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H_2O@open-cage fullerene C_{60}: control of the encapsulation property and the first mass spectroscopic identification

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Abstract—A novel open-cage C_{60} derivative (a 19-membered ring orifice), prepared by the sequential cage scission reactions of the ketolactam derivative of C_{60} with *o*-phenylenediamine, allows the encapsulation of one water molecule. The resulting endohedral water complexes were confirmed for the first time by mass spectroscopy. The efficiency of the encapsulation was affected by the substituent on the nitrogen atom.

Opening a hole on the fullerene surface by the carbon–carbon bond cleavage of the fullerene cage has received much attention, because the resulting open-cage derivatives allow small molecules access into their internal cavities.[1,2] Using this method, the first encapsulations of helium and hydrogen gas were recently achieved.[3,4] However, the drastic reaction conditions employed for these successful results suggest that the construction of a larger orifice is essential for practical application. Recently, we have found that the reactions of the open-cage diketone derivative of C_{60} with nitrogen reagents proceeded with controlled cage scissions to give ring-expanded products.[5–7] In particular, the reaction with *o*-phenylenediamine took place with multiple cage scissions to give a bowl-shaped fullerene (**1**) having a 20-membered ring orifice (Fig. 1).[7] The orifice in **1** is currently the largest produced so far allowing the encapsulation of one water molecule for the first time.

In respect to the molecular encapsulation into the open-cage fullerenes, Rubin et al. reported the important result that the encapsulation of helium into their open-cage C_{60} derivative was less efficient compared to that of hydrogen.[3a] This was due to the rapid emission of the smaller helium, and suggests that a bigger orifice is not always better than a smaller one for purpose of molecular storage. On this point, we found that the above cage-scission reaction was also applicable to the

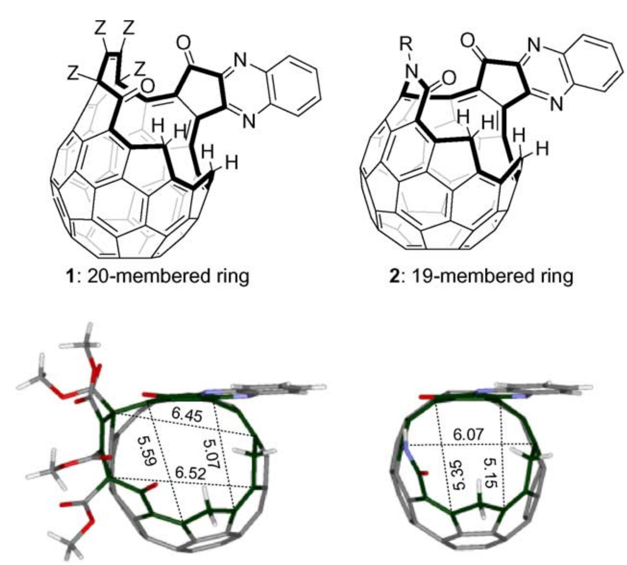

Figure 1. Molecular structures of **1** and **2**. Top views of the B3LYP/6-31G(d)—optimized structures of **1** (Z = CO_2Me) and **2c** (R = H) are shown as stick models. Atoms located at the bottoms of the structures are omitted for clarity. Selected interatom distances are shown in angstroms.

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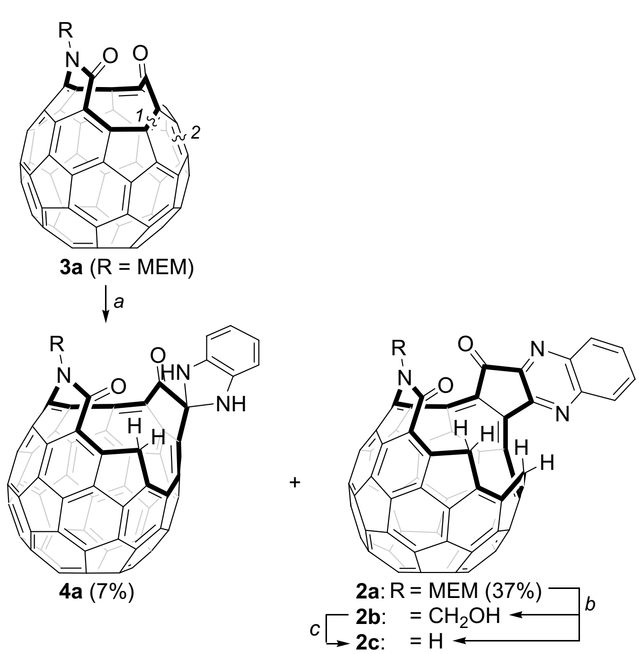
related ketolactam derivative of C_{60},[6b,8] and that the resulting orifice was smaller than that of the product prepared from the diketone derivative of C_{60}. Herein, we report the synthesis of a new open-cage C_{60} derivative (**2**). The calculated molecular structure of **2** given in Figure 1 indicates that the longer axis of **2** is approximately 0.4 Å shorter than that of **1**.[9] The smaller orifice brought about a change in the property of the water encapsulation, and allowed the first observation of the endohedral water complex of fullerene by mass spectroscopy.

