Supplementary Information

Alkali and alkaline earth metal ion binding by a foldamer capsule: selective recognition of magnesium hydrate

Pedro Mateus,[a] Barbara Wicher,[b] Yann Ferrand[a] and Ivan Huc*[a] ¶

[a] *Univ. Bordeaux and CNRS, CBMN (UMR 5248), IECB, 2 rue Robert Escarpit, F-33600 Pessac, France.*

[b] *Department of Chemical Technology of Drugs, Poznan University of Medical Sciences, Grunwaldzka 6, 60-780 Poznan, Poland.*

E-mail: i.huc@iecb.u-bordeaux.fr.

This PDF file includes:

1. Methods for NMR, Circular Dichroism and X-ray crystallography

Nuclear Magnetic Resonance. NMR spectra were recorded on two machines: an Avance II NMR spectrometer (Bruker Biospin) with a vertical 7.05T narrow-bore/ultrashield magnet operating at 300 MHz for ^{1}H observation and 75 MHz for ^{13}C observation by means of a 5-mm direct BBO H/X probe with Z gradient capabilities and an Avance 400 NMR spectrometer (Bruker Biospin) with a vertical 9.4T narrow-bore/ultrashield magnet operating at 400 MHz for ^{1}H observation by means of a 5-mm direct QNP $^{1}H/^{13}C/^{31}P/^{19}F$ probe with gradient capabilities. Chemical shifts are reported in parts per million (ppm, δ) with tetramethylsilane as an internal standard. ^{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. Data processing was performed with Topspin 2.0 software. Samples were not degassed. $CDCl_3$ from Aldrich was used after filtration through an alumina pad.

NMR titration. The metal ion guests were added in the form of solutions of their triflate salts by means of a Hamilton microsyringe to solutions of oligomer **1**[1] (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) at 298K. After homogenization and equilibration the ^{1}H NMR spectrum (400 MHz) was recorded.

NMR competition titration. Solutions of the **1** ⊃ Na^+ complex were prepared by adding a slight excess of NaOTf to oligomer **1** (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) at 298K. The metal ion competitors were added in the form of solutions of their triflate salts by means of a Hamilton microsyringe. After homogenization and equilibration the ^{1}H NMR spectrum (400 MHz) was recorded.

Circular Dichroism. The metal ion guests were added in the form of solutions of their triflate salts by means of a Hamilton microsyringe and after homogenization and equilibration CD spectra were recorded in the 340–450 nm region on a Jasco J-815 spectropolarimeter at 298.2±0.1 K using a 2 mm pathlength cell. Changes in ellipticity were analysed considering a 1:1 binding model, using the HypSpec program[2]. The errors quoted are the standard deviations of the overall constants given directly by the program for the input data, which include all the wavelengths of each experimental point.

Crystallography. The X-ray diffraction measurements were carried out on a Rigaku FRX rotating anode (2.9 kW) diffractometer at the IECB X-ray facility (UMS 3033 – UMS001). CuKα radiation monochromated with high flux Osmic Varimax mirrors was used for data collection. The X-ray source is equipped with a Dectris Pilatus 200K detector and partial chi goniometer. The Rigaku CrystalClear suite[3] was used to index and integrate data with a multiscan absorption correction. Structures were solved with Shelxt and refined by full-matrix least-squares method on F^2 with Shelxl-2016.[4]

For the **1**⊃Ca^{2+} complex, decrease in diffraction power was observed in the last scans, most probably due to radiation damage of the crystal. These scans were removed during data reduction thus data has only 91.6% of completeness up to θ=50.43º. For this structure, no counter ions were found, thus only C-bound hydrogen atoms for the backbone were placed at idealized position and were refined in the riding-model approximation, with Uiso(H)=1.2Ueq(C). Also, anisotropic displacement parameters were used only for the backbone.

In case of the **1**⊃Na^+ complex, a triflate anion was localized in the electron density map. However, high residual electron density peaks were observed near this ion that could not be reasonably modelled and were introduced in the refinement as dummy oxygen atoms. For this reason, the occupancy factor for the triflate molecule was refined and at final stages got a value of 0.7.

For the **1**⊃Na^+, **1**⊃K^+ and **1**⊃Ba^{2+} complexes, anisotropic displacement parameters were used for the backbone, some atoms of the isobutoxy side chains, triflate and some solvent molecules. Hydrogen atoms were placed at idealized position and were refined in the riding-model approximation, with Uiso(H)=1.2Ueq(CH, CH2, NH) and Uiso(H)=1.5Ueq(CH3). DFIX, AFIX, SIMU, RIGU, EADP and DELU instructions were employed to model the geometry of the molecules and temperature parameters.

Heavily disordered solvent molecules in **1**⊃K^+ and **1**⊃Ba^{2+} complexes were removed using the SQUEEZE[5] procedure. For the search and analysis of solvent accessible voids in the structures default parameters were used: grid 0.20 Å, probe radius 1.2 Å and NStep 6. Calculated total potential solvent accessible void volumes and electron counts per unit cell were 6199 $Å^3$ and 1590, and 3822 $Å^3$ and 882 for **1**⊃K^+ and **1**⊃Ba^{2+} complexes, respectively.

Despite many attempts to collect high quality data, only weak diffraction intensity and data with moderate resolution were obtained due to: radiation damage of the crystals; large volume fractions occupied with disordered solvent molecules; disorder of the isobutoxy substituents; and large size of the foldamer molecules. For these reasons, unavoidable A - level and B - level alerts remain in the check cif file but they are inherent to the data quality and refinement procedures and do not reflect errors. These alerts are listed below.

Group 1 alerts illustrate weak quality of the data and refinement statistics if compared to that expected for small molecule structures from highly diffracting crystals:

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

Calculated sin(theta_max)/wavelength = 0.5000

PLAT023_ALERT_3_A Resolution (too) Low [sin(theta)/Lambda < 0.6].. 50.43 Degree

PLAT084_ALERT_3_A High wR2 Value (i.e. > 0.25) ..... 0.50 Report

PLAT234_ALERT_4_A Large Hirshfeld Difference

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

PLAT082_ALERT_2_B High R1 Value

PLAT084_ALERT_3_B High wR2 Value (i.e. > 0.25)

PLAT090_ALERT_3_B Poor Data / Parameter Ratio (Zmax > 18)

PLAT230_ALERT_2_B Hirshfeld Test Diff for ...

PLAT234_ALERT_4_B Large Hirshfeld Difference ...

PLAT241_ALERT_2_B High 'MainMol' Ueq as Compared to Neighbors of...

PLAT242_ALERT_2_B Low 'MainMol' Ueq as Compared to Neighbors of ...

PLAT340_ALERT_3_B Low Bond Precision on C-C Bonds

PLAT911_ALERT_3_B Missing # FCF Refl Between THmin & STh/L= 0.500 375 Report

PLAT919_ALERT_3_B Reflection # Likely Affected by the Beamstop ...

PLAT934_ALERT_3_B Number of (Iobs-Icalc)/SigmaW > 10 Outliers ...

Group 2 alerts is connected with decision made during refinement and explained below:

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

As indicated above not all non-H atoms were refined with anisotropic displacement parameters.

PLAT602_ALERT_2_A VERY LARGE Solvent Accessible VOID(S) in Structure ! Info:

Not all electron density could be reasonably modeled thus in the structures solvent accessible voids are observed.

PLAT973_ALERT_2_A Check Calcd Positive Residual Density on Ba1 2.48 eA-3:

The atom type is correct and there is no evidence of twinning. The large residual density near Ba atom may be due to an anomalous dispersion effect and has no chemical significance.

PLAT306_ALERT_2_B Isolated Oxygen Atom (H-atoms Missing ?);
PLAT326_ALERT_2_B Possible Missing H on sp3? Carbon;
PLAT327_ALERT_2_B Possible Missing H on sp3? Carbon:
As indicated above not all H atoms were determined.

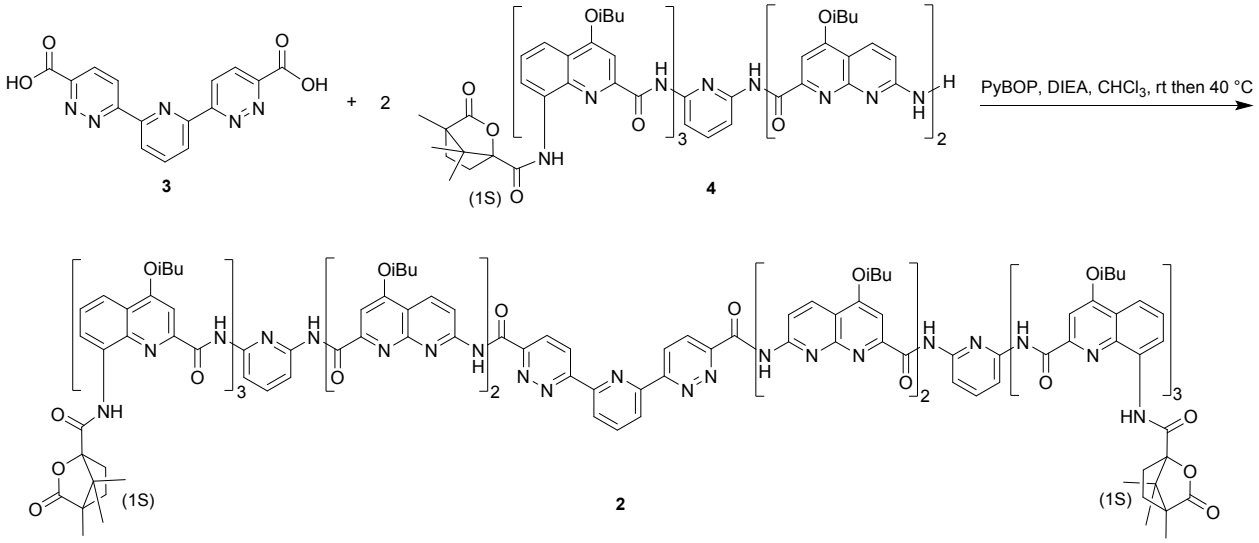
PLAT430_ALERT_2_B Short Inter D...A Contact :
Alerts concerns O···O distances between water molecules that most probably hydrogen bonded but H atoms were not determined.

PLAT987_ALERT_1_B The Flack x is >> 0 - Do a BASF/TWIN Refinement Please Check:
Alert concerns **1**⊃Ca^{2+} complex with very low completeness thus Flack parameter cannot be reliably determined.

2. Materials and Methods for chemical synthesis

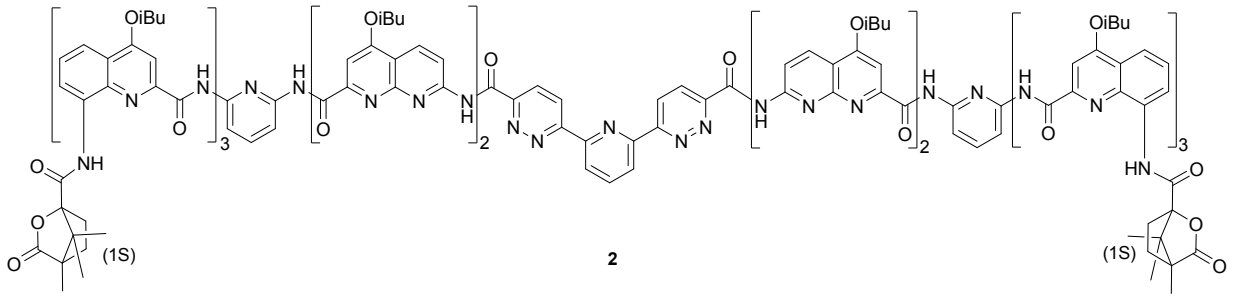
All reactions were carried out under a dry nitrogen atmosphere. Commercial reagents were purchased from Sigma-Aldrich, Alfa-Aesar or TCI and were used without further purification unless otherwise specified. Chloroform ($CHCl_3$) and diisopropylethylamine (DIEA) were distilled over calcium hydride (CaH_2) prior to use. Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel 60-F254 plates and observed under UV light. GPC purification was performed on an LC-9130G NEXT setup (Japan Analytical Industry Co., Ltd.) equipped with two preparative columns (Inner diameter of 20mm and length of 600mm): a JAIGEL 2.5H and a JAIGEL 3H, in conjugation with UV-600 NEXT UV detector and an FC-3310 fraction collector. Chloroform with 1% EtOH and 0.5% Et_3N was used as mobile phase, with a flow rate of 7.0 mL/min. ESI mass spectra were obtained from the Mass Spectrometry Laboratory at the European Institute of Chemistry and Biology (UMS 3033 - IECB), Pessac, France.

2.1 Synthesis of oligomer 2



Scheme S1. Synthesis of oligomer **2**.

