Electronic Supplementary Material (ESI) for CrystEngComm.

Electronic Supporting Information

Oligomeric phosphate clusters in macrocyclic channels

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S1. Materials and Instrumentation

Materials

All reagents, chemicals and deuterated solvents were purchased from commercial suppliers and used as received without further purification.

Instrumentation

All NMR spectra were recorded at 298K using DMSO-d_6 as solvent. Solution pH was measured by a Fischer Accumet pH meter. ^{1}H NMR spectra were recorded on Bruker AVIIIHD 400 MHz spectrometers; All ^{31}P NMR spectra were recorded on Bruker AVIIIHD 400 MHz (162 MHz) NMR spectrometer and referenced by absolute referencing with their corresponding ^{1}H NMR. DOSY NMRs were recorded at Bruker Avance AVIII 600 MHz NMR. All NMR data were analyzed using MestreLab Mnova software. HRESIMS^{+} were recorded in Waters Micromass LCT Premier spectrometer.

S2. Crystallization Procedures

Crystallization of phosphate complex 2·2H_2O

A solution of phosphoric acid (85 wt.% H_3PO_4) (25 μL) in 0.5 mL H_2O was added to a 1 mL CH_3OH solution of macrocycle **1** (10 mg), followed by addition of 0.5 mL CH_3CN. The resulting cloudy solution was sonicated and mild heated to get completely clear and allowed to sit for slow evaporation at room temperature. After a week, nice triclinic block like crystals of $[(H_3\mathbf{1}^{3+})\cdot(HPO_4^{2-})\cdot(H_2PO_4^{-})\cdot(H_3PO_4)_3]\cdot 2H_2O$ **(**CCDC No: 2113443) were obtained that were suitable for X-ray crystallography.

S3. Crystal Structure Overlays

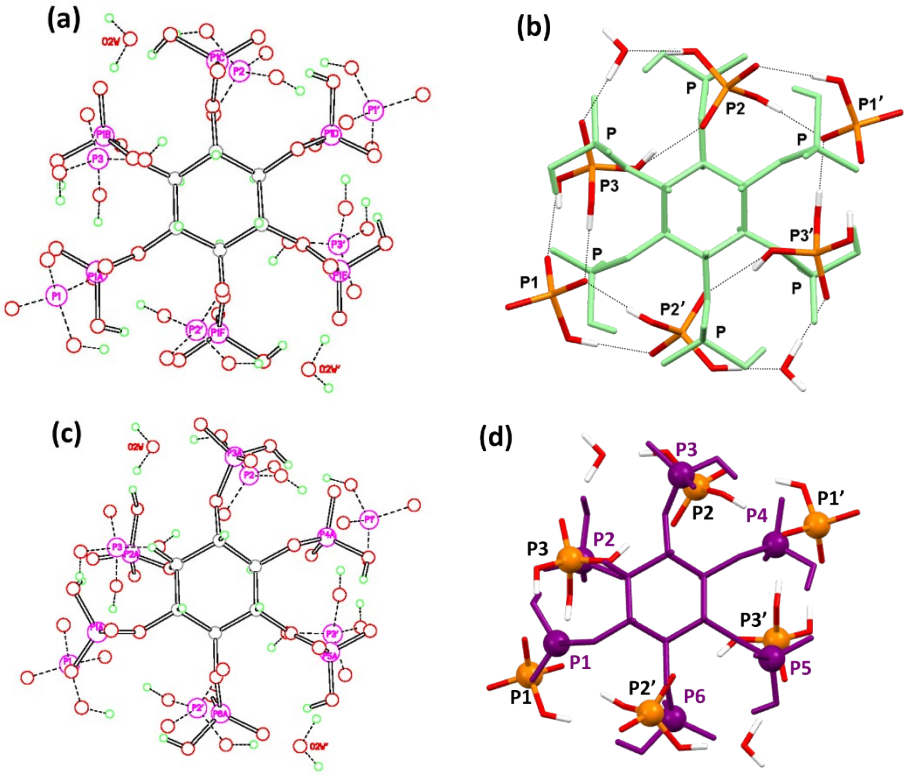

Fig. S1. Two different types overlay formats of the phosphorus atoms for the phosphate cluster with (a) and (b) *scyllo*-IP_6 (rms = 1.24 Å) and (c) and (d) with the *myo*-IP_6 (rms = 1.31Å).

