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Cage Compounds

Encapsulation of Formaldehyde and Hydrogen Cyanide in an Open-Cage Fullerene

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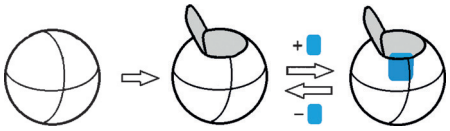
Dedicated to John R. Shapley

Abstract: Reaction of $C_{63}NO_2(Ph)_2(Py)$ (**1**) with *o*-phenylenediamine and pyridine produces a mixture of $C_{63}H_4NO_2(Ph)_2(Py)(N_2C_6H_4)$ (**2**) and H_2O@**2**. Compound **2** is a new open-cage fullerene containing a 20-membered heterocyclic orifice, which has been fully characterized by NMR spectroscopy, high-resolution mass spectrometry, and X-ray crystallography. The elliptical orifice of **2** spans 7.45 Å along the major axis and 5.62 Å along the minor axis, which is large enough to trap water and small organic molecules. Thus, heating a mixture of **2** and H_2O@**2** with hydrogen cyanide and formaldehyde in chlorobenzene affords HCN@**2** and H_2CO@**2**, respectively. The ^{1}H NMR spectroscopy reveals substantial upfield shifts for the endohedral species ($\delta = -1.30$ to -11.30 ppm), owing to the strong shielding effect of the fullerene cage.

The interior space of fullerenes is large enough to enclose atoms and small molecules.[1] Endohedral metallofullerenes (for example, Sc_3N@C_{80}) are currently being prepared by evaporation of graphite/metal oxide composites,[2] while individual nitrogen atoms, lithium atoms, or noble gases have been incorporated into fullerenes by forced plasma or high-pressure processes.[3] The disadvantages of these methods are the large amount of work involved, poor control of products, and extremely low yields.[4] Recently, creating a hole on the fullerene cage surface by chemical methods provides a promising approach.[5–10] Such open-cage fullerenes allow atoms, small molecules, or ions to enter and leave their inner sphere in a controllable and reversible manner (Scheme 1). This molecular-container-like feature may find wide applications in sensors, molecular storage and transport, hazard sequestration, and biomedicines.[11]

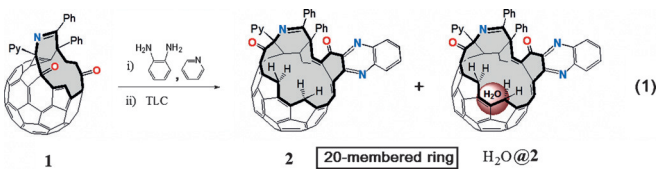
The first open-cage fullerene was reported in 1995 by Wudl and co-workers.[12] Later, Rubin et al. synthesized a bislactam



Scheme 1. An open-cage fullerene for the inclusion of substances.

derivative of C_{60} and successfully inserted a He or H_2 molecule into the cage,[13] though the filling ratio was low owing to a small orifice size. Komatsu et al. subsequently prepared a new derivative containing a larger orifice, which encapsulated H_2 quantitatively.[14] Up to now, noble gases (He, Ar, Kr),[13,15,16] N_2,[15] H_2,[13,14,15,17,18] H_2O,[18,19] CO,[15,20] NH_3,[21] CH_4,[22] and HF[23] molecules have been effectively stored inside the open-cage fullerenes, and completion of "molecular surgery"[24] to reform the pristine C_{60} cage was achieved for He@C_{60},[16] H_2@C_{60},[17a] and H_2O@C_{60}.[19b] Yet the incorporation of organic compounds bearing functional groups has not been reported. In our continuing interest in fullerene chemistry,[25] herein we present the successful insertion of $H_2C{=}O$ and $HC{\equiv}N$ into a new open-cage fullerene.

The open-cage fullerene $C_{63}NO_2(Ph)_2(Py)$ (**1**) with a 12-membered heterocyclic ring was prepared from C_{60} according to the method reported by Komatsu and Murata.[26] Furthermore, following the Iwamatsu's ring-enlargement process,[19a] compound **1** was treated with *o*-phenylenediamine and pyridine to afford an air-stable brown solid containing the mixture of $C_{63}H_4NO_2(Ph)_2(Py)(N_2C_6H_4)$ (**2**) and H_2O@**2** in 51% yield [Eq. (1)]. A suitable single crystal was studied by X-ray diffraction, where compounds **2** and H_2O@**2** were co-crystallized in the lattice. The ORTEP diagram of H_2O@**2**, depicted in Figure 1, is basically identical to **2**, except that one water molecule is located at the center of fullerene cage, with the O5···$C_{(cage)}$ distances from 3.43 Å to 3.58 Å. The bowl-shaped **2** contains a 20-membered heterocyclic ring, of which the C88–C95 edge is fused with an *o*-phenylenediimine moiety, and two CH_2 units (C132 and C135) are seated at the top of separate pentagons.



