Anion coordination chemistry has developed rapidly in recent years because of the important roles anions play in many biological, environmental, and chemical processes. Studies have shown that the coordination behavior of the anions, although less well-defined, is quite similar to the coordination of transition metals; for example, anions also display “coordination geometry” and “coordination number.” These analogies provide promising ideas for the self-assembly of novel supramolecular systems based on anion coordination.

In the past few decades, zero-dimensional, aesthetically pleasing metal coordination complexes, such as molecular squares, capsules, tetrahedra, and other complex polyhedral shapes, have attracted much interest. Tetrahedral cages that contain an isolated space have been intensely studied as mimics of the microenvironments of bioprocesses, in stabilizing reactive intermediates, and as catalysts for chemical transformations. There are two typical approaches for constructing tetrahedral metal cages: By using C2-symmetric bis-chelating ligands and octahedral metal ions, M4L6-type species (with four metal ions at the vertices and six ligands along the edges) can be obtained. The other type of tetrahedral cages, the M4L4 compounds, is less common and can be assembled from C3-symmetric tris-chelating ligands which are positioned on the faces of the tetrahedron. In addition, there are also covalent organic cages comprised of a single molecule.

In contrast to the rich chemistry of metal-based systems, supramolecular architectures driven by anion coordination are underdeveloped, although anions can play crucial roles in templating exciting structures (e.g., the starlike helicates). In recent years, anion-centered structures, such as catenanes, rotaxanes, foldamers, and helices, have emerged; however, the well-defined cage complexes have not yet been explored. Compared to the transition-metal complexes, the assembly/disassembly process of anion-based supramolecular systems may be controlled under mild conditions (e.g., by acid/base modulation or by solvent polarity), which may be more promising for biological processes.

As part of our studies on anion coordination, we recently developed a series of ortho-phenylene-bridged oligoureia ligands, which display excellent affinity and complementarity to the tetrahedral sulfate and phosphate anions. More importantly, the fully deprotonated phosphate ion (PO43−) shows a strong tendency for “coordination saturation” (12 hydrogen bonds), a characteristic of tetrahedral anions that is proven both theoretically and experimentally. This property can ensure the formation of desired structures by hydrogen bonding six urea groups to its six edges. Hence, we designed the tris(bisurea) ligand L (Scheme 1) by attaching three bisurea moieties to a central C3-symmetric tripheylamine platform. Here we report the assembly of the first tetrahedral anion cage ([A4L4]-type (A = anion); 1) and a unique pinwheel helical [A1L1]-complex (2) from ligand L and PO43− and SO42− ions, respectively.

Ligand L was synthesized by the reaction of p-nitrophenyldisocyanate with N,N′,N″-(nitrilotri-4,1-phenylene)tris(2-aminophenylurea). Treatment of L with an equimolar quantity of (TMA)3PO4 (generated in situ from (TMA)OH and (TMA)2SO4) results in the spontaneous self-assembly of the tetrahedral anion cage (Scheme 1).

**Scheme 1.** Assembly of the A4L4 tetrahedral anion cage from phosphate anions and ligand L.

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and \( \text{H}_3\text{PO}_4 \); TMA = tetramethylammonium ion) afforded a yellow crystalline product in almost quantitative yield. The compound is readily soluble in common solvents such as acetone, acetonitrile, DMF, and DMSO. NMR spectroscopy, ESIMS, and elemental analysis proved that this species (TMA)\(_2\)\(([PO_4]_3L_4\] (I) was the unique product, with no evidence for the occurrence of other stoichiometries (see below for solution studies).

Complex I crystallizes from diethyl ether/acetonitrile in the centrosymmetric cubic space group \( \text{P}4_3\text{m} \). The structure has the ideal \( T \) symmetry with one twelfth of the tetrahedral molecular cage (one third of a phosphate ion, one third of the ligand, one TMA as the counter cation) appearing in the asymmetric unit. The four \( C_3 \)-symmetric ligands position on the four triangular faces of the tetrahedron, and each vertex is defined by a phosphate ion which is coordinated by three bisurea arms (Figure 1). The four axial-chiral PO\(_4\)\(^{-3} \) centers have the same configuration (\( \text{AA} \text{AA} \) or \( \text{AAAA} \)) in the tetrahedral. However, as in most \( M_4L_4 \) tetrahedra with achiral ligands,\(^\text{[7]} \) both \( P \)- and \( M \)-handed \([\text{A}_x\text{L}_y \text{]} \) enantiomers are present in the crystal lattice of complex I.

