

# Inorganic Molecular Capsules: From Structure to Function

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The assembly of nanoscale capsules or cages using metal coordination represents one of the most interesting and challenging areas of chemical nanoscience. These high-symmetry capsules are invariably comprised of many metal–ligand components, which often self-assemble rapidly and in high yield into a single gigantic species—sometimes even protein-sized.<sup>[1]</sup> However, the interest in these systems goes far beyond aesthetics. An understanding of the mechanisms of the assembly process that leads to their formation will allow systems with unmatched physical properties and functionalities to be designed from first principles. As the emphasis changes from *structure* to *function*, cages have been constructed that can serve as supramolecular containers, reaction vessels, and ion channel models for biological cells. In this Highlight, the very recent advances in the formation of cages and capsules through metal ion coordination is explored.

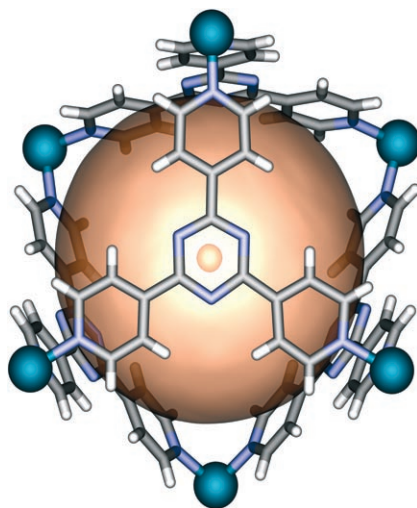
The self-assembly process of coordination cages mediated by metal–ligand coordination depends critically upon the building blocks chosen and their respective reactivities. One very important route to the formation of metallosupramolecular architectures involves the selection of building blocks that are preorganized, kinetically stable, that incorporate labile coordination sites, and are complementary. For instance, the  $[\text{Pd}(\text{en})]^{2+}$  unit (en = ethylenedia-

mine) has emerged as a versatile building block in molecular self-assembly.<sup>[2]</sup> Importantly, the  $90^\circ$  coordination angle present between one of the blocking groups and one of the labile ligands at the  $\text{Pd}^{\text{II}}$  metal ion has been judiciously used in the design of new discrete two- and three-dimensional structures ranging from cages, bowls, boxes, tubes, catenanes, and spheres. An example of an octahedral cage is  $[\{\text{Pd}(\text{en})\}_6\text{L}_4]^{12+}$  (**1**; Figure 1), which is based on the coordination of six  $\text{Pd}^{\text{II}}$  centers with  $[\text{Pd}(\text{en})]^{2+}$  corners and four 2,4,6-tris(4-pyridyl)-1,3,5-triazine units. The cage has a large hydrophobic cavity, yet the outer part is hydrophilic. The tricoordinated ligand in **1** is relatively electron-deficient,

therefore the cavity binds preferentially electron-rich aromatic guests.

The cavity of **1** is well-defined stereochemically and is able to control chemical reactions. For example, Diels–Alder reactions are dramatically accelerated by a factor of over 100, and [2+2] photodimerizations of olefins proceed faster and with high regio- and stereoselectivity.<sup>[3]</sup> The formation of “molecular ice” within variants of **1**, whereby ten water molecules are complexed within the cavity,<sup>[4]</sup> may help further the understanding of the reactivity and host–guest binding properties of such capsules. Indeed, the sequence-specific binding of tripeptides was observed with capsule **1**,<sup>[5]</sup> wherein the encapsulation of Trp-Trp-Ala was favored over other sequences and singly mutated tripeptides. The encapsulation of paramagnetic moieties has also revealed interesting results, and the pH-responsive switching of spin–spin interactions of stable organic radicals has been possible in **1**.

The design of a similar cage, **2**, comprising two 2,4,6-tris(4-pyridyl)-1,3,5-triazine units and three 4,4'-bipyridine ligands with six  $[\text{Pd}(\text{en})]^{2+}$  corner units yielded a pillared cylinder. The organic-pillared nature of the cylinder resulted in interesting guest-binding properties through a combination of interactions. The complexation of tetrathiafulvalene (TTF) allowed the generation of a mixed-valence radical dimer cation within the self-assembled cage **2**.<sup>[6]</sup> This result is significant because this noncovalently bound species can only be generated in such a cage or by covalent linking. A similar effect is observed in the complexation of **2** with large planar aromatic organic mole-



**Figure 1.** Molecular structure of  $[\{\text{Pd}(\text{en})\}_6\text{L}_4]^{12+}$  (**1**; L = 2,4,6-tris(4-pyridyl)-1,3,5-triazine), in which the  $\text{Pd}^{\text{II}}$  ions occupy the corners of an octahedron (the en ligands and guest molecule are omitted for clarity). The cavity is illustrated by the large orange–brown sphere;  $\text{Pd}^{\text{II}}$  ions blue spheres; stick representation: C gray, N blue, H white.