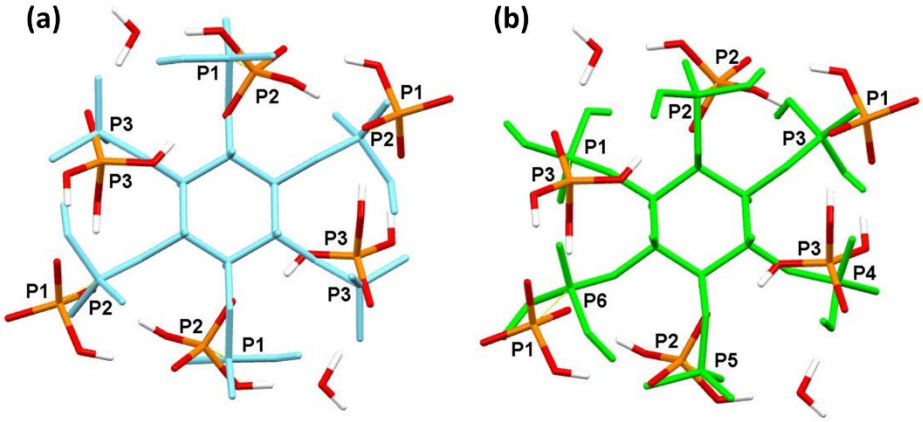

Fig. S2. Overlays of the phosphorus atoms for the phosphate cluster with (a) Na_8*scyllo*-IP_6 (rms = 1.00 Å) and (b) K_3*myo*-IP_6 (rms = 1.22Å).

S4. NMR Titrations and Binding Constants

^{1}H NMR titrations were conducted for each host on Bruker AVIIIHD 400 MHz spectrometer. Tetrabutylammonium (TBA) salts of dihydrogen phosphate ($H_2PO_4^-$) was used to make the guest titrant solution in DMSO-d_6. A 20 mM solution of guest anions were titrated into 0.5 mL of 2 mM host solution resulting in 20 NMR spectra to examine anion binding. ^{31}P NMR spectra of $TBAH_2PO_4$ (10 mM) were recorded with increasing addition of macrocycle **1** (40 mM) in DMSO-d_6 and ^{31}P NMR are referenced by absolute referencing with their corresponding ^{1}H NMR.

