Anion Binding in Water Drives Structural Adaptation in an Azaphosphatranne-Functionalized Fe\textsuperscript{II}₄L₄ Tetrahedron

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Supporting Information

ABSTRACT: Anion-templated aqueous self-assembly resulted in the formation of an endohedrally functionalized Fe\textsuperscript{II}₄L₄ tetrahedron from azaphosphatranne-based subcomponents. This new water-soluble cage is flexible and able to encapsulate anions with volumes ranging from 35 to 219 Å³ via hydrogen bonding and electrostatic interactions. It structurally adapts in response to the size and shape of the template anions, dynamically adopting a conformation either where all four azaphosphatranne +P–H vectors point inward, or else where one points outward and the other three inward. The two cage isomers can coexist in solution and interconvert. A shape memory phenomenon was observed during guest displacement because guest exchange occurs more rapidly than structural reconfiguration.

Self-assembly is an efficient tool for the construction of diverse functional architectures. One subset of these, metal–organic polyhedral complexes, have proven useful in a range of applications, including molecular recognition,† chirality sensing,‡ gas separation,§ stabilization of reactive species,¶ and catalysis.† The strategy of subcomponent self-assembly allows the preparation of a variety of capsules with different shapes and sizes, which bind many different guests.¶ Most such capsules contain cavities surrounded by aromatic panels.¶ The elaboration of the cavity microenvironment, through incorporation of functional moieties,¶ represents an attractive means by which specific substrate encapsulation might be achieved.

Azaphosphatranes, the conjugate acids of Verkade superbases,§ are attractive functional moieties for incorporation into the faces of tetrahedral capsules. Their polarized +P–H groups enable them to be employed as catalysts for CO\textsubscript{2} activation and lactide ring-opening polymerization.¶ Although both of these applications benefit from the hydrogen-bond donor ability of the +P–H group, their use as anion receptors has not been reported. Importantly, these cationic species can be rendered water-soluble via selection of a suitable counterion, potentially enabling their use as anion binders in water, the development of which has been identified as a key challenge in supramolecular chemistry.¶ Anion recognition in water is intimately involved in many chemical, biological, and environmental processes.¶ However, hydration of both the host and guest often hinders complexation.†¶ Nonetheless, several synthetic anion receptors able to operate in water have been reported, employing hydrophobic effects, metal-anion coordination, C–H hydrogen bonds, and halogen bonds.†¶ Here we report a new azaphosphatranne-functionalized tetrahedron 1 (Scheme 1), assembled from cationic triamine subcomponent A. The design of 1 was based on the following four principles. First, the cationic azaphosphatrane together with the metal ions provide an overall +12 charge, offering a strong electrostatic driving force for anion binding. Second, the cationic framework also inductively increases the affinity of the +P–H hydrogen bond donor for anionic species.¶ Third, the sulfate counterion was chosen to maximize the water solubility of 1. Fourth, methylene groups between the phenyl rings and azaphosphatranne nitrogen atoms were introduced to enhance cage flexibility, enabling the cavity to fit a diverse array of anions.

We first prepared cage 1 as the bis(trifluoromethanesulfonyl)imide (trilimide, Tf₂N⁻), hexafluorophosphate (PF₆⁻), and trifluoromethanesulfonate (triflate, TfO⁻) salts, all of which were soluble in acetonitrile (Scheme 1). The chloride salt of subcomponent A was obtained in four steps (Scheme S1). The Cl⁻ of A readily exchanged with Tf₂N⁻, PF₆⁻, or TfO⁻ via anion metathesis. The subsequent reaction of A (4 equiv) with the corresponding FeX₂ salt (4 equiv) and 2-formylpyridine (12 equiv) in acetonitrile gave a single product with one azaphosphatranne capping each face (Scheme 1). Products were characterized by NMR and mass spectrometry (Figures S1–S36).

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$^{19}$F NMR spectra (Figures S5, S17, and S29) indicated the encapsulation of one anion inside the cavity, in slow exchange on the NMR time scale with the external anions.

Single-crystal X-ray diffraction confirmed the structure of 1 in the solid state. As shown in Figure 1, 1 has a face-capped tetrahedral framework with approximate T-symmetry. Both enantiomers (ΔΔΔΔ and ΔΔΔΔ) are present in the unit cell. The 'P–H groups of the azaphosphatrane units point inward into the cavity, where a disordered TfO$^{-}$ is encapsulated. The Fe$^{III}$ centers are separated by an average of 14.7 Å, and the volume of the central cavity approximates 166 Å$^{3}$ (51% occupancy for TfO$^{-}$, Figure S72).

