opening generated in situ, followed by addition of a water molecule to regenerate bishemiketal encapsulating an H_2O molecule. The ^1H NMR spectrum of H_2O-encapsulated bishemiketal displayed a strongly shielded sharp signal at -9.87 parts per million (ppm), corresponding to the encapsulated H_2O molecule. The encapsulation was also supported by fast atom bombardment mass spectrometry analysis displaying the molecular ion peak at a mass-to-charge ratio m/z 1139 $(M+H^+)$, corresponding to H_2O-encapsulated bishemiketal. Our synthetic pathway for closing the 13-membered-ring opening on H_2O-encapsulated bishemiketal is a coupling reaction of two carbonyl groups with a phosphite ester. As shown in Scheme 1-79, the reaction of H_2O-encapsulated bishemiketal with excessive amounts of $P(Oi\text{-}Pr)_3$ (i-Pr, isopropyl) in refluxing toluene gave H_2O-encapsulated fullerenes in 50% isolated yield without the loss of the encapsulated H_2O molecule, followed by two successive carbonyl couplings. The final step in the synthesis of $H_2O@C_{60}$ is removal of the organic addend. They mixed H_2O-encapsulated fullerene (50 mg) with neutral Al_2O_3 (1 g) in a mortar, and the resulting mixture was heated at 360 °C for 1 hour under vacuum to give $H_2O@C_{60}$ as brown powder in 29% yield after purification with silica gel chromatography. This step likely proceeded though a [4+2]cyclization, retro[4+4]reaction, and formation of a bicylo[2.2.0]hexene moiety followed by a retro[4+2]reaction, which would be thereverse of the reaction of the addition, or radical cleavage of four C-C single bonds. Direct evidence for the existence of the encapsulated H_2O molecule inside C_{60} was obtained from single-crystal X-ray analysis. The ^{13}C NMR (ODCB-d_4) spectrum showed a sharp signal at 142.89 ppm, suggesting rapid rotation of the encapsulated H_2O molecule inside the C_{60} cage with respect to the time scale of NMR.
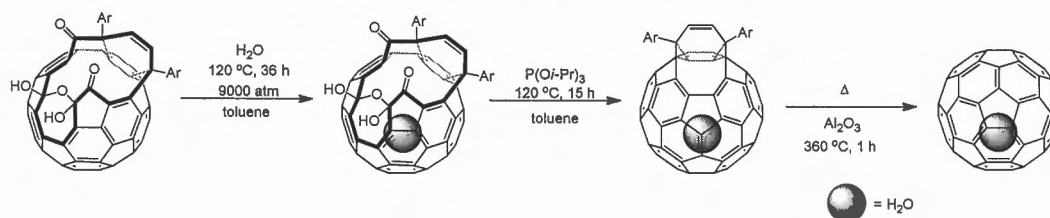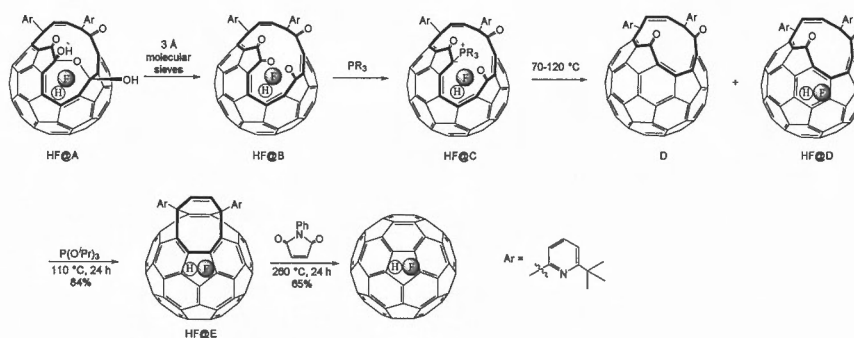

Scheme 1-80

The improved synthetic routes to the small-molecule endofullerenes $H_2O@C_{60}$, $D_2O@C_{60}$ and $H_2@C_{60}$ was reported by Whitby et al.[171] The use of high temperatures and pressures for the endohedral molecule incorporation are avoided. A new partial closure step using PPh_3, and final suturing using a novel Diels-Alder/retro-Diels-Alder sequence with maleimide are amongst the advances reported. When a solution of tetra-ketone or its bishemiketal intermediate for the improved syntheses was treated with a large excess of 70% w/w hydrogen fluoride in pyridine (HF-Py), HF-encapsulated fullerene was isolated after basic work-up and chromatography (Scheme 1-81). The filling factor of HF was established by ^1H NMR spectroscopy, comparing the integral values of the endohedral HF proton with the protons on the exohedral groups. The

highest filling factor (50%) was achieved by equilibrating a solution in dichloromethane with an excess (200 eq. HF) of HF-Py at room temperature. The ESI$^+$ MS spectrum of the isolated compounds displays signals at m/z 1121 and 1141 respectively for the molecular ions of empty and HF-encapsulated fullerenes. Solution state NMR typically reveals unusual chemical shifts for the endohedral nuclei due to the strong magnetic shielding effect of the fullerene cage. Indeed the ^{1}H signal from the HF molecule in HF-encapsulated fullerene appears as a doublet centred at δ = 6.55 ppm with a J_{HF} of 508 Hz. A doublet with a J_{HF} of 508 Hz is present in the ^{19}F NMR at δ 223.91 ppm; the two lines coalesce into a singlet in the proton decoupled spectrum.
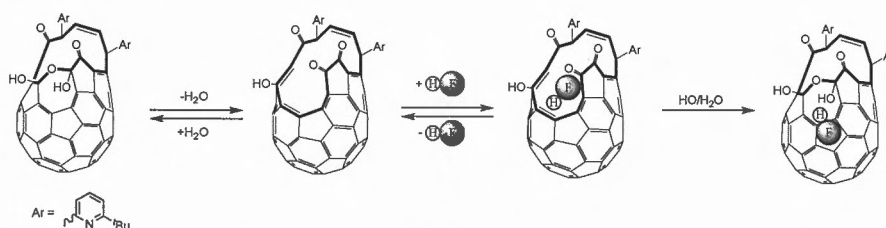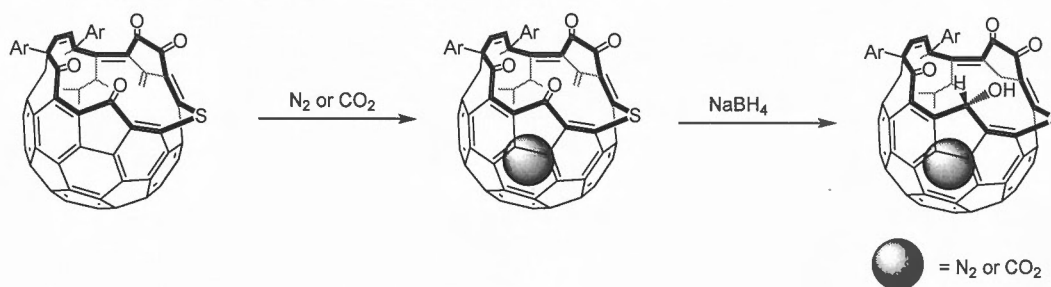

Scheme 1-81

Furthermore, Witby et al. reported the encapsulation of hydrogen fluoride inside C$_{60}$ using molecular surgery to give the endohedral fullerene HF@C$_{60}$ (Scheme 1-81).[173] Stirring HF@A with 3 Å molecular sieves at room temperature allowed the formation of HF@B without a significant loss of the endohedral molecule. HF@B reacted slowly with PPh$_3$ at room temperature to afford the unusual isolable phosphorous ylid HF@C (PR$_3$ = PPh$_3$), again with retention of HF. The regiochemistry of ylid C was confirmed by a 9.6 Hz coupling between the phosphorous and the adjacent carbonyl carbon, and by good agreement of the calculated ^{13}C NMR spectra of only the isomer shown with experimental values. The orifice of HF@D can be sutured, as reported for H$_2$O@D, without further loss of the endohedral molecule. Thus, 30% filled HF@C$_{60}$ was isolated after the reduction of HF@D with triisopropylphosphite to afford HF@E followed by reaction with N-phenylmaleimide. Overall, sublimed 30% filled HF@C$_{60}$ is produced in three steps and 36% yield from 50% filled HF@A. HPLC on a Buckyprep column can be used to separate HF@C$_{60}$ (retention time, 8.05 minutes) from C$_{60}$ (retention time, 7.81 minutes) to afford a quantitatively filled sample. The ^{1}H NMR spectrum of HF@C$_{60}$ shows a doublet with a $^1J_{HF}$ of 505.5 ± 0.5 Hz at δ_H = -2.68 ppm, with the upfield shift caused by the shielding effect of the C$_{60}$ cage.
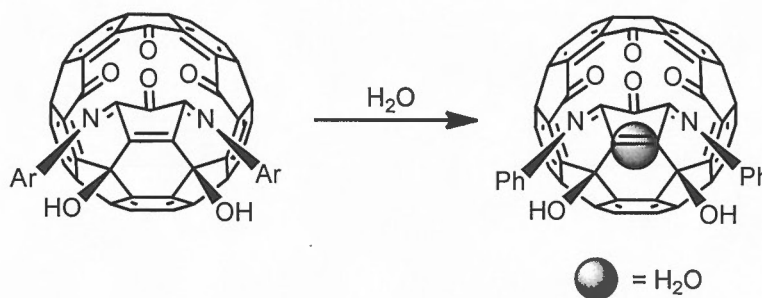
Scheme 1-82

