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## Solution structure of zinc-seamed C-alkylpyrogallol[4]arene dimeric nanocapsules†

 Harshita Kumari,<sup>a</sup> Wei G. Wycoff,<sup>b</sup> Collin M. Mayhan,<sup>b</sup> Steven R. Kline,<sup>c</sup> Joshua R. So,<sup>b</sup> Carol A. Deakne,<sup>\*b</sup> John E. Adams<sup>†b</sup> and Jerry L. Atwood<sup>†\*b</sup>

The structural stability and solution geometry of zinc-seamed-C-propylpyrogallol[4]arene dimers has been studied in solution using *in situ* neutron scattering and 2D-DOSY NMR methods. In comparison with the structures of the analogous copper-/nickel-seamed dimeric entities, the spherical geometry of the  $\text{PgC}_3\text{Zn}$  species ( $R = 9.4 \text{ \AA}$ ; diffusion coefficient =  $1.05 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ ) is larger due to the presence of ligands at the periphery in solution. This enhanced radius in solution due to ligation is also consistent with the findings of model molecular dynamics simulations of the zinc-seamed dimers.

A supramolecular assembly can be defined as a complex entity, such as a DNA double helix, held together by non-covalent bonds. Such complex large entities are formed *via* molecular self-assembly, a process taking far fewer steps than does a conventional synthesis of a single molecule of similar dimensions. The ease of formation, high yield, and possible practical applications as functional materials are some of the factors that have spurred a widespread interest in supra- and supermolecular assemblies.<sup>1–6</sup>

One group of such assemblies comprises the metal-seamed pyrogallol[4]arene nanocapsules (Fig. 1).<sup>1,7</sup> Although these nanocapsules have now been synthesized with a selection of alkyl groups, metals, guests and axial ligands, only a few have been examined in solution.<sup>8–15</sup> Our motivation in studying solution-phase architectures is to determine whether the solution structures conform to the solid-state geometries. Many nanocapsules, specifically transition metal (Cu/Ni)-seamed hexamers and dimers and hydrogen-bonded dimers, retain their solid-state geometry in solution.<sup>10,13</sup> In contrast, Ga- and Ga/Zn-seamed pyrogallol[4]arene hexamers rearrange from spheres in the solid state to toroids in solution.<sup>12</sup> Similarly, the hydrogen-bonded  $\text{PgC}_1\text{C}$  ferrocene/ $\text{PgC}_6\text{C}$  pyrene nanotubes rearrange to dimers in solution.<sup>14,15</sup> Solution-phase studies also have allowed us to discover novel structures of species that were either difficult to crystallize or expected to be unstable in solution.<sup>9,11</sup> For example, the ellipsoidal and tubular architectures of

the  $\text{PgC}_{17}\text{Cu}$  and  $\text{PgC}_1\text{Fe}$  nanoassemblies, respectively, have been studied exclusively in solution.<sup>9,11</sup>

The current study and analysis focus on the solution structure of the original dimeric pyrogallol[4]arene-based nanocapsules:

$[\text{Zn}_8(\text{C-propylpyrogallol[4]arene})_2(\text{pyridine})_7(\text{DMSO})_1\text{C-pyridine}]$ , with propyl R-groups, a pyridine guest and pyridine/DMSO axial ligands (Fig. 1C and D, propyl R-groups and guest pyridine molecule are removed for clarity).<sup>16</sup> The zinc dimer is composed of two pyrogallol[4]arene subunits that are coordinated by the ring of eight  $\text{Zn}^{+2}$  ions across the equatorial belt. The metal atoms displace 16 of the 24

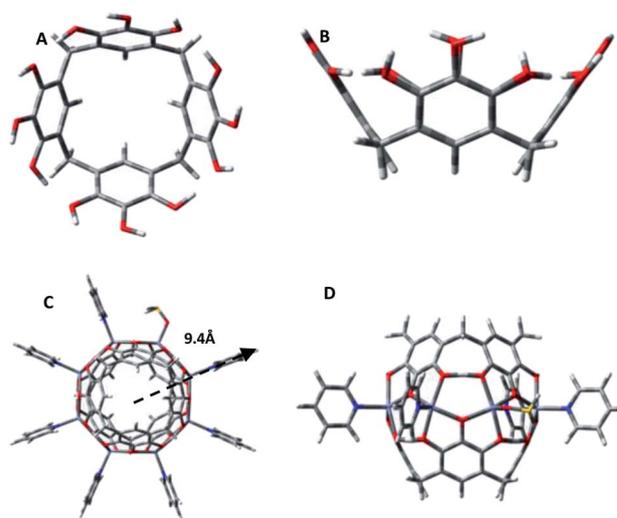


Fig. 1 (A) Top view of pyrogallol[4]arene; (B) front view of pyrogallol[4]arene; (C) top view of the C-alkylpyrogallol[4]arene zinc-seamed dimer illustrating the approximate radius of the capsule; (D) front view of the C-alkylpyrogallol[4]arene dimer. For clarity alkyl groups and guest pyridine molecule are removed from the figures. O: red, M (metal): light blue, C: grey, N: blue, H: white.