The reaction of **3a** (R = 2-methoxyethoxymethyl, MEM)[8a] with *o*-phenylenediamine proceeded at 80 °C in the presence of an excess amount of pyridine. The reaction was rather slow and sluggish compared to that of the diketone derivative, and **2a** was obtained in 37% yield together with **4a** (7%), which corresponded to the initial cage scission product (Scheme 1).[7] In order to evaluate the substituent effect on the molecular encapsulation, the MEM group in **2a** was removed by the treatment with trifluoroacetic acid. This reaction gave the *N*-hydroxymethyl derivative **2b** (86%) as a major product together with the desired **2c** (14%), but the former was gradually converted to the latter by stirring with silica-gel at ambient temperature in toluene.

^{1}H and ^{13}C NMR spectra of the products **2a–c** showed two methylene moieties, indicating that two bond scissions took place as well as did **1** [For **2a**: δ 4.97 (J = 18 Hz), 4.58 (J = 19 Hz), 3.67 (J = 19 Hz), 3.55 (J = 18 Hz) ppm (each 1H) in ^{1}H NMR; δ 42.38 and 41.83 ppm in ^{13}C NMR], and the structural changes in the series of **2a–c** were further confirmed by mass spectrometry. We concluded that the same cage scissions as in the case of **1** were most likely to have occurred based on the similarity of the spectroscopic data of the products as well as that of the structures of the starting materials at the present stage.[7,10]

In the ^{1}H NMR spectrum of **2a**, one sharp singlet signal was observed at δ −10.0 ppm (Fig. 2), and it was reasonably assigned to the water molecule inside **2** by comparison with that of H_2O@**1** (δ −11.4 ppm).[7] Reflecting the difference in the shielding effect, which was due mainly to the structure of the fullerene cage, it appeared downfield of the chemical shift relative to that of H_2O@**1**. The substituents on the nitrogen atom in **2a–c** did not affect the chemical shift of the incorporated water molecule (H_2O@**2b**: −9.8 ppm; H_2O@**2c**: −9.9 ppm). Likewise, the water molecule inside the cage scarcely affected the chemical shifts of the functionalized moieties. In the ^{1}H spectrum, methylene protons of H_2O@**2** were distinguishable from those assigned to the empty **2**; however, the differences of the chemical shifts were insignificant (<0.01 ppm).

The fraction of the endohedral complex H_2O@**2** in the product can be estimated by comparing the integral values between the signal assigned to the water molecule inside the cage and those assigned to the functionalized groups. After the usual purification by silica-gel column chromatography, the yields of H_2O@**2a–c** were less than 10% in all cases. A representative ^{1}H NMR spectrum of the isolated **2a** is shown in Figure 2a. These poor yields were in contrast to the spontaneous formation of H_2O@**1**;[7] however, they were easily improved by simple reflux in a mixture of toluene and water. As shown in



Scheme 1. Reactions of **3a** with *o*-phenylenediamine. Reagents and conditions: (a) *o*-phenylenediamine (20 equiv), pyridine (50 equiv), PhCl, 80 °C; (b) CF_3CO_2H (excess), toluene, rt; (c) SiO_2, toluene, rt.

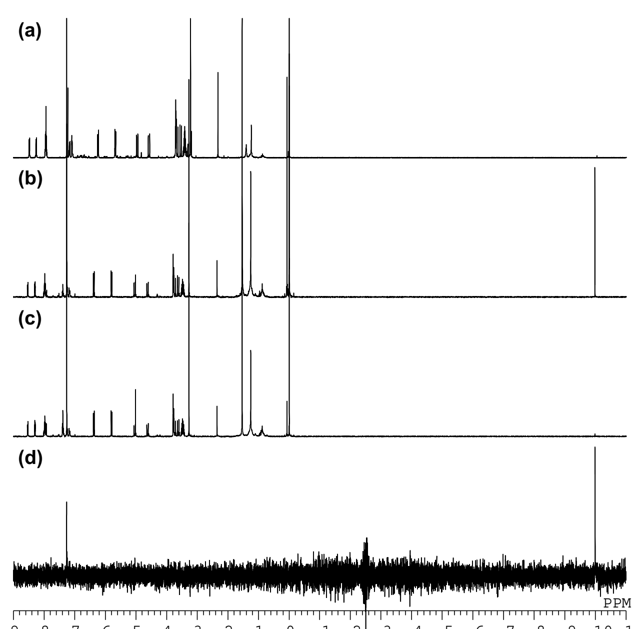


Figure 2. ^{1}H NMR spectra ($CDCl_3$) of (a) **2a** (after the purification by silica-gel chromatography), (b) H_2O@**2a** (after refluxing in a mixture of toluene/water (6/4) for 18 h), and (c) D_2O@**2a** (after refluxing in a mixture of toluene/deuterated water (6/4) for 18 h), (d) ^{2}H NMR spectrum of D_2O@**2a** in $CHCl_3$.

