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A Single Water Molecule Trapped Inside Hydrophobic C_{60}

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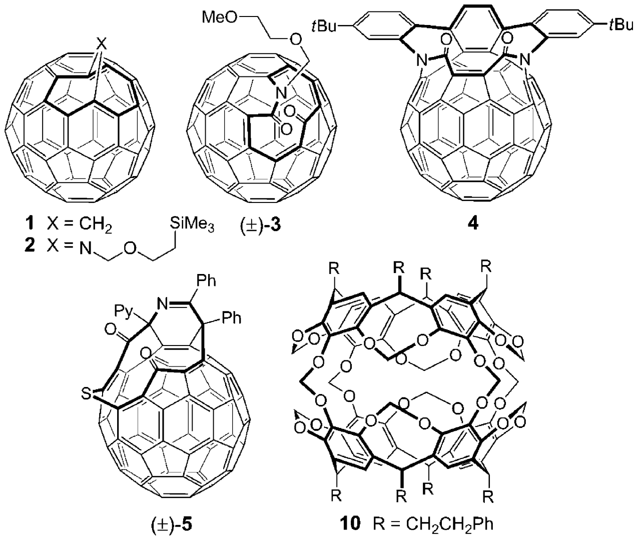
C_{60} · cage compounds · fullerene · mechanical bonding · host–guest systems

The properties of water, a ubiquitous medium and reagent essential for life and many abiotic processes on Earth, critically depend on strong intermolecular interactions. The remarkable dipolar and hydrogen-bonding interactions associated with its polar O−H bonds are responsible not only for the liquid nature of water under ambient conditions, but also for the course of many chemical and supramolecular processes taking place in it. To better understand these interactions, scientists have devised ways to investigate small, defined clusters of H_2O molecules in the gas phase or in confined nanoscopic spaces.[1] The isolation of a single molecule of water[2] inside the cage of buckminsterfullerene was recently achieved by Kurotobi and Murata.[3] The inner cavity of C_{60} has a diameter of approximately 3.6 Å and is completely lined by pyramidalized, formally sp^2-hybridized carbon atoms that form a network of 12 pentagons and 20 hexagons. Under normal conditions, it does not allow the escape or exchange of incarcerated species.

Endohedral fullerenes (gr. "within the faces") or fullerene incarceranes (lat. *carcer* = prison) are the names given to carbon polyhedra with enclosed guests.[4] They include a broad variety of metals, metal-containing clusters (for example, Sc_3N), noble gases (He, Ne, Ar, Kr, Xe), and other nonmetal atoms (such as N or P). Typical production methods are the covaporization of the metal and carbon by using salt-doped graphite electrodes in an arc furnace, the high-pressure/high-temperature treatment of empty fullerenes with rare gases, and the implantation of species into empty cages by beams of fast atoms or ions.

It is clear that the above techniques are too energetic for the incorporation of small molecules, which can, since recently, be done by the so-called surgical method.[5a] This method consists of chemically creating an aperture in the shell of an empty fullerene, thereby lowering the energy barrier for the insertion of a molecule, and restoring the original carbon skeleton with the guest locked up inside. While the idea is simple, the synthetic challenge is considerable. In particular, all "suturing" steps have to be done at a temperature low enough to prevent escape of the "captive".

The cleavage of a skeletal bond in the early days of fullerene chemistry was demonstrated in the synthesis of homo- and azahomofullerenes (e.g. **1** and **2**; Scheme 1).[6] A further step in cracking open the carbon shell was made by Wudl and co-workers in the mid 1990s, when they prepared lactam (±)-**3** by photooxygenation of an azahomofullerene.[7] Around the same time, Rubin opened the cage in a controlled way by rearrangement of benzo[60]fullerene through a photoinduced cycloaddition/cycloreversion sequence.[8] Significant further advances in creating or extending incisions in C_{60} and C_{70} were made by the research groups of Komatsu, Murata, Iwamatsu, Orfanopoulos, and Gan.[5]



Scheme 1. Some milestones (**1** to (±)-**5**; Py = 2-pyridyl) on the way to opening, filling, and reclosing carbon cages ("surgical" method for the preparation of fullerene incarceranes) and a carcerand (**10**).