<sup>a</sup>James L. Winkle College of Pharmacy, University of Cincinnati, OH 45267, USA. E-mail: kumariha@ucmail.uc.edu

<sup>b</sup>Department of Chemistry, University of Missouri-Columbia, Columbia, MO 65211, USA. E-mail: AtwoodJ@umsystem.edu; DeakneC@umsystem.edu; AdamsJE@umsystem.edu

<sup>c</sup>NIST Center for Neutron Research, National Institute of Standards and Technology, 100 Bureau Drive, Gaithersburg, MD 20899, USA

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hydroxyl protons of the pyrogallols to seam this spherical framework. Each of the zinc centers is ligated by four phenoxy groups, two from each pyrogallol, along with an axial DMSO or pyridine ligand, that gives a square pyramidal configuration to the metal center. The central phenoxy group from each pyrogallol is bridged between two adjacent zinc centers, whereas the two exterior phenoxy groups are each ligated to a single zinc center and hydrogen-bonded to a phenoxy group on the neighboring pyrogallol subunit, making the overall assembly neutral. In the transition from pentacoordinated Zn in the solid state to tetraordinated Zn in the gas phase, as a result of the MALDI-TOF analysis, this local Zn–O binding geometry is essentially preserved.<sup>16–18</sup> Of course, thermal fluctuations do occur, although, as we shall show *via* molecular dynamics simulations, the overall shape remains roughly spherical.

The  $\text{PgC}_3\text{Zn}$  dimeric nanocapsule was synthesized by adding 1 equiv. of  $\text{PgC}_3$  ( $0.01 \text{ mol L}^{-1}$ ), 4 equiv. of zinc(II) nitrate ( $0.04 \text{ mol L}^{-1}$ ), and 14 equiv. of pyridine in DMSO solvent. The solution was heated, sonicated, and left overnight to obtain yellow crystals of the dimer. The unit cell was confirmed and the crystals were filtered and dissolved in *d*6-DMSO at mass fractions of 1% and 5% for SANS measurements. Preferential deuteration of solvent for SANS studies enhances the coherent scattering and improves the contrast between the solute and the solvent. The samples were left overnight to ensure saturation without precipitation, and the SANS measurement was conducted at  $25^\circ\text{C}$  on the NG3 30m SANS instrument at the NIST Center for Neutron Research in Gaithersburg, MD.<sup>19</sup> The collected scattering data was reduced and analyzed using Igor-Pro<sup>20</sup> incorporating the instrumental *q*-resolution function.

The measurements on the dimeric sample at mass fractions of both 1% and 5% were conducted to ensure sufficient scattering and to detect a concentration dependence of the capsular structure. The scattering length densities (SLDs) of the solute and solvent were calculated and held fixed for data analyses. The SLDs of the solvent (*d*6-DMSO) and solute ( $\text{PgC}_3\text{Zn}$  dimer) were fixed at  $5.28 \times 10^{-6} \text{ \AA}^{-2}$  and  $1.37 \times 10^{-6} \text{ \AA}^{-2}$ , respectively.

The reduced SANS data was fitted globally, with the two data sets corresponding to different mass fractions being modelled simultaneously to obtain the best fit. The data was fitted to various cylindrical, ellipsoidal and core-shell models to detect the occurrence of structural transformation. It was quickly found, however, that the entity does not have a core-shell, ellipsoidal or cylindrical geometry (ESI†). Previous studies on copper and nickel nanocapsules have indicated the presence of both dimers and hexamers in solution;<sup>13</sup> hence, it was important to investigate the possible presence of multiple species with similar or different architectures. For this purpose, the data was globally fitted to the bimodal Schulz sphere and Schulz sphere models (ESI†). The calculated SLDs for the hexamer ( $1.56 \times 10^{-6} \text{ \AA}^{-2}$ ), dimer ( $1.37 \times 10^{-6} \text{ \AA}^{-2}$ ) and solvent ( $5.28 \times 10^{-6} \text{ \AA}^{-2}$ ) were held fixed for global fitting. An unphysical volume fraction was obtained for the second spherical species in the bimodal Schulz sphere global fit, clearly indicating that the  $\text{PgC}_3\text{Zn}$  sample has a unimodal distribution. In fact, the data for the  $\text{PgC}_3\text{Zn}$  was fit best to a polydisperse sphere (Schulz sphere) model<sup>21,22</sup> with a chi-sqrt value of 1.156 and a radius of

$\approx 9.4 \text{ \AA}$ , a result indicating the presence of only one spherical assembly in solution (ESI†; Fig. 1 and 2).

