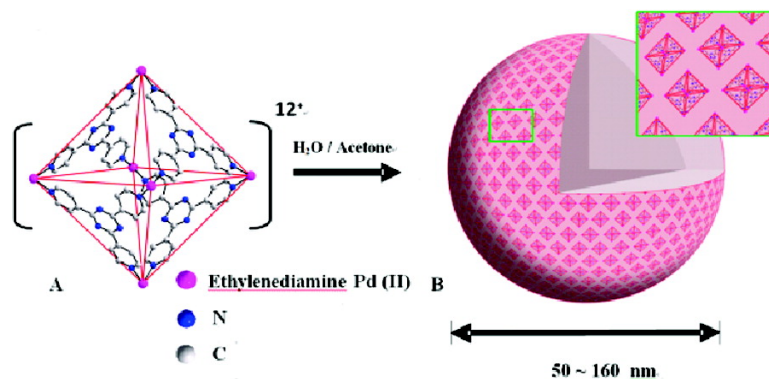


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Spontaneous Self-Assembly of Metal–Organic Cationic Nanocages to Form Monodisperse Hollow Vesicles in Dilute Solutions

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Metal–organic nanocages are an extensive class of giant, porous molecules that formed by small organic ligands and metal ions. Their shape, size, charge, and composition can be rationally designed by the choice of metal ion and organic ligands.^{1–3} Due to their molecular nature, the cages have precisely defined cage windows, or pore-openings, making the cages accessible to guest molecules.^{1–3} Therefore, the metal–organic cages not only are appealing by their aesthetic shape but also show a distinguished host–guest chemistry that has recently emerged.

Beyond their fascinating properties as nanoscaled molecules, herein we report the spontaneous self-assembly of highly water soluble metal–organic nanocages to form hollow, spherical, vesicle-like structures with tunable sizes. This is a completely new phenomenon observed for metal–organic nanocages (Figure 1).

The commercially available (Wako) Pd₆L₄(NO₃)₁₂ {Pd = ethylenediamine palladium(II), L = 2,4,6-tris(4-pyridyl)-triazine} metal–organic nanocage (Figure 1), first reported by Fujita,⁴ was used for this study, which has an octahedral shape and a diameter of ~2 nm.⁴ In pure water each nanocage carries 12 positive charges attributed to 6 Pd²⁺ ions, after releasing 12 NO₃[–] counterions into solution. The Pd₆L₄(NO₃)₁₂ solutions were studied by dynamic and static light scattering (DLS and SLS) techniques. In a pure aqueous solution, very low scattered intensity was collected by SLS after several weeks, indicating that there was no large structure forming in solution; i.e., the cages existed as discrete macrocations. This is due to the high charge density of the nanocages and not a surprise for highly soluble ions.

However, when different amounts of acetone were added into the aqueous solutions of nanocages, a significant and continuous increase of the total scattered intensity from SLS was observed, suggesting the formation of much larger structures. The nanocages are still quite soluble in such water/acetone mixtures (up to 75 v% acetone at 0.20 mg/mL) and form clear, stable, homogeneous solutions. Therefore, the growth of the scattered intensity is not due to the aggregation of insoluble species but a slow self-association process of individual cages. As revealed in Figure 2, the peaks obtained by Constrained Regularization (CONTIN) analysis⁵ from DLS studies of a 0.20 mg/mL nanocage solution with 22 v% acetone are attributed to supramolecular structures which are dominant in solution and have narrow size distributions. The average hydrodynamic radius (R_h) of the large structures does not change with time, indicating that such supramolecular structures have preferred curvatures in solution. Besides, in a 0.06 mg/mL nanocage solution containing 40 v% acetone, the average R_h is 38 ± 1.0 nm measured at a 90° scattering angle. Extrapolating the R_h values to a 0° scattering angle results in an $R_{h,0}$ of 40.5 nm. SLS measurements performed on the same solutions indicate that the average radius of gyration (R_g) of the supramolecular structures is 40.8 ± 0.8 nm. Therefore, the ratio R_g/R_h is very close to 1. For spherical objects (TEM evidence provided in Figure 3), if they are solid in nature, the general rule of $R_g/R_h = 0.77$ holds. When

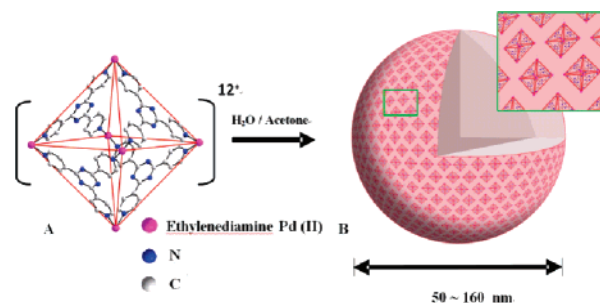


Figure 1. (A) Three-dimensional structure of a single metal–organic nanocage molecule. (B) The supramolecular blackberry type structure determined by laser light scattering measurements and TEM.

