Three's company: co-crystallization of a self-assembled S_4 metallacyclophane with two diastereomeric metallacycle intermediates[†]

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Three discrete supramolecular self-assembled arsenic(III) complexes including an unusual S_4 -symmetric tetranuclear [As₄L₂Cl₄] metallacyclophane and two diastereomeric *cis/trans*-[As₂LCl₂] metallacycle intermediates co-crystallize within a single crystal lattice.

Increasing interest in incorporating main-group elements into supramolecular assemblies has led to numerous new and fascinating coordination compounds previously unattainable using the more familiar geometries and binding modes afforded by transition metals.^{1,2} While common coordination geometries for transition metals include octahedral, tetrahedral, and square planar, integrating main-group elements in supramolecular self-assembly applications allows for markedly different structural motifs. For example, trivalent pnictogens such as arsenic, antimony, and bismuth all prefer a trigonal pyramidal coordination geometry when bonded to thiolate ligands.³ In this structure design, arsenic(III) maintains a stereochemically active lone pair of electrons-an important design consideration for supramolecular self-assembly applications. Past work in our laboratory has incorporated this structurally distinct feature into the synthesis and characterization of a series of dinuclear arsenic cryptands $\left[As_{2}L_{3}\right]^{4,5}$ and macrocycles [As₂L₂Cl₂]^{6,7} utilizing rigid dithiolates as bridging ligands $(e.g., H_2L = 1,4$ -bismercaptomethylbenzene).⁸

Our efforts in supramolecular arsenic coordination chemistry have exploited the sufficient lability of the As–S(thiolate) bond⁹ to synthesize a variety of new metalla and supramolecular cyclophanes. Although still a relatively young field, recent work has provided many inorganic analogs of traditional cyclophanes in the form of metallacyclophanes and metallacycles.^{10,11} Unlike their hydrocarbon counterparts, these distinct compounds form *via* coordination-directed self-assembly routes, greatly simplifying overall synthesis and increasing accessibility of novel structure types. In addition, metallacyclophanes provide a new approach to heteroatom bond formation, intramolecular interactions, and host–guest interactions.¹²



 $\label{eq:Scheme 1} Synthesis of the [As_2L^1Cl_2] and [As_4L^1_2Cl_4] assemblies.$

Herein we report the synthesis of a novel tetranuclear arsenic(III) [As₄L¹₂Cl₄] metallacyclophane with idealized S_4 symmetry using the tetradentate rigid bridging ligand H₄L¹ (1,2,4,5-tetrakis(mercaptomethyl)benzene,¹³ Scheme 1). In 1,1,2,2-tetrachloroethane (TCE) the reaction between H₄L¹ and AsCl₃ yields crystals of the [As₄L¹₂Cl₄]·C₂H₂Cl₄ complex (Fig. 1a and b) after three days of slow evaporation.¹⁴ Unexpectedly, when crystals are grown in dichloromethane, the [As₄L¹₂Cl₄] metallacyclophane co-crystallizes with two diastereomeric *cis/trans*-[As₂L¹Cl₂] metallacycle reaction intermediates (*trans* Fig. 1c, *cis* Fig. 1d).¹⁵ These results prove intriguing for a number of reasons: (1) the [As₄L¹₂Cl₄] structure, to the best of our knowledge, is the first reported example of a self-assembled tetranuclear arsenic-containing



Fig. 1 Crystallographic data: (a) stick representation of $[As_4L_2^1Cl_4]$, top view; ORTEP representations (ellipsoids set at 50% probability, hydrogen atoms and solvent molecules are omitted for clarity) of (b) $[As_4L_2^1Cl_4]$, side view, (c) *trans*- $[As_2L^1Cl_2]$, and (d) *cis*- $[As_2L^1Cl_2]$.

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structure, (2) S_4 symmetry is an unusual point group seldom encountered in self-assembling systems,¹⁶ (3) a remarkable four metal– π interactions per benzene ring stabilize the tetranuclear assembly, and (4) we observe the co-crystallization of *three discrete* supramolecular assemblies in the same single crystal by simply varying solvent conditions.

To prepare $[As_4L_2^1Cl_4]$, two equivalents of AsCl₃ were added to a suspension of H_4L^1 in 1,1,2,2-tetrachloroethane and the mixture was left overnight at room temperature, after which undissolved solids, most likely starting material and coordination polymer, were removed by filtration. Crystals suitable for X-ray diffraction were first observed after allowing the filtrate to slowly evaporate at room temperature for three days. Further crystallization in this manner yields the $[As_4L_2^1Cl_4]\cdot C_2H_2Cl_4$ complex in 14% isolated yield; however, ¹H NMR spectroscopy shows nearly complete conversion to the tetrameric species.

In the $[As_4L_2^1Cl_4]$ metallacyclophane, an *endo* configuration is observed for all four metalloid centers with the As(III) lone pairs pointing toward the cavity.¹⁷ This endohedral functionality is consistent with other trigonal thiolate arsenic(III) complexes.^{4,18} As···C_{aryl} distances in this structure range between 3.235 and 3.449 Å, within the expected range for metal–arene contacts and shorter than the sum of the van der Waals radii for As and C (3.7 Å).^{1,19} The $[As_4L_2^1Cl_4]$ assembly is unusual in that *each* aryl ring has four intramolecular As(III)··· π close-contacts. We hypothesize that these interactions serve as the weak, reversible guiding forces necessary for supramolecular self-assembly.

