The outside knows the difference inside: trapping helium by immediate reduction of the orifice size of an open-cage fullerene and the effect of encapsulated helium and hydrogen upon the NMR of a proton directly attached to the outside†

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A methodology to entrap He inside an open-cage fullerene by immediate reduction of the size of an orifice was developed, and the effects of encapsulated He and H_2 on the chemical shift of a proton directly attached to the outer fullerene sphere were revealed.

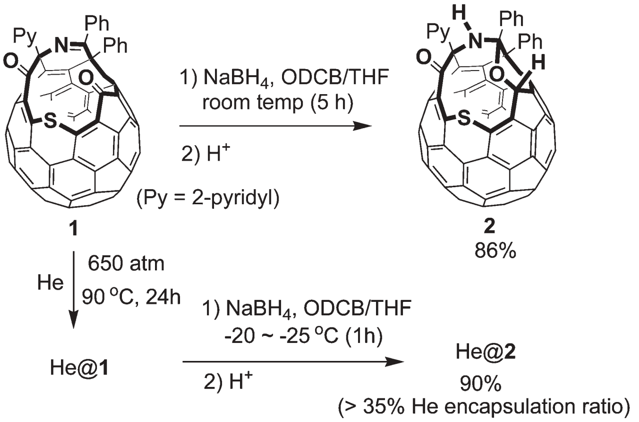
Recently, open-cage fullerenes that encapsulate atom(s) or molecule(s) inside the hole-containing cage have been one of the most interesting topics of fullerene chemistry besides their well developed exohedral functionalization chemistry.[1] Several groups have been able to chemically create a large enough orifice on the fullerene surface and have proved that insertion of a guest entity through the orifice is possible.[2] Helium and molecular hydrogen are two of the many possible guest entities that have been of interest for insertion because of their small atomic or molecular volume. The encapsulation ratio of hydrogen has been upped to 100% inside an open cage fullerene.[3] Furthermore, the isolation of $H_2@C_{60}$ has been successful through re-closure of the orifice.[2i]

Even though the van der Waals radii of helium (1.22 Å, V = 11.0 Å^3) and the hydrogen molecule (1.20 Å, V = 19.0 Å^3) are close,[4] open-cage fullerene **1** with helium inside the cage has not been isolated in high encapsulation ratio due to its low barrier for release from the cage.[5] In this paper, we present an approach to entrap helium within the cage by immediate reduction of the orifice size after helium is inserted into the cage of **1**, based on the reactivity of the two carbonyl and imine functional groups of compound **1**. We further discuss the non-covalent effect of encapsulated helium and hydrogen on the chemical shift of a proton that is directly attached to the fullerene skeleton.

Helium can enter and escape at room temperature from open-cage fullerene **1** based on previously reported kinetic results.[5] Its equilibrium constant K_{eq} at 50 °C was measured to be 3.1×10^{-4} atm^{-1} with overall uncertainty of 40%. This result predicts the incorporation ratio is *ca.* 20% at a pressure of 800 atm. A high pressure helium gas of 322580 atm will be necessary to achieve nearly 100% incorporation of helium at 50 °C!

The reduction of the orifice size was carried out by reaction of **1** with 15 equiv. of sodium borohydride in 1 g scale in a mixture of *o*-dichlorobenzene (ODCB) and THF (Scheme 1). The progress of the reaction was followed by HPLC (analytical Buckyprep column). A new peak with a retention time of 5.1 min (toluene, flow rate = 1 mL min^{-1}) corresponding to **2** appeared gradually. The reaction was worked up with 1 M HCl after **1** was consumed. After purification, compound **2** was isolated in 86% yield as brown solids. The orifice size is reduced from a 13-membered ring in **1** to an 11-membered ring in **2**.

The structure of empty **2** was first verified by ^{1}H and ^{13}C NMR, 2D-HMQC, 2D-HMBC, and MS spectral data.† The ^{1}H NMR of compound **2** exhibited two new peaks at 6.45 and 5.27 ppm ($CDCl_3$–CS_2 = 1 : 1) corresponding to methine and secondary benzylic amine protons, respectively. Two new sp^3 carbon signals appeared at 84.1 and 94.4 ppm corresponding to methine and aminooxy benzylic carbons, respectively. The disappearance of the carbonyl group on the five-membered ring of compound **2** was deduced from the lack of a carbonyl carbon signal at 185.0 ppm in ^{13}C NMR and also the lack of a C=O stretching band at 1748 cm^{-1} in FT-IR, which are characteristic signals for compound **1**. The carbonyl group of the six-membered ring remained unchanged based on the presence of a signal at 198.6 ppm in ^{13}C NMR and the corresponding stretching band at 1707 cm^{-1} in the IR spectrum. The proposed structure was unambiguously confirmed by single crystal X-ray crystallographic



Scheme 1 Synthesis of compound **2** and He@**2**.