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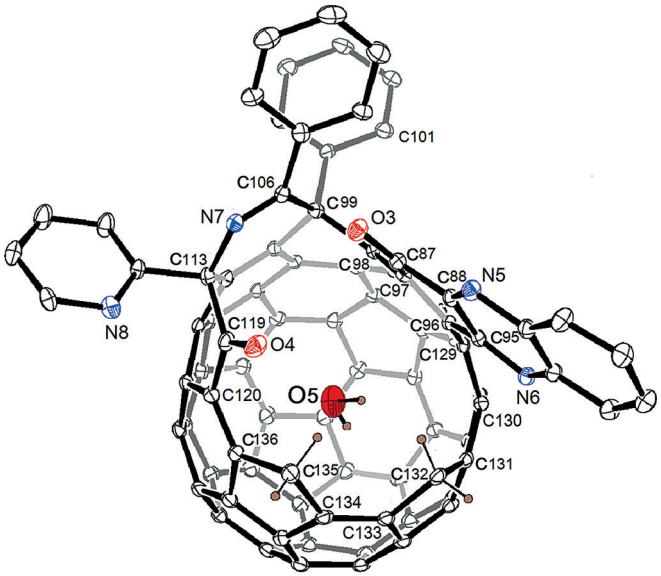

Figure 1. Molecular structure of H_2O@**2**. Ellipsoids are set at 30% probability; hydrogen atoms other than H_2O and CH_2 are omitted for clarity.

The ^{1}H NMR spectrum for the mixture of **2** and H_2O@**2** displays the aromatic proton resonances ranging from $\delta = 8.56$ to 6.88 ppm, which can be assigned on the basis of an H,H-COSY experiment. The four doublet signals from $\delta = 4.61$ to 3.13 ppm (Figure 2a) arise from the two diastereotopic CH_2 units at the rim of fullerene orifice. Three sets of the methylene proton resonances are distinguishable for H_2O@**2** and **2**, though the difference is small (0.01–0.03 ppm). It is noteworthy that the far upfield resonance at $\delta = -11.30$ ppm is attributed to the encapsulated water protons, which is shielded by 12.82 ppm compared to free water ($\delta = 1.52$ ppm). Unusual chemical shifts for the endohedral nuclei have been previously observed by NMR spectroscopy, owing to the strong magnetic shielding effect by the π-electron shell of the fullerene cage.[18–23,27] The fraction of endohedral water molecules can be estimated by comparing its integral value with the ^{1}H signal at $\delta = 8.56$ ppm. The filling factor varies depending on the experimental conditions such that the ratio of H_2O@**2** decreased to 25% by heating the toluene solution over molecular sieves, but it reached 85% when the solution was heated in the presence of trace water. Notably, the water-inclusion behavior of open-cage fullerenes was previously shown also depending on the polarity of solvents.[28]

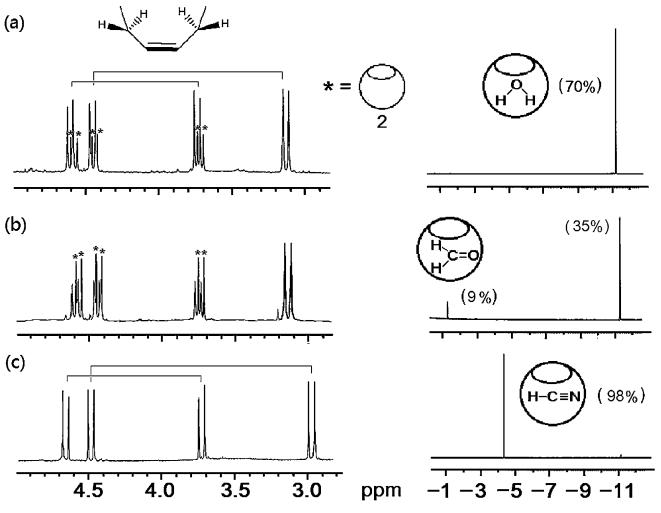

Figure 2. 500 MHz ^{1}H NMR spectra in the methylene and upfield resonance regions for **2**, H_2O@**2**, H_2CO@**2**, and HCN@**2** taken in CD_2Cl_2 at 23 °C.