Similar to the above procedure, slow evaporation of a 1 : 2mixture of H_4L^1 and $AsCl_3$ in dichloromethane yields crystals suitable for X-ray diffraction after two weeks at ambient temperature. X-Ray diffraction of these crystals reveals the co-crystallization of three discrete supramolecular structures: the previously described $[As_4L^1_2Cl_4]$ structure as well as two structurally discrete *cis/trans*- $[As_2L^1Cl_2]$ diastereomers. These dinuclear $[As_2L^1Cl_2]$ metallacycles crystallize as *cis* and *trans* structural isomers, as defined by the orientation of the stereochemically active As(III) lone pairs in relation to one another. As expected, each metalloid center maintains its predictable trigonal pyramidal coordination geometry and stereochemically active lone pair. The seven-membered rings each exhibit the same basic chair conformation in the solid state.

There are a number of intermolecular interactions observed in the crystal packing that may give hints as to how three distinct supramolecular structures have co-crystallized together within a single crystal (Fig. 2). Intermolecular As $\cdot \cdot \pi$ interactions are present in the crystal, with As. Carvl close-contact distances of 3.535 Å. The crystal structure also reveals other intermolecular short range interactions including As...S contacts ranging from 3.548 to 3.621 Å and S...S interactions of just 3.334 Å.²⁰ Previous work by Atwood and co-workers includes the synthesis and structural characterization of 3-chloro-4H,7H-5,6-benz-1,3,2-dithiarsepine, a sevenmembered arsenic(III) dithiolate metallacycle in the chair conformation in the solid state.¹⁸ These crystal structures also reveal intermolecular As $\cdot \cdot \pi$ close-contacts (3.546 Å in this case), providing further insight into the potential role of these non-trivial secondary bonding interactions as templates for



Fig. 2 Fragment of the *cis/trans*-[As₂L¹Cl₂] and [As₄L¹₂Cl₄] crystal packing (hydrogen atoms and solvent removed for clarity). Intermolecular contacts include As···S (red), S···S (green), and As··· π (blue).

crystal packing. This suggests a possible emerging interaction motif in crystal engineering.²¹

Essential to the formation of the $[As_4L_2^1Cl_4]$ metallacyclophane is the notion of dynamic covalent chemistry²² between the self-assembling components, made possible in this system by the reversibility and lability of the As-thiolate bond.^{5,9} ¹H and gCOSY NMR spectroscopy studies reveal constant relative ratios of the complexes throughout the crystallization process. When single crystals of $[As_4L^{1}_2Cl_4]$. C₂H₂Cl₄ are redissolved in TCE-d₂, dissociation into [As₂L¹Cl₂] is not observed in the ¹H NMR spectrum, even after heating at 80 °C. The [As₄L¹₂Cl₄] complex maintains S_4 symmetry in solution, as evidenced by the four doublets observed for its sixteen total methylene protons (Fig. 3). We attribute the increased thermodynamic stability of the $[As_4L_2^1Cl_4]$ assembly to the high number of $As(III) \cdots \pi$ interactions-four per benzene ring-as compared to the cis/trans-[As₂L¹Cl₂] metallacycles, which lack any such intramolecular As(III) $\cdots \pi$ close-contacts in the solid state.

The inorganic arsenic cryptands $[As_2L_3]$ and macrocycles $[As_2L_2Cl_2]$ previously synthesized in our laboratory bear strong resemblance to the corresponding organic π -prismands and bicyclophanes.^{5,23} In many respects, the $[As_4L^1_2Cl_4]$ complex presented here is analogous to another spectacular example from the organic cyclophane literature. The (1,2,4,5)(1,5,4,2) linkage found in our $[As_4L^1_2Cl_4]$ assembly closely parallels that of tetrathia[3.3.3.3]cyclophane, first synthesized and characterized by Klieser and Vögtle (Fig. 4).²⁴ To date, we have not isolated the $[As_4L^1_2Cl_4]$ assembly with corresponding (1,2,4,5)(1,2,4,5) connectivity,



Fig. 3 ¹H NMR spectrum of methylene region from isolated $[As_4L_2^1Cl_4]$ single crystals.



Fig. 4 (a) $[As_4L_2^1Cl_4]$ metallacyclophane with two structural isomers of tetrathia[3.3.3.3]cyclophane: (b) (1,2,4,5)(1,5,4,2) and (c) (1,2,4,5)(1,2,4,5).

nor do we see NMR evidence of its existence. Future studies of the dynamic covalent nature of the arsenic(III)–thiolate bond may allow access to the inorganic analogs of other important examples from the cyclophane literature through supramolecular self-assembly. The [As₄L¹₂Cl₄] metallacyclophane has a cavity volume of 28 Å³, so further development of this cage—either by transmetallation or through reactions involving larger pnictogens—could increase potential for host–guest interactions.²⁵

In summary, we report the synthesis of three discrete self-assembled supramolecular structures utilizing the trigonal pyramidal coordination geometry of trivalent arsenic, co-crystallized in a single crystal structure. Of particular interest, the $[As_4L_2^1Cl_4]$ structure exhibits S_4 symmetry, a point group rare in nature and relatively uncommon in synthetic chemistry. Importantly, the synthesis and characterization of these novel $[As_4L_2^1Cl_4]$ and $[As_2L^1Cl_2]$ structures support the claim that main group elements, with their distinct coordination geometries, can provide access to new and interesting supramolecular structure types and designs.

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