On the other hand, Murata et al. reported that an open-cage C_{60} tetraketone with a large opening was able to encapsulate N_2 and CO_2 molecules after its exposure to high pressures of N_2 and CO_2 gas. A subsequent selective reduction of one of the four carbonyl groups on the rim of the opening induced a contraction of the opening and trapped the guest molecules inside. The thus-obtained host-guest complexes with N_2 and CO_2 could be isolated by recycling HPLC, and were found to be stable at room temperature (Scheme 1-83).[174] The molecular structures of N_2- and CO_2-encapsulated fullerenes were determined by single-crystal X-ray diffraction analyses, and revealed the encapsulated fullerene with N_2 and CO_2.
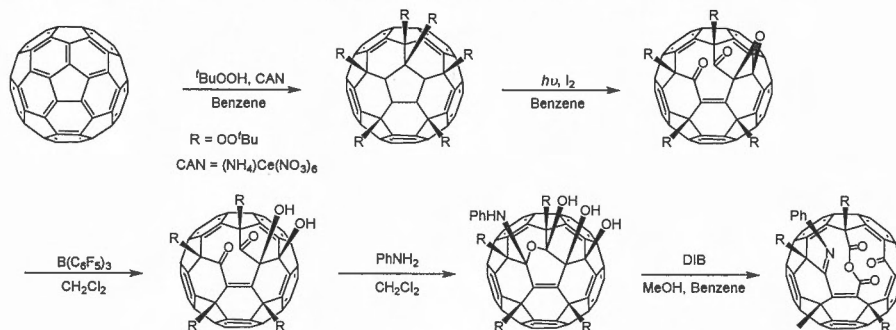

Scheme 1-83

Starting from open-cage fullerene prepared on Scheme 1-50, Gan, Wang and co-workers recently reported that heating a solution of it (Scheme 1-84)[130] in toluene-water at 70 °C for 5 h, results in water encapsulation at a 40% ratio as determined by ^{1}H NMR spectroscopy. Further heating for 24 h increased the incorporation up to 87%. Endohedral complex H_2O-encapsulated fullerene was identified through its single-crystal X-ray structure.
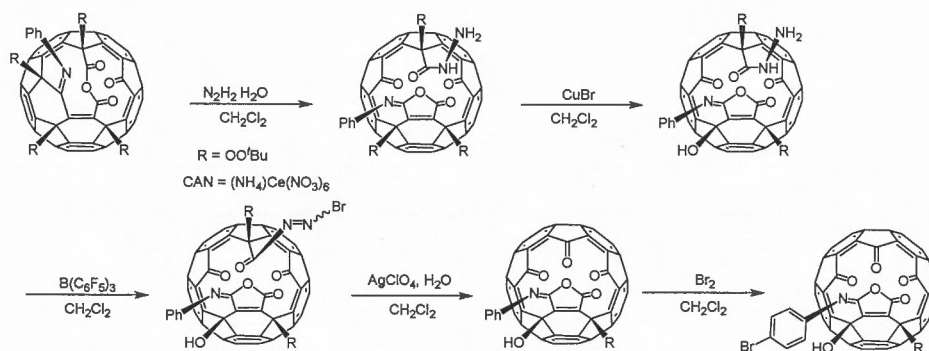

Scheme 1-84

The synthesis of open-cage fullerene derivatives with 18- and 19-membered-ring orifices was reported in 2007 by Gan, Wang and co-workers. Initially, aminoketal/hemiketal derivatives, derived from adduct in Scheme 1-85 after an epoxide ring opening reaction and coupling of the adjacent carbonyl groups through treatment with an arylamine, were oxidized by (diacetoxy)iodobenzene (DIB) to afford open-cage adducts (Scheme 1-85).[175] The three hydroxyl groups in it were converted into carbonyls, whereas the amino group was also transformed into an imine. These compounds bear an anhydride bridge, the removal of which could afford a large opening on the fullerene cage (Scheme 1-86). Indeed, primary amines (R'NH$_2$) reacted with this anhydride to give 18-membered-ring orifice products after multiple bond cleavages in one step. The structure of it, i.e. the exact positions of all functional groups, was elucidated by means of single-crystal X-ray analysis on one of these compounds. Although the compound bears a pretty large opening, the presence of the amide group blocks the entrance as evinced in its X-ray structure. Hence, in order to make the aperture more accessible, they attempted to remove the amide moiety. At first, hydrazine adduct was treated with Br$_2$ to provide bromoazo product as a mixture of E and Z isomers (Scheme 1-86). Then, treatment of it with AgClO$_4$ removed the acyl group. Conversion of it (R" = OH) into the p-bromo substituted adduct, in the presence Br$_2$, has been proven useful for the preparation of crystals suitable for X-ray analysis. The X-ray structure of it clearly shows that the amide moiety is absent, and that the access to the 18-membered-ring opening is now improved (Scheme 1-86).
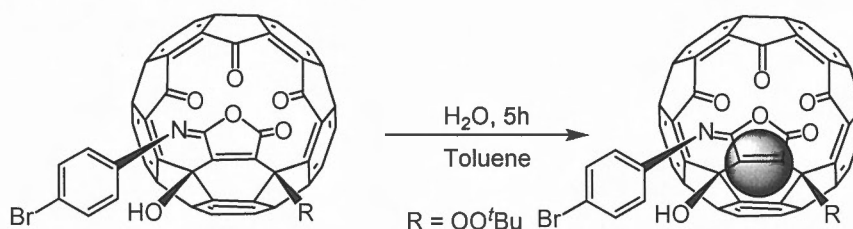

Scheme 1-85

Scheme 1-86

66

Gan et al. also reported that this open-cage compounds were also found capable of incorporating a water molecule within the cage (Scheme 1-87).[176] In particular, in the ^{1}H NMR spectra of the 18-membered-ring orifice adducts, low-intensity peaks were present at $\delta = -13.13$ ppm. This peak was attributed to encapsulated water molecules, in accordance with the water-encapsulated complexes reported by Iwamatsu. The encapsulation ratios were less than 5%, increasing to 78%, only after heating a solution in toluene/water at 80 °C for 5 h. Endohedral complexes H_2O-encapsulated fullerenes exchange H_2O with D_2O in a D_2O-added $CDCl_3$ solution. The enclosed water molecules in H_2O-encapsulated fullerenes were directly observed in their X-ray structures at 200 K.

Scheme 1-87

In general, water was found to enter the cavity of open-cage fullerenes. Considering the hydrophobic nature of carbon atoms on the fullerene skeleton, it is quite a surprising observation. What is the driving force for water encapsulation? A possible explanation is that the empty cavity of the fullerene cage is electropositive. Owing to the curvature of the fullerene cage, the electron density is greater on the outer surface than on the more crowded inner surface, to minimize electron repulsion (Figure 1-24). The presence of the multiple carbonyl groups in the present open-cage compounds probably increases the electron deficiency through their electron-withdrawing effect. Therefore, the cavity acts like an empty orbital of a Lewis acid. The encapsulation of water is thus a "Lewis acid and Lewis base" interaction between the encapsulated water and the cavity.
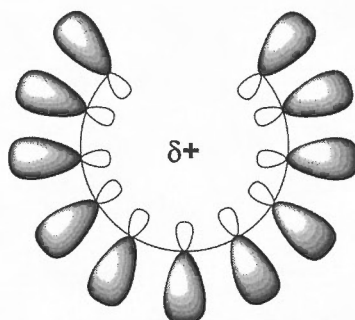

Figure 1-24

All the above open-cage fullerenes have an orifice large enough to encapsulate water efficiently, but at the same time, the trapped water molecule can also escape from the cavity rapidly because of the large size of the orifice. Thus, exchange of D_2O with trapped H_2O could be observed by

^{1}H NMR. Compound reported by Murata and Kurotobi was an exception. In this case, high pressure and longtime heating were needed to encapsulate the water molecule, and the trapped water molecule remained inside the cavity during successive orifice closing reactions. For potential application purposes such as delivery of trapped atom or molecule, it is desirable to control the encapsulation and release process. In other words, an open-cage fullerene with an easily switchable stopper is needed. Ideally, the trigger can be activated and stopped by an external stimulus such as photon, proton or electron. In an effort to prepare such a molecular vial, Gan et al. treated open-cage fullerene (Ar = Ph) with triethylphosphite and obtained compound with a phosphate group above the orifice (Scheme 1-88).[177] The phosphate group reduces the size of the orifice significantly, and thus the rate of water exchange rate of was drastically decreased compared to compound without phosphate (Ar = Ph) as shown by theoretical calculation and ^{1}H NMR D_2O exchange experiments. The calculated increase of energy barrier for water leaving the cavity in the gas phase is 23 kJ mol^{-1} from compound with phosphate (Ar = Ph) without the stopper to compound with a stopper. The phosphate group can be removed by hydrolysis under basic condition but only with moderate yield.
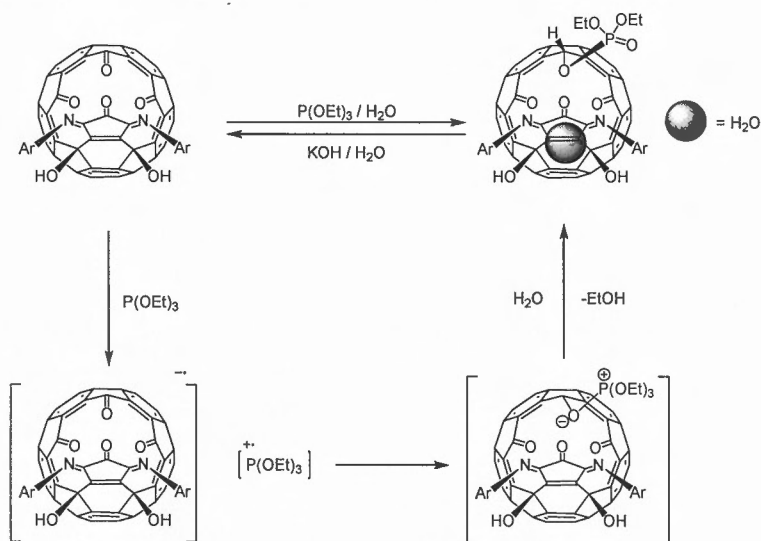
Scheme 1-88

