ChemComm

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Journal:	*ChemComm*
Manuscript ID	CC-COM-07-2018-005650
Article Type:	Communication

Journal Name

COMMUNICATION

Phase dependent structural perturbation of a robust multicomponent assembled icosahedral array

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Irene Ling*,[a,b] Harshita Kumari,[c] Marzieh Mirzamani,[c] Alexandre N. Sobolev,[d] Christopher J. Garvey,[e] Jerry L. Atwood[f] and Colin L. Raston*[b]

We report on the assembly of three-fold axially compressed icosahedral arrays of the bowl shaped p-sulfonatocalix[4]arene molecules in the solid-state, intricately bound to dipicolinate and yttrium(III) ions, with the compression reflected in Hirshfeld surface analyses. Solution studies show dissolution of the icosahedra intact, but with a geometrical rearrangement to regular icosahedra.

Polyhedral shells are prominent in structural mimicry of natural systems, including virus capsids and protein-based bacterial organelles, and in the buckminster fullerene array of carbon atoms[1-8]. Such polyhedral shells adopt the almost spherical form that affords a near-maximum internal volume for a given surface area. Polyhedral shells[9-12] derived from spontaneous self-assembly are of interest in confining space for a variety of applications, including in catalysis, molecular sensing, drug delivery, separation and purification[13-26]. They can have stunning structures and most importantly provide functionality for molecular recognition events[27-28]. The discovery of Platonic polyhedra shells has sparked the design and development of organic and inorganic assemblies.

Constructing polyhedral shell synthetically is possible by metal-organic ligand intercatenation or by host-guest molecular recognition. We are interested in the design and fabrication of polyhedral shells using the latter process, particularly involving p-sulfonatocalix[4]arene, **1**, which is essentially a rigid truncated cone macromolecule with distinct hydrophobic and hydrophilic segments, and is the focus in the present work. While this calixarene typically forms bilayers,[29] under specific conditions, polyhedral arrays are accessible but there is limited understanding of their behaviour in solution phase,[30] either under diffusion control or under shear stress.

Two polyhedral arrays of **1** have been authenticated, only in the solid state[30,31]. The first was a neo-spherical Platonic solid prepared from penta-sodium **1**, pyridine N-oxide, and lanthanum(III) ions, in a 1:2:2 ratio, respectively. The icosahedron is made up of twelve C_4-symmetry calixarenes, which are arranged at the vertices of an icosahedron with their cavities and sulfonate groups on the outer surface,[30] Fig. 1(a). Replacing pyridine N-oxide by 18-crown-6 and lanthanum(III) nitrate by praseodymium(III) (or neodymium(III) or samarium(III)) triflate in this ternary system however results in a different spheroidal array, consisting of twelve calixarenes arranged at the vertices of a cuboctahedron, similarly with the sulfonate groups facing outward,[31] Fig. 1(b). Polyhedra based on coordination driven self-assembly of the carboxylic acid derivative of calix[4 and 5]arene with the uranyl cation have also attracted attention[32]. Here, the carboxylate groups are directed towards the inner surface with the metal ions located at the faces of hexameric and dodecameric cages of calix[4]arene and calix[5]arene respectively, as an integral part of the cages, unlike the arrangement of metal ions for other polyhedral shells.

Herein, we report a new rationally designed spheroidal array, **3**, Fig. 1(c), derived from **1**, dipicolinic acid, **2**, and yttrium(III) chloride (2:1:2 ratio) in basic aqueous solution (pH ~ 10-11). In **3**, twelve calixarenes (each with 4- charge) and six dipicolinate molecules are present, requiring thirty-two counter ions (fourteen Y^{3+} and eighteen Na^+ ions) for overall charge balance. We systematically explored the synthetic parameter space and found that the conditions for the formation of **3** are critical, with a slight departure resulting in the formation of the common bilayer arrangement of the calixarene. This is consistent with a recently reported structure of **1** and **2** in the presence of cerium(III) which has a bilayer

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[a] *School of Science, Monash University Malaysia, Jalan Lagoon Selatan, Bandar Sunway, 46150 Selangor, Malaysia.*

