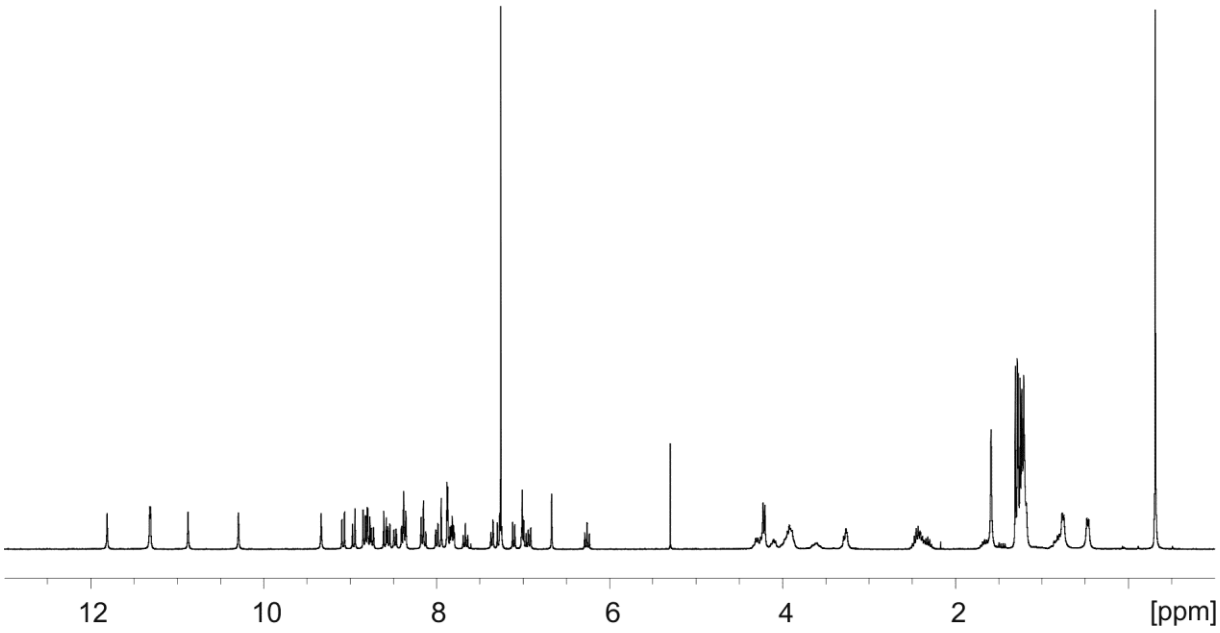


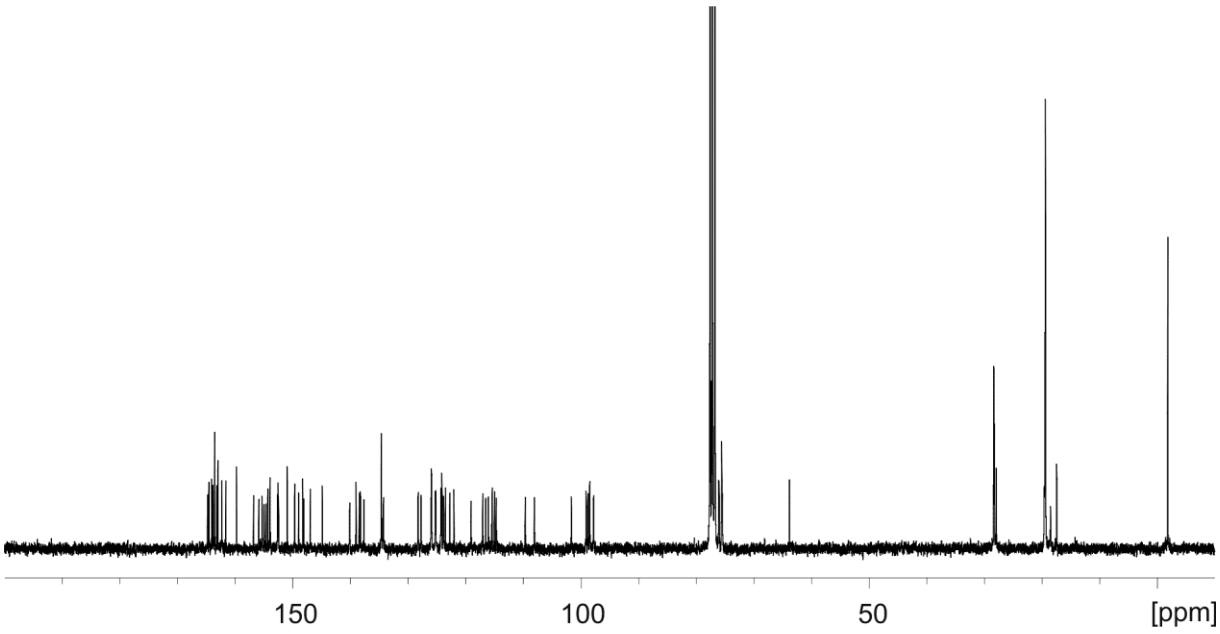
14