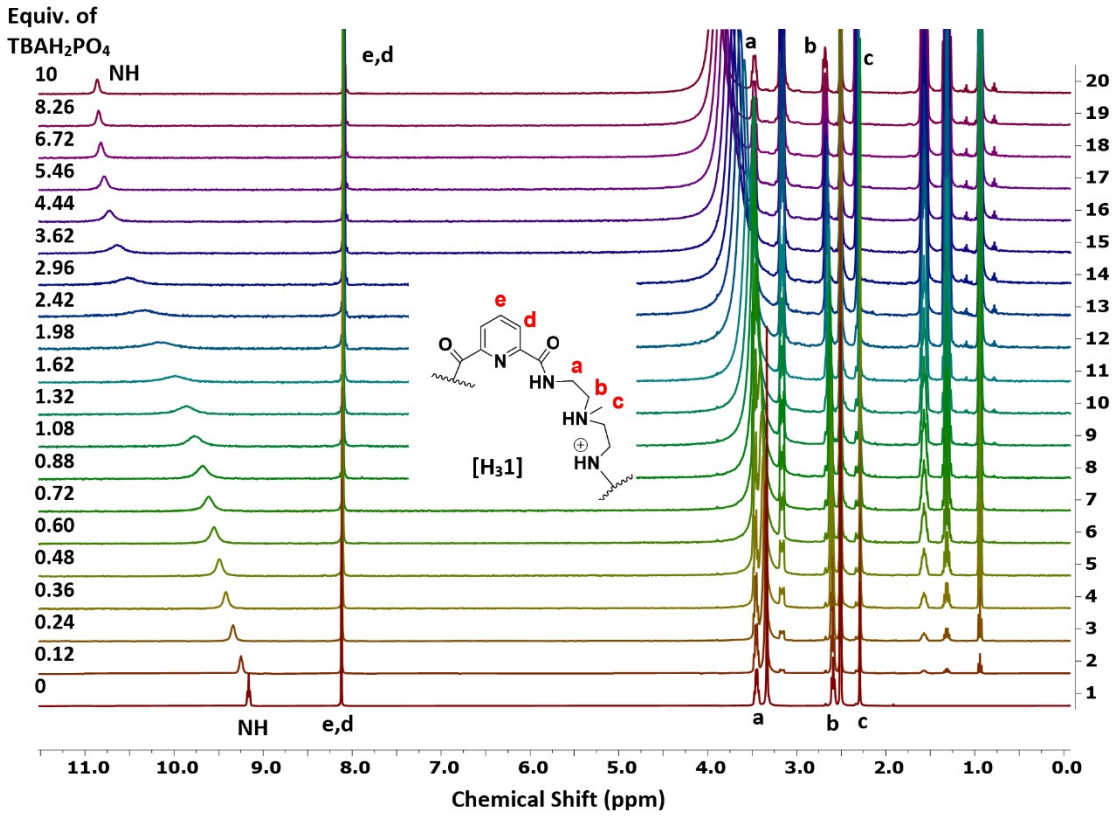

Fig. S3. Full 1H NMR spectra showing chemical shift changes of macrocycle **1** (2 mM) with increasing concentration of (TBA)(H2PO4) (20 mM) in DMSO-*d6* (400 MHz, 298 K).

In the ^{1}H NMR titration binding study, different proton resonances were investigated to determine the trends associated with the observed the chemical shift changes. Herein, four different proton resonances [amide (NH), methylene (b and a) and methyl (c)] were considered, providing multiple data sets from which the association constants (K_1, K_2, K_3) could be determined by a global fitting analysis to a 1:3 binding model in a custom written matlab program which together with the raw and processed data can be found at:

https://github.com/pallithordarson/Oligophosphate-1-3-model/

The 1:3 model and the methodology used here to select the best binding model is almost identical to a previously reported 1:3 binding model[S1] except here NMR data used instead of UV-Vis data.

Importantly, the data is fitted to all four possible "flavors"[S2] of the 1:3 binding model;
"**full 1:3**" binding model. This model assumes three non-identical binding sites per molecule of host **1** that allows for cooperativity (negative or positive).
"additive 1:3" binding model. To reduce the number of fitted parameters we note that in many circumstances it can be assumed that the chemical shifts of the 1:1, 1:2 and 1:3 are simply additive, i.e. for the chemical shift at any given titration point, the change in chemical shift (δ)on going on from the free host to the 1:1 complex is simply 1/2 of the change between the 1:2 complex and the free host and 1/3 of the change between the 1:3 complex and the free host.
"**non-cooperative 1:3**" model. Here we revert back to noting that the chemical shifts may not be correlated, instead we now make the assumption that the 1:3 complexation is non-cooperative and, hence, after considering statistical factors, that $K_1 = 3K_2 = 9K_3$.
"statistical 1:3" model. Here we not only make the assumption that the binding is non-cooperative ($K_1 = 3K_2 = 9K_3$) but also that the chemical shifts are all additive.