[b] *Centre for NanoScale Science and Technology, School of Chemical and Physical Sciences, Flinders University, Bedford Park, SA 5042, Australia.*

[c] *James L. Winkle College of Pharmacy, University of Cincinnati, 231 Albert Sabin Way, MSB # 3109C, Cincinnati, OH 45267, United States.*

[d] *School of Molecular Sciences, M310, The University of Western Australia, 35 Stirling Highway, Perth, WA 6009, Australia.*

[e] *Australian Nuclear Science and Technology Organization, New Illawara Road, Lucas Heights, NSW, Australia.*

[f] *Department of Chemistry, University of Missouri, 601 South College Avenue, Columbia, MO 65211, United States.† Footnotes relating to the title and/or authors should appear here.*

[g] *Electronic Supplementary Information (ESI) available: Synthesis method and analyses (PDF). Colour movie clips/animation of the cuboctahedron, icosahedron and distorted icosahedron. (Movie S1- Movie S3). See DOI: 10.1039/x0xx00000x*

arrangement of calixarenes with dipicolinate in each cavity[33]. The interplay of the three aforementioned components is controlled by a combination of both self-assembly and molecular templating. We reasoned that the aromatic ring in **2** has the potential to bind in the cavity of **1** with then the carboxylate moieties available for binding to Y^{3+} in building spheroidal arrays, noting that the sulfonate moieties of the calixarene can weakly coordinate to lanthanide ions. The extensive yttrium(III) metal coordination to **1** and **2** provides an extraordinary degree of directional control in the overall polyhedral assembly. It is important to note that each spheroidal array (nanocapsule) in **3** takes on the shape of a axially flattened icosahedron, which is distorted along a C_3 symmetry axis in the trigonal space group R$\overline{3}$, Fig. 1(c), as for the earlier structurally authenticated icosahedral structure, Fig. 1(a), whereas the cuboctahedral structure, Fig. 1(b), crystallizes in the tetragonal space group, P_4/nnc.

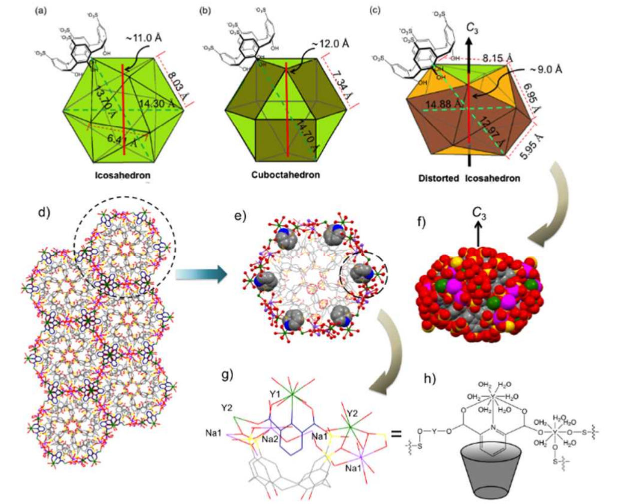

Figure 1. Diagrammatic representations of an (a) icosahedron[14] (b) cuboctahdron,[15] and (c) distorted icosahedron, **3**, of 12 calixarenes, showing selected inter O-phenolic centroid to O-phenolic centroid distances. Solid-state structure of **3** showing the packing of the distorted icosahedra, (d), and the de-construction of components to a single icosahedron, (e) and (f), and coordination and included dipicolinate, (g) and (h).