The tetrahedral cage I represents the first example of a new class of anion-coordination supramolecular hosts. Each phosphate ion is bound to six urea groups from three different ligands through 12 strong N···O hydrogen bonds (N···O distances range from 2.81\( \pm \)0.02 to 2.88\( \pm \)0.02 \( \AA \), average 2.81\( \pm \)0.02 \( \AA \); N···H···O angles range from 157 to 167\( \pm \)4\( \circ \), average 163\( \pm \)4\( \circ \); see Figure 1 and Table S2 in the Supporting Information). Altogether there are 48 N···H···O hydrogen bonds. In addition, there is also a C···H···O hydrogen bond (C···H: 3.34\( \pm \)0.05 \( \AA \); \( \alpha \)-CHO: 133\( \circ \)) from one \( \alpha \)-CH proton of each three terminal urea arms deviate from the triangular plane and point to the same side of the plane. Two ligands stack in a face-to-face fashion, with three \( \text{SO}_4^{2-} \) ions between. Notably, the structure is not \( C_3 \)-symmetric in the solid state. The S···S separations are 12.7 and 14.0 \( \AA \), and the central N···N separation between two ligands is 5.50 \( \AA \). Each sulfate ion is bound by four urea groups through eight N···O hydrogen bonds (see Figure S8 and Table S3 in the Supporting Information). Moreover, C···H···O hydrogen bonds also occur with the anions (see Figure S8 in the Supporting Information), and T-shaped CH···π interactions are formed between the terminal nitrophenyl rings and the o-phenylene planes, with CH···π distances of 3.67–3.98 \( \AA \) (see Figure S7 in the Supporting Information).

Notably, although the tetrahedral sulfate and phosphate ions can both potentially accept a maximum of 12 hydrogen bonds,\(^\text{[12]} \) we found that they lead to significantly different solid-state structures. The trianionic phosphate ion tends to accept 12 hydrogen bonds and, thus, can coordinate with three bisurea fragments, while the dianionic sulfate ion does not.

In the tetrahedral cage, the \( \text{PO}_4^{2-} \)···\( \text{PO}_4 \) separation is about 15 \( \AA \), and the internal volume was estimated with the VOIDOO program to be about 181 \( \text{Å}^3 \).\(^\text{[15]} \) The volume of the countercation TMA was calculated to be approximately 121 \( \text{Å}^3 \) by DFT using the B3LYP/6-31G* method. An optimum encapsulation of about 55% was observed in many host–guest systems (for neutral guests),\(^\text{[16]} \) and it would be expected that the tetrahedral cage is too small to include the TMA ion. Indeed, there is no guest inside the cage, and in the crystal structure the TMA cations and solvent molecules are found outside the cage.

Treatment of L with \([\text{K}([\text{18-crown-6}])]\text{SO}_4 \) afforded the sulfate complex \([\text{K}([\text{18-crown-6}])]_4 \text{[SO}_4\text{]}_3 \text{[L]}_4\text{·3CH}_3\text{COCH}_3 \) (2). Complex 2 (C2/c) shows a pinwheel-like helical structure, in which the bisurea arms cross over the \( \text{SO}_4^{2-} \)···\( \text{SO}_4^{2-} \) axes (Figure 2a).\(^\text{[17]} \) The ligand adopts a conformation such that the

![Figure 1](image1.png)

**Figure 1.** (a) The tetrahedral cage \([\text{PO}_4]_3\text{L}_4\]\(^{2-} \) in the crystal structure of 1, with the dark-blue facial ligand truncated so that the interior and opposite \( \text{PO}_4 \) corner can be seen; b) hydrogen bonds around the \( \text{PO}_4^{2-} \) ion; c,d) space-filling representation of the tetrahedron with a view onto a corner (c) or a face (d). Only a \( P \) enantiomer is shown, and non-acidic hydrogen atoms are omitted for clarity.

![Figure 2](image2.png)

**Figure 2.** a) The “pinwheel” helical sulfate complex \([\text{SO}_4\text{]}_3\text{L}_4\]\(^{2-} \) in the crystal structure of 2; b,c) top and side view of the space-filling representation. Only an \( M \) enantiomer is shown.
reach saturated coordination. This difference was also observed in the assembly of the triple anion helicate in the presence of a phosphate ion, whereas the sulfate ion only leads to a single-stranded 1:2 complex.\cite{11l} The reason might be the higher negative charge density and stronger basicity of the phosphate ion which requires more hydrogen bonds for efficient binding.

The assembly of L and PO$_4^{3-}$ in solution was investigated. The $^1$H NMR spectrum of complex I in [D$_6$]DMSO/5% water (v/v) revealed very large downfield shifts of the signals corresponding to all the urea NH protons ($\Delta\delta = 2.75$–3.58 ppm) compared to the free ligand, thus indicating strong hydrogen bonds to the PO$_4^{3-}$ ions. When 1.0 equivalent of PO$_4^{3-}$ ions (as the [K([18]crown-6)])$_3$PO$_4$ salt) were titrated into a solution of L ($5 \times 10^{-3}$M), similar downfield shifts of the NH protons were observed (Figure 3 and see Figure S9 in the Supporting Information). No further changes appeared with the strong hydrogen bonding, and there is no other phosphate species in solution.

