Synthesis of Endohedral Fullerenes and Dynamic Behavior of Encapsulated Water Molecules

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General Introduction

Abstract: A fullerene is one of carbon clusters, which forms ball-shaped or ellipsoidal sphere. Since the discovery¹ and macroscopic scale syntheses² of [60]fullerene (C_{60}) and [70]fullerene (C₇₀), various functionalization and structural modifications of fullerenes have been done for elucidating their intrinsic nature.³ The first report on C_{60} containing a lanthanum atom (La) inside its cavity gave a great impact into fullerene chemistry in 1985.⁴ Such fullerene family is so-called "endohedral fullerenes" and abbreviated to be $X@C_{60}$ (X = guest molecule(s)) which was first proposed by Smalley et al. in 1991.⁵ Rubin has advocated a sophisticated concept for synthesizing endohedral fullerenes by utilizing organic reactions in 1997.⁶ So far, several examples such as $H_2@C_{60}$,⁷ $He@C_{60}$,⁸ $H_2O@C_{60}$,⁹ $HF@C_{60}$,¹⁰ and $CH_4@C_{60}$ ¹¹ have been synthesized by the molecular surgery method in macroscopic quantities. Contrastingly, replacement of carbon atom(s) in the fullerene cage by heteroatom(s) has attracted much attention because of their unique electronic and structural features which are predicted to be different from parent fullerenes.¹² Evidences for such molecules, i.e. "heterofullerenes" have appeared in gas-phase under mass spectroscopic conditions. In 1995, Wudl and co-workers reported that the macroscopic synthesis of azafullerene C₅₉N as its dimer was achieved by the organic reactions using C_{60} as a starting material.¹³ Over the past decades, a number of derivatization on C_{59} N have been studied and some of them have been, indeed, applied in the electronic devices.¹² Note that azafullerene is still an exclusive example for heterofullerenes at the present time due to difficulty for accessing other heteroatom analogues.

Introduction

Since the discovery¹ of fullerene C_{60} by Kroto et al. and achievement of macroscopic preparation² by Kräschmer et al., fullerene chemistry has been intensively studied in not only organic area but also physical and medicinal research fields. The derivatives obtained from C_{60} by structural modifications can be classified into four types of fullerene families, i.e., (1) exohedral fullerenes, (2) fullerene ions, (3) endohedral fullerenes, and (4) heterofullerenes (Figure 1).³ The molecules synthesized by addition reactions on an external sphere of C_{60} are so-called exohedral fullerenes, which are, among four categories, the most widely investigated by utilizing common organic reactions. The fullerene salts or fullerene anion/cation are also fascinating species, which can be easily prepared by redox reaction in solution and used as reactive intermediates toward exohedral fullerenes. Fullerenes have a spherical cavity in which they have suitable inner space for accommodation of atom(s), molecule(s), or cluster(s). Such compounds are called as endohedral fullerenes and currently can be synthesized by both physical and organic methods. The remaining category of the fullerene family is elusive molecules, that is,

heterofullerenes, in which carbon atom(s) are replaced by heteroatom(s).



Figure 1. Fullerene C_{60} and its families including exohedral fullerenes, fullerene salts, endohedral fullerenes, and heterofullerenes.

Endohedral fullerenes have been widely investigated and the number of isolated endohedral fullerenes is exceeding much more than 100 at the present time.¹⁴ In sharp contrast to this fact, the substantial evidences on the existence of heterofullerenes have been gained only under gasphase conditions by mass spectrometry, scuh as $C_{59}X$ (X = B,¹⁵ N,¹⁶ O,¹⁷ Si,¹⁸ Fe,¹⁹ Co,¹⁹ Ni,¹⁹ Rh,¹⁹ P,²⁰ Pt,²¹ Ir,²¹ As,²² and Ge²²) and C₅₈YZ (YZ = B₂,¹⁵ N₂,²³ and BN²⁴) (Figure 2). Among them, macroscopic preparation and isolation has been achieved only for azafullerene C₅₉N.¹³ This suggests that the heterofullerene chemistry is lagging behind the endohedral fullerene chemistry. Thus, development of synthetic methods toward heterofullerene is a great topic of interest in



Figure 2. Representative examples of heterofullerenes: $C_{59}B$, $C_{59}N$, $C_{59}O$, $C_{59}Si$, $C_{58}N_2$, and $C_{58}BN$.

fullerene chemistry. The B and N-atoms have been considered as candidate atoms for forming feasible heterofullerenes because of their similarity to a C-atom in terms of electronegativity and atomic size. For instance, heterofullerenes, $C_{59}B^-$, $C_{59}N^+$, and $C_{58}BN$, are the most fascinating molecules having the isoelectronic structure to C_{60} .

Additionally, theoretical calculations of $C_{58}X_2$ provide a beneficial prediction that the properties of $C_{58}X_2$ should significantly depend on the arrangement where X-atoms are doped.²⁵ For such heterofullerene containing two heteroatoms, 23 different structures are considered as isomers in theory (Figure 3). The author calculated all isomeric diazafullerenes (1,n)- $C_{58}N_2$ at the B3LYP/6-31G(d) level of theory and summarized in Table 1.²⁶ This implies that, if the second heteroatom can be introduced at the desired position, it will be an efficient way to finely tune electronic structures of $C_{58}X_2$ (HOMO-LUMO levels as well) without changing their spherical structures. Herein, the author focused on heterofullerenes, which are expected to have intriguing properties different from parent C_{60} , and summarized (1) gas-phase generation and organic synthesis of heterofullerenes, (2) synthetic attempts toward novel heterofullerene families, (3) preparation and structures of endohedral fullerenes, and (4) effect of encapsulation: properties of endohedral fullerenes.



Figure 3. (a) The Schlegel diagram of (1,n)-C₅₈X₂ and (b) its molecular structure with positional numbers. The X-atoms in C₅₈X₂ (23 isomers in total) are indicated by blue spots.

п	$\Delta E_{tot}{}^a$ (kcal/mol)	E _{HOMO} (eV)	E _{LUMO} (eV)	$E_{ m gap}$ (eV)
2	32.8	-4.79	-3.47	1.32
3	14.3	-4.61	-3.44	1.17
6	11.9	-4.71	-3.50	1.21
7	0.0	-5.03	-3.33	1.70
9	15.2	-5.29	-3.29	1.99
13	6.2	-4.70	-3.34	1.36
14	5.8	-4.65	-3.36	1.29
15	6.5	-4.70	-3.43	1.27
16	9.1	-4.61	-3.46	1.15
23	1.4	-4.79	-3.35	1.44
24	9.7	-4.58	-3.51	1.07
31	10.1	-4.53	-3.51	1.02
32	7.2	-4.55	-3.35	1.19
33	8.8	-4.53	-3.44	1.10
34	11.4	-4.45	-3.51	0.94
35	12.4	-4.45	-3.54	0.90
41	3.1	-4.68	-3.33	1.35
49	9.2	-4.47	-3.48	0.99
50	6.4	-4.55	-3.43	1.12
52	6.1	-4.55	-3.35	1.20
56	7.9	-4.52	-3.45	1.07
57	11.6	-4.43	-3.52	0.91
60	7.4	-4.48	-3.36	1.13

Table 1. Calculated relative total electronic energies, HOMO-LUMO levels, and gaps of (1,n)-C₅₈N₂ (B3LYP/6-31G(d))

^{*a*}Total electronic energies are referenced to the value of the most stable isomer (1,7)-C₅₈N₂.

Gas-Phase Generation and Organic Synthesis of Heterofullerenes

The first heterofullerene was reported by Smalley et al. in 1991¹⁵ soon after the discovery of C_{60} .¹ They observed molecular ion peaks corresponding to boron-containing fullerenes from a graphite disk with 15 wt% boron nitride by applying the laser vaporization supersonic beam method. The FT-ICR (Fourier transform ion cyclotron resonance) mass spectra showed molecular ion peaks of borafullerenes containing boron atoms up to 6 in the form of molecular complex $(C_{60-n}B_n) \cdot (NH_3)$ n by exposure to ammonium-gas for two seconds (Figure 4).



Figure 4. FT-ICR spectra: (a) around 60-atom clusters produced from graphite containing 15 wt% boron nitride by laser vaporization method and (b) after exposure to ammonia vapor for two seconds.

In 1996, Muhr et al. reported an efficient method for the extraction of borafullerenes utilizing the Lewis acidic character of B-atoms embedding into the carbon network (Figure 5).²⁷ Whereas the mass spectrum of the CS₂ (carbon disulfide) extract includes molecular ion peaks of C₆₀, C₇₀, and higher-order fullerenes without considerable amount of borafullerenes, the mass spectrum of the pyridine-extract obviously showed the molecular ion peaks of borafullerenes, C₅₉B and C₆₉B. It is noteworthy that the fragment ion peaks of (C₅₉B)•(pyridine) were observed at m/z 745 and 771 with maintaining the B←N coordination bond, which implies that the B-atom in C₅₉B has a strong Lewis acidity (Figure 6). In 2013, Poblet, Kroto, and co-workers succeeded in the formation of borafullerenes C₅₉B and C₆₉B by direct exposure of C₆₀ and C₇₀ to boron



Figure 5. Concept of effective enrichment of borafullerenes from the soot produced by the arc evaporation of graphite containing 10–15 wt% of BN, B₄C or B.

vapor.²⁸ The molecular ion peak corresponding to $C_{59}B$ was clearly observed by FT-ICR mass only in the negative ionization mode despite the absence of $C_{59}B^+$ in the positive ionization mode. This indicates the high electron affinity of the $C_{59}B$ skeleton.



Figure 6. Fragment ion peaks of molecular complex (C₅₉B)•(pyridine).

In the case of azafullerene $C_{59}N$, since 1991, substantial evidences on its existence have been presented and confirmed in the gas-phase under mass spectroscopic conditions.²⁹ In 1995, the research group of Mattay and Abraham and the research group of Malcolm independently reported the organic synthesis of $C_{60}NH$ whose molecular formula is very close to azafullerene $C_{59}N$.³⁰ This compound can be synthesized from C_{60} in two steps: the reaction of C_{60} with *tert*butyloxycarbonyl azide and then deprotection on the nitrogen atom (Scheme 1).

Scheme 1. Synthesis of Aziridinofullerene C₆₀NH



The two types of mechanism can be considered for the reaction of C_{60} with azide: one is [2+1] cycloaddition of C_{60} with nitrene which is formed by N₂-extruction from azide, and the other is [3+2] cycloaddition of azide and C_{60} , followed by the formation of triazoline derivative **3** and then extrusion of N₂ to give aziridinofullerene **1** (Figure 7). In 1996, Hirsch et al. isolated the triazoline intermediate by the reaction of C_{60} with 2-methoxyethoxymethyl azide and the solid-state structure was unambiguously determined by the single crystal X-ray analysis.³¹ From this fact, the pathway (b) depicted in Figure 7 is most likely to rationally explain the addition reaction

of azide to C_{60} . In the same year, Mattay et al. reported the gas-phase generation of hydrogenated azafullerene $C_{59}NH^{++}$ and $C_{59}NH_2^{++}$ by DCI (desorptive chemical ionization) mass analysis of aziridinofullerene **2** ($C_{60}NH$) only when NH₃ was used as a reagent gas (Figure 8).³² These peaks were not observed under *iso*-butene gas. Although the mechanism is still unclear, this result indicates that the simplest N-bridged C_{60} derivative **2** can become a synthetic precursor toward azafullerene $C_{59}N$.



Figure 7. Plausible mechanism of the reaction of C₆₀ and azide.



Figure 8. DCI mass spectra of $C_{60}NH$ (2): (a) under *iso*-butene and (b) under ammmonia.

Since then, the great efforts on the research of N-bridged C_{60} derivatives were made by Hirsch and co-workers. They revealed that triazoline derivative **4**, which is obtained by the reaction of C_{60} and an alkyl azide, undergoes the formation of aziridinofullerene **5** and azafulleroid **7** by extrusion of N₂ (Scheme 2). Aziridinofullerene **5** has a nitrogen atom on the [6,6]-bond which connects two hexagonal rings in a closed fashion³³ whereas azafulleroid **7** has a nitrogen atom on the [5,6]-bond which connects one pentagonal and one hexagonal rings in an open fashion.³⁴ Each structural isomer can regioselectively react with one additional azide to afford corresponding bisadduct 6 or 8 (Scheme 2).

Scheme 2. Synthesis of aziridinofullerene and azafulleroid



In the meanwhile, Wudl et al. reported the further transformation of azafulleroids **7** and **8** into open-cage C_{60} derivatives **9** and **10** (Scheme 3).³⁵ This is the first report on the cage-opened derivative, which has a potential to be a precursor of endohedral fullerenes. Moreover, FAB (fast atom bombardment) mass spectra of these compounds showed the molecular ion peak corresponding to azafullerene $C_{59}N^+$.¹³

Scheme 3. Synthesis of open-cage C₆₀ derivatives (a) 9 and (b) 10



To get deeper insights into the formation mechanism of azafullerene $C_{59}N^+$, they subsequently analyzed the FAB mass spectra of compounds **9** and **10** (Figure 9).¹³ As a consequence, they figured out the fact that azafullerenyl cation $C_{59}N^+$ was formed stepwisely: elimination of 2-methoxyethanol followed by the closure of the opening with elimination of

HCHO and then release of CO. The deprotection of the N-MEM group in 9 and 10 is a key step to form the C₅₉N skeleton.



Figure 9. FAB mass spectra of (a) 9 and (b) 10.

According to these results, Wudl et al. treated **9** with a strong acid, *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H₂O) and for the first time successfully isolated azafullerene as its dimer $(C_{59}N)_2$ in macroscopic quantities (Scheme 4).¹³ In the next year, a monomeric azafullerene was also isolated in the form of hydroazafullerene HC₅₉N, which was obtained by the reaction of **9** with *p*-TsOH·H₂O in the presence of hydroquinone (Scheme 4).³⁶ From the DFT calculations at the B3LYP/6-31G(d) level of theory, HC₅₉N (HOMO, -5.49 eV; LUMO, -3.29 eV) has a slightly lower-lying LUMO level by 0.06 eV and an elevated HOMO level by 0.50 eV relative to C₆₀

Scheme 4. Synthesis of bisazafullerenyl (C59N)2 and monoazafullerene HC59N



(HOMO, -5.99 eV; LUMO, -3.23 eV). The cyclic voltammetry is in good agreement of this prediction: reduction potentials are comparable each other ($E_{1/2}$, 1.106 V for HC₅₉N and 1.123 V for C₆₀ in ODCB) while oxidation potential of HC₅₉N (E_{pa} , 0.823 V in ODCB) is cathodically shifted by 0.48 V compared to that of C₆₀ (E_{pa} , 1.300 V in PhCN³⁷).

Under the mass spectroscopic conditions, $C_{59}N^+$ is exclusively observed despite the absence of the parent peak corresponding to $(C_{59}N)_2$.^{13,38} This suggests that the $C(sp^3)-C(sp^3)$ single bond which connects two $C_{59}N$ cages is readily to be cleaved. From the optimized structure of $(C_{59}N)_2$ at the B3LYP/6-31G(d) level of theory, the bond length of the single bond is 1.582 Å which is elongated relative to typical $C(sp^3)-C(sp^3)$ single bond (1.54 Å). Additionally, the binding energy of this single bond was estimated to be ca. 18 kcal/mol using the BLYP method by Andreoni et al. in 1996.³⁹ Therefore, upon heating $(C_{59}N)_2$, azafullerene is considered to be in the thermal equilibrium with azafullerenyl radical $C_{59}N^*$ which is isoelectronic to radical anion C_{60}^- . However, the distribution of the electronic spin is quite different between these two radical species (Figure 10). In the case of $C_{59}N^*$, the spin is mainly localized on two hexagonal rings containing the Natom. In contrast, the spin of C_{60}^- is distributed on the entire skeleton.



Figure 10. Spin density map of (a) $C_{59}N^{\bullet}$ and (b) $C_{60}^{\bullet-}$ (B3LYP/6-31G(d)).

In 1997, ESR measurements of $C_{59}N^{\bullet}$ were reported. In sharp contrast to C_{60}^{\bullet} that exhibited one broad signal without hyperfine coupling with ¹³C (I = 1/2) (Figure 11d),⁴⁰ the three sharp lines are detected for $C_{59}N^{\bullet}$ in solution, which is assignable to a single ¹⁴N (I = 1) hyperfine splitting with a hyperfine coupling constant of ca. 3.7 G (Figure 11a,b).^{41,42} In the solid-state, the similar splitting was observed but somewhat broadened probably because the concentrated spin density enhanced the spin-spin interaction which leads to rapid relaxation (Figure 11c).⁴³ So far, a variety of derivatization of ($C_{59}N$)₂ have been investigated. As summarized in Figure 12, azafullerenyl radical $C_{59}N^{\bullet}$ and cation $C_{59}N^{+}$ can be used as reactive intermediates via radical coupling reaction and electrophilic reaction, respectively.¹² The multi-functionalization is also available for further functionalization (the reverse reaction as well) (Figure 12c).



Figure 11. ESR spectra of (a) CW ESR of $C_{59}N^{\bullet}$ in solution, (b) LESR of $C_{59}N^{\bullet}$ in solution, (c) CW ESR of $C_{59}N^{\bullet}$ in solid-state, and (d) CW ESR of $C_{60}^{\bullet}Ph_4P^{+}(Ph_4PCl)_2$ in solution.



Figure 12. Versatile derivatization of (C₅₉N)₂.

Unfortunately, the single crystal X-ray analysis of $(C_{59}N)_2$ has not yet been reported because of low solubility and poor crystallinity except for the report on synchrotron powder XRD (X-ray diffraction) analysis.⁴⁴ In 2003, Reed et al. reported the crystal structure of $C_{59}N^+$ with a counteranion of silver(I) bis-carborane complex, which was prepared by the oxidation of $(C_{59}N)_2$ by the radical cation of hexabromo(phenyl)carbazole (Figure 13a).⁴⁵ From this X-ray structure with severe disorder in the fullerene cage, they cannot judge the structural feature of $C_{59}N^+$ that should have an iminium cation character predicted by DFT calculations. In 2008, Gan et al. reported the well-resolved X-ray structure of a penta-adduct of $C_{59}N$ ($C_{59}N(OOt-Bu)_4Br$) (Figure 13b).⁴⁶ From bond lengths, the pentagonal ring containing the N-atom is found to have a pyrrole character. Very recently (in 2019), Chronakis, Tagmatarchis, and their co-workers reported the Xray structure of a bis-substituted $C_{59}N$ derivative (Figure 13c).⁴⁷ In this data, the local structure surrounding the N-atom was well-dissolved without any disorder.



Figure 13. Single crystal X-ray structures of (a) $C_{59}N^+$, (b) $C_{59}N(OOt-Bu)_4Br$, and (c) (RC₅₉N)CR₂.

Synthetic Attempts toward Novel Heterofullerene Families

The rational organic synthesis of C_{60} from a stable precursor had been a challenging issue. The synthetic strategy is based on the bottom-up synthesis from macrocyclic poly-yne derivatives or polycyclic aromatic hydrocarbons (PAHs), which is applicable to the synthesis of novel heterofullerene families. The extended approaches based on the Wudl's method,¹³ derivatization from C_{60} should be also beneficial (Figure 14).



Figure 14. Synthetic strategy toward novel heterofullerenes, based on the Wudl's method.¹²

In 1997, Rubin et al. proposed a molecule ($C_{60}H_6$, **11**) depicted in Figure 15a as a possible precursor of C_{60} in which two benzene rings are linked with three poly-yne chains.^{6a} Toward this molecule, they prepared macrocyclic compound $C_{60}H_{18}$ (**12**) which undergoes partial dehydrogenation to give $C_{60}H_{14}^-$ under mass spectroscopic conditions (Figure 15b). In the next year, Tobe et al. reported an analogous compound $C_{60}H_6$ (indane)₆ (**13**) in which each double bond in $C_{60}H_{18}$ (**12**) is replaced with indane.⁴⁸ Compound **13** is stable and expected to form $C_{60}H_6$ by the elimination of six aromatic indane fragments by thermal treatment (Figure 15c). The LD-TOF (laser desorption time-of-flight) mass spectra of **13** exhibited molecular ion peaks of desired **11**⁻ and C_{60}^{-} . In 2001 and 2002, Scott et al. reported PAHs **14-X** as suitable precursors of C_{60} (Figure 15d).⁴⁹ The overall process required 9 and 11 steps to synthesize **14-H** and **14-Cl**, respectively. Whereas **14-H** undergoes dehydrogenation to form C_{60} under mass spectroscopic conditions, **14**-**Cl** can be converted into C_{60} in macroscopic scale under pyrolytic conditions, albeit only in ca. 1%. The easier access to **14-H** was accomplished by a triple palladium-catalysed arylation of a trialkylated truxene by Echavarren et al.⁵⁰



Figure 15. Possible precursors for the bottom-up synthesis of C₆₀.

The pioneering work on the synthesis of novel heterofullerenes has been done by the research group of Hirsch.⁵¹ Inspired by the Wudl's report on azafullerene $C_{59}N$,¹³ they attempted to synthesize diazafullerene $C_{58}N_2$ as a novel heterofullerene. In the first stage, they focused on bisazafulleroid in which two nitrogen atoms are adjacent each other and bridged on the [5,6]-bond in an open fashion (Figure 16a, the same as **8** shown in Scheme 2). The *n*-butylamine-adduct of this compound was found to be transformed into $(C_{59}N)_2$ by the thermal treatment in the presence of *p*-TsOH·H₂O instead of the formation of $C_{58}N_2$.³⁸ Next, they performed the direct reaction of azafullerene $(C_{59}N)_2$ with 2-methoxyethoxymethyl azide but it resulted in an isomeric mixture (16 isomers) (Figure 16b). Thus, they moved focus to the reaction of C_{60} with a tether molecule bearing two azide groups. As a result of intermolecular addition reaction (Figure 16c), the FAB mass spectrum of the thus-obtained compound showed a fragment ion peak of $C_{59}N$ without formation of $C_{58}N_2$. In the case of intramolecular addition reaction (Figure 16d),⁵² however, the precursor of the tether molecule cannot be prepared due to the instability of azidomethylether as a key unit.⁵¹



Figure 16. Concepts and designed molecules toward diazafullerene $C_{58}N_2$ (proposed by Hirsch et al.).

Finally, Hirsch et al. found a way to access diazafullerene $C_{58}N_2$.⁵¹ As shown in Scheme 5, they designed and synthesized a $C_{59}N$ derivative bearing an azide group linked by a spacer unit (**15**). The azide group in **15** would react on the double bond marked by a blue arrow with a relatively high regioselectivity (Scheme 5). The resulting **16** was subsequently exposed to O_2 under light irradiation to give **17** which has a ketolactam moiety as a key structure for a nitrogenembedding. After the one-pot process, freshly-prepared **17** was immediately analyzed by FAB mass spectrometry. The fragmentation peak around m/z 720 corresponding to 60-cluster of carbons indicates the formation of $C_{59}N$ and $C_{58}N_2$ with a ratio of 4:1. Although desired $C_{58}N_2$ cannot be isolated, they still aimed to the synthesis of novel heterofullerenes, not limited to $C_{58}N_2$.



Scheme 5. Synthetic concept and route toward diazafullerene $C_{58}N_2$ proposed by Hirsch et al.

Recently, Gan et al. reported the new route to synthesize azafullerene in the form of $HC_{59}N$, which was derived from C_{60} in 8 steps (Scheme 6). They found that the reaction of C_{60} with *tert*butyl hydroperoxide provided pentakis-adduct **19** with an epoxide group⁵³ which can be cleaved to give diol derivative **20**.⁵⁴ Further treatment of **20** with (diacetoxyiode)benzene PhI(OAc)₂ (hypervalent iodine compound) afforded diketo-derivative **21** having a 10-membered-ring opening.⁵⁴ Hydroxylamine NH₂OH regioselectively reacted with **21** and resulted in the formation of **22** while the closure of the opening of **21** proceeded at the same time.⁴⁶ Phosphorus pentachloride PCl₅ induced the rearrangement in **22** and constructed the ketolactam moiety (**23**).⁴⁶ Just passing through a basic alumina column, **23** was found to be converted into azafullerene derivative **24** with loss of CO.⁴⁶ The X-ray structure of the analogous compound of **23** indicated that the driving force for the loss of lactam CO from **23** should be steric strain. Finally, they figured out the complete conversion of **24** into hydroazafullerene HC₅₉N by the sequential reaction utilizing BBr₃ and PPh₃.⁵⁵ It is important to note that the N-atom in hydroxylamine is the source of a heteroatom of HC₅₉N.

Scheme 6. Synthesis of HC₅₉N reported by Gan et al.



Toward the synthesis of diazafullerene $C_{58}N_2$, they focused on hydroazafullerene derivative **24** (Scheme 7).⁵⁶ After bromination of **24**,⁴⁶ compound **25** was consequently reacted with hydroxylamine to give **26**. In the similar way to Scheme 6, **26** was treated with PCl₅, which resulted in the successful incorporation of the second N-atom in the carbon network of the C₅₉N

skeleton (27). Continuously, the remaining Cl functional group in 27 was replaced by the alkoxy group (28) and the four *t*BuOO addends were removed by utilizing BBr₃ and PPh₃ (29). The final step is the deprotection of alkoxy group in 29 and furnished 30a which should be chemically transformed into 30b under protic conditions. Although full characterization of 30 ($C_{59}N_2OH_2$) could not be accomplished due to its poor solubility, the MALDI-TOF (matrix-assisted laser desorption/ionization time-of-flight) mass spectrum of 30 showed the undoubtable formation of diazafullerene $C_{58}N_2$ in the form of $C_{58}N_2H^+$ together with a parent peak corresponding to $C_{59}N_2OH^{++}$. Compared with the Hirsch's approach,⁵⁰ the Gan's method should provide single isomer of diazafullerene, namely 1,9- $C_{58}N_2$, in which two N-atoms are adjacent each other to make a [6,6]-bond. Though the Hirsch's method is inaccessible to the Gan's isomer, it would provide other isomers except for the 1,9-substitution position by changing the chain length of a spacer bearing an azide group.



Figure 17. MALDI-TOF mass spectra of 30, showing a peak corresponding to C₅₈N₂H⁺.



Scheme 7. Synthetic route toward diazafullerene $C_{58}N_2$ proposed by Gan et al.

In 2007, Gan et al. reported open-cage C_{60} derivative **31** derived from C_{60} in 3 steps (Scheme 8).⁵⁷ In 2012, further treatment of **31** by BBr₃ and PPh₃ was found to provide simple compound **32** with a molecular formula of $C_{59}O_3$ (Scheme 8).⁵⁵ The structure of **32** is quite similar to ketolactam derivative **9** used for the synthesis of $(C_{59}N)_2^{13}$ as well as a precursor of $C_{58}N_2$ (**30b**).⁵⁶ Therefore, **9** was analyzed by MALDI-TOF mass spectrometer in a way similar to **30** but the desired dioxafullerene $C_{58}O_2$ was not observed. The MALDI-TOF mass spectrum of **31** also showed no fragment peak of $C_{58}O_2$.

Scheme 8. Synthesis of $C_{60}O_3$ by Gan et al.



From the analyses of **31–33** by mass spectrometry, **32** can be generated from **31** and **33** but it is not accessible to hydrolyzed species $C_{59}O_4H$ (**34**) (Figure 18). However, only **33** induces the formation of dioxafullerene $C_{58}O_2$ via **34** by the loss of addends and further rearrangement. This indicates that partially-brominated intermediate **33** plays an important role in the gas-phase formation of $C_{58}O_2$ (Figure 19) although the chemical structure of **33** was hardly characterized owing to its facile reactivity, which presumably involves replacement of Br by OH.



Figure 18. MALDI-TOF mass spectra of 33.



Figure 19. Plausible mechanism of the formation of $C_{58}O_2$ from 33 under mass spectroscopic conditions.

On the basis of the bottom-up approach, Tobe et al. reported the gas-phase generation of diazafullerene $C_{58}N_2$ in 1999.⁵⁸ They prepared pyridinophane **35** fused by propellatriene units as a precursor of macrocyclic poly-yne **36**. Under the LD-TOF mass conditions, **35** was mainly converted into **36**⁻ together with a trace amount of $C_{58}N_2^-$ (Scheme 9).



Scheme 9. Gas-phase generation of $C_{58}N_2$ based on the bottom-up synthesis by Tobe et al.

Although a relatively high yield of C_{60} was confirmed in the case of $C_{60}H_6(indane)_6$ (13),^{48a} the production yield of $C_{58}N_2^-$ from $C_{58}H_4N_2(indane)_6$ was quite low (Figure 20). The conversion of $C_{58}H_4N_2^-$ (36⁻) into $C_{58}N_2^-$ is considered to take place in a stepwise fashion since intermediate species such as $C_{58}H_3N_2^-$ and $C_{58}H_2N_2^-$ were detected. In addition, the mass spectrum showed a strong peak corresponding to CN^- which should be extruded from $C_{58}N_2$ or its precursors. Anionic species $C_{57}N^-$ and C_{56}^- were also detected, which are formed by the loss of neutral CN fragment(s) from $C_{58}N_2$. Thus, the inefficient conversion of 35 into $C_{58}N_2$ is probably due to the thermodynamic and kinetic lability of $C_{58}N_2$. It is noteworthy that this is the first observation of $C_{58}N_2$ formed in a size selective manner.



Figure 20. LD-TOF mass spectra of 35 showing a peak corresponding to $C_{58}N_2^-$.

In 2004, Gómez-Lor and Echavarren reported the synthesis of a heterocyclic aromatic hydrocarbon (hetero-PAH) $C_{57}N_3H_{33}$ (**40**)⁵⁹ which is a heteroatom analogue of $C_{60}H_{27}X_3$ (**14**).⁴⁹ They synthesized **40** from **37** only in 3 steps. In the course of this reaction, triindole **38** is a key intermediate and the triple alkylation and intramolecular palladium-catalyzed arylation provided the facile access to **40** as a possible precursor of triazafullerene $C_{57}N_3$ (Scheme 10). Ideally, oxidation of **40** and subsequent dehydrogenation of 15H₂ should lead to the generation of $C_{57}N_3$.

Scheme 10. Synthesis of C₅₇N₃H₃₃ (40) by Gómez-Lor and Echavarren



In 2008, they reported that the surface-catalysed cyclodehydrogenation of **40** resulted in the quantitative conversion into triazafullerene $C_{57}N_3$.⁶⁰ The formation of $C_{57}N_3$ was clearly observed by the STM (scanning tunneling microscope) images (Figure 21). Hetero-PAH **40** deposited onto a Pt(111) surface can be visualized as a triangle-shape with 2.2 nm on each side (Figures 21a,b). Upon annealing at 750 K, a surface reaction took place and the triangular molecules **40** was transformed into round molecules $C_{57}N_3$ with an apparent height of ca. 0.38 nm and a diameter of 1.5 nm (Figures 21c,d). The underestimated height is caused by a strong bonding interaction between $C_{57}N_3$ and the Pt(111) surface.⁶¹ The 3-step synthesis of **14** from unsubstituted truxene was also reported in that paper and the complete conversion of **14** into C_{60} was achieved by applying the surface-catalysed cyclodehydrogenation.



Figure 21. STM images of 40 (a, b) and $C_{57}N_3$ (c, d) deposited on the Pt(111) surface.

Preparation and Structures of Endohedral Heterofullerenes

The examples of endohedral heterofullerenes are quite limited even though the combined chemistry of endohedral fullerenes and heterofullerenes has received attention. The first example was reported by Smalley et al. in 1991.⁵ In the paper, they also discovered the first heterofullerene $C_{59}B$. One day in the course of study, they faced to a severe problem: the laser vaporization apparatus was contaminated with KCl which cannot be completely removed. They finally decided to use this apparatus despite remaining contamination of KCl and after the experiment they noticed the molecular ion peaks corresponding to not only C_{60} and $C_{59}B$ but also K_nC_{60} , $KC_{59}B$, and $KC_{58}B_2$ in the FT-ICR mass spectra (Figure 22a). To confirm whether the potassium atom is exohedrally or endohedrally attached/encapsulated, they measured mass spectrum in an ammonia atmosphere, which clearly showed the formation of (K@C_{59}B)(NH_3) (Figure 22b).



Figure 22. FT-ICR mass spectra demonstrating the production of endohedral heterofullerenes: (a) before and (b) after reaction with NH₃.

In accordance with the Wudl's method,¹³ Akasaka, Nagase et al. synthesized La@C₈₂(NCH₂Ph) and La₂@C₈₀(NCH₂Ph) by the reaction of La₂@C₈₀ and La@C₈₂ with corresponding benzyl azides, respectively, in 1999 (Scheme 11).⁶² The evidences of the gas-phase generation of endohedral azafullerenes La₂@C₇₉N and La@C₈₁N were confirmed by the FAB mass fragmentation of La@C₈₂(NCH₂Ph) and La₂@C₈₀(NCH₂Ph). These cationic species La₂@C₇₉N⁺ and La@C₈₁N⁺ are isoelectronic with La₂@C₈₀ and La@C₈₂, respectively. Ab initio calculations of La₂@C₇₉N⁺ showed that almost all three valence electrons are transferred from each La-atom (5d¹6s²) to the LUMO, LUMO+1, and LUMO+2 of the azafullerene cage, as seen in La₂@C₈₀. In addition, La₂@C₇₉N⁺ has a closed shell electronic structure, which can accept one electron to give (La₂@C₇₉N)⁺ (Figure 23). Interestingly, the electronic spin is suggested not to be distributed on the caged surface whereas each La-atom in the C₇₉N cage has a spin density of 0.5. This electronic property is different from aza[60]fullerene C₅₉N which has an electronic spin on its cage. In consequence of the acceptance of one electron into the La–La bonding orbital and the decreased positive charge on each La-atom, the La–La distance of La₂@C₇₉N (3.585 Å) is shorter than those of La₂@C₇₉N⁺ (3.622 Å) and La₂@C₈₀ (3.655 Å).

Scheme 11. Synthesis of $La@C_{82}(NCH_2Ph)$ and $La_2@C_{80}(NCH_2Ph)$ and gas-phase formation of corresponding endohedral azafullerenes



Figure 23. Redox species of La₂@C₇₉N based on ab initio calculations with related molecules.

In 2009, Stevenson and Zhang et al. reported the gas-phase formation of trimetallic nitride azafullerene La₃N@C₇₉N (Figure 24a).⁶³ They applied the CAPTEAR (chemically adjusting plasma temperature, energy, and reactivity) method⁶⁴ to a graphite rod packed with Sc₂O₃/La₂O₃ with a ratio of 1:3 in the presence of Cu(NO₃)₂·2.5H₂O as a catalyst. Notably, La₃N@C₈₀ was not observed even though the cage-size is almost the same as that of C₇₉N. For a long time, it has been believed that C₈₀ cannot encapsulate M₃N consisting metal-atoms with the ionic radius equal to or larger than the La-atom (Figure 24b). This implies that, during the formation process of La₃N@C₈₀ from the metallic and carbon-nitrogen pieces, there is the strong force to attract each other, which cannot be expected for the normal carbon pieces.



Figure 24. (a) MALDI mass spectrum of the soot extract obtained by CAPTEAR conditions and (b) overview of preferred cages for M_3N clusters.

