

Electronic supporting information

**Snapshots of “Crystalline” Salt-Water Solutions Inositol  
Hexaphosphate Conformers**

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### Experimental Procedures:

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

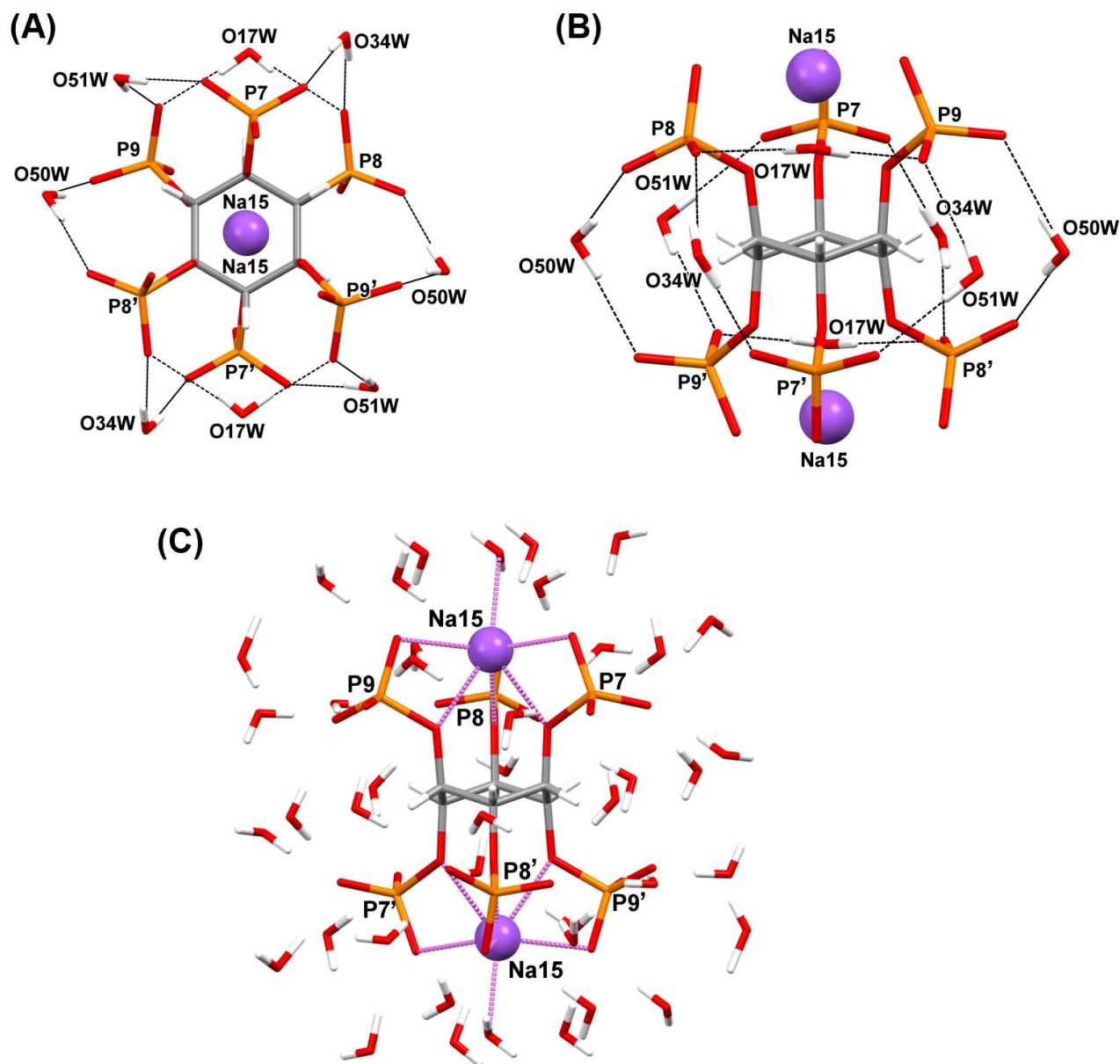
**Instrumentation.**  $^1\text{H}$  and  $^{31}\text{P}$  NMR spectra were recorded on a Bruker AVIIIHD 400 MHz (162 MHz for  $^{31}\text{P}$ ) NMR spectrometer. All  $^{31}\text{P}$  NMR (proton decoupled) spectra were referenced by absolute referencing with their corresponding  $^1\text{H}$  NMR. NMR data were analyzed using MestreLab MestreNova software and pHs were measured by a Fischer Accumet pH meter. HREIMS+ were recorded in Waters Micromass LCT Premier spectrometer.

