A Double-Walled Tetrahedron with Ag$_4^1$ Vertices Binds Different Guests in Distinct Sites


Abstract: A double-walled tetrahedral metal-organic cage assemblage in solution from silver(I), 2-formyl-1,8-naphthyridine, halide, and a threefold-symmetric triamine. The Ag$_4^1$X clusters at its vertices bring together six naphthyridine-imine moieties, leading to a structure in which eight tritopic ligands bridge four clusters in an (Ag$_4^1$X)$_4$L$_4$ arrangement. Four ligands form an inner set of tetrahedron walls that are surrounded by the outer four. The cage has significant interior volume, and was observed to bind anionic guests. The structure also possesses external binding clefts, located at the edges of the cage, which bound small aromatic guests. Halide ions bound to the silver clusters were observed to exchange in a well-defined hierarchy, allowing modulation of the cavity volume. The principles uncovered here may allow for increasingly more sophisticated cages with silver-cluster vertex architectures, with post-assembly tuning of the interior cavity volume enabling targeted binding behavior.

The potential utility of Ag$_1^+$ as a structural metal ion in such complex cages is highlighted by an elegant series of topologically entangled cages bound with silver(I) reported by Fujita and co-workers,[9] as well as a range of Ag$_1^+$-carbene cages and metallacycles.[10] The flexible coordination environment of Ag$_1^+$ has also been used to synthesize a range of Ag$_1^+$-dipyridylpeptide coordination complexes, achieving even greater topological complexity.[11]

Self-assembled metal-organic structures that incorporate polymetallic clusters as vertices,[12] as opposed to single metal ions, are beginning to be developed.[13] Strategies that enable the rational design of these more intricate assemblies are likewise under investigation. The ability of the ‘soft’ metal Ag$_1^+$ to form clusters[14] and to support differing coordination numbers and environments makes this metal well suited to the formation of cluster-vertex assemblies.[15] We have reported a trigonal-prismatic structure containing disilver vertices,[16] and a series of hexameric helicates containing tetra- and hexa-silver clusters as vertices.[17] These structures demonstrate the diverse coordination environments that emerge when naphthyridine-imine ligands direct the formation of Ag$_1^+$ clusters. However, previous structures provided relatively small internal volumes for guest binding.

In this work, we report the incorporation of [Ag$_4^1$I]$^{2-}$ clusters into a previously unreported type of double-walled tetrahedral structure,[18] and explore its guest binding potential. This structure exhibits both interior and peripheral guest binding, with distinct groups of guests favoring each site. Furthermore, we found that the silver clusters at the tetrahedron vertices underwent halide exchange, which enabled us to finely tune the volume of the interior cavity.

Supporting information for this article is given via a link at the end of the document.

[a] S. E. Clark, Dr A. W. Heard, Dr C. T. McTernan, Dr T. K. Ronson, Prof J. R. Nitschke
Yusuf Hamied Department of Chemistry
University of Cambridge
Lensfield Road, Cambridge, CB2 1EW, U.K.
E-mail: jm34@cam.ac.uk
[b] Dr A. W. Heard
Astex Pharmaceuticals
436 Cambridge Science Park, Milton Road, Cambridge, CB4 0QA, U.K.
[c] Dr C. T. McTernan
The Francis Crick Institute
Midland Road, London, NW1 1AT, U.K.
[d] Dr C. T. McTernan
Department of Chemistry
King’s College London
7 Trinity Street, London, SE1 1DB, U.K.
[e] Dr B. Rossi
Eleftra Sincrotrone Trieste
Basovizza, Trieste, IT-34149, Italy
[f] P. Rozhin, Prof S. Marchesan
Department of Chemical and Pharmaceutical Science
University of Trieste
Trieste, IT-34127, Italy
E-mail: smarchesan@units.it