After correcting for statistical factors this corresponds to binding energies of ΔG_1 = -6.2 kJ mol^{-1}, ΔG_2 = -12.0 kJ mol^{-1} and ΔG_3 = -8.6 kJ mol^{-1} indicating some positive cooperativity (binding gets stronger after 1:1 complex is formed) (Table S1).

Table S1. Chemical shift for amide (NH), methylene (b and a) and methyl (c) (see Fig. S1) fitted with the four proton resonances using the "full" (unconstrained) 1:3 model.

	Statistical analysis				Binding constants		
Model (flavour)	BIC (Bayesian)[a]	ΔBIC compared to full model[b]	Data Points	Degrees of freedom	K_1 / M^{-1}	K_2 / M^{-1}	K_3 / M^{-1}
full	-559.03	n/a	80	65	**968**	**68204**	**1024**
additive	-429.56	129.47	80	73	912	1084	3 x 10^{-8}
Non-cooperative	-513.03	46.00	80	67	12551	4184[c]	1395[c]
statistical	-380.78	178.26	80	75	12143	4048[c]	1349[c]

[a] Bayesian Information Criteria (BIC).[S3] The lower BIC, the better. BIC can be negative and if so, the more negative the better.
[b] Defined here as BIC(X model)-BIC(full model). A ΔBIC > 6-10 is usually considered as strong evidence in favor of the model with a lower (more negative) BIC.
[c] By default, in these models $K_1 = 3K_2 = 9K_3$.

