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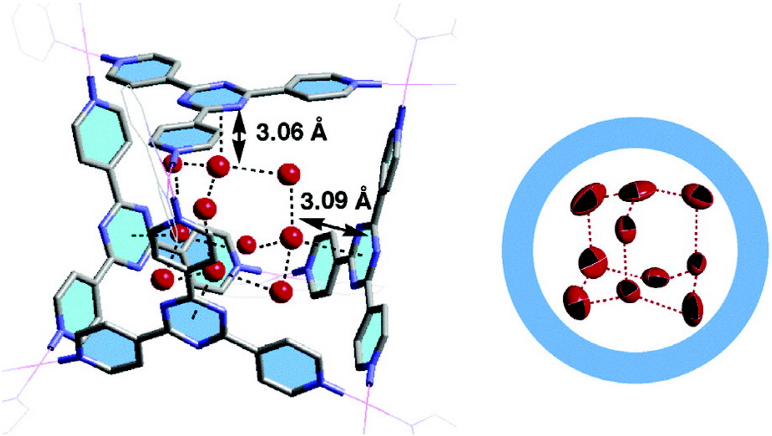

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Endohedral Clusterization of Ten Water Molecules into a “Molecular Ice” within the Hydrophobic Pocket of a Self-Assembled Cage

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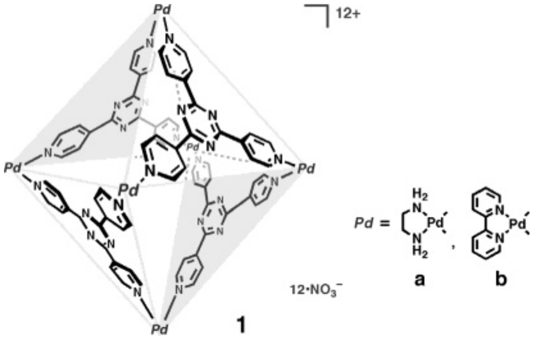
One of the most characteristic features of water molecules is their ability to make themselves rather “hydrophobic” by neutralizing their intrinsic high polarity by forming hydrogen-bonded networks.[1,2] In particular, when they are in contact with a hydrophobic solute, hydrogen-bonded water networks (or clusters if the number of water molecules is limited) spontaneously grow at the surface of the solute, often giving rise to stable hydrate complexes such as methane hydrate.[3] The growth of such hydrogen-bonded water clusters/networks may occur not only at the surface of hydrophobic molecules but also within hydrophobic pockets of large hollow compounds.[4] Here we report that, within the hydrophobic cavity of a self-assembled coordination cage (**1**),[5] an adamantanoid $(H_2O)_{10}$ cluster is formed, which is termed “molecular ice” because this structure is the smallest unit of naturally occurring I_c-type ice.[1,2] The X-ray structural analysis, coupled with neutron diffraction study, reveals that the molecular ice is not simply formed by filling the void space but is a result of specific $H_2O{:}\cdots\pi$ interaction within the cage. Whereas there are numerous examples of the crystallographic observation of water clusters in crystals,[6,7] relatively few have been reported on the endohedral clusterization of water molecules within hollow discrete compounds, except for those in small host compounds.[8]



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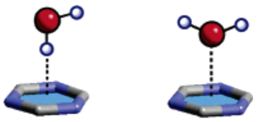
In expectation of endohedral clusterization of water within the large hollow framework of **1**, we examined the crystallographic analysis of the cage after crystallization from water. The diffraction study of **1a** suffered from many technical and crystallographical problems such as brittle crystals and severe disorder of solvent molecules and anions, allowing the rough display of only the framework of cage **1a**. However, the replacement of ethylenediamine by 2,2′-bipyridine[5] and crystallization under slightly acidic conditions (HNO_3) afforded, after 3 days at room temperature, high-quality single crystals of **1b**.