The icosahedra in **3** with calculated volume (from crystal structure) of 1996.8 $Å^3$ can be segmented into equatorial and axial parts, Fig. 2(b). The former is comprised of six calixarenes with the sulfonate groups involved in Y^{3+} metal coordination along with each cavity containing the dipicolinate guest molecule connected through extensive metal ion coordination (chelation and bridging through the carboxylic groups), forming a toroidal arrangement. The formation of a toroidal array, without taking up the capping axial calixarenes devoid of dipicolinate, may result in destabilization relative to the formation of the common bilayer arrangement of calixarenes. Indeed, bilayer formation prevails for other ratios of the components used in the synthesis, Fig. 2. The calixarenes take on a splayed conformation involving inter-calixarene C···π interactions (3.44 to 3.97 Å). The N-atom and two O atoms from the carboxylic groups of the dipicolinate molecules act as a tridentate ligand to Y^{3+} (Y–N 2.507(5), Y–O 2.390(4) and 2.402(4) Å). The same Y^{3+} center is also coordinated by six water molecules (Y–O 2.376(5) Å to 2.432(6) Å). Each carboxylate group of a dipicolinate molecule is coordinated to another Y^{3+} (Y–O 2.296(4) and 2.321(4) Å), two oxygen atoms of two adjacent calixarene sulfonate groups (Y–O 2.355(3) and 2.393(3) Å) and four water molecules (Y–O 2.328(5) Å to 2.354(4) Å). Binuclear aquated carboxylato-yttrium(III) species readily form with functionalized carboxylate molecules[34].

Another salient feature of **3** is that sodium ions are also present in binding directly to sulfonate groups and aquated Y^{3+} or form a secondary coordination sphere interaction through coordinated water molecules. In the extended solid-state, each distorted icosahedron is connected through hydrogen bonded water molecules, hydrated Y^{3+} and Na^+, with a unique Na^+ common to two icosahedra (see below), Fig. 2(a). Na1 coordinates with three adjacent calixarene sulfonate groups (Na–O 2.33 to 2.41 Å), one crystalline water molecule (Na-O 2.93 Å) and aquated Y^{3+} center Y2 (Na–O 2.59 to 2.69 Å), while Na2 coordinates two sulfonate groups (Na–O at 2.23 to 2.34 Å) with the remaining coordination sphere occupied by three water molecules. In addition, Na3 is located at a R$\overline{3}$ position connecting two icosahedra at the outer layer, involving bridging to six calixarene sulfonate groups (Na–O 2.46 Å), Fig. 2. These are positioned along the C_3 distortion axis of the array of calixarenes. For the cuboctahedron, neighboring spheres share the 18-crown-6 guest, and thus the calixarenes are eclipsed relative to one another, whereas for the symmetrical icosahedron the neighbouring spheres are bridged by multi-sphere coordination involving {1-pyridine-N-oxide-lanthanum-pyridine-N-oxide-1} dimer.

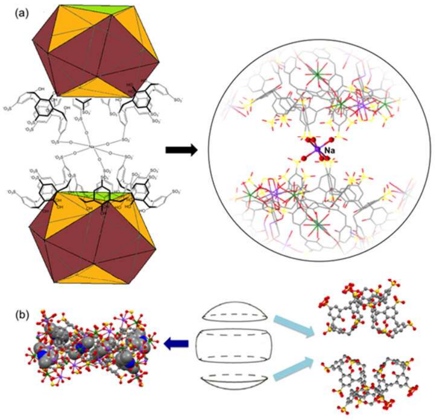

Figure 2. (a) Linking of the distorted icosahedral arrays in **3** through Na^+ coordination involving sulfonate groups from three different *p*-sulfonatocalix[4]arene on a triangular face of adjacent icosahedral arrays. (b) Diagrammatic representation of the segments of the arrays relative to the bilayer arrangement of *p*-sulfonatocalix[4]arene, devoid of dipicolinate inclusion (complex **4**), which forms from a 2:1:1 ratio of calixarene, dipicolinic acid and yttrium(III) (See Fig. S14), compared with 2:1:2 for forming **3**.