Basket **4** was the first open-cage fullerene to be filled with gaseous guests (He and H_2), albeit in yields of less than 5 % because of the small orifice and the corresponding high activation barrier.[9] By contrast, the larger opening of (±)-**5** allowed the capture of 100 % H_2. It was with this compound that Komatsu, Murata, and co-workers demonstrated the feasibility of the "surgical" method, by perfectly restoring the fullerene skin with the dihydrogen staying entrapped.[5a]

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Other open-cage fullerenes have been shown to encapsulate molecules such as N_2, CO, H_2O, NH_3, CH_4, and $2H_2$.[5]

Similar to the pioneering "surgery" studies, the incision of C_{60} in the synthesis of $H_2O@C_{60}$[3] starts with a sequence of cycloadditions and cycloreversions that partly follows a sequence elaborated by Rubin[8] and affords dihomofullerene **6** (Scheme 2). In situ cleavage of a butadiene-type double bond at its rim by photogenerated $^1O_2$ (→ (±)-**7**) and further double-bond oxidation of the butadiene fragment newly appearing at the lip, led to the isolation of empty hydrate (±)-**9**. This is formed via tetrone (±)-**8**, with which it appears to be in equilibrium in hot toluene.

The temperature-dependent ketone/hydrate equilibrium plays a key role in the efficient encapsulation of water, thus making the system a receptor with a variable portal, that is, a 13-membered ring in (±)-**9** and a 16-membered ring in (±)-**8**. Thanks to this versatility, quantitative formation of $H_2O@$(±)-**9** was achieved by heating (±)-**9** in wet toluene at 120 °C under a pressure of 9000 atm and then returning to ambient conditions. This process presumably proceeds via the intermediacy of (±)-**8** and $H_2O@$(±)-**8** (not shown), with the narrower aperture of (±)-**9** keeping the water entrapped at room temperature.

Seamless "suturing" of the orifice was achieved in only two preparative steps. First, treatment of $H_2O@$(±)-**9** with an excess of triisopropyl phosphite afforded $H_2O@$**6** without loss of incarcerated water. In this transformation, tetrone $H_2O@$(±)-**8**, in equilibrium with $H_2O@$(±)-**9**, undergoes two sequential 1,6-dione coupling reactions with regeneration of two benzenoid rings of the cage. Final ejection of the remaining addend with generation of the endohedral fullerene $H_2O@C_{60}$ was attained by heating a ground mixture of $H_2O@$**6** and Al_2O_3 to 360 °C under vacuum. Treatment of (±)-**9** with a H_2O/D_2O mixture led to $HDO@C_{60}$ and $D_2O@C_{60}$ being obtained in addition to $H_2O@C_{60}$. No water was lost upon heating pure $H_2O@C_{60}$ at 420 °C for 30 min under vacuum.

$H_2O@C_{60}$ differs in various respects from endohedral metallofullerenes, which are typically characterized by electron transfer from the metal to the cage, in which it often adopts an off-center location and may not be able to move about freely.[4]

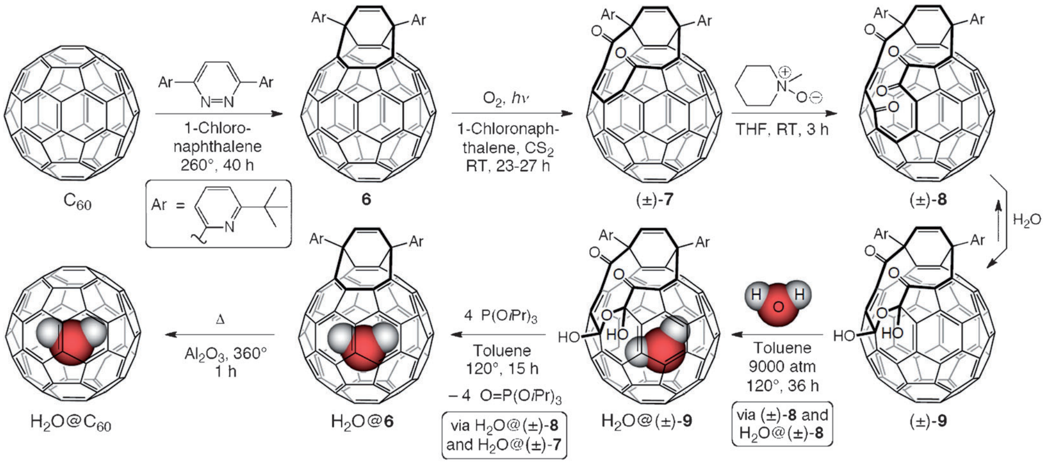
Single-crystal X-ray analysis (−173 °C) of the complex $[H_2O@C_{60}\cdot(\text{NiOEP})_2]$ (OEP = octaethylporphyrin; the complexation prevents orientational disorder of the carbon spheres which, otherwise, exhibit fast rotation) reveals the O atom to be located at the center of the fullerene, with the O−H bonds pointing towards the Ni atoms (experimental refinement of the position of the H atoms). Comparison with the crystal structure of empty $[C_{60}\cdot(\text{NiOEP})_2]$ shows that the endohedral H_2O does not affect the bond lengths or angles of the fullerene.