In an effort to encapsulate hydrogen fluoride in open-cage fullerene like Witby's work, Gan et al. treated a mixture of empty and H_2O-encapsulated fullerenes with aqueous hydrogen fluoride (Scheme 1-89).[178] The HF addition product was produced slowly instead of the expected hydrogen fluoride encapsulation product. ^{1}H NMR spectra of it showed clearly that there is hardly any detectable signal for trapped water, which should appear in the high-field range above 0 ppm owing to the shielding effect of the fullerene cage. The HF adduct is not stable and decomposes to empty open-cage fullerene in a few days. Treating HF adduct with $B(C_6F_5)_3$ eliminates hydrogen fluoride to give empty open-cage fullerene in 10 min. Trifluoroacetic acid

could also convert HF adduct into open-cage fullerene. The ^{1}H-decoupled ^{19}F fluorine NMR spectrum of HF adduct showed two doublets. The high-field signal at -205.10 ppm is most likely due to the fluorine atom that is well-shielded by the fullerene cage.
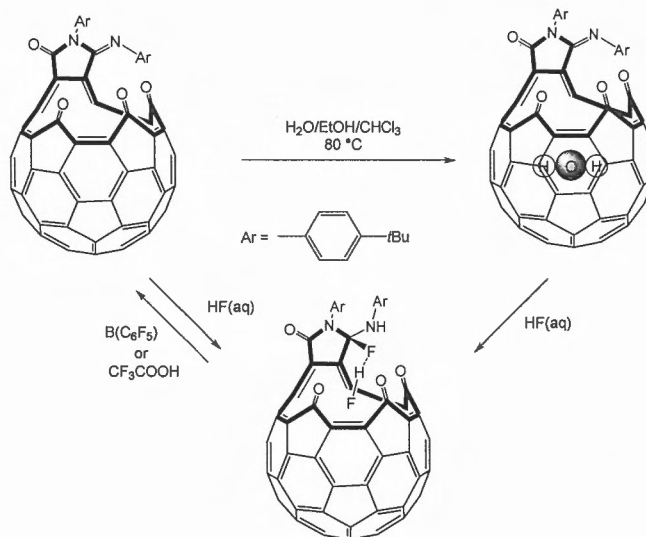
Scheme 1-89

Recently, open-cage fullerenes with a dynamic orifice were reported by Gan et al. (Scheme 1-90).[179] Compound has an aryl imide group above the orifice. Unlike the rigid orifices in the above open-cage compounds, rotation of the aryl group about the Ar-N bond makes the size of the orifice flexible within a range defined by the substituent on the aryl group. When the aryl group is parallel to the imide ring, the size of the orifice is the largest and water can go in and out of the cage with a barrier close to that of the compound. When the aryl group is perpendicular to the imide ring, the orifice size is the smallest. The flexibility of the orifice is demonstrated by the ability of compounds (Ar = 2,4-dimethylphenyl) to trap either water or hydrogen. All the compounds mentioned earlier with a large rigid orifice can trap water but not hydrogen due to rapid escape. The methyl group at the 6-position of the aryl group in the compound is relatively bulky. When this methyl group is located directly above the orifice, the compound has a very small orifice compared to the other conformation with H-atom above the orifice (Scheme 1-90). Rotation of the aryl-N bond back and forth thus could in principle act as a stopper for the orifice. But at present, it is not possible to control the rotation. The two conformations exist in thermaldynamic equilibrium as observed by ^{1}H NMR spectroscopy.
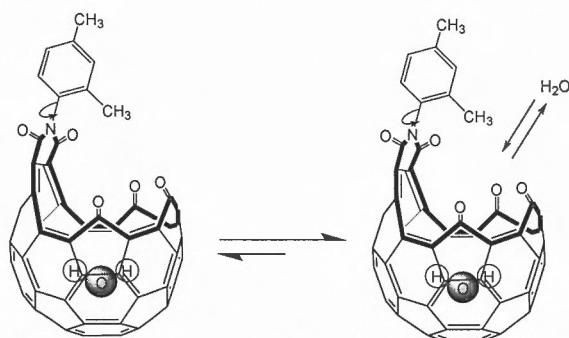
Scheme 1-90

To expand the orifice Gan et al. treated a triol component with diacetoxyl iodobenzene (DIB). To their surprise, compound with a CO molecule trapped in the cavity was isolated.[152] Spectroscopic data are in agreement with the CO-trapped structure. Conclusive structural assignment came from the single-crystal X-ray diffraction structure of its Diels-Alder derivative. Two regioisomers were obtained from the addition of 1,4-diphenyl butadiene. Steric hindrance favors the less crowded product. A possible mechanism for the key step of CO encapsulationis shown in Scheme 1-91. The first step is replacement of the two acetoxyl groups by two hydroxyl groups to form intermediate **A**. The regioselective formation of the dioxolane is controlled by the most reactive hemiketal hydroxyl group. The driving force for the rearrangements from **A** to **B** to **C** should be mainly the release of ring strain. The S_N2-type process from intermediate **C** to **D** pushes the carbon mon-oxide into the cavity of the cage. The presence of the tertbutyl and phenyl groups must play an important role as well in pushing in the carbon monoxide inside the cavity.
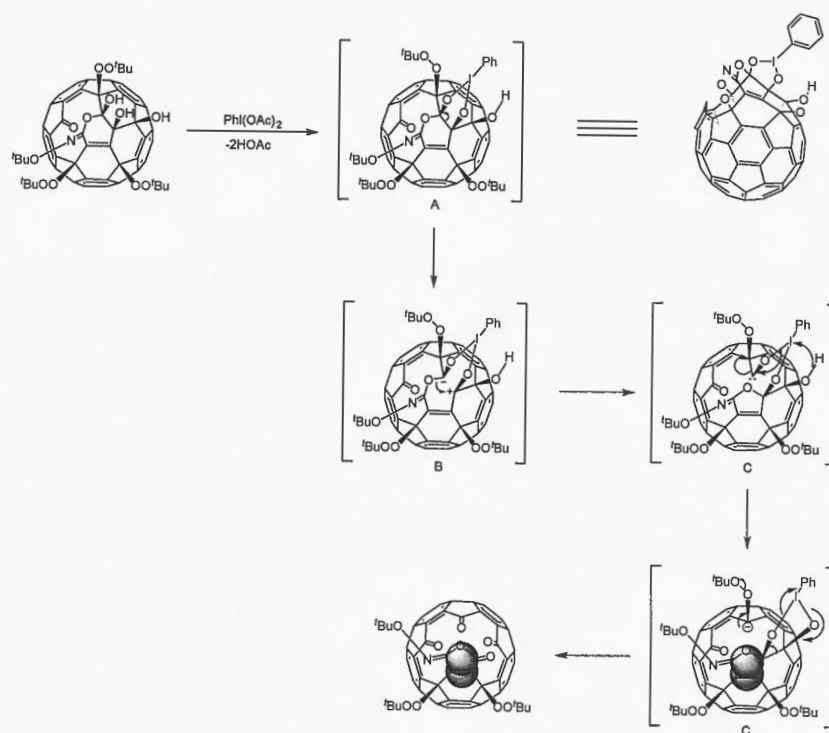
Scheme 1-91

Reference

1) a) R. Ananthaiah, *RESONANCE*, January, **1997**, 68.

   b) E. Osawa, *Kagaku*, **1970**, *25*, 850.

   c) Z. Yoshida, E. Osawa, *Aromaticity* (in Japanese) (Kagakudoujin, Kyoto, **1971**).

2) H. W. Kroto, J. R Heath, S. C. O'Brien, R. F. Curl and R. E. Smalley, *Nature*, **1985**, *318*, 162.

3) a) R. E. Smalley, *The Sciences*, March/April, **1991**, 22.

   b) H. W. Kroto, *Angew. Chem. Int. Ed.* Engl., **1992**, *31*, 111.

   c) G. Taubes, *Science*, **1991**, *253*, 1476.

4) W. Krätchmer, L. D. Lamb, K. Fostiropoulos and D. R. Huffman, *Nature*, **1990**, *347*, 354.

5) W. Krätchmer, K. Fostiropoulos and D. R. Huffman, *Chem. Phys. Lett.*, **1990**, *170*, 167.

6) L. D. Lamb and D. R. Hoffman, *J. Phys. Chem. Solids*, **1993**, *54*, 1635.

7) R. E. Haufler, J. Conceicao, L. P. F. Chibante, Y. Chai, N. E. Byrne, S. Flanagan, M. M. Haley, S. C. O'Brien, C. Pan, Z. Xiao, W. E. Billups, M. A. Ciufolini, R. H. Hauge, J. L. Margrave, L. J. Wilson, R. F. Curl and R. E. Smalley, *J. Phys. Chem.*, **1990**, *94*, 8634.

8) R. E. Haufler, *Proc. Sympo. Recent Advances Chem. Phys. Fullerenes and Related Materials*, The *Electrochemical Society*, **1994**, *94-24*, 50.

9) J. C. Winter, R. O. Loufty and T. P. Lowe, *Fullerene Sci. Technol.*, **1997**, *5*, 1.

10) a) J. B. Howard, J. T. McKinnon, Y. Makarovsky, A. L. Laufleur and M. E. Johnson, *Nature*, **1991**, *352*, 139.

    b) J. B. Howard, J. T. Mckinnon, M. E. Johnson, Y. Makarovsky and A. L. Laufleur, *J. Phys. Chem.*, **1992**, *96*, 657.

11) L. P. F. Chibante, A. Thess, J. M. Alford, M. D. Diener and R. E. Smalley, *J. Phys. Chem.*, **1993**, *97*, 8696.

12) C. L. Field, J. R. Pitts, M. J. Hale, C. Bingham, A. Lewandowski and D. E. King, *J. Phys. Chem.*, **1993**, *97*, 8701.

13) R. Taylor, G. J. Langley, H. W. Kroto and D. R. M. Walton, *Nature*, **1993**, *366*, 728.

14) R. Boese, A. J. Matzger and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **1997**, *119*, 2052.

15) R. F. Bunshah, S. Jou, S. Prakash, H. J. Doerr, L. Isaacs, A. Wehrsig, C. Yeretzian, H. Cynn and F. Diederich, *J. Phys. Chem.*, **1992**, *96*, 6866.

16) M. M. Boorum, Y. V. Vasil'ev, T. Drewello and L. T. Scott, *Science*, **2001**, *294*, 828.

17) L. T. Scott, M. M. Boorum, B. J. McMahon, S. Hagen, J. Mack, J. Blank, H. Wegner and A. de Meijere, *Science*, **2002**, *295*, 1500.