In comparison with the radii of the  $\text{PgC}_3\text{Cu}$  and  $\text{PgC}_3\text{Ni}$  dimers, the radius obtained for the  $\text{PgC}_3\text{Zn}$  dimer is  $\approx 2.4 \text{ \AA}$  larger, and the size/diameter of the  $\text{PgC}_3\text{Zn}$  dimer ( $\approx 18.8 \text{ \AA}$ ) is intermediate between that of a  $\text{PgC}_3\text{Cu/Ni}$  dimer ( $\approx 14 \text{ \AA}$ ) and that of a  $\text{PgC}_3\text{Cu/Ni}$  hexamer ( $\approx 20 \text{ \AA}$ ). This comparison indicates that  $\text{PgC}_3\text{Cu}$  and  $\text{PgC}_3\text{Ni}$  most likely lose their ligands in solution. As this was the case, we examined the dimensions of the solid-state  $\text{PgC}_3\text{Zn}$  dimer (XRD). The solid-state radius of the  $\text{PgC}_3\text{Zn}$  dimer is  $\approx 9.4 \text{ \AA}$  and  $\approx 7 \text{ \AA}$  with and without external pyridine/DMSO ligands, respectively.<sup>16</sup> The geometric dimensions obtained for the  $\text{PgC}_3\text{Zn}$  dimer in the solution phase are nearly identical to those obtained in the solid state. Thus, SANS data analysis for the solvent-solubilized  $\text{PgC}_3\text{Zn}$  dimer not only confirms its spherical shape and structural stability in solution but also reveals the preference for a square pyramidal metal bonding geometry, which differs from the distorted square planar geometry found in other metal-seamed ( $\text{PgC}_3\text{Cu}$ ,  $\text{PgC}_3\text{Ni}$ ) dimers in solution.

These radii obtained for the  $\text{PgC}_3\text{Zn}$  dimer are also commensurate with those calculated from molecular dynamics simulations of  $\text{PgC}_0\text{Zn}$  dimers with and without 8 ligated molecules. These mixed quantum-classical calculations were performed using the AMBER program suite,<sup>23</sup> with a tight-binding DFT scheme (DFTB3)<sup>24</sup> being used to model the Zn, O, and bridging H atoms as well as the atoms of the ligand. All other atoms of the dimer were treated classically using the gaff2 force field.<sup>25</sup> The simulation results reported here reflect the dynamics of room-temperature gas-phase species. In the absence of the ligands, the average dimer radius was found to be  $4.9 \pm 0.1 \text{ \AA}$ , whereas with 8 ligated ammonia molecules the

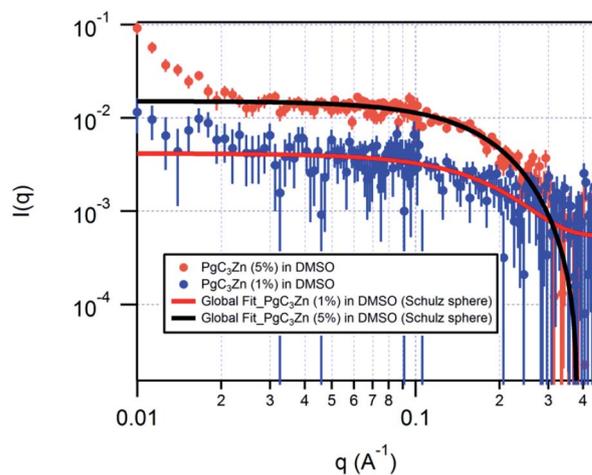


Fig. 2 SANS intensity from the zinc-seamed C-propylpyrogallol[4] arene dimer at mass fractions of 1% and 5%. The solid line is the model fit with a polydisperse sphere model. The error bars on the SANS data points represent one standard deviation in the measured intensity. The upturn seen at  $q < 0.02 \text{ \AA}^{-1}$  is likely due to the presence of a small fraction of aggregates of nanocapsules in solution. Analysis is restricted to larger *q*-values to focus on the scattering from individual nanocapsules.



average radius was  $7.1 \pm 0.1 \text{ \AA}$ , with 8 ligated pyridine molecules the average radius was found to be  $9.8 \pm 0.1 \text{ \AA}$ , and with 8 ligated DMSO molecules the average radius was found to be  $8.4 \pm 0.7 \text{ \AA}$  (the uncertainties here are standard deviations of the average radii as measured from the instantaneous center of mass of the 8 Zn atoms. That is, they reflect the time-dependent thermal fluctuations of the dimer capsule rather than uncertainties in the calculated forces and simulation methodology). The larger uncertainty associated with the calculated average radius for the DMSO-ligated species here derives from the nonlinear bonding at the oxygen and nonplanar bonding at the sulfur in DMSO and the rotation about the oxygen–sulfur bond. In the above ligated species, the calculated radius of the roughly spherical dimer cage itself also differs from that of the non-ligated dimer, being larger by about  $0.1 \text{ \AA}$  in each case.