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† Electronic supplementary information (ESI) available: Experimental procedures, ^{1}H and ^{13}C NMR, UV–vis, IR spectral data of all new compounds and CIF. See DOI: 10.1039/b702589k

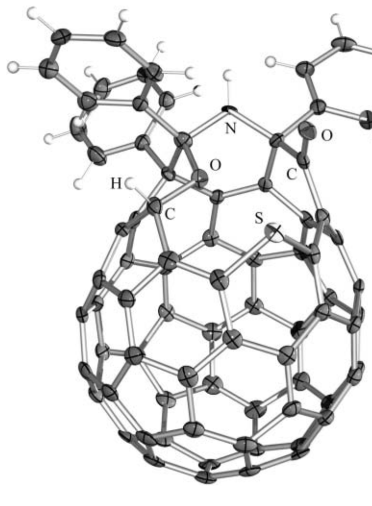

Fig. 1 Single crystal X-ray structure of compound **2** drawn at 50% probability (the structure shown here is the enantiotopic isomer of the structure **2** drawn in Scheme 1).†

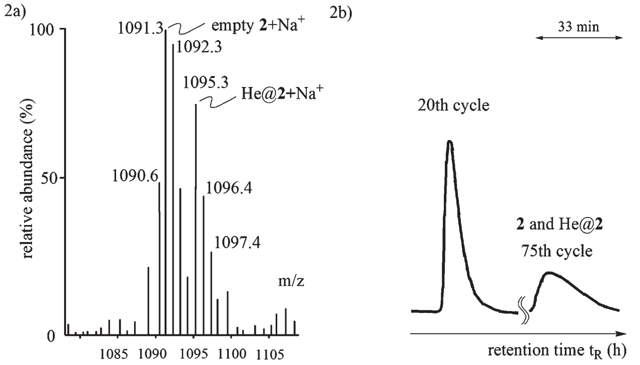

Fig. 2 (a) APCI mass spectrum (positive mode) of a mixture of He@**2** and empty **2**. (b) Recycling preparative HPLC chromatogram of a mixture of He@**2** and empty **2** in about 1 : 1 ratio (t_R = 11 h for 20th cycle; t_R = 41 h for 75th cycle).

analysis (Fig. 1).[6] Formation of compound **2** could be interpreted by addition of hydride to the carbonyl group on the five-membered ring followed by the addition of the resulting alkoxide anion to the imino carbon (6-*exo*-trig) located in close proximity. The formation of this 11-membered-ring product **2** demonstrated the higher reactivity of the carbonyl group on the five-membered ring compared to that on the six-membered ring of compound **1**, presumably due to the release of strain.

DFT calculations at the B3LYP/6-31G**//B3LYP/3-21G level of theory[7] showed a barrier of 50.4 kcal mol^{-1} for helium release from He@**2**.[8] This barrier is about twice as large as that for helium escape from He@**1** (24.6 kcal mol^{-1}).[5] Therefore, this computational result suggests that the helium would not escape from the cage of **2** at room temperature once the orifice size was reduced from a 13-membered ring to an 11-membered ring.

After confirmation of the reduction process and determination of the product structure, we carried out insertion of He and H_2 into compound **1** to obtain He@**2** and H_2@**2**, respectively. ^{4}He was chosen as the inserted entity rather than ^{3}He because ^{4}He was more readily available in larger amounts for high pressure experiments.[9] The insertion of helium into **1** was carried out at a relatively lower temperature at 90 °C (650 atm, 24 h) as compared to the hydrogen insertion temperature (200 °C, 800 atm).[2k] Cooling of the product and subsequent reduction at −20 to −25 °C was crucial to obtain He encapsulation in **2**.† The mixture was worked up as described for the synthesis of empty **2**. Flash silica-gel chromatography gave 90% of a mixture of He@**2** and empty **2** as brown solids (Scheme 1). The encapsulation ratio of helium was estimated to be 35% based on atmospheric pressure chemical ionization (APCI, positive mode) mass spectroscopic data by comparison of the peak intensities of *m/z* 1091.3 (**2** + Na$^+$) and 1095.3 (He@**2** + Na$^+$) as shown in Fig. 2a. The incorporation ratio of helium was assumed to be higher than 35% because some amounts of helium might have escaped under the condition of ionization. A peak corresponding to He_2@**2** was not observed under this condition.[10]

Next, the procedure for synthesis of He@**2** by chemical reduction was applied similarly to the synthesis of H_2@**2** using H_2@**1**[3] as starting material, which gave a mixture of H_2@**2** and empty **2** in 83% isolated yield. The encapsulation ratio of H_2 in **2** was estimated to be 75% based on APCI-MS (Fig. 3a). The ^{1}H NMR signal corresponding to encapsulated hydrogen of H_2@**2** was observed at −7.79 ppm, which was upfield shifted by 0.54 ppm as compared to that of H_2@**1**, revealing slight disruption of the π-conjugated system of **1** by chemical modification of the orifice. This is consistent with our previous observation for the chemical shift change of encapsulated H_2 upon exohedral functionalization of $H_2@C_{60}$.[2i]

The relative degree of non-covalent interaction of He and H_2 with the fullerene moiety could be reflected from chromatography and ^{1}H NMR spectroscopy. Separation of H_2@**2** from empty **2** by recycling preparative Buckyprep dual sequential columns (20 mm × 250 mm × 2) was attained after the 10th cycle (toluene, flow rate = 6.0 mL min^{-1}, 50 °C, Fig. 3b). After the 31st cycle, complete purification of H_2@**2** was achieved. However, separation of He@**2** from empty **2** was not seen even after 75 cycles under the same conditions. Only a broadened peak was observed thereafter (Fig. 2b), presumably due to little interaction of helium with the fullerene framework. This evident difference in chromatography results showed that H_2 exhibited more appreciable non-covalent interaction with the outer fullerene cage than He.