The −180 °C X-ray diffraction study of the crystal showed a large unit cell (volume: ca. 27 000 Å^3) including four crystallographically independent (yet almost identical) **1b** cages, which were hidden among a very complicated network composed of 48 nitrate ions and ca. 200 oxygen atoms derived from water molecules.[9]

A T_d-symmetric adamantanoid $(H_2O)_{10}$ cluster, a molecular ice, is revealed within the cage (Figure 1a) when the outside water molecules are removed.[10] In the literature, only one example of an adamantanoid cluster has been reported by Atwood et al.; the cluster exists in the void space of a Cu(II) complex and seems considerably stabilized by the coordination of bridgehead H_2O lone pairs to Cu(II) centers along with hydrogen bonding of bridged H_2O with NO_3 anions and the framework.[6] In contrast, the molecular ice in cage **1b** is not sustained by any metal or anion coordination. It is noncovalently accommodated by the hydrophobic pocket with close contacts of 3.06 and 3.09 Å, providing a reminiscent endohedral cluster of hypothetical reversed hydrate complexes. Surprisingly, the molecular ice does not “melt” even at room temperature; the adamantanoid framework of 10 water molecules can be located roughly even in a room-temperature diffraction study.

The structural parameters of the molecular ice are quite similar to those of I_c-type ice (Figure 1b).[1,2,11] The adjacent O···O distances are 2.72−2.93 Å (2.84 Å on average) in the molecular ice and are close to 2.74 Å in I_c-type ice. The O···O···O angles at the bridgeheads are 108.8−122.3°, whereas those at the other corners are 96.7−104.1°; the former is slightly larger than the ideal 109.47°, whereas the latter is slightly smaller than ideal. These observations indicate that the molecular ice is slightly compressed by the four planar ligands.

Since the thermal parameter of the bridgehead oxygen is small and the distance between the oxygen and the ligand is very short (3.06 and 3.09 Å), we assume that the molecular ice is formed not by a simple void-filling effect but by efficient molecular recognition. The recognition of the molecular ice by the cage at the bridgehead oxygen atoms can be explained by two possible binding modes: OH···π hydrogen bonding vs $H_2O{:}\cdots\pi$ interaction. These two possibilities cannot be distinguished by X-ray crystallography because no hydrogen atoms can be located.



Therefore, we carried out a single-crystal neutron diffraction study on deuterated molecular ice to specify the position of hydrogen (deuterium) atoms.[12] Crystals with dimensions of 3.5 mm × 3.5 mm × 2.0 mm were prepared from a D_2O solution of **1b** and, after being sealed in a quartz tube, subjected to neutron

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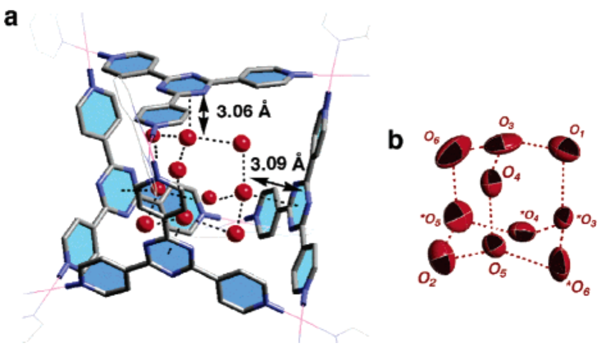

Figure 1. (a) X-ray crystal structure of **1b** along with oxygen atoms (water molecules) around the cage. (b) ORTEP drawing (50% probability ellipsoids) of 10 oxygen atoms (molecular ice) within **1b**. Interatomic distances (Å): $O_1-O_3 = 2.87$, $O_2-O_5 = 2.78$, $O_3-O_4 = 2.93$, $O_3-O_6 = 2.72$, $O_4-O_5 = 2.85$, $O_5-O_6 = 2.92$.