S5. Mass Spectral Analyses

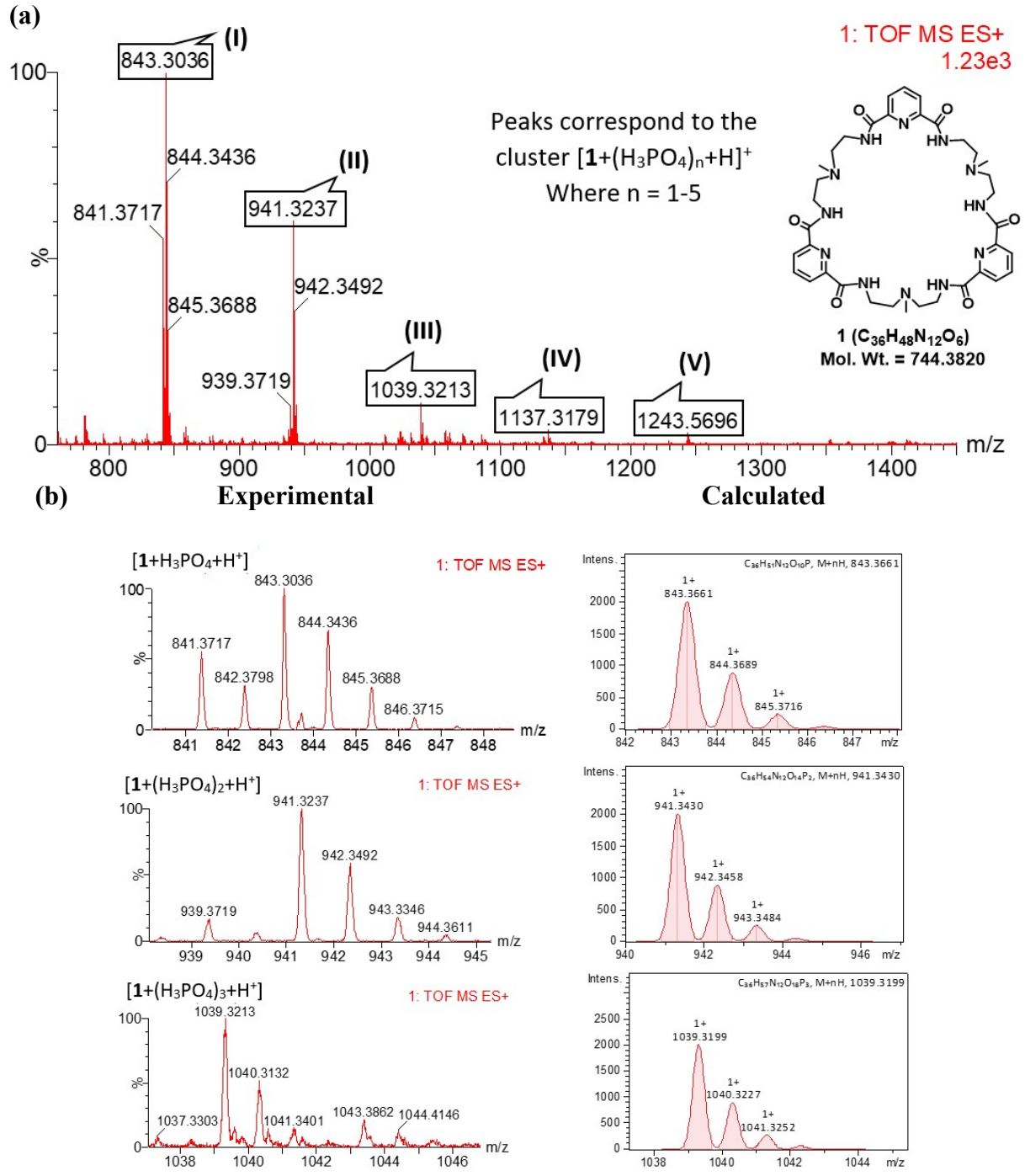

Fig. S4. **(a)** ESI-MS (+ve) spectrum of crystal solution of **2** shows the appearance of peaks correspond to [**1**+$(H_3PO_4)_n$+H]$^+$ cluster where m/z at (I) 843.3036, [**1**+H_3PO_4+H^+]; (II) 941.3237, [**1**+$(H_3PO_4)_2$+H^+]; (III) 1039.3213, [**1**+$(H_3PO_4)_3$+H^+]; (IV) 1137.3179, [**1**+$(H_3PO_4)_4$+H^+] and (V) 1243.5696, [**1**+$(H_3PO_4)_5$+0.5H_2O+H^+] suggest the formation of phosphate oligomer. **(b)** Correlation of two different experimental (left) and calculated (right) peaks of the ESI-MS spectrum of the complex, respectively.\

S6. X-ray Crystallographic Studies

Data Collection and Structure Solution for $[(H_3I^{3+})\cdot(HPO_4^{2-})\cdot(H_2PO_4^{-})\cdot(H_3PO_4)_3]\cdot 2H_2O$

A complete set of diffraction data were collected with monochromated CuKα radiation for a single-domain crystal. A total of 2620 1.0°-wide ω- or ϕ-scan frames with counting times of 5-10 seconds were collected on a Bruker APEX II CCD area detector. X-rays were provided by a Bruker MicroStar microfocus rotating anode operating at 45kV and 60 mA and equipped with Helios multilayer x-ray optics. Preliminary lattice constants were obtained with the Bruker program SMART.[S4] Integrated reflection intensities were produced using the Bruker program SAINT[S5] and the data set was corrected empirically for variable absorption effects using equivalent reflections. The Bruker software package SHELXTL was used to solve the structure using "direct methods" techniques. All stages of weighted full-matrix least-squares refinement were conducted by minimizing $\Sigma w(F_o^2-F_c^2)^2$ with the SHELXTL v2014 software package.[S6]

The final structural model incorporated anisotropic thermal parameters for all nonhydrogen atoms and isotropic thermal parameters for all hydrogen atoms. The lattice contains two water molecules as solvent of crystallization of which one was disordered. The disorder was modeled with partial occupancies over two position and the occupancies were refined to 80:20%. Displacement parameter were constrained (EADP) for the two partial O atoms.

All macrocycle H-atoms were calculated in idealized positions and treated with appropriate riding models (AFIX m3). The O-H hydrogen atoms were located from difference Fourier maps and were allowed to ride on the corresponding O atoms they are bonded to with geometrical restraints.
The relevant crystallographic and structure refinement data are given in Table S1.