2.2 Experimental procedures



Oligomer 2: Diacid **3**[1] (9.2 mg, 0.028 mmol), and hexamer amine **4**[6] (87 mg, 0.058 mmol) and PyBOP (148 mg, 0.285 mmol) were dissolved in dry $CHCl_3$ (1 mL). Then, DIEA (0.05 mL, 0.285 mmol) was added at room temperature and the reaction mixture was heated to 40 °C. After two days, the mixture was washed with saturated aqueous. NH_4Cl, followed by saturated aqueous $NaHCO_3$ and finally water. The organic phase was dried on anhydrous $MgSO_4$, filtered and evaporated to dryness. The residue was purified by GPC to yield **2** as a yellow solid (60 %, 56 mg). ^1H NMR (300 MHz, $CDCl_3$) δ ppm = 12.07 (s, 2H); 12.04 (s, 2H); 11.35 (s,

2H), 11.10 (s, 2H); 9.85 (s, 2H); 9.83 (s, 2H); 9.82 (s, 2H); 8.86-8.68 (m, 12H); 8.51-8.47 (m, 4H); 8.17 (t, *J* = 4.41, 2H); 7.90-7.83 (m, 12H); 7.68-7.65 (m, 4H); 7.37 (d, *J* = 7.96, 2H); 7.29 (s, 1H); 7.14 (s, 2H); 7.11-7.05 (m, 4H); 6.83 (d, *J* = 8.30, 2H); 6.71 (s, 2H); 6.42 (t, *J* = 7.96, 2H); 4.34-4.20 (m, 8H); 4.15-4.10 (m, 2H); 4.00-3.94 (m, 2H); 3.63-3.50 (m, 8H); 2.48-2.34 (m, 6H); 2.02 (m, 2H); 1.87-1.76 (m, 4H); 1.68-1.61 (m, 2H); 1.44-1.33 (m, 4H); 1.27-1.20 (m, 37H); 0.86-0.82 (m, 18H); 0.67-0.65 (m, 17H); 0.31 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 176.2, 164.4, 164.3, 163.9, 163.8, 163.5, 163.3, 163.2, 162.5, 161.8, 161.7, 160.3, 158.7, 154.7, 154.2, 154.1, 153.8, 153.0, 151.4, 151.3, 150.8, 149.6, 148.9, 147.5, 139.9, 138.8, 137.9, 137.4, 134.5, 134.3, 134.1, 132.3, 127.0, 126.2, 126.0, 124.8, 122.6, 122.3, 121.8, 121.6, 116.8, 116.6, 116.4, 115.9, 115.5, 115.3, 114.9, 114.6, 110.3, 108.9, 100.1, 99.1, 98.7, 98.6, 98.1, 91.6, 75.9, 75.8, 75.2, 75.0, 74.9, 54.6, 54.0, 29.7, 29.0, 28.6, 28.3, 28.2, 27.9, 19.3, 19.1, 18.9, 18.7, 16.1, 9.6. HRMS (ESI+): *m/z* calcd for $C_{181}H_{181}N_{35}O_{28}$ [M+2H]+ 1646.19075 found 1646.19673.

1⊃Na$^+$ complex. Oligomer **1** (2.99 mg, 1.0 μmol) was first dissolved in an NMR tube in $CDCl_3$ (300 μL), then a solution (0.005 M) of NaOTf in CD_3CN (200 μL) was added. The tube was agitated manually at room temperature and NMR was recorded ten minutes after the addition. ^{1}H NMR (400 MHz, $CDCl_3$/CD_3CN 6:4): δ ppm 11.72 (s, 2H), 11.20 (s, 2H), 10.42 (s, 2H), 10.28 (s, 2H), 9.96 (s, 2H), 9.89 (s, 2H), 9.19 (s, 2H), 8.99 (d, J = 7.1 Hz, 2H), 8.77 (d, J = 7.1 Hz, 2H), 8.41 (d, J = 9.5 Hz, 2H), 8.27 - 8.23 (m, 4H), 8.19 - 8.17 (m, 2H), 8.13 (d, J = 7.1 Hz, 2H), 8.05 (d, J = 8.6 Hz, 2H), 7.94 (t, J = 6.2 Hz, 1H), 7.85 (s, 3H), 7.83 (s, 1H), 7.73 (d, J = 7.7 Hz, 2H), 7.32 (d, J = 6.7 Hz, 2H), 7.29 (s, 2H), 7.18 (s, 2H), 7.16 - 7.08 (m, 6H), 7.03 (s, 1H), 7.01 (s, 1H), 6.98 – 6.94 (m, 4H), 6.73 (d, J = 6.7 Hz, 2H), 6.59 (s, 1H), 6.00 (t, J = 6.7 Hz, 2H), 4.62 - 4.58 (m, 1H), 4.56 - 4.52 (m, 2H), 4.41 - 4.37 (m, 2H), 4.30 - 4.27 (m, 2H), 4.21 – 4.17 (m, 2H), 3.73 - 3.64 (m, 4H), 3.40 (d, J = 6.7 Hz, 2H), 3.11 - 3.07 (m, 2H), 2.96 - 2.92 (m, 2H), 2.57 - 2.46 (m, 4H), 2.20 - 2.11 (m, 7H), 1.42 - 1.00 (m, 48H), 0.62 (d, J = 6.9 Hz, 6H), 0.48 (d, J = 6.9 Hz, 6H). HRMS (ESI+): calcd. for $C_{161}H_{152}N_{35}O_{26}Na$ [M + Na + H]$^{2+}$ 1508.0807, found 1508.0211

1⊃K$^+$ complex. Oligomer **1** (2.99 mg, 1.0 μmol) was first dissolved in an NMR tube in $CDCl_3$ (300 μL), then a solution (0.005 M) of KOTf in CD_3CN (200 μL) was added. The tube was agitated manually at room temperature and NMR was recorded ten minutes after the addition. ^{1}H NMR (400 MHz, $CDCl_3$/CD_3CN 6:4): δ ppm 11.71 (s, 2H), 11.28 (s, 2H), 10.20 (s, 2H), 10.17 (s, 2H), 9.76 (s, 2H), 9.39 (s, 2H), 8.94 – 8.87 (m, 4H), 8.56 (d, J = 8.9 Hz, 2H), 8.25 – 8.02 (m, 13H), 7.93 (s, 3H), 7.91 (s, 1H), 7.40 (s, 2H), 7.28 (s, 2H), 7.18 – 7.13 (m, 4H), 7.07 (d, J = 7.7 Hz, 2H), 7.02 (d, J = 7.7 Hz, 2H), 6.85 – 6.78 (m, 4H), 6.61 (s, 2H), 6.54 (t, J = 8.1 Hz, 2H), 6.03 (t, J = 8.1 Hz, 2H), 5.91 (s, 2H), 4.61 - 4.58 (m, 1H), 4.52 - 4.48 (m, 2H), 4.32 - 4.25 (m, 4H), 4.20 - 4.17 (m, 2H), 3.75 - 3.66 (m, 4H), 3.43 - 3.35 (m, 4H), 2.97 – 2.93 (m, 2H), 2.56 – 2.43 (m, 5H), 2.32 - 2.28 (m, 2H), 2.23 - 2.14 (m, 4H), 1.38 - 1.05 (m, 48H), 0.59 (d, J = 6.4 Hz, 6H), 0.40 (d, J = 6.3 Hz, 6H). HRMS (ESI+): calcd. for $C_{161}H_{152}N_{35}O_{26}K$ [M + K + H]$^{2+}$ 1515.5659, found 1515.5699.

1⊃Mg^{2+} complex. Oligomer **1** (2.99 mg, 1.0 μmol) was first dissolved in an NMR tube in $CDCl_3$ (300 μL), then a solution (0.005 M) of $Mg(OTf)_2$ in CD_3CN (200 μL) was added. The tube was agitated manually at room temperature and NMR was recorded ten minutes after the addition. ^{1}H NMR (400 MHz, $CDCl_3$/CD_3CN 6:4): 11.39 (s, 2H), 10.91 (s, 2H), 10.24 (s, 2H), 10.01 (s, 2H), 9.94 (s, 2H), 9.46 (s, 2H), 9.08 (d, J = 8.5 Hz, 2H), 8.54 (d, J = 9.4 Hz, 2H), 8.42 (d, J = 10.6 Hz, 2H), 8.41 (d, J = 11.0 Hz, 2H), 8.32 - 8.28 (m, 4H), 8.15 (d, J = 7.9 Hz, 2H), 8.00 – 7.96 (m, 2H), 7.91 – 7.87 (m, 5H), 7.68 (s, 2H), 7.50 – 7.44 (m, 5H), 7.34 -7.32 (m, 2H), 7.29 - 7.25 (m, 4H), 7.01 – 6.93 (m, 5H), 6.80 (d, J = 8.1 Hz, 2H), 6.74 (s, 2H), 6.70 (d, J = 8.1 Hz, 2H), 6.10 (s, 2H), 6.00 (t, J = 7.7 Hz, 2H), 4.61 - 4.58 (m, 1H), 4.56 - 4.52 (m, 2H), 4.35 - 4.29 (m, 6H), 3.87 - 3.78 (m, 4H), 3.58 - 3.51 (m, 4H), 3.13 - 3.06 (m, 2H), 2.98 – 2.94 (m, 2H), 2.63 – 2.47 (m, 5H),

2.31 - 2.17 (m, 4H), 1.37 - 1.07 (m, 48H), 0.59 (d, J = 6.4 Hz, 6H), 0.41 (d, J = 6.3 Hz, 6H). HRMS (ESI+): calcd. for $C_{161}H_{151}N_{35}O_{26}Mg$ $[M + Mg]^{2+}$ 1508.0744, found 1508.0357.

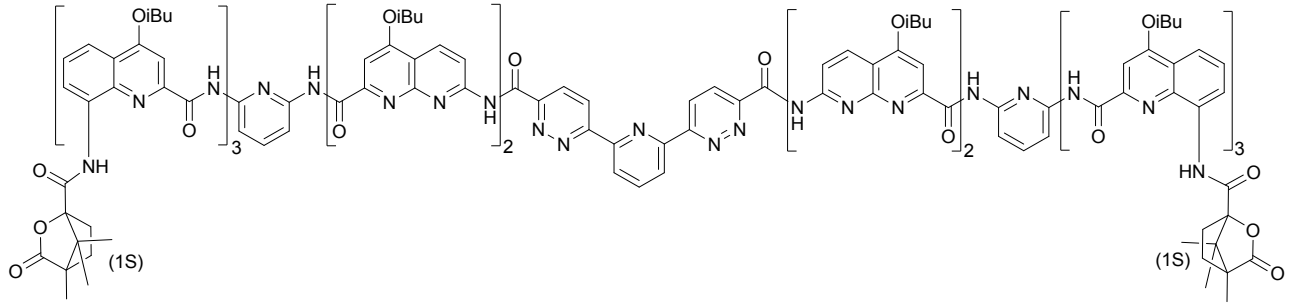
1⊃Ca^{2+} complex. Oligomer **1** (2.99 mg, 1.0 μmol) was first dissolved in an NMR tube in $CDCl_3$ (300 μL), then a solution (0.005 M) of $Ca(OTf)_2$ in CD_3CN (200 μL) was added. The tube was agitated manually at room temperature and NMR was recorded ten minutes after the addition. ^1H NMR (400 MHz, $CDCl_3/CD_3CN$ 6:4): 11.49 (s, 2H), 10.78 (s, 2H), 10.37 (s, 2H), 9.96 (s, 2H), 9.76 (s, 2H), 9.69 (s, 2H), 9.07 (d, J = 8.5 Hz, 2H), 8.50 (d, J = 8.6 Hz, 2H), 8.49 (d, J = 8.2 Hz, 2H), 8.44 – 8.39 (m, 4H), 8.29 (d, J = 8.2 Hz, 2H), 8.18 (d, J = 7.1 Hz, 2H), 8.00 – 7.86 (m, 7H), 7.49 (s, 2H), 7.45 (s, 2H), 7.36 – 7.23 (m, 12H), 6.92 (t, J = 7.1 Hz, 2H), 6.81 (t, J = 7.8 Hz, 2H), 6.68 (s, 2H), 6.67 (d, J = 8.1 Hz, 2H), 6.16 (s, 2H), 6.07 (t, J = 7.9 Hz, 2H), 4.61 - 4.56 (m, 3H), 4.44 - 4.26 (m, 6H), 3.75 - 3.74 (m, 4H), 3.56 - 3.55 (m, 4H), 3.14 - 3.08 (m, 2H), 2.95 – 2.91 (m, 2H), 2.61 – 2.47 (m, 5H), 2.25 - 2.18 (m, 4H), 1.40 - 1.11 (m, 48H), 0.61 (d, J = 6.4 Hz, 6H), 0.43 (d, J = 6.3 Hz, 6H). HRMS (ESI+): calcd. for $C_{161}H_{151}N_{35}O_{26}Ca$ $[M + Ca]^{2+}$ 1516.0632, found 1516.0102.

1⊃Ba^{2+} complex. Oligomer **1** (2.99 mg, 1.0 μmol) was first dissolved in an NMR tube in $CDCl_3$ (300 μL), then a solution (0.005 M) of $Ba(OTf)_2$ in CD_3CN (200 μL) was added. The tube was agitated manually at room temperature and NMR was recorded ten minutes after the addition. ^1H NMR spectrum could not be precisely assigned due to the presence of multiple overlapping peaks as a result of incomplete folding (see text).

3. Solution studies: Circular Dichroism (CD) and Nuclear Magnetic Resonance (NMR)

3.1 Circular dichroism titrations

Titrations with oligomer **2**



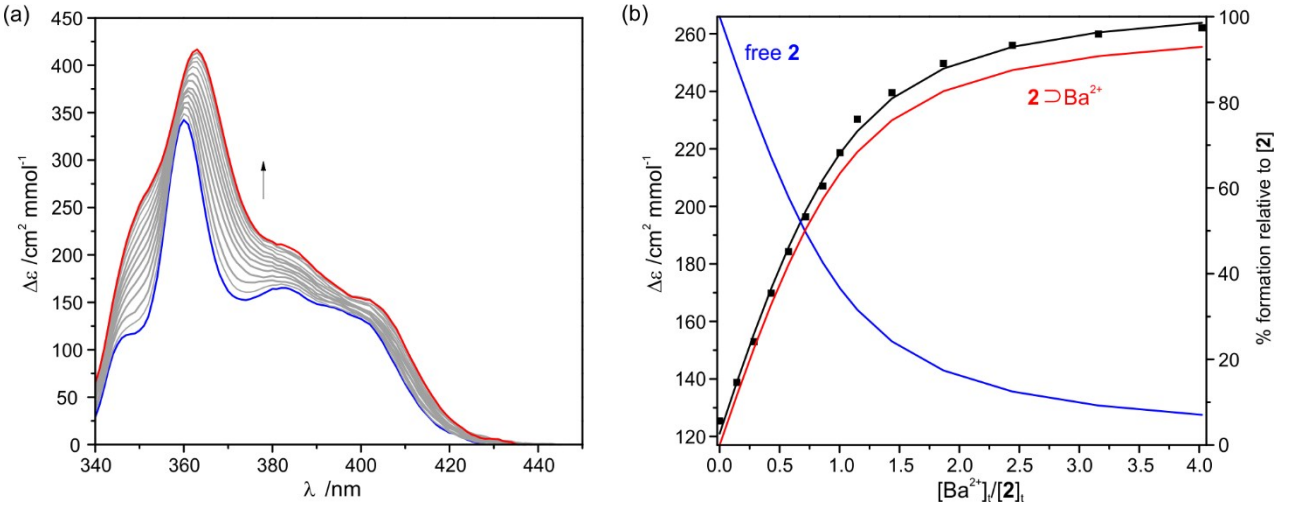


Figure S1. (a) CD spectra recorded at 298 K for the binding study of oligomer **2** vs. Ba^{2+} in $CHCl_3$/MeCN (6:4 vol/vol). $[\mathbf{2}]_{initial}$ = 0.015 mM, $[Ba(OTf)_2]_{titrant}$ = 0.41 mM; (b) Experimental and calculated values for the ICD binding study of oligomer **2** vs. Ba^{2+} in $CHCl_3$/MeCN (6:4 vol/vol) with the corresponding species distribution diagram. Although only Δε values at 350 nm are shown here, all wavelengths in the 340-450 nm region were used for the calculation of the binding constant. Log K_a = 5.53±0.01. Limiting Δε = 275 cm^2 $mmol^{-1}$.