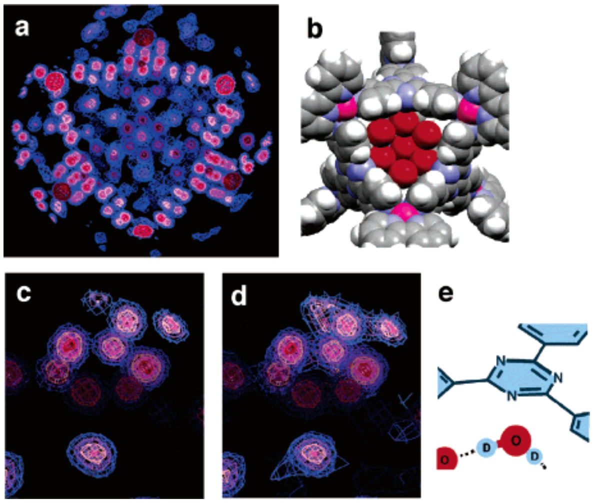

Figure 2. (a) The electron density map of **1b** by X-ray superimposed on the nuclear density map. (b) The corresponding structural drawing by space-filling model (red = oxygen atom). A partial structure around a bridgehead D_2O molecule: (c) the electron density map by X-ray diffraction, (d) its superimposition on the nuclear density map by neutron diffraction, and (e) the corresponding structural drawing.

diffraction at room temperature for 13 days. Due to the large crystal size and long exposure at room temperature, the quality of the data was inferior. However, refinement with the atomic coordinates determined by the X-ray diffraction provided a reasonable nuclear density map. Figure 2a shows the electron density map superimposed on the nuclear density map (X-ray + neutron) around the cage.[13] Partial structures of a bridgehead water molecule and the nearest triazine core of the ligand are shown in Figures 2c (X-ray) and 2d (X-ray + neutron).

In Figure 2d, no nuclear density is observed between bridgehead D_2O and the ligand. Two deuterium atoms of the D_2O molecule are clearly shown to be involved in the adamantanoid cluster framework. Therefore, we conclude that the bridgehead water molecules interact with the ligand via $D_2O{\cdots}\pi$ (lone pair$-\pi$ electron) interaction. This result strikingly contrasts with the general understanding that aromatic π-systems donate electron density to electron-deficient or cationic species, as suggested by many examples of cation$-\pi$ interactions.[14]

From the results of X-ray and neutron diffraction studies, we propose that the molecular ice donates electrons from the lone pair of the bridgehead water to the ligand of **1b**, which is considerably electron-deficient due to metal coordination of the three pyridyl groups. Deuterium atoms of nonbridgehead water could not be located because the thermal disorder of these D_2O molecules was relatively large. The nonbridgehead water molecules are weakly hydrogen-bonded with outside water molecules through the window of the cage to balance the insufficient number of hydrogen bonds. These hydrogen bonds are more dynamic because the thermal parameters of the outside waters are considerably larger.

The presence of highly ordered water clusters inside the binding pockets of proteins has been predicted[15] and considered to be crucial in entropy-driven substrate binding.[16] We suggest that the molecular recognition by cage **1** is entropy-driven, in which the binding of guests is compensated by the "melting" of the molecular ice into free water molecules. The endohedral water cluster therefore plays an important role in the molecular recognition of the cage, as in protein binding pockets.