Metal-organic cages that assemble from metal ions and organic ligands possess well-defined interior cavities that can bind guests selectively. These molecular containers have applications in molecular recognition and chemical separations,[7] stabilization of highly reactive molecules,[2] catalysis,[3] and sensing.[4] Subcomponent self-assembly, whereby higher-order cage structures emerge from simple precursors through the simultaneous formation of covalent C=N and coordinative N→ metal coordination bonds, has allowed others[5][6] and our group[15] to prepare intricate three-dimensional structures, encompassing Platonic and Archimedean solids, and beyond.[7] Different design strategies produce architectures with different sizes and symmetries,[5] allowing tuning of the interior cavity’s sizes and properties.
The reaction between 1,3,5-tris(4-aminophenyl)benzene (A, 8 equiv.) with 2-formyl-1,8-naphthyridine (B, 24 equiv.), Ag bis(trifluoromethanesulfonyl)imide (triflimide or \(\text{NTf}_2\), 16 equiv.) and tetra-n-butylammonium iodide (TBAI, 4 equiv.) produced cage 1 (Figure 1a). The \(^1\text{H}\) NMR spectra of 1 exhibited two magnetically distinct ligand environments (Figure 1b), with two distinct imine signals assigned by HSQC (Figure S6). The DOSY NMR spectrum confirmed that both environments corresponded to a single discrete structure, with a diffusion coefficient of \(3.06 \times 10^{-6} \text{ cm}^2\text{s}^{-1}\) in CD\(_2\)CN, giving a solvodynamic radius of 21.2 Å (Figure 1d). The mass spectrum (Figure S10-14) indicated a \([\text{Ag}_{16}\text{L}_2]\)\(^{12+}\) composition.

Single-crystal X-ray diffraction revealed the molecular structure of 1 to be a \(T\)-symmetric double-walled tetrahedron. Two tritopic ligands span each face of the tetrahedron (Figure 1a), consistent with NMR and MS. Each vertex consists of a \([\text{Ag}^\text{II}]^{3+}\) cluster (Figure 1c), with \(\text{Ag}^+ - \text{Ag}^+\) distances of 3.03 Å between the capping \(\text{Ag}^+\) and each of the three \(\text{Ag}^+\) centers closer to iodide. This distance is within the sum of the Van de Waals radii \(3.44 \text{ Å}\) for two \(\text{Ag}^+\) ions, and similar to the 2.97-3.00 Å distance reported for previous vertex clusters\(^{17}\) and other naphthyridine-bridged \(\text{Ag}^+\) clusters\(^{19}\). The phenyl core of the inner and outer ligands is separated by 3.67 Å, in the typical range for a \(\pi-\pi\) stacking interaction. The structure has a distance between farthest-spaced silver ions of 18.7 Å, comparable to the solvodynamic radius observed in DOSY. The innermost triads of \(\text{Ag}^+\) ions were separated by 4.32 Å, suggesting that these \(\text{Ag}^+\) ions do not undergo argentophilic interactions with each other.

Three observations help clarify how the naphthyridine-imine ligand binding groups help shape the silver clusters at the vertices of 1. First, the imine nitrogen atoms of the inner panels (blue in Figure 1) are oriented away from the \(\text{Ag}^+\) centers, and are therefore uncoordinated. Second, the outer ligands (green in Figure 1) adopt a bridging role, with each naphthyridine N-atom bound to a different \(\text{Ag}^+\) center (Figure 1b). Third, in contrast with these outer-ligand naphthyridines, one in each pair of naphthyridine N-atoms of the inner (blue) ligands effectively chelates \(\text{Ag}^+\) ions from the inner set closest to iodide (Figure 1c, coordination bond shown in white). Each inner \(\text{Ag}^+\) thus coordinates to one imine nitrogen from an inner (blue) ligand and one from an outer (green) ligand. The flexibility of naphthyridine to either bridge or chelate \(\text{Ag}^+\) thus appears to again play an important role in bringing the silver-cluster vertices of 1 together, as has been observed elsewhere\(^{16,17,20}\).

The tight arrangement of tritopic ligands around the cage interior results in a high degree of enclosure. The available cavity space within 1 was calculated to be 103 Å\(^3\) using Molosol\(^{21}\). With this available volume in mind, small neutral and anionic species were screened as potential guests for 1.
Figure 2. Schematic depicting the exterior (left) and interior (right) binding modes of double-walled tetrahedron 1. Anionic guests bound within 1 are depicted in the blue circle at right. Small aromatic guests bound at the exterior of 1 are shown in the green circle at left. No binding was observed for the molecules shown in the central (black) circle. BrO$_3^-$ was introduced as the potassium salt; all other anionic guests were used as the tetra-n-butylammonium salts.