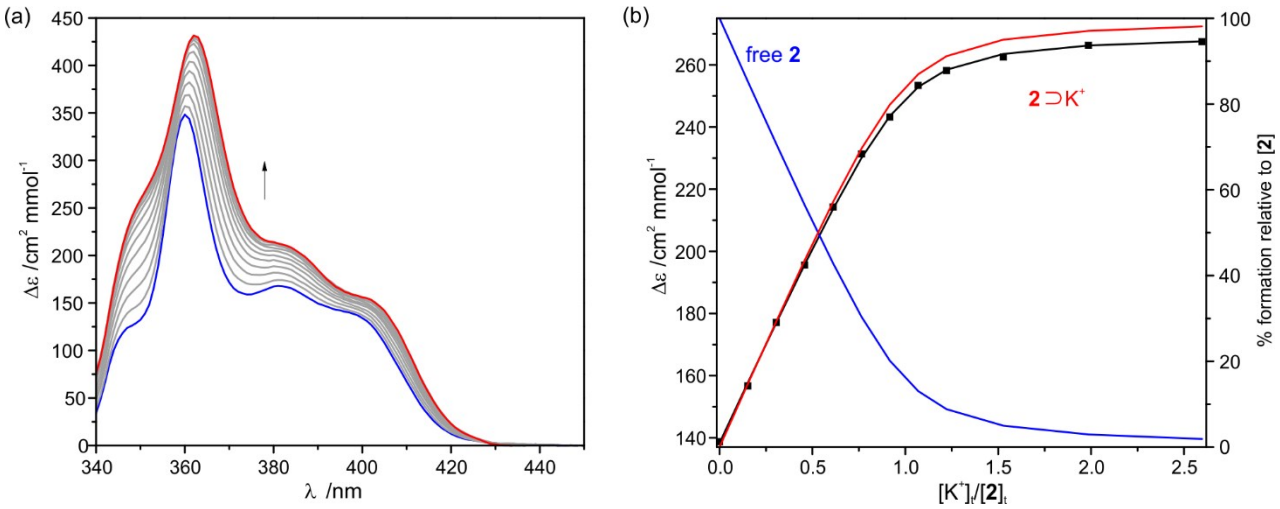


Figure S2. (a) CD spectra recorded at 298 K for the binding study of oligomer **2** vs. K^+ in $CHCl_3$/MeCN (6:4 vol/vol). $[\mathbf{2}]_{initial}$ = 0.015 mM, $[KOTf]_{titrant}$ = 0.41 mM; (b) Experimental and calculated values for the ICD binding study of oligomer **2** vs. K^+ in $CHCl_3$/MeCN (6:4 vol/vol) with the corresponding species distribution diagram. Although only Δε values at 350 nm are shown here, all wavelengths in the 340-450 nm region were used for the calculation of the binding constant. Log K_a = 6.08±0.01. Limiting Δε = 270 cm^2 $mmol^{-1}$.

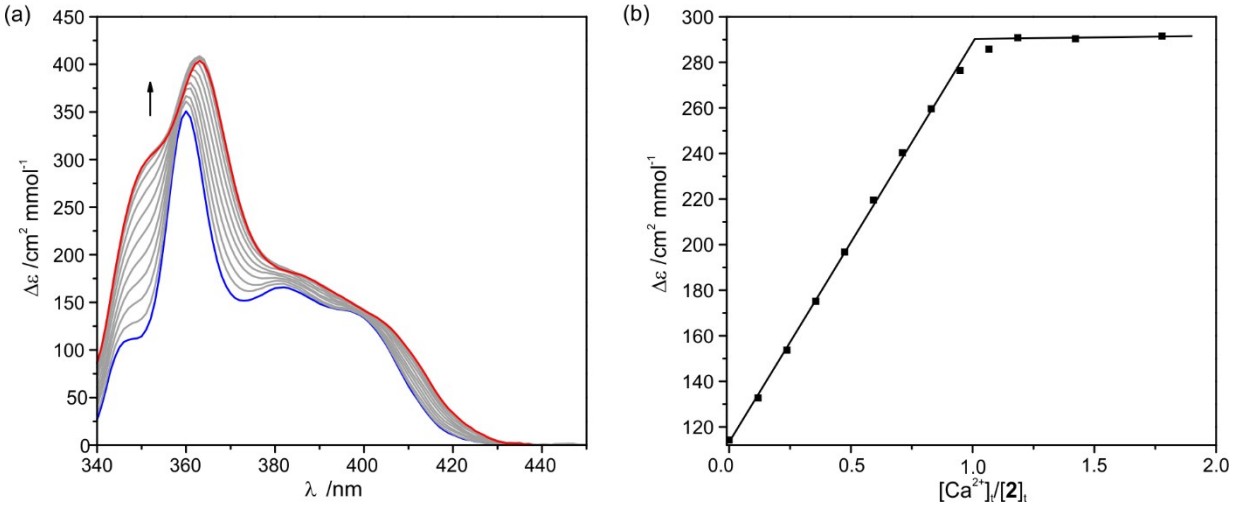


Figure S3. (a) CD spectra recorded at 298 K for the binding study of oligomer **2** vs. Ca^{2+} in $CHCl_3$/MeCN (6:4 vol/vol). $[\mathbf{2}]_{initial}$ = 0.030 mM, $[Ca(OTf)_2]_{titrant}$ = 0.80 mM; (b) Experimental values for the ICD binding study of oligomer **2** vs. Ca^{2+} in $CHCl_3$/MeCN (6:4 vol/vol). Δε values at 350 nm are shown. $K_a > 10^7\ M^{-1}$. Lines are for guiding the eye only.

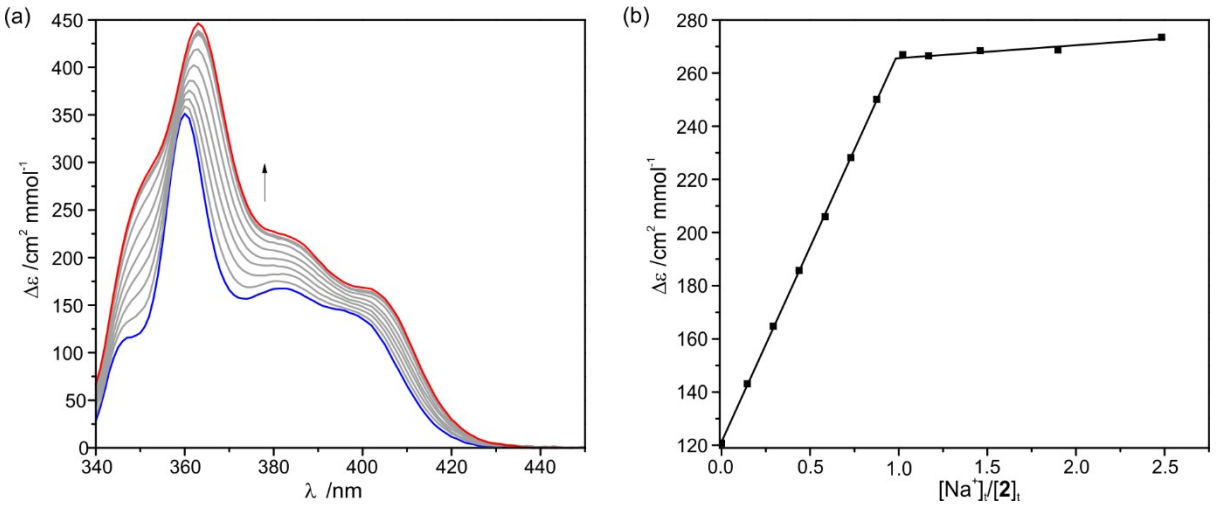


Figure S4. (a) CD spectra recorded at 298 K for the binding study of oligomer **2** vs. Na^+ in $CHCl_3$/MeCN (6:4 vol/vol). $[\mathbf{2}]_{initial}$ = 0.030 mM, $[NaOTf]_{titrant}$ = 0.80 mM; (b) Experimental values for the ICD binding study of oligomer **2** vs. Na^+ in $CHCl_3$/MeCN (60:40). Δε values at 350 nm are shown. $K_a > 10^7\ M^{-1}$. Lines are for guiding the eye only.

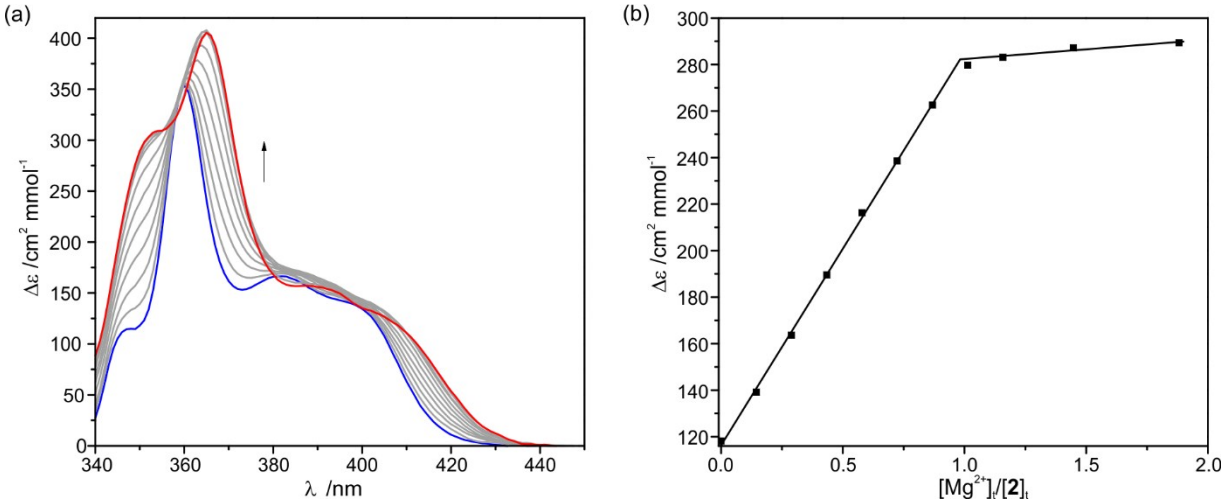


Figure S5. (a) CD spectra recorded at 298 K for the binding study of oligomer **2** vs. Mg^{2+} in $CHCl_3$/MeCN (6:4 vol/vol). $[\mathbf{2}]_{initial}$ = 0.030 mM, $[Mg(OTf)_2]_{titrant}$ = 0.80 mM; (b) Experimental values for the ICD binding study of oligomer **2** vs. Mg^{2+} in $CHCl_3$/MeCN (6:4 vol/vol). Δε values at 369 nm are shown. $K_a > 10^7\ M^{-1}$. Lines are for guiding the eye only.

3.2 ^{1}H NMR titrations

Titrations with oligomer **1**

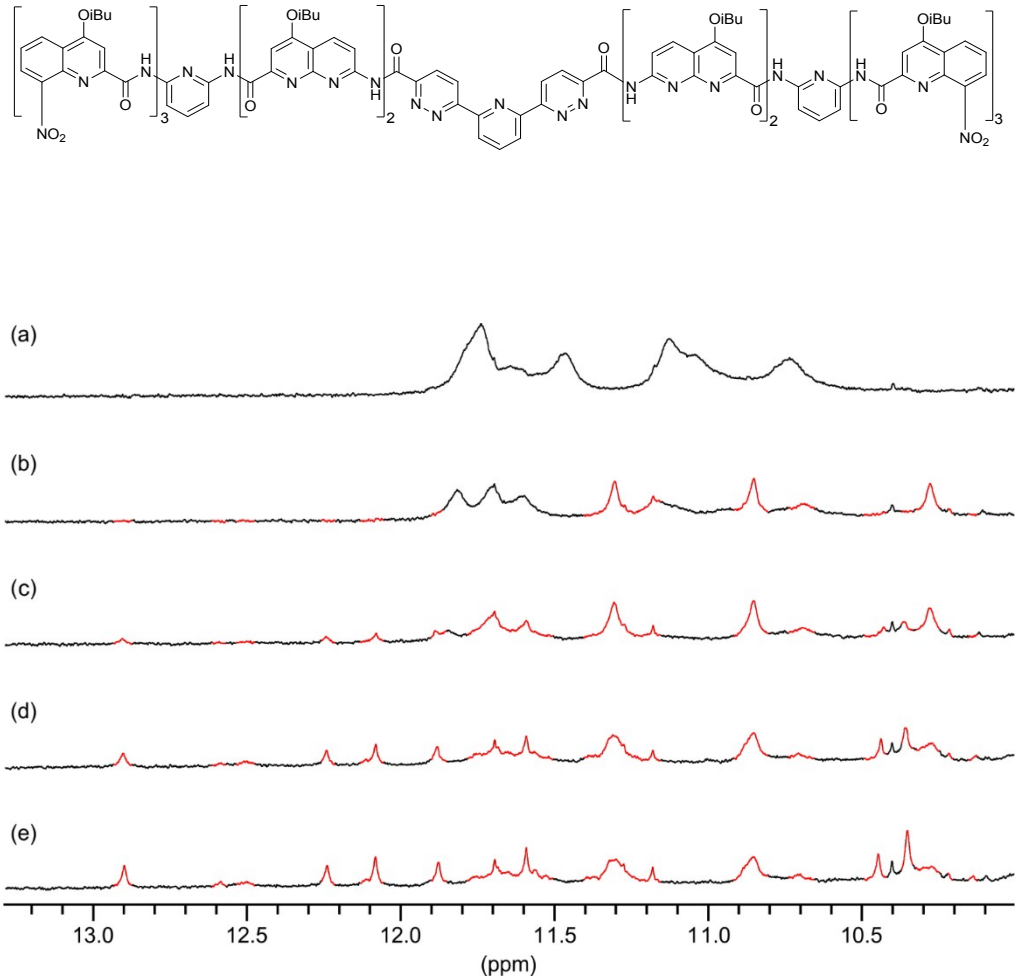


Figure S6. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of oligomer **1** (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 0.25 equiv.; (c) 0.50 equiv.; (d) 0.75 equiv.; (e) 1 equiv. of $Ba(OTf)_2$. Peaks belonging to the **1** ⊃ Ba^{2+} complex are marked in red. $K_a > 10^5\ M^{-1}$.