**NMR titration with pH variation.** 1 mL 10 mM solution of *scyllo*-inositol-1,2,3,4,5,6-hexakisphosphate hexasodium salt,  $[(\text{Na})_6(\textit{scyllo}\text{-H}_6\text{IP}_6)]$  and 1 mL 20 mM *myo*-inositol-hexaphosphate sodium salt solution were prepared in  $\text{D}_2\text{O}$ . All NMR spectra were recorded at  $25^\circ\text{C}$ , and trimethylsilylpropanoic acid sodium salt (TMSP) was used as an internal reference. NMR spectra of the solutions were recorded at different pH intervals altered by dropwise addition of NaOH solution (1 M).

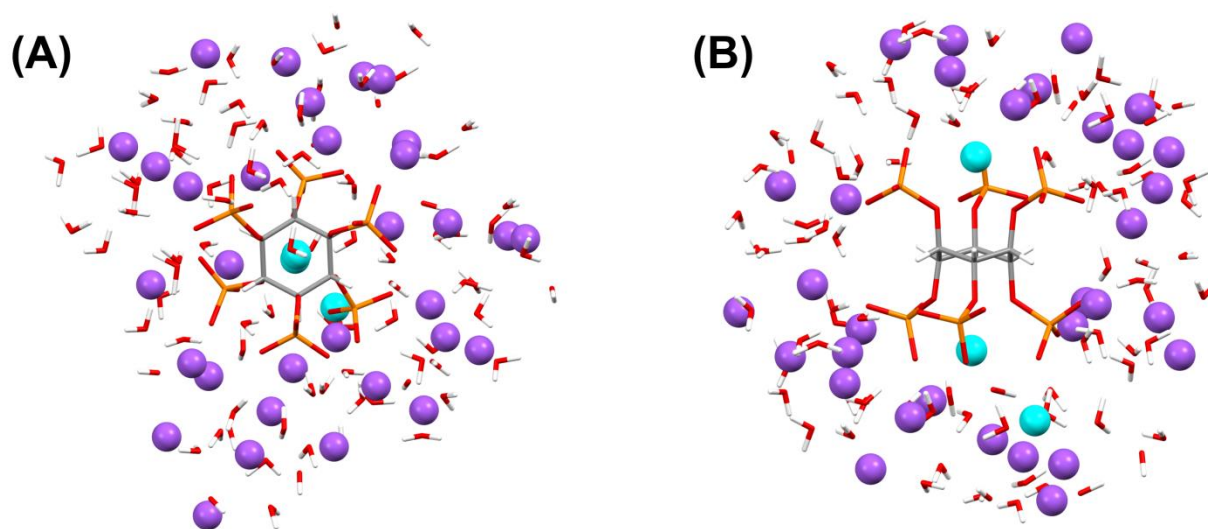
### Crystallization Procedures:

**Crystallization of  $[(\text{Na})_{12}(\textit{scyllo}\text{-IP}_6)]$  (6a conformation):** An aqueous solution of NaOH (1 M) was added dropwise to the 0.2 mL aqueous solution of  $[(\text{Na})_6(\textit{scyllo}\text{-H}_6\text{IP}_6)]$  (5 mg) until the pH reached to 12.68. The solution was set up for vapor diffusion under acetone. After 3 days, colorless triclinic crystals ( $\text{P}\bar{1}$ ) of  $\{[\text{Na}]_{12}[\textit{scyllo}\text{-C}_6\text{H}_6(\text{PO}_4)_6]\}_{1.5}\cdot 60.8\text{H}_2\text{O}$  (**1**) (CCDC No: 2027581) suitable for X-ray crystallography were obtained.