In 2008 and 2011, Balch, Dorn, and co-workers reported the macroscopic-scale synthesis of $M_2@C_{79}N$ (M = Tb, Y, and Gd).⁶⁵ They prepared $M_2@C_{79}N$ from composite graphite rods containing a mixture of Tb₄O₇, Y₂O₃, or Gd₂O₃, graphite powder, and metallic Cu by applying the electric arc method. The single crystals of Tb₂@C₇₉N were obtained by cocrystallization with

nickel(II) octaethylporphyrin Ni^{II}(OEP) from a benzene solution.^{65a} As shown in Figure 25a, the X-ray structure of Tb₂@C₇₉N definitively ruled out the alternative possibilities such as Tb₂CN@C₇₈ or Tb₂C₂@C₇₇N. Each Tb-atom coordinates with an adjacent hexagon of the cage in an η^6 -fashion. By comparison with the X-ray data of $[Sc_3N@C_{80}][NiOEP][2C_6H_6]$, ⁶⁶ they decided that there is no specific intermolecular interaction between the C₇₉N cage and NiOEP since the close-set distances of [Tb₂@C₇₉N][NiOEP] (2.805(3), 3.044(8) Å) are comparable to that of $[Sc_3N@C_{80}][NiOEP][2C_6H_6]$ (2.812(3), 3.078(3) Å). In the case of $Gd_2@C_{79}N$, the overall yield reaches up to 0.05–0.1% (Gd₂@C₇₉N/C₆₀) and 0.5–1 mg of Gd₂@C₇₉N was isolable for every gram of C₆₀.^{65b} In 2018, Shi, Jiang, Gao, and their co-workers reported the crystal structure of Gd₂@C₇₉N (Figure 25b) and its properties as molecular magnet with a collective high-spin ground state (S = 15/2) generated by strong magnetic coupling.⁶⁷ In 2019, the similar research work on Tb₂@C₇₉N as a single molecular magnet has been investigated by Dorn, Popov, and their coworkers.⁶⁸ Very recently, as a collaborative research with Dorn, Wang reported that the nuclear polarization of ¹H and ¹³C spins from 40 mM 4-oxo-TEMPO (TEMPO: 2,2,6,6tetramethylpiperidine 1-oxyl) was increased by ca. 40 and 50% at 5 and 1.2 K, respectively, by adding a 60 µM dosage of Gd₂@C₇₉N.⁶⁹ To the best of the author's knowledge, this is the first report on DNP (dynamic nuclear polarization)⁷⁰ utilizing fullerenes.



Figure 25. X-ray structure of (a) $Tb_2@C_{79}N$ and (b) $Gd_2@C_{79}N$. The solvent molecules are omitted for clarity.

Effect of Encapsulation: Properties of Endohedral Fullerenes

Beside the researches on the synthesis of endohedral fullerenes and heterofullerenes, it has been elucidated that single molecules inside nanoconfined environments exhibit intriguing properties largely different from those in bulk, i.e., nuclear spin relaxation,⁷¹ rotational behavior,⁷² *ortho-para* conversion,⁷³ dielectric constant,⁷⁴ rotational and vibrational transitions,^{73f,75} electron densities,⁷⁶ and chemical reactivities⁷⁷ (Figure 26). Thus, it is of particular importance to study the nature of the inner sphere and the effect of encapsulation on properties of the external sphere.

To investigate whether the encapsulated species such as H_2 and H_2O are magnetically isolated or not, Turro and co-workers studied the effect of the electron spin existing outside of the cage by using ¹H NMR relaxation time.⁷¹ As the results, the relaxation becomes rapid due to the dipolar interaction between the electron spin and the encapsulated species. This clearly indicates that the encapsulated molecules are geometrically isolated but not magnetically isolated. Importantly, C_{60} can provide opportunities to investigate the quantum dynamics such as quantum rotation and interconversion between *ortho*-H₂O and *para*-H₂O.^{73–75} So far, these two different spin states of H₂O were confirmed by inelastic neutron scattering, far-infrared spectroscopy, cryogenic nuclear magnetic resonance, and dielectric constant measurements. Interestingly, the encapsulated water molecule isotropically rotates even at 20 K^{73d,f} and its rotational motion is not frozen upon cooling down to 8 K.⁷⁴ In contrast to H₂O@C₆₀, Suzuki and co-workers reported that the lithium cation inside the C₆₀ cage shows a librational mode below 120 K, associated with the Li⁺@C₆₀ molecules and counter anions.^{72b} The encapsulation of Li⁺ inside the C₆₀ cage results in

Specific nature of H₂O@C₆₀:



- 1. Ortho-para conversion of H₂O
- 2. Rapid free rotation at 20 K
- 3. Increasing permittivity upon cooling



Figure 26. Properties of endohedral [60] fullerenes.

localization of the Li⁺ ion due to the electrostatic interactions with the C₆₀ cage as well as with the neighboring lowering the LUMO level. In the Diels-Alder reaction with 1,3-cyclohexadiene, the reaction rate for Li⁺@C₆₀ was increased by 2400-fold relative to empty C₆₀ at 303 K.⁷⁸ Recently, Martín and co-workers reported that the reaction rate for polar endofullerenes such as H₂O@C₆₀ and HF@C₆₀ slightly enhances in the *cis-trans* isomerization compared with pristine C₆₀ due to the intramolecular H-bonding leading to the stabilization of the intermediates and transition states.⁷⁹ These results unambiguously show that the intramolecular interaction between the C₆₀ cage and the encapsulated species, which leads to the specific properties different from pristine C₆₀. Furthermore, the geometrically isolated species inside the C₆₀ cage have distinct nature that cannot be seen in the bulk conditions.

Survey of This Thesis

As described above, endohedral heterofullerenes are an elusive class of fullerene family. Most importantly, endohedral heterofullerenes are regarded as models suitable for the investigation of the single molecular properties. In this thesis, the author attempted to synthesize the first endohedral aza[60]fullerenes and examined the properties of the encapsulated molecules by utilizing ¹H NMR relaxation times in terms of rotational behavior (Chapters 1–3). So far, in the fullerene chemistry, it has been of particular importance to get insights into the intramolecular interaction between the encapsulated molecules and the C₆₀ cages whereas there is quite limited methodologies to describe such interaction or contact. To verify the availability of the method based on the ¹H NMR relaxation time, the author further investigated how the circumstances, especially rotational behavior of the H₂O molecule, are influenced by the structural modification of the outer sphere (Chapters 4 and 5). During the course of these studies, the author has recognized that the endohedral fullerenes are not confined in the fullerene chemistry but can provide the specific interior which enables to experimentally demonstrate physicochemical phenomena, leading to the deeper insights or knowledges in the fundamental chemistry.

In Chapter 1, the author focused on the synthesis and properties of an endohedral opencage C_{60} derivative which is potentially converted into the first endohedral aza[60]fullerene (Figure 27). In order to encapsulate a hydrogen molecule, the author developed a method to enlarge the 11-membered-ring opening of the C_{59} N-precurosr, giving a 15-membered-ring opening which allows for a hydrogen molecule to pass through. Regarding the enlargement reaction, the regioselectivity was examined by theoretical calculations following the rational mechanism. Upon exposure to high-pressure H₂-gas, the open-cage C_{60} derivative was found to encapsulate a hydrogen molecule and the subsequent closing step was also studied.



Figure 27. Enlargement of the opening and accommodation of a hydrogen molecule inside the cage studied in Chapter 1.

In Chapter 2, using the method developed in Chapter 1, the author have synthesized endohedral aza[60]fullerene encapsulating a hydrogen molecule, that is, $H_2@RC_{59}N$ as both monomeric and dimeric forms (Figure 28). Since this method was not applicable in the case of H_2O due to the larger molecular size, the author demonstrated the direct method to derive $H_2O@RC_{59}N$ commenced with $H_2O@C_{60}$. Utilizing the encapsulated H_2 and H_2O molecules as magnetic probes, the author investigated the nature of the internal sphere of the fullerene cages including C_{60} and $C_{59}N$ on the basis of ¹H NMR relaxation time and theoretical calculations. Additionally, the effect of encapsulation was examined by kinetic studies using $H_2O@C_{59}N$ and $H_2@C_{59}N$ dimers, indicating the acceleration of the reaction rate only for $H_2O@RC_{59}N$ due to the intramolecular electrostatic interaction.



Figure 28. Endohedral fullerenes and azafullerenes studied in Chapter 2.

In Chapter 3, the author focused on $C_{59}N^+$ which is isoelectronic to C_{60} (Figure 29). Thus, the quantitative conversion of $(C_{59}N)_2$ to $C_{59}N^+$ was investigated. The author found the facile method applicable for endohedral species, affording $H_2@C_{59}N^+$ and $H_2O@C_{59}N^+$ from the corresponding dimers. Utilizing these materials, the author investigated the shielding effect and electrostatic interaction between the encapsulated molecules and the fullerene cages.



Figure 29. Isoelectronic endohedral fullerenes studied in Chapter 3.

In Chapter 4, the author studied the dynamic behavior of the encapsulated H₂O molecule inside the fullerene cages such as C₆₀CR₂, C₆₀NR, C₆₀O, and C₆₀O₂ (Figure 30). The ¹H NMR relaxation time measurements clearly demonstrated the effect of atoms (E) introduced on the C₆₀ cage, closely related to the polarization degree of E–C(C₆₀) bonds. In other words, the author succeeded for the first time in the experimental rating of electronegativities followed in the order of O > N > C.



Figure 30. Endohedral fullerenes studied in Chapter 4.

For exploring the potential utilizability of the nano-confined H₂O molecule as a magnetic probe, the author thought that the rational way to desirably modify the C₆₀ cage should be required. However, the regioselective functionalization of the C₆₀ cage is, in principle, difficult since it has at most 30 double bonds as the candidate reaction sites. Especially for the open-cage C₆₀ derivatives, the reaction usually takes place on the opening which can efficiently release the strain energy. In other words, for the second reaction to the open-cage C₆₀ derivative, it is difficult to realize the functionalization at the desired position different from double bonds on the opening.

In Chapter 5, the author focused on the structural modification of C_{60} with high regioselectivity by using pre-functionalized C_{60} derivatives in the presence of a palladium catalyst (Figure 31). The author demonstrated that this method is applicable to an endohedral open-cage C_{60} derivative. The orientation of the encapsulated H₂O molecule was also examined by both X-ray crystallography and theoretical calculations.



Figure 31. Endohedral open-cage C₆₀ derivatives studied in Chapter 5.

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Chapter 1

Synthesis of Open-Cage Ketolactam Derivatives of Fullerene C₆₀ Encapsulating a Hydrogen Molecule

ABSTRACT: A novel open-cage fullerene C_{60} derivative having a bis(hemiketal) moiety was synthesized by the reaction of C_{60} -*N*-MEM-ketolactam (MEM: 2-methoxyethoxymethyl) with *N*-methylmorpholine *N*-oxide in the presence of water. The structure was clearly determined by single crystal X-ray analysis. Further enlargement of the opening was performed by treatment with trifluoroacetic anhydride to give the tetraketo derivative having a 15-membered ring opening. For H₂-insertion into the cage, the derivative was exposed to high pressure of H₂. After the encapsulation, the opening-size was reduced to the original one with keeping the hydrogen molecule inside the cage. This compound is a possible precursor for endohedral azafullerenes encapsulating a hydrogen molecule.



Introduction

Open-cage fullerene derivatives¹ have been attracting considerable attention because they are interesting molecules in host–guest chemistry and can be used as precursors for endohedral fullerenes encapsulating atom(s) or small molecule(s) as well as heterofullerenes.² Komatsu and Murata et al. have previously synthesized several endohedral fullerenes, which encapsulate hydrogen molecule(s),^{3,4} a helium atom,⁵ and a water molecule,⁶ by applying the molecular surgery method.⁷ In this method, open-cage fullerene derivatives play an important role, which should meet two requirements for the synthesis of endohedral fullerenes: (a) the opening-size is large enough for a guest molecule to be inserted into the cage and (b) the opening can be readily reduced to a smaller one to prevent the escape of the guest molecule.

As shown in Figure 1, C_{60} -*N*-MEM-ketolactam **1** is the first open-cage C_{60} derivative reported by Wudl et al. in 1995,⁸ and also known as a precursor for azafullerenes such as $(C_{59}N)_2^9$ and $C_{59}NH$,¹⁰ in which one of the carbon atoms of C_{60} is replaced by a nitrogen atom. At the present time, these azafullerenes are the only example for heterofullerenes, for which rational synthetic pathways have been successfully accomplished.^{9–11} The author expected that, if a small molecule is entrapped inside the $C_{59}N$ cage, magnetically intriguing properties, which are different from those for endohedral C_{60} , would be observed due to the unpaired valence electron on the cage of the $C_{59}N$ radical. However, the size of the 11-membered ring opening of **1** is too small even for a helium atom to enter the cage.⁸ Thus, enlargement of the opening of **1** is needed for the first step to obtain endohedral azafullerenes.



Figure 1. MEM-substituted ketolactam derivatives of C_{60} , having an *n*-membered ring opening; (a) n = 11 as C_{60} -*N*-MEM-ketolactam **1**, reported by Wudl et al. and the LUMO near the opening (B3LYP/6-31G*), (b) n = 15 and 19, reported by Iwamatsu et al., (c) n = 12 and 13, reported by Orfanopoulos et al.

Results and Discussion

Regarding the chemical modification of the opening of 1, structural determination for its derivatives is critical because there are four conjugated reactive olefins \mathbf{a} -d on the rim of the opening. In 2003, the first example was reported by Iwamatsu et al.¹² They synthesized an opencage C_{60} derivative having a 15-membered ring opening by the reaction of 1 with aromatic hydrazines through the migration of two hydrogen atoms with the regioselective cleavage of a C=C double bond. They also performed the related reaction using o-phenylenediamine to give an open-cage C₆₀ derivative having a 19-membered ring opening in 2004.¹³ Orfanopoulos et al. also reported two ketolactam derivatives having 12- and 13-membered ring openings, of which contain sulfur atom(s) on the rim, in 2004¹⁴ and 2007,¹⁵ respectively. The development of the method to repair the enlarged opening on these derivatives¹²⁻¹⁵ remains as a challenging issue. Herein, the author report the enlargement of the opening of 1 to provide novel open-cage C_{60} derivatives, their encapsulation of a hydrogen molecule, and the restoration of the opening to the original one. Murata et al. previously reported a method to enlarge the opening by N-methylmorpholine Noxide (NMO) as a nucleophilic oxidant in the presence of a small amount of water.⁶ As shown in Scheme 1, the author applied this method to 1 in o-dichlorobenzene (ODCB) to give C₆₀-N-MEMbis(hemiketal) 4a in 40% yield. Under the same conditions, trimethylamine N-oxide (TMAO) instead of NMO resulted in a similar yield (37%) of 4a. Since 4a was found to be reactive to methanol, ethanol, and 2-propanol (even trace amounts of ethanol as stabilizer in chloroform), these alcohols cannot be used as eluents for chromatographic purification of 4a. When 4a was exposed to these alcohols, mono-alkylated derivative **6a** ($\mathbf{R}' = \mathbf{Me}$, Et, or *i*Pr) having a ketal moiety was formed (confirmed by the ¹H NMR and APCI mass spectra). In addition, the HPLC analyses using the Buckyprep (toluene) column revealed that 4a tends to be adsorbed on the stationary phase and no peak was observed. The Buckyprep-M (toluene) and ODS (octadecylsilyl, toluene/acetonitrile) columns were also unsuitable. The 5PBB column, which is silica-based column modified with pentabromobenzyl groups, is available for the analysis of 4a (retention time, 14.3 min for 4a and 22.4 min for 1; mobile phase, toluene/acetonitrile = 7/3; flow rate, 1 mL/min; temperature, 50 °C; detection, 326 nm). The structure of 4a was confirmed by APCI MS, ¹H and ¹³C NMR, UV-vis, and IR. The molecular ion peak of **4a** was observed at m/z 905 with a fragment peak at m/z 887 corresponding to tetraketo derivative **3a**, which would be formed by the elimination of a water molecule from the rim of the opening under the mass spectroscopic conditions. The ¹H NMR spectrum in DMSO- d_6 showed two signals for OH groups at δ 9.46 and 9.63 ppm, and the ¹³C NMR spectrum in CDCl₃ showed two characteristic sp³-carbon signals corresponding to hemiketal carbons at δ 95.90 and 109.25 ppm. These NMR data support the structure of **4a** shown in Scheme 1.





The theoretical calculations explained the selective formation of bis(hemiketal) that occurred on bond **a**. The epoxidation of **1**, which takes place at one of the C=C double bonds **a**, **b**, **c**, and **d**, is considered to be the first step of this reaction. The theoretical calculations at the B3LYP/6-31G* level of theory¹⁶ demonstrated that the LUMO is relatively localized at the butadiene unit (C1=C2-C3=C4) including bonds **a** and **b** (Figure 1a). Epoxide **2a** formed by the reaction on bond **a** is more stable by 9.0 kcal mol⁻¹ than the other epoxide formed by the reaction on bond b. To discuss more details of the epoxidation with kinetic and thermodynamic perspectives, the author investigated the reaction mechanism using model compound 1', in which the MEM group was replaced by a methyl group. The calculations were conducted at the M06-2X/6-31G* level of theory with the SMD solvation model¹⁷ in THF. Table 1 summarizes the Gibbs energies of the stationary points and transition structures for the epoxidation on the C=C double bonds a-d. Regarding the nucleophilic attack of TMAO to one of the double bonds on 1', formation of each INT on C1-C4 seems less selective because all A and B values are quite similar to each other. Then, the subsequent elimination of trimethylamine (TMA) from each INT was predicted to give product **2a'** or **2b'**. Among the possible reaction pathways, the reaction on C1 needs the least value of C (16.2 kcal/mol), and formation of epoxide 2a' is more exothermic than 2b' as indicated by the value of D (-33.6 kcal/mol for 2a' and -25.4 kcal/mol for 2b'). These results can explain the regioselective formation of epoxide 2a, which reacts with the second oxidant to give **3a**. The resulting **3a** affords **4a** by the addition of a water molecule to carbon C2 on the opening.⁶



Table 1. Changes in Gibbs energies for the epoxidation of 1' with TMAO

^{*a*}The labeling numbers are shown in Figure 1a and Scheme 1.

2b'

2b'

C3

C4

^bThe changes in Gibbs energies (M06-2X/6-31G* with the SMD solvation model in THF at 25 °C).

+4.2

+6.2

+25.9

+19.1

-25.4

-25.4

+11.1

+11.0

After many trials, single crystals of **4a** were obtained from *p*-xylene solution and the solid state structure was unambiguously determined by X-ray analysis (Figure 2).¹⁸ This is a rare example for the solid-state structure of C₆₀ derivatives with a flexible MEM group.¹⁹ It was shown that **4a** has a 12-membered ring opening with an ellipsoidal shape with diameters of 3.319(16) Å along the minor axis and 5.209(18) Å along the major axis (Figure 3). The size of the opening is slightly smaller than that of open-cage C₆₀ derivative **7** having a 13-membered ring opening reported by Komatsu and Murata et al. (3.75 Å along the minor axis and 5.64 Å along the major axis.^{20,21}), which can encapsulate a hydrogen molecule quantitatively. Therefore, the opening-size of **4a** is considered to be insufficient to insert a hydrogen molecule into its cage. For the larger opening, tetraketo derivative **3a** would be a suitable candidate. The theoretical calculations at the B3LYP/6-31G* level of theory showed that **3a** has a 15-membered ring opening with 3.49 Å



Figure 2. X-ray structure of **4a**; (a) side and (b) front views. Thermal ellipsoids are shown at 50% probability level. Solvent molecules and hydrogen atoms are omitted for clarity.



Figure 3. Opening-sizes of **4a**, **3a**, and **7** (**4a**¹⁸ and **7**, ^{20,21} crystal structures; **3a**, calculated structure (B3LYP/6-31G*). 2-Pyridyl group was abbreviated as Py.).

The enlargement of the opening of **4a** was investigated through a dehydration reaction from the bis(hemiketal) moiety. The reaction of **4a** with an excessive amount of trifluoroacetic anhydride (TFAA) at room temperature for 3 h gave tetraketo derivative **3a**, quantitatively. In the presence of water or by column chromatography on silica gel, **3a** readily turned back to **4a**. Other dehydrating agents such as molecular sieves 4A (MS4A) did not work well, resulting in unrecoverable adsorption on MS4A and/or decomposition. In the case of the reaction of **4a** with *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H₂O), removal of the MEM group took place to give hardly soluble **5a** in 50% yield (Scheme 1). This result is consistent with the report by Orfanopoulos et al. on the reactivity of the ketolactam derivative containing a sulfur atom in the rim of the opening shown in Figure 1c.¹⁴

Electrochemical properties of 1, 4a, and 3a were studied by cyclic voltammetry in ODCB. The first reduction potential of ketolactam 1 (-0.96 V vs. Fc/Fc⁺) was close to that of 4a having a bis(hemiketal) moiety (-0.98 V). On the other hand, the first reduction potential of 3a (-0.66 V) was anodically shifted by 0.30 V compared with that of 1, due to the two more carbonyl groups generated from the bis(hemiketal) moiety, which lead to significant decrease of the LUMO level. Bis(hemiketal) 4a showed interesting electrochemical behaviors. After the first scan from -0.23 to -2.3 V for 4a, the new redox wave was observed at -0.66 V, keeping appearance in the following scans. Since this reduction potential is the same value as 3a, tetraketo derivative 3a was probably generated from 4a after electrochemical reduction followed by elimination of a water molecule in EC mechanism.



Figure 4. Cyclic voltammograms of **1**, **4a**, and **3a** using 1 mM samples with 0.1 M n-Bu₄N·BF₄ in ODCB at a scan rate of 20 mV s⁻¹. (a) scans for the first redox waves and (b) full scans within the electrochemical window of the solvent.

In advance of experiments for H₂-insertion, opening-sizes of **3a** and **4a** were estimated by theoretical calculations at the M06-2X/3-21G level of theory. By comparison of the energies required for insertion of a hydrogen molecule, it was shown that **3a** has a larger opening than that of **4a** (total electronic energies; 23.5 kcal mol⁻¹ for **3a** and 58.4 kcal mol⁻¹ for **4a**). Thus, H₂-insertion experiments were conducted using both **3a** and **4a** as powders, as well as in ODCB solutions under high-pressure conditions of H₂. It was found that **3a** and **4a** were not stable over 100 °C and a part of them thermally changed into MEM-deprotected derivative **5a** and 2-

methoxyethylated derivative **6a** (2-methoxyethyl group supposedly came from the eliminated MEM group). However, H₂-insertion into **3a** was found to be possible above 150 °C, and that **4a** can be also used as a substrate for H₂-insertion probably due to *in-situ* dehydration to give **3a** at this temperature. Under the high-pressure conditions (165 atm, 150 °C, 24 h), formation of H₂@**3a** and H₂@**4a** were confirmed by ¹H NMR with the encapsulation ratio of 20–30% (Scheme 2). After purification by column chromatography on silica gel, H₂@**4a** was isolated in 48% yield.

Scheme 2. Synthesis of H₂@3a and H₂@4a



Finally, the author attempted to reduce the opening-size of **4a**. In 2011, Murata et al. reported a coupling reaction of two carbonyl groups on the rim of an open-cage C_{60} derivative by using triisopropyl phosphite.⁶ Under the similar conditions (at 100 °C in toluene with an excessive amount of triisopropyl phosphite), mono- and di- isopropylated **4a** were formed as by-products together with desired **1**. In contrast, when triphenylphosphine was used in place of triisopropyl phosphite, **4a** was converted to original **1** in 70% yield without considerable amounts of by-products. Thus, the author applied the same conditions to H₂@**4a** (16% encapsulation) in ODCB/toluene. The isolation of H₂@**1** was successful in 65% yield, maintaining the encapsulation ratio of the original 16%. This is the first example for a possible precursor of endohedral azafullerenes such as (H₂@C₅₉N)₂ and H₂@C₅₉NH. The proton signals corresponding to the hydrogen molecule encapsulated inside **1**, **3a**, and **4a** appeared at -4.63, -5.94, and -5.54 ppm, respectively, which reflects the structural changes of the outer cage.²²





Conclusion

In conclusion, the author synthesized a novel open-cage fullerene derivative having a 12membered ring opening (**4a**) as well as a 15-membered ring opening (**3a**). With regard to **4a**, the structure was clearly determined by X-ray analysis. H₂-insertion into these compounds was achieved by applying high pressure of H₂. Finally, the formation of H₂@**1** was successfully accomplished by the treatment of H₂@**4a** with triphenylphosphine. This compound is considered to be a precursor for endohedral azafullerenes encapsulating a hydrogen molecule, i.e., $(H_2@C_{59}N)_2$.

Experimental Section

General. Melting points were determined on a Yanaco MP-500D apparatus. The ¹H and ¹³C NMR measurements were carried out with a JEOL JNM ECA500 instrument and a JEOL JNM ECA600 instrument. The NMR chemical shifts were reported in ppm with reference to residual protons and carbons of CDCl₃ (δ 7.26 ppm in ¹H NMR, δ 77.0 ppm in ¹³C NMR), and DMSO- d_6 (δ 2.49 ppm in ¹H NMR). UV-vis absorption spectra were measured with a Shimadzu UV-3150 spectrometer. IR spectra were taken with a Shimadzu FTIR-8400S spectrometer. APCI mass spectra were measured on a Bruker micrOTOF-Q II. The high-performance liquid chromatography (HPLC) was performed with the use of a Cosmosil Buckyprep column (250 mm in length, 4.6 mm in inner diameter) and a 5PBB column (250 mm in length, 4.6 mm in inner diameter) for analytical purpose. Cyclic voltammetry was conducted on a BAS Electrochemical Analyzer ALS620C using a three-electrode cell with a glassy carbon working electrode, a platinum wire counter electrode, and a Ag/AgNO₃ reference electrode. The measurements were carried out in 1 mM solutions of substrate using 0.1 M tetrabutylammonium tetrafluoroborate (n-Bu₄N·BF₄) as a supporting electrolyte, and the potentials were calibrated with ferrocene used as an internal standard which was added after each measurement. C₆₀-N-MEM-ketolactam 1 was prepared according to the previous report.⁸ Fullerene C₆₀ was purchased from SES Research Co. 2-Methoxyethoxymethyl chloride, 18-crown-6, and trimethylamine N-oxide (TMAO) were purchased from Tokyo Chemical Industries Co., Ltd. Sodium azide, N-methylmorpholine N-oxide (NMO), trifluoroacetic anhydride (TFAA), and p-toluenesulfonic acid monohydrate (p-TsOH·H₂O) were purchased from Wako Pure Chemical Industries, Ltd.

Computational methods. All calculations were conducted with Gaussian 09 program packages. The structures were optimized at the M06-2X/3-21G, M06-2X/6-31G*, and B3LYP/6-31G* levels of theory without any symmetry assumptions. All structures including the stationary states and the transition states were confirmed by the frequency analyses at the same level of

theory.

Synthesis of C₆₀-*N*-MEM-bis(hemiketal) (4a). C₆₀-*N*-MEM-ketolactam 1 (200 mg, 234 μ mol) was dissolved in ODCB (80 mL) and heated to 50 °C for 0.5 h under Ar atmosphere. To the solution were added a 20-mL THF solution of NMO (54.8 mg, 468 μ mol) and distilled water (8.43 μ L, 468 μ mol). After 3 h, the solution was evaporated for removal of THF. The reaction mixture was purified by column chromatography (silica gel, toluene/acetone = 20/1 to 9/1). 4a was obtained as dark brown solids in 40% yield.

4a: mp >300 °C (decomposed into insoluble solids after heated at 300 °C for 0.5 h.); UVvis (toluene) λ_{max} (log ε) 330 (4.55), 396 (sh, 4.09), 437 (sh, 3.76), 640 (sh, 2.67), 703 (2.51); IR (KBr) $\nu = 1678$ (C=O, lactam), 1753 (C=O, ketone), 3160 cm⁻¹ (OH); ¹H NMR (500 MHz, CDCl₃) δ 7.98 (br s, 1H), 7.39 (br s, 1H), 6.65 (d, J = 10.9 Hz, 1H), 5.96 (d, J = 10.9 Hz, 1H), 4.16–4.06 (m, 2H), 3.68–3.59 (m, 2H), 3.36 (s, 3H); ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.63 (s, 1H), 9.46 (s, 1H), 6.22 (d, J = 10.9 Hz, 1H), 5.68 (d, J = 10.9 Hz, 1H), 3.80–3.76 (m, 2H), 3.47–3.41 (m, 2H), 3.18 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 194.91, 166.48, 151.90, 149.53, 149.50, 149.34, 149.16, 149.14, 148.76, 147.26, 146.89, 146.77, 146.29, 146.25, 146.22, 146.00, 145.94, 145.67, 145.58, 145.55, 145.47, 145.43, 145.09, 144.67, 144.62, 144.50, 144.14, 143.72, 143.47, 143.27, 143.12, 142.96, 142.58, 142.21, 142.14, 141.55, 140.17, 139.49, 139.02, 138.89, 138.84, 138.69, 138.40, 137.38, 136.39, 135.54, 134.63, 132.96, 132.63, 132.38, 132.06, 131.79, 130.49, 130.11, 109.25, 095.90, 81.58, 71.67, 70.01, 59.08 (four sp²-carbon signals were overlapped); HRMS (APCI, negative ionization mode), calcd for C₆₄H₁₁NO₇ (M⁻) 905.0536, found 905.0524. The fragment peak for **3a** was also observed (calcd for C₆₄H₉NO₆ (M⁻) 887.0435, found 887.0461).

Synthesis of C₆₀-*N*-MEM-tetraketone (3a). To a solution of 4a (20.0 mg, 22.1 μ mol) in dry CDCl₃ (6.25 mL) was added trifluoroacetic anhydride (62.5 μ L, 1.5165 g/mL, 451 μ mol) with checking the ¹H NMR during the reaction. After stirred for 3 h at room temperature, the solution was evaporated and pumped up for removal of trifluoroacetic anhydride and trifluoroacetic acid to give powdery 3a as black solids. The ¹H NMR spectrum showed a quantitative formation of 3a.

3a: mp >300 °C (decomposed into insoluble solids after heated at 300 °C for 0.5 h.); UVvis (toluene) λ_{max} (log ε) 324 (4.56), 441 (sh, 3.77); IR (KBr) v = 1690 (C=O, lactam), 1747 cm⁻¹ (C=O, ketone); ¹H NMR (500 MHz, CDCl₃) δ 6.65 (d, J = 10.9 Hz, 1H), 5.84 (d, J = 10.9 Hz, 1H), 4.02–4.00 (m, 2H), 3.75–3.65 (m, 2H), 3.41 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 188.15, 183.09, 182.86, 159.84, 154.38, 149.89, 149.83, 149.17, 148.95, 148.67, 147.66, 147.05, 146.82, 146.73, 146.43, 146.07, 145.91, 145.89, 145.68, 145.64, 145.44, 145.38, 145.29, 145.13, 145.07, 144.68, 144.64, 144.20, 143.83, 143.73, 143.68, 143.41, 143.05, 142.60, 142.58, 141.54, 141.46, 141.11, 141.01, 140.95, 140.48, 139.51, 139.50, 139.27, 138.98, 138.88, 138.76, 137.59, 137.28, 135.85, 135.08, 132.43, 131.53, 131.43, 131.05, 129.40, 127.97, 82.68, 71.42, 70.02, 58.92 (three sp²-carbon signals were overlapped); HRMS (APCI, negative ionization mode), calcd for $C_{64}H_9NO_6$ (M⁻) 887.0435, found 887.0440.

H₂-insertion: synthesis and isolation of **H**₂@4a. Powdery 3a (10 mg) wrapped in aluminum foil was put into a 50-mL autoclave. The autoclave was purged with H₂ gas 3 times and heated at 150 °C under a high-pressure of H₂ (165 atm) for 24 h. The ¹H NMR (500 MHz, CDCl₃) analysis of the resulting material showed formation of the following compounds; 55% of H₂@3a (H₂-encapsulation 29%), 13% of H₂@4a (H₂ 20%), 9% of H₂@5a (H₂ 41%), and 23% of H₂@6a (H₂ 33%, R' = 2-methoxyethyl). After several experiments, all materials were conbined and separated by silica gel column (toluene/acetone = 20/1 to 9/1 as eluent) to isolate H₂@4a in 48% yield.

H₂@**4a**: ¹H NMR (500 MHz, CDCl₃) δ 8.04 (br s, 1H), 7.53 (br s, 1H), 6.72 (d, *J* = 10.9 Hz, 1H), 6.02 (d, *J* = 10.9 Hz, 1H), 4.23–4.12 (m, 2H), 3.71–3.61 (m, 2H), 3.37 (s, 3H), -5.93 (s, 0.32H).

Closure of the opening: synthesis of H₂@1. H₂@4a (9.7 mg, 10.7 µmol, encapsulation ratio of 16%) and triphenylphosphine (28.1 mg, 107 µmol) were dissolved in the solvent mixture of degassed ODCB/toluene = 1/9 (6.78 mL). The resulting solution was heated at 100 °C for 6 h under Ar atmosphere. The reaction mixture was evaporated and then purified by column chromatography (silica gel, toluene/acetone = 20/1 to 9/1) to afford H₂@1 in 65% yield as black solids, maintaining the encapsulation ratio of 16%.

H₂@1: ¹H NMR (500 MHz, CDCl₃) δ 6.45 (d, *J* = 11.0 Hz, 1H), 6.06 (d, *J* = 11.0 Hz, 1H), 4.08–4.01 (m, 2H), 3.67–3.59 (m, 2H), 3.37 (s, 3H), -4.63 (s, 0.32H).

Deprotection of the MEM group: synthesis of C₆₀-*N*-**H**-**bis(hemiketal) (5a). 4a** (51.9 mg, 57.3 µmol) and *p*-toluenesulfonic acid monohydrate (164 mg, 862 µmol) were dissolved in ODCB (41.5 mL). The solution was heated at 150 °C. After 1 h, the reaction mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene/acetone = 9/1) to afford **5** in 50% yield as black solids.

5a: mp >300 °C (decomposed into insoluble solids after heated at 300 °C for 0.5 h.); UVvis (toluene) λ_{max} (log ε) 336 (4.43), 394 (sh, 4.02), 443 (sh, 3.63), 656 (sh, 2.52), 721 (2.41); IR (KBr) v = 1684 (C=O, lactam), 1740 (C=O, ketone), 3229 cm⁻¹ (OH); ¹H NMR (500 MHz, CDCl₃) δ 11.4 (s, 1H for NH), 9.55 (s, 1H for OH), 9.37 (s, 1H for OH); ¹³C NMR (sufficient data could not be obtained due to its poor solubility); HRMS (APCI, negative ionization mode), calcd for $C_{60}H_3NO_5$ (M⁻) 817.0017, found 817.0042. The fragment peak for the dehydrated compound was also observed (calcd for $C_{60}HNO_3$ (M⁻) 798.9911, found 798.9929).

Single crystal X-ray structure of 4a. Single crystals of 4a were grown from a *p*-xylene solution of 4a by slow evaporation of the solvent. Intensity data were collected at 103 K on a Rigaku Single Crystal CCD X-ray Diffractometer (Saturn 70 with MicroMax-007) with Mo Ka radiation ($\lambda = 0.70926$ Å). A total of 15546 reflections were measured at the maximum 2θ angle of 50.0°, of which 6906 were independent reflections ($R_{int} = 0.0626$). The structure was solved by direct methods (SHELXS-2013²³) and refined by the full-matrix least-squares on F^2 (SHELXL-2013²³). All non-hydrogen atoms were refined anisotropically. The hydrogen atoms of water molecule (H8A–H8B) were placed and restrained using DFIX instruction during the refinement. All hydrogen atoms, except for the water molecule (H8A–H8B), were placed using AFIX instructions. The crystal data are as follows: $C_{72}H_{23}NO_8$; FW = 1029.91, crystal size 0.15 × 0.10 × 0.05 mm³, Triclinic, P-1, a = 10.128(5) Å, b = 10.497(5) Å, c = 20.664(5) Å, $a = 85.270(5)^{\circ}$, $\beta = 77.477(5)^{\circ}$, $\gamma = 78.869(5)^{\circ}$, V = 2102.4(15) Å³, Z = 2, $D_c = 1.627$ g cm⁻³. The refinement converged to $R_1 = 0.1784$, $wR_2 = 0.4210$ ($I > 2\sigma(I)$), GOF = 1.111.



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Chapter 2

Synthesis and Properties of Endohedral Aza[60]fullerenes: H₂O@C₅₉N and H₂@C₅₉N as Their Dimers and Monomers

ABSTRACT: The macroscopic-scale syntheses of the first endohedral aza[60]fullerenes X@C₅₉N (X = H₂O, H₂) were achieved in two different ways: (1) synthesis from endohedral C₆₀ as a starting material and (2) molecular surgical synthesis from a C₅₉N precursor having a considerably small opening. In the neutral state of H₂O@C₅₉N, the author expected the H-bonding interaction or repulsive N–O interaction between entrapped H₂O and a nitrogen atom on the C₅₉N cage. However, an attractive electrostatic N–O interaction was suggested from the results of VT NMR, nuclear magnetic relaxation times (T_1 , T_2), and DFT calculations. Upon the reaction with acetone via cationic intermediate C₅₉N⁺, the difference in reaction rates was found between H₂O@C₅₉N and H₂@C₅₉N dimers (observed reaction rates: $k'(H_2O)/k'(H_2) = 1.74 \pm 0.16$). The DFT calculations showed thermal stabilization of C₅₉N⁺ by entrapped H₂O through the electrostatic interaction.