Figure 2b, the signal intensity at δ −10.0 ppm was significantly increased, and the yield of H_2O@**2a** reached 85%. In the same manner, treatment of **2a** with D_2O afforded D_2O@**2a**, which was confirmed by ^{2}H NMR (Fig. 2d).

As reported previously,[7] in solution, H_2O@**1** showed rapid H_2O–D_2O exchange behavior at ambient temperature due to the equilibrium with water outside the cage. Unlike H_2O@**1**, escape of the water molecule from H_2O@**2** was quite slow even at high temperature. The yield of H_2O@**2a** gradually decreased from 48% to 13% after heating for 27 h at 120 °C (sealed tube) in toluene-d_8/D_2O (4/1).

The rate retardation of the emission of the water molecule enabled us to observe the molecular ion peaks of the endohedral water complexes of the open-cage fullerene by mass spectroscopy. As shown in Figure 3, the molecular ion peaks of H_2O@**2a** (m/z = 981) and D_2O@**2a** (m/z = 983) were observed together with that of the empty **2a** (m/z = 963). The signal intensities of the spectra were coincident with the yield of the endohedral complex estimated by ^{1}H NMR. In contrast, attempts to detect H_2O@**1** by mass spectroscopy have been still unsuccessful due to the rapid emission during measurement.[7]

It is notable that a significant substituent effect was observed in the encapsulation efficiency by refluxing with

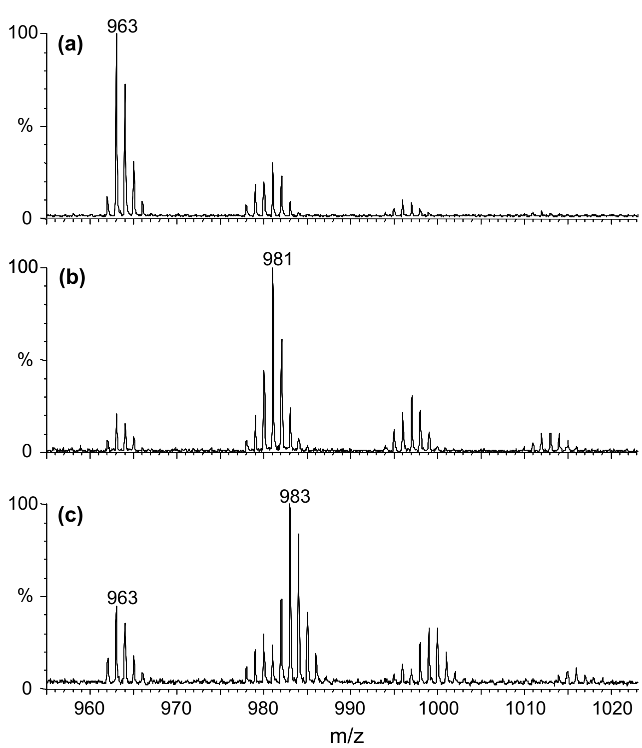


Figure 3. Electrospray mass spectrum (negative) of (a) **2a**, (b) H_2O@**2a**, and (c) D_2O@**2a**. Note that the ion peaks in the regions of $[M+16]^-$ (e.g., m/z = 979 and 980 in Fig. 3a) and $[M+32]^-$ correspond to the oxidations of the samples during the measurements. These peaks are commonly observed in fullerene derivatives.

water. The yield of H_2O@**2c** reached only 35% under the same condition. Initially, we might attribute this finding to the fact that the activation barrier of escape from **2c** is lower than that from the sterically crowded **2a**. However, the escape of H_2O from H_2O@**2c** was slower than that from H_2O@**2a**. The yield of H_2O@**2c** decreased from 35% to 26% under the identical condition to that of the escape experiment regarding H_2O@**2a** (48–13%) described above. Since the encapsulations were carried out under biphasic conditions, we suppose that the amphiphilic character of the MEM group may be more important than the steric hindrance or the size of the orifice.

In summary, we have demonstrated that the ring expansion of the open-cage ketolactam derivative of C_{60} by the cage scission reactions with *o*-phenylenediamine gave a novel open-cage C_{60} derivative having a 19-membered ring orifice. The smaller orifice afforded us additional evidence of the endohedral water complex of the open-cage C_{60} derivative. The remarkable substituent effect on the molecular encapsulation suggests the importance of the organic addends as well as that of the size and shape of the orifice. Further investigations are now in progress.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.07.008. Experimental procedures as well as spectroscopic data of compounds **2a–c** are available. This material is available online with the paper in ScienceDirect.

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9. All calculations were performed using the GAUSSIAN 03 program (Gaussian Inc., Pittsburgh, PA, 2003).
10. Recently, Orfanopoulos et al. reported a difference in the reactivity between **3a** and the related diketone derivatives (Refs. 4c,6c). At present, however, we lack reliable data for resolving the structure.