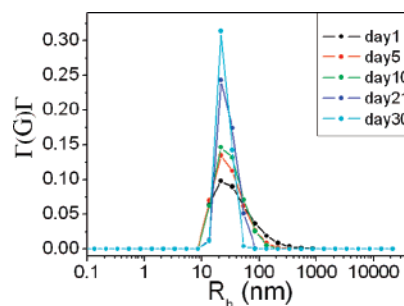


Figure 2. Hydrodynamic radius (R_h) distributions of 0.20 mg/mL Pd₆L₄ cationic nanocage aqueous solution with 22 v% acetone (Ac) after 1, 5, 10, 21, and 30 days. The scattering angle is set at 90°.

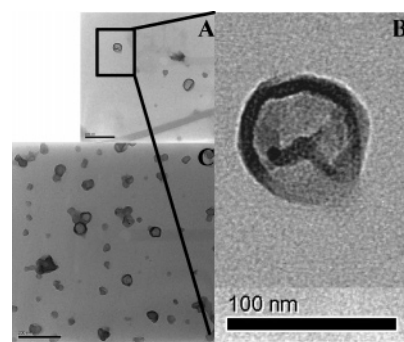


Figure 3. TEM studies of a 0.06 mg/mL Pd₆L₄ cationic nanocage aqueous solution containing 40 v% acetone. (A) 38–40 nm radius vesicles; (B) a zoom-in image of A; (C) a comprehensive view of burst and intact vesicles which show soft, membrane-like property.

$R_g/R_h \approx 1$, it implies that the mass of the particle is almost entirely distributed on its surface. Accordingly, it serves as strong evidence that the assemblies formed by Pd₆L₄ cationic nanocages observed at this circumstance have a hollow, vesicle-like structure.

TEM studies also clearly show the presence of uniform, hollow, vesicle-like structures formed by Pd₆L₄ cationic nanocages, with the average radius of ~40 nm in 40 v% acetone solution (Figure

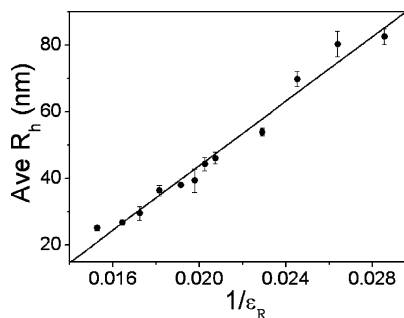


Figure 4. Average R_h of vesicle-like structures in 0.20 mg/mL cationic nanocage aqueous solutions containing different volume of acetone is plotted over the inverse dielectric constant of the solvent.

3), which is consistent to the DLS and SLS studies. Some of the vesicle-like structures are burst due to the loss of internal and external solvent during the drying process. The burst vesicles showed a wrinkly feature which is indicative of a soft, flexible, and biomembrane-like nature (Figure 3B and C).

An interesting question is about the wall structure of the nanocage vesicles. It is known that the amphiphilic surfactants and phospholipids form bilayer vesicle structures due to the hydrophobic interactions. In contrast, fully hydrophilic inorganic polyoxometalate (POMs) macroanions can form single layer, vesicle-like “blackberry” structures due to the counterion-mediated attraction and hydrogen bonds.^{6–12}

The current Pd_6L_4 nanocages are macrocations, which certainly show similarities to POM macroanions. A major difference between nanocages and POMs is that the POMs are fully hydrophilic while the nanocages contain both hydrophilic (Pd^{II} ions) and hydrophobic parts (tridentate aromatic ligands). On the other hand, the nanocages also differ from amphiphilic surfactants, which usually have a hydrophilic polar head and a hydrophobic “end”. The nanocages lack such “ends” because of their highly isotropic symmetry. Therefore, both electrostatic and hydrophobic interactions could contribute to their vesicle formation.