Endohedral [60]Fullerene

The First Endohedral Aza[60]fullerene

Introduction

Fullerene C₆₀ has an internal space with a diameter of ca. 3.7 Å, which is suitable for accommodating a small atom or molecule. Several endohedral fullerenes X@C₆₀ (X = atom(s) and molecule(s)) have been synthesized in macroscopic quantities. Examples of an entrapped molecule include not only neutral species such as He,¹ Ne,¹ H₂,² and H₂O³ but also radical or cationic species such as N⁴, P,⁵ or Li⁺.⁶ Recently, the nature of an H₂O molecule inside the C₆₀ cage has been investigated. In 2012, Levitt et al. observed an apparent *ortho-para* conversion of entrapped H₂O as well as a rapid isotropic rotation inside the restricted space at temperatures below 20 K.⁷ In 2014, Aoyagi et al. reported an increase of the dielectric permittivity for a single crystal of H₂O@C₆₀ upon cooling to 8 K.⁸

Contrastingly, reports on synthetic development of a heterofullerene family are quite limited. In 1990s, heterofullerenes $C_{59}Y$ (Y = B,⁹ N,¹⁰ Si,¹¹ Ir,¹² and Pt¹²) had been reported and their existence was confirmed only under mass spectroscopic conditions in gas-phase without any structural information except for computational predictions. Despite some substantial evidences for metallic endohedral heterofullerenes (vide infra), examples of effective syntheses are almost confined exclusively to azafullerenes $C_{n-1}N$ (n = 60, 70). In 1995, Wudl et al. reported the first open-cage C_{60} derivative which has a ketolactam moiety on the opening.¹³ In the same year, they achieved the synthesis of bis(aza[60]fullerenyl) ($C_{59}N$)₂ from the open-cage C_{60} derivative.¹⁴ They proposed that a MEM-substituted ketolactam moiety is a key structure to form a $C_{59}N$ skeleton.¹⁵ In the next year, Hirsch et al. succeeded in the synthesis of ($C_{59}N$)₂ by utilizing another method and also reported bis(aza[70]fullerenyl) ($C_{69}N$)₂.¹⁶ These discoveries provide useful methods to synthesize N-doped fullerenes in bulk quantities.

In recent years, combination of *endohedral fullerenes* and *heterofullerenes* has been attracting great attention. So far, these two types of chemical modifications have been almost-independently developed. The first evidence of endohedral heterofullerenes was represented by Smalley et al. in 1991.¹⁷ They revealed that the FT-ICR (Fourier transform ion cyclotron resonance) mass spectrum of a material, prepared from a boron/graphite composite rod, showed the existence of K@C₅₉B and K@C₅₈B₂ which were accidentally formed by contamination of KCl. In 1999, Akasaka et al. reported the synthesis of La@C₈₂(NCH₂Ph) by an addition reaction of benzyl azide to La@C₈₂ and found that the FAB (fast atom bombardment) mass spectrum of La@C₈₂(NCH₂Ph) exhibited a fragment peak corresponding to endohedral heterofullerene La@C₈₁N⁺.¹⁸ They also proved the existence of La₂@C₇₉N⁺ from the FAB mass fragmentations of La₂@C₈₀(NCH₂Ph). In 2008, Balch and Dorn et al. reported the prepared M₂@C₇₉N from cored graphite rods packed with Y₂O₃ or Tb₄O₇ by applying the Krätschmer-Huffman electric-arc method. The crystallographic data of Tb₂@C₇₉N cocrystallized with NiOEP (OEP:

octaethylporphyrin) conclusively excluded alternative possibilities of chemical formula such as Tb₂CN@C₇₈ and Tb₂C₂@C₇₇N. The crystallographic analysis of Tb₂@C₇₉N showed that there is no specific interaction between a nitrogen atom on the cage and a nickel atom of the NiOEP molecule which was located outside the cage. In the same manner, $Gd_2@C_{79}N$ was synthesized by the group in 2011 from graphite powder containing Gd_2O_3 with metallic Cu as a catalyst and isolated in ~0.05–0.1% as a relative yield ratio of $Gd_2@C_{79}N/C_{60}$.²⁰ In addition, Stevenson and Zhang et al. brought out an experimental evidence of trimetallic nitride endohedral aza[80]fullerene, La₃N@C₇₉N in 2009.²¹ They applied the CAPTEAR(chemically adjusting plasma temperature, energy, and reactivity)²² approach to a graphite rod packed with Sc₂O₃/La₂O₃. The MALDI (matrix assisted laser desorption ionization) mass spectrum of the resulting soot extract contained molecular ion peaks of C₆₀, C₇₀, Sc₃N@C₈₀, and LaSc₂N@C₈₀ as major components together with La₃N@C₇₉N as a minor component in spite of the absence of La₃N@C₈₀.

Of importance is to study properties and behaviors of a small molecule inside the cage of N-doped fullerene. Doping of a nitrogen atom on the carbon cage is expected to influence the nature of the inside of the cage. Thus, the author focused on the rational preparation of endohedral heterofullerenes using the C₅₉N cage. The author studied two possible routes to obtain sufficient amount of endohedral aza[60]fullerene X@C₅₉N: (1) synthesis from endohedral fullerene X@C₆₀ and (2) molecular surgical synthesis²³ which contains a size-expansion of an opening of C₅₉N precursor **2**, insertion of a guest molecule, and closing of the opening. Herein, the author reports these two synthetic pathways, characteristic NMR properties, and difference in reactivity between H₂O@C₅₉N and H₂@C₅₉N.

Results and Discussion

Synthesis of H₂O@C₅₉N dimers. In an analogous way for the preparation of $(C_{59}N)_{2,}^{14}$ the author obtained the first endohedral aza[60]fullerene from H₂O@C₆₀. The synthetic pathway was shown in Scheme 1. According to the reported procedures,^{3,24} H₂O@C₆₀ was synthesized from C₆₀ in 16% overall yield (6 steps). First, the 1,3-dipolar cycloaddition reaction of 2-methoxyethoxymethyl azide (MEM-N₃)^{13,25} was conducted using H₂O@C₆₀ with the encapsulation ratio of 28%. After chromatographic purification, H₂O@1 was obtained in 16% yield. Subsequently, the author synthesized H₂O@2 by photooxygenation¹³ of H₂O@1 under O₂ atmosphere. The encapsulation ratio of H₂O@C₅₉N was obtained as its dimers in 85% yield (Scheme 1). The overall yield is calculated to be 1.6% from C₆₀. Pure (H₂O@C₅₉N)₂ was also able to be synthesized from H₂O@C₆₀ with the encapsulation ratio of 100%.





^aEncapsulation ratio estimated by APCI mass, ^bEstimated by ¹H NMR, ^cApparent value for a mixture of dimers of $C_{59}N$ and $H_2@C_{59}N$.

Synthesis of $H_2@C_{59}N$ dimers. Open-cage fullerene derivatives have great potential as precursors not only for endohedral fullerenes but also for heterofullerenes. As described in Chapter 1,²⁶ the way to introduce a hydrogen molecule into the cage of a ketolactam derivative of

 C_{60} (2) has already developed. As shown in Scheme 2, an 11-membered-ring opening of 2 was firstly enlarged by the reaction with *N*-methylmorpholine *N*-oxide (NMO) to form a 12-membered-ring opening (3). Further enlargement was achieved by heating, which led to *in-situ* generation of a 15-membered-ring opening (4), and subsequently H₂-insertion was performed. Under the optimized conditions (150 °C, 165 atm, 24 h) (Table S1), the encapsulation ratio of H₂ reached to 33% which was confirmed by ¹H NMR spectrum. The opening of H₂@4 was partially closed to afford H₂@2 while retaining the ratio of entrapped H₂. It should be mentioned that H₂@2 is a possible precursor of endohedral aza[60]fullerene H₂@C₅₉N.²⁶ Finally, H₂@C₅₉N was obtained as its dimers by the reaction of H₂@2 (H₂: 33%) under the Wudl's conditions¹⁴ in 72% yield (Scheme 2). The overall yield was 2.2% from C₆₀, which is higher than that of H₂O@C₅₉N



Scheme 2. Synthesis of endohedral bis(aza[60]fullerenyl) encapsulating hydrogen molecule(s)

^aEncapsulation ratio estimated by ¹H NMR. ^bEstimated by APCI mass, ^cApparent value for a mixture of dimers of $C_{59}N$ and $H_2@C_{59}N$.

attempted H₂O-insertion using **3** as a host molecule (150 °C, 10,000 atm, 24 h in PhCl) but no encapsulation was observed by APCI mass and ¹H NMR spectra. This suggests that the 15-membered-ring opening of **4** is still small for H₂O to be inserted into the cage. Thus, the latter synthetic approach would be effective to gain endohedral aza[60]fullerene X@C₅₉N especially for encapsulating a molecule such as H₂ and He, which are smaller than H₂O.

Characterization by mass spectroscopy and HPLC analysis. The APCI mass spectrum in the positive ion mode of H₂O@C₅₉N dimers showed two signals corresponding to monomeric $C_{59}N^+$ (m/z 722.0011) and H₂O@C₅₉N⁺ (m/z 740.0161) generated by cleavage of the C(sp³)– C(sp³) bond connecting two C₅₉N cages, instead of signals of dimers (Figure 1a). Assuming the similar ionization abilities both of C₅₉N and H₂@C₅₉N, an apparent encapsulation ratio of H₂O@C₅₉N dimers was determined to be 28% from the mass intensities. This indicates no escape of entrapped H₂O in the course of the reactions. The fragment ion peaks of H₂@C₅₉N dimers were observed in the negative ion mode at m/z 722.0065 and 724.0166, respectively, corresponding to monomeric C₅₉N⁻ and H₂@C₅₉N⁻ with no signal of dimers (Figure 1b). An apparent encapsulation ratio of H₂@C₅₉N dimers was estimated to be 33% from the mass intensities.



Figure 1. APCI mass spectra of (a) $H_2O@C_{59}N$ dimers in positive ion mode and (b) $H_2@C_{59}N$ dimers in negative ion mode.

The HPLC (Buckyprep column, toluene, 50 °C) analysis clearly showed the dimeric configuration of X@C₅₉N in an analogous way for empty C₅₉N (retention time t_R : 7.10 min for HC₅₉N and 14.0 min for (C₅₉N)₂). It was also found that H₂O@C₅₉N dimers are comprised of three components (Figure 2(a)), corresponding to empty (C₅₉N)₂ ($t_R = 14.0$ min), singly-encapsulating H₂O@(C₅₉N)₂ ($t_R = 14.6$ min), and doubly-encapsulating (H₂O@C₅₉N)₂ ($t_R = 15.2$

min). These results were quite similar to those observed for H₂O@C₆₀ dimers.²⁷ The composition ratio of (C₅₉N)₂, H₂O@(C₅₉N)₂, and (H₂O@C₅₉N)₂ was determined to be 55:39:6 according to the peak area which is in close accordance with the value (53:40:7) predicted from the encapsulation ratio of precursor H₂O@**2** (H₂O: 27%). In a similar fashion of H₂O@C₅₉N dimers, H₂@C₅₉N dimers should contain (C₅₉N)₂, H₂@(C₅₉N)₂, and (H₂@C₅₉N)₂ with the production ratio of 45:44:11. However, only one peak was observed at the retention time of 14.2 min which is almost the same value of empty one ($t_R = 14.0$ min) but slightly broadened compared to empty one (Figures 2c,d). These results indicate that there is a stronger interaction between H₂O@C₅₉N dimers, probably due to the difference in van der Waals interaction between the C₅₉N cage and entrapped molecules.



Figure 2. HPLC (Buckyprep column, toluene, 50 °C) charts of (a) $H_2O@C_{59}N$ dimers, (b) pure $(H_2O@C_{59}N)_2$, (c) $H_2@C_{59}N$ dimers, and (d) $(C_{59}N)_2$.

Chemical shifts. The ¹H NMR signals of H₂O and H₂ inside the C₅₉N cage were shown in Figure 3, as well as residual H₂O and free H₂ in ODCB- d_4 at room temperature. The proton signals of X@C₅₉N dimers containing (X@C₅₉N)₂ and X@(C₅₉N)₂ were fully overlapped as a sharp singlet at δ –6.96 ppm for entrapped H₂O and δ –3.43 ppm for entrapped H₂, respectively (Figure

3(a)(b)). This shows that there is no detectable magnetic interaction between two entrapped molecules which were separated by the C₅₉N cage.²⁷ In comparison with residual H₂O (δ 1.37 ppm) and free H₂ (δ 4.54 ppm) in ODCB-*d*₄ (Figure 3(c)), entrapped molecule inside the C₅₉N cage displayed a significant upfield-shift by ca. –8 ppm, reflecting slightly larger shielding effects than C₆₀ (ca. –6 ppm).^{2,3} The theoretical calculations²⁸ of NICS(0) for each hexagon and pentagon were conducted for C₆₀, (C₅₉N)₂, and MeC₅₉N at the HF/6-311G(d,p)//B3LYP/6-31G(d) level of theory. The results suggested a decrease in anti-aromaticity of all five-membered rings of C₅₉N, especially in an N-containing five-membered ring: NICS(0) +8.17 for C₆₀, –2.26 to +6.97 for (C₅₉N)₂, and –3.28 to +6.82 for MeC₅₉N.



Figure 3. ¹H NMR spectra (500 MHz, ODCB- d_4 , r.t.) of (a) H₂O@C₅₉N dimers with a 55:39:6 ratio of (C₅₉N)₂, H₂O@(C₅₉N)₂, and (H₂O@C₅₉N)₂, (b) H₂@C₅₉N dimers with a 45:44:11 ratio of (C₅₉N)₂, H₂@(C₅₉N)₂, and (H₂@C₅₉N)₂, and (c) a 3:4 mixture of free H₂ and H₂O.

Variable temperature NMR (VT NMR) experiments. The temperature dependence of chemical shifts is primarily associated with the electronic structures surrounding the nuclei or the degree of inter- and intramolecular interactions.²⁹ The VT NMR measurements were performed at the temperature range of 260–360 K in ODCB- d_4 . The upper limit was set to 360 K so as to avoid the formation of C₅₉N radicals and lower limit was set to 260 K in consideration of the low solubility of dimeric C₅₉N as well as the melting point of ODCB- d_4 . The results showed that the temperature dependence of chemical shifts for entrapped H₂O is slightly stronger than that for entrapped H₂ (0.78 ppb/K for H₂@C₆₀, 0.75 ppb/K for H₂@C₅₉N dimers, 0.91 ppb/K for H₂O@C₆₀, and 1.35 ppb/K for H₂O@C₅₉N dimers) (Figure 4a). These chemical shift profiles most likely

arise from the size effect of entrapped molecules (H₂O molecule is somewhat larger than H₂ molecule and might be closer contact to the wall of the carbon cage.^{30a}). However, the remarkably larger shift for H₂O@C₅₉N dimers seems to be affected by an additional factor. To discuss in more detail, the difference in chemical shifts $\Delta\delta(X)$ was defined as the following equation and plotted as a function of temperature (Figure 4b).

$$\Delta\delta(\mathbf{X}) = \delta(\mathbf{X}@\mathbf{C}_{59}\mathbf{N} \text{ dimers}) - \delta(\mathbf{X}@\mathbf{C}_{60})$$

In contrast to the $|\Delta\delta(H_2)|$ values without temperature dependence, the $|\Delta\delta(H_2O)|$ values became larger with decreasing temperatures, indicating the stronger shielding effects for H₂O in C₅₉N (Figure 4b). This suggests the existence of a certain kind of intramolecular interactions which are dominant at lower temperatures and may restrict the rotational motion of entrapped H₂O. The author first considered the possibility of hydrogen-bonding (H-bonding) effect between entrapped H₂O and nitrogen atom on the C₅₉N cage. Generally, H-bonding results in downfield shift due to electron-deficient protons of H₂O (deshielding effect). However, the chemical shift of H₂O@C₅₉N dimers monotonically moved to upfield with decreasing temperatures. A plausible explanation for this phenomena is that the rotational motion of H₂O in C₅₉N is more restricted than that for H₂O@C₆₀ by weak intramolecular interaction different from hydrogen bonding effect. This might account for the temperature dependence of chemical shifts for H₂O@C₅₉N dimers.



Figure 4. (a) ¹H NMR spectra (500 MHz, ODCB-*d*₄, 260–360 K) of H₂O@C₆₀ and H₂O@C₅₉N dimers and (b) chemical shifts of X@C₅₉N dimers with reference to X@C₆₀, $\Delta\delta(X) = \delta(X@C_{59}N \text{ dimers}) - \delta(X@C_{60})$.

Relaxation times. The author found that the full widths at half maximum of the proton signals of entrapped H₂ were approximately 2.5 times larger than that of entrapped H₂O, regardless of the type of fullerene cages such as C_{60} and $C_{59}N$. In general, the line width of the NMR signal is inversely proportional to the relaxation time at which is required for nucleic spins excited by radio frequency pulse to return to thermal equilibrium. In this case, the relaxation time of entrapped H₂ inside the fullerene cage is known to be shorter than that of entrapped H₂O under the influence of the dipole-dipole interaction depending on a short distance between two protons.³¹ The mechanism of nuclear magnetic relaxation is commonly related to molecular motions. In order to gain further insights into dynamics of entrapped molecules, the author focused on the proton magnetic relaxation time for X@C₅₉N dimers and X@C₆₀.



Figure 5. The relaxation rates (500 MHz, ODCB- d_4 , 260–360 K), (a) $1/T_1$ for entrapped H₂, (b) $1/T_2$ for entrapped H₂, (c) $1/T_1$ for entrapped H₂O, and (d) $1/T_2$ for entrapped H₂O: blue points on a purple line; H₂@C₆₀, blue points on a green line; H₂@C₅₉N dimers, red points on a purple line; H₂O@C₆₀, red points on a green line; H₂O@C₅₉N dimers. The T_1 and T_2 values were measured by using inversion recovery method and the CPMG (Carr Purcell Meiboom Gill) method, respectively. These values are the average at least two measurements having errors within 5% and follow the general trend ($T_1 \ge T_2$) at each temperature.

The spin-lattice relaxation times T_1 of entrapped H₂ and H₂O were measured by the inversion recovery method in ODCB- d_4 at 300 K at a field strength of 500 MHz (Figures 5a,c). The T_1 values of H₂@C₆₀ and H₂O@C₆₀ were determined to be 0.101 and 0.615 s, respectively, being in good agreement with the reported value in toluene- d_8 at 300 K.³⁰ In the case of entrapped H₂, there was almost no difference between the T_1 values of H₂@C₆₀ (0.101 s) and H₂@C₅₉N dimers (0.113 s), suggesting the similar molecular motion of the hydrogen molecule inside each cage. For entrapped H₂O, the T_1 value of H₂O@C₅₉N dimers (1.72 s) is approximately three times longer than that for H₂O@C₆₀ (0.615 s) (Figure 5c). The contributions to the longer T_1 values may include the influences of (1) rotation of entrapped H₂O, (2) N····H₂O interaction, (3) rotation of fullerene cage, and (4) residual C₅₉N radical. Because of little difference of the T_1 values between H₂@C₆₀ and H₂@C₅₉N dimers, the latter contributions (3)(4) could be ruled out. However, the former contributions (1)(2) still remain.

To unveil the detailed relaxation mechanism and the dynamic behavior of entrapped molecules, spin-lattice relaxation times T_1 were measured over the temperature range of 260–360 K in a 20-K interval, as well as spin-spin relaxation times T_2 by applying the CPMG (Carr Purcell Meiboom Gill) method (Figures 5b,d). All of the T_2 values followed the general trend ($T_1 \ge T_2$). As mentioned in the literature,^{30a} the T_1 values of H₂@C₆₀ in toluene- d_8 vary depending on the spin relaxation at higher temperatures (>240 K). The spin-rotation interactions must be enhanced with increasing temperature and lead to rapid relaxation.^{30a} The temperature dependence of the T_2 values of $H_2@C_{60}$ were in agreement with this explanation (Figure 5b). In contrast, the T_2 relaxation of $H_2@C_{59}N$ dimers became rapid at lower temperatures. The origin of the rapid relaxation at lower temperatures is considered to be a dipole-dipole interaction which should be stronger with decreasing temperature according to the faster reorientation of the magnetic dipoles. Note that H₂@C₆₀ has maximum point $T_{1,max}$ in toluene- d_8 at 240 K and the major relaxation mechanism is a dipole-dipole interaction at temperatures below $T_{1,max}$ while a spin-rotation interaction becomes predominant at temperatures above $T_{1,max}$.^{30a} For H₂@C₅₉N dimers, the wider temperature range of the dipole-dipole interaction was found as a major relaxation mechanism and the maximum point of T_1 was not observed within the measured range. The possible reason is an additional dipolar interaction between nuclei ¹H (I = 1/2) of H₂ and ¹⁴N (I = 1)/¹⁵N (I = 1/2) in C₅₉N. On the other hand, for H₂O@C₆₀, the temperature dependence of T_1 and T_2 values exhibited a typical spin-rotation mechanism in an analogous way for $H_2@C_{60}$. However, $H_2O@C_{59}N$ dimers have three-times longer T_1 values compared to $H_2O@C_{60}$ probably due to the restrained rotational molecular motion (Figure 5c). Though the major relaxation mechanism for H₂O@C₅₉N dimers seems to be the spin-rotation interaction, such interaction cannot be explained from the T_2 values because its temperature dependence was totally different from that for H₂O@C₆₀ whose magnetic relaxation mainly relies on the spin-rotation interaction (Figure 5d).

According to the computational results of the electrostatic potentials for model compound HC₅₉N (MP2/6-31G(d,p)//M06-2X/6-31G(d,p)) (Figure 6a), unexpectedly, the positive charge was distributed on the nitrogen atom on the inner surface of the HC₅₉N cage whereas the nitrogen atom was negatively-charged on the outer surface. Additionally, the author found two conformers of H₂O@HC₅₉N having different molecular orientations of H₂O at the M06-2X/6-31G(d,p) level of theory (Figure 6b). The most stable conformer adopts a structure where the positive potential, located on the backside of the nitrogen atom, should be canceled out by the negative charge of lone pair electrons of the oxygen atom in entrapped H₂O. The rotational barrier of entrapped H₂O inside the HC₅₉N cage was also determined to be 1.46 kcal/mol. These results suggest the electrostatic interaction between entrapped H₂O and the nitrogen atom. For the above reasons, the plausible relaxation mechanism for H₂O@C₅₉N dimers is considered as follows: the rotational motion restricted by the N–O interaction would reduce the effect of the spin-rotation interaction and the magnetic energy coherently-induced on the nuclei should move to the C₅₉N cage via electrostatic N–O interaction and then further energy-transfer would occur from the cage to the lattice.



Figure 6. DFT calculations: (a) electrostatic potentials of $H_2O@HC_{59}N$ (MP2/6-31G(d,p)//M06-2X/6-31G(d,p)) and (b) relative energies for two conformers of $H_2O@HC_{59}N$ and TS (M06-2X/6-31G(d,p)).

Herein, the author discusses again the DFT calculations which suggest the positivelycharged nitrogen atom on the inner surface of HC₅₉N. The author further calculated electrostatic potentials for additional related compounds: the simplest amine (DABCO) and amine embedded into the curved π -conjugated system (diazabuckybowl and pentabenzoazacorannulene³²) (Figure S1). According to the calculations, DABCO has negatively-charged nitrogen atom on the outer surface due to naked lone pair electrons. However, the positive potential was also found inside the caged structure of DABCO. Diazabuckybowl exhibited a similar potential map despite reduced sp³-amine character which was induced by the curved π -conjugation. In the case of pentabenzoazacorannulene, the positive charge was suggested to be distributed on the backside of the nitrogen atom in an analogous way for HC₅₉N even though negative potential was not found on the outer surface based on the sp²-pyrrol character. In all examples above, however, it would be difficult to experimentally discriminate this bilateral potential character. As mentioned above, the unique molecular system, H₂O@RC₅₉N, provided an elusive evidence of the positive potential of backside of the nitrogen atom.

Reactivity. For elucidation of the difference in reactivity between $H_2O@C_{59}N$ and $H_2@C_{59}N$ dimers, the author made a choice of the known reaction for $(C_{59}N)_2$ with acetone under oxidative conditions.³³ The reaction mechanism was explained as follows: thermal dissociation of $(C_{59}N)_2$ to give two $C_{59}N$ radicals, oxidation of $C_{59}N$ radicals to $C_{59}N^+$ by O_2 , and electrophilic attack to enolizable ketones to afford Mannich bases involving a $C_{59}N$ sphere ($CH_3COCH_2C_{59}N$, **5**). If there is an undisputed interaction between polar H_2O and cationic center of $C_{59}N^+$, the reactivity would be different between $H_2@C_{59}N$ and $H_2O@C_{59}N$ due to the stabilization of $C_{59}N^+$ by entrapped H_2O . Recently, regarding an enantiospecific *cis-trans* isomerization of chiral fulleropyrrolidines, Martín et al. reported that anionic intermediate $H_2O@RC_{60}^-$ should be stabilized by the intramolecular H-bonding induced by entrapped H_2O inside the C_{60} cage.³⁴

First, the author conducted the reaction using H₂O@C₃₉N and H₂@C₅₉N dimers, separately (Scheme 3). The reaction progress was monitored by HPLC and it has almost completed within 20 min at 150 °C. After chromatographic purification, X@5 was obtained in the similar yields both for H₂O and H₂. The proton signals of X@5 in ODCB-*d*₄ appeared at δ –7.34 ppm for H₂O and –3.87 ppm for H₂, which were distinguishable from parent X@C₃₉N dimers. For the competition experiment, a mixture of X@C₅₉N dimers was prepared with a 1: 1 encapsulation ratio of H₂O and H₂ (H₂O@C₅₉N/H₂@C₅₉N/C₅₉N = 22/22/56). The encapsulation ratio was determined by ¹H NMR spectrum (Figure 7b, **A**). The reaction was conducted at 100 °C in ODCB-*d*₄ and the reaction progress was monitored by ¹H NMR. The results were shown in Figure 7. After 0.5 h (point **B**), the molar ratio of starting material to target compound is ca. 2:1 for H₂@C₅₉N dimers and ca. 1:2 for H₂O@C₅₉N dimers, indicating the faster reaction for H₂O@C₅₉N dimers.

Scheme 3. Synthesis of 1-Azafullereneylpropnan-2-one Encapsulating a Small Molecule, X@5 $(X = H_2O, H_2)$



^aEstimated by APCI MS, ^bEstimated by ¹H NMR.

The keto form of acetone is more stable than the enol form under acidic conditions. However, during the reaction, the enol form of acetone should be constantly formed in the ketoenol tautomeric equilibrium while the enol form is consumed to afford Mannich base X@5. Therefore, if the concentration of enolizable acetone is enough high compared to X@C₅₉N dimers and X@C₅₉N⁺ is so reactive that the electrophilic addition to the enol form of acetone promptly takes place, this reaction can be assumed as pseudo-first-order reaction in both cases where X@C₅₉N dimers are in pre-equilibrium with their radicals and where the changes in concentration of X@C₅₉N radicals is much smaller than the formation rate of X@C₅₉N⁺. Since the reaction rate should heavily depend on the step of C₅₉N⁺ formation as demonstrated in the previous report,^{24a} one can roughly estimate the apparent rate constants *k'* under the assumption of pseudo-first-order reaction expressed as follows:

- dC/dt = k'C (*C* = [X@C₅₉N dimers]).

The concentrations of X@C₅₉N dimers and X@RC₅₉N were determined by the integration of proton signals for entrapped molecules. The concentration of empty adduct **5** was calculated by subtracting the concentration of X@RC₅₉N from the concentration of acetone-adducts determined from integration of overlapped proton signals of α -H on C1 of oxopropyl group (The labeling number was shown in Scheme 3). Using these values, the concentration of empty (C₅₉N)₂ was also estimated. According to the rate law, the pseudo-first-order rate constant k' (10⁴ s⁻¹) was obtained from the slope of plots as ln (C/C_0) versus reaction time (Figure 8b): 7.50 ± 0.33 for H₂O@C₅₉N dimers, 4.32 ± 0.35 for H₂@C₅₉N dimers, and 4.06 ± 0.31 for (C₅₉N)₂. The rate constant k' for H₂O@C₅₉N dimers was found to be absolutely larger than that for (C₅₉N)₂ (by 1.85 ± 0.16) even though there was little practical difference between H₂@C₅₉N dimers and empty (C₅₉N)₂ (k'(H₂)/k'(empty) = 1.06 ± 0.12).



Figure 7. Competition experiment of X@C₅₉N dimers (X = H₂O, H₂) with acetone at 100 °C in O₂ atmosphere under acidic conditions: (a) changes in conversion against reaction time and (b) selected ¹H NMR spectra (500 MHz, ODCB-*d*₄, r.t.) at each point of **A**–**D**. All values of conversion were determined by integrated ¹H NMR signals of three measurements. The four singlet signals correspond to H₂@C₅₉N dimers (-3.43 ppm), H₂@**5** (-3.87 ppm), H₂O@C₅₉N dimers (-6.96 ppm), and H₂O@**5** (-7.34 ppm), respectively.



Figure 8. Plots of ln (C/C_0) versus reaction time, where *C* is the concentration of X@C₅₉N dimers, C_0 is the initial concentration of X@C₅₉N dimers, *t* is the reaction time, R^2 is the coefficient of determination, R_f^2 is the adjusted R^2 , and k' is the pseudo-first-order rate constant: red for H₂O@C₅₉N dimers, blue for H₂@C₅₉N dimers, and gray for (C₅₉N)₂.

Theoretical calculations. The author estimated the stabilization energies for trapping H₂O inside the cage of C_{60} , MeC_{60}^- , MeC_{60}^+ , $HC_{59}N$, $C_{59}N^-$, and $C_{59}N^+$ at the MP2/6-31G(d,p)//M06-2X/6-31G(d,p) level of theory with the BSSE (basis set superposition error) correction (Table S2 and Figure S2). For all species except for C₆₀, two conformers of a water molecule were found. Upon seeing the most stable conformers, the relative stabilization energy was calculated to be -7.3 kcal/mol for H₂O@MeC₆₀, which was larger than that for C₆₀ (-6.4 kcal/mol). The extra stabilization may come from the effect of H-bonding between anionic center of MeC₆₀⁻ and H₂O as reported by Martín et al.³³ For N-doped fullerene, H₂O@HC₅₉N has the stabilization energy of -7.0 kcal/mol which was almost the same value as H₂O@MeC₆₀⁻ (isoelectronic carbon cage). Thus, it is no wonder even if some kind of interaction exist in $H_2O@HC_{59}N$. This result supports the N-O interaction anticipated from relaxation time measurements and electrostatic potential maps. For $H_2O@C_{59}N^+$ with the largest stabilization energy (-8.8 kcal/mol), there should be a possible interaction between cationic center of $C_{59}N^+$ and entrapped H₂O (Figure 9). This may cause the difference in reactivity upon the reaction of $X@C_{59}N$ dimers and acetone. In conclusion, the electrostatic interaction was suggested both in neutral state (H₂O@HC₅₉N) and in cationic state $(H_2O@C_{59}N^+)$ from experimental and theoretical points of view.



Figure 9. The most stable conformers suggested by DFT calculations (Table S2 and Figure S2): (a) $H_2O@C_{59}N^+$ having both carbenium and iminium cation characters and (b) an analogous structure of neutral $H_2O@HC_{59}N$. The caged bonds were partially omitted for clarity.

Conclusion

In summary, the author developed methods for the synthesis of endohedral aza[60]fullerenes and obtained $X@C_{59}N$ (X = H₂O and H₂) as their dimers and monomers in several tens of milligrams quantities. The author showed that endohedral heterofullerenes have unprecedented significance as a unique molecular system. The ¹H NMR spectrum of X@ $C_{59}N$ dimers consisting of $(C_{59}N)_2$, $X@(C_{59}N)_2$, and $(X@C_{59}N)_2$ showed that there is no detectable magnetic interaction between two entrapped molecules separated by each cage and that the inner space of the $C_{59}N$ cage is more shielded than that of C_{60} . From the HPLC analyses, $(C_{59}N)_2$, $H_2O@(C_{59}N)_2$, and $(H_2O@C_{59}N)_2$ were found to be distinguishable from each other in contrast to $H_2@C_{59}N$ dimers. The T_1 measurements demonstrated that $H_2O@C_{59}N$ dimers have a three-fold value compared to that of $H_2O@C_{60}$. The author revealed the different relaxation mechanisms among X@C₆₀ and X@RC₅₉N. The DFT calculations suggested the possible attractive electrostatic interaction between a nitrogen atom on the $C_{59}N$ cage and entrapped H₂O with a rotational energy barrier of H₂O inside the C₅₉N cage (1.46 kcal/mol). This might drastically make an impact toward the longer T_1 value for H₂O@C₅₉N dimers. The author provided an experimental evidence for the existence of positive potential which is located on the backside of nitrogen atom. From the competition experiment of X@C59N dimers and acetone under oxidative conditions, the difference in reactivity between $H_2O@C_{59}N$ and $H_2@C_{59}N$ dimers was observed $(k'(H_2O)/k'(H_2))$ = 1.74 ± 0.16). This result was in accordance with the prediction from the DFT calculations that $C_{59}N^+$ should be stabilized by entrapped H₂O via electrostatic interaction.

Experimental Section

General. The ¹H and ¹³C NMR measurements were carried out at room temperature with a JEOL JNM ECA500 instrument. The NMR chemical shifts were reported in ppm with reference to residual protons and carbons of CDCl₃ (δ 7.26 ppm in ¹H NMR, δ 77.0 ppm in ¹³C NMR) and

ODCB- d_4 (δ 7.20 ppm in ¹H NMR, δ 132.35 ppm in ¹³C NMR). The relaxation time measurements were conducted at a field strength of 500 MHz at 260–360 K in each interval of 20 K using sample solutions in ODCB- d_4 . The 90° pulse widths were determined using single pulse sequence prior to relaxation time measurements. The inversion recovery method (180°- τ -90° sequence) was applied to measure spin-lattice relaxation time T_1 . The CPMG (Carr Purcell Meiboom Gill) method was applied to measure spin-spin relaxation time T_2 . APCI mass spectra were measured on a Bruker micrOTOF-Q II. The high-performance liquid chromatography (HPLC) was performed with the use of a Cosmosil Buckyprep column (250 mm in length, 4.6 mm in inner diameter) for analytical purpose. Fullerene C₆₀ was purchased from SES Research Co. 2-Methoxyethoxymethyl chloride and 18-crown-6 were purchased from Tokyo Chemical Industries Co., Ltd. Sodium azide, *N*-methylmorpholine *N*-oxide (NMO), *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H₂O), and acetone were purchased from Wako Pure Chemical Industries, Ltd. Triphenylphosphine was purchased from Nacalai Tesque, INC. ODCB was purchased from Sigma-Aldrich Co. LLC.

Computational methods. All calculations were conducted with Gaussian 09 program packages. The structures were optimized at the B3LYP/6-31G(d) or M06-2X/6-31G(d,p) level of theory without any symmetry assumptions. The MP2 calculations were performed using the geometries optimized at the M06-2X/6-31G(d,p) level of theory. All structures including the stationary states and the transition state were confirmed by the frequency analyses at the same level of theory.