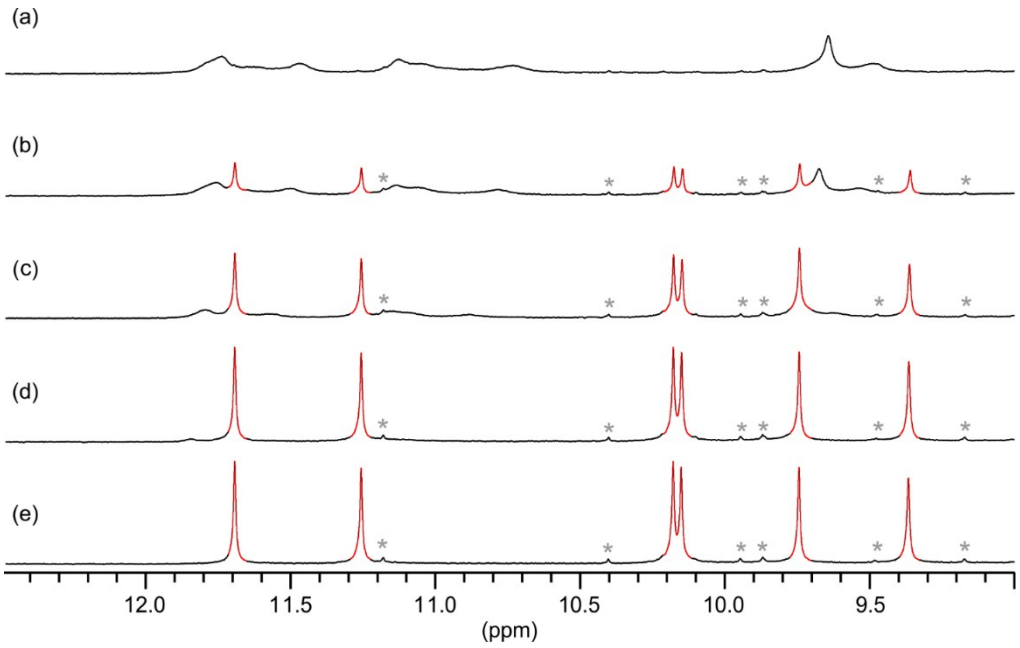


Figure S7. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of oligomer **1** (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 0.25 equiv.; (c) 0.50 equiv.; (d) 0.75 equiv.; (e) 1 equiv. of KOTf. Peaks belonging to the **1** ⊃ K^+ complex are marked in red. $K_a > 10^5$ M^{-1}. Additional peaks marked as * correspond to the **1** ⊃ Na^+ complex which is present even though no Na^+ was added, as this metal ion is a well-known, ubiquitous contaminant of, for instance, glassware.

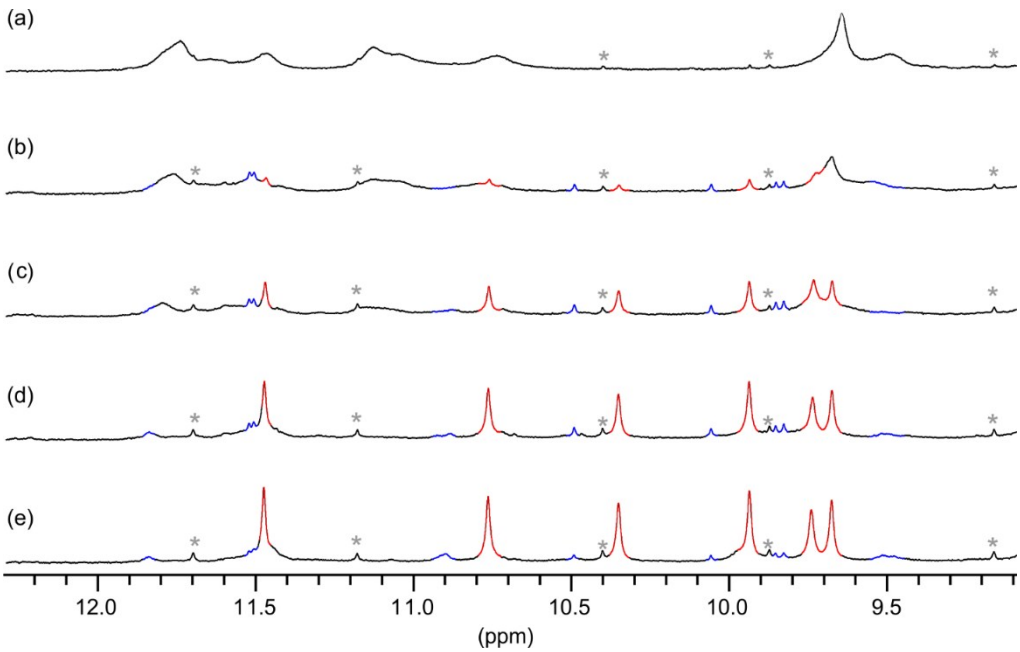


Figure S8. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of oligomer **1** (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 0.25 equiv.; (c) 0.50 equiv.; (d) 0.75 equiv.; (e) 1 equiv. of $Ca(OTf)_2$. Peaks belonging to the **1** ⊃ Ca^{2+} complex are marked in red. $K_a > 10^5$ M^{-1}. Peaks marked in blue correspond to the empty, protonated oligomer, formed probably from proton transfer from the calcium hydrate to the pyz-pyr-pyz unit. Additional peaks marked as * correspond to the [**1** ⊃ $Na]^+$ complex which is present even though no Na^+ was added, as this metal ion is a well-known, ubiquitous contaminant of, for instance, glassware.

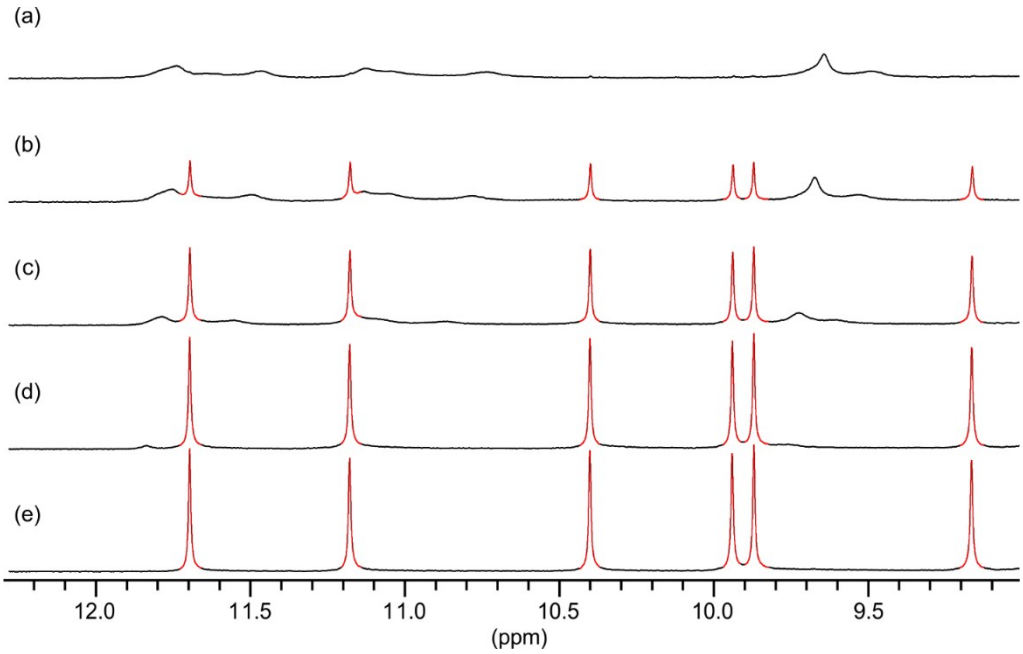


Figure S9. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of oligomer **1** (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 0.25 equiv.; (c) 0.50 equiv.; (d) 0.75 equiv.; (e) 1 equiv. of NaOTf. Peaks belonging to the **1**⊃Na^{+} complex are marked in red. $K_a > 10^5$.

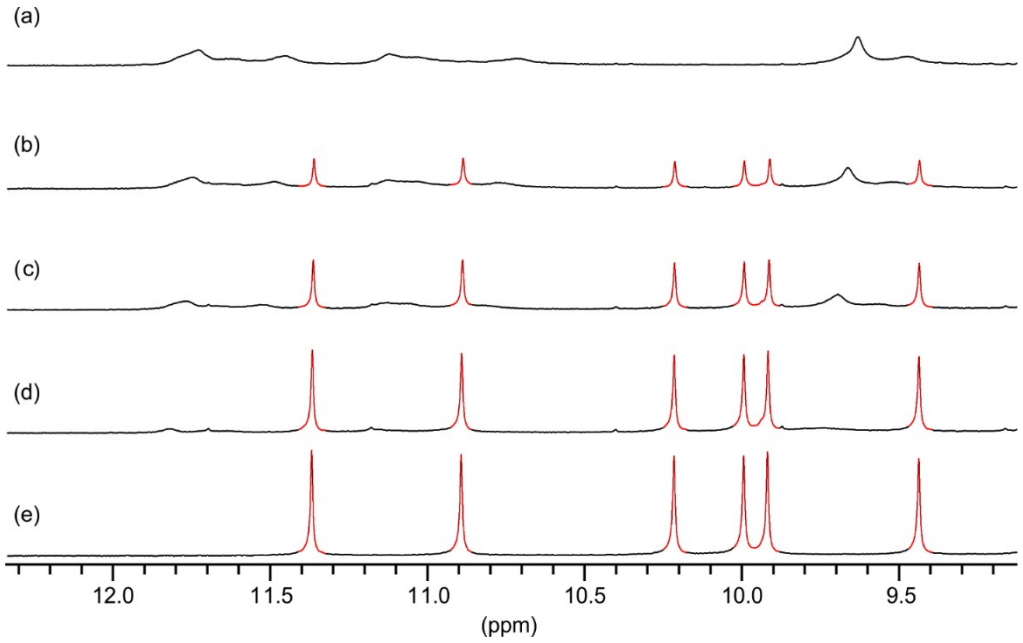


Figure S10. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of oligomer **1** (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 0.25 equiv.; (c) 0.50 equiv.; (d) 0.75 equiv.; (e) 1 equiv. of $Mg(OTf)_2$. Peaks belonging to the **1**⊃Mg^{2+} complex are marked in red. $K_a > 10^5\ M^{-1}$.

3.3 ^{1}H NMR competition titrations

As can be seen in Figs S6 to S10, addition of the metal ion guests to a 1 mM solution of **1** produces a separated set of proton resonances for the free and bound capsule indicating that the binding process is slow in the NMR time scale. In all cases, addition of 1 equiv. of guest leads to saturation of the capsule in agreement with association constants that are higher than 10^5 M^{-1}, thus impossible to be accurately measured by NMR. As an alternative, competition experiments were performed to determine the selectivity ratios.

Considering a host H that can bind two different guests A and B in a 1:1 binding stoichiometry, the two processes can be described by the following equilibria:

$H + A \rightleftharpoons HA$; $K_{HA} = [HA]/[A][H]$
$H + B \rightleftharpoons HB$; $K_{HB} = [HB]/[B][H]$

The selectivity ratio is defined as the ratio between binding constants:

$K_{A/B} = K_{HA}/K_{HB} = [HA][B]/[HB][A]$ which is the equilibrium constant of the following competition equilibrium:

$HB + A \rightleftharpoons HA + B$

Starting with conditions such that the HB complex is fully formed and adding guest A leads to displacement of guest B from the host. When the binding process is slow in the NMR time scale the concentrations of HA, HB, A and B in equilibrium can be known by integration of the HA and HB peaks and thus $K_{A/B}$ can be determined.

Since it was possible to determine the association constants for the binding of Ba^{2+} and K^+ by CD spectroscopy, the knowledge of the selectivity ratios allows the determination of all association constants (see Table 1).