We then attempted the preparation of a water-soluble cage by employing SO$_4^{2-}$ counterions. The initial Cl$^{-}$ of A was exchanged for SO$_4^{2-}$ (Scheme S2). However, the subsequent reaction of the sulfate salt of A (4 equiv) with Fe$_2$SO$_4$ (4 equiv) and 2-formylpyridine (12 equiv) in water failed to give the expected cage complex (Figure S37). We infer that the hydrophilic character of SO$_4^{2-}$ prevents it from acting as a template for the formation of 1. Therefore, a series of other anions with different shapes and volumes, listed in Figure 2, were added to the aqueous reaction mixture to investigate their template effects (1 equiv of anion was added in each case with regard to the final cage).

All of the anions listed in Figure 2, with volumes ranging from 35 Å$^{3}$ (I$^{-}$) to 219 Å$^{3}$ (CB$_{11}$H$_{12}$), were observed to serve as competent templates for 1 in water, indicating that its cavity adapted readily to guests having different sizes and shapes.

Cage 1 manifested this adaptability in a novel way: for the smaller template anions, with volumes ≤53 Å$^{3}$, part of the population of 1 consisted of a C$_3$-symmetric isomer (C$_3$-1) in which one of the azaphosphatrane 'P–H groups was oriented away from the inner cavity (exo) with the other three points inward (endo). A T-symmetric isomer (T-1), containing four endo 'P–H groups, constituted the other part of the population. For the larger anionic templates, having volumes ≥55 Å$^{3}$, the T-symmetric isomer (T-1) of the cage was observed exclusively.

The $^1$H NMR spectra of 1 templated by BF$_4^{−}$, NO$_3^{−}$, or I$^{-}$ in water thus show five sets of ligand signals (Figures S38) in which one set belongs to T-1, while the other four sets in a 1:1:1:1 ratio belong to C$_3$-1 (for full structural assignment of C$_3$-1, see Figure S43). The corresponding $^{31}$P NMR spectra exhibit three peaks, one for T-1 and two in a 3:1 ratio for C$_3$-1 (Figure S39). The two cage isomers were observed to interconvert, taking at least 2 weeks at 298 K to reach equilibrium, as monitored by both $^1$H and $^{31}$P NMR.

For the self-assembly with NO$_3^{−}$ as a template, gradual conversion from T-1 to C$_3$-1 was observed, with the ratio changing from 58:42 at 24 h to 10:90 at 215 h (Figures 3 and S40–S42). This observation indicates that the initially formed mixture between NO$_3^{−}$CT-T$^{-}$1-[SO$_4^{2-}$]$_{1.5}$ (●) and NO$_3^{−}$CC$_3$-1-[SO$_4^{2-}$]$_{1.5}$ (▲) at 298 K by monitoring the integration of the corresponding imine peaks in the $^1$H NMR spectra (D$_2$O, 500 MHz, 298 K). DOSY NMR indicated that the two species diffuse at the same rate.

Figure 2. Schematic representation of the two cage isomers X$^{−}$CT-1 and X$^{−}$CC$_3$-1 obtained by aqueous self-assembly in the presence of 1 equiv of template anion. The cage faces colored orange represent endo-azaphosphatrane ligands, with 'P–H pointing inward, while the cyan face represents exo 'P–H.

Figure 3. Time evolution of the ratio between NO$_3^{−}$CT-T$^{-}$1-[SO$_4^{2-}$]$_{1.5}$ (●) and NO$_3^{−}$CC$_3$-1-[SO$_4^{2-}$]$_{1.5}$ (▲) at 298 K by monitoring the integration of the corresponding imine peaks in the $^1$H NMR spectra (D$_2$O, 500 MHz, 298 K). DOSY NMR indicated that the two species diffuse at the same rate.

This observation indicates that the initially formed mixture between NO$_3^{−}$CT-T$^{-}$1 and NO$_3^{−}$CC$_3$-1 is kinetically metastable. The ratio further shifted to a constant value of 5:95 after 2 weeks at 298 K (Figure S43), corresponding to a Gibbs free energy change ($\Delta G$) of 7.3 kJ mol$^{-1}$ in favor of the C$_3$ isomer. The free energy of activation ($\Delta G^*$) from NO$_3^{−}$CT-T$^{-}$1 to NO$_3^{−}$CC$_3$-1 was calculated to be 105 kJ mol$^{-1}$ at 298 K (Supporting Information section 2.4.4 and Figure S68).

In the cases of BF$_4^{−}$ (Figures S51 and S52) and I$^{-}$ (Figures S54 and S55), T-1 was observed to be thermodynamically favored over C$_3$-1, giving equilibrium ratios of 90:10 and 56:44. These values correspond to $\Delta G$ differences of 5.4 and 0.64 kJ mol$^{-1}$, respectively. The $\Delta G$ values at 298 K for the conversion from...
The volume of the preorganized planar cavity approximates 59 Å³ relative to

Figure 4. MM3-optimized molecular model of NO₃⁻⊂C₃-I based on the crystal structure of TfO⁻⊂C₁ shown in Figure 1. Non-P-bound hydrogen atoms are omitted for clarity. The exo-azaphosphatrane ligand is colored cyan.

centrally bound by the three endo ‘P–H groups. The methylene groups of the exo-azaphosphatrane occupy the rest of the cavity. The volume of the preorganized planar cavity approximates 59 Å³ (69% occupancy for NO₃⁻, Figure S72), significantly smaller than that of TfO⁻⊂T-1 (166 Å³). This model also suggests that the shape-fit between C₃-I and NO₃⁻ may account for the greater favoring by this anion of this isomer, as compared to BF₄⁻ (Figure S53) or I⁻ (Figure S56).