The charge balanced discrete spheroidal arrays confine an aqueous core (water molecules), with the shell made up of a combination of hydrophilic and hydrophobic segments that are in close contact. In the present structure the estimated internal volume (for the confinement of other molecules) for the distorted icosahedral array of calixarenes is ca. 1300 Å^3. This volume was determined from the distance between the centroids of methylene carbon atoms for each calixarene. The distances in the equatorial plane in **3** are slightly larger than that for the maximum distance in the symmetrical icosahedral and cuboctahedral arrays. As for the case of the symmetrical icosahedral array, Fig. 1(a), the core of the symmetrical icosahedral sphere contains a cluster of water molecules and sodium ions, with an internal volume of ca. 975 Å^{330} while the cuboctahedral array in Fig. 1(b), has a larger internal volume ca. 1258 Å^3 that confined six aquated praseodymium(III) ions[31]. NMR and mass spectrometry experiments were uninformative as to the nature of the species present in solution. Also critical is the need for a small lanthanide(III) ion (Y^{3+}), with the ratio in solution required for the synthesis the same as in the structure, noting larger lanthanide ions favor icosahedral and cuboctahedral arrays, Fig. 1(a), and (b), at least in the presence of pyridine N-oxide and crown ether molecules respectively.

Hirshfeld surface analysis was undertaken using CrystalExplorer[35] to ascertain any prominent interactions that are distinctly different to interactions in the symmetrical icosahedral and cuboctahedral arrays. Hirshfeld surface analysis of **3** revealed more bright red spots for calixarenes accommodating the dipicolinate molecules relative to those devoid of such molecules, (see Supporting Information). Short O···H contacts dominate the interactions (32.7%) where the dipicolinate resides in the cavity, followed by H···H and C···H close contacts at 19.0% and 18.6% respectively. For the calixarene devoid of dipicolinate molecules, O···H interaction contributes 25.6% while H···H and C···H both contribute 9.7% and 12.2% respectively. Hirshfeld surface analysis of the symmetrical icosahedral and cuboctahedral structures reveals less bright spots relative to those with dipicolinate molecules in the cavities of six of the calixarenes in **3** (see Supporting Information). The origin of the distortion in **3** possibly arises from the geometrical requirements of Y^{3+} bridging carboxylate groups of dipicolinate with its aromatic ring residing in the cavity of a calixarene, and a sulfonate group from an adjacent calixarene, coupled with the inter-icosahedra Na^+ bridging.

As an initial assessment on the stability of complex **3** in solution, we studied the particle size distribution using volume distribution because scattering intensity of larger particles can override the contribution from smaller particles. Particle size distribution for crystals of complex **3** (~ 0.7 mg/mL) dissolved in water, using dynamic light scattering (DLS), yielded a bimodal histogram of particles with a hydrodynamic diameter range of 0.6 to 10 nm and a larger size range of 10-100 nm suggesting the presence of both the monomeric spherical assembly **3** and the aggregates/super self-assembly of **3**, respectively. The results thus provide credence for the presence of spheroidal arrays found in **3** also present in solution. We also isolated an amorphous white precipitate form of complex **3** and dissolution in water, yielded a monomodal distribution with aggregates of size range 100-1000 nm. The differences observed for crystalline and amorphous forms indicate that the individual monomers were organized in a crystal lattice, which then dissolve in solution. The addition of dilute NaCl (0.01 M) followed by mild sonication to the solution of **3** yielded particles 0.6 to 7.5 nm in diameter for the crystalline form and 0.4 nm to 10 nm for the amorphous form. In both cases, excess sodium ions most likely disrupted the bridging sodium ions of the solid-state structure of **3**, Fig. 2(a). Particle analysis using transmission electron microscopy (TEM) correlate well with the size of the icosahedra in the solid state, Fig. 3(b) and 3(c), and interestingly aggregations of these small particles are evident in TEM images. Although intriguing, DLS failed to provide a narrower size range of **3** in solution that could be directly correlated with solid-state structure. In addition, DLS could only be used effectively in dilute solution and provides the hydrodynamic diameter of a sphere, regardless of the actual shape. Similar to DLS, the extensive diffusion NMR experiments were inconclusive due to the limitation of the technique in assessing the shape of nanoassemblies in solution. We therefore conducted small angle neutron scattering (SANS) experiments to provide complementary bulk state (nanoassemblies) information, i.e. form factor (shape and size) and structure factor (interaction) in solution.

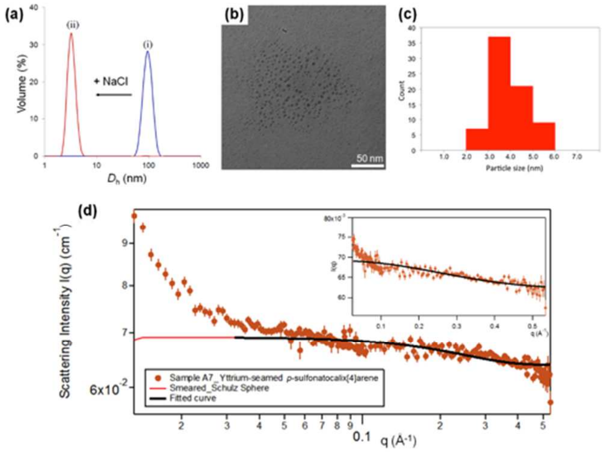

Figure. 3. (a) DLS particle size distribution showing (i) diluted white precipitate of complex **3** in aqueous solution, and (ii) addition of dilute NaCl solution to (i) along with (b) corresponding TEM image for (ii). (c) Particle size distribution measured from TEM. (d) Small-angle neutron scattering curve of **3**, showing a fit to the Schulz sphere model (Inset: scattering curve in linear scale). High q data points fits a Schulz sphere and low q data points show some aggregation.

For SANS, scattering length density, SLD (calculated by summing the coherent scattering lengths of all atoms over a small volume and dividing by that volume) of **3** (SLD= 1.714×10^{-6} Å^{-2}) and that of D_2O (SLD= $6.335\ \times10^{-6}$ Å^{-2}) was held constant and the high-q region of scattering curve (inset Fig. 3c) was fitted to a variety of spherical and ellipsoidal models [36]. The data fitted well to the sphere model, suggesting that the distorted icosahedra in **3** rearranges to a more spherical icosahedron geometry in solution. The sphere fit yielded a radius of ~6 Å, which corresponded to ~12 Å diameter. The radius of gyration/R_g (6 Å) obtained from SANS corresponds to a volume of 904 Å^3, which is smaller overall than for the distorted icosahedra determined from the X-ray structure. Here the distance from the centroid to the van der Waals limit is 8.91 Å along the compression axis and 11.15 Å in the equatorial plane, Fig. 1c, which corresponds to a volume of 3041 Å^3. The decrease in size/R_g suggests that the linkages with yttrium centres remain intact to hold the nano-assembly together, but the sodium ions are either located outside the surface of sphere or enclosed within the sphere in providing the counter balance. Interestingly, the radius of hydration/R_h (10.5 Å, obtained from correlation R_g/R_h=0.57) that corresponds to a volume of 4850 Å^3, is larger than that observed for distorted icosahedra. This difference can be attributed to the inherent difference between R_g (radius calculated based of center of gravity of **3**) and R_h (radius of hypothetical sphere with volume equal to the volume of sphere **3**). Note that R_h accounts for the solvent drag of the sphere and in this case a significant amount of solvent drag is associated with forming the nano-assembly in solution.

Hydrogen-bonded supramolecular assemblies are typically not stable in solution[37]. The stability of spheroidal geometry in solution in the present study can be attributed to the seam of Y^{3+}/dipicolinate and sulfonate complexation involving six calixarenes, Fig. 2(b). Given the persistence of the spheroidal array in solution and a distorted icosahedral array in solid state, the sphere may be fluxional in solution.

Conclusions

We have established the formation of an axially compressed icosahedral array of *p*-sulfonatocalix[4]arenes in the solid-state. The choice of yttrium(III) rather than a large lanthanide(III), is critical in forming the compressed array, as is the ratio of the trivalent metal ions to calixarene, which is understood in terms of Hirshfeld surface analysis. There is also evidence for the persistence of the new icosahedral array in solution, but without the axial compression present in the solid state, as evidenced by SANS results. Overall, the findings open the way for constructing robust spheroidal arrays in the solid and aqueous solution as a route to confining space in a controlled way.

Acknowledgment

We gratefully acknowledge support of this work by the Australian Research Council and The Government of South Australia (C.L.R.) and National Science Foundation (J. L. A.)

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