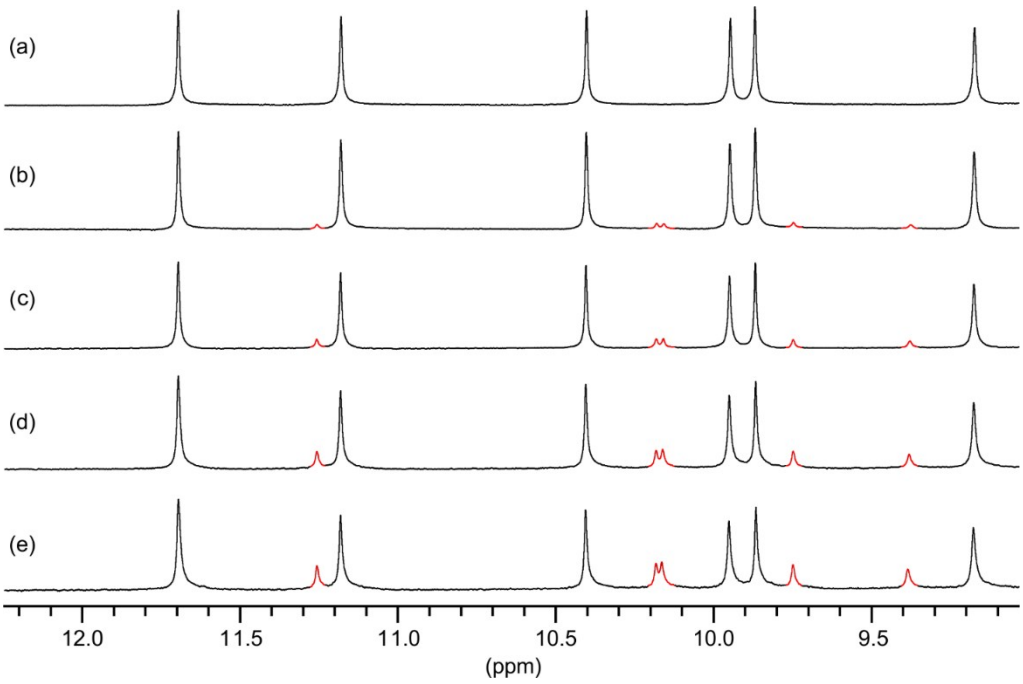


Figure S11. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of **1**⊃Na^+ (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 1 equiv.; (c) 3 equiv.; (d) 8 equiv.; (e) 15 equiv. of KOTf. Signals of **1**⊃K^+ amide resonances are marked in red. K_a(**1**⊃Na^+)/K_a(**1**⊃K^+) = 271.

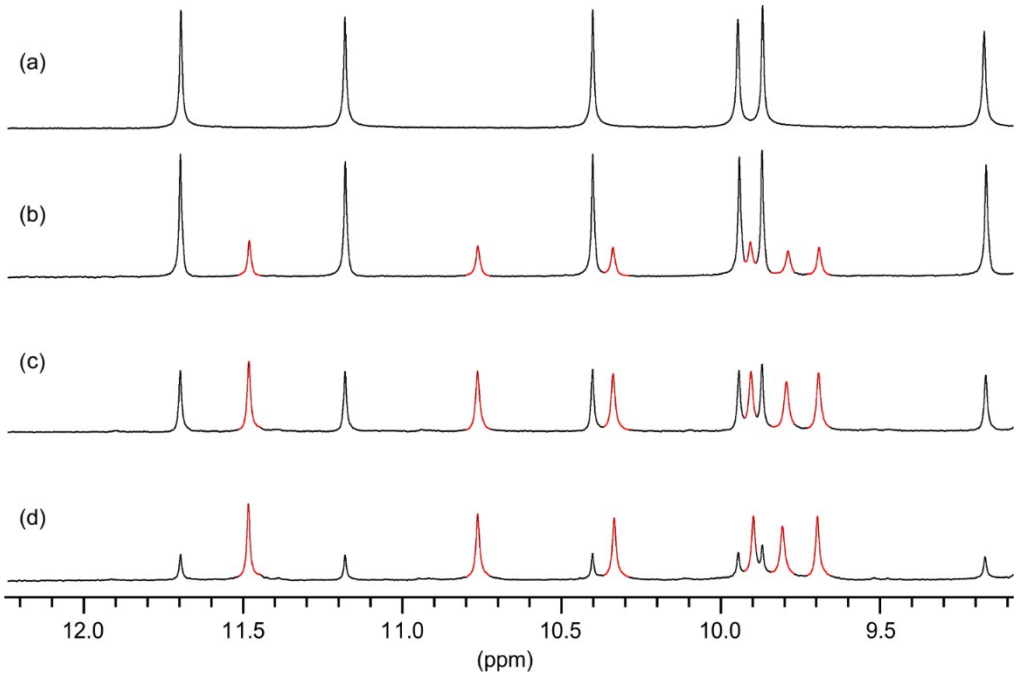


Figure S12. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of **1**⊃Na^+ (1 mM) in $CDCl_3/d_3$-MeCN (60:40) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 0.5 equiv.; (c) 1.5 equiv.; (d) 4.5 equiv. of $Ca(OTf)_2$. Signals of **1**⊃Na^+ and of **1**⊃Ca^{2+} amide resonances are marked with filled circle and empty circle, respectively. K_a(**1**⊃Na^+)/K_a(**1**⊃Ca^{2+}) = 1.7.

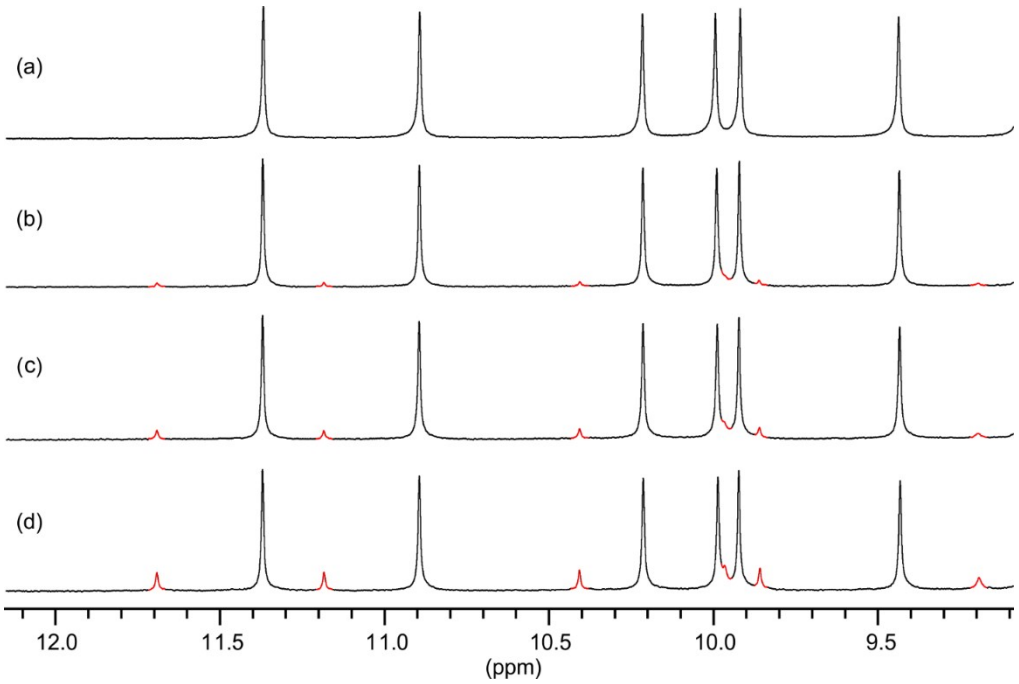


Figure S13. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of **1** ⊃ Na^+ (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 10 equiv.; (c) 20 equiv.; (d) 40 equiv. of NaOTf. Signals of **1**⊃Mg^{2+} amide resonances are marked in red. K_a(**1**⊃Na^+)/K_a(**1**⊃Mg^{2+}) = 0.002.

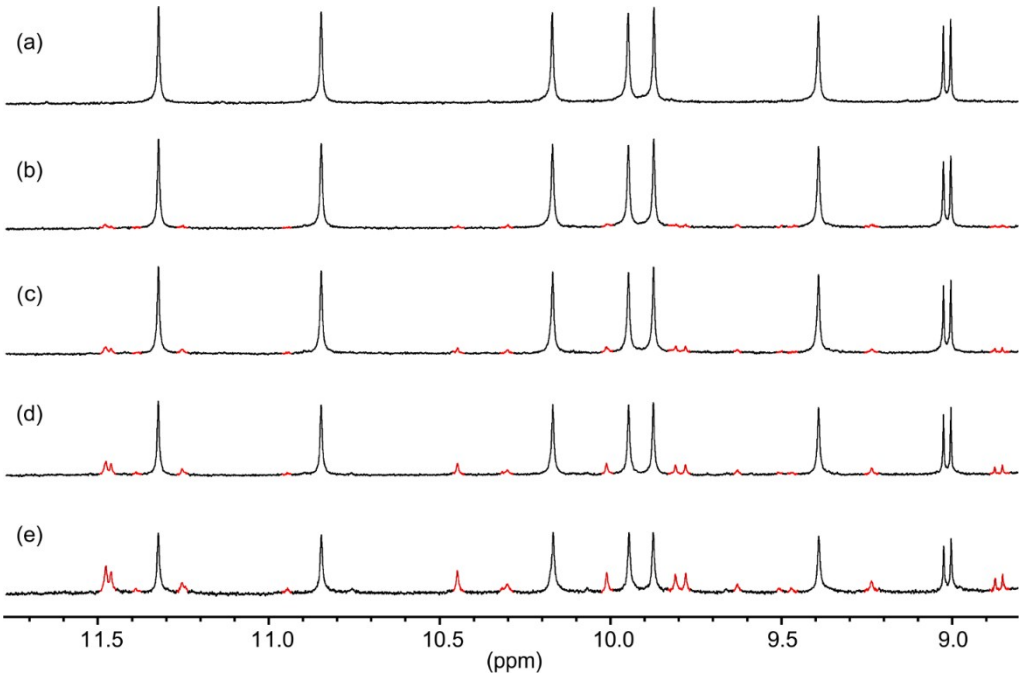


Figure S14. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of **1**⊃Mg^{2+} (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 1 equiv.; (c) 2 equiv.; (d) 4 equiv. and (e) 6 equiv. of $Cu(MeCN)_4BF_4$. Signals of **1**⊃Cu^+ amide resonances are marked in red.

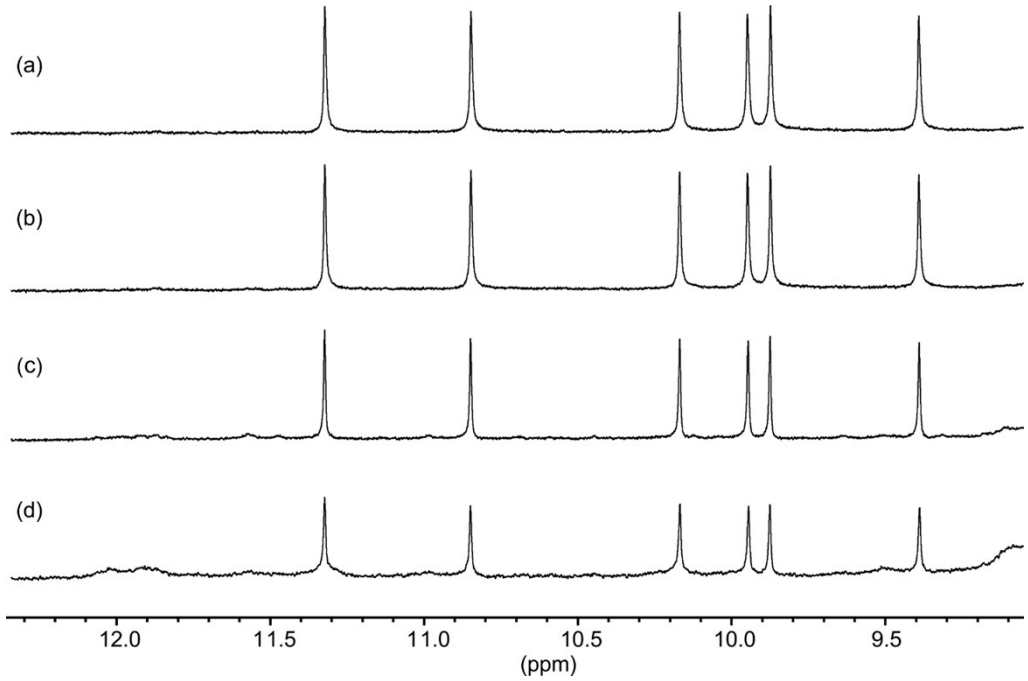


Figure S15. Part of the ^{1}H NMR spectrum (400 MHz) at 298K of **1**⊃Mg^{2+} (1 mM) in $CDCl_3/CD_3CN$ (6:4 vol/vol) showing the amide resonances in the presence of: (a) 0 equiv.; (b) 1 equiv.; (c) 5 equiv.; (d) 10 equiv. of $Zn(OTf)_2$.

4. Solid state X-Ray Crystallography

4.1 X-Ray crystallographic data for the 1⊃Na^+ complex

Table S1. Crystal data and refinement details for the **1**⊃Na^+ complex.