H, ¹³C, and ³¹P NMR spectra of 1 templated by ClO₄⁻, ReO₄⁻, PF₆⁻, TfO⁻, Tf₂N⁻, or CB₁₁H₁₂NO₃⁻ in water show only one set of ligand signals (Figures S57–S60), consistent with the exclusive formation of T-1. The ¹H–¹⁹F HMQC spectra of the TfO⁻ and PF₆⁻ adducts of T-1 exhibited strong NOE correlations between the F atoms of the encapsulated guest and the ‘P–H of the azaphosphatrane, underlining the hydrogen bonding interactions (Figures S61, S66, and S67).

Although the cage was unstable in the absence of a template anion, competitive guest exchange offers a way of measuring the relative binding affinities of the different anions. We first chose TfO⁻⊂C₁-[SO₄]₅.₅₋ as the reference to determine the hierarchy of binding affinities of these latter anions. We observed by ‘H NMR that 1.7 equiv of CB₁₁H₁₂NO₃⁻ completely displaced the encapsulated Tf₂N⁻ (Figure S76), while a larger excess (>6 equiv) of BF₄⁻ or I⁻ was needed for Tf₂N⁻ displacement, with BF₄⁻ binding more strongly than I⁻ (Figures S77 and S78). NO₃⁻ (12 equiv) was unable to displace the bound Tf₂N⁻. Combining these results, we observe the following anion binding hierarchy in water: PF₆⁻ > ReO₄⁻ > TfO⁻ > ClO₄⁻ > CB₁₁H₁₂NO₃⁻ > Tf₂N⁻ > BF₄⁻ > I⁻ > NO₃⁻.

Although tetrahedron 1 templated by BF₄⁻ was observed in two distinct isomeric forms (T-1 ⇌ C₃-I), we noted during the titration of BF₄⁻ into Tf₂N⁻⊂T-1 that only BF₄⁻⊂T-1 was observed within 5 h. BF₄⁻⊂C₃-I appeared only thereafter, indicating a short-term shape memory effect (Figure 5).

Figure 5. Schematic representation of two successive processes: fast guest displacement of Tf₂N⁻ or NO₃⁻ by BF₄⁻, giving rise to a shape memory phenomenon, followed by slow isomeric reconfiguration.

experiments showed that, after addition of BF₄⁻ (2 equiv) to 5:95 ratio of NO₃⁻⊂CT-1:NO₃⁻⊂C₃-I in solution, a 5:95 ratio of BF₄⁻⊂CT-1/BF₄⁻⊂C₃-I was observed immediately after the anion displacement (Figure S79). BF₄⁻⊂C₃-I then gradually converted to BF₄⁻⊂T-1. These results indicate the occurrence of two successive processes: rapid guest displacement, with maintenance of the initial ratio of cage diastereomers, followed by slower BF₄⁻ templated isomeric reconfiguration.

Taking advantage of the larger population of BF₄⁻⊂C₃-I (95%) following anion exchange from NO₃⁻⊂C₁, we were able to observe heteronuclear NOE correlations between the bound BF₄⁻ and the methylene protons of the exo-azaphosphatrane of BF₄⁻⊂C₃-I in ¹H–¹⁹F HOESY spectrum (Figure S80). These correlations provide important structural evidence for the exo conjugation of one face of C₃-I, but they could not be observed directly in the BF₄⁻ templated assembly, wherein the population of BF₄⁻⊂C₃-I constituted less than 25%.

In summary, this study has demonstrated the feasibility of introducing azaphosphatrane into polyhedral complexes using subcomponent self-assembly and also shown the utility of azaphosphatrane as anion binding moieties. The designed flexibility of the structures reported herein enables the aequous binding of anions with volumes ranging from 35 to 219 Å³ via hydrogen bonding and electrostatic interactions. Structural adaptation of the cage framework was observed in response to the sizes and shapes of template anions, enabling the selective formation of either a T- or a C₃-symmetric cage framework, which...
are capable of interconversion. A shape memory phenomenon was observed during guest displacement, due to its faster kinetics compared to those of framework reconfiguration. Future work will seek to use this tailored cage or one of its derivatives as a catalyst, benefitting from the internally oriented azaphosphatrane H-bond donors, for instance, for CO₂ conversion.

**ASSOCIATED CONTENT**

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b02950.

Experimental details (PDF)

Crystallographic data for TfO⁻C1 (CCDC 1529220) (CIF)

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Notes

The authors declare no competing financial interest.

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