Figure 3. Successive halide exchange at the Ag$_4$ clusters resulted in sequential transformations, allowing us to assign silver cluster halide affinity in the order I$^-$ > Br$^-$ > Cl$^-$. Halides were added as the tetra-n-butylammonium salts. See Supporting Information, Figure S43-48 for $^1$H NMR data.

In most cases, no change was observed in the NMR spectrum (Figure 2) upon adding the prospective guest to host 1 in solution. The addition of anionic guests nitrate (NO$_3^-$), periodate (IO$_4^-$), bromate (BrO$_3^-$), tetrafluoroborate (BF$_4^-$), and perchlorate (ClO$_4^-$) led to $^1$H NMR shifts of 0.04-0.10 ppm for the inward-facing imine $^1$H signal, with no shift observed for externally-oriented imine (see Supplementary Information, Section 8). This observation supports the assignment of internal binding, taking place in fast exchange on the NMR time scale. The volume of the anionic guests lay in the range 41.1–67.7 Å$^3$; all guests are of appropriate volume for the measured cavity volume of 1. We infer the binding of these anions to be driven by coulombic interactions between the guests and the cationic Ag$^+$ ions of the cage framework.

Small aromatic molecules were observed to bind externally to 1. The presence of these guests (Figure 2) resulted in shifts to NMR signals of 1 assigned to externally-oriented hydrogen atoms, as opposed to the internal ones observed to shift for anionic guests. For these prospective guests, binding was inferred to have taken place when chemical shifts changed by at least 0.04 ppm upon guest addition. A 2D ROESY NMR spectrum showed correlations between added benzene and $^1$H NMR signals assigned to the tetrahedron edges (Figure S57). We thus infer that binding of these species occurs externally, involving aromatic stacking and van der Waals interactions between the guest and the large aromatic surface area exposed on the exterior of cage 1 at the six edges of the tetrahedron. A Job plot showed a clear maximum at a molar fraction of benzene at 0.85, supporting a 6:1 binding stoichiometry (Figure S66). The assignment of this binding mode is further supported by the lack of NMR changes observed for larger aromatics, such as naphthalene.

Synthesis of 1 was repeated using other halides, as TBAF, TBACl and TBABr, in place of TBAI. While fluoride did not lead to clean assembly, the formation of analogs of 1 were observed with bromide (2) and chloride (3) as templating ions. The DOSY NMR confirmed the formation of a similarly sized species, with two distinct ligand environments in the $^1$H NMR spectrum. Mass spectrometry confirmed the presence of the [Ag$_{16}$X$_4$L$_8$](NTf$_2$)$_{12}$ species in solution.

We hypothesized that stronger binding between iodide and Ag$^+$ could provide a driving force for halide exchange within the silver cluster. Such exchanges were observed to proceed, with a binding hierarchy of I$^-$ > Br$^-$ > Cl$^-$, shown in Figure 3. These processes were monitored by $^1$H NMR spectroscopy (Figures S43-S48). These NMR spectra indicated the presence of
intermediate species that incorporated two different halides, in slow exchange on the NMR time scale. Broadening of the $^1$H NMR spectra was observed alongside halide addition both in the case of halide exchange and excess of a lighter halide, attributed to possible aggregation or interior halide binding.

Numerous attempts did not result in the isolation of single crystals of 2 or 3 with sufficient quality for X-ray analysis. However, modeling using the Scigress extended-MM3 method$^{[23]}$ with the crystal structure of 1 as a starting point allowed estimation of the differences in interior volume.$^{[24]}$ Analyses of the interiors in the modeled structures of cages 2 and 3 using Molovol$^{[25]}$ gave cavity volumes of 111 Å$^3$ and 113 Å$^3$ respectively.