Synthesis of MEM-N₃. 18-Crown-6 (0.700 g, 2.65 µmol, 3.00 mol%) and NaN₃ (17.2 g, 265 mmol, 3.00 equiv) were suspended in dry THF (150 mL) and stirred for 0.5 h at room temperature. MEM-Cl (10.0 mL, $\rho = 1.10$ g/mL, 88.3 mmol, 0.589 M) was added slowly. After 25 h, the resulting mixture was filtered and evaporated under reduced pressure for removal of THF. The concentrated solution was diluted with diethyl ether (15 mL), washed with brine (10 mL × 3), and dried over anhydrous Na₂SO₄. After filtration, the solvent was evaporated. MEM-N₃ was obtained in 90% yield as colorless oil (10.6 g, 79.6 mmol, 98% purity). The assignments were conducted according to the literature.³⁵



MEM-N₃: ¹H NMR (500 MHz, CDCl₃) δ 4.68 (s, 1H), 3.75–3.73 (m, 2H), 3.57–3.55 (m, 2H), 3.37 (s, 3H).
Synthesis of C₆₀-*N*-**MEM (1).** C₆₀ (5.00 g, 6.94 mmol) was dissolved in ODCB (SPR grade, 500 mL, 13.9 mM) and the resulting solution was degassed through five vacuum-Ar cycles. MEM-N₃ (1.86 g, 13.9 mmol, 2.00 equiv) was added to the solution. After stirred at 60 °C for 20 h, the reaction mixture was heated up to reflux for 3 h under Ar stream. The resulting mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene to toluene/ethyl acetate, 4:1). Unreacted C₆₀ (2.15 g, 2.98 mmol, 43%) was eluted first, followed in order by **1** (1.07 g, 1.29 mmol, 19%), **6** (0.149 g, 0.181 mmol, 2.6%), and **7** (trace). The assignments were conducted according to the literature.³⁵



1: ¹H NMR (500 MHz, CDCl₃/CS₂ (2:1)) δ 5.34 (s, 2H), 4.25–4.23 (m, 2H), 3.78–3.76 (m, 2H), 3.48 (s, 3H); HRMS (APCI, negative ion mode) calcd for C₆₄H₉NO₂ (M⁻) 823.0639, found 823.0660.

6: ¹H NMR (500 MHz, CDCl₃/CS₂ (2:1)) δ 5.26 (s, 2H), 4.35–4.33 (m, 2H), 3.84–3.82 (m, 2H), 3.51 (s, 3H); ¹³C NMR (126 MHz, ODCB-*d*₄) 144.91, 144.85, 144.40, 144.28, 143.89, 143.52, 142.89, 142.80, 142.60, 141.99, 141.88, 140.55, 140.02, 83.35, 82.49, 72.31, 69.59, 58.75 (The sum of carbon signals must be 21 in theory. Observed 18. Three sp² carbon signals are overlapped.); HRMS (APCI, negative ion mode) calcd for C₆₄H₉NO₂ (M⁻) 823.0639, found 823.0670.

7: ¹H NMR (500 MHz, CDCl₃/CS₂ (4:1)) δ 5.61 (d, *J* = 9.45 Hz, 2H), 5.47 (d, *J* = 9.45 Hz, 2H), 4.24–4.20 (m, 2H), 4.07–4.03 (m, 4H), 3.76 (t, *J* = 4.58 Hz, 2H), 3.48 (s, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 158.63, 147.54, 146.95, 145.46, 145.28, 144.88, 144.76, 144.53, 144.49, 144.13, 144.07, 143.91, 143.69, 143.51, 143.39, 142.72, 142.29, 141.75, 141.63, 140.27, 139.54, 139.36, 139.14, 138.23, 136.55, 135.36, 134.61, 132.97, 132.87, 130.38, 83.79, 71.91, 68.26, 59.13 (The sum of carbon signals must be 36 in theory. Observed 34. Two sp² carbon signals are overlapped.); HRMS (APCI, negative ion mode) calcd for C₆₈H₁₈N₂O₄ (M⁻) 926.1272, found 926.1290.

Synthesis of C₆₀-N-MEM-ketolactam (2). C₆₀-N-MEM 1 (587 mg, 713 μ mol) was dissolved in CS₂/CCl₄ (1:1, 466 mL, 1.53 mM). The resulting solution was bubbled with O₂ for 0.5 h and subsequently irradiated with LED. The reaction progress was monitored by HPLC. After 44 h at room temperature, the reaction was almost completed. The resulting solution was

evaporated and purified by column chromatography (silica gel, toluene : ethyl acetate, 9:1) to give 2 (585 mg, 684 µmol) in 96% yield as a black powder. The assignments were conducted according to the literature.³⁵

2: ¹H NMR (500 MHz, CDCl₃) δ 6.44 (d, J = 10.9 Hz, 1H), 6.05 (d, J = 10.9 Hz, 1H), 4.08–4.00 (m, 2H), 3.67–3.57 (m, 2H), 3.36 (s, 3H).

Synthesis of $(C_{59}N)_2$. C₆₀-*N*-MEM-ketolactam **2** (50.0 mg, 58.4 µmol) was dissolved in ODCB (23.3 mL, 2.51 mM) and the resulting solution was degassed through three vacuum-Ar cycles. *p*-Toluenesulfonic acid monohydrate (222 mg, 1.17 mmol, 20.0 equiv) was added and heated at 150 °C for 1.5 h. The reaction mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene) to give $(C_{59}N)_2$ (35.6 mg, 24.6 µmol) in 84% yield as a black powder. The assignments were conducted according to the literature.³⁶

 $(C_{59}N)_2$: ¹³C NMR (126 MHz, ODCB- d_4) δ 156.01, 148.59, 147.86, 147.72, 147.57, 147.44, 146.70, 146.63, 146.34, 145.88, 145.85, 145.21, 145.03, 144.89, 144.69, 144.39, 144.02, 143.29, 142.89, 142.23, 141.88, 141.75, 141.39, 141.06, 140.98, 140.13, 137.92, 136.35, 124.93, 90.24 (One sp² carbon signal was overlapped. The sum of carbon signals must be 31 in theory.).

Synthesis of H₂O@C₆₀-*N*-MEM (H₂O@1). H₂O@C₆₀ (encapsulation ratio: 100% estimated by MS) was prepared according to the literatures.^{3,24} H₂O@C₆₀ (124 mg, 168 µmol) was dissolved in ODCB (SPR grade, 14.1 mL, 11.9 mM) and the resulting solution was degassed through three vacuum-Ar cycles. MEM-N₃ (47.6 mg, 336 µmol, 2.00 equiv) was added to the solution. After stirred at 60 °C for 20 h, the reaction mixture was heated up to reflux for 3 h under Ar stream. The resulting mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene to toluene/ethyl acetate). Unreacted H₂O@C₆₀ (41.0 mg, 55.5 µmol, 33%) was eluted first, followed in order by H₂O@1 (21.8 g, 25.9 µmol, 15%), H₂O@6 (3.7 mg, 4.4 µmol, 2.6%), and H₂O@7 (11.4 mg, 12.1 µmol, 7.2%).



H₂O@1: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 5.34 (s, 2H), 4.25–4.23 (m, 2H), 3.78– 3.76 (m, 2H), 3.48 (s, 3H), -5.36 (s, 2H); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 147.69, 144.82, 144.70, 144.62, 144.45, 144.30, 144.13, 143.92, 143.85, 143.74, 143.56, 143.41, 143.37, 143.22, 143.07, 142.95, 142.88, 142.70, 142.60, 141.66, 140.75, 140.48, 139.38, 138.49, 138.36, 138.20,

137.85, 136.80, 136.32, 135.89, 133.38, 83.85, 71.92, 68.24, 58.91 (One sp² carbon signal was supposedly overlapped at 144.30. The sum of carbon signals must be 36 in theory.); HRMS (APCI, negative ion mode) calcd for $C_{64}H_{11}NO_3$ (M⁻) 841.0739, found 841.0750.

H₂O@**6**: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 5.26 (s, 3H), 4.34–4.33 (m, 2H), 3.83– 3.81 (m, 2H), 3.51 (s, 3H), -6.40 (s, 2H); ¹H NMR (500 MHz, ODCB- d_4) δ 5.18 (s, 3H), 4.34– 4.32 (m, 2H), 3.77–3.75 (m, 2H), 3.41 (s, 3H), -6.54 (s, 2H); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 145.92, 145.04, 144.60, 144.49, 144.47, 144.45, 144.03, 143.67, 143.08, 142.98, 142.76, 142.11, 142.01, 140.75, 140.17, 83.07, 82.27, 71.96, 69.35, 58.92 (The sum of carbon signals must be 21 in theory. Observed 20. One sp² carbon signal is overlapped.); ¹³C NMR (126 MHz, ODCB- d_4) δ 145.77, 144.98, 144.53, 144.49, 144.42, 144.39, 144.00, 143.61, 143.00, 142.90, 142.69, 142.11, 141.95, 140.63, 140.18, 83.44, 82.50, 72.31, 69.59, 58.75 (Observed 20. One sp² carbon signal is overlapped.); HRMS (APCI, negative ion mode) calcd for C₆₄H₁₁NO₃ (M⁻) 841.0739, found 841.0763.

H₂O@**7**: ¹H NMR (500 MHz, CDCl₃) δ 5.61 (d, J = 9.74 Hz, 2H), 5.48 (d, J = 9.74 Hz, 2H), 4.25–4.21 (m, 2H), 4.07–4.03 (m, 4H), 3.76 (t, J = 4.59 Hz, 2H), 3.48 (s, 6H), -5.82 (s, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 159.09, 147.57, 147.08, 145.84, 145.53, 145.19, 144.93, 144.90, 144.83, 144.45, 144.36, 144.02, 143.67, 142.85, 142.50, 142.01, 141.73, 140.24, 139.74, 139.39, 138.36, 136.58, 135.52, 134.94, 132.93, 130.46, 83.87, 71.95, 68.33, 59.19 (The sum of carbon signals must be 36 in theory. Observed 30. Six sp² carbon signals are overlapped.); HRMS (APCI, negative ion mode) calcd for C₆₈H₂₀N₂O₅ (M⁻) 944.1372, found 944.1407.

Synthesis of H₂O@C₆₀-*N*-MEM-ketolactam (H₂O@2). H₂O@1 (40.6 mg, 48.2 μ mol, encapsulation ratio: 100% estimated by MS and ¹H NMR) was dissolved in CS₂/CCl₄ (1:1, 31.6 mL, 1.53 mM). The resulting solution was bubbled with O₂ for 0.5 h and subsequently irradiated with LED. The reaction progress was monitored by HPLC. After 50 h at room temperature, the reaction was almost completed. The resulting solution was evaporated to give H₂O@2 (36.6 mg, 41.9 μ mol) in 87% yield as a black powder.

H₂O@**2**: ¹H NMR (500 MHz, CDCl₃) δ 6.44 (d, J = 10.9 Hz, 1H), 6.05 (d, J = 10.9 Hz, 1H), 4.08–4.00 (m, 2H), 3.67–3.57 (m, 2H), 3.36 (s, 3H), -7.96 (s, 2H); ¹³C NMR (126 MHz, CDCl₃ : CS₂ = 1 : 1) δ 198.52, 163.53, 150.26, 149.56, 147.92, 147.50, 147.10, 146.84, 146.72, 146.70, 146.52, 146.50, 146.27, 146.16, 146.02, 145.89, 145.53, 145.43, 145.26, 145.02, 144.93, 144.74, 144.48, 144.33, 144.28, 144.22, 144.13, 144.01, 143.95, 143.70, 143.51, 143.47, 142.70, 141.67, 141.34, 141.23, 140.47, 140.44, 139.72, 139.56, 139.41, 139.35, 138.71, 138.05, 136.65, 136.16, 135.98, 135.80, 135.73, 134.00, 133.96, 133.01, 132.38, 132.05, 127.90, 80.57, 71.55, 69.98, 59.09 (Four sp² carbon signals were overlapped.); HRMS (APCI, negative ion mode) calcd for C₆₄H₁₁NO₅ (M⁻) 873.0637, found 873.0643.

Synthesis of H₂O@C₅₉N dimers. H₂O@2 (25.2 mg, 29.4 µmol, encapsulation ratio: 27%, estimated by ¹H NMR) was prepared in 12% yield (2 steps) from H₂O@C₆₀ (186 mg, 256 µmol, encapsulation ratio: 28% estimated by MS). H₂O@2 was dissolved in ODCB (11.7 mL, 2.51 mM) and the resulting solution was degassed through five vacuum-Ar cycles. *p*-Toluenesulfonic acid monohydrate (112 mg, 588 µmol, 20.0 equiv) was added and heated at 150 °C for 1.5 h. The reaction mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene) to give H₂O@C₅₉N dimers (18.1 mg, 12.5 µmol) in 85% yield as a black powder. The apparent encapsulation ratio was determined to be 28% by APCI MS. This shows no escape of entrapped H₂O. The composition ratio of (C₅₉N)₂, H₂O@(C₅₉N)₂, and (H₂O@C₅₉N)₂ was determined to be 55:39:6 by HPLC analysis.

H₂O@C₅₉N dimers consisting of (C₅₉N)₂, H₂O@(C₅₉N)₂, and (H₂O@C₅₉N)₂: ¹H NMR (500 MHz, ODCB- d_4) δ –6.96 (singlet); ¹³C NMR (126 MHz, ODCB- d_4) δ <u>156.62</u>, 156.01, <u>149.16</u>, 148.59, <u>147.93</u>, 147.85, <u>147.79</u>, <u>147.74</u>, 147.71, <u>147.69</u>, 147.57, 147.44, 146.69, <u>146.65</u>, 146.63, 146.34, <u>146.31</u>, <u>145.99</u>, 145.88, <u>145.85</u>, 145.76, 145.21, <u>145.15</u>, 145.11, 145.03, 144.89, <u>144.85</u>, <u>144.79</u>, 144.68, <u>144.38</u>, <u>144.05</u>, 144.02, <u>143.44</u>, 143.29, 142.88, <u>142.82</u>, 142.22, <u>142.13</u>, <u>141.91</u>, 141.88, <u>141.83</u>, 141.75, <u>141.46</u>, 141.38, <u>141.20</u>, <u>141.06</u>, 140.97, 140.12, 140.06, <u>138.40</u>, 137.91, <u>136.77</u>, 136.35, 132.35, <u>125.29</u>, 124.93, 90.24 (The carbon signals of H₂O@C₅₉N cage were partially separated from that of C₅₉N cage. Carbon signals for H₂O@C₅₉N were represented with underline.); HRMS (APCI, positive ion mode) calcd for C₅₉N (M⁺) 722.0025, found 722.0011 and calcd for C₅₉H₂NO (M⁺) 740.0131, found 740.0161 (The parent peak corresponding to dimer was not observed.).

 $H_2O@2$ (36.6 mg, 42.3 µmol, encapsulation ratio: 100%, estimated by ¹H NMR and APCI MS) was dissolved in ODCB (16.85 mL, 2.51 mM) and the resulting solution was degassed through three vacuum-Ar cycles. *p*-Toluenesulfonic acid monohydrate (161 mg, 846 µmol, 20.0 equiv) was added and heated at 150 °C for 1.5 h. The reaction mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene) to give ($H_2O@C_{59}N$)₂ (21.8 mg, 14.9 µmol) in 71% yield as a black powder.

 $(H_2O@C_{59}N)_2$: ¹H NMR (500 MHz, ODCB-*d*₄) δ –6.95 (singlet); ¹³C NMR (126 MHz, ODCB-*d*₄) δ 156.63, 149.18, 147.93, 147.81, 147.75, 147.70, 146.66, 146.31, 146.00, 145.85, 145.82, 145.16, 144.85, 144.79, 144.36, 144.06, 143.44, 142.83, 142.14, 141.91, 141.83, 141.46, 141.22, 141.20, 140.06, 138.41, 136.77, 125.32, 90.34 (Two sp² carbon signals were overlapped. The sum of carbon signals must be 31 in theory.); HRMS (APCI, negative ion mode) calcd for C₅₉H₂NO (M⁻) 740.0142, found 740.0131 (The parent peak corresponding to dimer was not observed.).

Synthesis of C₆₀-*N*-MEM-bis(hemiketal) (3). Compound 3 was synthesized according to the previous report.²⁶ C₆₀-*N*-MEM-ketolactam 2 (400 mg, 467 µmol) was dissolved in ODCB (160 mL, 2.92 mM) and degassed through three vacuum-Ar cycles. The solution was heated up to 50 °C. To the solution were added NMO (109.6 mg, 936 µmol, 2.00 equiv) dissolved in THF (40 mL) and distilled water (16.86 µL, 936 µmol, 2.00 equiv). After 3 h, the solution was evaporated for removal of THF. The reaction mixture was purified by column chromatography (silica gel, toluene/acetone, 20:1 to 9:1) to give unreacted 2 (81.5 mg, 95.2 µmol, 20%) and 3 (201 mg, 222 µmol, 47%).

3: ¹H NMR (500 MHz, CDCl₃) δ 7.98 (br s, 1H), 7.39 (br s, 1H), 6.65 (d, *J* = 10.9 Hz, 1H), 5.96 (d, *J* = 10.9 Hz, 1H), 4.16–4.06 (m, 2H), 3.68–3.59 (m, 2H), 3.36 (s, 3H); ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.63 (s, 1H), 9.46 (s, 1H), 6.22 (d, *J* = 10.9 Hz, 1H), 5.68 (d, *J* = 10.9 Hz, 1H), 3.80–3.76 (m, 2H), 3.47–3.41 (m, 2H), 3.18 (s, 3H).

Synthesis of H₂@C₆₀-*N*-MEM-ketolactam (H₂@2). Compound H₂@2 was synthesized according to the previous report.²⁶ Powdery **3** (100 mg, 110 µmol) wrapped in aluminum foil was placed into a 50-mL autoclave. The autoclave was purged with H₂ gas three times and heated at 150 °C under high-pressure H₂ (750 atm) for 24 h. ¹H NMR (500 MHz, CDCl₃) spectrum of the resulting material showed the formation of H₂@**3** (51%, encapsulation ratio: 20%), H₂@**4** (26%, encapsulation ratio: 50%), and two kinds of decomposed derivatives (23%). The optimized conditions were shown in Table S1. The mixture was used for the next reaction without further purification. Subsequently, the mixture was dissolved in ODCB (5.65 mL, 19.5 mM) and the solution was degassed through three vacuum-Ar cycles. Triphenylphosphine (290 mg, 1.10 mmol) was added and the resulting solution was heated up to 100 °C for 6 h under Ar atmosphere. The reaction progress was monitored by HPLC and TLC. The reaction mixture was purified by column chromatography (silica gel, toluene, toluene/acetone, 40:1 to 9:1) to give H₂@**2** (33.1 mg, 38.7 µmol) in 35% yield (2 steps). The encapsulation ratio was determined to be 30% by ¹H NMR spectrum.

H₂@**2**: ¹H NMR (500 MHz, CDCl₃) δ 6.45 (d, *J* = 11.0 Hz, 1H), 6.06 (d, *J* = 11.0 Hz, 1H), 4.08–4.01 (m, 2H), 3.67–3.59 (m, 2H), 3.37 (s, 3H), -4.63 (s, 0.60H).



Table S1. H₂-insertion under high-pressure conditions

^aEstimated by ¹H NMR spectra of crude products.

Synthesis of $H_2@C_{59}N$ dimers. $H_2@2$ (43.7 mg, 51.0 µmol, encapsulation ratio: 33%) was dissolved in ODCB (20.4 mL, 2.50 mM) and the resulting solution was degassed through five vacuum-Ar cycles. *p*-Toluenesulfonic acid monohydrate (194 mg, 1.02 mmol, 20.0 equiv) was added and heated at 150 °C for 1.5 h under Ar atmosphere. The reaction mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene) to give a mixture of ($C_{59}N$)₂, H₂@($C_{59}N$)₂, and (H₂@ $C_{59}N$)₂ (26.5 mg, 18.3 µmol) in 72% yield as a black powder. The apparent encapsulation ratio was determined to be 33% by APCI MS. This shows no escape of entrapped H₂.

H₂@C₅₉N dimers consisting of (C₅₉N)₂, H₂@(C₅₉N)₂, and (H₂@C₅₉N)₂: ¹H NMR (500 MHz, ODCB-*d*₄) δ –3.43 (singlet); ¹³C NMR (126 MHz, ODCB-*d*₄) δ <u>156.13</u>, 156.01, <u>148.71</u>, 148.59, <u>147.92</u>, 147.86, <u>147.80</u>, 147.72, <u>147.62</u>, 147.57, <u>147.54</u>, 147.44, <u>146.79</u>, <u>146.72</u>, 146.70, 146.63, <u>146.43</u>, 146.34, <u>145.99</u>, <u>145.93</u>, 145.89, 145.85, <u>145.30</u>, 145.21, <u>145.17</u>, 145.03, <u>144.98</u>, 144.89, <u>144.79</u>, 144.69, <u>144.44</u>, 144.39, <u>144.10</u>, 144.02, <u>143.34</u>, 143.29, <u>142.96</u>, 142.89, <u>142.31</u>, 142.23, <u>141.96</u>, 141.88, <u>141.84</u>, 141.75, <u>141.46</u>, 141.39, <u>141.14</u>, 141.06, <u>141.00</u>, 140.98, <u>140.18</u>, 140.13, <u>137.99</u>, 137.92, <u>136.49</u>, 136.35, <u>125.07</u>, 124.93, 90.24 (The carbon signals of H₂@C₅₉N cage were separated from that of C₅₉N cage. Carbon signals for H₂@C₅₉N were represented with underline); HRMS (APCI, negative ion mode) calcd for C₅₉N (M⁻) 722.0036, found 722.0065 and calcd for C₅₉H₂N (M⁻) 724.0193, found 724.0166 (The parent peak corresponding to dimer was not observed.).

Synthesis of CH₃COCH₂(H₂O@C₅₉N) (H₂O@5). H₂O@C₅₉N dimers (11.5 mg, 7.93 μ mol, apparent encapsulation ratio: 26% estimated by APCI MS) and *p*-toluenesulfonic acid monohydrate (60.4 mg, 318 μ mol, 40.0 equiv) were dissolved in ODCB (SPR grade, 4.0 mL, 1.98 mM) and The resulting solution was bubbled with O₂. Acetone (0.10 mL) was added and heated at 150 °C. The reaction progress was monitored by HPLC. After 20 min, the reaction was almost completed. The reaction mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene) to give H₂O@**5** (8.3 mg, 10.6 μ mol) in 67% yield as a black powder. The encapsulation ratio was determined to be 26% by ¹H NMR spectrum.

H₂O@**5**: ¹H NMR (500 MHz, ODCB-*d*₄) δ 4.671, 4.667 (s, 2H), 2.599, 2.595 (s, 3H), – 7.338 (s, 0.52H) (The proton signals of H₂@**5** were separated from that of **5**.); HRMS (APCI, negative ion mode) calcd for C₆₂H₅NO (M⁻) 779.0377, found 779.0388 and calcd for C₆₂H₇NO₂ (M⁻) 797.0482, found 797.0490.

Synthesis of CH₃COCH₂(H₂@C₅₉N) (H₂@5). H₂@C₅₉N dimers (5.7 mg, 3.94 μ mol, apparent encapsulation ratio: 29% estimated by MS) and *p*-toluenesulfonic acid monohydrate (30.0 mg, 158 μ mol, 40.0 equiv) were dissolved in ODCB (SPR grade, 2.0 mL, 1.97 mM) and The resulting solution was bubbled with O₂. Acetone (0.10 mL) was added and heated at 150 °C. The reaction progress was monitored by HPLC. After 20 min, the reaction was almost completed. The reaction mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene) to give H₂@**5** (3.9 mg, 5.00 μ mol) in 63% yield as a black powder. The encapsulation ratio was determined to be 30% by ¹H NMR spectrum.

H₂@**5**: ¹H NMR (500 MHz, ODCB-*d*₄) δ 4.667 (s, 2H), 2.594 (s, 3H), -3.869 (s, 0.60H); HRMS (APCI, negative ion mode) calcd for C₆₂H₅NO (M⁻) 779.0377, found 779.0358 and calcd for C₆₂H₇NO (M⁻) 781.0533, found 781.0472.

Competition experiment. A 1:1 encapsulation mixture of X@C₃₉N dimers (6.00 mg, 4.14 μ mol) was prepared from H₂O@C₅₉N dimers (2.80 mg, 1.93 μ mol, H₂O: 47%) and H₂@C₅₉N dimers (3.20 mg, 2.21 μ mol, H₂: 41%). The actual mixing ratio was calculated to be 21.87% for H₂O, 21.92% for H₂, and 56.21% for empty. The encapsulation ratio was also confirmed by ¹H NMR spectrum (H₂O/H₂ (1.00:1.00)). The mixture was dissolved in ODCB-*d*₄ (2.10 mL, 1.97 mM) together with an excessive amount of *p*-toluenesulfonic acid monohydrate (31.5 mg, 166 μ mol, 40.0 equiv) and the resulting solution was saturated with O₂. Acetone (0.10 mL) was added and heated at 100 °C. The reaction progress was monitored by ¹H NMR spectrum at intervals of 0.5 h with using ca. 0.4 mL of the reaction mixture which was passed through silica gel for removal of residual *p*-toluenesulfonic acid.



Figure S1. Electrostatic potentials calculated at the MP2/6-31G(d,p)//M06-2X/6-31G(d,p) of (a) DABCO, (b) pentabenzoazacorannulene, and (c) diazabuckybowl.

Table	S2.	Stabilization	energies	calculated	at	the	MP2/6-31G(d,p)	level	of	theory	using
geometries optimized at the M06-2X/6-31G(d,p) level of theory											

MP2/6-31G([Hartree]					
H ₂ O	-76.21977468					[kcal/mol]
11						
metastable	C ₆₀	MeC ₆₀ ⁻	MeC_{60}^{+}	HC ₅₉ N	$C_{59}N^{-}$	$C_{59}N^{-}$
Host	-2279.622908	-2319.472511	-2319.146939	-2296.81917	-2296.296779	-2295.998623
H ₂ O@Host ^a	-2355.852854	-2395.700461	-2395.375817	-2373.048	-2372.524868	-2372.225467
Host	0.0	0.0	0.0	0.0	0.0	0.0
H ₂ O@Host ^a	-6.4	-5.1	-5.7	-5.7	-5.2	-4.4
most stable	C ₆₀	MeC_{60}^{-}	${\rm MeC_{60}}^+$	HC ₅₉ N	$C_{59}N^-$	$C_{59}N^+$
Host	-2279.622908	-2319.472511	-2319.146939	-2296.81917	-2296.296779	-2295.998623
H ₂ O@Host ^a	-2355.852854	-2395.703985	-2395.378571	-2373.050147	-2372.530547	-2372.232388
Host	0.0	0.0	0.0	0.0	0.0	0.0
H ₂ O@Host ^a	-6.4	-7.3	-7.4	-7.0	-8.8	-8.8
		10	J			

^{*a*} Stabilization energies including the BSSE correction.



Figure S2. Stabilization energies of $H_2O@C_{60}$, $H_2O@MeC_{60}^-$, $H_2O@MeC_{60}^+$, $H_2O@HC_{59}N$, $H_2O@C_{59}N^-$, and $H_2O@C_{59}N^+$, calculated at the MP2/6-31G(d,p)//M06-2X/6-31G(d,p) level of theory. Two types of conformers with different orientations of entrapped H_2O were found for each species except for $H_2O@C_{60}$.

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Chapter 3

Facile Access to Azafullerenyl Cation C₅₉N⁺ and Specific Interaction with Entrapped Molecules

ABSTRACT: The facile preparation of azafullerenyl cation $C_{59}N^+$ has been achieved by the assistance of trifluoromethanesulfonic acid. The thus formed $C_{59}N^+$ was quite stable in solution over one month and can be used as an intermediate for the electrophilic reaction. Applying this method to endohedral azafullerenes, corresponding cations (H₂@C₅₉N⁺ and H₂O@C₅₉N⁺) were prepared and the dynamic behavior of entrapped molecules was studied on the basis of ¹H NMR relaxation time measurements. The results indicated that there is strong intramolecular $C_{59}N^+\cdotsO^{\delta-}H_2$ interaction in H₂O@C₅₉N⁺, which stands in contrast to isoelectronic H₂O@C₆₀ with no electrostatic interaction. The author also demonstrated that the magnetic shielding environment inside the C₅₉N⁺ cage closely resembles that for isoelectronic C₆₀.



Introduction

Heterofullerenes, in which carbon atoms of fullerene C_{60} are partially replaced by heteroatoms, have been a great topic of interest and predicted to have properties different from parent C_{60} in terms of electronic and structural features.¹ The existence of heterofullerenes has been demonstrated mainly in gas-phase under the mass spectroscopic conditions.² In 1995, Wudl and co-workers marked the beginning of a new chapter in the history of fullerene chemistry, i.e., synthesis of azafullerene $C_{59}N$ as its dimer in macroscopic quantities by a solution process starting from C_{60} .³ At the present time, $C_{59}N$ is the only example of heterofullerenes while the replacement of carbon atom(s) in the C_{60} cage with heteroatom(s) still remains a crucial issue due to the difficulty for accessing other heteroatom analogues. Under the mass spectroscopic conditions, azafullerenyl cation $C_{59}N^+$ is known to be exclusively observed despite the absence of the parent peak corresponding to $(C_{59}N)_2$.^{3,4} This suggests that the $C(sp^3)-C(sp^3)$ single bond which connects two $C_{59}N^+$ cages is readily cleaved to form $C_{59}N^+$. In the presence of oxidant such as O_2 or chloranil, $C_{59}N^+$ can be converted in-situ into azafullerenyl cation $C_{59}N^+$.⁵ These monomeric azafullerenes $(C_{59}N^+)^+$ enable to expand the versatility of their functionalization.¹

In Chapter 2, the author described the rational way to prepare endohedral azafullerenes, $H_2O@C_{59}N$ and $H_2@C_{59}N$, as their dimers and monomers.⁶ According to the NMR and kinetic studies, it was concluded that the magnetic environment inside the $C_{59}N$ cage is remarkably shielded than that for C_{60} and the reaction rate is approximately two times accelerated by encapsulation of H_2O owing to the stabilization of the intermediate ($C_{59}N^+$). From the computational study on $C_{59}N^*$ (Chapter 4), encapsulation of H_2O affects its electronic nature depending on the orientation of entrapped H_2O .⁷ The author now moved focus to the cationic species of endohedral azafullerenes, $X@C_{59}N^+$, which has an isoelectronic structure with $X@C_{60}$ (Figure 1). Very recently, based on the single-molecular junction study of $H_2O@C_{60}$, the author



Figure 1. Schematic representation of $H_2O@C_{59}N^+$ and its isoelectronic endohedral fullerene, $H_2O@C_{60}$.

and co-workers have demonstrated that the electrostatic interaction between the carbon wall of C_{60} and entrapped H₂O is negligibly small.⁸ In the anionic state, i.e., RC_{60}^{-} , Martín and co-workers reported that entrapped H₂O and HF can interact with the anionic cage via intramolecular hydrogen bonding, which resulted in the accelerated reaction rate relative to empty one.⁹ Herein, the author presents the acid-assisted facile preparation of azafullereneyl cation $C_{59}N^+$ and studies on the magnetic environment inside the $C_{59}N^+$ cage as well as dynamic behavior of entrapped molecules, which revealed the existence of a specific intramolecular interaction.

Results and Discussion

In 2003, the isolation of $C_{59}N^+$ has been carried out by Reed and co-workers for the first time. They reported the crystal structure of $C_{59}N^+$ with a counteranion of silver(I) bis-carborane complex, which was prepared from $(C_{59}N)_2$ by the oxidation using the radical cation of hexabromo(phenyl)carbazole.¹⁰ It is known that nitrogen-doped electron-rich nanocarbons undergo oxidation to form radical cation or cationic species in the presence of oxygen with acids. For example, trifluoroacetic acid (TFA) promotes oxidation of hexabenzoazacorannulene by air to give corresponding radical cation.¹¹ Similarly, bicarbazole and biacridine derivatives are also oxidized by oxygen with a variety of Brønsted or Lewis acids.¹² The generation of cationic species is likely due to the electron transfer involving air oxidation.¹³ As to the acids that can act as strong oxidizing agents, concentrated sulfuric acid (H₂SO₄) is a prototypical example. For the rapid and easy preparation of $C_{59}N^+$, $(C_{59}N)_2$ was subjected to sulfuric acid (Figure 2). However, the conversion and the solubility was quite limited (less than 1 mg/mL). Contrastingly, (C₅₉N)₂ exhibited an excellent solubility in trifluoromethanesulfonic acid (TfOH) presumably due to the effective conversion into $C_{59}N^+$ (surprisingly, the solubility was increased up to 100 mg/mL). While TfOH has no oxidizing ability, its acidity is appreciably stronger than that of H₂SO₄.¹⁴ The possible reason is that the oxidation of $C_{59}N^{+}/C_{59}N^{+}$ highly depends on pH in the presence of oxygen as predicted by Hirsch and co-workers.⁵



Figure 2. (a) Acid-assisted formation of $C_{59}N^+$ from $(C_{59}N)_2$ and (b) solubility of $C_{59}N^+$ in H_2SO_4 and TfOH.

To verify the conclusive formation of $C_{59}N^+$ in TfOH, the ¹³C NMR spectrum was recorded. The sample solution was prepared under ambient conditions in the NMR tube containing a glasssealed capillary insert for the D_2O lock. The obtained signal pattern was apparently different from that of $(C_{59}N)_2$ in ODCB- d_4 (o-dichlorobenzene- d_4) (Figure 3a). The absence of the ¹³C(sp³) signal at ca. 90 ppm strongly suggests the formation of $C_{59}N^+$. The author also conducted the GIAO calculations for $(C_{59}N)_2$, $C_{59}N^+$, and $(C_{59}NH^+)_2$ at the B3LYP/6-311G(d,p)//B3LYP/6-31G(d) level of theory.¹⁵ The simulated data is well-reproducible for the spectrum of $(C_{59}N)_2$ in ODCB- d_4 (Figures 3a,c). Likewise, the simulated pattern of $C_{59}N^+$ shows close resemblance to experimental data which exhibits a diagnostic signal at ca. 155 ppm for the sp²-hybridized carbocation adjacent to the N-atom (Figures 3b,d). It should be noted that protonated azafullerene (C₅₉NH⁺)₂ as the possible product was completely excluded because of the absence of a signal at ca. 107 ppm corresponding to the C(sp³)-atom (Figure 3e). The oxidation progress of $(C_{59}N)_2/C_{59}N^+$ was also monitored by the spectral change of UV-Vis absorption in the ODCB-CH₃CN (4:1) solution upon addition of TfOH as an additive (Figure S2). The maximum absorption wavelengths (λ_{max}) at 440, 596, 722, and, 804 nm were responsive to the addition amount of TfOH. After addition of 2500 equiv of TfOH, the quantitative conversion of $(C_{59}N)_2$ into $C_{59}N^+$ was observed. These results convince the author of the formation of $C_{59}N^+$ in TfOH.



Figure 3. The comparison of ¹³C NMR spectra in the aromatic region: experimental data (126 MHz) of (a) $(C_{59}N)_2$ in ODCB-*d*₄ and (b) $C_{59}N^+$ in TfOH (The deuterium lock was established by D₂O in a glass-sealed capillary insert which was placed at the center of the NMR tube. The ¹³C chemical shifts were referenced with the residual signals of ODCB.) and simulated data (GIAO-B3LYP/6-311G(d,p)//B3LYP/6-31G(d)) of (c) $(C_{59}N)_2$, (d) $C_{59}N^+$, and (e) $(C_{59}NH^+)_2$.

Furthermore, the author found that $C_{59}N^+$ prepared in TfOH smoothly underwent solvolysis by treating with ethanol to furnish ethoxyazafullerene (1) in 74% yield (Scheme 1). This reaction was high-yielding and proceeded even at room temperature within 1 min. The conditions are rather mild compared with the conventional electrophilic reaction of $C_{59}N^+$, which requires 150– 180 °C for few hours using *p*-toluenesulfonic acid under oxygen.^{1b}





It is noteworthy that $C_{59}N^+$ prepared using this method is remarkably stable in the TfOH solution. Even though one month has passed since the preparation, no spectral change was observed by ¹³C NMR. Here, it is of particular importance to study both magnetic and electrostatic environment inside the $C_{59}N^+$ cage for comparison with isoelectronic C_{60} . For this purpose, $C_{59}N^+$ possessing a small molecule inside its cavity becomes an appropriate model since entrapped molecules can be used as a magnetic probe.¹⁶ Thus, the author synthesized X@C₅₉N⁺ from X@C₆₀ (X = H₂ and H₂O). Among two approaches for synthesizing endohedral azafullerenes X@RC₅₉N,⁶ the author adopted the direct conversion method (Scheme 2). First, X@C₆₀ was prepared according to literatures.¹⁷ The reaction of X@C₆₀ with 2-methoxyethoxymethyl azide (MEM-N₃) gave X@2 via 1,3-dipolar cycloaddition and N₂-extrusion. Subsequent photooxygenation of X@2 yielded X@3 which was further converted into X@C₅₉N dimers. Finally, X@C₅₉N⁺ was obtained by dissolution of corresponding X@C₅₉N dimers in TfOH (Scheme 2).