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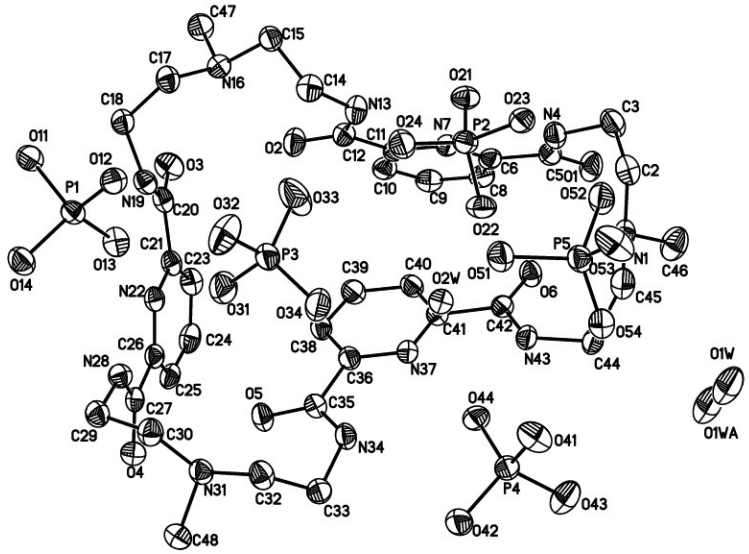

Fig. S5. Projection view with 50% probability ellipsoids- H atoms omitted for clarity.

Table S2. Crystal Data and Structure Refinement for $[(H_3\mathbf{1}^{3+})\cdot(HPO_4^{2-})\cdot(H_2PO_4^{-})\cdot(H_3PO_4)_3]\cdot 2H_2O$

	$\mathbf{2}\cdot 2H_2O$
Empirical formula	$C_{36}H_{67}N_{12}O_{28}P_5$
Formula weight	1270.86
Temperature	200(2) K
Wavelength	1.54178 Å
Crystal system	Triclinic
Space group	$\overline{P1}$ - C_i^1 (No. 2)
a	14.1582(2) Å
b	14.7759(3) Å
c	14.9206(3) Å
α	70.4003(10)°
β	73.1350(10)°
γ	69.4031(10)°
Volume	2699.64(10) $Å^3$
Z	2
Density (calculated)	1.563 g/cm^3
Absorption coefficient	2.464 mm^{-1}
F(000)	1332
Crystal size	0.075 × 0.060 × 0.030 mm^3
Theta range	5.18 to 70.39°
Index ranges	$-14 \le h \le 17$, $-17 \le k \le 17$, $-17 \le l \le 17$
Reflections collected	24062
Independent reflections	9422 [R_{int} = 0.049]
Completeness/θ_{max}	94.7%/67.679°
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8644 and 0.7008
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9422 / 19 / 735
Goodness-of-fit on F^2	1.037
Final R indices [I>2σ(I)]	R1 = 0.0430, wR2 = 0.1059
R indices (all data)	R1 = 0.0654, wR2 = 0.1181
Largest diff. peak and hole	0.397 and -0.399 $e^-/Å^3$

S6. References

S1 M. Kudisch, C.-H. Lim, P. Thordarson and G. M. Miyake, *J. Am. Chem. Soc.*, **2019**, *141*, 19479-19486.

S2 D. B. Hibbert and P. Thordarson, *Chem. Commun*., **2016**, *52*, 12792-12805.

S3 G. Schwarz, *Annals Stat.*, **1978**, *6*, 461-464

S4 Data Collection: SMART Software in APEX2 v2014.11-0 Suite. Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA.

S5 Data Reduction: SAINT Software in APEX2 v2014.11-0 Suite. Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA.

S6 Refinement: SHELXTL Software in APEX2 v2014.11-0 Suite. Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA.