Conformationally Flexible p-Sulfonated Calix[5]arene Binding with Large Bis-Phosphonium Cations

Irene Ling,*† Yatimah Alias,‡ Brian W. Skelton,† and Colin L. Raston*§

†Chemistry Department, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia
‡Centre for Microscopy, Characterisation and Analysis, M313, University of Western Australia, Perth, Western Australia 6009, Australia
§Centre for Strategic Nano-Fabrication, School of Biomedical, Biomolecular and Chemical Sciences, University of Western Australia, 35 Stirling Highway, Crawley, Western Australia 6009

Supporting Information

ABSTRACT: Water-soluble p-sulfonated calix[5]arene forms a multicomponent complex with aquated Gd(III) ions and bis-phosphonium cations, where the calixarenes are arranged in bilayers with the bis-phosphonium cations embedded between and within the bilayers. The calixarenes are significantly distorted from the common “cone” conformation and are linked from one bilayer to another through the sulfonate groups via secondary coordination sphere interactions associated with homolectic aminated metal ions.

INTRODUCTION

The development of bowl-shaped molecules for recognition events is becoming more intriguing and of greater complexity, particularly for applications in biology. In general such molecules can accommodate molecular guests through complementary noncovalent interactions and can self-assemble into micelles or bilayers at the nanoscale. Calix[n]arenes are one of the most studied synthetic molecules for molecular recognition, where the size of the cavity can be varied, depending on the number of phenolic rings bridged by the methylene groups in the macrocycle. They have two segments, the so-called upper rim and lower rim, which can be modified chemically to provide higher structural and functional diversity.

Calix[n]arenes bearing upper rim water solubilizing sulfonated groups have been extensively studied as supramolecular tectons in building complex multicomponent materials. Most of the studies focus on p-sulfonatocalix[4]arene, the smallest macrocycle in the family. A diverse range of guest molecules of different sizes and shapes, as neutral and charged species, can bind in the cavity of calixarenes, both in solution, and in the extended solid state structures. Apart from selective inclusion properties, the aforementioned molecule can self-organize into the simplest bilayer arrangement or form complex materials, which includes molecular capsules, “Russian dolls”, two- or three-dimensional (2-D or 3-D) coordination polymers, “Ferris wheels” and nanometer-scale dodecahedral arrays, in the form of icosahedra and cuboctahedra. There have been limited studies on the larger ring size p-sulfonatocalix[6 and 8]arenes which are conformational more flexible than the almost exclusively cone conformation for the calix[4]arene.

For the synthetically difficult to access p-sulfonatocalix[5]-arene, a few host–guest and inclusion complexes have been reported, where it usually adopts a “cone” conformation with all the phenolic oxygen atoms in a plane. The cavity is larger in diameter but shallower than that of p-sulfonatocalix[4]arene. In forming host guest and inclusion complexes, p-sulfonatocalix[5]arene can form bilayers with a distorted cone conformation. Interestingly the packing of 5-fold symmetry molecules into extended sheets while retaining this symmetry crystallographically is not possible. The iso-electronic p-phosphonatocalix[5]arene is always isolated as an amorphous solid, forming lower rim to upper rim stacked fibers from solutions containing molecular capsules based on two calixarenes held together by a seam of hydrogen bonds.

p-Sulfonatocalix[5]arene is similar to p-sulfonatocalix[4]-arene in forming bilayers in the extended structures. A unique densely packed bilayer of p-sulfonatocalix[5]arenes forms in the presence of ytterbium(III) and tetraphenylphosphonium ions, with the latter acting as an auxiliary molecule in facilitating the crystallization of the metal complex of the calixarene. The calixarene can form complicated motifs such as the Ferris wheel-like coordination polymers involving complexation of the macrocycle with aza-crown ether and lanthanides. The presence of lanthanides is also important in the formation of a molecular capsule based on two p-sulfonatocalix[5]arenes in the cone conformation. Atwood et al. established the self-assembly in the solid state of several aquated lanthanide ions (Eu, Tb, Gd, and Yb) that bind to sulfonato oxygen atoms, while Su et al. have established complexation of bis-pyridinium in a molecular capsule comprised of two p-sulfonatocalix[5]- arenes.

Received: December 6, 2011
Revised: January 9, 2012
Published: January 11, 2012
p-Sulfonic acid calix[5]arene itself forms a hydrogen bonded molecular capsule, confining two sulfuric acid molecules. In the present study, we report a detailed analysis of the self-assembly of p-sulfonatocalix[5]arene complexed with large organic cations, namely, bis-phosphonium cations, in the presence of lanthanide(III) ions. Previously we carried out extensive studies on the complexation of p-sulfonatocalix[4]arene with imidazolium based cations of varying size and functionality, along with phosphonium cations, establishing that the imidazolium cations are selectively drawn into the cavity of the calixarene. We now find that the same approach involving p-sulfonatocalix[5]arene, for several imidazolium cations and selected organic phosphonium cations, results in crystalline material devoid of imidazolium cations, with bis-phosphonium cations taking on a dual role, both endo- or exo-relative to the cavity of the bowl shaped calix[5]arenes. The endo-interplay of the two components involves phenyl rings of the bis-phosphonium cations with the calixarenes essentially arranged into “molecular capsules”, whereas for exo-interplay the cations are positioned within bilayers of calixarenes. In the present study, the absence of the imidazolium cations results in the same complex.

RESULTS AND DISCUSSION

A mixture of p-sulfonatocalix[5]arene, the large bis-phosphonium cation and several different imidazolium cations, either 1-hexyl-3-methylimidazolium or 1-octyl-3-methylimidazolium, and gadolinium(III) chloride, afforded a complex based on three of the components, which vary only slightly in their water content, as established with the isolation of 1 and 2, respectively, Figure 1. These complexes have slightly different cell dimensions in the solid state, with subtle differences evident from their Hirshfeld surface analyses. In both structures two bis-phosphonium molecules are encapsulated by two calix[5]arenes, with the larger cations, that is, bis-phosphonium cations, drawn into the larger cavity of the calixarene, rather than the smaller imidazolium cations. Other bis-phosphonium cations are within a bilayer arrangement of the calixarenes. This finding contrasts with our previous finding for p-sulfonatocalix[4]arene where the charged headgroup of the imidazolium is preferentially drawn into the cavity in the solid state, and also in solution, yet similar with bis-phosphonium cations embedded in a bilayer arrangement of calixarenes. In the present study, the absence of the imidazolium cations results in the same complex.

Complexes 1 and 2 crystallize in the triclinic space group with the asymmetric unit consisting of one calixarene anion (with disordered SO$_3^-$ groups), two bis-phosphonium cations (with disordered phenyl rings), and one homolectic...
gadolinium(III) ion coordinated by eight water molecules, along with some disordered water molecules. However, the site occupancies of the [Gd(H₂O)₈]³⁺ is 1/3 for both complexes, noting that population of sites ≤1 is a common occurrence for inorganic cations included with p-sulfonatocalix[4]arene for lanthanide(III) and transition metal(III) ions (M³⁺ = Gd³⁺, Tb³⁺, Rh³⁺, Y³⁺, Eu³⁺, Pr³⁺, Nd³⁺). In the extended structure, the sulfonated calixarenes are assembled in bilayers generated by skewed “molecular capsules” where the upper rims are aligned in a head-to-head fashion essentially providing a hydrophilic regions interposed with disordered water molecules, and both components are involved in mutual hydrogen bonding, as evidenced by short O···O contacts at 2.69(1)–2.98(2) Å involving [Gd(H₂O)₈]³⁺. The calixarenes take on an unusual conformation possessing a pseudo cavity (see below) with the bis-phosphonium cations located contiguously in two regions: (i) confined directly between the hydrophobic regions of the directionally opposed calixarenes (endo-cavity), and (ii) embedded in hydrophobic regions of the bilayers of calixarenes (exo-cavity), Figure 2. The aquated metal ions have secondary coordination sphere interactions with the calixarenes associated with hydrogen bonding to sulfonate groups, evidenced by short GdO···O distances at 2.86(2) and 2.90(3) Å, for complexes 1 and 2, respectively. The coordination around the Gd atom is the same for both complexes and is best described as a distorted square antiprism, Figure 3 with the opposite planes consisting of (i) O101, O102, O103, O108 and O104, O105, O106, O107 for complex 1 and (ii) O101, O102, O104, O107 and O103, O105, O106, O108 for complex 2. Similar coordination environments have been reported for lanthanide (M³⁺ = Gd³⁺, Tb³⁺, and Tm³⁺) complexes with p-sulfonatocalix[4]arene, with the metal centers a slightly distorted square antiprism arrangement of eight water molecules.²⁰

The structures can be considered as being built of skewed “molecular capsules” based on two calixarenes, approximately 17 Å in height as measured along the principal axis, shrouding the ends of two bis-phosphonium cations. The “molecular capsules” are arranged in an intertwined network with other bis-phosphonium cations exo-relative to the calixarene cavity, in an expanded bilayer approximately 12.0 Å thick. A bilayer built exclusively of p-sulfonatocalix[5]arene in its sodium salt is 8.4 Å thick.¹² There are small differences between complexes 1 and 2, mainly in relation to the interplay between the calixarenes and the bis-phosphonium cations.

For the space between the central parts of opposing calixarenes in the "molecular capsules", two phenyl rings of two centro-symmetrically related bis-phosphonium cations are positioned in the distorted-cavity of the same calixarene. One phenyl ring has close π···π interplay ring-centroid to ring-centroid distances at 4.24 and 4.00 Å respectively for complexes 1 and 2. The exo-cavity phosphonium cation has a phenyl ring with close C–H···π(centroid) contact to a calixarene methylene carbon atom, at 2.87 Å for both complexes, Figure 4 (corresponding C···π(centroid) distance at 3.67 Å). The triphenylphosphine moieties and associated methylene bridges of the endo-cavity bis-phosphonium cations have weak hydrogen bonding to calixarene sulfonate groups, as judged by close C–H···O contacts at 2.48(1) to 2.85(1) Å (corresponding C···O distance at 3.16(1)–3.29(1) Å and 2.36(1)–2.71(1) Å (corresponding C···O distance at 3.20(1)–3.51(1) Å), for both complexes. Phenyl rings of two independent endo-cavity bis-phosphonium cations are in the phenyl embrace face-to-face arrangement, with π(centroid)···π(centroid) distance at 4.06 Å for both complexes.
Figure 5. Distortion of the cone conformation for p-sulfonatocalix[5]arene associated with both endo- and exo-pseudo cavity interplay with the bis-phosphonium cations.

The conformation of the p-sulfonatocalix[5]arene is perturbed from the usual cone conformation, with the aryl groups flattened, Figure 5; the dihedral angles between the phenyl plane and the basal plane containing the five methylene carbon atoms of the calixarene are summarized in Table 1.

<table>
<thead>
<tr>
<th>phenolic ring</th>
<th>dihedral angle (°) Complex 1</th>
<th>dihedral angle (°) Complex 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ring 1</td>
<td>82.2</td>
<td>99.4</td>
</tr>
<tr>
<td>Ring 2</td>
<td>31.6</td>
<td>28.2</td>
</tr>
<tr>
<td>Ring 3</td>
<td>29.2</td>
<td>32.6</td>
</tr>
<tr>
<td>Ring 4</td>
<td>29.3</td>
<td>24.6</td>
</tr>
<tr>
<td>Ring 5</td>
<td>47.7</td>
<td>53.6</td>
</tr>
</tbody>
</table>

Table 1. Dihedral Angles between the Aryl Plane and the Basal Plane of the Calixarene

Figure 6. Projections highlighting the arrangement of the exo-cavity bis-phosphonium cations (green) relative to each other and the calixarene in forming the bilayer arrangement (for complex 1, with the same arrangement in 2).

Departure from the cone conformation of p-sulfonatocalix[5]arene has been noted for inclusion complexes of 1,2-bis(pyridinium)ethane and 1,4-diazabicyclo[2.2.2]octane, respectively, either as a partial-cone or where one of the sulfonate groups is directed in the opposite direction, as a pseudodouble cone conformation.9,15

The exo-cavity bis-phosphonium are involved in self-association through attractive edge-to-face (ef) interplay.21 Figure 6, with C–H···π(centroid) distances at 3.24 Å and 3.25 Å (corresponding C···π(centroid) distances at 3.97 and 3.98 Å) for complexes 1 and 2, respectively. These cations are also involved in (i) hydrogen bonding with the O-atoms of the phenolic groups of the calixarene, with close C–H···O contacts at 2.531(4)–3.002(4) Å (corresponding C···O distances 3.345(8)–3.521(9) Å), (ii) C–H···π(centroid) interactions with the methylene moieties of the calixarenes, with the closest contacts ranging from 2.63 Å to 2.64 Å (corresponding CH···π(centroid) distances at 3.42–3.87 Å), and (iii) hydrogen bonding interactions with O-atoms of the calixarene sulfonate groups, with close contacts at 2.530(4)–2.996(4) Å (corresponding C···O distances 3.454(8)–3.515(9) Å).