18) V. M. Tsefrikas and L. T. Scott, *Chem. Rev.*, **2006**, *106*, 4868.

19) R. Taylor, J. P. Hare, A. Abdul-Sada and H. W. Kroto, *J. Chem. Soc., Chem. Commun.*, **1990**, 1423.

20) C. S. Yannoni, R. D. Johnson, G. Meijer, D. S. Bethune and J. R. Salem, *J. Phys. Chem.*, **1991**,

95, 9.

21) J. M. Hawkins, A. L. Meyer, A. Timothy, S. Loren and F. J. Hollander, *Science*, **1991**, *252*, 312.

22) P. J. Fagan, J. C. Calabrese and B. Malone, *Science*, **1991**, *252*, 1160.

23) H. Kroto, *Nature*, **1987**, *329*, 529.

24) T. G. Schmalz, W. A. Seitz, D. J. Klein and G. E. Hite, *J. Am. Chem. Soc.*, **1988**, *110*, 1113.

25) A. Bax and R. Freeman, T. A. Frenkiel, *J. Am. Chem. Soc.*, **1981**, *103*, 2102.

26) A. Bax and R. Freeman, S. P. Kempsell, *J. Am. Chem. Soc.*, **1980**, *102*, 4849.

27) A. Bax and R. Freeman, *J. Magn. Reson.*, **1980**, *41*, 507.

28) J. M. Hawkins, S. Loren, A. Meyer and R. Nunlist, *J. Am. Chem. Soc.*, **1991**, *113*, 7770.

29) J. M. Hawkins, *Acc. Chem. Res.*, **1992**, *25*, 150.

30) J. M. Hawkins, A. Meyer, T. A. Lewis, U. Bunz, R. Nunlist, G. E. Ball, T. W. Ebbesen and K. Tanigaki, *J. Am. Chem. Soc.*, **1992**, *114*, 7954.

31) F. Wudl, A. Hirsh, K. C. Khemani, T. Suzuki, P.-M. Allemand, A. Koch, H. Eckert, G. Srdanov and H. M. Webb, "Fullerenes", G. S. Hammond and V. J. Kuck (eds.), ACS Symposium Series 481, ACS, Washington, DC, **1992**, *Chapter 11*.

32) R. Taylor, J. P. Hare, A. Abdul-Sada and H. W. Kroto, *J. Chem. Soc., Chem. Commun.*, **1990**, 1423.

33) J. M. Hawkins, A. Meyer, T. A. Lewis and S. Loren, "Fullerenes", G. S. Hammond and V. J. Kuck (eds.), ACS Symposium Series 481, ACS, Washington, DC, **1992**, *Chapter 6*.

34) P. J. Fagan, J. C. Calabrese and B. Malone, *Acc. Chem. Res.*, **1992**, *25*, 134.

35) R. C. Haddon, L. E. Brus and K. Raghavachari, *Chem. Phys. Lett.*, **1986**, *125*, 459.

36) A. Hirsch, "The Chemistry of Fullerenes", Thieme, Stuttgart, **1994**.

37) M. Dresselhaus, G. Dresselhaus and P. C. Eklund, "Science of Fullerenes and Carbon Nanotubes", Academic Press, San Diego, **1995**, *Chapter 10*.

38) a) F. Diederich and C. Thilgen, *Science*, **1996**, *271*, 317.
   b) F. Diederich, *Pure. Appl. Chem.*, **1997**, *69*, 395.

39) Q. Xie, E. P.-Coedero and L. Echegoten, *J. Am. Chem. Soc.*, **1992**, *114*, 56.

40) A. Hirsch, *Synthesis*, **1995**, 895.

41) E. W. Godly and R Taylor, *Pure. Appl. Chem.*, **1997**, *69*, 1411.

42) R. C. Haddon, *Science*, **1993**, *261*, 1545.

43) G. Schick, K.-D. Kampe and A. Hirsch, *J. Chem. Soc., Chem. Commun.*, **1995**, 2023.

44) K.-D. Kampe and N. Egger, *Liebigs Ann.*, **1995**, 115.

45) M. Ohno, A. Yashiro and S, Eguchi, *J. Chem. Soc., Chem. Commun.*, **1996**, 291.

46) A. W. Jensen, A. Khong, M. Saunders, S. R. Wilson and D. I. Schuster, *J. Am. Chem. Soc.*, **1997**, *119*, 7303.

47) G.-W. Wang, K. Komatsu, Y. Murata and M. Shiro, *Nature*, **1997**, *387*, 583.

48) M. Sawamura, H. Iikura and E. Nakamura, *J. Am. Chem. Soc.*, **1996**, *118*, 12850.

49) M. Maggini, G. Scorrano and M. Prato, *J. Am. Chem. Soc.*, **1993**, *115*, 9798.

50) F. Adrian, M. Ruebsam, K.-P. Dinse, D. Fuchs, H. Rietschel, R. M. Michel, M. Benz and M. M. Kappes, *Fullerene Sci. Technol.*, **1996**, *4*, 655.

51) S. R. Wilson and Q. Lu, *Tetrahedron Lett.*, **1993**, *34*, 8043.

52) M. Tsuda, T. Ishida, T. Nogami, S. Kurono and M. Ohashi, *J. Chem. Soc., Chem. Comm.*, **1993**, 1296

53) C. Bingel, *Chem. Ber.*, **1993**, *126*, 1957.

54) A. Hirsch, I. Lamparth and H. R. Karfunkel, *Angew. Chem. Int. Ed. Engl.*, **1994**, *33*, 437.

55) A. Hirsch, I. Lamparth, T. Gröser and H. R. Karfunkel, *J. Am. Chem. Soc.*, **1994**, *116*, 9385.

56) I. Lamparth, C. Maichle-Mössmer and A. Hirsch, *Angew. Chem. Int. Ed. Engl.*, **1995**, *34*, 1607.

57) S. R. Wilson and Q. Lu, *Tetrahedron. Lett.*, **1995**, *36*, 5705.

58) P. J. Fagan, P. J. Krusic, D. H. Evans, S. A. Lerke and E. Johnston, *J. Am. Chem. Soc.*, **1992**, *114*, 9697.

59) T. Tanaka, T. Kitagawa, K. Komatsu and K. Takeuchi, *J. Am. Chem. Soc.*, **1997**, *119*, 9313.

60) T. Suzuki, Q. C. Li, K. C. Khemani and F. Wudl, *J. Am. Chem. Soc.*, **1992**, *114*, 7301.

61) F. Wudl, *Acc. Chem. Res.*, **1992**, *25*, 157.

62) T. Suzuki, Q. C. Li, K. C. Khemani, F. Wudl and Ö. Almarsson, *Science*, **1991**, *254*, 1186.

63) T. Suzuki, Q. C. Li, K. C. Khemani, F. Wudl and Ö. Almarsson, *J. Am. Chem. Soc.*, **1992**, *114*, 7300.

64) S. Shi, K. C. Khemani, Q. C. Li and F. Wudl, *J. Am. Chem. Soc.*, **1992**, *114*, 10656.

65) A. B. Smith III, R. M. Strongin, L. Brard, G. T. Furst, W. J. Romanow, K. G. Owens and R. C. King, *J. Am. Chem. Soc.*, **1993**, *115*, 5829.

66) M. Prato, V. Lucchini, M. Maggini, E. Stimpfl, G. Scorrano, M. Eiermann, T. Suzuki and F. Wudl, *J. Am. Chem. Soc.*, **1993**, *115*, 8479.

67) L. Isaacs and F. Diederich, *Helv. Chim. Acta.*, **1993**, *76*, 2454.

68) F. Diederich, L. Isaacs and D. Philp, *J. Chem. Soc., Perkin Trans. 2*, **1994**, 391.

69) L. Isaacs, A. Wehrsig and F. Diederich, *Helv. Chim. Acta.*, **1993**, *76*, 1231.

70) A. Skiebe and A. Hirsch, *J. Chem. Soc., Chem. Comm.*, **1994**, 335.

71) R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, **1992**, 3.

72) R. Taylor, *Philos. Trans. R. Soc. London, Ser. A*, **1993**, *23*, 243.

73) M. Cases, M. Duran, J. Mestres, N. Martin and M. Sola, *J. Org. Chem.*, **2001**, *66*, 433.

74) V. V. Zverev, V. I. Kovalenko, I. P. Romanova and O. G. Sinyashin, *Int. J. Quant. Chem.*, **2007**, *107*, 2442.

75) A. Vasella, P. Uhlmann, C. A. A. Waldraff, F. Diederich and C. Thilgen, *Angew. Chem. Int. Ed.*, **1992**, *31*, 1388.

76) G. Schich and A. Hirsch, *Tetrahedron*, **1998**, *54*, 4283.

77) Y. Kabe, H. Hachiya, T. Saito, D, Shimizu, M. Ishiwata, K. Suzuki, Y. Yakushigawa and W. Ando, *J. Organometallic Chem.*, **2009**, *694*, 1988.

78) a) L. Isaacs, A. Wehrsig and F. Diederich, *Helv. Chim. Acta.*, **1993**, *76*, 1231.

b) L. Isaacs and F. Diederich, *Helv. Chem. Acta.*, **1993**, *76*, 2454.

79) a) Y. Nakamura, K. Inamura, R. Oomura, R. Laurenco, T. T. Tidwell and J. Nishimura, *Org. Biomol. Chem.*, **2005**, *3*, 3032.

b) Y. Nakamura, N. Takano, T. Nishimura, E. Yashima, M. Sato, T. Kudo and J. Nishimura, *Org. Lett.*, **2001**, *3*, 1193.

80) H. L. Anderson, C. Boudon, F. Diederich, J.-P. Gisselbrecht, M. Gross and P. Seiler, *Angew. Chem. Int. Ed.*, **1994**, *33*, 1628.

81) A. F. Kiely, R. C. Haddon, M. S. Meier, J. P. Selegue, C. P. Brock, B. O. Patrich, G.-W. Wang and Y. Chen, *J. Am. Chem. Soc.*, **1999**, *121*, 7971.