Scheme 2. Synthesis of $H_2@C_{59}N^+$ and $H_2O@C_{59}N^+$



^aEncapsulation ratio (30% for H₂ and 28% for H₂O) was determined by mass spectroscopic analysis.

The ¹H NMR spectra of X@C₅₉N⁺, X@C₆₀, and X@C₅₉N dimers were shown in Figure 4. The chemical shifts of entrapped H₂ and H₂O inside the C₅₉N⁺ cage were found to be obviously down-field shifted by ca. 3 ppm relative to that for X@C₅₉N dimers. These values are relatively close to that of X@C₆₀ without consideration of the solvation and counteranion effects. To understand the shielding profile of C₅₉N⁺, the NICS calculations were performed for C₆₀, C₅₉N⁺, and MeC₅₉N at the HF/6-311G(d,p)//B3LYP/6-31G(d) level of theory (Figures S3–4). Interestingly, the inner magnetic environment of azafullerene drastically changes by oxidation. It becomes more deshieled and shows the similarity to that of C₆₀, reflecting the isoelectronic structure with C₆₀. From these results, the author concluded that there is a little difference in shielding effect inside the C₆₀ and C₅₉N⁺ cages and the observed difference in chemical shifts might arise from the effect of solvent and/or counteranion.



Figure 4. ¹H NMR spectra (500 MHz, 300 K) of (a) $H_2@C_{59}N^+$ and $H_2O@C_{59}N^+$ (in TfOH, D₂O lock) and (b) $H_2@C_{60}$, $H_2O@C_{60}$, $H_2@C_{59}N$ dimers, and $H_2O@C_{59}N$ dimers (in ODCB-*d*₄).

To verify the presence or absence of specific intramolecular interaction for X@C₅₉N⁺, the author measured spin-lattice relaxation time T_1 and spin-spin relaxation time T_2 by applying the inversion recovery and CPMG (Carr-Purcell-Meiboom-Gill) methods, respectively (Figure 5). The field strength is 800 MHz equipped with a cryogenic probe system. The sample concentration of H₂O@C₅₉N⁺ in TfOH was set to 2.6 mM with 30% encapsulation ratio. For H₂@C₅₉N⁺ with 33% encapsulation ratio, the concentration was increased up to 5.2 mM to improve the S/N (signal-to-noise) ratio since the signal of H₂ was considerably broadened owing to its rapid relaxation.^{6b}



Figure 5. (a,b) Relaxation times T_1 (solid line) and T_2 (dashed line) and (c,d) relaxation time ratio T_1/T_2 at variable temperatures for H₂O@C₅₉N⁺ (red), H₂O@C₅₉N dimers (pink), H₂O@C₆₀ (grey), H₂@C₅₉N⁺ (blue), H₂@C₅₉N dimers (sky blue), and H₂@C₆₀ (grey). The T_1 and T_2 values were measured at 500 MHz for X@C₅₉N dimers and X@C₆₀ in ODCB- d_4^{6b} and at 800 MHz for X@C₅₉N⁺ in TfOH containing a D₂O capillary for an external lock.

Generally, in the solution NMR spectroscopy, the T_1 value is as almost the same as the T_2 value.¹⁸ As described in Chapter 5, the author has revealed that the T_1-T_2 gap becomes larger if the molecular motion is restricted via specific interaction at lower temperatures.^{6b,16,} The temperature dependence of T_1 and T_2 values for $X@C_{59}N^+$ was found to be similar to that for $X@C_{59}N$ dimers. This suggests that the relaxation mechanism depends on spin-rotation interaction for $H_2O@C_{59}N^+$ and dipole-dipole (^{14/15}N•••¹H₂) interaction for $H_2@C_{59}N^+$ as seen in $X@RC_{59}N^{6b}$ (Figures 5a,b). Subsequently, the T_1/T_2 values were plotted against temperature in order to clarify the effect of the interaction in $H_2O@C_{59}N^+$. The T_1/T_2 values of $H_2O@C_{60}$ and all endohedral H_2 molecules are constant without dependence on temperature over the measured range (Figures 5c,d). This is due to negligible van der Waals interaction between entrapped

molecules and the carbon wall. In contrast, H₂O@C₅₉N dimers has larger T_1/T_2 values at lower temperatures ($T_1/T_2 = 2.5$ at 280 K), reflecting the attractive N–O interaction.^{6b} Surprisingly, at the same temperature, H₂O@C₅₉N⁺ has much larger value ($T_1/T_2 = 6$) and the T_1/T_2 curve is shifted by a factor of +40 K relative to that of H₂O@C₅₉N dimers. This indicates that there is strong intramolecular electrostatic C₅₉N⁺•••O⁶-H₂ interaction and the electrostatic perturbation from the cationic center is large enough to significantly prevent the rotational motion of entrapped H₂O. From the electrostatic potential maps (Figure 6), the partial positive charge under the cationic center inside the C₅₉N⁺ cage was suggested to become stronger when compared with neutral HC₅₉N. This can provide the rational explanation for the stronger C₅₉N⁺•••O⁶-H₂ interaction, which should contribute to the remarkable stabilization of the cationic center and enhance the reactivity.^{6b}



Figure 6. Electrostatic potential maps of (a) $HC_{59}N$ and (b) $C_{59}N^+$, calculated at the MP2/6-31G(d,p)//M06-2X/6-31G(d,p) level of theory.

Conclusion

In summary, the author found that the dissolution of $(C_{59}N)_2$ in TfOH readily undergoes oxidation to yield azafullerenyl cation $C_{59}N^+$, which exhibits remarkable stability in solution over one month. It can be trapped by ethanol under solvolytic conditions to give ethoxyazafullerene. The DFT calculations suggested that the shielding environment inside the $C_{59}N^+$ cage are comparable to that for C_{60} due to its isoelectronic structure, which was confirmed by ¹H NMR chemical shifts of X@C₅₉N⁺ (X = H₂ and H₂O). From the relaxation time measurements, the author demonstrated that H₂O@C₅₉N⁺ has the intramolecular C₅₉N⁺•••O^{δ}-H₂ interaction which is rather stronger than that observed for neutral H₂O@C₅₉N dimers. The method demonstrated herein would be a diagnostic tool to evaluate such interaction. Thus, the elucidation of yetunknown interaction, between entrapped molecules and the fullerene cage, plays an important role to understand the change in the reactivity from the inside, some of which have been investigated.¹⁹

Experimental Section

General. The ¹H and ¹³C NMR measurements were carried out at room temperature (unless otherwise noted) with JEOL JNM ECA500 and Bruker Avance III 800US Plus instruments. The NMR chemical shifts were reported in ppm with reference to residual protons and carbons of CDCl₃ (δ 7.26 ppm in ¹H NMR, δ 77.00 ppm in ¹³C NMR), D₂O (δ 4.80 ppm in ¹H NMR), *o*-dichlorobenzene (ODCB, δ 132.35 ppm in ¹³C NMR). APCI mass spectra were measured on a Bruker micrOTOF-Q II. UV-vis absorption spectra were measured with a Shimadzu UV-3150 spectrometer. The high-performance liquid chromatography (HPLC) was performed with the use of a Cosmosil Buckyprep column (250 mm in length, 4.6 mm in inner diameter) for analytical purpose. Fullerene C₆₀ was purchased from SES Research Co. Toluene was purchased from Kanto Chemical Co., Inc. ODCB (SPR grade), and ethyl acetate were purchased from Nacalai Tesque, Inc. Trifluoromethanesulfonic acid was purchased from Tokyo Chemical Industry Co. Ltd. Carbon disulfide, *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H₂O), acetone, and ethanol (super dehydrated) were purchased from Wako Pure Chemical Industries, Ltd. ODCB (99%) was purchased from Sigma-Aldrich Co. LLC. (C₅₉N)₂, ^{6b} H₂@C₆₀, ^{17a} H₂O@C₆₀, ^{17b} and H₂O@C₅₉N dimers^{6b} were synthesized according to literatures.

Computational methods. All calculations were conducted with Gaussian 09 program packages. The structures were optimized at the B3LYP/6-31G(d) level of theory without any symmetry assumptions. All structures at the stationary states were confirmed by the frequency analyses at the same level of theory.

Synthesis of ethoxyazafullerene (1). Azafullerene dimer $(C_{59}N)_2$ (5.00 mg, 3.46 µmol) was dissolved in TfOH (0.150 mL, 46.1 mM) to quantitatively give $C_{59}N^+$ (6.92 µmol). To the solution, dehydrated EtOH (20 µL) was added and stirred at room temperature for 1 min. The reaction mixture was reprecipitated by addition of the excessive amount of dehydrated EtOH. After filtration, the precipitates were dissolved in CS₂ and passed through a Celite pad to afford EtOC₅₉N (1) (3.93 mg, 5.12 µmol, 74%).

1: ¹H NMR (500 MHz, CDCl₃/CS₂ (2:1)) δ 4.97 (q, 2H, *J* = 7.16 Hz), 1.89 (t, 3H, *J* = 7.16 Hz); ¹³C NMR (201 MHz, CDCl₃/CS₂ (2:1)) δ 153.64, 147.01, 146.92, 146.74, 146.70, 145.73, 145.72, 145.57, 145.32, 145.27, 145.17, 145.11, 144.66, 144.47, 144.35, 143.84, 143.61, 142.96, 142.84, 142.62, 141.96, 141.87, 141.21, 141.07, 140.88, 140.75, 139.20, 136.61, 135.16, 124.98,

100.38, 61.86, 15.78 (The sum of carbon signals must be 33 in theory. Observed 33.); HRMS (APCI, negative ion mode) calcd for $C_{61}H_5NO(1^{-})$ 767.0377, found 767.0353.

Synthesis of H₂@C₆₀-*N*-MEM (H₂@2). H₂@C₆₀ (encapsulation ratio: 30%, 100 mg, 139 μ mol) was dissolved in ODCB (SPR grade, 11.6 mL, 12.0 mM) and the resulting solution was degassed through three vacuum-Ar cycles. MEM-N₃ (39.3 mg, 278 μ mol, 2.00 equiv) was added to the solution. After stirred at 60 °C for 20 h, the reaction mixture was refluxed for 3 h under Ar atmosphere. The resulting mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene to toluene/ethyl acetate (4:1)). Unreacted H₂@C₆₀ (43.4 mg, 60.2 μ mol, 43%) was eluted first, followed in the order by H₂@2 (19.5 mg, 23.6 μ mol, 17%), H₂@4 (3.6 mg, 4.4 μ mol, 3.1%), and H₂@5 (10.6 mg, 11.4 μ mol, 8.2%). From ¹H NMR spectra, the encapsulation ratio of all endohedral derivatives was determined to be 30%.



H₂@2: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 5.34 (s, 2H), 4.23 (dd, J = 4.58, 9.16 Hz, 2H), 3.77 (dd, J = 4.58, 9.16 Hz, 2H), 3.48 (s, 3H), -2.03 (s, 0.60H); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ <u>147.73</u>, 147.63, <u>144.83</u>, 144.75, <u>144.66</u>, 144.58, <u>144.55</u>, 144.48, <u>144.33</u>, 144.26, <u>144.21</u>, <u>144.17</u>, 144.13, 144.10, <u>144.05</u>, 143.99, <u>143.89</u>, <u>143.87</u>, <u>143.83</u>, 143.76, <u>143.72</u>, <u>143.53</u>, 143.45, 143.34, 143.24, <u>143.13</u>, 143.05, <u>142.99</u>, <u>142.97</u>, 142.91, 142.86, <u>142.83</u>, 142.74, <u>142.68</u>, 142.60, <u>142.58</u>, 142.51, <u>141.62</u>, 141.55, <u>140.74</u>, 140.65, <u>140.53</u>, 140.31, <u>139.29</u>, 139.18, <u>138.45</u>, 138.41, 138.32, <u>138.21</u>, 138.14, <u>137.74</u>, 137.66, <u>136.87</u>, 136.77, <u>136.28</u>, 136.23, <u>135.90</u>, 135.69, <u>133.51</u>, 133.45, <u>83.89</u>, <u>71.94</u>, <u>68.25</u>, <u>58.90</u> (The carbon signals of H₂@2 and 2 were distinguishable. The δ values corresponding to H₂@2 were shown with underline. The δ values overlapped at the same position between H₂@2 and 2 were indicated with double underline. The sum of carbon signals must be 36 in theory. For each compound, the sum of observed signals was 34 while two sp² signals were overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for C₆₄H₁₁NO₂ (H₂@2⁻) 825.0795 and C₆₄H₉NO₂ (2⁻) 823.0639, found 825.0821 and 823.0625, respectively.

H₂@**4**: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 5.25 (s, 3H), 4.33 (dd, J = 4.58, 9.16 Hz, 2H), 3.82 (dd, J = 4.58, 9.16 Hz, 2H), 3.51 (s, 3H), -3.03 (s, 0.60H); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ <u>145.08</u>, <u>145.03</u>, 145.00, 144.94, <u>144.59</u>, 144.51, <u>144.46</u>, <u>144.44</u>, 144.37, <u>144.31</u>, <u>144.03</u>, 143.96, <u>143.68</u>, 143.61, <u>143.07</u>, 143.01, 142.92, <u>142.80</u>, 142.71, 142.08, <u>142.02</u>,

141.99, <u>140.80</u>, 140.72, <u>140.17</u>, 140.05, <u>83.08</u>, 83.03, <u>82.30</u>, <u>72.00</u>, <u>69.38</u>, <u>58.94</u>, <u>29.82</u> (The carbon signals of H₂@4 and 4 were distinguishable. The δ values corresponding to H₂@4 were shown with underline. The δ values overlapped at the same position between H₂@4 and 4 were indicated with double underline. The sum of carbon signals must be 21 in theory. For each compound, the sum of observed signals was 19 while two sp² signals were overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for C₆₄H₁₁NO₂ (H₂@4⁻) 825.0795 and C₆₄H₉NO₂ (4⁻) 823.0639, found 825.0799 and 823.0634, respectively.

H₂@5: ¹H NMR (500 MHz, CDCl₃) δ 5.61 (d, J = 9.74 Hz, 2H), 5.47 (d, J = 9.74 Hz, 1.4H), 5.45 (d, J = 9.74 Hz, <u>0.60H</u>), 4.23 (ddd, J = 4.58, 4.58, 10.88 Hz, 2H), 4.06 (ddd, J = 4.58, 4.58, 10.88 Hz, 2H), 3.76 (t, J = 4.58 Hz, 4H), 3.48 (s, 6H), -2.55 (s, <u>0.60H</u>); ¹³C NMR (126 MHz, CDCl₃) δ <u>158.93</u>, 158.70, <u>147.68</u>, 147.61, <u>147.11</u>, 147.04, <u>145.64</u>, 145.54, <u>145.43</u>, 145.36, <u>145.04</u>, 144.97, <u>144.89</u>, 144.85, <u>144.70</u>, <u>144.66</u>, 144.62, 144.59, <u>144.31</u>, 144.22, 144.16, <u>144.11</u>, 144.00, <u>143.87</u>, 143.78, <u>143.65</u>, 143.59, <u>143.55</u>, 143.47, <u>142.84</u>, 142.81, <u>142.50</u>, 142.37, <u>141.91</u>, 141.84, <u>141.73</u>, 141.70, 140.35, <u>139.70</u>, 139.62, <u>139.54</u>, 139.45, <u>139.42</u>, 139.22, <u>138.42</u>, 138.31, 136.63, <u>135.51</u>, 135.43, <u>134.79</u>, 134.70, <u>133.14</u>, 133.08, 132.93, <u>130.59</u>, 130.46, <u>83.88</u>, <u>71.97</u>, <u>68.32</u>, <u>59.17</u> (The carbon signals of H₂@**5** and **5** were distinguishable. The δ values corresponding to H₂@**5** were shown with underline. The sum of carbon signals must be 36 in theory. The sum of observed signals was 30 for H₂@**5** and 34 for **5** while six and two sp² signals were overlapped in the aromatic region, respectively.); HRMS (APCI, negative ion mode) calcd for C₆₈H₂₀N₂O₄ (H₂@**5**⁻) 928.1429 and C₆₈H₁₈N₂O₄ (**5**⁻) 926.1272, found 928.1442 and 926.1308, respectively.

Synthesis of $H_2@C_{60}$ -*N*-MEM-ketolactam ($H_2@3$). $H_2@2$ (19.5 mg, 23.6 µmol, encapsulation ratio: 30% determined by ¹H NMR) was dissolved in CS₂/CCl₄ (2:1, 15.4 mL, 1.53 mM). The resulting solution was bubbled with O₂ and then it was irradiated with LED lamps. The reaction progress was monitored by HPLC. After 38 h at room temperature, the reaction was almost completed. The resulting solution was evaporated and purified by column chromatography (CS₂/acetone (40:1)) to give $H_2@3$ (13.3 mg, 15.6 µmol, encapsulation ratio: 30% determined by ¹H NMR) in 66% yield as a black powder.

H₂@**3**: ¹H NMR (500 MHz, CDCl₃) δ 6.44 (d, J = 10.9 Hz, 1H), 6.05 (d, J = 10.9 Hz, 1H), 4.08–4.00 (m, 2H), 3.67–3.58 (m, 2H), 3.37 (s, 3H), –4.63 (s, 0.60H); ¹³C NMR (126 MHz, CDCl₃) δ <u>198.50</u>, <u>163.58</u>, <u>150.18</u>, 150.07, <u>149.44</u>, 149.36, <u>147.83</u>, 147.73, <u>147.50</u>, 147.38, <u>147.09</u>, 147.06, <u>146.77</u>, 146.71, 146.68, 146.59, <u>146.46</u>, <u>146.37</u>, 146.28, <u>146.20</u>, <u>146.17</u>, <u>146.11</u>, 146.08, 146.04, <u>146.00</u>, 145.90, <u>145.84</u>, 145.76, 145.51, 145.46, 145.43, <u>145.36</u>, 145.31, <u>145.17</u>, 145.11, <u>144.91</u>, <u>144.87</u>, 144.80, <u>144.66</u>, <u>144.51</u>, 144.43, 144.27, 144.21, <u>144.19</u>, 144.12, 144.09, <u>144.03</u>, 143.96, <u>143.92</u>, 143.82, 143.74, <u>143.67</u>, 143.60, <u>143.55</u>, <u>143.52</u>, <u>143.48</u>, <u>143.46</u>, 143.41, <u>142.74</u>, 142.66, <u>141.65</u>, 141.60, <u>141.30</u>, 141.18, <u>141.11</u>, 141.00, <u>140.50</u>, <u>140.44</u>, 140.39, 140.35, <u>139.76</u>, 139.71, <u>139.61</u>, 139.52, <u>139.49</u>, 139.45, <u>139.28</u>, 139.23, <u>138.71</u>, 138.68, <u>137.92</u>, 137.88, <u>136.72</u>, 136.68, <u>136.12</u>, 135.96, 135.91, <u>135.83</u>, <u>135.72</u>, 135.67, 135.64, <u>135.56</u>, 134.07, <u>134.00</u>, 133.92, <u>133.01</u>, 132.93, <u>132.46</u>, 132.37, <u>132.10</u>, 132.01, <u>127.97</u>, 127.90, <u>80.55</u>, <u>71.58</u>, <u>70.00</u>, <u>59.09</u> (The carbon signals of H₂@**3** and **3** were distinguishable. The δ values corresponding to H₂@**3** were shown with underline. The δ values overlapped at the same position between H₂@**3** and **3** were indicated with double underline. The sum of carbon signals must be 64 in theory. The sum of observed signals was 55 for H₂@**5** and 58 for **5** while nine and six sp² signals were overlapped in the aromatic region, respectively.); HRMS (APCI, negative ion mode) calcd for C₆₄H₁₁NO₄ (H₂@**3**⁻) 857.0694 and C₆₄H₉NO₄ (**3**⁻) 855.0537, found 857.0693 and 855.0543, respectively.

Synthesis of H₂@C₅₉N Dimers. H₂@3 (43.7 mg, 51.0 μ mol, encapsulation ratio: 30% determined by ¹H NMR) was dissolved in ODCB (20.4 mL, 2.50 mM) and the resulting solution was degassed through five vacuum-Ar cycles. *p*-Toluenesulfonic acid monohydrate (194 mg, 1.02 mmol, 20.0 equiv) was added and heated at 150 °C for 1.5 h under Ar atmosphere. The reaction mixture was cooled down to room temperature and purified by column chromatography (silica gel, toluene) to give H₂@C₅₉N dimers (26.5 mg, 18.3 μ mol, encapsulation ratio: 30% determined by APCI mass) in 72% yield as a black powder.

H₂@C₅₉N dimers: ¹H NMR (500 MHz, ODCB-*d*₄) δ –3.43 (s, 2H); ¹³C NMR (126 MHz, ODCB-*d*₄) δ <u>156.13</u>, 156.01, <u>148.71</u>, 148.59, <u>147.92</u>, 147.86, <u>147.80</u>, 147.72, <u>147.62</u>, 147.57, <u>147.54</u>, 147.44, <u>146.79</u>, <u>146.72</u>, 146.70, 146.63, <u>146.43</u>, 146.34, <u>145.99</u>, <u>145.93</u>, 145.89, 145.85, <u>145.30</u>, 145.21, <u>145.17</u>, 145.03, <u>144.98</u>, 144.89, <u>144.79</u>, 144.69, <u>144.44</u>, 144.39, <u>144.10</u>, 144.02, <u>143.34</u>, 143.29, <u>142.96</u>, 142.89, <u>142.31</u>, 142.23, <u>141.96</u>, 141.88, <u>141.84</u>, 141.75, <u>141.46</u>, 141.39, <u>141.14</u>, 141.06, <u>141.00</u>, 140.98, <u>140.18</u>, 140.13, <u>137.99</u>, 137.92, <u>136.49</u>, 136.35, <u>125.07</u>, 124.93, <u>90.24</u> (The carbon signals of H₂@C₅₉N and C₅₉N dimers were distinguishable. The *δ* values corresponding to H₂@C₅₉N dimers were shown with underline. The *δ* values overlapped at the same position between H₂@C₅₉N and C₅₉N dimers were indicated with double underline. The sum of carbon signals must be 31 in theory. For each dimer, the sum of observed signals was 30 while one sp² signal was overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for C₅₉N (M⁻) 722.0036, found 722.0065 and calcd for C₅₉H₂N (M⁻) 724.0193, found 724.0166 (The parent peak corresponding to dimer was not observed.).

Preparation and Characterization of $C_{59}N^+$ **.** Azafullerenyl cation $C_{59}N^+$ was prepared by dissolution of ($C_{59}N$)₂ in TfOH and characterized by ¹³C NMR and UV-Vis absorption spectra.

C₅₉N⁺: ¹³C NMR (126 MHz, TfOH as solvent, D₂O as an external lock) δ 154.53, 148.61,

147.43, 145.67, 145.56, 145.40, 145.38, 145.13, 145.06, 144.88, 144.63, 144.57, 144.49, 144.32, 144.24, 144.12, 143.88, 143.77, 143.26, 143.20, 143.09, 143.01, 142.26, 140.67, 139.88, 137.64, 135.29, 133.95, (The sum of carbon signals must be 31 in theory. The sum of observed signals was 28 while three sp² signal were overlapped in the aromatic region.)



Figure S1. UV-Vis absorption spectra of $C_{59}N^+$ in H_2SO_4 (50.0 μ M).



Figure S2. The spectral change in UV-Vis absorption of $(C_{59}N)_2$ in ODCB-CH₃CN (4:1) upon addition of TfOH. The red and blue curves correspond to the spectra of $(C_{59}N)_2$ and $C_{59}N^+$, respectively.

NICS scans. The calculation results on C_{60} and $MeC_{59}N$ were referenced from Chapter 2.^{6b} The inner sphere of neutral $MeC_{59}N$ is suggested to be remarkably shielded compared to that of C_{60} . However, the shielding environment becomes comparable to that of C_{60} by the oxidation of the $C_{59}N$ cage since $C_{59}N^+$ has an isoelectronic structure with C_{60} .



Figure S3. NICS scans along an axis of symmetry inside the cages of C_{60} , $MeC_{59}N$, and $C_{59}N^+$ at the HF/6-311G(d,p)//B3LYP/6-31G(d) level of theory.



Figure S4. Schlegel diagrams of C_{60} , MeC₅₉N, and $C_{59}N^+$ calculated at the HF/6-311G(d,p)//B3LYP/6-31G(d) level of theory.

¹H NMR relaxation times of X@C₅₉N⁺. The spin-spin relaxation time T_2 was measured by the CPMG (Carr Purcell Meiboom Gill) method. The field strength is 800 MHz equipped with a cryogenic probe system. The sample concentration of H₂O@C₅₉N⁺ in TfOH was set to 2.6 mM with 30% encapsulation ratio of H₂O. The NMR lock was established by D₂O inside a capillary which was inserted into the NMR tube. For H₂@C₅₉N⁺ with 33% encapsulation ratio, the concentration was increased up to 5.2 mM to improve the S/N (signal-to-noise) ratio since the signal of H₂ was considerably broadened owing to its rapid relaxation. The T_1 and T_2 values for X@C₅₉N dimers and X@C₆₀ (500 MHz in ODCB-*d*₄) were referenced from Chapter 2.^{6b}

Electrostatic potential maps. The structures of $HC_{59}N$ and $C_{59}N^+$ were optimized at the M06-2X/6-31G(d,p) level of theory. Using these geometries,¹ the single point calculations were conducted at the MP2/6-31G(d,p) level of theory for the visualization of the electrostatic potential maps.

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Chapter 4

H₂O Entrapped inside Fullerene Cages: Potential Probe for Evaluation of Bond Polarization

ABSTRACT: The concept of the bond polarization is a useful tool to understand chemical reactions and fundamental properties of compounds. However, experimental considerations are limited due to its difficulty of reliable description. The author demonstrated that geometrically isolated H₂O inside the cage of fullerene C₆₀ is a possible probe to evaluate the polarization degree of covalent bonds C(C₆₀)–X (X = heteroatom) on the C₆₀ cage. The ¹H NMR relaxation times of entrapped H₂O have been systematically measured at variable temperatures for H₂O@C₆₀X (X = CR₂, NR, O, and O₂). The results followed in the order by electronegativities of C (2.55), N (3.04), and O (3.44), indicating that entrapped H₂O can sensitively respond to the degree of the bond polarization.



Introduction

Chemical reactions and their mechanisms are usually considered in terms of polarity of reagents and solvents as well as electro- or nucleophilicity of substrates.^{1,2} Today, one can roughly understand such kind of properties (i.e., electronic structure of a molecule) according to a conception of the bond polarization which is recognized as an axis of classical organic chemistry. The bond polarization has been so far understood from the viewpoint of the electronegativity (vide infra). In 1811, the concept was first introduced by Berzelius³ and a chemical scale of electronegativity χ was proposed on the basis of the bond valence theory by Pauling in 1932 (original definition of electronegativity: the power of an atom in a molecule to attract electrons to itself).⁴ Soon after, Ingold built a conceptual scale of electrophilicity ω to describe electro- or nucleophile based on the valence electron theory in 1934.⁵ These two parameters are closely related to each other by a simple equation: $\omega = \chi^2/(2\eta)$, where η is the hardness of the system.²

Unfortunately, the electronegativity is not a physical observable and cannot be determined experimentally. Thus, the correlation with other physicochemical parameters has been investigated over the years.^{4,6,7} The evaluation of the bond polarization in gas-phase mainly depends on the theoretical calculations using the density functional theory (DFT),⁸ conceptual density functional theory (CDFT),⁹ or bond polarization theory (BPT).¹⁰ In solid- and liquid-phases, bond lengths, chemical shifts, IR absorbance, and binding energies (X-ray photoelectron spectroscopy, XPS) have been used as convenient parameters even in cases where the influences from the packing force, molecular interactions, surrounding electronic structures, and steric effects are not negligible.¹¹

Herein, the author proposes a reliable experimental methodology to evaluate the polarization degree of covalent bonds, $C(C_{60})$ –X (X = heteroatom), which were introduced on the cage of H₂O@C₆₀. The author expected that the polarization of the C(C₆₀)–X bonds on the C₆₀ cage would influence the electrostatic environment inside the cage which leads to restriction of the rotational motion of entrapped H₂O; this would be a detectable changes in ¹H relaxation times as an observable (Figure 1). In Chapters 2 and 3, the author described macroscopic-scale syntheses of endohedral aza[60]fullerenes H₂@RC₅₉N and H₂O@RC₅₉N (R = 2-oxopropyl or azafullerenyl) and revealed the existence of the remarkably positive potential *on the back side* of the nitrogen atom according to the NMR study of entrapped H₂ and H₂O@C₆₀X as a potential probe to evaluate the polarization degree of the C(C₆₀)–X bonds.



Figure 1. Selected electronegativities in the Pauling's scale and the concept of an experimental methodology to evaluate the polarization degree of covalent bonds.

Results and Discussion

For this purpose, the author made a choice of model compounds bearing the $C(C_{60})$ –X bonds on the C₆₀ cage (i.e., C₆₀CR₂, C₆₀NR, and C₆₀O_n). Note that entrapped H₂O inside the C₆₀X cage is geometrically isolated from outside environment. C₆₀CR₂,¹³ C₆₀NR,¹⁴ C₆₀O,¹⁵ and C₆₀O₂¹⁵ were synthesized from empty C₆₀ according to reported methods. Endohedral derivatives H₂O@C₆₀X were also synthesized in a similar manner using H₂O@C₆₀ (100% encapsulation), which was prepared in 6 steps from C₆₀¹⁶ using the molecular surgery method.¹⁷ The [6,6]isomer of H₂O@C₆₀CR₂ (R = phenyl) was synthesized from H₂O@C₆₀ in 23% yield by 1,3-dipolar cycloaddition of diphenyldiazomethane generated in-situ and subsequent thermal isomerization (Scheme 1a). Aziridinofullerene H₂O@C₆₀NR (R = 2-methoxyethoxymethyl (abbreviated as MEM)) was obtained in 2.7% yield by 1,3-dipolar cycloaddition of MEM-N₃ to H₂O@C₆₀ (Scheme 1b). Oxidation of H₂O@C₆₀O and H₂O@C₆₀O₂ in 23 and 6.3% yields, respectively (Scheme 1c).





^aThe yields in parentheses are results of empty C₆₀ uesd as a starting material.

The NMR chemical shifts are generally governed by both electronic density (electronic effects) and magnetic current density (shielding effects).^{111-m} The ¹³C chemical shifts δ (¹³C) of the C(C₆₀)–X bonds for empty C₆₀CR₂, C₆₀NR, and C₆₀O were summarized in Table 1 as well as natural charges (NC) calculated using natural population analysis (NPA)¹⁸ at the M06-2X/6-31G(d,p) level of theory.¹⁹ The NC values allow to know the electron distribution of the atomic charge based on occupancies of orthonormal natural atomic orbitals (NAO) of constituent atoms. The author defined the Δ NC values which were obtained by subtracting the NC(C) values from the NC(X) values. The Δ NC values suggest the stronger polarization of the C(C₆₀)–O bond (Δ NC = -0.738) relative to the C(C₆₀)–N bond (Δ NC = -0.574) whereas the C(C₆₀)–C bond has a negligible effect of polarization (Δ NC = -0.008). There exists a linear correlation between the Δ NC values and δ (¹³C), implying the existence of the polarization of the C(C₆₀)–X bonds, which was also supported by the temperature dependence of ¹H chemical shifts of entrapped H₂O (Figure S1 and Table S1).

Table 1. Natural charges (NC) calculated using the NPA method at the M06-2X/6-31G(d,p) level of theory and ¹³C NMR chemical shifts δ (¹³C) of the C(C₆₀)–X bonds

δ- χ - δ+	NC(X) NC(C), δ(¹³ C)							
and the second second								
Compound	NC(X)	NC(C)	ΔΝC	δ (ppm)				
$C_{60}CR_2 (R = Ph)$	-0.034	-0.026	-0.008	78.64^{a}				
$C_{60}NR (R = MEM)$	-0.442	+0.133	-0.574	83.35 ^{<i>a</i>}				
C ₆₀ O	-0.476	+0.262	-0.738	89.77^{b}				
^a Measured in ODCB- d_4 . ^b Measured in CS ₂ /CDCl ₃ (1:1).								

To get further insights into the bond polarization degree and its effects on the electrostatic environment surrounding sp³-C atoms of the C(C₆₀)–X bonds, electrostatic potentials were calculated for C₆₀CPh₂, C₆₀N-MEM, C₆₀O, and C₆₀O₂ at the MP2/6-31G(d,p)//M06-2X/6-31G(d,p) level of theory (Figure 2). The partial positive charge is suggested to be located inside the C₆₀ cage. The differences were indicated by the more intense positive potential charge (blue spot) *on the back side* of the C(C₆₀)–X bonds attached outside the cage, in ascending order of electronegativities of C, N, and O. The author expected that this electrostatic influence on inner potentials is magnetically detectable by using entrapped H₂O as a probe.



Figure 2. Electrostatic potentials calculated at the MP2/6-31G(d,p)//M06-2X/6-31G(d,p) level of theory: (a) $C_{60}CPh_2$, (b) $C_{60}N$ -MEM, (c) $C_{60}O$, and (d) $C_{60}O_2$.

The 10 mM solutions of $H_2O@C_{60}X$ in ODCB- d_4 were prepared for measurements of relaxation times. Only for $H_2O@C_{60}CR_2$, a saturated solution (1.1 mM) was used due to its poor solubility in ODCB- d_4 . Any oxygen present in the ODCB- d_4 solution was thoroughly removed by bubbling with argon gas and then pumping. To avoid the contamination of oxygen, the dry argon gas was introduced over the sample solution in the NMR tube (internal diameter, 5 mm). All measurements were conducted at a field strength of 500 MHz over temperatures between 260 and 360 K in each interval of 20 K. The temperature of the sample solution was kept constant within error value of 0.1 K. The inversion recovery method and the CPMG method were applied to measure spin-lattice relaxation time T_1 and spin-spin relaxation time T_2 , respectively. Prior to the measurements of relaxation times T_1 and T_2 , the widths of 90° pulse were determined at each temperature (10.1–10.4 µs for $H_2O@C_{60}CR_2$, 9.85–10.1 µs for $H_2O@C_{60}NR$, 9.90–10.3 µs for $H_2O@C_{60}O$, and 9.88–10.2 µs for $H_2O@C_{60}O_2$). The relaxation times were obtained from the average of at least two measurements with measuring error less than 3%. The relaxation times for the reference compounds, $H_2O@C_{60}$ and $H_2O@C_{59}N$ dimers, were picked up from Chapter 2.^{12b}

As shown in Figure 3, spin-lattice relaxation times T_1 for H₂O@C₆₀CR₂, H₂O@C₆₀NR, and H₂O@C₆₀O lied between the values of H₂O@C₆₀ and H₂O@C₅₉N dimers. In accordance with the degree of the bond polarization, the relaxation times T_1 became longer in the order by H₂O@C₆₀CR₂, H₂O@C₆₀NR, and H₂O@C₆₀O (Figure 3a). Especially for H₂O@C₆₀O₂ having four C(C₆₀)–O bonds on itself, the relaxation times T_1 exceed the values for H₂O@C₅₉N dimers.

For common small molecules in solution, spin-spin relaxation time T_2 is known to coincide with the value of T_1 .²⁰ Whereas H₂O@C₆₀ followed the typical trend, the difference between T_1 and T_2 values for H₂O@C₅₉N dimers became larger with decreasing temperature. As mentioned in Chapters 2 and 3,^{12b} the attractive electrostatic interaction between entrapped H₂O and the nitrogen atom on the C₅₉N cage should restrict the rotational motion of entrapped H₂O and reduce the contribution of the spin-rotation mechanism for T_2 relaxation, resulting in the larger gap between T_1 and T_2 values at lower temperatures. This gap should be affected by dynamic behavior of entrapped H₂O and become larger in order by C₆₀CR₂, C₆₀NR, C₆₀O, and C₆₀O₂ (Figures 3c–f). The positive correlation was also found between $|\Delta NC|$ values and the T_1 values at 300 K for H₂O@C₆₀CR₂, H₂O@C₆₀NR, and H₂O@C₆₀O (Figure 3b), suggesting that entrapped H₂O is a possible probe on the degree of the bond polarization.