The elliptic orifice of **2** spans 7.45 Å along the major axis and 5.62 Å along the minor axis (Figure 3a). This size is large enough to trap water molecule from wet solvents spontaneously. We consequently studied insertion of small organic substrates into the cavity of **2**. Formaldehyde ($H_2C{=}O$) and hydrogen cyanide (HC≡N) were investigated because they are important precursors to many other materials and chemical compounds, significant considerations for human health, and have suitable dimensions for inclusion (Figure 3b).[29] It should be noted that, taking account of the size of the π-electron cloud, the inner space of C_{60} is about 3.5 Å in diameter,[1,5e] and the CH_4 molecule (with a kinetic diameter of 3.8 Å) has been suggested to be one of the largest guests for C_{60}.[22]

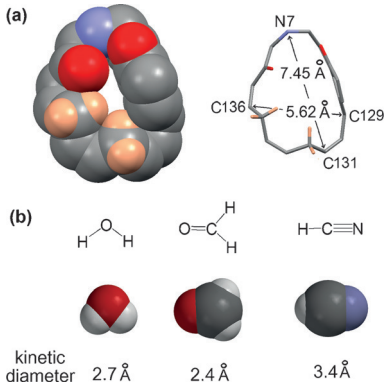

Figure 3. a) Orifice dimensions of **2**. b) Kinetic diameters for water, formaldehyde, and hydrogen cyanide.

Gaseous formaldehyde was generated by depolymerization of solid paraformaldehyde at 150 °C under N_2. The gas was bubbled through a chlorobenzene solution of **2** + H_2O@**2** at 100 °C for 15 min. After cooling the solution, *n*-hexane was added to precipitate a brown solid, which was washed and dried under vacuum. The LD-TOF mass spectrum of the product displays three peaks at *m/z* 1172, 1160, and 1142 corresponding to the molecular ion of H_2CO@**2**, H_2O@**2**, and **2**, respectively. The ^{1}H NMR spectrum (Figure 2b) shows the endohedral H_2CO proton resonance at $\delta = -1.30$ ppm, which is shielded by 11.03 ppm compared to free formaldehyde ($\delta = 9.73$ ppm). The percentages of empty **2**, H_2O@**2**, and H_2CO@**2** are estimated to be 56%, 35%, and 9%, respectively, based on the integral values. Since polymerization of formaldehyde proceeded facilely, a prolonged reaction time did not afford a higher filling factor for H_2CO@**2**. On the contrary, no H_2CO was included at room temperature. Attempts to separate

H_2CO@**2** from H_2O@**2** and **2** by TLC or HPLC were not successful, where only one eluting band was observed, and the fraction of H_2CO@**2** was found to decrease after workup.

Pure hydrogen cyanide can be obtained by adding diluted $H_2SO_{4(aq)}$ into $NaCN_{(s)}$, drying over $CaCl_2$, and condensing at $-20\,^{\circ}C$ under dinitrogen. Treating the mixture of **2** and H_2O@**2** with HCN (ca. 700 equiv) in chlorobenzene at $90\,^{\circ}C$ afforded HCN@**2** in high yield (>98%). Stirring the solution without heating for 48 h could also produce HCN@**2** in 40%. Presumably, hydrogen bonding between HCN and H_2O facilitates escape of the trapped water, and the linear HCN molecule is easier to pass through the orifice; that accounts for the high filling factor of HCN. Solid HCN@**2** is very stable, but it slowly releases HCN molecules in solution. The ESI mass spectrum displays the molecular ion peak at *m/z* 1170 for $[HCN@\mathbf{2}+H]^+$. The 2D $^{13}C/^{1}H$ NMR correlation spectrum records the endohedral HCN carbon resonance at $\delta = 119.2$ ppm, which is 15.2 ppm upfield of free HCN ($\delta = 134.4$ ppm). The ^{1}H NMR spectrum of HCN@**2** presents similar aromatic proton resonances to those of **2** and H_2O@**2**, indicating that the encapsulated molecule scarcely affects the chemical shifts of the exohedral aromatic addends. However, the rim CH_2 proton resonances are moderately altered (Figure 2c). The trapped HCN displays a sharp singlet at $\delta = -4.37$ ppm ($\delta = 3.78$ ppm for free HCN), which broadens at $-90\,^{\circ}C$, to imply fast rotation of HCN molecule inside the cage on the NMR timescale.[20,22] Meanwhile, the C≡N stretching frequency for HCN@**2** (2087 cm^{-1}; taken in chlorobenzene) is red-shifted merely 8 cm^{-1} from free HCN (2095 cm^{-1}), suggesting little interactions between encaged HCN and fullerene core.

In summary, we have prepared a new open-cage fullerene **2** containing a 20-membered heterocyclic orifice and report the first example of inserting functional organic compounds, HCN and H_2CO, into the cavity of fullerenes. Heating the reaction mixture is necessary for efficient encapsulation. The large upfield ^{1}H chemical shifts ($\delta = -1.30$ to -11.30) and the mass spectral data provide a solid evidence for the presence of endohedral species. The endohedral molecules are slowly released upon standing in solution or heating under vacuum. Attempt to enclose larger organic molecules or transition metal atoms (ions) by expanding the orifice of **2** is undergoing.

Experimental Section

Details of the reaction procedures, characterization data and diagrams, and details of the structural determination of H_2O@**2** are given in the Supporting Information. CCDC 1445024 contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

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Keywords: cage compounds · fullerenes · host–guest systems · inclusion compounds · structure elucidation

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