Identification code	**1** ⊃ Na^+
Chemical formula	$C_{161}H_{151}N_{35}O_{26}Na \cdot 0.7(CF_3O_3S) \cdot C_6H_5Cl \cdot 4.17(CHCl_3) \cdot 6(H_2O) \cdot 6.43(O)$*
Formula weight	3934.93
Temperature	100(2)
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a=20.5626 (4), α=90
	b=49.2607 (11), β=105.218 (3)
	c=22.2525 (6), γ=90
Volume	21749.8 (9)
Z	4
Density (calculated)	1.202
Absorption coefficient	2.27
Absorption correction	Multi-scan
Crystal size	0.20 × 0.07 × 0.02
Index ranges	h = -20→20, k = -48→42, l = -21→21
Completeness to theta = 50.43°	98.9
Reflections collected	89947
Reflections observed [$I > 2\sigma(I)$]	18677
R_{int}	0.055
Data/parameters/restrains	22533/2249/148
Goodness-of-fit on F^2	3.74
Final R indices [$I > 2\sigma(I)$]	R1 = 0.1971, wR2 = 0.4819
R indices (all data)	R1 = 0.2100, wR2 = 0.4971
Lasgest diff. peak and hole	1.56, -0.87
CCDC #	1561023

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

(a) (b)

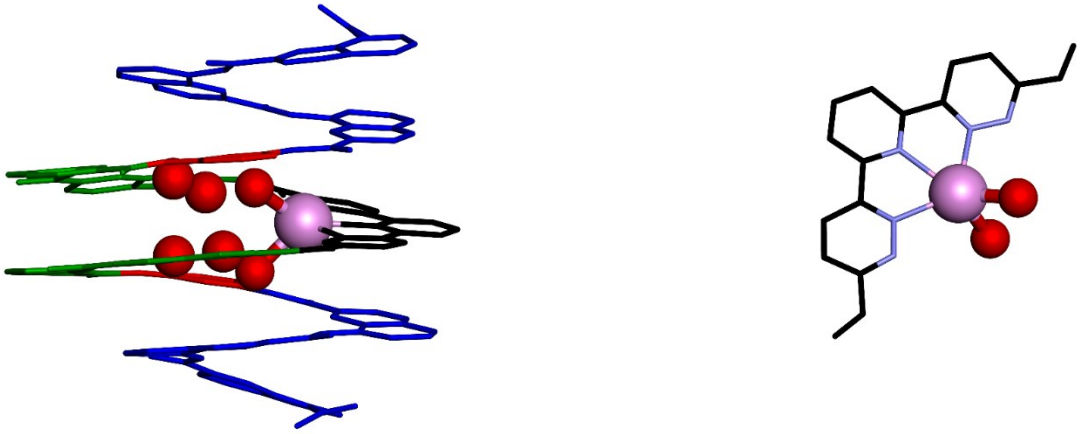


Figure S16. Solid-state structure of the ***P*-1**⊃Na^+ complex: (a) side view; (b) Na coordination sphere. Isobutoxy side chains and cavity-excluded solvent molecules are omitted for clarity. The capsule backbone is represented in sticks. Sodium atoms are represented in pink balls and oxygen atoms of water molecules are depicted as red balls.

Table S2. First-coordination sphere bond lengths (Å) in the **1**⊃Na^+ complex.[a]

Bond	Bond length (Å)[b]
Na01–O1W	2.344(8)
Na01–O2W	2.330(8)
Na01–N17A	2.701(8)
Na01–N18A	2.625(8)
Na01–N19A	2.586(8)

[a] Atom numbers are those of the cif file. [b] Values in parenthesis are standard deviations in the last significant figure.

Table S3. O···N distances shorter than 3.25 Å between water molecules and capsule heteroatoms in the **1**⊃Na^+ complex.[a]

	d (Å)[b]
O1W···N7A	2.93(1)
O2W···N29A	3.02(1)
O2W···N28A	3.16(1)
O2W···N30A	3.24(1)
O3W···N22A	3.11(1)
O4W···N25A	3.14(1)
O4W···N26A	3.22(1)
O5W···N10A	3.15(1)
O5W···N11A	3.25(1)
O6W···N14A	2.96(1)

[a] Atom numbers are those of the cif file. [b] Values in parenthesis are standard deviations in the last significant figure.

4.2 X-Ray crystallographic data for 1⊃K^+ complex

Table S4. Crystal data and refinement details for **1**⊃K^+ complex.

Identification code	**1** ⊃ K^+
Chemical formula	$C_{161}H_{151}N_{35}O_{26}K \cdot CF_3O_3S \cdot 3(CHCl_3) \cdot 6(H_2O)$*
Formula weight	3646.53
Temperature	100(2)
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a=20.339 (4), α=90
	b=49.532 (10), β=103.33 (3)
	c=21.904 (4), γ=90
Volume	21473 (8)
Z	4
Density (calculated)	1.128
Absorption coefficient	1.93
Absorption correction	Multi-scan
Crystal size	0.15 × 0.10 × 0.05
Index ranges	h = -20→20, k = -48→49, l = -21→20
Completeness to theta = 50.43°	99.5
Reflections collected	99522
Reflections observed [$I > 2\sigma(I)$]	15657
R_{int}	0.108
Data/parameters/restrains	22365/1764/448
Goodness-of-fit on F^2	2.73
Final R indices [$I > 2\sigma(I)$]	R1 = 0.2008, wR2 = 0.4668
R indices (all data)	R1 = 0.2266, wR2 = 0.4875
Lasgest diff. peak and hole	1.16, -0.73
CCDC #	1561024

*SQUEEZE procedure was used to remove severely disordered solvent molecules

(a) (b)

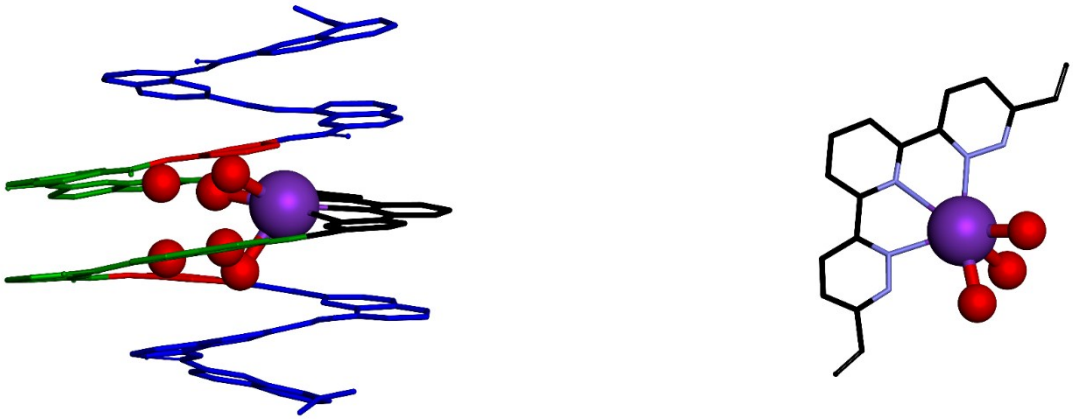


Figure S17. Solid-state structure of the ***P*-1⊃K$^+$** complex: (a) side view; (b) K coordination sphere. Isobutoxy side chains and cavity-excluded solvent molecules are omitted for clarity. The capsule backbone is represented in sticks. Potassium atoms are represented in purple balls and oxygen atoms of water molecules are depicted as red balls.

Table S5. First-coordination sphere bond lengths (Å) in the **1**⊃K$^+$ complex.[a]

Bond	Bond length (Å)[b]
K01–O1W	2.592(8)
K01–O2W	3.428(12)
K01–O3W	2.723(10)
K01–N17A	3.031(10)
K01–N18A	3.119(8)
K01–N19A	2.747(9)

[a] Atom numbers are those of the cif file. [b] Values in parenthesis are standard deviations in the last significant figure.

Table S6. O···N distances shorter than 3.25 Å between water molecules and capsule heteroatoms in the **1**⊃K$^+$ complex.[a]

	d (Å)[b]
O1W···N7A	2.91(1)
O2W···N29A	3.11(1)
O2W···N28A	2.84(1)
O3W···N22A	3.23(1)
O4W···N14A	2.96(1)
O5W···N10A	3.22(1)
O5W···N11A	3.11(1)
O6W···N25A	2.90(1)

[a] Atom numbers are those of the cif file. [b] Values in parenthesis are standard deviations in the

last significant figure.

4.3 X-Ray crystallographic data for 1⊃Ca^{2+} complex

Table S7. Crystal data and refinement details for **1**⊃Ca^{2+} complex.

Identification code	**1** ⊃ Ca^{2+}
Chemical formula	C_{161} H_{151} N_{35} O_{26}, Ca O_7, 2(O)*
Formula weight	3176.24
Temperature	100(2)
Wavelength	1.54178 Å
Crystal system	Tetragonal
Space group	$I4_1cd$
Unit cell dimensions	a=b=21.7945 (19), c=71.588 (9)
Volume	34004 (7)
Z	8, (Z'=0.5)
Density (calculated)	1.241
Absorption coefficient	0.99
Absorption correction	Multi-scan
Crystal size	0.20 × 0.10 × 0.05
Index ranges	h = -21→10, k = -13→12, l = -71→66
Completeness to theta = 50.43°	91.6
Reflections collected	14207
Reflections observed [$I > 2\sigma(I)$]	5429
R_{int}	0.023
Data/parameters/restrains	7297/795/292
Goodness-of-fit on F^2	1.62
Final R indices [$I > 2\sigma(I)$]	R1 = 0.1364, wR2 = 0.3608
R indices (all data)	R1 = 0.1672, wR2 = 0.3932
Lasgest diff. peak and hole	0.80, -0.48
CCDC #	1561025

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

(a) (b)

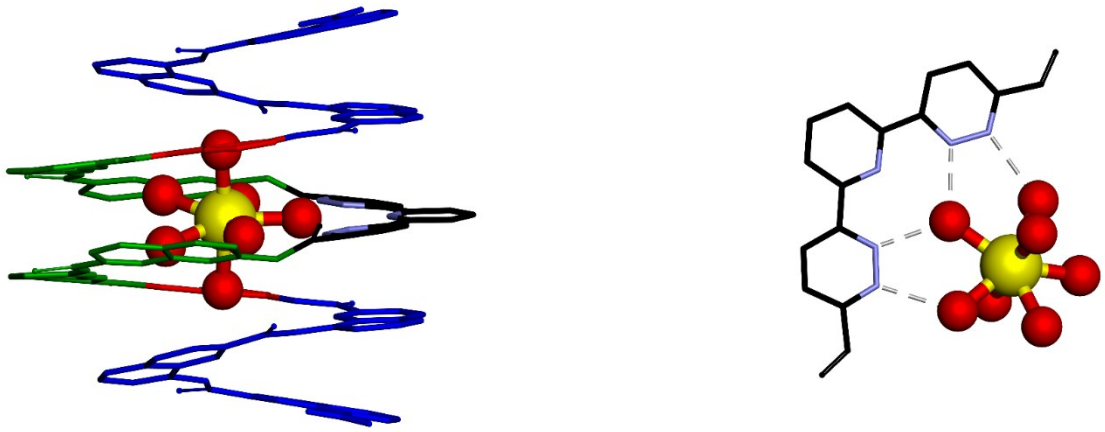


Figure S18. Solid-state structure of the ***P*-1**⊃Ca^{2+} complex: (a) side view; (b) detail of the hydrogen bonding interactions between the calcium hydrate and the central pyz-pyr-pyz monomer. Isobutoxy side chains and cavity-excluded solvent molecules are omitted for clarity. Dashed lines indicate hydrogen bonds. The capsule backbone is represented in sticks. Calcium atoms are represented in yellow balls and oxygen atoms of water molecules are depicted as red balls.

Table S8. First-coordination sphere bond lengths (Å) in the **1**⊃Ca^{2+} complex.[a]

Bond	Bond length (Å)[b]
Ca1–O1W	2.378(19)
Ca1–O2W	2.413(12)
Ca1–O3W	2.344(13)
Ca1–O4W	2.50(3)

[a] Atom numbers are those of the cif file. [b] Values in parenthesis are standard deviations in the last significant figure.

Table S9. O···N distances shorter than 3.25 Å between water molecules and capsule heteroatoms in the **1**⊃Ca^{2+} complex.[a]

	d (Å)[b]
O1W···N17A	2.77(2)
O1W···N18A	3.10(3)
O2W···N14A	3.01(1)
O2W···N15A	3.25(2)
O2W···N16A	2.88(2)
O3W···N8A	2.71(2)
O4W···N11A	2.80(3)
O4W···N12A	3.05(3)

[a] Atom numbers are those of the cif file. [b] Values in parenthesis are standard deviations in the

last significant figure.

4.4 X-Ray crystallographic data for 1⊃Ba^{2+} complex

Table S10. Crystal data and refinement details for **1**⊃Ba^{2+} complex.

Identification code	**1** ⊃ Ba^{2+}
Chemical formula	$C_{161}H_{151}N_{35}O_{26}$ Ba·2(CF_3O_3S)·6($CHCl_3$)·7(H_2O) *
Formula weight	4269.96
Temperature	100 (2) K
Wavelength	1.54178 Å
Crystal system	Triclinic
Space group	*P*-1
Unit cell dimensions	a=21.6820 (6), α=70.405 (3), b=23.7632 (9), β=78.648 (2) c=26.0862 (7), γ=75.477 (3)
Volume	12163.5 (7)
Z	2
Density (calculated)	1.166 Mg/m^3
Absorption coefficient	3.84
Absorption correction	Multi-scan
Crystal size	0.20 × 0.07 × 0.02 mm^3
Index ranges	h = -21→21, k = -23→23, l = -26→26
Completeness to theta = 50.43°	98.9
Reflections collected	78956
Reflections observed [$I > 2\sigma(I)$]	13996
R_{int}	0.158
Data/parameters/restrains	25179/1756/727
Goodness-of-fit on F^2	1.75
Final R indices [$I > 2\sigma(I)$]	R1 = 0.1517, wR2 = 0.3653
R indices (all data)	R1 = 0.1977, wR2 = 0.4009
Lasgest diff. peak and hole	1.58, -1.05
CCDC #	1561026

*SQUEEZE procedure was used to remove severely disordered solvent molecules

(a) (b)

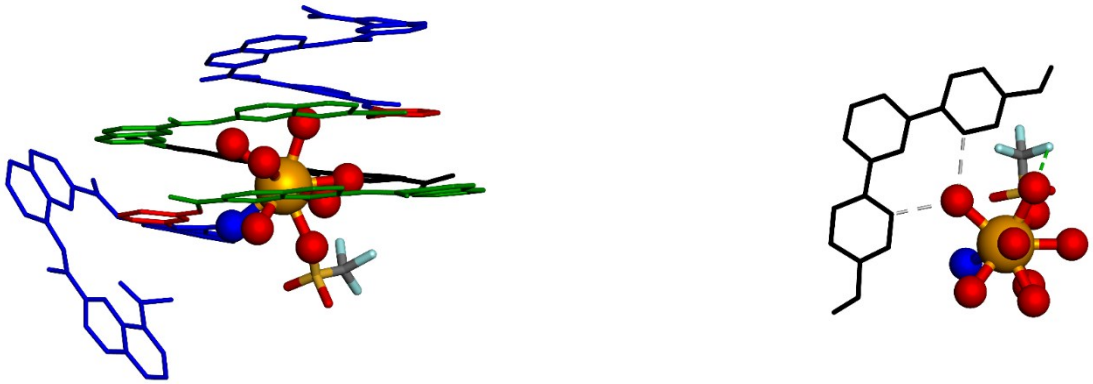


Figure S10. Solid-state structure of the ***P*-1**⊃Ba^{2+} complex: (a) side view; (b) detail of the hydrogen bonding interactions between the barium hydrate and the central pyz-pyr-pyz monomer. Isobutoxy side chains and cavity-excluded solvent molecules are omitted for clarity. Dashed lines indicate hydrogen bonds. The capsule backbone is represented in sticks. Barium atoms are represented in orange balls and oxygen atoms of water molecules are depicted as red balls.