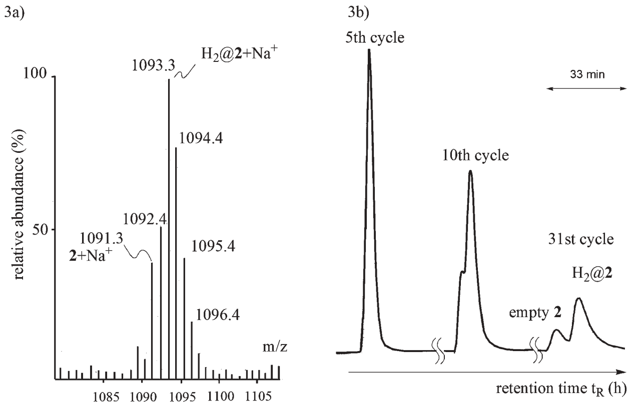

Fig. 3 (a) APCI mass spectrum (positive mode) of a mixture of H_2@**2** and empty **2**. (b) Recycling preparative HPLC chromatogram of a mixture of H_2@**2** and empty **2** in 3 : 1 ratio (t_R = 2.8 h for 5th cycle; t_R = 5.5 h for 10th cycle; t_R = 17 h for 31st cycle).

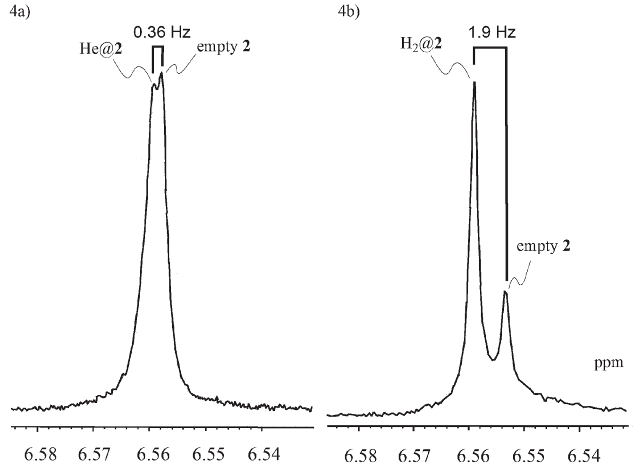

Fig. 4 ^{1}H NMR spectra (300 MHz, ODCB-d_4) of (a) a ~1 : 1 mixture of He@**2** and empty **2**, and (b) a 3 : 1 mixture of H_2@**2** and empty **2**.

Our interest in addressing the viewpoint of "the outside knows the difference inside" can be accounted for by the chemical shift of the methine proton. The chemical shifts of the methine protons in empty **2**, He@**2**, and H_2@**2** were dependent on the encapsulated species inside the cage. The ^{1}H NMR spectrum of the mixture of He@**2** and empty **2** showed two signals with a difference of 0.36 Hz centered at 6.56 ppm (Fig. 4a). This notion suggested that a non-covalent interaction between helium and the fullerene cage does exist. Furthermore, a clear downfield-shift of 1.9 Hz was observed for the methine proton signal of H_2@**2** as compared to that of empty **2** (Fig. 4b). The observed difference suggested that the encapsulated hydrogen molecule interacts more with the cage than helium. No similar and pronounced peak splitting was observed for other proton signals both in He@**2** and H_2@**2**.

In conclusion, we have demonstrated an approach to entrap helium inside open-cage fullerene **2** by immediate orifice-size reduction of He@**1**. The encapsulation ratio (> 35%) of helium using this present method is higher than those previously reported (~ 2%).[2f,5] The difference inside the cage could be recognized from the chemical shift of the methine proton directly attached to the outside of the C_{60} cage. The degree of non-covalent interaction between the encapsulated helium and the fullerene moiety was minute and less than that of H_2.

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6 Crystallographic data of compound **2**: black cube, approximate dimensions 0.09 mm × 0.11 mm × 0.18 mm, $C_{80}H_{16}N_2O_2S\cdot 2CS_2$, M = 1221.27, orthorhombic, space group $P2(1)2(1)2(1)$, $Z = 4$, a = 15.7008 (9), b = 16.1532 (9), c = 19.0307 (11) Å, V = 4826.5 (5) Å^3, T = 100 (2) K, μ = 0.308 mm^{-1}, R_{int} = 0.0442, $R1$ = 0.0421, w$R2$ = 0.0645, GOF = 1.005. Flack parameter 0.17(5). CCDC 637541. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b702589k.

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