82) A. S. Pimenova, A. A. Kozlov, A. A. Goryunkov, V. Y. Markov, P. A. Khavrel, S. M. Avdoshenko, I. N. Ioffe, S. G. Sakharov, S. I. Troyanov and L. N. Sidorov, *Chem. Comm.*, **2007**, 374.

83) A. S. Pimenova, A. A. Kozlov, A. A. Goryunkov, V. Y. Markov, P. A. Khavrel, S. M. Avdoshenko, I. N. Ioffe, S. G. Sakharov, S. I. Troyanov and L. N. Sidorov, *Dalton Transactions*, **2007**, 5322.

84) N. A. Samoylova, N. H. Belov, V. A. Brotsman, I. N. Ioffe, N. S. Lukonina, V. Y. Markov, A. Ruff, A. V. Rybalchenko, P. Schuler, O. O. Semivrazhskaya, B. Speiser, S. I. Troyanov, T. V. Magdesieva and A. A. Goryunkov, *Chem. Eur. J.*, **2013**, *19*, 17969.

85) Y. Kabe, H. Ohgaki, T. Yamagaki, H. Nakanishi, W. Ando, *J. Organomet. Chem.*, **2001**, *82*, 636.

86) J. Nagatsuka, S. Sugitani, M. Kako, T. Nakahodo, N. Mizorogi, M. O. Ishitsuka, Y. Maeda, T. Tsuchiya, T. Akasaka, X. Gao and S. Nagase, *J. Am. Chem. Soc.*, **2010**, *132*, 12106.

87) M. Prato, Q. C. Li, F. Wudl and V. Lucchini, *J. Am. Chem. Soc.*, **1993**, *115*, 1148.

88) B. Nuber, F. Hampel and A. Hirsch, *Chem. Commun.*, **1996**, 1799.

89) J. Averdung and J. Mattay, *Tetrahedron*, **1996**, *52*, 5407.

90) T. Grösser, M. Prato, V. Lucchini, A. Hirsch and F. Wudl, *Angew. Chem. Int. Ed. Engl.*, **1995**, *34*, 1343.

91) M. R. Banks, J. I. G. Cadogan, I. Gosney, P. K. G. Hodgson, P. R. R. Langridge-Smith, J. R. A. Millar and A. T. Taylor, *J. Chem. Soc., Chem. Commun.*, **1995**, 885.

92) M. R. Banks, J. I. G. Cadogan, I. Gosney, P. K. G. Hodgson, P. R. R. Langridge-Smith, J. R. A. Millar, J. A. Perkinson, D. W. H. Rankin and A. T. Taylor, *J. Chem. Soc., Chem. Commun.*, **1995**, 887.

93) G. Schick, T. Grosser and A. Hirsch, *J. Chem. Soc., Chem. Commun.*, **1995**, 2289.

94) A. B. Smith III and H. Tokuyama, *Tetrahedron*, **1996**, *52*, 5257.

95) H. Hachiya, T. Kakuta, M. Takami and Y. Kabe, *J. Organometallic Chem.*, **2009**, *694*, 630.

96) T. Nakahodo, M. Okada, H. Morita, T. Yoshimura, M. O. Ishitsuka, T. Tsuchiya, Y. Maeda, H. Fujihara, T. Akasaka, X. Gao and S. Nagase, *Angew. Chem. Int. Ed.*, **2008**, *47*, 1298.

97) L.-L. Shiu, K.-M. Chien, T.-Y. Liu, T.-I. Lin, G.-R. Her and T.-Y. Luh, *J. Chem. Soc. Chem. Commun.*, **1995**, 1159.

98) G.-X. Dong, J.-S. Li and T.-H. Chan, *J. Chem. Soc. Chem. Commun.*, **1995**, 1725.

99) C. K. -F. Shen, H.-H. Yu, C.-G. Juo, K.-M. Chien, G..-R. Her and T.-Y. Luh, *Chem. Eur. J.*, **1997**, *3*, 744.

100) C. K.-F. Shen, K.-M. Chien, C.-G. Juo, G.-R. Her and T.-Y. Luh, *J. Org. Chem.*, **1996**, *61*, 9242.

101) P. P. Kanakamma, S.-L. Huang, C.-G. Juo, G.-R. Her and T.-Y. Luh, *Chem. Eur. J.*, **1998**, *4*, 2037.

102) A. Ikeda, C. Fukuhara and S. Shinkai, *Chem. Lett.*, **1998**, *27*, 915.

103) C.-F. Chen, J.-S. Li, G.-J. Ji, Q.-Y. Zheng and D.-B. Zhu,. *Synth. Commun.*, **1998**, *28*, 3097.

104) G.-S. Tang, X.-L. Chen, S.-Y. Zhang and J. Wang, *Org. Lett.*, **2004**, *6*, 3925.

105) M. Chen, L. Bao, P. Peng, S. Zheng, Y. Xie and X. Lu, *Angew. Chem. Int. Ed.*, **2016**, *55*, 11857.

106) H. Hachiya, T. Kakuta, M. Takami and Y. Kabe, *J. Organometallic Chem.*, **2009**, *694*, 630.

107) T. Nakahodo, M. Okada, H. Morita, T. Yoshimura, M. O. Ishitsuka, T. Tsuchiya, Y. Maeda, H. Fujihara, T. Akasaka, X. Gao and S. Nagase, *Angew. Chem. Int. Ed.*, **2008**, *47*, 1298.

108) S. Minakata, R. Tsuruoka, T. agamachi and M. Komatsu, *Chem. Commun.*, **2008**, 323.

109) R. Tsuruoka, T. Nagamachi, Y. Murakami, M. Komatsu and S. Minakata, *J. Org. Chem.*, **2009**, *74*, 1691.

110) T. Nagamachi, Y. Takeda, K. Nakayama and S. Minakata, *Chem. Eur. J.*, **2012**, *18*, 12035.

111) Y. Nakamura, N. Takano, T. Nishimura, E. Yashima, M. Sato, T. Kudo, J. Hishimura, *Org. Lett.*, **2001**, *3*, 1193.

112) G. Kim, K. C. Lee, J. Kim, J. Lee, S. M. Lee, J. C. Lee, J. W. Seo, W.-Y. Choi and C. Yang, *Tetrahedron*, **2013**, *69*, 7354.

113) 中村吉宏　神奈川大学化学科卒業論文 **(2014)**

114) G.-W. Wang and B. Zhu, *Chem. Commun.*, **2009**, 1769.

115) Y. Rubin, *Chem. -Eur. J.*, **1997**, *3*, 1009.

116) Y. Rubin, *Top. Curr. Chem.*, **1999**, *199*, 67.

117) J. C. Hummelen, M. Prato and F. Wudl, *J. Am. Chem. Soc.*, **1995**, *117*, 7003.

118) G. Schick, T. Jarrosson and Y. Rubin, *Angew. Chem. Int. Ed.*, **1999**, *38*, 2360.

119) M. R. Ceron, M. Izquierdo, A. Aghabali, J. A. Valdez, K. B. Ghiassi, M. M. Olmstead, A. L. Balch, F. Wudl and L. Echegoyen, *J. Am. Chem. Soc.*, **2015**, *137*, 7502.

120) S.-C. Chuang, M. Sander, T. Jarrosson, S. James, E. Rozumov, S. I. Khan and Y. Rubin, *J. Org. Chem.*, **2007**, *72*, 2716.

121) M. Sander, T. Jarrosson, S.-C. Chuang, S. I. Khan and Y. Rubin, *J. Org. Chem.*, **2007**, *72*, 2724.

122) M.-J. Arce, A. L. Viado, Y.-Z. An, S. I. Khan and Y. Rubin, *J. Am. Chem. Soc.*, **1996**, *118*, 3775.

123) H. Inoue, H. Yamaguchi, T. Suzuki, T. Akasaka and S. Murata, *Synlett*, **2000**, 1178.

124) H. Inoue, H. Yamaguchi, S.-I. Iwamatsu, T. Uozaki, T. Suzuki, T. Akasaka, S. Nagase and S. Murata, *Tetrahedron Lett.*, **2001**, *42*, 895.

125) Y. Murata, M. Murata and K. Komatsu, *Chem. -Eur. J.*, **2003**, *9*, 1600.

126) Y. Murata, N. Kato and K. Komatsu, *J. Org. Chem.*, **2001**, *66*, 7235.

127) Y. Murata and K. Komatsu, *Chem. Lett*, **2001**, 896.

128) Y. Kabe, H. Hachiya, T. Saito, D. Shimizu, M. Ishiwata, K. Suzuki, Y. Yakushigawa and W. Ando, *J. Organomet. Chem.*, **2009**, *694*, 1988.

129) H. Hachiya and Y. Kabe, *Chem. Lett.*, **2009**, *38*, 372.

130) O. Z. Z. Jia, S. Liu, G. Zhang, Z. Xiao, D. Yang, L. Gan, Z. Wang and Y. Li, *Org. Lett.*, **2009**, 11, 2772.

131) S. Huang, Z. Xiao, F. Wang, L. Gan, X. Zhang, X. Hu, S. Zhang, M. Lu, Q. Pan and L. Xu, *J. Org. Chem.*, **2004**, *69*, 2442.

132) L. Gan, *Pure Appl. Chem.*, **2006**, *78*, 841.

133) F. Wang, Z. Xiao, Z. Yao, Z. Jia, S. Huang, L. Gan, J. Zhou, G. Yuan and S. Zhang, *J. Org. Chem.*, **2006**, *71*, 4374.

134) Y. Yu, X. Xie, T. Zhang, S. Liu, Y. Shao, L. Gan and Y. Li, *J. Org. Chem.*, **2011**, *76*, 10148-10153.

135) N. Lou, Y. Li and L. Gan, *Angew. Chem. Int. Ed.*, **2017**, *56* 2403.

136) S.-I. Iwamatsu, F. Ono and S. Murata, *Chem. Lett.*, **2003**, *7*, 614.

137) G. C. Vougioukalakis, K. Prassides, J. M. Campanera, M. I. Heggie and M. Orfanopoulos, *J. Org. Chem.*, **2004**, *69*, 4524.