Table S11. First-coordination sphere bond lengths (Å) in the **1**⊃Ba^{2+} complex.[a]

Bond	**Bond length (Å)**[b]
Ba1–O1C	2.804(14)
Ba1–O12A	2.789(11)
Ba1–O1W	2.790(11)
Ba1–O2W	2.827(9)
Ba1–O3W	2.746(12)
Ba1–O4W	2.861(9)
Ba1–O5W	2.917(9)
Ba1–O6W	2.729(8)
Ba1–O7W	2.718(9)

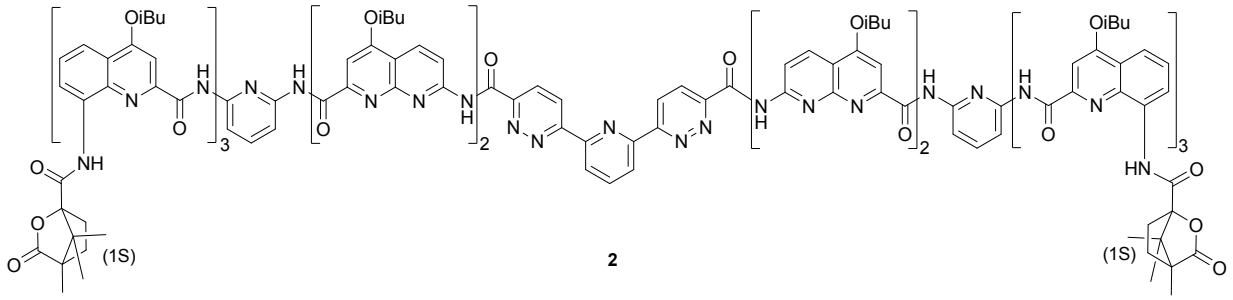
[a] Atom numbers are those of the cif file. [b] Values in parenthesis are standard deviations in the last significant figure.

Table S12. O···N distances shorter than 3.25 Å between water molecules and capsule heteroatoms in the **1**⊃Ba^{2+} complex.[a]

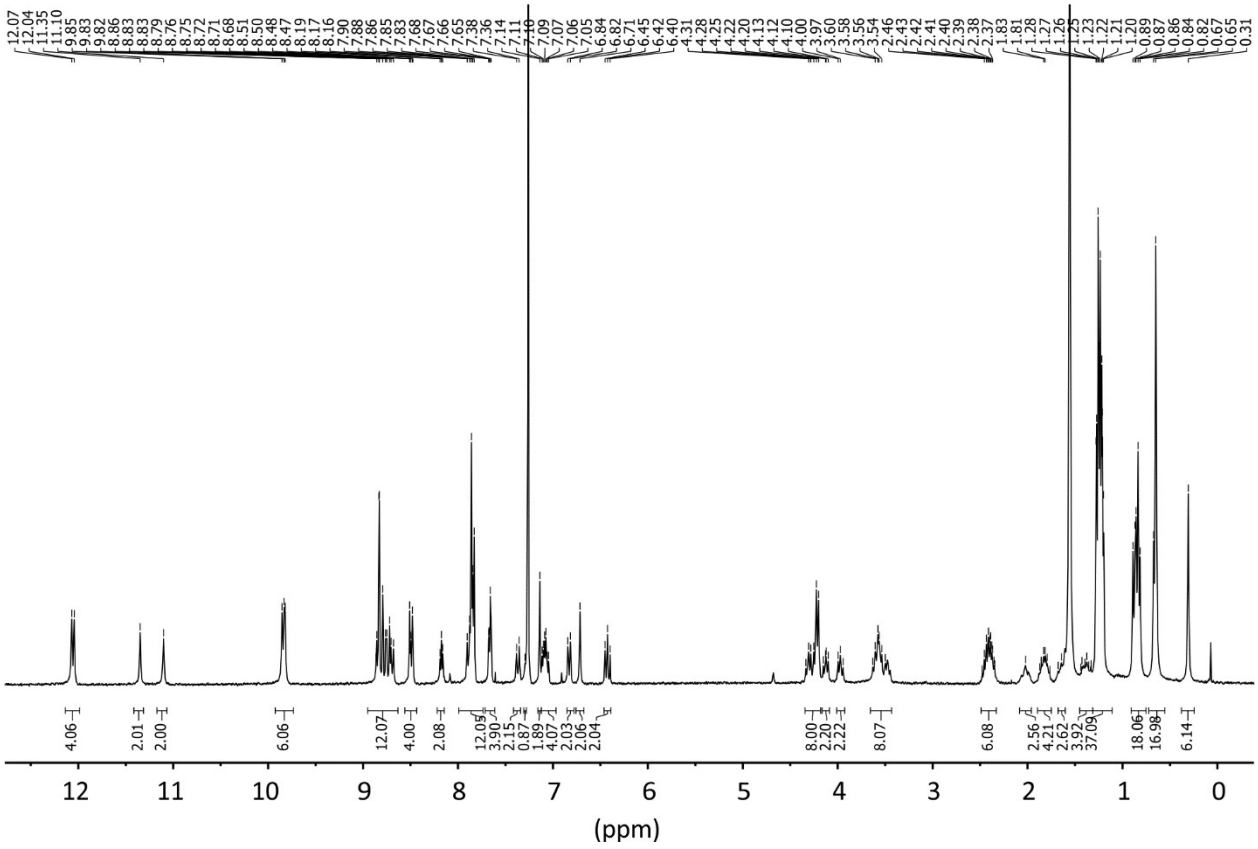
	d **(Å)**[b]
O1W···N4A	3.02(2)
O1W···N7A	3.24(2)
O1W···N8A	2.81(2)
O3W···N14A	2.85(2)
O4W···N24A	3.033(2)
O4W···N25A	2.85(1)
O5W···N27A	2.930(2)
O5W···N28A	2.93(2)
O6W···N17A	2.80(2)
O6W···N18A	3.10(2)
O6W···N19A	2.85(2)
O7W···N20A	3.07(2)
O7W···N21A	3.16(2)
O7W···N22A	3.03(1)

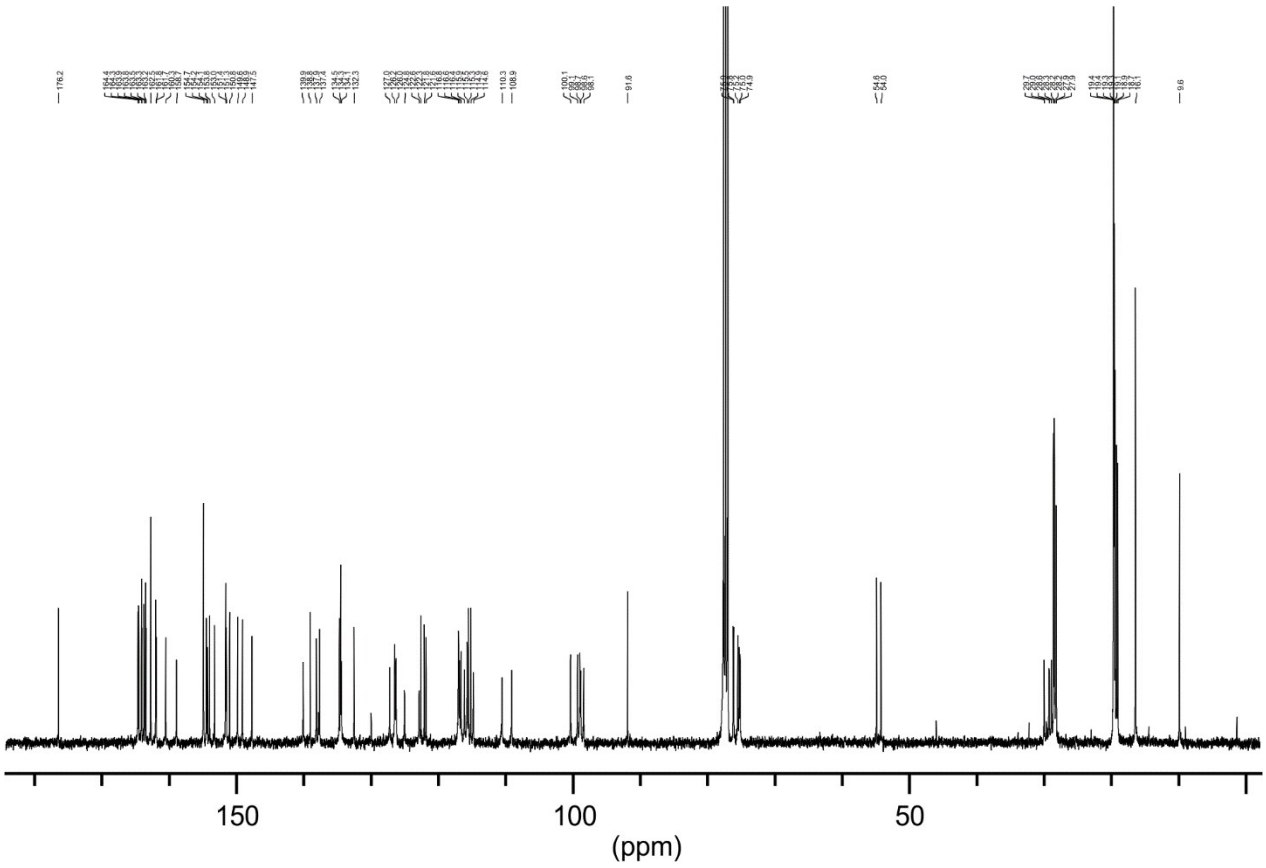
[a] Atom numbers are those of the cif file. [b] Values in parenthesis are standard deviations in the last significant figure.