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cles<sup>[7]</sup> and causes the stacking of  $[M^{II}(\text{acac})_2]$  moieties ( $M = \text{Pt}, \text{Pd}, \text{Cu}$ ;  $\text{acac} = \text{acetylacetonate}$ ), which exhibit  $M-M$  interactions.<sup>[8]</sup>

Another way to construct spherical capsules with well-defined pores was demonstrated using polyoxometalate-based building blocks. Polyoxometalates are clusters based on  $\text{MO}_x$  units (typically  $M = \text{Mo}, \text{W}, \text{V}$ ;  $4 \leq x \leq 7$ ), which form structures that contain between 6 and 368 metal atoms.<sup>[9]</sup> Interestingly, even comparably small clusters can display remarkable physical properties as a result of encapsulating electronically or chemically active moieties.<sup>[10]</sup> However, by far the most interesting cluster types for nanoscience are those with ring and spherical shapes, comprising pentagonal  $\{(\text{Mo})\text{Mo}_5\}$  (pent) building blocks.<sup>[9]</sup>

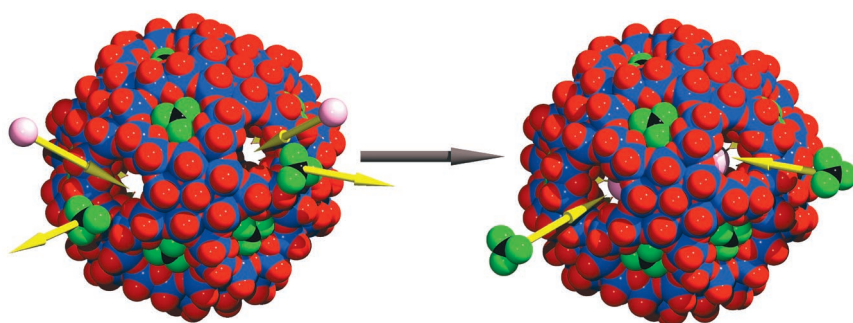
All the spherical and approximately icosahedral clusters have the general formula  $[(\text{pent})_{12}(\text{link})_{30}]$  (link = binuclear linker). One example is the capsule  $[(\text{Mo})\text{Mo}_5\text{O}_{21}(\text{H}_2\text{O})_6]_{12}[\text{Mo}_2\text{O}_4(\text{L})]_{30}]^{n-}$  ( $n = 72$ ;  $\text{L} = \text{sulfate}$ ), in which 12 central pentagonal units span an icosahedron and the linkers form a distorted truncated icosahedron. The highly charged nanoscale capsule, with an inner cavity diameter of approximately 2.5 nm, allows different types of encapsulations. For example, well-structured large water assemblies (up to 100 molecules) were observed with an onionlike layer structure enforced by the outer shell.<sup>[9,11]</sup> Most importantly, the capsule contains 20 well-defined pores and the functionalities of the internal shell can be tuned precisely through the nature of the

bidentate ligands. With binuclear  $\{\text{Mo}^V_2\text{O}_4\}^{2+}$  linkers, the pores are  $\{\text{Mo}_9\text{O}_9\}$  rings with diameters of 0.6–0.8 nm that function as crown ethers. The pores can be reversibly closed, for example, through hydrogen-bonding interactions between guanidinium cations and the rings.<sup>[11]</sup> In a related smaller capsule with mononuclear linkers, the  $\{\text{Mo}_6\text{O}_6\}$  pores are closed upon complexation with smaller potassium ions.<sup>[12]</sup>

Perhaps the most intriguing and exciting property of such highly negatively charged capsules is that they can mediate cation transfer from the solution to the inner nanocavity. Indeed, reaction of the above-mentioned 72-fold negatively charged capsule with different cations such as  $\text{Na}^+$ ,  $\text{Cs}^+$ ,  $\text{Ce}^{3+}$ ,  $\text{C}(\text{NH}_2)_3^+$ , and  $\text{OC}(\text{NH}_2)\text{NH}_3^+$  in aqueous solution leads to assemblies that exhibit well-defined cation separations within the channels of the capsules (“nano-ion-chromatograph” behavior).<sup>[13]</sup> A temperature-dependent equilibrium process that involves the uptake and release of  $\text{Li}^+$  ions through the capsule pores was also observed. In this process, the porous capsule behaves as a semipermeable inorganic membrane, allowing only  $\text{H}_2\text{O}$  and small cations through.<sup>[14]</sup> Furthermore, the 20 pores of the same capsule that are blocked by protonated urea as “stoppers” could be opened in solution, thus allowing uptake of calcium(II) ions, before closing occurred again (see Figure 2).<sup>[15]</sup> Thus, pore-gating (a model of biological ion transport) can be demonstrated: After initial cation uptake, the negative charge (or more precisely the electrochemical

gradient) of the capsule decreases and subsequent cations are resultantly found hydrated outside the pores.<sup>[16]</sup>

In summary, recent work has shown that the designed assembly of nanoscale capsules by using coordinative interactions can open doors to new areas of chemistry. In particular, parallels can be drawn between such systems under confined conditions and processes in biological cells, such as cell response and ion transport. Generally speaking, matter can be studied under confined conditions; however, new systems resulting from encapsulation often reveal new phenomena that are not observable by bulk-phase investigations. Examples include the study of “confined water” with or without electrolytes, as well as chemical reactions. Programming of the architectures of the inner cluster walls to give well-defined cavities and gated pores results in the specific interaction of capsules with their environments and the selective uptake and binding of guests. The future of capsule systems is exciting, and a better understanding of the principles that underpin the assembly mechanisms of such capsules should allow the designed construction of extremely complex and specifically interacting systems, thus, in the broadest sense, bringing inorganic chemistry to life.



**Figure 2.** Space-filling representation of  $[(\text{Mo})(\text{Mo}_5\text{O}_{21}(\text{H}_2\text{O})_6)_{12}\{\text{Mo}_2\text{O}_4(\text{SO}_4)\}_{30}]^{72-}$  and a simplified view of the uptake of  $\text{Ca}^{2+}$  ions by the capsule. The pores are initially closed, but treatment of a solution of the capsule with  $\text{Ca}^{2+}$  ions (pink spheres) leads to cation uptake (left); following their uptake, the pores close again (right). Mo blue, O red, C black, N/O(urea) green; yellow arrows indicate the direction of motion.

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