The solution-phase behavior of  $\text{PgC}_4\text{Zn}$  was further investigated using diffusion-ordered NMR spectroscopy (DOSY). Specifically, we investigated the encapsulation of pyridine within zinc dimers.

Note that we are reporting here the first DOSY NMR study of the metal-seamed pyrogallol[4]arene dimeric framework. The diffusion NMR studies reported by Cohen and co-workers were on hydrogen-bonded pyrogallol[4]arene, octahydroxypyridine[4]arene<sup>26,27</sup> and resorcin[4]arene nanocapsules in  $\text{CDCl}_3$ .<sup>28</sup> Atwood *et al.* have more recently reported DOSY NMR studies on  $\text{PgC}_4\text{Ga}$  hexamers,  $\text{PgC}_4\text{GaZn}$  toroids and hydrogen-bonded  $\text{PgC}_6\text{C}$  pyrene nanoassemblies in *d*-6-acetone.<sup>29</sup>

Capsules of  $\text{PgC}_4\text{Zn}$  in pyridine for the NMR studies were synthesized by mixing methanolic solutions of *C*-butylpyrogallol[4]arene, zinc nitrate and pyridine in the ratio of 1 : 4 : 14. Sonication yielded a precipitate of zinc dimers. A 2% solution of  $\text{PgC}_4\text{Zn}$  in pyridine was prepared in *d*-6-DMSO for the NMR measurements. Notably, we used a different tail (butyl) here, *versus* the previously studied *C*-propyl tail, as the tail length has been shown to not impact the self-assembled metal-coordinated core architecture of the nanocapsule.

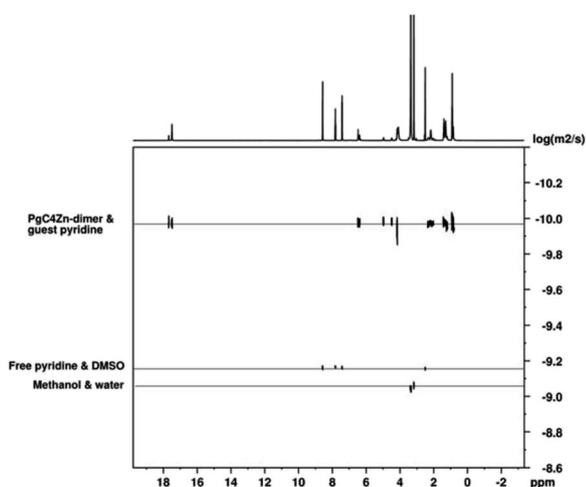


Fig. 3 The DOSY NMR spectra of the  $[\text{PgC}_4\text{Zn} \subset (\text{pyridine})]$  dimer. The Y-axis on the DOSY plot is displayed as  $\log D$ .

The diffusion coefficients of the phenoxy hydroxyls, alkyl moieties and bound pyridine are similar (Fig. 3), indicating the structural integrity of the  $\text{PgC}_4\text{Zn}$  dimer in DMSO solvent. Overall, the macrocycle/capsule and bound guest pyridine have a diffusion coefficient of  $1.04 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ . The integration of bound *versus* free pyridine is 1 : 8 suggesting that the external pyridine ligand has exchanged with DMSO. The diffusion coefficients of the “free” pyridine ligand, solvent DMSO, methanol and water are  $6.79 \times 10^{-10}$ ,  $7.00 \times 10^{-10}$ ,  $8.71 \times 10^{-10}$  and  $9.08 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ , respectively. The diffusion coefficient of the bound pyridine is about 6.5 times lower than that of a free pyridine.

Overall, the combined neutron scattering, diffusion-ordered NMR spectroscopy and molecular dynamics results indicate (a) the structural stability of the dimer in solution; (b) guest encapsulation; (c) fast external ligand exchange with solvent, which can only be captured through SANS; and (d) an increase in the effective radius of the zinc dimer due to ligation at zinc centers showing a preference for square pyramidal bonding.

The robustness of dimers demonstrated in this study justifies the use of these frameworks for guest encapsulation. Furthermore, the presence of exterior ligands affords valuable insight into the nature of guest–ligand communication. Future studies thus will focus on studying these robust frameworks and on variations in their structural properties in response to varying the encapsulated guest.

## Conflicts of interest

There are no conflicts to declare.

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