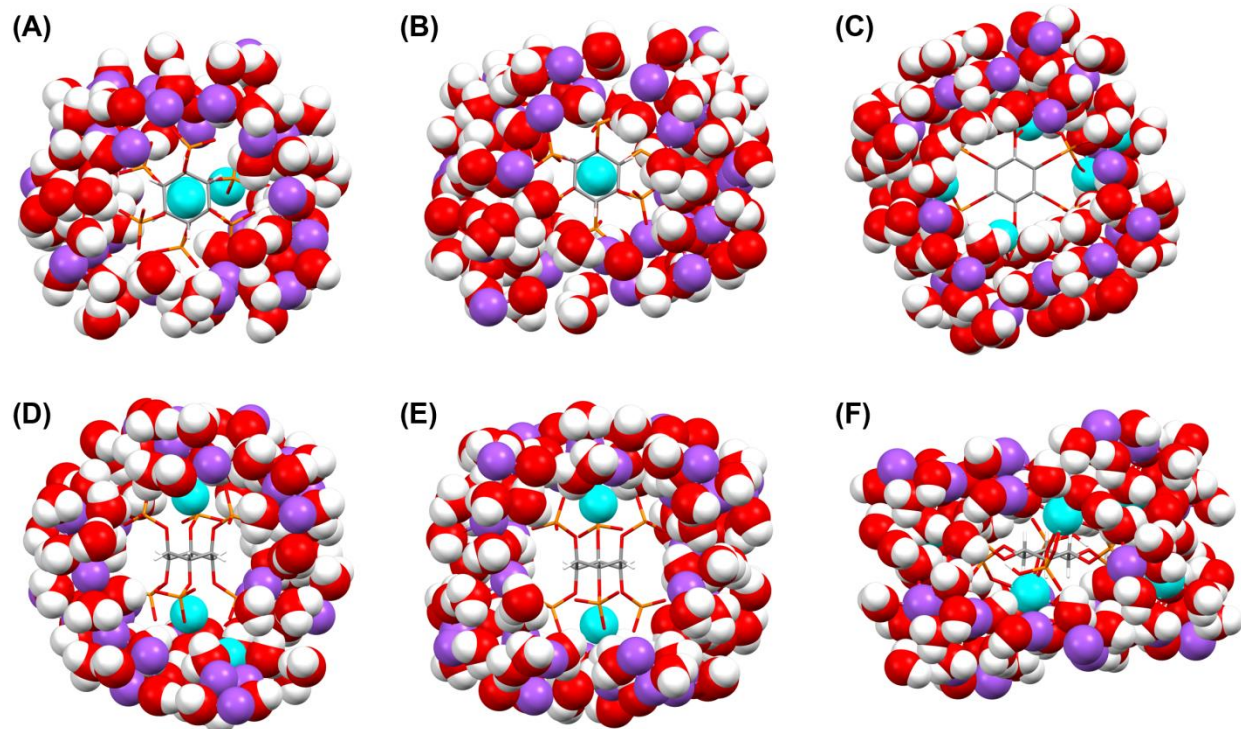
**Crystallization of  $[(\text{Na})_8(\textit{scyllo}\text{-H}_4\text{IP}_6)]$  (6e conformation):** 5 mg of the sodium salt of *scyllo*-inositol-hexakisphosphate was dissolved in 0.2 mL of water and the resulting solution (pH = 6.36) was set up for vapor diffusion under acetone. After 1 day, colorless triclinic crystals ( $\text{P}\bar{1}$ ) of  $[\text{Na}]_8[\textit{scyllo}\text{-C}_6\text{H}_6(\text{HPO}_4)_4(\text{PO}_4)_2]\cdot 26\text{H}_2\text{O}$  (**2**) (CCDC No: 2027582) suitable for X-ray crystallography were obtained.