Raman spectroscopy was used to verify the structure of cages 1-3 in thin films and in solution. Visible-light Raman spectra of thin films of cages 1-3 were dominated by signals arising from aromatic ligand coordination to the metal centers in the region 1550-1650 cm$^{-1}$. Aniline signals were not observed, confirming the absence of cage hydrolysis (Figure S39). Evidence was observed for the presence of silver clusters in the region below 500 cm$^{-1}$ (Figure S40). The Ag–Ag distance of 2.94 Å between the basal and apical Ag$^+$ centers, obtained from the crystal structure of 1, was used in conjunction with Herschbach–Laurie relationships$^{[26]}$ as implemented by Harvey et al.$^{[27]}$ From this relationship, a predicted Ag–Ag force constant of 0.236 mdyr Å$^{-1}$ was obtained, which corresponds to a stretching frequency of 86 cm$^{-1}$ (see Supporting Information, Page S35). Force constants determined this way have previously shown good agreement with experimentally determined Raman shifts.$^{[28]}$ While we were not able to observe the Ag–Ag stretching band directly due to instrumental limits of Rayleigh rejection, the fundamental frequency was confirmed by two overtone peaks at 323 cm$^{-1}$ and 409 cm$^{-1}$, with the corresponding spacing ($\Delta \nu = 86$ cm$^{-1}$) as previously reported for Ag clusters.$^{[29]}$

Similar results were obtained for thin films of cages 2 and 3 (319-320 cm$^{-1}$, 409 cm$^{-1}$, Figure S40), corresponding to overtones of a fundamental stretching band at 89-90 cm$^{-1}$. This corresponds to a Ag–Ag force constant of ~0.25 mdyr Å$^{-1}$, with a shorter Ag–Ag distance consistent with Ag-Br and Ag-Cl bonding being weaker relative to Ag–I. and the atomic radii of Br and Cl being smaller than for I. These observations support our hypothesis that the cage framework remains unchanged upon substitution of the halide. Importantly, solution-state UV Resonance Raman measurements, performed at the Elettra synchrotron radiation facility using deep-UV excitation wavelength ($\lambda = 266$ nm, Figure S41) close to the resonance of the aromatic moieties, resulted in the appearance of two signals at 1587 and 1603 cm$^{-1}$, likely resulting from non-covalent interactions between the double walls of the cage.

These Raman measurements thus provided evidence to support three conclusions. Firstly, that the double-walled cage framework persists in both the solid and solution states. Secondly, that subtle differences in Ag–Ag stretching overtones report the presence of the different halides. Thirdly, that the ligands comprising the double walls of the cage are more mobile in solution than in the solid state. Absence of aniline peaks also confirmed cage integrity in solution. In the future, this spectroscopic approach may be useful for the structural characterization of cages for which single-crystal X-ray structure data is not available.

The structures of 1-3 thus make a significant addition to the small set of known double-walled container molecules,$^{[18,29]}$ with the added unusual property of having identical ligands occupying both interior and exterior faces and the ability to bind guests in two distinct environments. The assembly of 1-3 was enabled by the remarkable ability of napthyridine-imine ligands to support and shape silver(I) clusters. Analogous structures with extended ligands and thus the capacity to enclose larger guests may enable the design of chemical sensors, where luminescent silver cluster vertices$^{[30]}$ report on guest presence and identity.

Acknowledgements

We thank Diamond Light Source (UK) for synchrotron beamtime on I19 (CV12497). S.E.C is the recipient of a PhD Studentship from BP through the BP International Centre for Advanced Materials (bp-ICAM). A.W.H. is the recipient of an Astex Pharmaceutical Sustaining Innovation Post-Doctoral Award. C.T.M. thanks the Leverhulme Trust, the Isaac Newton Trust, and Sidney Sussex College, Cambridge, for financial support. We acknowledge Elettra Sincrotrone Trieste for providing access to its synchrotron radiation facilities (proposal number 20220534) and networking support from COST Action CA17139 (eutopia.unitn.eu) funded by COST (www.cost.eu).

Keywords: Metal-Organic Cages • Supramolecular Chemistry • Self-assembly • Metal Clusters


A double-walled tetrahedron assembled via the formation of atomically-precise [Ag$_4$X]$^{3+}$ silver clusters at the vertices, where X = I, Br, or Cl. The cage binds guests in two distinct modes: small aromatic guests bind externally, and anionic guests bind in the central cavity. Further binding behavior is observed through the substitution of halides on the silver cluster, with preference for softer halides.

@ChemCambridge @SamECClark