To clarify the driving force for the self-assembly of nanocages, we first investigated the effect of solvent polarity (in the form of dielectric constant ϵ_R) on the vesicle size. At a concentration of 0.20 mg/mL, the R_h of nanocage vesicles increases monotonically from 25 to 80 nm with increasing acetone content, as shown in Figure 4. By plotting the R_h of the vesicles versus $1/\epsilon_R$ of the solvent, a linear relationship is demonstrated, indicating that the cage vesicles with preferred curvatures are stabilized by the charge regulation mechanism.¹³ It suggests that the nanocage macrocations can spontaneously and reversibly form vesicle-like structures in polar solvents as long as they possess appropriate charge density. The hydrophobic interaction raised from the aromatic ligands does not play a major role in the self-assembly. If the hydrophobic interaction is the dominant driving force, then it would be much easier and probably faster for the nanocage vesicle formation in pure water than in water/acetone mixtures, because a stronger hydrophobic interaction is expected to be present in the former solution (the hydrophobic ligands become better solvated when acetone is introduced). However, no supramolecular structures formed in pure water, which is a clear argument against the possibility of hydrophobic interaction being the major attractive force. Similar results were obtained in other mixed solvent systems

such as water/EtOH. Therefore, we conclude that the nanocage macrocations behave similarly to macroanionic POMs in solution, i.e., form “blackberry”-type structures with the help of counterion-mediated attractions. Additional evidence comes from the very slow vesicle formation process (takes days to weeks, revealed by the very slow increment of the scattered intensity), which is very similar to the process of the POM blackberry formation¹⁰ but certainly different from the formation of bilayer vesicles.

In summary, we demonstrate for the first time that the $\{\text{Pd}_6\text{L}_4\}^{12+}$ cationic metal–organic nanocages can self-assemble into unique supramolecular vesicular structures in solution. The vesicle size can be accurately adjusted by varying the solution polarity. This suggests a tremendous scope for metal–organic nanocage vesicles due to the large variety of nanocages that can be made in practically any shape, size, and organic functionality by design. The dependence of vesicle size on solvent polarity and their slow formation process indicate that the vesicles formed by macrocations are analogous to our previously observed blackberry structures formed by POM macroanions.¹⁴ The present work indicates that macrocations behave similarly to macroanions in dilute solution: they also tend to strongly attract with each other and form conserved, stable supramolecular structures with the help of counterions. Therefore, the blackberry structure is likely to be a universal type of self-assembly for soluble macroions. In addition, our findings may serve as an intriguing model for understanding biological macroionic structures and their solution behavior such as the virus shell construction and dissociation,¹⁴ some of which involves hundreds of positively charged protein macrocations subunits. Moreover, the self-assembled nanocages can provide blackberry structures a wide range of organic functionalities that are impossible to reach with purely inorganic systems, which may open the door to new types of biomembranes, hierarchically structured delivery systems, nanocontainers, nanoreactors, sensors, and nanocatalysts.

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References

- (1) Caulder, D. L.; Raymond, K. N. *Acc. Chem. Res.* **1999**, *32*, 975.
- (2) Fujita, M.; Umemoto, K.; Yoshizawa, M.; Fujita, N.; Kusukawa, T.; Biradha, K. *Chem. Commun.* **2001**, *6*, 509.
- (3) Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853.
- (4) Fujita, M.; Oguro, D.; Miyazawa, M.; Oka, H.; Yamaguchi, M.; Ogura, K. *Nature* **1995**, *378*, 469.
- (5) Provencher, S. W. *Comput. Phys. Commun.* **1982**, *27*, 229.
- (6) Liu, T.; Diemann, E.; Li, H.; Dress, A. W.; Muller, A. *Nature* **2003**, *426*, 59.
- (7) Liu, G.; Cai, Y.; Liu, T. *J. Am. Chem. Soc.* **2004**, *126*, 16690.
- (8) Liu, G.; Liu, T. *J. Am. Chem. Soc.* **2005**, *127*, 6942.
- (9) Liu, T. *J. Am. Chem. Soc.* **2002**, *124*, 10942.
- (10) Liu, T. *J. Am. Chem. Soc.* **2003**, *125*, 312.
- (11) Liu, T.; Imber, B.; Diemann, E.; Liu, G.; Cokleski, K.; Li, H.; Chen, Z.; Muller, A. *J. Am. Chem. Soc.* **2006**, *128*, 15914.
- (12) Kistler, M. L.; Bhatt, A.; Liu, G.; Casa, D.; Liu, T. *J. Am. Chem. Soc.* **2007**, *129*, 6453.
- (13) Verhoeff, A. A.; Kistler, M. L.; Bhatt, A.; Pigga, J.; Groenewold, J.; Klokkenburg, M.; Veen, S.; Roy, S.; Liu, T.; Kegel, W. K. *Phys. Rev. Lett.* **2007**, *99*, 066104.
- (14) Johnson, J. E.; Speir, J. A. *J. Mol. Biol.* **1997**, *269*, 665.

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