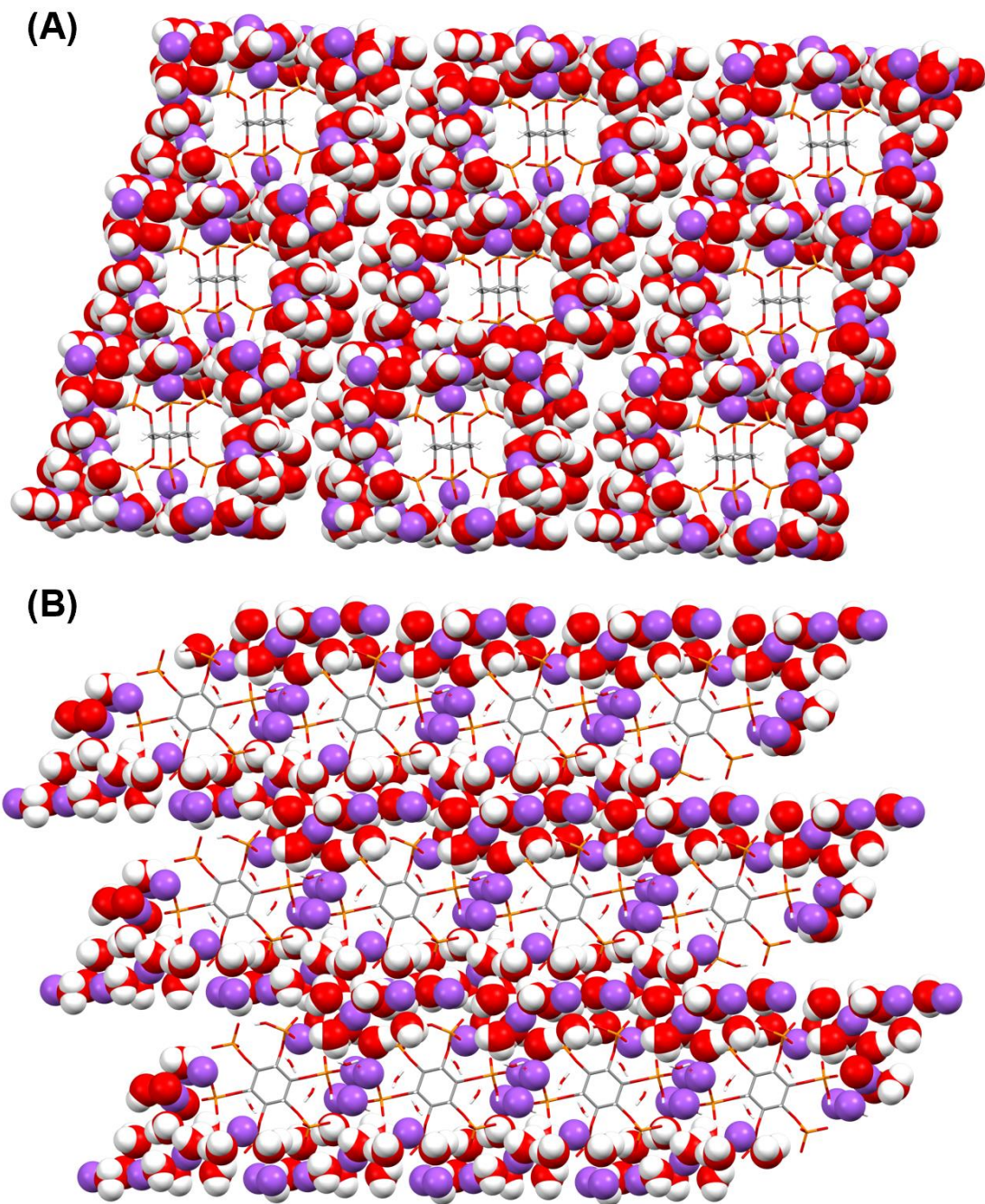
**Fig. S1.** Overhead and side perspective views of chelated water molecules for the 6a conformation for *scyllo-2*, (A) and (B), respectively, showing Na<sup>+</sup> ions within 3.0 Å of the center of the inositol. (C) Side views of the surrounding water coordination sphere for waters molecules directly interacting with *scyllo-2*.