While UV/Vis spectroscopy points to no discernable electronic interaction between the C_{60} cage and the enclosed H_2O molecule, $H_2O@C_{60}$ and the empty fullerene can be separated relatively easily by HPLC on a pyrenylated stationary phase, in stark contrast to the cases of He, Ar, Kr, Xe, and H_2 incarceranes. This behavior may be due to the dipole moment of $H_2O@C_{60}$, which DFT calculations by the authors show to be almost equal (2.03 D) to that of H_2O.

The ^{1}H NMR spectrum ([D$_4$]*o*-dichlorobenzene) of $H_2O@C_{60}$ contains a sharp singlet at $\delta = -4.81$ ppm, which is 6.2 ppm upfield from that of dissolved free H_2O ($\delta = 1.39$ ppm). This shift reflects a strong shielding at the interior of the fullerene, similar to that experienced by incarcerated H_2 or ^{3}He. The latter has been widely used as a ^{3}He NMR probe for fullerene aromaticity. Apparent H/D couplings (^{1}H and ^{2}H NMR spectroscopy) indicate that H/D exchange does not occur in $HDO@C_{60}$. $H_2O@C_{60}$ also displays a single sharp ^{13}C NMR resonance, which indicates rapid rotation of the encapsulated water molecule on the NMR time scale.

Water is electrochemically stable inside the fullerene cage, and the incarcerane undergoes an irreversible oxidation and four quasireversible reductions at nearly the same potentials as empty C_{60}.

The redox stability of the encapsulated H_2O molecule parallels the astounding chemical stability of $N@C_{60}$, with its extremely reactive nitrogen atom.[4e] The interior of the fullerene cage seems to be exceptionally chemically inert, thus allowing the room-temperature investigation of species



Scheme 2. Synthesis of $H_2O@C_{60}$ from C_{60}.

that otherwise persist only in inert gas matrices at low temperature. Such “inner phases” are known in supramolecular chemistry from cyclophane-type container molecules such as Cram’s carcerands (e.g. **10**, Scheme 1) that irreversibly entrap guests during their formation by covalent macrocyclization.[10] Related, but less rigid, systems allow dynamic guest exchange at higher temperatures. They were used for the room-temperature investigation of highly reactive species such as benzyne or cyclobutadiene, which were generated photochemically as isolated molecules in the receptor cavity from appropriate precursors. Controlled guest release or inner-phase reactions have been investigated with resorcinarene-based basket molecules fitted with switchable portals[11] (cf. equilibrium (±)-**8** ⇄ (±)-**9**) and capsules self-assembled through hydrogen bonding or metal coordination.[12]

Compared to these versatile container molecules, fullerenes are rather difficult to “stuff”, as cage opening and reclosure requires stepwise breaking and making of covalent bonds. However, even open fullerene cages can keep guests imprisoned for a prolonged time if the energy barrier for escape is high enough, a property of interest for the reversible storage of a cargo. On the other hand, a completely “mended” close fullerene framework allows the retention and investigation of even small atoms under harsh conditions. As exemplified by $H_2O@C_{60}$, this is actually possible without the mechanically entrapped species having a particular affinity for the receptacle (intrinsically hydrophilic H_2O in extremely hydrophobic fullerene). Further investigations into the intrinsic properties of a single, non-hydrogen-bonded H_2O molecule inside the apolar, highly symmetric fullerene as well as the modification of the exohedral chemical reactivity of the C_{60} globe by polar “groundwater” are eagerly awaited.

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