5. ^{1}H NMR and ^{13}C NMR spectra of new synthetic compounds

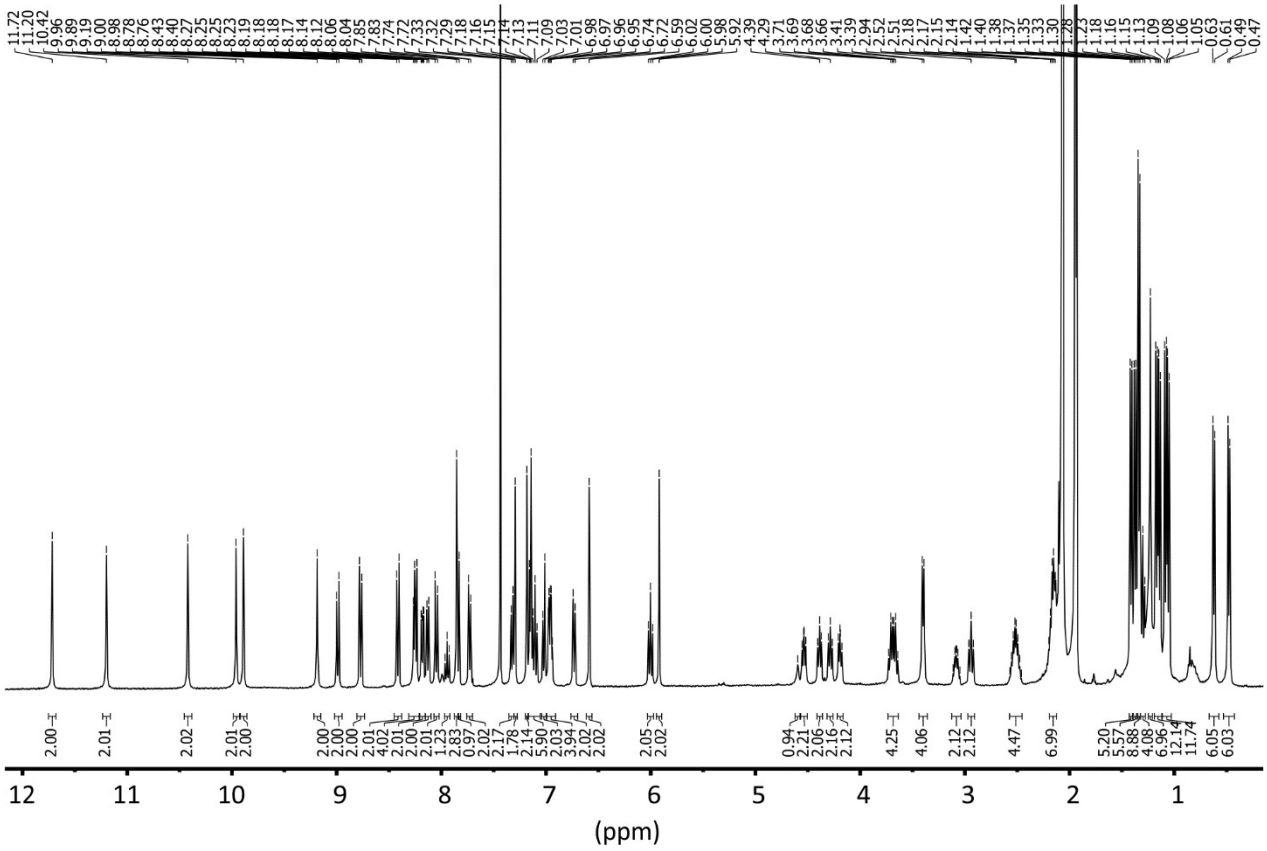


2

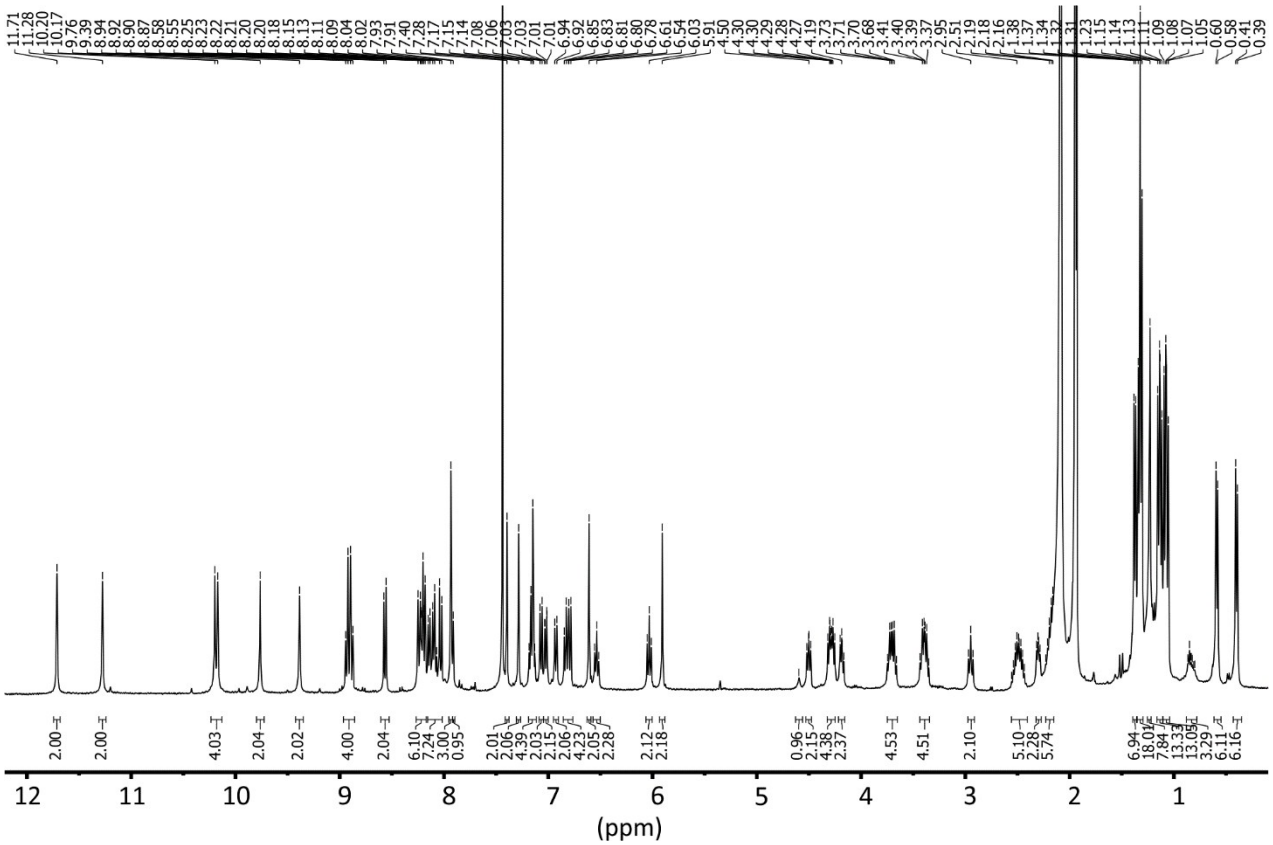




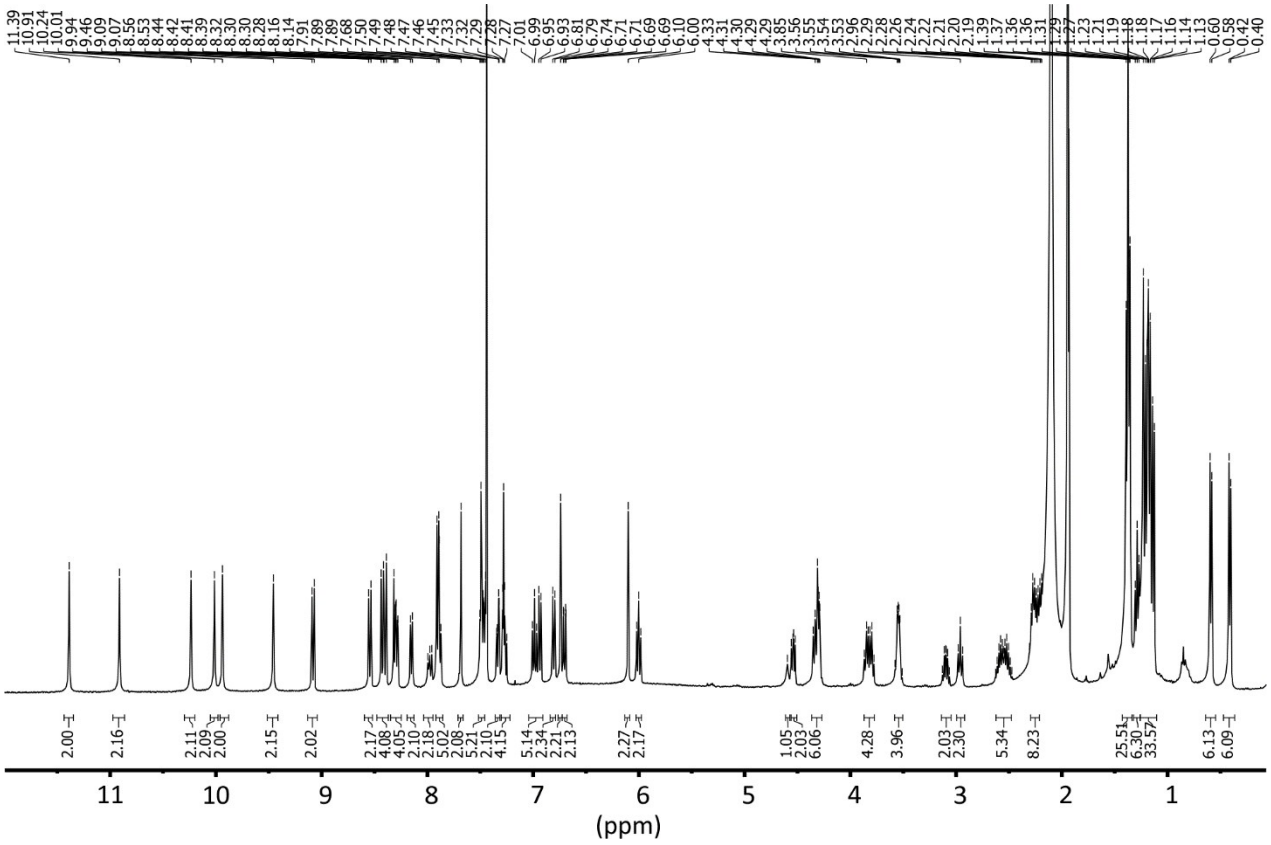
1⊃Na$^+$ complex.



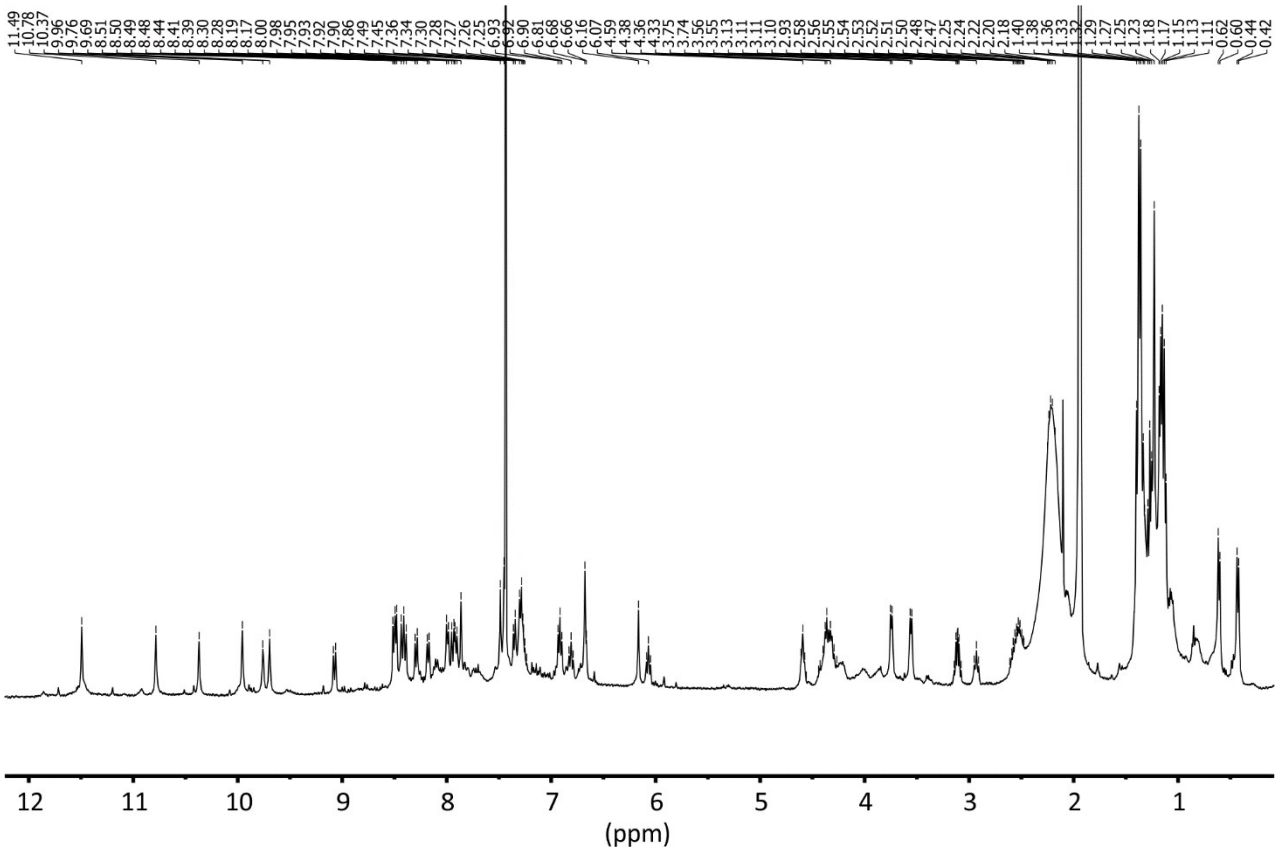
1⊃K^+ complex.



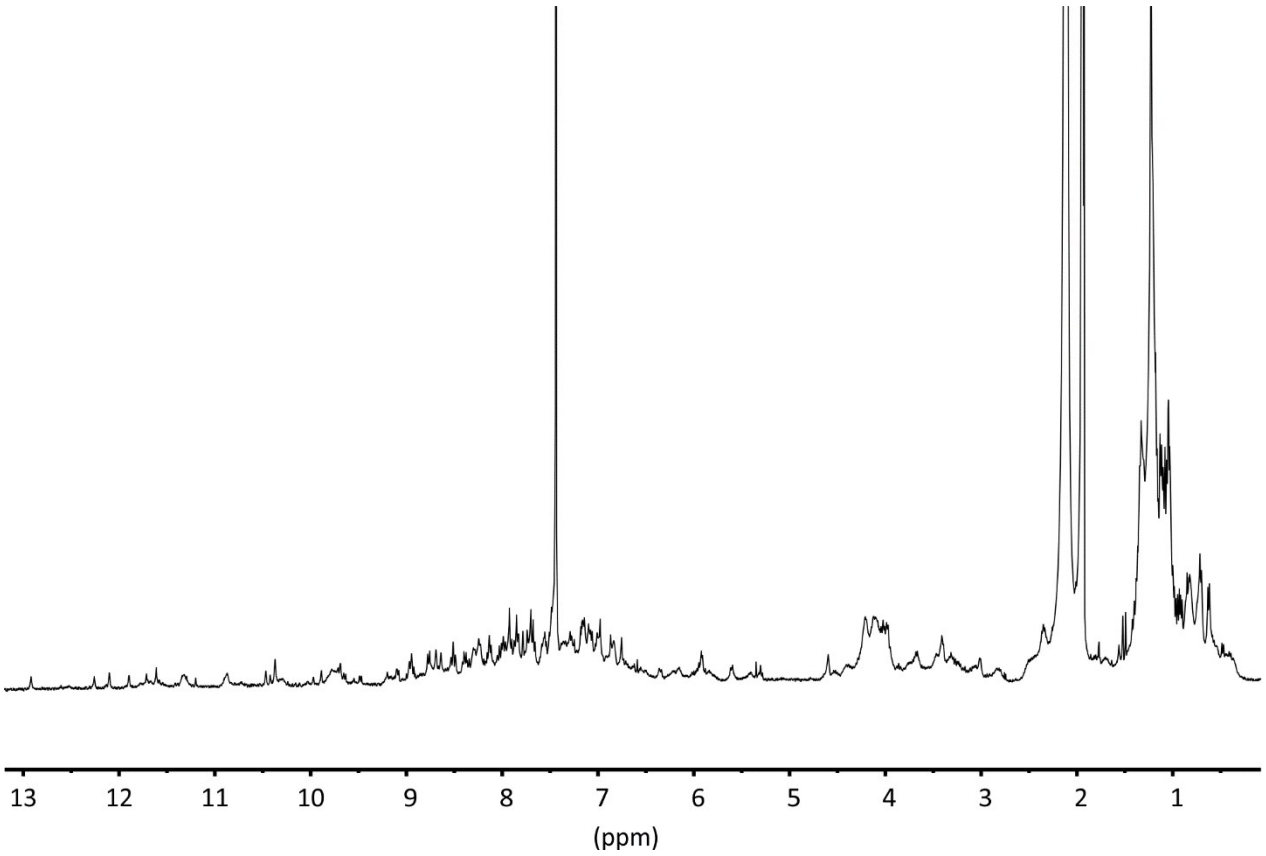
1⊃Mg^{2+} complex.



1⊃Ca^{2+} complex.



1⊃Ba^{2+} complex



6. References

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