Figure 3. Temperature dependence of relaxation times T_1 and T_2 of entrapped H₂O (500 MHz, ODCB- d_4 , 260–360 K), (a) graphical overview of T_1 , (b) T_1 (300 K) plotted against $|\Delta NC|$ values, (c) H₂O@C₆₀CR₂, (d) H₂O@C₆₀NR, (e) H₂O@C₆₀O, and (f) H₂O@C₆₀O₂. The data for H₂O@C₆₀ and H₂O@C₅₉N dimers were referenced from Chapter 2.^{12b}

The theoretical calculations at the M06-2X/6-31G(d,p) level of theory provided two types of conformers of H₂O@C₆₀X having different orientations of entrapped H₂O (Table 2 and Figure S2). The most stable conformer I has a structure where the oxygen atom of entrapped H₂O is attracted by the positive potential and faces *on the back side* of the C(C₆₀)–X bonds. The entrapped H₂O in metastable conformer II adopts an opposite orientation. From the difference in the Gibbs free energies, the ratio of conformers I and II was calculated under the assumption of thermal equilibrium at 298 K. The results exhibited that contribution of conformer I except for H₂O@C₆₀CH₂ is significantly dominant and should restrict the rotational motion of entrapped H₂O via electrostatic interaction, which causes larger T_1 values and T_1 – T_2 gap (Figure 3). As clearly depicted in Figure 3b, this method is quite satisfactory to evaluate the degree of the bond polarization and the electrostatic environment near polarized bonds.

Table 2. Computational results of energy differences between two types of conformations,calculated at the M06-2X/6-31G(d,p) level of theory (298 K)



^{*a*}Units in kcal/mol (at 298 K), $\Delta E = E(\mathbf{I}) - E(\mathbf{II})$, $\Delta H = H(\mathbf{I}) - H(\mathbf{II})$, $\Delta G = G(\mathbf{I}) - G(\mathbf{II})$. ^{*b*}Calculated using the values of ΔG .

Conclusion

In summary, the author experimentally demonstrated that the geometrically isolated H₂O molecule inside the C₆₀ cage works as a good indicator to describe the polarization degree of the C(C₆₀)–X bonds on the C₆₀ cage. The existence of the polarization of the C(C₆₀)–X bonds was proved by the ¹³C chemical shifts of sp³-C(C₆₀) atoms and temperature dependence of ¹H chemical shifts of entrapped H₂O. The ¹H NMR relaxation times T_1 and T_2 of H₂O@C₆₀X (X = CR₂, NR, O, and O₂) were found to be followed in order by the polarization degree: C(C₆₀)–C < C(C₆₀)–N < C(C₆₀)–O, giving a positive correlation between the T_1 values and | Δ NC| values

Experimental Section

General. The ¹H and ¹³C NMR measurements were carried out at room temperature with a JEOL JNM ECA500 instrument. The NMR chemical shifts were reported in ppm with reference to residual protons and carbons of CDCl₃ (δ 7.26 ppm in ¹H NMR, δ 77.00 ppm in ¹³C NMR), CD₂Cl₂ (δ 5.32 ppm in ¹H NMR, δ 53.80 ppm in ¹³C NMR), and ODCB-d₄ (δ 7.20 ppm in ¹H NMR, δ 132.35 ppm in ¹³C NMR). The relaxation time measurements were conducted at a field strength of 500 MHz at 260-360 K in each interval of 20 K using sample solutions in ODCB-d₄. The 90° pulse widths were determined using single pulse sequence prior to relaxation time measurements. The inversion recovery method (180° - τ - 90° sequence) was applied to measure spin-lattice relaxation time T_1 . The CPMG (Carr Purcell Meiboom Gill) method was applied to measure spin-spin relaxation time T_2 . APCI mass spectra were measured on a Bruker micrOTOF-Q II. The high-performance liquid chromatography (HPLC) was performed with the use of a Cosmosil Buckyprep column (250 mm in length, 4.6 mm in inner diameter) for analytical purpose and the same columns (two directly connected columns; 250 mm in length, 20 mm in inner diameter) for preparative purpose. Fullerene C_{60} was purchased from SES Research Co. Toluene and tetrahydrofuran (THF) were purchased from Kanto Chemical Co., INC. Tosylhydrazone, ptoluenesulfonic acid monohydrate, 2-methoxyethoxymethyl chloride, and 18-crown-6 were purchased from Tokyo Chemical Industries Co., Ltd. Methanol and sodium azide were purchased from Wako Pure Chemical Industries, Ltd. Benzophenone and o-dichlorobenzene (ODCB, SPR garade) were purchased from Nacalai Tesque, INC. ODCB, sodium hydride NaH (60%, dispersion in mineral oil), and *m*-chloroperoxybenzoic acid (*m*-CPBA) were purchased from Sigma-Aldrich Co. LLC. Prior to use NaH (60%, dispersion in mineral oil), the mineral oil was removed by washing with dry hexane and filtered under inert atmosphere. $H_2O@C_{60}$ (encapsulation ratio: 100% confirmed by MS and HPLC) was prepared according to the literatures.^{16a}

Computational method. All calculations were conducted with Gaussian 09 program packages. The structures were optimized at the M06-2X/6-31G(d,p) level of theory without any symmetry assumptions. The MP2 calculations were performed using the geometries optimized at the M06-2X/6-31G(d,p) level of theory. All structures including the stationary states were confirmed by the frequency analyses at the same level of theory.

Synthesis of benzophenone tosylhydrazone. Benzophenone tosylhydrazone 2 was synthesized according to the literature.²¹ Benzophenone 1 (1.00 g, 5.49 mmol) and tosylhydrazone (TsNHNH₂, 1.29 g, 6.93 mmol, 1.20 equiv) were dissolved in methanol (20.0 mL). To the solution, a catalytic amount of *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H₂O, 10.5 mg, 55.2 µmol,

1.01 mol%) was added and stirred for 4 h at the reflux temperature. The resulting solution was cooled down to room temperature. The precipitation was filtered, washed with cold Et_2O , and pumped up. Benzophenone tosylhydrazone **2** was obtained in 93% yield as a white powder (1.79 g, 5.11 mmol).

$$\begin{array}{c} O \\ Ph \end{array} \xrightarrow{P} Ph \end{array} \xrightarrow{P-TsOH \cdot H_2O (1.2 \text{ equiv})} \\ \hline MeOH, \text{ reflux, 4 h} \\ 1 \end{array} \xrightarrow{Ph } Ph \end{array} \xrightarrow{P} \begin{array}{c} N \\ Ph \\ Ph \end{array}$$

2: ¹H NMR (500 MHz, CD₂Cl₂) δ 7.82 (d, *J* = 8.59 Hz, 2H), 7.58 (br s, 1H), 7.55–7.52 (m, 3H), 7.43–7.41 (m, 2H), 7.38–7.34 (m, 3H), 7.32–7.29 (m, 2H), 7.14–7.12 (m, 2H), 2.43 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 154.20, 144.13, 136.39, 135.49, 131.08, 130.08, 129.83, 129.76, 129.65, 128.25, 128.18, 127.89, 127.55, 21.60; ¹³C NMR (126 MHz, CD₂Cl₂) δ 154.89, 144.82, 136.91, 135.90, 131.47, 130.47, 130.24, 130.12, 130.08, 128.69, 128.61, 128.14, 127.84, 21.71; HRMS (APCI, positive ion mode) calcd for C₂₀H₁₉N₂O₂S (M+H⁺) 351.1162, found 351.1155.

Synthesis of C_{60} CPh₂. The [6,6]isomer of C_{60} CPh₂ **4** was synthesized according to the literature.^{13c} Benzophenone tosylhydrazone **2** (48.6 mg, 139 µmol) and sodium hydride (NaH, 5.0 mg, 208 µmol, 1.5 equiv) were dissolved in pyridine (1.0 mL). After 10 min, the white suspension changed into a white solid. To the reaction mixture, C_{60} (100 mg, 139 µmol, 1.0 equiv) in ODCB (12.0 mL) was added and heated at reflux temperature for 3 h. For removal of residual NaH and **2**, methanol was added and the resulting powder was filtered and pumped up. The black powder containing isomers **3** and **4** was dissolved in ODCB (5.0 mL) again and heated at reflux temperature to thermally isomerize **3** into **4**. After 4 h, the reaction mixture was cooled down to room temperature and purified by HPLC (Buckyprep column, 50 °C, 7.5 mL/min) to give unreacted C_{60} (14.0 mg, 19.4 µmol, 14%), isomer **4** (37.3 mg, 42.1 µmol, 30%), and bis-adducts (21.2 mg, 20.1 µmol, 15%).



4: ¹H NMR (500 MHz, CDCl₂) δ 8.11–8.08 (m, 2H), 7.48 (tt, J = 7.56 Hz, J = 1.81 Hz, 2H), 7.38 (tt, J = 7.56 Hz, J = 1.81 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 147.92, 145.13, 144.99, 144.92, 144.51, 144.46, 144.43, 144.12, 143.64, 142.81, 142.75, 142.00, 141.94, 140.73, 138.73, 138.04, 130.74, 128.61, 127.99, 78.64, 58.03 (The sum of carbon signals must be 22 in theory. Observed 21. One sp² carbon signal is supposedly overlapped at 142.75 ppm.); HRMS (APCI, negative ion mode) calcd for C₇₃H₁₀ (M⁻) 886.0788, found 886.0808.

Synthesis of H₂O@C₆₀CPh₂. Benzophenone tosylhydrazone 2 (11.9 mg, 34.0 µmol) and sodium hydride (NaH, 1.2 mg, 50 µmol, 1.5 equiv) were dissolved in pyridine (0.25 mL). After 10 min, the white suspension changed into a white solid. To the reaction mixture, H₂O@C₆₀ (25.0 mg, 33.8 µmol, 1.0 equiv) in ODCB (3.0 mL) was added and heated at reflux temperature for 3 h. For removal of residual NaH and **2**, methanol was added and the resulting powder was filtered and pumped up. The black powder containing isomers H₂O@**3** and H₂O@**4** was dissolved in ODCB (1.25 mL) again and heated at reflux temperature to thermally isomerize H₂O@**3** into H₂O@**4**. After 4 h, the reaction mixture was cooled down to room temperature and purified by HPLC (Buckyprep column, 50 °C, 7.5 mL/min) to give unreacted H₂O@C₆₀ (5.04 mg, 6.82 µmol, 20%), H₂O@**4** (7.14 mg, 7.89 µmol, 23%), and H₂O@bis-adducts (3.80 mg, 3.55 µmol, 10%).



H₂O@**4**: ¹H NMR (500 Hz, CDCl₃/CS₂ (1:1)) δ 8.09 (d, 2H, J = 8.02 Hz), 7.48 (t, 2H, J = 8.02 Hz), 7.38 (t, 1H, J = 8.02 Hz); ¹H NMR (500 Hz, ODCB-*d*₄) δ 8.14–8.12 (m, 2H), 7.36 (t, 2H, J = 7.64 Hz), 7.23 (t, 1H, J = 7.64 Hz); ¹³C NMR (126 Hz, CDCl₃/CS₂ (1:1)) δ 148.08, 145.26, 145.16, 145.03, 144.65, 144.60, 144.51, 144.25, 143.73, 142.94, 142.90, 142.85, 142.08, 141.98, 140.81, 138.73, 138.17, 130.75, 128.61, 127.99, 78.70, 58.05 (The sum of carbon signals must be 22 in theory. Observed 22.); ¹³C NMR (126 Hz, ODCB-*d*₄) δ 148.33, 145.39, 145.12, 145.00, 144.61, 144.58, 144.42, 144.18, 143.68, 142.84, 142.06, 141.97, 140.82, 139.39, 138.21, 131.05, 128.75, 128.11, 79.06, 58.33 (Observed 20. Two sp² carbon signals are overlapped.); HRMS (APCI, negative ion mode) calcd for C₇₃H₁₂O (M⁻) 904.0894, found 904.0917.

Synthesis of $C_{60}O$ and $C_{60}O_2$. Fullerene epoxides $C_{60}O$ and $C_{60}O_2$ were synthesized according to the literature.^{15b} C_{60} (100 mg, 139 µmol) was dissolved in toluene (50.0 mL) and heated up to 80 °C. To the solution, *m*-chloroperoxybenzoic acid (*m*-CPBA, 77% purity, 311 mg, 1.39 mmol, 10.0 equiv) in toluene (50.0 mL) was added slowly and stirred at 80 °C for 2 h. After reaction, the solution was concentrated to ca. 5-mL portion and methanol was added. The resulting precipitation was filtered and subjected to recycle HPLC (Buckyprep column, 50 °C, 7.5 mL/min) to give unreacted C_{60} (47.2 mg, 65.5 µmol, 47%) was eluted first, followed in order by $C_{60}O$ (24.8 mg, 33.7 µmol, 24%), minor isomers of $C_{60}O_2$ (2.0 mg, 2.7 µmol, 1.9%), and a single product of major isomer $C_{60}O_2$ (8.3 mg, 11 µmol, 7.9%).



 $C_{60}O$: ¹³C NMR (126 MHz, CDCl₃) δ 145.07, 145.05, 144.95, 144.83, 144.14, 144.03, 143.76, 143.66, 143.32, 142.86, 142.34, 142.15, 141.96, 141.75, 140.64, 89.77 (The sum of carbon signals must be 17 in theory. Observed 16. One sp² carbon signal is overlapped at 142.85 ppm.); HRMS (APCI, negative ion mode) calcd for $C_{60}O$ (M⁻) 735.9955, found 735.9950.

 $C_{60}O_2$ (major): ¹³C NMR (126 MHz, CDCl₃) δ 149.31, 147.49, 146.88, 146.44, 145.89, 145.87, 145.73, 145.65, 145.28, 144.84, 144.62, 144.59, 144.06, 144.05, 143.76, 143.24, 143.09, 142.95, 142.87, 142.32, 142.26, 142.22, 142.19, 141.54, 141.32, 141.14, 140.46, 139.88, 138.88, 82.15, 78.22 (The sum of carbon signals must be 32 in theory. Observed 31. One sp² carbon signal is overlapped.); HRMS (APCI, negative ion mode) calcd for $C_{60}O_2$ (M⁺) 751.9904, found 751.9891.

Synthesis of H₂O@C₆₀O and H₂O@C₆₀O₂. H₂O@C₆₀ (100 mg, 135 µmol) was dissolved in toluene (50.0 mL) and heated up to 80 °C. To the solution, *m*-chloroperoxybenzoic acid (*m*-CPBA, 77% purity, 304 mg, 1.35 mmol, 10.0 equiv) in toluene (47.4 mL) was added slowly and stirred at 80 °C for 2 h. After reaction, the solution was concentrated to ca. 5-mL portion and methanol was added. The resulting precipitation was filtered and subjected to recycle HPLC (Buckyprep column, 50 °C, 7.5 mL/min) to give unreacted H₂O@C₆₀ (48.1 mg, 65.1 µmol, 48%) was eluted first, followed in order by H₂O@C₆₀O (23.0 mg, 30.5 µmol, 23%), minor isomers of H₂O@C₆₀O₂ (2.5 mg, 3.2 µmol, 2.4%), and a single product of major isomer H₂O@C₆₀O₂ (6.6 mg, 8.6 µmol, 6.3%).



 $H_2O@C_{60}O: {}^{1}H NMR (500 MHz, CDCl_3/CS_2 (1:1)) \delta -6.50 (s, 2H); {}^{1}H NMR (500 MHz, ODCB-$ *d* $_4) \delta -6.70 (s, 2H); {}^{1}3C NMR (126 MHz, CDCl_3) \delta 140.68, 141.80, 142.14, 142.34, 142.36, 142.86, 142.97, 143.48, 143.85, 144.00, 144.20, 144.45, 144.90, 145.01, 145.11, 145.14, 89.86 (The sum of carbon signals must be 17 in theory. Observed 17.); HRMS (APCI, negative ion mode) calcd for C₆₀H₂O₂ (M⁻) 754.0060, found 754.0035.$

H₂O@C₆₀O₂ (major): ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ –8.01 (s, 2H); ¹H NMR (500 MHz, ODCB-*d*₄) δ –8.26 (s, 2H); ¹³C NMR (126 MHz, ODCB-*d*₄) δ 149.91, 148.04, 146.90, 146.45, 146.31, 145.90, 145.70, 145.58, 145.32, 144.93, 144.69, 144.57, 144.22, 144.08, 143.80, 143.31, 142.99, 142.95, 142.92, 142.48, 142.44, 142.38, 142.36, 142.16, 141.96, 141.26, 141.22, 141.14, 139.91, 139.34, 82.29, 78.41 (The sum of carbon signals must be 32 in theory. Observed 32.); HRMS (APCI, negative ion mode) calcd for C₆₀H₂O₃ (M⁻) 770.0009, found 770.0001.

VT NMR. For all compounds, chemical shifts corresponding to the entrapped H₂O molecules shifted to higher field at lower temperatures, reflecting the local magnetization induced by the molecular rotation of entrapped H₂O.^{12b} In comparison with H₂O@C₆₀CR₂, the differences in chemical shifts ($\Delta\delta$) of entrapped H₂O inside the cages of C₆₀NR and C₆₀O became larger and the chemical shifts for H₂O@C₆₀O₂ significantly shifted. This indicates that the bond polarization of C(C₆₀)–X bonds on the C₆₀ cage would affect the electronic structure inside the C₆₀ cage.



Figure S1. ¹H NMR spectra (500 MHz, ODCB- d_4 , 260–360 K) of H₂O@C₆₀CPh₂, H₂O@C₆₀N-MEM, H₂O@C₆₀O, and H₂O@C₆₀O₂.

temp.		chemical shift δ (ppm)					
(°C)	(K)	H ₂ O@C ₆₀ CR ₂	H ₂ O@C ₆₀ NR	H ₂ O@C ₆₀ O	H ₂ O@C ₆₀ O ₂		
87	360	-6.551	-6.464	-6.625	-8.164		
67	340	-6.565	-6.487	-6.645	-8.194		
47	320	-6.581	-6.510	-6.668	-8.221		
27	300	-6.598	-6.535	-6.693	-8.251		
7	280	-6.615	-6.561	-6.719	-8.285		
–13	260	-6.634	-6.588	-6.746	-8.320		
Δδ (ppm)		0.083	0.124	0.121	0.156		

Table S1. Chemical shifts of the entrapped H₂O molecules inside the cage of $C_{60}CR_2$, $C_{60}NR$, $C_{60}O$, and $C_{60}O_2$ (500 MHz, ODCB- d_4)

Relaxation time. The 10 mM solutions of $H_2O@C_{60}X$ in ODCB- d_4 were prepared for measurements of relaxation times. Only for $H_2O@C_{60}CR_2$, a saturated solution (1.1 mM) was used due to its poor solubility in ODCB- d_4 . Any oxygen present in the ODCB- d_4 solution was thoroughly removed by bubbling with argon gas and then pumping. To avoid the contamination of oxygen, the dry argon gas was introduced over the sample solution in the NMR tube (internal diameter, 5 mm). All measurements were conducted at a field strength of 500 MHz over temperatures between 260 and 360 K in each interval of 20 K. The temperature of the sample solution was kept constant within error value of 0.1 K. The inversion recovery method and the CPMG method were applied to measure spin-lattice relaxation time T_1 and spin-spin relaxation time T_2 , respectively. Prior to the measurements of relaxation times T_1 and T_2 , the widths of 90° pulse were determined at each temperature (10.1–10.4 µs for $H_2O@C_{60}CR_2$, 9.85–10.1 µs for $H_2O@C_{60}NR$, 9.90–10.3 µs for $H_2O@C_{60}O$, and 9.88–10.2 µs for $H_2O@C_{60}O_2$). The relaxation times were obtained from the average of at least two measurements and the measuring error was less than 3%. **Single crystal X-ray structure of C**₆₀**CPh**₂. Single crystals of C₆₀CPh₂ were obtained from a toluene solution by slow evaporation. Intensity data were collected at 100 K on a Bruker Single Crystal CCD X-ray Diffractometer (SMART APEX II) with Mo K α radiation (λ = 0.71073 Å) and graphite monochromater. A total of 16393 reflections were measured at the maximum 2 θ angle of 50.1°, of which 6174 were independent reflections (R_{int} = 0.0391). The structure was solved by direct methods (SHELXS-97²²) and refined by the full-matrix least-squares on F^2 (SHELXL-97²²). All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were placed using AFIX instructions. The crystal data are as follows: C₇₃H₁₀; FW = 886.81, crystal size 0.08 × 0.05 × 0.03 mm³, Orthorhombic, *Pca2*₁, *a* = 19.675(3) Å, *b* = 10.3836(14) Å, *c* = 17.138(2) Å, α = 90°, *V* = 3501.2(8) Å³, Z = 4, *D_c* = 1.682 g cm⁻³. The refinement converged to *R*₁ = 0.0391, *wR*₂ = 0.0848 (*I* > 2 σ (*I*)), GOF = 1.027.



Single crystal X-ray structure of H₂O@C₆₀CPh₂. Single crystals of H₂O@C₆₀CPh₂ were obtained from a toluene solution by slow evaporation. Intensity data were collected at 100 K on a Bruker Single Crystal CCD X-ray Diffractometer (SMART APEX II) with Mo K α radiation (λ = 0.71073 Å) and graphite monochromater. A total of 16821 reflections were measured at the maximum 2 θ angle of 51.0°, of which 5235 were independent reflections ($R_{int} = 0.0411$). The structure was solved by direct methods (SHELXS-97²²) and refined by the full-matrix least-squares on F^2 (SHELXL-97²²). All non-hydrogen atoms were refined anisotropically. The positions of hydrogen atoms of the entrapped H₂O molecule were refined. All other hydrogen atoms were placed using AFIX instructions. The crystal data are as follows: C₇₃H₁₂O; FW = 904.83, crystal size 0.10 × 0.08 × 0.05 mm³, Orthorhombic, *Pca2*₁, *a* = 19.652(4) Å, *b* = 10.3869(18) Å, *c* = 17.174(3) Å, α = 90°, *V* = 3505.6(11) Å³, Z = 4, *D_c* = 1.714 g cm⁻³. The refinement converged to *R*₁ = 0.0404, *wR*₂ = 0.0798 (*I* > 2 $\sigma(I)$), GOF = 1.068.



DFT calculations: conformers of H₂O@C₆₀X. According to the DFT calculations, two types of conformers were obtained. The most stable conformer I has a structure where the oxygen atom of entrapped H₂O is attracted by the positive potential and faces on the back side of the $C(C_{60})$ –X bonds. Entrapped H₂O in metastable conformer II adopts an opposite orientation. Except for H₂O@C₆₀CR₂, conformation of entrapped H₂O of I is significantly preferable. This suggests that there is the electrostatic interaction between entrapped H₂O and partial positive charge on the back side of $C(C_{60})$ –X bonds and should restrict the rotational motion of entrapped H₂O.



Figure S2. Computational results of energy differences between two types of conformations, calculated at the M06-2X/6-31G(d,p) level of theory (298 K): (a) $H_2O@C_{60}H_2$, (b) $H_2O@C_{60}NH$, (c) $H_2O@C_{60}O$, and (d) $H_2O@C_{60}O_2$.

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Chapter 5

Palladium-Catalyzed Cyclization:

Regioselectivity and Structure of Arene-Fused C₆₀ Derivatives

ABSTRACT: The palladium-catalyzed cyclization on the fullerene C_{60} cage has been achieved using several aryl halides and C_{60} . This reaction was found to be accelerated by the addition of pivalic acid, which can be rationally explained by the computational study based on the concerted metalationdeprotonation mechanism. The author also demonstrated the regioselective π -functionalization using pre-functionalized designed molecules possessing the same substructure on the C_{60} cage. The single crystal X-ray analysis and electrostatic potential map revealed that the orientation of entrapped H₂O inside the naphthalene-fused open-cage C_{60} derivative is electrostatically demanded due to the naphthalene-fusion and construction of the opening.



Introduction

The multi-functionalization of fullerenes has received attention over the past decades and a great deal of efforts has been done for both elucidation on the nature of multiple adducts of C_{60} and applications in electronic devices and bio-medical field.¹ So far, several methods have been established for syntheses of multiple functionalized fullerenes. The representative isolable multiple adducts of C_{60} were shown in Figure 1. The most conventional way is a direct sequential multi-addition which provides highly functionalized C_{60} derivatives including fulleroids² and η^2 -metal complexes.³ To introduce functional groups at the desired positions, a sophisticated way based on the tethering control has been proposed. The addition pattern is likely to depend on the length of the linker of the tether molecule.⁴ However, these methods are mostly uncontrollable and makes isolation to be difficult.

Even though only several examples of the successful stepwise multi-addition of C_{60} were reported,⁵ there still remains an elusive subject to control the addition degree and pattern which should determine the electronic nature of multiple functionalized fullerenes. In addition, functionalization and skeletal modification applying these methods have been mostly limited to pristine fullerenes C_{60} and C_{70} while the further functionalization of pre-functionalized and/or open-cage C_{60} derivatives is still under development. As to open-cage C_{60} derivatives, in general, the reaction takes place on their rims of the opening, which enables to create a larger opening.⁶ The high reactivity of the opening is governed by the degree of coefficients of the HOMO and LUMO. Owing to this electronic nature, it is possible to expand the π -conjugation⁷ whereas functionalization of the fullerene skeleton excluding the rim of the opening is not likely to be occurred.

In lieu of these approaches, modification of the electronic structure of substrates is expected to become a useful methodology toward the regiocontrolled functionalization of C_{60} and its derivatives since the electronic factor contributes to the selectivity. In this context, the author has developed a palladium-catalyzed functionalization of C_{60} and theoretically examined the reaction mechanism. Furthermore, the author demonstrated that an open-cage C_{60} derivative and its structural analogue (i.e., 1,4-substituted C_{60} derivative) effectively undergo cyclization to give the sole product. Endohedral derivatives were also able to be synthesized by this method. Using ¹H NMR signals of entrapped H₂O as a magnetic probe, the author studied the effects of naphthalenefusion on the shielding environment inside the fullerene cages. As to the naphthalene-fused opencage C_{60} derivative, the author got single crystals for endohedral one. Both the X-ray analysis and electrostatic potential map suggested that the orientation of entrapped H₂O is conclusively controlled by the electrostatic effects of the naphthalene-fusion and construction of the opening.



Figure 1. Representative examples and concepts for synthesizing isolable multi-adducts of C_{60} and Pd-catalyzed regioselective functionalization reported herein (this work).

Results and Discussion

Palladium-catalyzed cyclization on the C₆₀ **cage.** Recently, transition-metal-mediated functionalization of C₆₀ has received growing attention because of the potential feasibility of high conversion and yield.^{8–16} For example, the successful syntheses of chiral C₆₀ derivatives using asymmetric catalysts such as Cu(II) or Ag(I) salt have been reported by Martin and co-workers.^{11d,e} In most cases, however, a stoichiometric amount of transition metal reagents is required.^{10a,11b-c,12–16} Most recently, several methods for structural modification of C₆₀ using rhodium- or palladium-catalyst have been developed.^{8,9} In particular, the research groups of Wang and Itami have been independently made a remarkable contribution to this research field.^{9c-m} As the simplest arene-fused C₆₀ derivatives, there is a report on the synthesis of naphthalene-fused C₆₀ derivative **1** containing one pentagonal ring.¹⁷ According to this report, **1** was prepared from C₆₀ and 1,8-diiodonaphthalene under the pyrolytic conditions and the yield lies in the range of 1–

14%. Initially, the author examined the efficient and facile synthesis of **1** from C_{60} and 1-halonaphthalene in the presence of palladium catalyst.

The results were summarized in Table 1. The reaction was monitored by HPLC (high performance liquid chromatography) equipped with the Buckyprep column. Naphthalene-fused C_{60} derivative **1** appeared at 5.93 min, which is distinguishable from the peak for C_{60} at 7.43 min. After chromatographic purification using silica gel, the resultant compound (**1**) was characterized by APCI (atmospheric pressure chemical ionization) mass and ¹H NMR analyses. To the best of the author's knowledge, this is the first metal-catalyzed direct arene-fusion using pristine C_{60} and aryl halides.



Table 1. Reaction conditions for the synthesis of naphthalene-fused $C_{60}(1)$

^{*a*}Estimated by HPLC analyses. The value in parenthesis is isolated yield. ^{*b*}Conducted in the presence of pivalic acid (30 mol%) as an additive. ^{*c*}1-Chloronaphthalene (1-ClNp) was used as a solvent instead of *o*-dichlorobenzene (ODCB).

The conversion of C_{60} and 1-bromonaphthalene into **1** was found to be slightly increased in the order of PdCl₂, Pd₂(dba)₃•CHCl₃, and Pd(OAc)₂ albeit in low yields (entries 1–3). It is noteworthy to mention that the use of pivalic acid as an additive (30 mol%)¹⁸ without changing the temperature and reaction time has a significant role in the improvement of the conversion up to 46% (entry 4). However, the yield of **1** still remained low (29%) due to the inevitable formation of multiple adducts. When 1 equiv. of 1-chloronaphthalene was used instead of 1bromonaphthalene, the conversion was decreased to 12% from 25% (entry 5). This indicates that the oxidative addition of the C–X bond to the Pd center is accelerated in X = Br. In the case where 1-chloronaphthalene was used as a solvent, the conversion was drastically improved to 40% and desired **1** was formed in 24% yield (entry 6). Increasing the temperature up to 200 °C resulted in the good conversion (78%) and yield (52%) (entry 7). Under the similar conditions to entry 7, addition of pivalic acid again reproduced a higher conversion (85%) with inevitable formation of multi-adducts as seen in entry 4 (entry 8).

Synthesis of π -functionalized C₆₀ derivatives. To explore the scope of this palladiumcatalyzed reaction, the author conducted the reaction of C₆₀ with several aryl bromides under the optimized conditions (Scheme 1). For these reactions, the solvent was replaced from 1halonaphthalene to 1-methylnaphthalene to avoid the fusion of naphthalene rings.



Scheme 1. Reaction scope of the palladium-catalyzed cyclization on the C_{60} cage

In the similar way to the case of 1-halonaphthalene, the Pd-catalyzed reaction of C_{60} was conducted with a stoichiometric amount of 1-bromo-4-*n*-butylnaphthalene. Compound **2** possessing a *n*-butyl group on the fused naphthalene ring was formed and isolated in 46% yield. By replacing the aryl bromide with 1-bromo-7-*tert*-butylpyrene, corresponding pyrene-fused C_{60} (**3**) was obtained in 48% yield. Even when the aryl bromide with an electron-deficient core was

used, this reaction can work well to provide fused derivative **4** with keeping the moderate yield (45%).

Molecular design toward the regioselective functionalization of C₆₀. Next, the author moved attention to regioselective functionalization of C₆₀ by utilizing the Pd-catalyzed reaction. For the regiocontrol, the design of the electronic structure of substrates is of particular importance. After consideration of potential substrates by association with DFT calculations¹⁹ (B3LYP/6-31G(d)), 1,4-di-alkylated C₆₀ (R₂C₆₀) was found to have large coefficients of the HOMO which is dominantly localized on bonds *a* and *b* as shown in Figure 3a for **5** (R = *n*-Bu). This stands in contrast to C₆₀ in which the HOMO delocalizes on the whole of the skeleton. In terms of bond lengths, 1,4-di-alkylated C₆₀ has a structural feature of acenaphtylene. Thus, the author expected that the construction of the similar structural motif on the C₆₀ cage induces the localized HOMO with large coefficients. Based on this expectation, the author designed open-cage C₆₀ derivative **6** bearing the similar molecular orbitals to **5** (Figure 3b). It is envisaged that open-cage C₆₀ derivative **6** would undergo the regiocontrolled functionalization on bond *a*, but not on the rim of the opening.



Figure 3. Representation of the HOMO on the cages of (a) $1,4-(n-Bu)_2C_{60}$ (**5**) and (b) open-cage C_{60} derivative **6'** calculated at the B3LYP/6-31G(d) level of theory (orbitals inside the cages are omitted for clarity. The *t*-butyl groups in **6** were replaced with the methyl groups in **6'**.).

1,4-Di-*n*-butyl[60]fullerene (**5**) was synthesized by the reaction of C_{60} with *n*-butyl magnesium chloride followed by quenching with *n*-butyl iodide (Scheme 2). In this reaction, 1,4-adduct **5** was preferably formed without considerable amount of 1,2-substituted isomer due to the steric contribution of the two *n*-butyl groups.²⁰

Scheme 2. Synthesis of $1,4-(n-Bu)_2C_{60}$ (5)



In order to synthesize designed molecule **6**, the author prepared **8** with an eight-memberedring opening. As already reported, open-cage C_{60} derivative **8** can be obtained by one-step reaction starting from C_{60} .²¹ However, separation of **8** from the reaction mixture is inconvenient for a gramscale reaction because of the similar polarity of C_{60} and **8**. To obtain **8** in a large scale, more polar **7** having two keto groups was firstly synthesized from C_{60} (52%) through the one-pot process (Scheme 3). After easy separation of **7** by silica gel column chromatography, **7** was further treated with an excessive amount of tri(isopropyl)phosphite P(O*i*Pr)₃, which underwent intramolecular carbonyl coupling^{21,22} to afford **8** (69%) in a gram-scale.

Scheme 3. Gram-scale synthesis of 8 and conversion into 6.



Subsequently, the author tried hydrogenation of **8** under several conditions. Firstly, the author generated dianion 8^{2-} by CH₃SNa in CH₃CN but the quenching with sat. NH₄Cl aq. resulted in the formation of multi-hydrogenated compounds and 48% recovery of **8**. The reduction of **8** by BH₃·THF gave a mixture of 1,2-/1,4-hydrogenated **8** in <10% yield. In contrast to these reductants, sodium dithionite Na₂S₂O₄ under phase transfer conditions²³ at 100 °C was found to be effective

for the exclusive formation of isomerically pure **6** in 73% yield (Scheme 3). In this reaction, HSO_2^- is considered to be a reactive species²³ which reacts with **8** in 1,2-fashion and then protonation led to the formation of 1,2-hydrogenated derivative of **8**, followed by thermal transformation into **6**.

Regioselective naphthalene-fusion on the pre-functionalized C₆₀ derivatives. The Pdcatalyzed reaction was applied to **5** and **6**. Under the neat conditions using 1-chloronaphthalene (1-ClNp), only the sole product was obtained from **5** in 35% yield (Scheme 5). The APCI MS, ¹H NMR, and ¹³C NMR spectra determined the structure to be **9** in which a naphthalene ring is fused on bond *a*. Even though the HOMO also localizes on bond *b*, the reaction took place only on bond *a* probably because of the steric effects from the *n*-butyl groups. 1-Bromonaphthalene (1-BrNp) also worked well to furnish **9** in 50% yield. In the case of open-cage C₆₀ derivatives, the reactions usually take place on the rim of the opening. However, naphthalene-fused compound **10** was formed from **6** and 1-ClNp under 200 °C for 3 h, albeit in 6% yield together with 11% of **8**. In this reaction, the formation of any other naphthalene-fused derivatives of **6** was not observed. By increasing the temperature at 220 °C for 1 h, **10** was isolated in 17% yield while the conversion into **8** predominantly occurred (43%) (Scheme 5). The low yield of **10** arises from the side reaction, i.e., thermal dehydrogenation from the opening of **6**. To prevent this side-reaction, 1-BrNp was employed at lower temperature (180 °C). As the result, the yield of **10** was improved up to 53% without thermal dehydrogenation of **6**.

Scheme 5. Regioselective naphthalene-fusion



It should be noted that the reaction of **8** (structurally similar to **6**) and 1-halonaphthalene (1-XNp) in the presence of the palladium catalyst resulted in the formation of a mixture of inseparable multi-adducts since the HOMO is distributed on the whole of the skeleton. This indicates that the Pd-catalyzed cyclization can be regiocontrolled by the proper modification of electronic structures such as **5** and **6**.

Preparation of endohedral derivatives and effects of naphthalene-fusion on shielding environment inside the fullerene cages. To study the effects of naphthalene-fusion on the magnetic environment inside the fullerene cages, naphthalene-fused derivatives would become model compounds when a water molecule is incarcerated inside their cavities. It is because the incarcerated water molecule could be potentially used as a magnetic probe to evaluate the shielding and/or electrostatic effects.²⁴ Thus, a series of endohedral derivatives were prepared from H₂O@C₆₀ or H₂O@8.²¹



Figure 4. Structures of endohedral derivatives and ¹H NMR chemical shifts (500 MHz, r.t.) of entrapped H₂O for H₂O@C₆₀, H₂O@1, H₂O@8, H₂O@6, and H₂O@10.