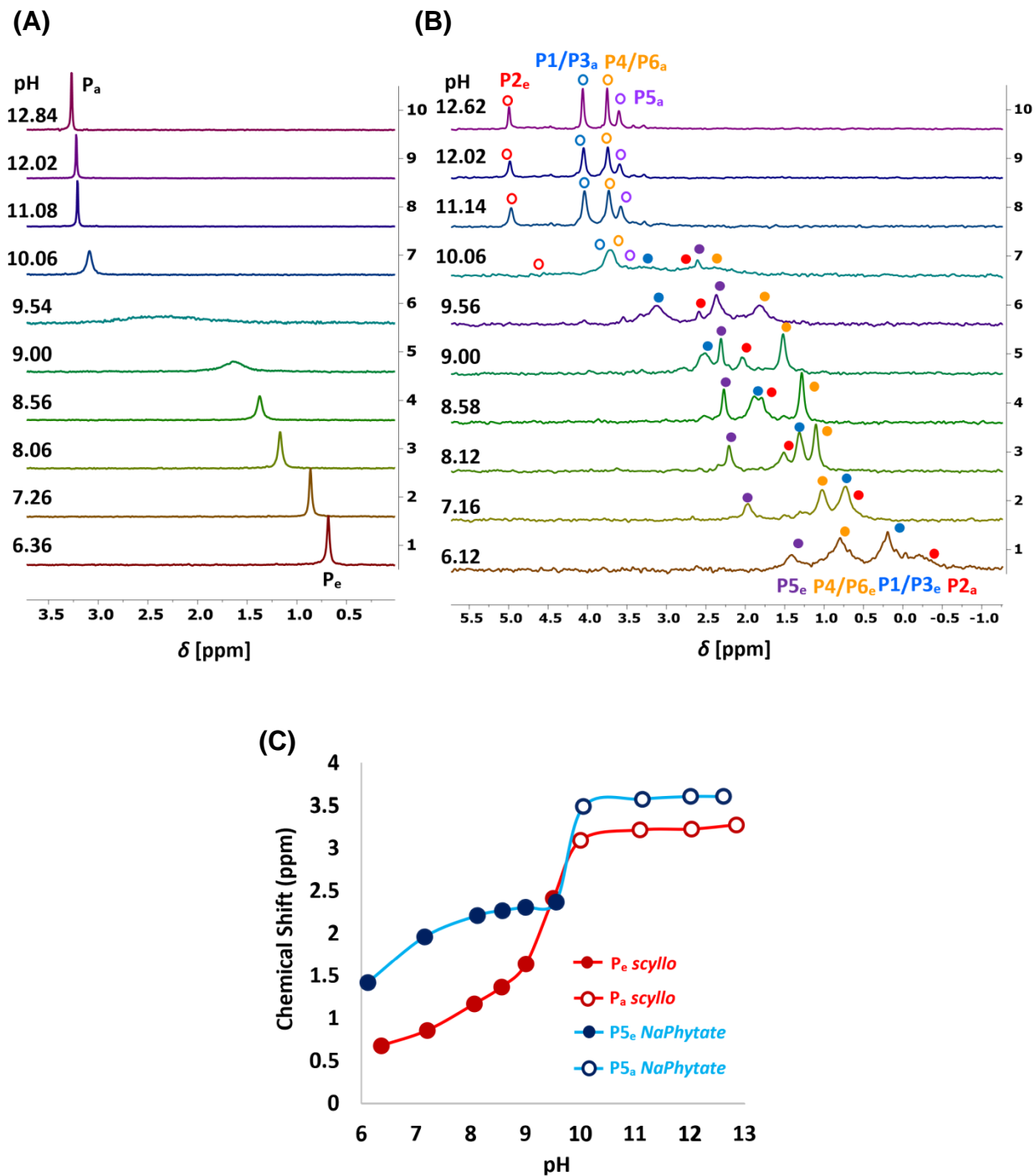
**Fig. S2.** Views of salt-water buffer zones around single *scyllo* ions showing overhead (A) and side (B) views of 6a conformations of *scyllo-1*. Sodium ions are represented by balls; waters and *scyllo-IP*<sub>6</sub> ions with stick-style bonds. Turquoise spheres represent Na<sup>+</sup> ions directly interacting with the *scyllo* phosphates.



**Fig. S3.** Space-filled views of salt-water buffer zones around single *scyllo* ions showing overhead and side views, respectively for 6a conformations: (A) and (D) of *scyllo-1*; (B) and (E) of *scyllo-2*, 6a conformations; and for the 6e conformation: (C) and (F) *scyllo-IP<sub>6</sub>*. Waters and sodium ions are represented by space-filled and *scyllo-IP<sub>6</sub>* as stick-style atoms. Turquoise spheres represent Na<sup>+</sup> ions directly interacting with the *scyllo* phosphates.