Supporting Information Available: Experimental details and crystallographic data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Eisenberg, D.; Kauzmann, W. *The Structure and Properties of Water*; Oxford University Press: New York, 1969.
(2) (a) Stillinger, F. H. *Science* **1980**, *209*, 451−457. (b) Ludwig, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 1808−1827.
(3) Jeffrey, G. A. Hydrate Inclusion Compounds. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Academic Press: 1984; Vol. 1, Chapter 5.
(4) Koga, K.; Gao, G. T.; Tanaka, H.; Zeng, X. C. *Nature* **2001**, 802−805.
(5) (a) Fujita, M.; Oguro, D.; Miyazawa, M.; Oka, H.; Yamaguchi, K.; Ogura, K. *Nature* **1995**, 378, 469−471. (b) Kusukawa, T.; Fujita, M. *J. Am. Chem. Soc.* **2002**, *124*, 13576−13582.
(6) Barhour, L. J.; Orr, G. W.; Atwood, J. L. *Nature* **1998**, *393*, 671−673.
(7) (a) Blanton, W. B.; Gordon-Wylie, S. W.; Clark, G. R.; Jordan, K. D.; Wood, J. T.; Geiser, U.; Collins, T. J. *J. Am. Chem. Soc.* **1999**, *121*, 3551−3552. (b) Müller, A.; Fedin V. P.; Kuhlmann, C.; Bögge, H.; Schmidtmann, M. *Chem. Commun.* **1999**, 927−928. (c) Ermer, O.; Neudörfl, J. *Chem. Eur. J.* **2001**, *7*, 4961−4980.
(8) (a) Manor, P. C.; Saenger, W. *Nature* **1972**, *237*, 392−393. (b) Atwood, J. L.; Hamada, F.; Robinson, K. D.; Orr, G. W.; Vincent, R. L. *Nature* **1991**, *349*, 683−684.
(9) Crystal data for **1b**: $C_{132}H_{96}N_{48}O_{126}Pd_6$, $M = 5012.97$, tetragonal, space group $P4_12_12$, $a = b = 30.626(2)$ Å and $c = 28.408(4)$ Å, $V = 26646(5)$ Å^3, $T = 93(2)$ K, $Z = 4$, $D_c = 1.250$ g cm^{-3}, λ (Mo Kα) = 0.71073 Å, 168 463 reflections measured, 30 622 unique ($R_{int} = 0.1159$) which were used in all calculations. The structure was solved by direct methods (SHELXL-97) and refined by full-matrix least-squares methods on F^2 with 1376 parameters. $R_1 = 0.0895$ ($I > 2\sigma(I)$) and w$R_2 = 0.2292$, GOF = 0.999; max/min residual density 1.087/−0.932 e Å^{-3}. CCDC reference number 248 450. See also Supporting Information.
(10) Region defined by the six Pd(II) centers is regarded as a boundary to discriminate inside and outside water molecules.
(11) Theoretical studies have predicted that a pentagonal prism structure is the most stable among numerous possible $(H_2O)_{10}$ cluster structures. The adamantanoid cluster is rather unfavorable. (a) Dang, L. X. *J. Chem. Phys.* **1999**, *110*, 1526−1532. (b) Sadlej, J.; Buch, V.; Kazimirski, J. K.; Buck, U. *J. Phys. Chem. A* **1999**, *103*, 4933−4947.
(12) Kurihara, K.; Tanaka, I.; Muslih, M. R.; Ostermann, A.; Niimura, N. *J. Synchrotron Rad.* **2004**, *11*, 68−71.
(13) Atomic parameters were not refined with neutron diffraction data because the number of neutrons reflection collected was not sufficient for lease-squares refinement. Therefore, to obtain the nuclear density of the deuterated hydrogen atoms of water molecules inside of **1b**, the difference Fourier calculation ($|2F_o - F_c|$) was performed by SHELX-97 using the atomic coordinates obtained by X-ray analysis.
(14) (a) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768−4774. (b) Karlström, G.; Linse, P.; Wallqvist, A.; Jönsson, B. *J. Am. Chem. Soc.* **1983**, *105*, 3777−3782.
(15) (a) Neidle, S.; Berman, H. M.; Shieh, H. S. *Nature* **1980**, *288*, 129−133. (b) Teeter, M. M. *Proc. Natl. Acad. Sci. U.S.A.* **1984**, *81*, 6014−6018.
(16) (a) Kang, J.; Rebek, J., Jr. *Nature* **1996**, *382*, 239−241. (b) Parac, T. N.; Caulder, D. L.; Raymond, K. N. *J. Am. Chem. Soc.* **1998**, *120*, 8003−8004. (c) Rekharsky, M.; Inoue, Y.; Tobey, S.; Metzger, A.; Anslyn, E. *J. Am. Chem. Soc.* **2002**, 124, 14959−14967.

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