138) S.-I. Iwamatsu, F. Ono and S. Murata, *Chem. Commun.*, **2003**, 1268.

139) S.-I. Iwamatsu and S. Murata, *Synlett*, **2005**, 2117.

140) M. M. Roubelakis, Y. Murata, K. Komatsu and M. Orfanopoulos, *J. Org. Chem.*, **2007**, *72*, 7042.

141) S.-I. Iwamatsu, T. Uozaki, K. Kobayashi, R. Suyong, S. Nagase and S. Murata, *Synthesis*, **2004**, 2962.

142) S.-I. Iwamatsu, T. Uozaki, K. Kobayashi, R. Suyong, S. Nagase and S. Murata, *J. Am. Chem. Soc.*, **2004**, *126*, 2668.

143) S.-I. Iwamatsu and S. Murata, *Tetrahedron Lett.*, **2004**, *45*, 6391.

144) Z. Xiao, G. Ye, Y. Liu, S. Chen, Q. Peng, Q. Zuo and L. Ding, *Angew. Chem. Int. Ed.*, **2012**, *51*, 9038.

145) Y. Yu, L. Xu, X. Huang and L. Gan, *J. Org. Chem.*, **2014**, 79, 2156.

146) K. Kurotobi, and Y. Murata, *Science*, **2005**, *307*, 238.

147) T. Futagoishi, M. Murata, A. Wakamiya, T. Sasamori and Y. Murata, *Org. Lett.*, **2013**, *15*, 2750.

148) Y. Hashikawa, M. Murata, A. Wakamiya, and Y. Murata, *Org. Lett.*, **2014**, *16*, 2970.

149) L. Gan and G. Zhang, *Eur. J. Org. Chem.*, **2013**, *32*, 7272.

150) L. Gan and S. Zhang, *J. Org. Chem.*, **2013**, *78*, 1157.

151) N. Xin, H. Huang, J. Zhang, Z. Dai and L. Gan, *Angew. Chem. Int. Ed.*, **2012**, *51*, 6163.

152) L. Shi, D. Yang, F. Colombo, Y. Yu, W.-X. Zhang and L. Gan, *Chem. -Eur. J.*, **2013**, *19*, 16545.

153) C.-S. Chen, Y.-F. Lin and W.-Y. Yeh, *Chem. Eur. J.*, **2014**, *20*, 936.

154) W.-Y. Yeh, *J. Organometallic Chem.*, **2015**, *784*, 13.

155) S.-I. Iwamatsu and S. Murata, *Synlett*, **2005**, 2117.

156) M. Murata, Y. Murata and K. Komatsu, *Chem. Comm.*, **2008**, 6083.

157) G. C. Vougioukalakis, M. M. Roubelakis and M. Orfanopoulos, *Chem. Soc. Rev.*, **2010**, *39*, 817.

158) L. Gan, D. Yang, Q. Zhang and H. Huang, *Adv. Mater*, **2010**, *22*, 1498.

159) Y. Rubin, T. Jarrosson, G.-W. Wang, M. D. Bartberger, K. N. Houk, G. Schick, M. Saunders and R. J. Cross, *Angew. Chem. Int. Ed.*, **2001**, *40*, 1543.

160) Y. Murata, M. Murata and K. Komatsu, *J. Am. Chem. Soc.*, **2003**, *125*, 7152.

161) S.-C. Chuang, Y. Murata, M. Murata, S. Mori, S. Maeda, F. Tanabe and K. Komatsu, *Chem. Commun.*, **2007**, 1278.

162) S.-I. Iwamatsu, S. Murata, Y. Andoh, M. Minoura,K. Kobayashi, N. Mizorogi and S. Nagase, *J. Org. Chem.*, **2005**, *70*, 4820.

163) S.-I. Iwamatsu, C. M. Stanisky, R. J. Cross, M. Saunders, N. Mizorogi, S. Nagase and S. Murata, *Angew. Chem. Int. Ed.*, **2006**, *45*, 5337.

164) K. E. Whitener Jr, R. J. Cross, M. Saunders, S.-I. Iwamatsu, S. Murata, N. Mizorogi and S. Nagase, *J. Am. Chem. Soc.*, **2009**, *131*, 6338.

165) K. E. Whitener Jr, M. Frunzi, S.-I. Iwamatsu, S. Murata, R. J. Cross and M. Saunders, *J. Am. Chem. Soc.*, **2008**, *130*, 13996.

166) C.-S. Chen, T.-S. Kuo and W.-Y. Yeh, *Chem. -Eur. J.*, **2016**, *22*, 8773.

167) C.-S. Chen and W.-Y. Yeh, *Chem. -Eur. J.*, **2016**, *22*, 16425.

168) M. Murata, Y. Morinaka, K. Kurotobi, K. Komatsu and Y. Murata, *Chem. Lett.*, **2010**, *39*, 298.

169) K. Komatsu, M. Murata and Y. Murata, *Science*, **2005**, *307*, 238.

170) K. Kurotobi and Y. Murata, *Science*, **2011**, *333*, 613.

171) A. Krachmalnicoff, M. H. Levitt and R. J. Whitby, *Chem. Comm.*, **2014**, *50*, 13037.

172) A. Krachmalnicoff, R. Bounds, S. Mamone, M. H. Levitt, M. Carravett and R. J. Whitby, *Chem. Comm.*, **2015**, *51*, 4993.

173) A. Krachmalnicoff, R. Bounds, S. Mamone, S. Alom, M. Concistrè, B. Meier, K. Kouřil, M. E. Light, M. R. Johnson, S. Rols, A. J. Horsewill, A. Shugai, U. Nagel, T. Rõõm, M. Carravetta, M. H. Levitt and R. J. Whitby, *Nat. Chem.*, **2016**, *8*, 953.

174) T. Futagoishi, M. Murata, A. Wakamiya and Y. Murata, *Angew. Chem. Int. Ed.*, **2015**, *54* 14791.

175) Z. Xiao, J. Yao, D. Yang, F. Wang, S. Huang, L. Gan, Z. Jia, Z. Jiang, X. Yang, B. Zheng, G. Yuan, S. Zhang and Z. Wang, *J. Am. Chem. Soc.*, **2007**, *129*, 16149.

176) T. Pankewitz and W. Klopper, *Chem. Phys. Lett.*, **2008**, *465*, 48.

177) Q. Zhang, T. Pankewitz, S. Liu, W. Klopper and L. Gan, *Angew. Chem. Int. Ed.*, **2010**, *49*, 9935.

178) L. Xu, H. Ren, S. Liang, J. Sun, Y. Liu and L. Gan, *Chem. –Eur. J.*, **2015**, *22*, 13539.

179) L. Shi and L. Gan, *J. Phys. Org. Chem.*, **2013**, *26*, 766.

Chapter 2

Direct benzyne-C$_{60}$ addition does not generate a [5,6] open fulleroid

2. Direct benzyne-C_{60} addition does not generate a [5,6] open fulleroid

2.1 Introduction

Fulleroids, azafulleroids and bisfulleroids with [5,6] open structures are key intermediates in the syntheses of open-cage fullerenes,[1,2] encapsulated[3] fullerenes and heterofullerenes.[4] Singlet oxygenation of these fullerenes results in the opening of a hole in the fullerene surface, which can be expanded via several different reactions.[1,2] Since cycloaddition (e.g., Diels-Alder or 1,3-dipolar addition) occurs at a [6,6] double bond rather than a [5,6] single bond of fullerene (C_{60}), [5,6] open fulleroids are normally only secondary products, produced by extrusion of N_2 from the initially formed [2+3] cycloadduct with diazo and azide compounds,[5] as well as from [4+4] cycloaddition and retro [2+2+2] reaction of a [4+2] adduct with a diene.[6] The reaction of benzyne (B) generated in situ from diazotization via (A) of 2-amino-4,5-dimethoxybenzoic acid (**1a**) with C_{60} affords the [6,6] closed adduct (**2a**) via [2+2] cycloaddition.[7] However, Yang and coworkers reported the unprecedented [5,6] fulleroid (**3b**) from the analogous reaction of 2-amino-4,5-dibutoxybenzoic acid (**1b**) with C_{60}, as shown in Scheme 2-1.[8] Further surprising were the different products reportedly obtained from the same reactants with amine: Wang and coworkers isolated the [6,6] closed adduct (**4a**) via betaine intermediate (C).[9] Thus, we attempted to reproduce the [5,6] fulleroid (**3b**) to then generate a new open-cage fullerene (**5b**) via singlet oxygenation; however, only **3b** was recovered, as shown in Scheme 2-2. In order to clarify the inconsistencies in the literature, we decided to reinvestigate the thermal or amine-promoted reaction of C_{60} with anthranilic acid derivatives (**1a** and **1b**) and isoamyl nitrite. We found that these reactions do not generate the [5,6] open fulleroids (**3a,b**), but rather, the [6,6] closed betaine adducts (**4a,b**) under both sets of reaction conditions.

Scheme 2-1.