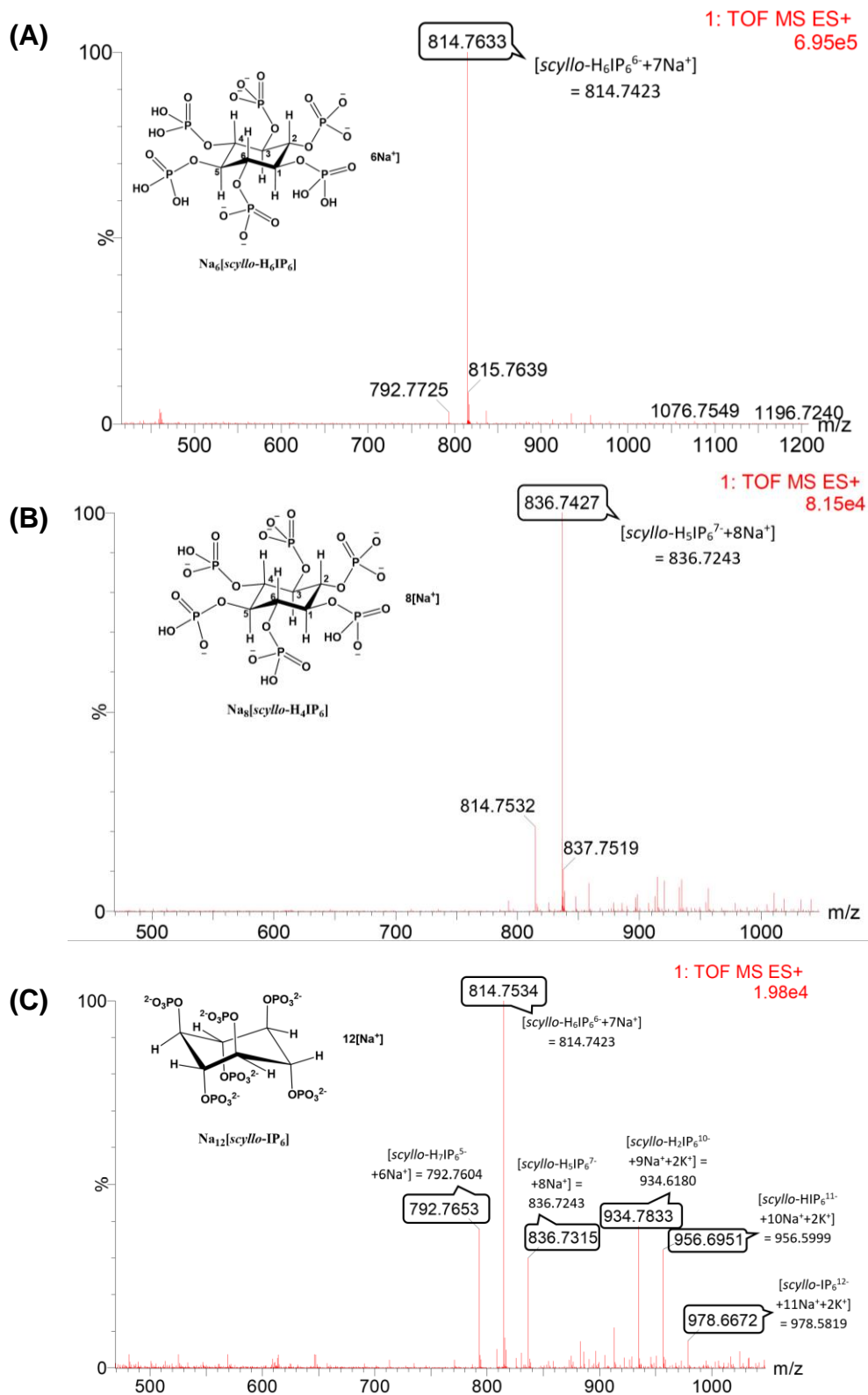


**Fig. S4.** Crystal packing of the (A) side view of *scyllo*-2 (6a) and (B) overhead view of *scyllo*-IP<sub>6</sub> (6e) with salt-water layers.



**Fig. S5.** Proton decoupled  $^{31}\text{P}$  NMR spectra (162 MHz) as a function of pH (Na(OH)) in  $\text{D}_2\text{O}$  at  $25^\circ\text{C}$ : (A) the  $\text{Na}^+$  salt of *scyllo*-IP<sub>6</sub> (10 mM) and (B) the  $\text{Na}^+$  salt of *myo*-IP<sub>6</sub> (20 mM); (C) Comparison of  $^{31}\text{P}$  chemical shift changes for the *scyllo* P singlet (red line) and the *myo* P5 signal (blue line), as a function of pH.





**Fig. S6.** ESI-MS (positive ion mode) spectrum of (A) purchased reagent  $\text{Na}_6[\text{scyllo-H}_6\text{IP}_6^{6-}]$ ; re-dissolved crystals of (B)  $\text{Na}_8[\text{scyllo-H}_4\text{IP}_6]$  and (C)  $\text{Na}_{12}[\text{scyllo-IP}_6]$ . Peaks has been denoted by the speciation along with calculated mass.

**Table S1.**  $^1\text{H}$  NMR chemical shift changes (ppm) of  $\text{Na}^+$  salt of *scyllo*-IP<sub>6</sub> (10 mM) and *myo*-IP<sub>6</sub> (20 mM) as a function of pH (Na(OH)) in D<sub>2</sub>O at 25°C.