Hirshfeld Surface Analysis. In determining the nature of interplay of the different ionic species in the solid state, analysis of close intermolecular interactions has been undertaken using Hirshfeld surface analysis generated by Crystal Explorer.22 The parameter d_{norm} displays a surface with a red-white-blue color scheme where bright red spots are designated for contacts shorter than the sum of their van der Waals radii, while blue regions are devoid of close contacts.22 The analysis also provides an equivalent 2D-fingerprint plot that demonstrates the summary of the frequency of each combination of d_{norm} and d_{norm} across the surface of a molecule. Overall, the analysis shows subtle differences between the two complexes. Figure 7 compares the Hirshfeld surfaces and the corresponding fingerprint plots for calixarene and bis-phosphonium molecules for complexes 1 and 2. For the calixarene, the dominant intermolecular interaction is the C–H···π contacts, evident from the herringbone arrangement in the fingerprint plot. The nature of the C–H···π interactions between the calixarene and bis-phosphonium cation for complexes 1 and 2 are similar to each other, making up the large percentage contribution of the Hirshfeld surface (~20% of overall interaction) with such interactions reflected as pairs of wings at the upper left and lower right of the fingerprint plot for the calixarene (areas circled in yellow), associated with the C–H···π donor and acceptor, respectively. The Hirshfeld surface mapped with d_{norm} reveals a bright red spot on the surface (yellow arrow) which is assigned to the close C–H···π contact involving the calixarene methylene bridge to the bis-phosphonium phenyl ring. For the bis-phosphonium component, short C–H···π contacts are also evident, which is reflected in the pair of spikes at the bottom left of the fingerprint plot (circled in yellow) for complexes 1 and 2 with the upper spike corresponding to the C–H···π donor, and the lower spike to the acceptor. Also, fingerprint plots for the bis-phosphonium component show symmetry along the diagonal of the plot which indicates a compact...
arrangement of the ion with small intermolecular voids, and this is consistent with the evidence from the Hirshfeld surface where less blue area is observed.

Hydrogen bonding involving hydrogen atoms and oxygen atoms for the calixarene and bis-phosphonium molecules are the major and important intermolecular interaction in both complexes. The H⋯H regions for both components (circled in red) show close H⋯H contacts for both complexes, with $d_e + d_i$ around 2.1 Å for the calixarene and 2.0 Å for the bis-phosphonium cation. The Hirshfeld surface of the calixarene and bis-phosphonium cations for both complexes reveals strong O⋯H hydrogen bonds highlighted by the red spots on the surface, and these contribute significantly to attractive interactions between crystal components with appreciable percentage contribution. Other close interactions for both components in complexes 1 and 2 are summarized as contribution percentages to the Hirshfeld surface area in Figure 8.

### CONCLUSIONS

Water-soluble $p$-sulfonatocalix[5]arene and a large bis-phosphonium cation in the presence of aquated gadolinium(III) ions form a multicomponent self-assembled material, at the exclusion of imidazolium cations present in solution. The material has a skewed molecular capsule arrangement of calixarenes shrouding the bis-phosphonium cations, and these are embedded in a bilayer arrangement with other bis-phosphonium cations. Complex formation is associated with a perturbation of the calixarene from the usual more symmetrical cone conformation, and this conformational flexibility, and the preferential binding of larger cations, establish a design strategy for building complex materials based on the $p$-sulfonated calix[5]arene, for which its use in self-assembly processes has been limited. Moreover, the formation of the multicomponent system suggests that the larger $p$-sulfonatocalix[6 and 8]arenes are likely to form analogous structures with the calixarene able to vary its conformation to optimize the interplay with
phosphonium cations between the bilayers, and embedded in the bilayers, and similarly for large organic cations in general, including drug molecules.

**EXPERIMENTAL SECTION**

p-Sulfonatocalix[5]arene, 1-hexyl-3-methylimidazolium, and 1-octyl-3-methylimidazolium halide salts were synthesized according to the literature procedures. \(^{14}\) Bis(triphenylphosphonium)methylbenzene chloride and gadolinium(III) chloride in the form of GdCl\(_3\) \((\text{H}_2\text{O})_8\) were purchased from Sigma Aldrich and used as received. Crystals of 1 and 2 were grown by slow evaporation of an acidified solution (using 1 M HCl) containing equimolar amounts (0.01 M) of calixarene, imidazolium salts (1-hexyl-3-methylimidazolium chloride and 1-octyl-3-methylimidazolium chloride respectively), bis-phosphonium salt and gadolinium(III) chloride. On standing over several days, small colorless crystals suitable for X-ray diffraction studies deposited.

Crystallography. All data were measured using an Oxford Diffraction Gemini CCD diffractometer at \(T = 100(2)\) K with monochromatic Mo-K\(_\alpha\) radiation (\(\lambda = 0.71073\) Å) for 1 and Cu-K\(_\alpha\) radiation (\(\lambda = 1.54178\) Å) for 2. The data were corrected for Lorentz and polarization effects, with absorption corrections applied using multiple symmetry equivalent reflections. The structures were solved by direct methods and refined using full matrix least-squares on \(F^2\) and polarization effects, with absorption corrections applied using \(c = 25.2906(7)\) Å, \(\Delta = 18.1333(13),\) \(I_{\text{max}} = 134.3\) ° and \(\Delta = 65.590(7)\) ° for 1 and 2 respectively. The values of the \(R\) and \(R_{\text{wp}}\) parameters listed in Table 1 were obtained from calculations using the program SHELXL-97. \(^{24}\) Crystallographic data files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org/.

**REFERENCES**