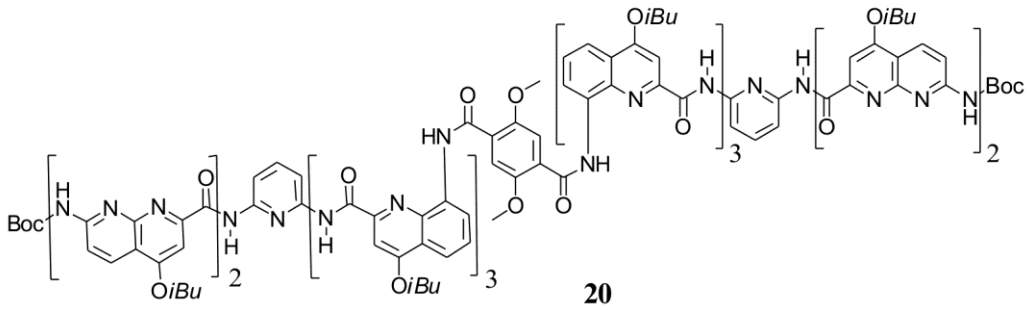




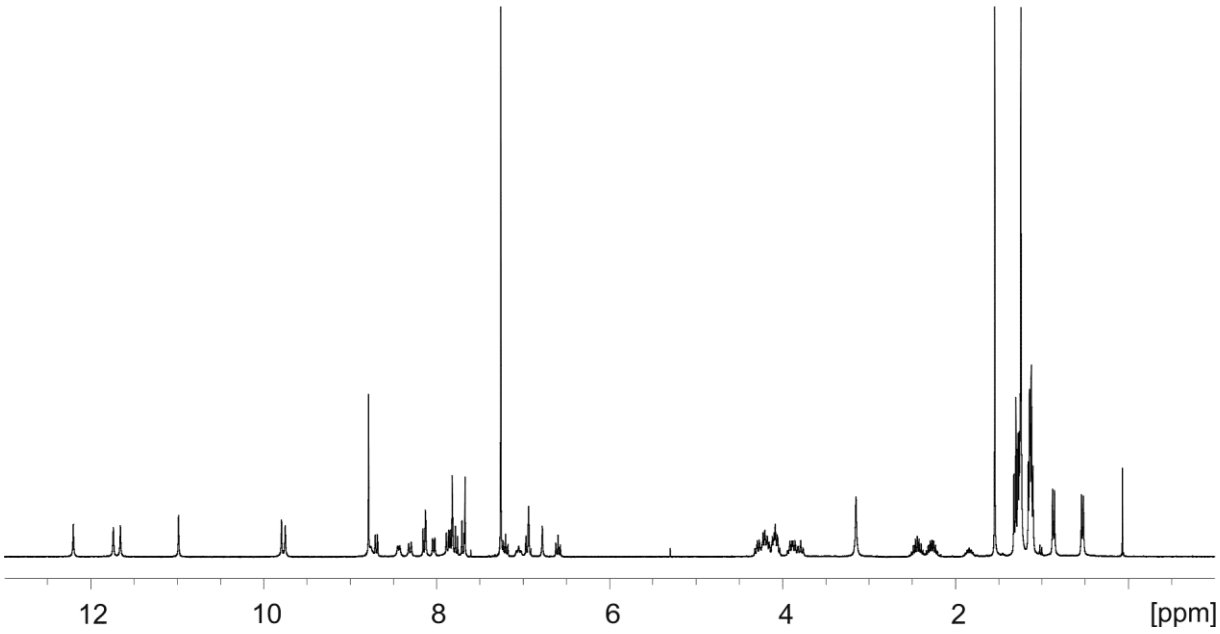
15