The structures and chemical shifts of proton signals of entrapped H₂O were displayed in Figure 4. By naphthalene-fusion on the C₆₀ cage, the chemical shift of entrapped H₂O was found to be upfield-shifted by $\Delta\delta$ 2.86 ppm from δ –4.64 (H₂O@C₆₀) to –7.50 ppm (H₂O@**1**). The enhanced shielding of ¹H resonance of H₂O is substantially due to the vanishing of the interrupted

paramagnetic π -electron ring currents in the two pentagonal rings highlighted with blue.²⁵ Even though open-cage derivative H₂O@**8** also loses the pentagonal ring currents at the two positions, the water signal appeared at δ –6.09 ppm, indicating that the effect of paramagnetic π -electron ring currents is weaker than that for H₂O@**1**. This is because of the scission of two closest [5,6]bonds with retaining the 60 π electron system. It has been proven that the cleavage of the [5,6]bond is less sensitive to change of the magnetic environment inside the fullerene cages, as seen in ³He@C₆₀CH₂²⁶ and H₂O@C₆₀NR.²⁷ The reduction of H₂O@**8** into H₂O@**6** results in the destruction of the 60 π electron system, which drastically reflects the shielding environment (δ – 8.23 ppm for H₂O@**6**) probably due to the change in diamagnetic ring currents extending around the entire fullerene sphere in addition to further weakening the paramagnetic ring current. In addition, introduction of the fused-naphthalene ring on the cage of H₂O@**6** induces the enhanced shielding and the proton signal of entrapped H₂O appeared at higher-field region (δ –10.22 ppm for H₂O@**10**).

Single crystal X-ray analysis. The single crystals of $H_2O@10$ which are suitable for X-ray analysis were obtained from CS_2 solution by slow evaporation. The solid-state and packing structures of $H_2O@10$ were shown in Figure 5.



Figure 5. (a) Single crystal X-ray structure of H₂O@10 and (b,c) packing structures with short contacts of π - π interaction and intra-/intermolecular CH/ π interaction. Thermal ellipsoids are shown in 50% probability.

The crystal structure of H₂O@10 demonstrated that two molecules of CS₂ was cocrystallized and the naphthalene ring was fused on bond *a*. From the packing structure of H₂O@10 (Figures 5b), the short contacts between adjacent molecules were observed. The short contacts arise from the π - π interaction with the distance of 3.204–3.398 Å, which was also seen in the crystal structures of **7** and **8** (see Supporting Information). the unique short contacts were also found among fused-naphthalene rings and *t*-butyl groups on the pyridyl moieties in H₂O@**10** (Figure 5c). The closest CH/ π distances between the H-atom in the *t*-butyl group and the mean plane of the naphthalene ring are 2.701–3.127 Å.

The position of entrapped H₂O was determined at the final stage of the X-ray analysis. After placing the O(1)-atom of entrapped H₂O, there still remained a low Q peak inside the fullerene cage, which was assignable to the H(1)-atom. Another H-atom (i.e., H(2)) was placed and restrained using DFIX instructions during the refinements. Without DFIX instructions, the position of H(2) cannot be determined. This results suggest that the entrapped water molecule is located at the center of the cage with the H(1)–O(1) bond facing to the opening. To unveil the origin of the unique orientation of entrapped H₂O, the electrostatic potential map was calculated for **10** at the MP2/6-31G(d,p)//M06-2X/6-31G(d,p) level of theory (Figure 6). Interestingly, inside the cage of **10**, the positive potential is located under the double bond in the opening. These positive and negative electrostatic potentials should contribute to the orientation of entrapped H₂O, concomitantly suggesting the restriction of the rotational motion of entrapped H₂O. This can rationally explain the orientation of entrapped H₂O in the single crystal X-ray structure of H₂O@**10**.



Figure 6. Electrostatic potential map of 10, calculated at the MP2/6-31G(d,p)//M06-2X/6-31G(d,p) level of theory.

Electrochemical and photophysical properties. The cyclic voltammetries and UV-vis absorption measurements were conducted for **2–6** and **8–10** (Table 2 and Figure 7). For each compound, three reversible reduction waves were observed and the first reduction potentials are mostly proportional to the values of calculated LUMO levels (B3LYP/6-31G(d)) (Table 2). By

the naphthalene-fusion, the reduction potentials of **2**, **9**, and **10** are cathordically shifted by 0.063, 0.119, and 0.122 eV with reference to those for C_{60} , **5**, and **6**, respectively. Pyrene-fused derivative **3** exhibited a quasi-reversible oxidation wave at +0.918 eV. The DFT calculations suggested that the HOMO and LUMO are localized on the pyrene core and the C_{60} cage, respectively. Thus, the stable radical cation and radical anion species are considered to be (*t*-butylpyrene)⁺⁺(C_{60}) and (*t*-butylpyrene)(C_{60})⁻⁻, respectively. Whereas **3** contains a pyrene core in its structure, the characteristic emission of pyrene is quenched by the effective energy transfer from the pyrene core to the C_{60} cage. In the case of **4**, the cathordic shift by the naphthalene fusion was canceled out to show the same reduction potential as C_{60} because of the introduction of an imide moiety and thus it has a good solubility in common solvents in contrast to C_{60} .

Since the first reduction potentials for fused derivatives 2–4 lie within the range between corresponding potentials of C_{60} (–1.09 eV)^{12c} and PC₆₁BM (–1.17 eV),²⁸ these have a potential application into *n*-type materials for solar cells. Particularly, 2 and 3 possess reduction potentials, which are comparable to that of PC₆₁BM. Furthermore, 1,4-substituted derivative 5, open-cage derivatives 6 and 8, and fused derivatives 9 and 10 have the higher-lying LUMO levels, which are expected to endow the higher open-circuit voltage (V_{OC}) in solar cells.²⁸

a a man d	$E_{ m ox}$	$E_{\rm red}{}^1$	$E_{\rm red}^2$	$E_{\rm red}{}^3$	LUMO ^a
compa.	(V)	(V)	(V)	(V)	(eV)
2	-	-1.156	-1.543	-2.066	-3.10
3	+0.918	-1.145	-1.530	-2.047	-3.11
4	-	-1.093	-1.503	-1.932	-3.35
5	-	-1.199	-1.609	-2.117	-3.07
6	$+1.037^{b}$	-1.247	-1.627	-2.139	-2.88
8	$+1.071^{b}$	-1.234	-1.623	-2.150	-2.93
9	-	-1.318	-1.697	-2.382	-2.90
10	$+0.901^{b}$	-1.369	-1.733	-2.463	-2.76
$C_{60}{}^{c}$	_	-1.093	-1.482	-1.947	-3.23
$PC_{61}BM^d$	_	-1.17	-1.57	-2.09	-3.09

Table 2. Electrochemical half-wave potentials and calculated LUMO levels of 2-6, 8-10, C_{60} and $PC_{61}BM$

Conditions: 0.50 mM samples with 0.10 M *n*-Bu₄N•BF₄ in ODCB at a scan rate of 100 mV s⁻¹. The values were calibrated with the oxidation potential of ferrocene/ferrocenium. *a*Calculated at the B3LYP/6-31G(d) level of theory. *t*-Butyl groups in **6**, **8**, and **10** were replaced with methyl groups for calculations. ${}^{b}E_{pa}$. *c*Ref. 12c. *d*Ref. 28.

The UV-vis absorption spectra of C_{60} , **5**, **6**, and **8–10** were recorded using 50 µM sample solutions in ODCB (Figure 7). In terms of the absorption property, **8** shows a close resemblance to C_{60} which is the 60 π electron system. The color of these solutions is purple. By the modification of the electronic structures in C_{60} by 1,4-addition, the 58 π electron system should be constructed in **5**. The similar spectral view and color (yellow) was again observed for **6** retaining the original 58 π electronic configuration. The fusion of the naphthalene ring influenced absorption intensities of **9** and **10** bearing 56 π electrons on their body, which showed an intense yellow color with increasing extinction coefficients in the measured range of 300–800 nm except around 330 nm.



Figure 7. UV-vis absorption spectra of (a) C_{60} , **5**, and **9** and (b) **8**, **6**, and **10** for 50 μ M solutions in ODCB. The dotted curves are enlarged views (by 10-fold) for each spectrum.

Mechanistic study for the palladium-catalyzed cyclization of the naphthalene ring on the C₆₀ cage. To get deep insights into the reaction mechanism of Pd-catalyzed cyclization of a naphthalene ring on the C₆₀ cage, DFT calculations were performed at the M06-2X level of theory with basis sets of SDD for Pd and Br and 6-31G(d,p) for the rest. Trimethylphosphine was used instead of tricyclohexylphosphine for calculations to be simplified. During the calculations, the author noticed that there are two possible pathways, that is, the concerted metalationdeprotonation (CMD) mechanism²⁹ (Figure 8) and the Heck-type mechanism³⁰ (Figure 9). At the first stage in these mechanisms, palladium (0) undergoes oxidative addition into the C–Br bond of 1-bromonaphthalene and then carbopalladation of thus resultant palladium (II) complex (**INT** 1) against C₆₀, which forms **INT2**. In the case of CMD mechanism, **INT2** is further converted into palladacycle **INT3** through a six-membered transition state **TS2** with transferring hydrogen. After conformational change of **INT3**, the C–C bond formation in **INT4** affords product 1 through **TS3**, which leads to regeneration of palladium (0). The DFT calculations based on the CMD mechanism suggest that the metalation-deprotonation process (**TS2**) is most likely to be a ratedetermining step with the energy barrier (ΔG^{\ddagger} , 298 K) of 39.9 kcal/mol in which carbonate anion arising from the stoichiometric carbonate base acts as a ligand. Interestingly, addition of pivalic acid as a co-catalyst is predicted to have a significant impact to a decrease of energy barrier for cleaving the C–H bond of the naphthalene moiety (**TS2**, 34.5 kcal/mol) by 5.4 kcal/mol compared to that for carbonate anion whereas there is less considerable effect of acetate anion (39.7 kcal/mol) arising from palladium diacetate as a palladium (II) source. The structure of **INT2** only for *t*-butyl derivative has remarkable distortion compared to other possible intermediates possessing a carbonate (HCO₃⁻) or acetate (CH₃CO₂⁻) ligand. This indicates that **INT2** (R = *t*-butyl) is enough reactive to readily pass through **TS2** in the presence of a pivalate ligand. These results could finely reproduce the experimental observation that the addition of pivalic acid resulted in higher conversion of C₆₀ (Table 1, entries 4 and 8).



Figure 8. Plausible reaction pathway for the formation of naphthalene-fused C_{60} (1) via CMD mechanism,²⁹ calculated at the M06-2X level of theory with basis sets of SDD for Pd and Br and 6-31G(d,p) for the rest. Trimethylphosphine was used for calculations to be simplified instead of tricyclohexylphosphine. Gibbs energies (at 298 K) were given in kcal/mol.

The alternative pathway via Heck-type mechanism was also considered (Figure 9). Even though the intermediate **INT3'** in the Heck-type mechanism is calculated to be more stable (13.4 kcal/mol) than that in the CMD mechanism (31.4 kcal/mol), the activation energy required for the intramolecular C_{60} insertion (**TS2'**) is rather high (46.0 kcal/mol) when compared to the **TS2** value

in the CMD mechanism (39.9 kcal/mol). This is probably because that the formation of the fourmembered transition state on the C_{60} cage in the Heck-type TS is less favored by the structural disturbance. From these points of view, the author concluded that the Heck-type mechanism can be excluded for the rational explanation of this reaction.



Figure 9. Plausible reaction pathway for the formation of naphthalene-fused C_{60} (1) via the Heck-type mechanism.³⁰ Calculation methods are the same as described in Figure 8.

Conclusion

In conclusion, the author has developed a palladium-catalysed cyclization for the concise syntheses of arene-fused C₆₀ derivatives. Using this method, naphthalene-, pyrene-, and naphthalimide-fused C₆₀ derivatives (1–4) were synthesized. For the regioselective functionalization of C₆₀, the author designed and synthesized pre-functionalized C₆₀ derivatives **5** and **6**. These compounds have the similar electronic structures, which were also supported by UV-vis absorption spectra. By applying the palladium-catalysed reaction to **5** and **6**, regio-controlled products **9** and **10** were obtained in each reaction. Endohedral derivatives such as H₂O@**1** and H₂O@**10** were also prepared, which indicated that the ¹H NMR signals of entrapped H₂O highly depend on their structural features with π -electron ring currents. The combined study based on the single-crystal X-ray analysis and DFT calculations revealed that the orientation of entrapped

 H_2O inside **10** is restrained by the electrostatic factor originated from the naphthalene-fusion and construction of the opening. The reduction potentials for arene-fused derivatives were also verified by cyclic voltammetries, implying the potential application into solar cells due to high electron-accepting abilities. Finally, to elucidate the reaction mechanism for this palladium-catalysed cyclization, the author performed the DFT calculations along with the CMD and Heck-type mechanisms. The author experimentally observed that the addition of pivalic acid promotes the conversion of C_{60} into **1**. It should be mentioned that the CMD mechanism is preferable for the rational explanation of this reaction and the pivalate ligand has a significant role for the enhanced reactivity. This reaction demonstrated herein is believed to have a potential versatility to synthesize π -functionalized C_{60} derivatives and create a new class of structural motifs in the nanocarbon chemistry.

Experimental Section

General. The ¹H and ¹³C NMR measurements were carried out at room temperature with a JEOL JNM ECA500 instrument. The NMR chemical shifts were reported in ppm with reference to residual protons and carbons of CDCl₃ (δ 7.26 ppm in ¹H NMR, δ 77.00 ppm in ¹³C NMR) and CD_2Cl_2 (δ 5.32 ppm in ¹H NMR, δ 53.80 ppm in ¹³C NMR). APCI mass spectra were measured on a Bruker micrOTOF-Q II. UV-vis absorption spectra were measured with a Shimadzu UV-3150 spectrometer. Cyclic voltammetry was conducted on a BAS Electrochemical Analyzer ALS620C using a three-electrode cell with a glassy carbon working electrode, a platinum wire counter electrode, and a Ag/AgNO3 reference electrode. The measurements were carried out under N_2 atmosphere using ODCB solutions of 0.50 mM samples and 0.10 M tetrabutylammonium tetrafluoroborate (n-Bu₄N·BF₄) as a supporting electrolyte. The redox potentials were calibrated with ferrocene used as an internal standard which was added after each measurement. The high-performance liquid chromatography (HPLC) was performed with the use of a Cosmosil Buckyprep column (250 mm in length, 4.6 mm in inner diameter) for analytical purpose and the same columns (two directly connected columns; 250 mm in length, 20 mm in inner diameter) for preparative purpose. Thin layer chromatography (TLC) was performed on glass plates coated with 0.25 mm thick silica gel 60F-254 (Merck). Column chromatography was performed using PSQ 60B or PSQ 100B (Fuji Silysia).

Fullerene C_{60} was purchased from SES Research Co. Tetrahydrofuran (THF), dichloromethane, toluene, and *n*-butylmagnesium chloride in THF were purchased from Kanto Chemical Co., INC. Propionic acid, *n*-butyllithium in hexane, dichloromethane, *t*-butyl chloride, aluminum chloride, bromine, carbon tetrachloride, carbon disulfide, sodium hydrosulfite, sodium bicarbonate, acetonitrile, palladium(II) acetate, tricyclohexylphosphine tetrafluoroborate,

potassium carbonate, and 1-methylnaphthalene were purchased from Wako Pure Chemical Industries, Ltd. 4-Bromo-1,8-naphthalic anhydride, 2,6-diisopropylaniline, *n*-Butyl iodide, triisopropyl phosphite, tetrabutylammonium chloride, and 1-bromonaphthalene were purchased from Tokyo Chemical Industry Co. Ltd. Pyrene and hexane were purchased from Nacalai Tesque, Inc. *o*-Dichlorobenzene (ODCB) and 1-chloronaphthalene were purchased from Sigma-Aldrich Co. LLC. Dinitrogen and dioxygen gases were purchased from Kyoto Teisan Co., Ltd.

All reactions were carried out under Ar atmosphere. 2,6-Di-(6-*tert*-butylpyridin-2-yl)pyridazine was synthesized according to the literature.²¹

Computational methods. All calculations were conducted using the Gaussian 09 program. A part of molecular geometries for transition states were first estimated by the Reaction plus Pro software package³¹ based on the nudged elastic band (NEB) method³² and subsequently reoptimized using the Gaussian 09 program. For calculations of HOMO-LUMO energy levels, the structures were optimized at the B3LYP/6-31G(d) level of theory without any symmetry assumptions. For the visualization of the electrostatic potential map, the single point calculations were carried out at the MP2/6-31G(d,p) level of theory using the geometry optimized at the M06-2X/6-31G(d,p) level of theory. For the computational analyses for the mechanism of Pd-catalyzed naphthalene-fusion on C₆₀, the geometries were optimized at the M06-2X level of theory with the basis sets of SDD for Pd and Br and 6-31G(d,p) for the other elements. The calculated energy levels were reported with the Gibbs free energies (units in kcal/mol) at the temperature of 298 K. All structures at the stationary and transition states were confirmed by the frequency analyses at the same level of theory. The energy values of all structures regarding the mechanistic analyses were summarized in Table S1.

Compd.	E _{tot} (Hartree)	Gibbs energy (Hartree)	Imaginary frequency (cm ⁻¹)
SM & BYPROD			
1-BrNp	-398.454067	-398.349466	_
Pd(PMe ₃) ₂	-1049.8397316	-1049.655708	-
KHCO3	-864.2517697	-864.252026	-
H_2CO_3 (R = OH)	-264.9053936	-264.890716	-
AcOH (R = CH_3)	-228.9910855	-228.954983	-
PivOH (R = t-Bu)	-346.8813278	-346.764820	-
KBr	-613.2908219	-613.314974	-
PMe ₃	-460.9904288	-460.906140	-
C ₆₀	-2285.4561909	-2285.117695	-
INT1 (CMD mechanism)			
INT1 (R = OH)	-1238.2791751	-1238.045989	-
INT1 ($R = CH_3$)	-1202.3615894	-1202.107117	-
INT1 (R = <i>t</i> -Bu)	-1320.2507094	-1319.915183	-
TS1 (CMD mechanism)			
TS1 (R = OH)	-3523.6974593	-3523.102374	-338.63
TS1 (R = CH_3)	-3487.7807604	-3487.164710	-336.65
TS1 (R = <i>t</i> -Bu)	-3605.6719976	-3604.973812	-327.21
INT2 (CMD mechanism)			
INT2 (R = OH)	-3523.7399364	-3523.140177	-
INT2 ($R = CH_3$)	-3487.8221506	-3487.202108	-
INT2 (R = <i>t</i> -Bu)	-3605.7065685	-3605.003182	-
TS2 (CMD mechanism)			
TS2 (R = OH)	-3523.6713538	-3523.076624	-1435.18
TS2 (R = CH ₃)	-3487.7549056	-3487.138839	-1461.38
TS2 (R = <i>t</i> -Bu)	-3605.6461115	-3604.948176	-1439.49
INT3 (CMD mechanism)			
INT3 (R = OH)	-3523.6985276	-3523.103810	-
INT3 ($R = CH_3$)	-3487.7772776	-3487.159004	-
INT3 (R = <i>t</i> -Bu)	-3605.6642898	-3604.965495	-
INT4 (CMD mechanism)			
INT4 (R = OH)	-3523.7049465	-3523.107894	-
INT4 ($R = CH_3$)	-3487.7852473	-3487.165148	-
INT4 (R = <i>t</i> -Bu)	-3605.6778501	-3604.976747	-
TS3 (CMD mechanism)			
TS3 (R = OH)	-3523.6878112	-3523.093523	-209.62
TS3 (R = CH ₃)	-3487.7649830	-3487.149276	-204.51
TS3 (R = <i>t</i> -Bu)	-3605.6572022	-3604.957826	-222.37
PROD			
1	-2670.0152200	-2669.555535	-
TS2' (Heck-type mechanism)			
TS2' (R = OH)	-3523.6678951	-3523.066897	-208.32
INT3' (Heck-type mechanism)			
INT3' (R = OH)	-3523.7347150	-3523.132406	-

Table S1. Summary of total electronic and Gibbs free energies calculated at the M06-2X level of theory with basis sets of SDD for Pd and Br and 6-31G(d,p) for the rest.

Synthesis of 2-bromo-4-*n*-butylnaphthalene (11). 1,4-Dibromonaphthalene (1.00 g, 3.50 mmol, 350 mM) was dissolved in THF (10.0 mL) and the solution was cooled down to -78 °C. *n*-Butyllithium (1.41 M, 2.48 mL, 3.50 mmol, 1.00 equiv) was slowly added to the solution whose color changed from colorless to yellow. After stirred for 0.5 h, *n*-butyl iodide (distilled, $\rho = 1.6155$ g/mL, 0.478 mL, 4.20 mmol, 1.20 equiv) was added and the solution was allowed to warm up to 0 °C. After stirred for further 0.5 h, the reaction mixture was quenched by water and extracted with CH₂Cl₂. The extract was dried over MgSO₄, filtrated, and evaporated. The chromatographic purification by silica gel (hexane) gave 1-bromo-4-*n*-butylnaphthalene **11** (562 mg, 2.13 mmol) as white powder in 61% yield.



11: ¹H NMR (500 MHz, CDCl₃) δ 8.28 (d, 1H, J = 8.02 Hz), 8.04 (d, 1H, J = 8.02 Hz), 7.69 (d, 1H, J = 7.45 Hz), 7.57 (quin, 2H, J = 8.02 Hz), 7.17 (d, 1H, J = 7.45 Hz), 3.04 (dd, 2H, J = 7.45 Hz), 1.72 (quin, 2H, J = 7.45 Hz), 1.45 (sext, 2H, J = 7.45 Hz), 0.97 (t, 3H, J = 7.45 Hz); ¹³C NMR (126 MHz, CDCl₃) δ 139.15, 133.17, 132.09, 129.57, 127.90, 126.76, 126.41, 126.32, 124.36, 120.73, 32.88, 32.66, 22.78, 13.95 (The sum of carbon signals must be 14 in theory. Observed 14.); HRMS (APCI, positive ion mode) calcd for C₁₄H₁₅Br (**11**⁺⁺) 262.0357, found 262.0341.

Synthesis of 1-bromo-7-(*tert*-butyl)pyrene (13)³³. Pyrene (1.00 g, 4.94 mmol, 618 mM) was dissolved in CH₂Cl₂ (8.00 mL) and *t*-BuCl (distilled, $\rho = 0.8425$ g/mL, 0.600 mL, 5.46 mmol, 1.10 equiv) was added. The reaction mixture was cooled down to 0 °C and AlCl₃ (0.726 g, 5.44 mmol, 1.10 equiv) was added by one portion. The color of the solution immediately changed from yellow to brown. The resulting solution was allowed to warm up to room temperature. After stirred for 3 h, the reaction mixture was quenched with ice water, neutralized by sat. NaHCO₃ aq., and extracted with CH₂Cl₂. The extract was filtrated and evaporated. After chromatographic purification by silica gel (CH₂Cl₂/hexane (1:10)), 2-*tert*-butylpyrene **12** (1.28 g, 4.94 mmol) was obtained as white powder in 100% yield.

2-*tert*-Butylpyrene **12** (0.500 g, 1.93 mmol, 138 mM) was dissolved in CH_2Cl_2 (4.00 mL) and the solution was cooled down to -78° C. Bromine ($\rho = 3.1028$ g/mL, 0.100 mL, 1.94 mmol, 1.01 equiv) diluted with CH_2Cl_2 (10.0 mL) was slowly added to the solution which was allowed to warm up to room temperature. After stirred for 14 h, the reaction mixture was quenched by sat. Na₂S₂O₃ aq. and extracted with CH_2Cl_2 . The extract was washed with brine, dried over Na₂SO₄,

filtrated, and evaporated. The resultant powder was dissolved in hexane (50 mL) at reflux temperature. The hexane solution was filtrated and recrystallized by the temperature gradient to afford 1-bromo-7-(*tert*-butyl)pyrene **13** (0.525 g, 1.55 mmol) as white crystalline powder in 80% yield.



12: ¹H NMR (500 MHz, CDCl₃) δ 8.23 (s, 2H, H(1,3)), 8.15 (d, 2H, H(6,8), J = 7.45 Hz), 8.06 (s, 4H, H(4,5,9,10)), 7.97 (t, 1H, H(7), J = 7.45 Hz), 1.59 (s, 9H, *t*-Bu); HRMS (APCI, positive ion mode) calcd for C₂₀H₁₉ ([**12**+H]⁺) 259.1481, found 259.1487.

13: ¹H NMR (500 MHz, CDCl₃) δ 8.41 (d, 1H, J = 9.16 Hz), 8.27–8.25 (m, 2H), 8.20 (d, 1H, J = 8.02 Hz), 8.17 (d, 1H, J = 9.16 Hz), 8.08 (d, 1H, J = 9.16 Hz), 8.01 (d, 1H, J = 9.16 Hz), 7.99 (d, 1H, J = 8.02 Hz), 1.59 (s, 9H); HRMS (APCI, positive ion mode) calcd for C₂₀H₁₇Br (**13**⁺⁺) 336.0508, found 335.0518.

Synthesis of 4-bromo-*N*-(2,6-diisopropylphenyl)-1,8-naphthalimide $(14)^{34}$. 4-Bromo-1,8-naphthalic anhydride (5.00 g, 18.0 mmol, 277 mM) was placed into the 2-neck flask and degassed through three vacuum-Ar cycles. 2,6-Diisopropylaniline ($\rho = 0.9415$ g/mL, 10.2 mL, 54.2 mmol, 3.00 equiv) and propionic acid (55.0 mL) were added. The resulting solution was further degassed through three vacuum-Ar cycles and heated at the reflux temperature for 17 h. After reaction, the reaction mixture was poured into water and extracted with CH₂Cl₂. The organic layer was dried over anhydrous Na₂SO₄, filtrated, and evaporated. The resultant powder was washed with hexane and purified by column chromatography (CH₂Cl₂) to give **14** (7.53 g, 17.3 mmol) in 96% yield as white powder.



14: ¹H NMR (500 MHz, CDCl₃) δ 8.73 (d, 1H, *J* = 7.45 Hz), 8.67 (d, 1H, *J* = 8.59 Hz), 8.49 (d, 1H, *J* = 7.45 Hz), 8.10 (d, 1H, *J* = 7.45 Hz), 7.91 (dd, 1H, *J* = 7.45, 8.59 Hz), 7.48 (t, 1H, *J* = 7.45 Hz), 7.33 (d, 2H, *J* = 7.45 Hz), 2.71 (sep, 2H, *J* = 6.87 Hz), 1.15 (d, 12H, *J* = 6.87 Hz); HRMS (APCI, negative ion mode) calcd for C₂₄H₂₃BrNO₂ ([**14**+H]⁺) 436.0918, found 436.0923.

Synthesis of 1,4-di-*n*-butyl[60]fullerene (5). C_{60} (100 mg, 139 µmol, 13.9 mM) was dissolved in ODCB (10.0 mL). *n*-BuMgCl in THF (0.719 M, 0.290 mL, 0.209 µmol, 1.50 equiv) was slowly added at room temperature. After stirred for 15 min, *n*-BuI (distilled, 1.00 mL) was added to the solution and heated at 60 °C for 18 h. The reaction mixture was passed through a Celite pad and purified by HPLC (Buckyprep column, 50 °C, 7.5 mL/min) to give hexa-*n*-butyl derivatives (19.6 mg, 18.4 µmol, 13%), 1,4-di-*n*-butyl[60]fullerene **5** (43.0 mg, 51.5 µmol, 37%), 4-*n*-butyl-1-hydro[60]fullerene (1.98 mg, 2.54 µmol, 1.8%), and unreacted C_{60} (33.0 mg, 45.8 µmol, 33%).



5: UV-vis (ODCB) λ_{max} (log ε) 332 (4.48), 440 (3.71), 548 (sh, 3.07), 624 (2.75), 694 (2.45); ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 3.15–3.00 (m, 4H), 2.42–2.32 (m, 4H), 1.77 (sext, 4H, *J* = 7.45 Hz), 1.20 (t, 6H, *J* = 7.45 Hz); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 157.56, 151.66, 148.45, 148.34, 147.22, 146.94, 146.67, 146.60, 146.09, 145.19, 144.87, 144.64, 144.50, 144.15, 144.02, 143.84, 143.66, 143.52, 142.92, 142.89, 142.70, 142.43, 142.38, 142.21, 141.84, 141.73, 140.51, 138.67, 138.11, 130.24, 127.31, 59.13, 42.92, 29.32, 23.60, 14.30 (The sum of carbon signals must be 36 in theory. Observed 36.); HRMS (APCI, negative ion mode) calcd for C₆₈H₁₈ (**5**⁻) 834.1414, found 834.1443.

15: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 6.49 (s, 1H), 3.49–3.46 (m, 2H), 2.63–2.57 (m, 2H), 1.93 (sext, 2H, J = 7.45 Hz), 1.31 (t, 3H, J = 7.45 Hz); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 155.80, 153.45, 147.21, 147.08, 146.84, 146.19, 146.15, 146.13, 146.01, 145.96, 145.62, 145.26, 145.22, 145.18, 145.16, 144.47, 144.40, 143.05, 142.37, 142.36, 141.98, 141.83, 141.80, 141.76, 141.45, 141.42, 140.03, 140.01, 136.35, 135.61, 64.75, 59.68, 47.06, 29.11, 23.70, 14.46 (The sum of carbon signals must be 36 in theory. Observed 36.); HRMS (APCI, negative ion mode) calcd for C₆₄H₁₀ (**15**⁻) 778.0788, found 778.0789.

Synthesis of open-cage C₆₀ derivatives (7 and 8). C₆₀ (3.00 g, 4.16 mmol, 34.6 mM) and 2,6-di-(6-*tert*-butylpyridin-2-yl)pyridazine (1.73 g, 4.99 mmol, 1.20 equiv) were dissolved in 1-chloronaphthalene (120 mL). The resulting solution was degassed through three vacuum-Ar cycles and heated at 270 °C for 91 h. After cooled down to room temperature, the resulting mixture was diluted with CCl₄ (480 mL) and bubbled with O₂ for 20 min. The solution was

irradiated with six LED lamps at room temperature for 48 h. After reaction, CCl₄ was removed under the reduced pressure. The chromatographic purification (hexane/toluene (1:1) to toluene) gave unreacted C_{60} (0.748 g, 1.04 mmol, 25%) and open-cage C_{60} derivative **7** (2.33 g, 2.18 mmol, 52%).

Open-cage C₆₀ derivative **7** (1.00 g, 934 µmol, 23.3 mM) was placed into the Schlenk tube and degassed through five vacuum-Ar cycles. Toluene (40.0 mL) and P(O*i*Pr)₃ (distilled, $\rho =$ 0.9035 g/mL, 4.30 mL, 20.0 equiv) were added and the resulting solution was heated at 120 °C for 3 h. The reaction mixture was evaporated and pumped up. The chromatographic purification (CS₂/hexane (1:1) to CS₂) gave **8** (665 mg, 640 µmol) as brown powder in 69% yield.

Endohedral derivatives including $H_2O@C_{60}$ and $H_2O@{\bf 8}$ were prepared according to the literature.^21

H₂O@C₆₀: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ –4.64 (s, 2H); HRMS (APCI, negative ion mode) calcd for C₆₀H₂O (H₂O@C₆₀-) 738.0113, found 738.0140.

H₂O@8: ¹H NMR (500 MHz, CDCl₃) δ 7.78 (t, 2H, *J* = 7.45 Hz), 7.71 (d, 2H, *J* = 7.45 Hz), 7.32 (d, 2H, *J* = 7.45 Hz), 6.47 (s, 2H), 1.36 (s, 18H), -6.09 (s, 1.84H, 92%); HRMS (APCI, negative ion mode) calcd for C₈₂H₂₈N₂O (H₂O@8⁻⁻) 1056.2209, found 1056.2201.

7: ¹H NMR (500 MHz, CDCl₃) δ 7.68 (t, 1H, *J* = 7.45 Hz), 7.65 (t, 1H, *J* = 7.45 Hz), 7.51 (d, 1H, *J* = 7.45 Hz), 7.38 (d, 1H, *J* = 7.45 Hz), 7.24–7.16 (m, 4H); HRMS (APCI, negative ion mode) calcd for C₈₂H₂₆N₂O₂ (**7**⁻) 1070.2000, found 1070.2027.

8: UV-vis (ODCB) λ_{max} (log ε) 334 (4.67), 432 (3.36), 538 (3.12), 588 (sh, 2.97), 674 (sh, 2.17); ¹H NMR (500 MHz, CDCl₃) δ 7.76 (t, 2H, J = 6.87 Hz), 7.71 (d, 2H, J = 6.87 Hz), 7.32 (d, 2H, J = 6.87 Hz), 6.45 (s, 2H), 1.36 (s, 18H); ¹³C NMR (126 MHz, CDCl₃) δ 168.84, 164.84, 152.31, 149.83, 145.72, 145.67, 145.28, 144.55, 144.38, 144.36, 144.31, 144.23, 144.13, 144.03, 143.84, 143.77, 143.69, 143.65, 143.62, 143.53, 143.27, 142.19, 141.45, 140.47, 140.44, 140.09, 138.06, 137.20, 136.97, 136.93, 136.81, 135.31, 134.88, 130.74, 127.68, 120.75, 117.11, 57.46, 37.72, 30.00 (The sum of carbon signals must be 41 in theory. Observed 40. One sp² carbon signal is overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for C₈₂H₂₆N₂ (**8**⁻) 1038.2101, found 1038.2115.
Synthesis of open-cage C₆₀ derivative (6). Open-cage C₆₀ derivative 8 (50.0 mg, 48.1 μ mol, 4.81 mM) was placed into the Schlenk tube and degassed through five vacuum-Ar cycles and dissolved in ODCB (10.0 mL). Na₂S₂O₄ (86.6%, 145 mg, 722 μ mol, 15.0 equiv), NaHCO₃ (162 mg, 1.92 mmol, 40.0 equiv), and NBu₄Cl (6.7 mg, 24.1 μ mol, 50 mol%) were further added and dissolved in degassed H₂O (distilled, 10.0 mL). The resulting two-layered solution was sonicated and then stirred at 100 °C for 3 h. Note that vigorous stirring results in overreaction to give highly-hydrogenated derivatives. The reaction mixture was extracted with ODCB and evaporated. The chromatographic purification (CS₂/hexane (1:5) to CS₂) gave 6 (36.5 mg, 35.1 μ mol, 73%) and unreacted 8 (3.54 mg, 3.41 μ mol, 7.1%).

Endohedral derivative $H_2O@6$ was also prepared in a similar manner using $H_2O@8$ as a starting material.

6: UV-vis (ODCB) λ_{max} (log ε) 332 (4.51), 392 (sh, 4.16), 452 (3.74), 542 (sh, 3.09), 578 (sh, 2.96), 628 (2.82), 700 (2.44); ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 7.68 (t, 2H, *J* = 7.45, 8.02 Hz), 7.51 (d, 2H, *J* = 8.02 Hz), 7.27 (d, 2H, *J* = 7.45 Hz), 7.02 (s, 2H), 6.69 (s, 2H), 1.41 (s, 18H); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 167.53, 161.93, 148.78, 147.98, 147.26, 146.17, 145.56, 145.49, 145.32, 145.08, 144.98, 144.70, 144.20, 143.97, 143.91, 143.69, 143.47, 143.44, 143.30, 142.77, 141.92, 141.76, 141.53, 140.72, 139.34, 139.21, 139.14, 138.57, 138.54, 137.36, 136.73, 136.10, 132.17, 130.61, 121.07, 116.84, 58.56, 48.73, 37.43, 29.93 (The sum of carbon signals must be 41 in theory. Observed 40. One sp² carbon signal is overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for C₈₂H₂₈N₂ (**6**⁻) 1040.2258, found 1040.2259.