<b>pH</b>	<b>H<sub>Nascyllo</sub></b>	<b>pH</b>	<b>H<sub>5NaPhytate</sub></b>
6.36	<b>4.24</b>	6.12	<b>4.2</b>
7.26	<b>4.21</b>	7.16	<b>4.18</b>
8.06	<b>4.18</b>	8.12	<b>4.17</b>
9	<b>4.24</b>	9	<b>4.16</b>
9.54	<b>4.42</b>	9.56	<b>4.17</b>
10.06	<b>4.53</b>	10.06	<b>4.57</b>
11.08	<b>4.53</b>	11.14	<b>4.56</b>
12.02	<b>4.53</b>	12.02	<b>4.56</b>
12.84	<b>4.53</b>	12.62	<b>4.56</b>

**Table S2.**  $^{31}\text{P}$  NMR chemical shift changes (ppm) of  $\text{Na}^+$  salt of *scyllo*-IP<sub>6</sub> (10 mM) and *myo*-IP<sub>6</sub> (20 mM) as a function of pH (Na(OH)) in D<sub>2</sub>O at 25°C.

<b>pH</b>	<b>P<sub>Nascyllo</sub></b>	<b>pH</b>	<b>P<sub>5NaPhytate</sub></b>
6.36	<b>0.68</b>	6.12	<b>1.42</b>
7.26	<b>0.86</b>	7.16	<b>1.96</b>
8.06	<b>1.17</b>	8.12	<b>2.21</b>
8.56	<b>1.37</b>	8.58	<b>2.27</b>
9	<b>1.64</b>	9	<b>2.31</b>
9.54	<b>2.41</b>	9.56	<b>2.37</b>
10.06	<b>3.09</b>	10.06	<b>3.49</b>
11.08	<b>3.21</b>	11.14	<b>3.58</b>
12.02	<b>3.22</b>	12.02	<b>3.61</b>
12.84	<b>3.27</b>	12.62	<b>3.61</b>

**X-ray Crystallographic Studies for 6a conformation  $[\text{Na}]_{12}[\text{scyllo-C}_6\text{H}_6(\text{PO}_4)_6]_{1.5} \cdot 60.8\text{H}_2\text{O}$  (1) and 6e conformation  $[\text{Na}]_8[\text{scyllo-C}_6\text{H}_6(\text{HPO}_4)_4(\text{PO}_4)_2] \cdot 26\text{H}_2\text{O}$  (2).**

Complete sets of unique reflections were collected with monochromated  $\text{CuK}\alpha$  radiation for single-domain crystals of both compounds. Totals of 3932 (1) and 2771(2)  $1.0^\circ$ -wide  $\omega$ - or  $\phi$ -scan frames with counting times of 4-6 seconds were collected with an Apex2 CCD (1) or Platinum 135 CCD (2) area detector. X-rays were provided by a shared high-flux Bruker MicroStar microfocus rotating anode operating at 45kV and 60 mA and equipped with dual CCD detectors and Helios high-brilliance multilayer (Platinum 135) or multilayer (Apex2) x-ray optics. Preliminary lattice constants were obtained with the Bruker program SMART.<sup>[S1]</sup> Integrated reflection intensities for both crystals were produced using the Bruker program SAINT.<sup>[S2]</sup> Each data set was corrected empirically for variable absorption effects using equivalent reflections. The Bruker software package SHELXTL was used to solve each structure using “direct methods” techniques. All stages of weighted full-matrix least-squares refinement were conducted using  $\text{Fo}^2$  data with the SHELXTL v2014.11-0 software package.<sup>[S3]</sup> The relevant crystallographic and structure refinement data for both structures are given in Table S1.

The final structural model for both structures incorporated anisotropic thermal parameters for all nonhydrogen atoms and isotropic thermal parameters for all included hydrogen atoms. The structure of (2) is well-ordered but the structure of (1) has very minor disorder. Phosphate oxygen atom O52 is 61%/39% disordered over two sites (O52 and O52') and their anisotropic thermal parameters were restrained to have equal values. One water is 82%/18% disordered over two sites (O58W and O58') and water oxygen O46W is included in the structure model with an occupancy factor of 0.80. One sodium is also 64%/36% disordered over two sites (Na19 and Na20)

All (2) or nearly all (1) of the hydrogen atoms in both compounds were located in a difference Fourier and incorporated into the structural models with isotropic thermal parameters that were initially allowed to vary in least-squares refinement cycles. Only one hydrogen could be located for O46w in the structure of (1) and no hydrogens for disordered water oxygens O58W and O58'.