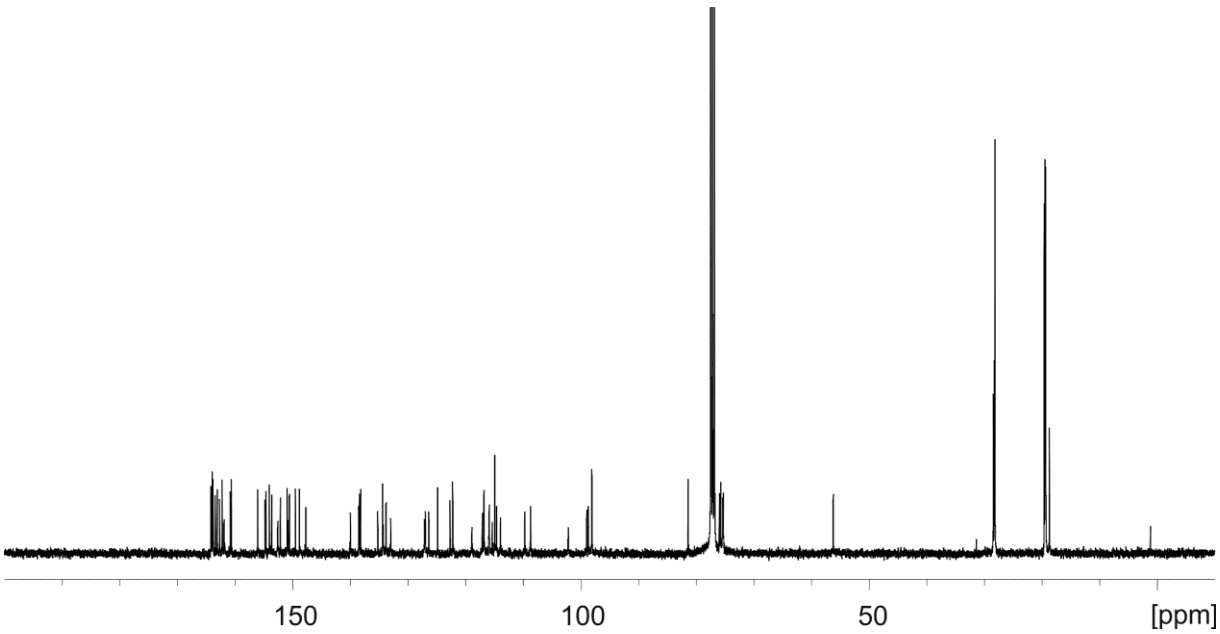


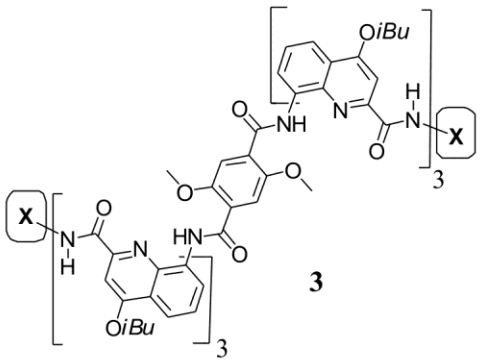




20







3

X =