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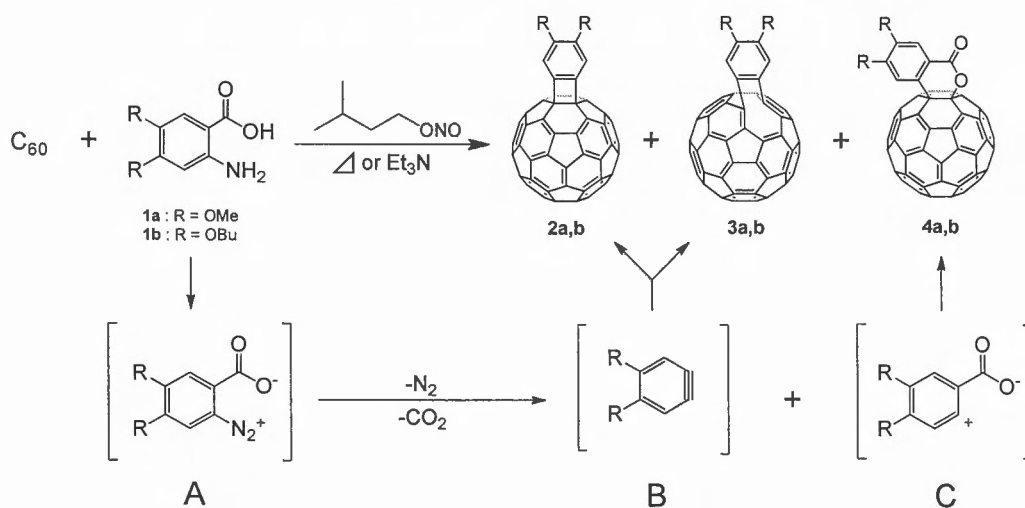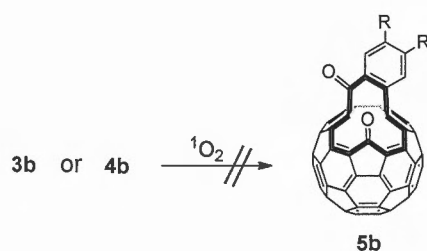
Scheme 2-2

2.2 Results and Discussion

Following the procedure reported by Yang and coworkers, C_{60} was reacted with **1a** at 100 °C for 24 h in o-dichlorobenzene (ODCB). After removal of the solvent, the crude product was obtained via silica gel column chromatography (benzene:AcOEt = 10:1; ^{1}H NMR spectra (CDCl$_3$) 7.64 ppm, 7.52 ppm, 3.99 ppm and 3.92 ppm). Insolubility prevented further purification or characterization of the crude products. Yang and coworkers encountered similar difficulties in spectral characterization of the reaction product of C_{60} with **1a** due to its limited solubility. They assigned only the ^{1}H NMR spectrum (CS$_2$:acetone-d_6 =3:1) of the monoadduct and methoxy protons corresponding to the [6,6] closed structure (**2a**) with C_{2v} symmetry.[7] When 2 equiv. of triethylamine were employed as the base according to the report by Wang (chlorobenzene, 60 °C, 1.5 h), the reaction gave product **4a** in 23.4% yield after removal of solvent and column chromatography (CS$_2$ and CS$_2$/CH$_2$Cl$_2$). No other products were detected in significant amounts. The ^{1}H NMR and ^{13}C NMR spectra of product **4a** were rigorously consistent with those reported by Wang and coworkers. As shown in Figure 2-1a, the two methoxy singlets and two aromatic protons in the ^{1}H NMR spectrum of **4a** reveal the presence of an asymmetrical 2,3-dimethoxy-o-phenylene moiety. The ^{13}C NMR spectrum of **4a** shown in Figure 2-1c exhibits less than thirty peaks with two half-intensity signals in the 134-154 ppm range for the sp^2 carbons of the fullerene cage, and two weak peaks at 95.0 and 58.0 ppm for the two sp^3 carbons of the C_{60} fullerene skeleton. Wang and coworkers assigned these C_{60} sp^3 carbons to the carbons with the oxygen atom[10a,b] and aryl group[10c] attached to the C_{60} skeleton via comparison to their previous work on C_{60}-fused γ lactones and naphthalene/indane. The ^{13}C NMR spectrum of **4a** is indicative of C_s molecular symmetry. The MALDI-TOF mass spectrum of **4a** (see Figure 2-2a) shows two apparent molecular ions, consistent with [M+H] at m/z 901.06 and [M-CO$_2$] at m/z 856.05, which represent the sum of C_{60}, benzyne (B) and CO$_2$. The ^{13}C NMR chemical shift at 160 ppm is assignable to the carbonyl carbons. The absorption at 1728 cm^{-1} in the IR spectra also supports the presence of a lactone. With these considerations, we concluded that structure of **4a** is the [6,6] closed C_{60}-fused δ lactone shown in Scheme 2-1. Further structural assignment was obtained with HMQC/HMBC NMR, since it is possible to identify the connectivity of the C_{60} sp^3 carbon adjacent to two aromatic protons by examining one-bond, two-bond and three-bond hydrogen-carbon ($^1J_{CH}$, $^2J_{CH}$ and $^3J_{CH}$) correlations. HMQC spectra of **4a** show the ^{13}C NMR

resonance at 115.0 ppm and 112.1 ppm connected to two aromatic methine protons, respectively (see supporting information). Figure 2-3 shows the HMBC and the expanded HMBC spectra of **4a** in the sp^2 region. The most important feature is that one aromatic methine proton is correlated with the C$_{60}$ sp^3 carbons at 58.0 ppm, and two aromatic quaternary carbons at 115.4 ppm and 149.3 ppm, the latter attached to a methoxy group. Another aromatic methine proton shows three-bond coupling with the carbonyl carbons at 160 ppm, and another two aromatic quaternary carbons at 129.9 ppm and 154.6 ppm, the latter attached with another methoxy group. These HMBC results are completely consistent with the structural assignment of **4a**.
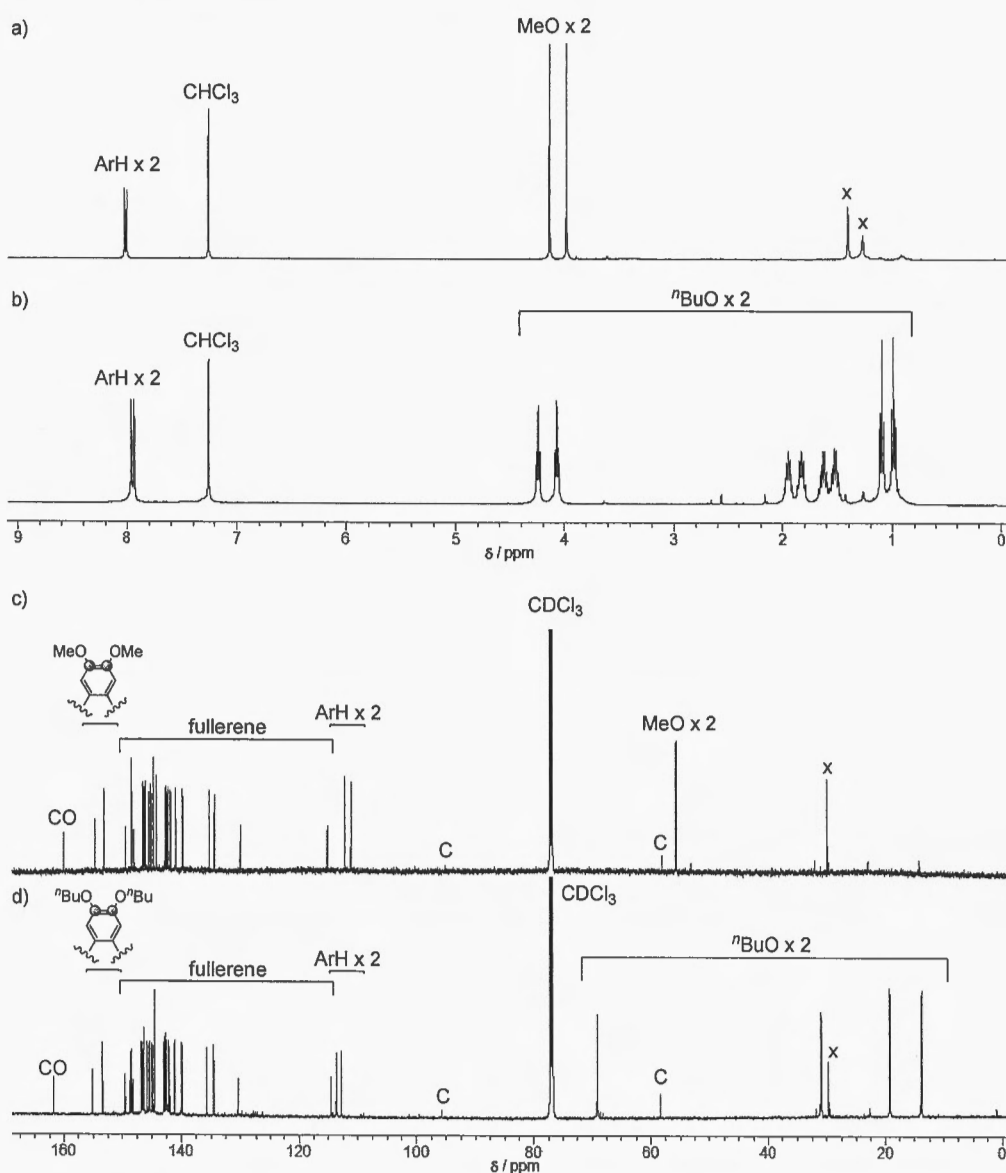