Furthermore, 2D-DOSY was also performed in [D$_6$]DMSO at 298 K. The DOSY spectrum of complex I (see Figure S14 in the Supporting Information) showed that all of the signals that correlate to the chemical shifts of ligand L are in a horizontal line, with a diffusion coefficient ($D$) of $9.0 \times 10^{-11}$ m$^2$s$^{-1}$. The hydrodynamic radius ($r_h$) of this species was calculated from the Stokes–Einstein equation to be about 12.0 Å, which is slightly smaller than that found in the crystal structure (see Figure S15 in the Supporting Information).

The high-resolution ESI mass spectrum of (TMA)$_4$[(PO$_4$)$_4$L$_3$] exhibited intense signals for [A,L$_3$] species ([TMA)$_4$][H]$_2$[(PO$_4$)$_4$L$_3$]$^{4+}$ at $m/z = 1068.707$ (x = y = z = 4), 1083.326 (x = 4, y = 5, z = 5), 1354.409 (x = y = 4, z = 4), and 1372.679 (x = 5, y = 3, z = 4; see Figure S17 and Table S4 in the Supporting Information). The observed isotopic patterns agree well with the simulated ones. These results suggest that the tetrahedral structure also persists in solution. The phosphate ion can be protonated or deprotonated to different states (PO$_4^{3-}$, HPO$_4^{2-}$, H$_2$PO$_4^-$, and HPO$_4^-$) when the external environment is changed, which could greatly influence the binding affinity and regulate the structure of the anion complex. Thus, a reversible formation of complex I was established by acid/base modulation and monitored by $^1$H NMR spectroscopy ([D$_6$]DMSO/5% H$_2$O). The addition of HClO$_4$ to a solution of complex I resulted in the PO$_4^{3-}$ ion being protonated gradually and the tetrahedral structure was disassembled (Figure 4). In contrast, when a base (TMAOH) was introduced, the protonated anions were deprotonated again, and the tetrahedral structure was reassembled (see Supporting Information for details). These results demonstrate that the assembly/disassembly of the anion-coordination-based cage can be readily controlled by the addition of acid or base. Moreover, the effects of other conditions such as temperature, solvent, and concentration on complex I were also examined, and the results revealed the complex to be...
remarkably stable. The variable-temperature 1H NMR spectra recorded in [D$_6$]DMSO showed that complex 1 is stable up to 80°C (see Figure S18 in the Supporting Information), and the cage can persist in different solvents (acetone, acetonitrile, DMSO), as indicated by NMR spectroscopy and ESIMS studies. Dilution of complex 1 in [D$_6$]DMSO resulted in no signs of disassembly on the NMR scale (see Figure S19 in the Supporting Information).

The 1H NMR spectrum of the sulfate complex 2 recorded in [D$_6$]DMSO revealed that all of the resonances of the urea NH groups underwent downfield shifts (Δδ = 0.46–1.62 ppm) relative to the signal of free ligand. The NOESY spectrum gave a diffusion coefficient of $D = 9.8 \times 10^{-11}$ m$^2$s$^{-1}$, which corresponds to an $R_g$ value of about 11.0 Å (see Figures S14 and S15 in the Supporting Information). The evolution of the spectrum was easy to follow in the 1H NMR titration experiments (see Figure S10 in the Supporting Information). Detailed discussion of the titration process is given in the Supporting Information. Notably, the titration revealed both 2:3 and 2:1 (host to guest) binding modes. This difference between the binding stoichiometry in the solid state and common and has been observed for many anion-binding receptors.

In conclusion, a C$_x$-symmetric tri(bisurea) ligand (L) has been designed. Self-assembly of L and phosphate anions (PO$_4^{3-}$) affords the expected highly negatively charged [A$_n$L]$_i$-type tetrahedral cage [PO$_4$$_i$L]$_{12}^-$ (complex 1) held together by 48 hydrogen bonds. In the complex, the phosphate ions occupy the vertices and the ligands lie on the faces. This conceptual study represents the first example of the successful assembly of tetrahedral cages through anion coordination, further proving the resemblance of metal coordination and anion coordination behavior in terms of the coordination number and geometry. Notably, the reversible assembly/disassembly of the tetrahedral cage 1 can be readily modulated under mild conditions by the addition of acid and base. Extension to bigger cages and higher polyhedra as well as investigation of their host–guest properties are currently underway.

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[13] CCDC 909133 (1) and 909134 (2) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[14] The structure of the tetrahedral cage \([\text{PO}_4]_{12}\) was optimized at the B3LYP/6-31G level using the Gaussian03 program suit (for full citation, see the Supporting Information).

[15] The cavity volume was calculated using the VOIDOO program, with a 1.4 Å diameter rolling ball on the crystal structure of complex 1.