H₂O@**6**: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 7.68 (t, 2H, J = 7.45 Hz), 7.51 (d, 2H, J = 7.45 Hz), 7.27 (d, 2H, J = 7.45 Hz), 7.05 (s, 2H), 6.70 (s, 2H), 1.41 (s, 18H), -8.22 (s, 2H); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 167.57, 161.83, 149.20, 148.41, 147.62, 146.63, 145.64, 145.62, 145.13, 145.02, 144.88, 144.72, 144.31, 144.29, 143.94, 143.89, 143.56, 142.98, 142.11, 141.74, 141.71, 140.72, 139.63, 139.44, 139.12, 138.62, 138.54, 137.53, 136.77, 135.72, 131.82, 130.61, 121.06, 116.88, 58.72, 48.73, 37.43, 29.92, (The sum of carbon signals must be 41 in theory. Observed 38. Three sp² carbon signals are overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for C₈₂H₃₀N₂O (H₂O@**6**⁻) 1058.2365, found 1058.2373.

Synthesis of naphthalene-fused C₆₀ derivative (1). C₆₀ (50.0 mg, 69.4 µmol, 29.2 mM), Pd(OAc)₂ (0.94 mg, 4.2 µmol, 6.0 mol%), PCy₃•HBF₄ (3.08 mg, 8.36 µmol, 12 mol%), and K₂CO₃ (19.2 mg, 139 µmol, 2.00 equiv) were placed into the Schlenk tube using an aluminum boat and degassed through five vacuum-Ar cycles. Degassed 1-chloronaphthalene (distilled, 2.38 mL) was added. The resulting solution was sonicated for 1 min and then heated at 200 °C for 3 h. The reaction mixture was reprecipitated by addition of acetone and filtered using the PTFE membrane. The column chromatography (CS₂/hexane (1:5 to 1:1)) was repeated five times to give unreacted C₆₀ (11.2 mg, 15.5 µmol, 22%), mono-functionalized **1** (30.6 mg, 36.2 µmol, 47%), and bis-functionalized derivatives (7.2 mg, 7.4 µmol, 11%). The reaction conditions were summarized in Tables S2 and S3.

Endohedral derivative $H_2O@1$ was also prepared in a similar manner using $H_2O@C_{60}$ as a starting material.



1: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 8.18 (2H, d, J = 6.98 Hz), 8.04 (2H, d, J = 8.12 Hz), 7.87 (2H, dd, J = 6.98, 8.12 Hz); HRMS (APCI, negative ion mode) calcd for C₇₀H₆ (1⁻) 846.0502, found 846.0475.

H₂O@1: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 8.17 (d, 2H, *J* = 7.45 Hz), 8.03 (d, 2H, *J* = 8.02 Hz), 7.87 (dd, 2H, *J* = 7.45, 8.02 Hz), -7.50 (s, 1.84H, 92%); HRMS (APCI, negative ion mode) calcd for C₇₀H₈O (H₂O@1⁻⁻) 864.0581, found 864.0569.

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	entry	Х	Pd cat. (mol%)		conversion (%) ^a	1 (%) ^a
	1	CI	Pd(OAc) ₂	(6)	12	1
	2	Br	Pd(OAc) ₂	(6)	25	20
	3 ^b	Br	Pd(OAc) ₂	(6)	46	29
	4	Br	PdCl ₂	(6)	3	1
	5	Br	Pd ₂ (dba) ₃ •CHCl ₃	(3)	14	9

Table S2. Optimization of reaction conditions using the stoichiometric amount of 1-halonaphthalene

^aValues were estimated by HPLC analyses.

^bThe reaction conducted in the presence of 30 mol% pivalic acid as an additive.

entry	Х	temp. (°C)	conversion (%) ^a	1 (%) ^a
1	CI	150	0	0
2	CI	180	40	24
3	CI	200	78	51 (52)
4 ^b	CI	200	85	35
5	CI	220	89	46
6	CI	270	99	10
7	Br	140	13	3
8	Br	160	16	8
9	Br	180	52	25
10	Br	200	94	26

Table S3. Optimization of reaction conditions using 1-halonaphthalene as a solvent

^aValues were estimated by HPLC analyses and those in parenthesis are isolated yields. ^bThe reaction conducted in the presence of 30 mol% pivalic acid as an additive.

Synthesis of *n*-butylnaphthalene-fused C₆₀ derivative (2). C₆₀ (20.0 mg, 27.8 µmol, 29.2 mM), **11** (7.4 mg, 28.1 µmol, 1.0 equiv), Pd(OAc)₂ (0.40 mg, 1.8 µmol, 6 mol%), PCy₃•HBF₄ (1.27 mg, 3.45 µmol, 12 mol%), and K₂CO₃ (7.80 mg, 5.64 µmol, 2.0 equiv) were placed into the Schlenk tube using an aluminum boat and degassed through five vacuum-Ar cycles. Degassed 1-methylnaphthalene (0.950 mL) was added. The resulting solution was sonicated for 1 min and then heated at 200 °C for 3 h. The reaction mixture was reprecipitated by addition of CH₃CN and filtered using the PTFE membrane. The precipitates were purified by HPLC (Buckyprep column, 50 °C, 7.5 mL/min) to give *n*-butylnaphthalene-fused **2** (11.6 mg, 12.8 µmol, 46%) and unreacted C₆₀ (7.58 mg, 10.5 µmol, 38%).

2: UV-vis (ODCB) λ_{max} (log ε) 310 (4.71), 326 (sh, 4.66), 430 (3.52), 466 (sh, 3.30), 562 (sh, 2.95), 646 (sh, 2.63), 710 (2.45); ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 8.15 (d, 1H, J = 6.87 Hz), 8.13 (d, 1H, J = 8.02 Hz), 8.07 (d, 1H, J = 6.87 Hz), 7.86 (dd, 1H, J = 6.87, 8.02 Hz), 7.66 (d, 1H, J = 6.87 Hz), 3.28 (t, 2H, J = 7.45 Hz), 1.94 (quin, 2H, J = 7.45 Hz), 1.62 (sext, 2H, J = 7.45 Hz), 1.10 (t, 3H, J = 7.45 Hz); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 153.56, 147.20, 145.99, 145.97, 145.86, 145.82, 145.77, 145.77, 145.13, 145.12, 144.93, 144.91, 144.30, 144.27, 144.26, 143.01, 142.54, 142.19, 142.13, 142.07, 141.86, 141.77, 140.46, 140.45, 138.02, 136.91, 135.64, 135.51, 132.34, 128.81, 128.69, 122.28, 121.48, 121.31, 79.90, 75.88, 33.26, 32.19, 23.09, 14.20 (The sum of carbon signals must be 46 in theory. Observed 40. Six sp² carbon signals are overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for C₇₄H₁₄ (**2**⁻) 902.1101, found 902.1077.

Synthesis of *t*-butylpyrene-fused C₆₀ derivative (3). C₆₀ (20.0 mg, 27.8 µmol, 29.2 mM), 13 (9.4 mg, 28 µmol, 1.0 equiv), Pd(OAc)₂ (0.40 mg, 1.8 µmol, 6 mol%), PCy₃•HBF₄ (1.27 mg, 3.45 µmol, 12 mol%), and K₂CO₃ (7.80 mg, 5.64 µmol, 2.0 equiv) were placed into the Schlenk tube using an aluminum boat and degassed through five vacuum-Ar cycles. Degassed 1methylnaphthalene (0.950 mL) was added. The resulting solution was sonicated for 1 min and then heated at 200 °C for 3 h. The reaction mixture was reprecipitated by addition of CH₃CN and filtered using the PTFE membrane. The precipitates were purified by HPLC (Buckyprep column, 50 °C, 7.5 mL/min) to give *t*-butylpyrene-fused **3** (12.9 mg, 13.2 µmol, 48%) and unreacted C₆₀ (6.95 mg, 9.64 µmol, 35%).

3: UV-vis (ODCB) λ_{max} (log ε) 340 (4.68), 356 (sh, 4.61), 432 (3.61), 478 (sh, 3.38), 562 (3.04), 624 (sh, 2.75), 642 (sh, 2.66), 706 (2.48); ¹H NMR (500 MHz, CD₂Cl₂/CS₂ (1:1)) δ 8.68 (s, 1H), 8.60 (d, 1H, *J* = 8.02 Hz), 8.48 (d, 1H, *J* = 8.02 Hz), 8.25 (s, 2H), 1.69 (s, 9H); ¹³C NMR (126 MHz, CD₂Cl₂/CS₂ (1:1)) δ 154.75, 153.16, 150.84, 147.79, 147.76, 146.56, 146.44, 146.41, 146.34, 145.74, 145.70, 145.56, 145.48, 144.85, 144.78, 143.56, 143.38, 143.13, 143.11, 142.72, 142.68, 142.65, 142.43, 142.31, 141.18, 141.03, 139.99, 136.43, 136.19, 134.57, 133.86, 131.79, 130.94, 130.69, 129.32, 128.15, 127.33, 126.92, 124.57, 123.76, 123.29, 123.10, 122.96, 122.31, 78.69, 77.09, 35.82, 32.43 (The sum of carbon signals must be 50 in theory. Observed 48. Two sp² carbon signals are overlapped in the aromatic region.); HRMS (APCI, positive ion mode) calcd for C₈₀H₁₇ ([**3**+H]⁺) 977.1330, found 977.1334.

Synthesis of naphthalimide-fused C₆₀ derivative (4). C₆₀ (20.0 mg, 27.8 µmol, 29.2 mM), 14 (24.3 mg, 55.7 µmol, 2.0 equiv), Pd(OAc)₂ (0.40 mg, 1.8 µmol, 6 mol%), PCy₃•HBF₄ (1.27 mg, 3.45 µmol, 12 mol%), and K₂CO₃ (7.80 mg, 5.64 µmol, 2.0 equiv) were placed into the Schlenk tube using an aluminum boat and degassed through five vacuum-Ar cycles. Degassed 1methylnaphthalene (0.950 mL) was added. The resulting solution was sonicated for 1 min and then heated at 200 °C for 3 h. The reaction mixture was reprecipitated by addition of CH₃CN and filtered using the PTFE membrane. The precipitates were purified by the silica gel column chromatography (CS₂ to CS₂/acetone (40:1)) to give unreacted C₆₀ (6.12 mg, 8.49 µmol, 31%) and a mixture containing **4** (23.6 mg). The mixture was further purified by HPLC (Buckyprep column, 50 °C, 7.5 mL/min) to give purely isolated **4** (13.4 mg, 12.5 µmol, 32%).

4: UV-vis (ODCB) λ_{max} (log ε) 336 (4.69), 394 (sh, 4.32), 432 (sh, 3.62), 464 (sh, 3.27), 488 (sh, 3.21), 550 (sh, 3.00), 620 (sh, 2.68), 640 (sh, 2.56), 702 (2.47); ¹H NMR (500 MHz, CD₂Cl₂/CS₂ (1:1)) δ 8.93 (d, 2H, J = 7.45 Hz), 8.53 (d, 2H, J = 7.45 Hz), 7.55 (t, 1H, J = 8.02 Hz), 7.39 (d, 2H, J = 8.02 Hz), 2.88 (sep, 2H, J = 6.87 Hz), 1.24 (d, 12H, J = 6.87 Hz); ¹³C NMR (126 MHz, CD₂Cl₂/CS₂ (1:1)) δ 163.90, 153.16, 152.30, 147.91, 146.80, 146.62, 146.38, 146.23, 145.97, 145.92, 145.87, 144.84, 143.69, 143.29, 142.74, 142.51, 142.48, 141.25, 136.36, 136.25, 134.81, 131.92, 129.81, 129.52, 124.45, 123.51, 122.28, 77.42, 29.71, 24.37 (The sum of carbon signals must be 31 in theory. Observed 30. One sp² carbon signal is overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for $C_{84}H_{21}NO_2$ (4⁻) 1075.1578, found 1075.1583.

Synthesis of naphthalene-fused 1,4-di-*n*-butyl C₆₀ derivative (9). 1,4-Di-*n*-butyl[60]fullerene 5 (20.0 mg, 27.8 µmol, 24.0 mM), Pd(OAc)₂ (0.34 mg, 1.5 µmol, 6 mol%), PCy₃•HBF₄ (1.06 mg, 2.88 µmol, 12 mol%), and K₂CO₃ (6.70 mg, 4.85 µmol, 2.0 equiv) were placed into the Schlenk tube using an aluminum boat and degassed through five vacuum-Ar cycles. Degassed 1-chloronaphthalene (distilled, 1.00 mL) was added. The resulting solution was sonicated for 1 min and then heated at 200 °C for 3 h. The reaction mixture was reprecipitated by addition of acetone and filtered using the PTFE membrane. The precipitates were purified by the silica gel column chromatography (CS₂/hexane (1:5)) to give unreacted 5 (3.20 mg, 3.83 µmol, 16%) and 9 (8.06 mg, 8.39 µmol, 35%).

1,4-Di-*n*-butyl[60]fullerene **5** (20.0 mg, 27.8 μ mol, 24.0 mM), Pd(OAc)₂ (0.34 mg, 1.5 μ mol, 6 mol%), PCy₃•HBF₄ (1.06 mg, 2.88 μ mol, 12 mol%), and K₂CO₃ (6.70 mg, 4.85 μ mol, 2.0 equiv) were placed into the Schlenk tube using an aluminum boat and degassed through five vacuum-Ar cycles. Degassed 1-bromonaphthalene (1.00 mL) was added. The resulting solution was sonicated for 1 min and then heated at 200 °C for 2 h. The reaction mixture was reprecipitated by addition of CH₃CN and filtered using the PTFE membrane. The precipitates were purified by the silica gel column chromatography (CS₂/hexane (1:5)) to give unreacted **5** (1.61 mg, 1.93 μ mol, 8.1%) and **9** (11.5 mg, 12.0 μ mol, 50%).

9: UV-vis (ODCB) λ_{max} (log ε) 362 (4.35), 450 (3.73), 570 (sh, 2.98), 628 (sh, 2.73), 690 (sh, 2.23); ¹H NMR (500 MHz, CDCl₃) δ 7.95 (d, 1H, J = 7.45 Hz), 7.94 (d, 1H, J = 7.45 Hz), 7.92 (d, 1H, J = 7.45 Hz), 7.83 (dd, 1H, J = 7.45 Hz), 7.79 (d, 1H, J = 7.45 Hz), 7.70 (dd, 1H, J = 7.45 Hz), 2.98–2.92 (m, 2H), 2.81–2.75 (m, 1H), 2.24 (quin, 2H, J = 8.02 Hz), 2.17–2.11 (m, 2H), 1.76–1.65 (m, 2H), 1.71–1.61 (m, 1H), 1.58–1.48 (m, 1H), 1.24–1.07 (m, 2H), 1.14 (t, 3H, J = 7.45 Hz), 0.68 (t, 3H, J = 7.45 Hz); ¹³C NMR (126 MHz, CDCl₃) δ 161.63, 157.71, 156.20, 155.08, 153.62, 153.13, 151.67, 150.10, 149.42, 149.25, 149.15, 148.69, 148.14, 148.07, 147.81, 147.71, 147.64, 147.46, 146.98, 146.92, 146.78, 146.65, 146.48, 146.13, 145.87, 145.70, 145.61, 145.45, 145.35, 145.18, 145.13, 144.97, 144.84, 144.78, 144.76, 144.74, 144.40, 144.38, 144.31, 144.01, 143.88, 143.86, 143.60, 143.23, 142.71, 142.55, 142.33, 142.04, 141.65, 141.16, 140.80, 136.75, 136.73, 135.89, 135.05, 134.39, 133.23, 129.04, 128.88, 125.05, 124.96, 120.68, 119.831, 76.01, 70.41, 59.52, 56.16, 41.38, 40.83, 29.62, 29.20, 23.31, 22.66, 14.21, 13.68 (The sum of carbon signals must be 78 in theory. Observed 75. Three sp² carbon signals are overlapped in the aromatic region.); HRMS (APCI, negative ion mode) calcd for C₇₈H₂₄ (**9**⁻) 960.1883, found

960.1881.

Synthesis of naphthalene-fused open-cage C_{60} derivative (10). Open-cage C_{60} derivative 6 (15.0 mg, 14.4 µmol, 19.2 mM), Pd(OAc)₂ (0.21 mg, 0.94 µmol, 6 mol%), PCy₃•HBF₄ (0.65 mg, 1.8 µmol, 12 mol%), and K₂CO₃ (4.08 mg, 29.5 µmol, 2.0 equiv) were placed into the Schlenk tube using an aluminum boat and degassed through five vacuum-Ar cycles. Degassed 1-chloronaphthalene (distilled, 0.750 mL) was added. The resulting solution was sonicated for 1 min and then heated at 220 °C for 1 h. The reaction mixture was reprecipitated by addition of CH₃CN and filtered using the PTFE membrane. The precipitates were purified by the silica gel column chromatography (CS₂/hexane (1:1)) to give unreacted 6 (0.44 mg, 0.42 µmol, 2.9%), 10 (2.85 mg, 2.44 µmol, 17%), and dehydrogenated 8 (6.39 mg, 6.15 µmol, 43%).

Open-cage C₆₀ fullerene derivative **6** (15.0 mg, 14.4 μ mol, 19.2 mM), Pd(OAc)₂ (0.21 mg, 0.94 μ mol, 6 mol%), PCy₃•HBF₄ (0.66 mg, 1.8 μ mol, 12 mol%), and K₂CO₃ (4.08 mg, 29.5 μ mol, 2.0 equiv) were placed into the Schlenk tube using an aluminum boat and degassed through five vacuum-Ar cycles. Degassed 1-bromonaphthalene (distilled, 0.750 mL) was added. The resulting solution was sonicated for 1 min and then heated at 180 °C for 3 h. The reaction mixture was reprecipitated by addition of CH₃CN and filtered using the PTFE membrane. The precipitates were purified by the silica gel column chromatography (CS₂/hexane (1:1)) to give unreacted **6** (3.20 mg, 3.07 μ mol, 21%) and **10** (8.96 mg, 7.68 μ mol, 53%).

Endohedral derivative $H_2O@10$ was also prepared in a similar manner using $H_2O@6$ as a starting material.



10: UV-vis (ODCB) λ_{max} (log ε) 374 (4.34), 460 (2.68), 560 (sh, 2.97), 640 (sh, 2.55), 714 (sh, 2.16); ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 7.90 (t, 2H, J = 8.02 Hz), 7.86 (d, 1H, J = 6.87 Hz), 7.78 (t, 1H, J = 8.02 Hz), 7.69 (t, 1H, J = 6.87 Hz), 7.66 (t, 1H, J = 6.87 Hz), 7.59 (t, 1H, J = 8.02 Hz), 7.53 (t, 1H, J = 8.02 Hz), 7.34 (d, 1H, J = 8.02 Hz), 7.28 (d, 1H, J = 8.02 Hz), 7.07 (d, 1H, J = 8.02 Hz), 6.49 (d, 1H, J = 9.74 Hz), 6.47 (d, 1H, J = 3.44 Hz), 6.23 (d, 1H, J = 9.74 Hz), 5.72 (d, 1H, J = 3.44 Hz), 1.39 (s, 9H), 0.90 (s, 9H); ¹³C NMR (126 MHz, CDCl₃/CS₂ (1:1)) δ 167.55, 166.93, 161.85, 161.09, 156.24, 155.10, 154.52, 154.14, 150.52, 150.15, 149.49, 149.28, 148.90, 148.83, 148.74, 148.69, 148.16, 148.00, 147.96, 147.19, 147.14, 146.85, 146.76, 146.65, 146.54, 146.38, 145.92, 145.81, 145.30, 145.16, 145.03,

144.50, 144.34, 144.25, 144.12, 143.83, 143.23, 143.18, 143.07, 142.85, 142.34, 142.23, 141.86, 141.75, 140.64, 140.53, 139.92, 139.79, 139.42, 139.25, 138.88, 138.37, 137.48, 136.59, 136.55, 136.45, 136.11, 135.09, 134.81, 133.96, 133.72, 133.64, 132.66, 132.59, 132.30, 131.93, 130.62, 130.28, 128.83, 128.69, 124.66, 124.51, 120.86, 120.64, 120.22, 120.07, 116.72, 116.68, 77.97, 73.14, 54.57, 54.53, 48.37, 48.08, 37.32, 36.99, 29.88, 29.23 (The sum of carbon signals must be 88 in theory. Observed 88.); HRMS (APCI, negative ion mode) calcd for $C_{92}H_{34}N_2$ (**10**⁻) 1166.2811, found 1166.2751.

H₂O@**10**: ¹H NMR (500 MHz, CDCl₃/CS₂ (1:1)) δ 7.94 (t, 2H, J = 8.59 Hz), 7.89 (d, 1H, J = 6.87 Hz), 7.80 (t, 1H, J = 8.02 Hz), 7.73 (d, 1H, J = 6.87 Hz), 7.68 (t, 1H, J = 8.02 Hz), 7.58 (t, 1H, J = 8.02 Hz), 7.53 (t, 1H, J = 8.02 Hz), 7.34 (d, 1H, J = 7.45 Hz), 7.29 (d, 1H, J = 7.45 Hz), 7.19 (d, 1H, J = 8.02 Hz), 7.06 (d, 1H, J = 8.02 Hz), 6.48 (d, 1H, J = 3.44 Hz), 6.48 (d, 1H, J = 9.74 Hz), 6.24 (d, 1H, J = 9.74 Hz), 5.75 (d, 1H, J = 3.44 Hz), 1.35 (s, 9H), 0.87 (s, 9H), - 10.2 (s, 1.84H, 92%); HRMS (APCI, negative ion mode) calcd for C₉₂H₃₄N₂ (**10**⁻) 1166.2811, found 1166.2777 and for C₉₄H₃₄N₂O (H₂O@**10**⁻) 1185.2867, found 1184.2846.

Crystal structure of 8•(toluene)₂. Single crystals of 8 were obtained from a toluene solution by slow evaporation. Intensity data were collected at 100 K on a Bruker Single Crystal CCD X-ray Diffractometer (SMART APEX II) with Mo K α radiation ($\lambda = 0.71073$ Å) and graphite monochromater. A total of 14004 reflections were measured at the maximum 2θ angle of 50.1°, of which 5420 were independent reflections ($R_{int} = 0.0201$). The structure was solved by direct methods (SHELXS-97³⁵) and refined by the full-matrix least-squares on F^2 (SHELXL-97³⁵). The *t*-butyl group on the 2-pyridyl group was disordered, which was solved using appropriate models.. Thus, two sets of t-butyl groups, i.e., (C41-C43) and (C58-C60), were placed and their occupancies were refined to be 0.80 and 0.20, respectively. This crystal contains two disordered toluene molecules, i.e., [(C44-C50) and (C44#-C50#)] and [(C51-C57) and (C51#-C57#)]which laid on the special position. The occupancies were refined to be 0.50 in each molecule. All non-hydrogen atoms except for the minor components were refined anisotropically. All hydrogen atoms were placed using AFIX instructions. The crystal data are as follows: $C_{48}H_{21}N$; FW = 611.66, crystal size $0.33 \times 0.23 \times 0.07 \text{ mm}^3$, monoclinic, $P2_1/m$, a = 11.7973(8) Å, b =16.8078(11) Å, c = 14.2706(9) Å, $\beta = 94.0714(9)^{\circ}$, V = 2822.5(3) Å³, Z = 4, $D_c = 1.439$ g cm⁻³. The refinement converged to $R_1 = 0.0487$, $wR_2 = 0.1256$ ($I > 2\sigma(I)$), GOF = 1.102.



Figure S1. (a) Crystal structure of **8** with 50% probability of thermal ellipsoids, (b) molecular structure, and (c) packing structure.

Crystal structure of 7•(benzene)_{0.5}. Single crystals of **7** were obtained from a benzene solution by slow evaporation. Intensity data were collected at 100 K on a Bruker Single Crystal CCD X-ray Diffractometer (SMART APEX II) with Mo K α radiation ($\lambda = 0.71073$ Å) and graphite monochromater. A total of 23075 reflections were measured at the maximum 2θ angle of 50.1°, of which 8426 were independent reflections ($R_{int} = 0.0867$). The structure was solved by direct methods (SHELXS-97³⁵) and refined by the full-matrix least-squares on F^2 (SHELXL-97³⁵). The *t*-butyl group on the 2-pyridyl groups, i.e., (C79–C81) and (C82–C84), were placed and their occupancies were refined to be 0.67 and 0.33, respectively. All non-hydrogen atoms except for the minor components were refined anisotropically. All hydrogen atoms were placed using AFIX instructions. The crystal data are as follows: C₈₅H₂₉N₂O₂; FW = 1110.10, crystal size 0.09 × 0.09 × 0.07 mm³, monoclinic, $P_{1/n}$, a = 10.8066(12) Å, b = 23.950(3) Å, c = 19.315(2) Å, $\beta = 105.8611(18)^\circ$, V = 4808.8(10) Å³, Z = 4, $D_c = 1.533$ g cm⁻³. The refinement converged to $R_1 = 0.0663$, $wR_2 = 0.1334$ ($I > 2\sigma(I)$), GOF = 1.026.



Figure S2. (a) Crystal structure of **7** with 50% probability of thermal ellipsoids, (b) molecular structure, and (c) packing structure.

Crystal structure of 7•(CS_{2})_{1.5}. Single crystals of 7 were obtained from a toluene solution by slow evaporation. Intensity data were collected at 100 K on a Bruker Single Crystal CCD Xray Diffractometer (SMART APEX II) with Mo K α radiation ($\lambda = 0.71073$ Å) and graphite monochromater. A total of 24215 reflections were measured at the maximum 2θ angle of 50.1°, of which 8958 were independent reflections ($R_{int} = 0.0256$). The structure was solved by direct methods (SHELXS-97³⁵) and refined by the full-matrix least-squares on F^2 (SHELXL-97³⁵). The t-butyl groups on the 2-pyridyl groups were disordered, which was solved using appropriate models. Thus, two sets of t-butyl groups, i.e., [(C71-C73) and (C85-C87)] and [(C80-C82) and (C88–C90)], were placed and their occupancies were refined to be 0.86 and 0.14 for the former and 0.84 and 0.14 for the latter, respectively. This crystal contains one disordered CS_2 molecule, i.e., (S1–C83–S2) and (S1#–C83#–S2#), which laid on the special position, and the occupancies were refined to be 0.50. This crystal contains one additional CS₂ molecule, i.e., $(S3-C83-S3^{\#})$, in which the occupancy was refined to be 0.50. All non-hydrogen atoms except for the minor components and the CS_2 molecule (S3–C83–S3#) were refined anisotropically. All hydrogen atoms were placed using AFIX instructions. The crystal data are as follows: C_{82.75}H₂₆N₂O₂S_{1.50}; FW = 1128.15, crystal size $0.37 \times 0.33 \times 0.16$ mm³, monoclinic, $P2_1/n$, a = 10.7378(6) Å, b = 10.7378(6)24.2061(15) Å, c = 19.2129(12) Å, $\beta = 104.9002(8)^\circ$, V = 4825.9(5) Å³, Z = 4, $D_c = 1.553$ g cm⁻ ³. The refinement converged to $R_1 = 0.0613$, $wR_2 = 0.1631$ ($I > 2\sigma(I)$), GOF = 1.075.



Figure S3. (a) Crystal structure of **7** with 50% probability of thermal ellipsoids, (b) molecular structure, and (c) packing structure.

Crystal structure of H₂**O**@**10**•(**CS**₂)₂. Single crystals of H₂O@**10** were obtained from a CS₂ solution by slow evaporation. Intensity data were collected at 100 K on a Bruker Single Crystal CCD X-ray Diffractometer (SMART APEX II) with Mo K α radiation ($\lambda = 0.71073$ Å) and graphite monochromater. A total of 27850 reflections were measured at the maximum 2 θ angle of 50.1°, of which 10156 were independent reflections ($R_{int} = 0.0311$). The structure was solved by direct methods (SHELXS-97³⁵) and refined by the full-matrix least-squares on F^2 (SHELXL-97³⁵). All non-hydrogen atoms were refined anisotropically. The hydrogen atoms of water molecule in the fullerene cage (H1 and H94) were placed and restrained using DFIX instruction during the refinement. All hydrogen atoms except for the water molecule (H1 and H94) were placed using AFIX instructions. The crystal data are as follows: C₉₄H₃₆N₂OS₄; FW = 1337.49, crystal size 0.20 × 0.05 × 0.03 mm³, orthorhombic, *P*2₁2₁2₁, *a* = 12.0669(15) Å, *b* = 17.883(2) Å, *c* = 26.759(3) Å, *V* = 5774.4(13) Å³, Z = 4, *D*_c = 1.538 g cm⁻³. The refinement converged to *R*₁ = 0.0600, *wR*₂ = 0.1490 (*I* > 2 σ (*I*)), GOF = 1.064.



Figure S4. (a) Crystal structure of $H_2O@10$ with 50% probability of thermal ellipsoids, (b) molecular structure, and (c) packing structure.

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List of Publications

Publications Included in This Thesis

Chapter 1

Synthesis of Open-Cage Ketolactam Derivatives of Fullerene C₆₀ Encapsulating a Hydrogen Molecule <u>Yoshifumi Hashikawa</u>, Michihisa Murata, Atsushi Wakamiya, Yasujiro Murata *Org. Lett.* **2014**, *16*, 2970–2973. (Letter) DOI: org/10.1021/ol501113y.

Chapter 2

Synthesis and Properties of Endohedral Aza[60]fullerenes: H₂O@C₅₉N and H₂@C₅₉N as Their Dimers and Monomers <u>Yoshifumi Hashikawa</u>, Michihisa Murata, Atsushi Wakamiya, Yasujiro Murata *J. Am. Chem. Soc.* **2016**, *138*, 4096–4104. (Article) DOI: 10.1021/jacs.5b12795.

Chapter 3

Facile Access to Azafullerenyl Cation C₅₉N⁺ and Specific Interaction with Entrapped Molecules <u>Yoshifumi Hashikawa</u>, Yasujiro Murata *J. Am. Chem. Soc.* 2017, *139*, 18468–18471. (Communication)
DOI: 10.1021/jacs.7b11322.
Selected as Journal Cover

Chapter 4

Water Entrapped inside Fullerene Cages: A Potential Probe for Evaluation of Bond Polarization.
<u>Yoshifumi Hashikawa</u>, Michihisa Murata, Atsushi Wakamiya, Yasujiro Murata *Angew. Chem., Int. Ed.* 2016, 55, 13109–13113. (Communication)
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Chapter 5

Palladium-Catalyzed Cyclization: Regioselectivity and Structure of Arene-Fused C₆₀ Derivatives
<u>Yoshifumi Hashikawa</u>, Michihisa Murata, Atsushi Wakamiya, Yasujiro Murata *J. Am. Chem. Soc.* 2017, *139*, 16350–16358. (Article)
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Other Publications not Included in This Thesis

(1) Co(I)-Mediated Removal of Addends on the C₆₀ Cage and Formation of Monovalent Cobalt Complex CpCo(CO)(η^2 -C₆₀) <u>Yoshifumi Hashikawa</u>, Michihisa Murata, Atsushi Wakamiya, Yasujiro Murata *Org. Lett.* **2016**, *18*, 6348–6351. (Letter) DOI: 10.1021/acs.orglett.6b03238.

(2) Structural Modification of Open-Cage Fullerene C₆₀ Derivatives Having a Small Molecule inside Their Cavities
<u>Yoshifumi Hashikawa</u>, Michihisa Murata, Atsushi Wakamiya, Yasujiro Murata *Can. J. Chem.* 2017, *95*, 320–328. (Article)
DOI: 10.1139/cjc-2016-0465.
Special issue to honor Professor Reginald Mitchell

(3) Orientation of a Water Molecule: Effects on Electronic Nature of the C₅₉N Cage <u>Yoshifumi Hashikawa</u>, Michihisa Murata, Atsushi Wakamiya, Yasujiro Murata *J. Org. Chem.* 2017, 82, 4465–4469. (Note) DOI: 10.1021/acs.joc.7b00453.

(4) Single Molecular Junction Study on H₂O@C₆₀: H₂O is "Electrostatically Isolated"
Satoshi Kaneko, <u>Yoshifumi Hashikawa</u>, Shintaro Fujii, Yasujiro Murata, Manabu Kiguchi *Chem. Phys. Chem.* 2017, *18*, 1229–1233. (Communication)
DOI: 10.1002/cphc.201700173.
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(5) Solvent-Coordinated Tin Halide Complexes as Purified Precursors for Tin-Based Perovskites Masashi Ozaki, Yukie Katsuki, Jiewei Liu, Taketo Handa, Ryosuke Nishikubo, Shinya Yakumaru, <u>Yoshifumi Hashikawa</u>, Yasujiro Murata, Takashi Saito, Yuichi Shimakawa, Yoshihiko Kanemitsu, Akinori Saeki, Atsushi Wakamiya *ACS Omega* **2017**, *2*, 7016–7021. (Article)

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(6) High-Resolution Photoelectron Imaging of Cryogenically-Cooled $C_{59}N^-$ and $(C_{59}N)_2^{2-}$ Azafullerene Anions

Guo-Zhu Zhu, <u>Yoshifumi Hashikawa</u>, Yuan Liu, Qian-Fan Zhang, Ling Fung Cheung, Yasujiro Murata, Lai-Sheng Wang

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(7) Synthesis and Properties of Open-Cage Fullerene C_{60} Derivatives: Impact of the Extended π -Conjugation

Yoshifumi Hashikawa, Hidefumi Yasui, Kei Kurotobi, Yasujiro Murata

Mater. Chem. Front. 2018, 2, 206–213. (Advance Article)

DOI: 10.1039/c7qm00449d.

Invited paper on the themed collection: Pi conjugated system bricolage (figuration) toward functional organic molecular systems

Selected on the themed collection: 2018 Materials Chemistry Frontiers Review-type Articles

(8) Probing the Interaction between the Encapsulated Water Molecule and the Fullerene Cages in $H_2O@C_{60}^-$ and $H_2O@C_{59}N^-$

Guo-Zhu Zhu, Yuan Liu, <u>Yoshifumi Hashikawa</u>, Qian-Fan Zhang, Yasujiro Murata, Lai-Sheng Wang

Chem. Sci. 2018, 9, 5666–5671. (Edge Article)

DOI: 10.1039/C8SC01031E.

Selected as 2018 Chemical Science HOT Article

(9) Construction of a Metal-Free Electron Spin System by Encapsulation of an NO Molecule inside an Open-Cage Fullerene C₆₀ Derivative. Shota Hasegawa, <u>Yoshifumi Hashikawa</u>, Tatsuhisa Kato, Yasujiro Murata

Angew. Chem., Int. Ed. 2018, 138, 4096–4104. (Communication)

DOI: 10.1002/anie.201807823.

(10) A Single *but* Hydrogen-Bonded Water Molecule Confined in an Anisotropic Subnanospace <u>Yoshifumi Hashikawa</u>, Shota Hasegawa, Yasujiro Murata *Chem. Commun.* 2018, *54*, 13686–13689. (Communication) DOI: 10.1039/c8cc07339b. (11) Wavelength-Dependent Efficiency of Sequential Photooxygenation: C=C Bond Cleavage on Open-Cage C₆₀ Derivatives
<u>Yoshifumi Hashikawa</u>, Yasujiro Murata *ChemPlusChem* 2018, 83, 1179–1183. (Communication)
DOI: 10.1002/cplu.201800464.
Invited paper on the official special issue of ISNA-18: Novel Aromatics
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(12) Probing the Regioselectivity Using an Entrapped H₂: Diels-Alder Reaction of a Cage Opened C₆₀ Derivative with Anthracene
<u>Yoshifumi Hashikawa</u>, Yasujiro Murata *Chem.-Eur. J.* 2019, 25, 2482–2485. (Communication)
DOI: 10.1002/chem.201806030.

(13) Rotational Motion and Nuclear-Spin Interconversion of H₂O Encapsulated in C₆₀ Appeared in the Low-Temperature Heat Capacity
Hal Suzuki, Motohiro Nakano, <u>Yoshifumi Hashikawa</u>, Yasujiro Murata *J. Phys. Chem. Lett.* **2019**, *10*, 1306–1311. (Letter)
DOI: 10.1021/acs.jpclett.9b00311.

Book Chapter

(1) Cutting-edge Technology in Fullerene Derivatives and Endohedral Fullerenes.
Yasujiro Murata, Rui Zhang, <u>Yoshifumi Hashikawa</u>
Chapter 3. Synthesis and Derivatization of Endohedral Fullerenes: Endohedral Fullerene
Encapsulating a Water Molecule
pp.135–142, CMC Publishing, 2014

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