All of the hydrogen atoms for (2) refined well and gave reasonable structural parameters. However, some of the hydrogen atom parameters for (1) refined to unreasonable values. The positions for these atoms (H352, H381, H382, H392, H452 and H461) were therefore fixed at their difference Fourier positions and their isotropic thermal parameters were fixed at values equal to 1.5 times the value of the equivalent isotropic thermal parameter of the oxygen atom to which they are covalently bonded. The isotropic thermal parameter of H251 was similarly fixed.

CCDC: 2027581 (1) and 2027582 (2).

**Table S3.** Crystal Data and Structure Refinement for **1** and **2**.

	<b>1</b>	<b>2</b>
Empirical formula	C <sub>9</sub> H <sub>129.44</sub> Na <sub>18</sub> O <sub>96.80</sub> P <sub>9</sub>	C <sub>6</sub> H <sub>62</sub> Na <sub>8</sub> O <sub>50</sub> P <sub>6</sub>
Formula weight	2479.91	1304.30
Temperature	200(2) K	200(2) K
Wavelength	1.54178 Å	1.54178 Å
Crystal system	Triclinic	Triclinic
Space group	P $\bar{1}$ – C <sub>i</sub> <sup>1</sup> (No. 2)	P $\bar{1}$ – C <sub>i</sub> <sup>1</sup> (No. 2)
<i>a</i>	11.8896(2) Å	7.7646(4) Å
<i>b</i>	20.6949(4) Å	12.0563(6) Å
<i>c</i>	22.3509(4) Å	13.7450(7) Å
<i>α</i>	113.5603(7)°	77.8930(10)°
<i>β</i>	90.6255(8)°	89.7550(10)°
<i>γ</i>	104.8657(8)°	89.0880(10)°
Volume	4832.24(15) Å <sup>3</sup>	1257.92(11) Å <sup>3</sup>
Z	2	2
Density (calculated)	1.704 Mg/m <sup>3</sup>	1.722 Mg/m <sup>3</sup>
Absorption coefficient	3.550 mm <sup>-1</sup>	3.830 mm <sup>-1</sup>
F(000)	2582	1352
Crystal size	0.160 x 0.150 x 0.035 mm <sup>3</sup>	0.580 x 0.070 x 0.060 mm <sup>3</sup>
Theta range	2.174 to 70.453°	6.780 to 68.150°
Index ranges	-13<= <i>h</i> <=14, -24<= <i>k</i> <=24, -26<= <i>l</i> <=26	-5<= <i>h</i> <=9, -14<= <i>k</i> <=14, -16<= <i>l</i> <=16
Reflections collected	68111	9678
Independent reflections	17055 [R(int) = 0.0382]	4325 [R(int) = 0.0272]

Completeness to $\theta = 66.00^\circ$	96.4%	96.6%
Absorption correction	Multi-scan	Multi-scan
Max. and min. transmission	1.000 and 0.7683	1.000 and 0.575
Refinement method	Full-matrix least-squares on $F^2$	Full-matrix least-squares on $F^2$
Data / restraints / parameters	17055 / 0 / 1715	4325 / 0 / 440
Goodness-of-fit on $F^2$	1.035	1.061
Final R indices [ $I > 2\sigma(I)$ ]	$R_1 = 0.0410$ , $wR_2 = 0.1047$	$R_1 = 0.0329$ , $wR_2 = 0.0926$
R indices (all data)	$R_1 = 0.0445$ , $wR_2 = 0.1082$	$R_1 = 0.0340$ , $wR_2 = 0.0936$
Largest diff. peak and hole	1.295 and $-0.826 \text{ e}^-/\text{\AA}^3$	0.646 and $-0.425 \text{ e}^-/\text{\AA}^3$

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## References

- [S1] Data Collection: SMART Software in APEX2 v2014.11-0 Suite. Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA.
- [S2] Data Reduction: SAINT Software in APEX2 v2014.11-0 Suite. Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA.
- [S3] Refinement: SHELXTL Software in APEX2 v2014.11-0 Suite. Bruker-AXS, 5465 E. Cheryl Parkway, Madison, WI 53711-5373 USA.