Figure 2-1. ^{1}H NMR spectra (400 MHz, CDCl$_3$:CS$_2$ = 1:4) of **4a** (a) and **4b** (b), and ^{13}C NMR spectra (150 MHz, CDCl$_3$:CS$_2$ = 1:4) of **4a** (c) and **4b** (d).
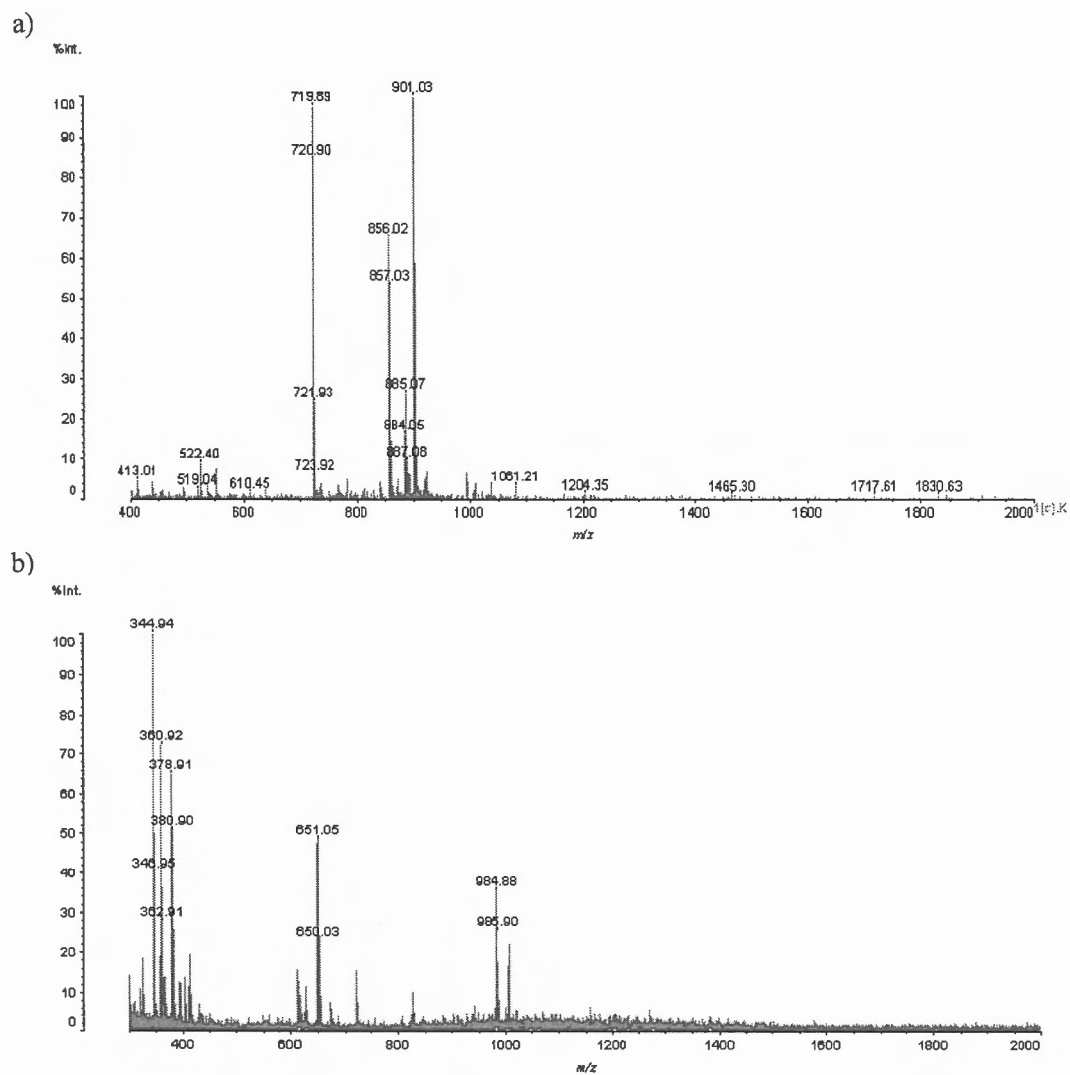
a)

b)

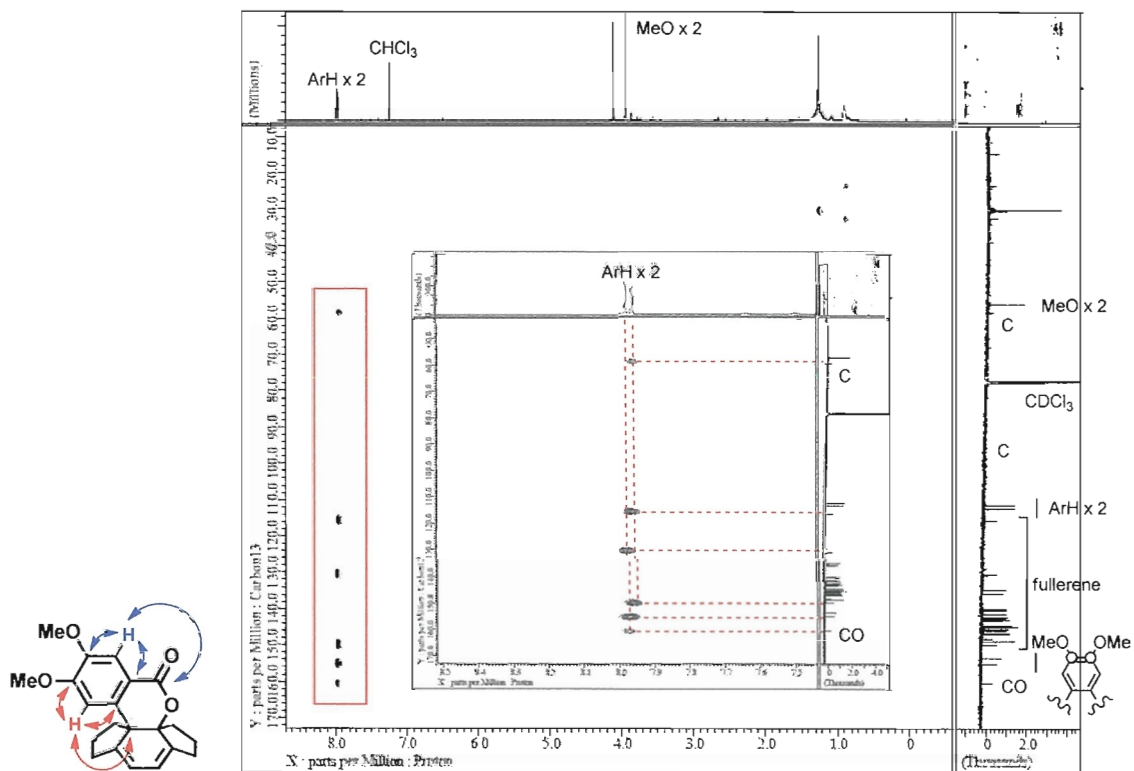Figure 2-2. MALDI-TOF MS of **4a** (a) and **4b** (b). (Matrix: 2,5-dihydroxybenzoic acid (DHB).)

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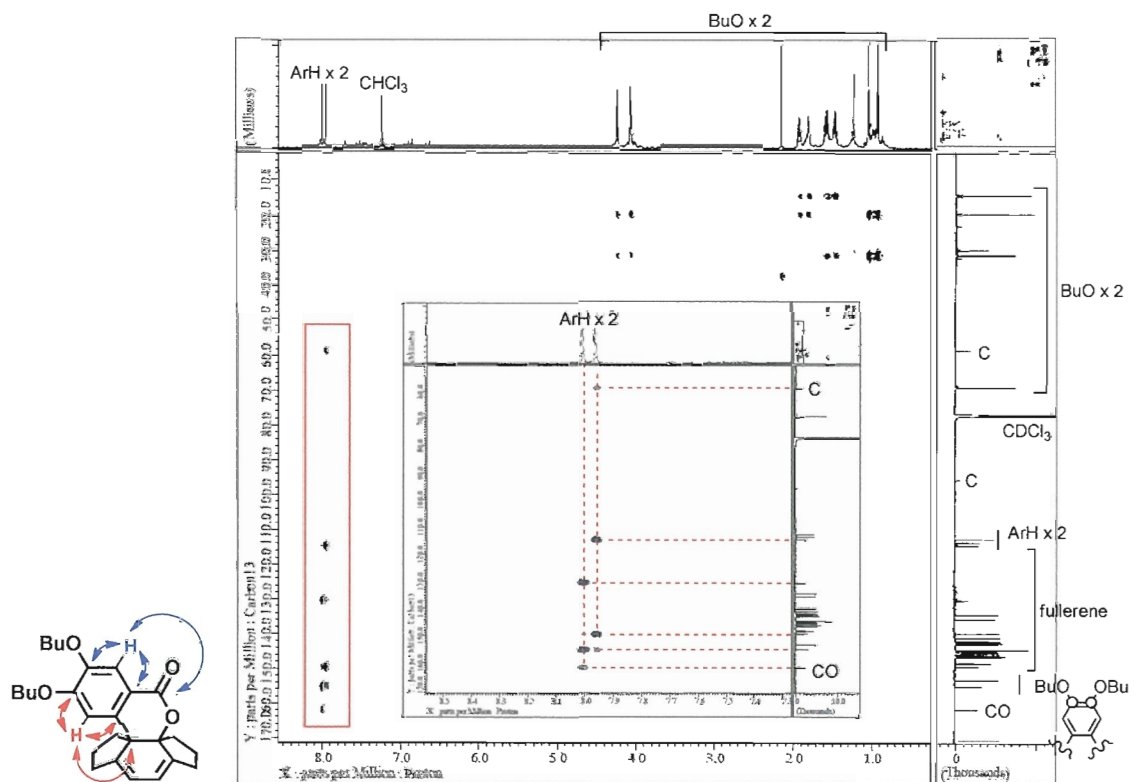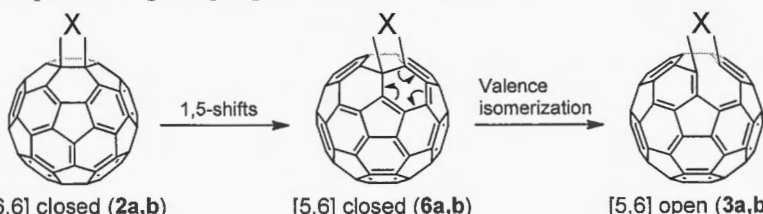Figure 2-3. HMBC spectrum of **4a** and correlations (^{1}H-^{13}C ^{3}J coupling).

Figure 2-4. HMBC spectrum of **4b** and correlations (^{1}H-^{13}C ^{3}J coupling).
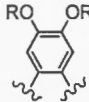
Next, we investigated the reaction of C_{60} with **1b** (ODCB, 100 °C, 24 h). After the solvent was removed under reduced pressure, the residue was separated on a silica gel column with CS_2/$CHCl_3$ as the eluent to afford product **4b** in 3% yield. When 2 equiv. of triethylamine were used in the reaction (chlorobenzene, 60 °C, 1.5 h), the yield of **4b** increased to 21.4%. No isomeric product of C_{60} other than **4b** was obtained. The ^1H and ^{13}C NMR spectra of **4b** shown in Figures 2-1b and 1d are quite similar to those reported by Yang as the [5,6] open structure (**3b**). There are two sets of butoxy protons and carbons, as well as two aromatic methine protons, revealing the asymmetry of the structure. The sp^2 carbons of the fullerene cage constitute less than thirty peaks, indicative of C_s symmetry. This is in sharp contrast with the report by Yang and coworkers, wherein the two C_{60} sp^3 carbons at 58.4 ppm and 95.7 ppm were not assigned. This is probably due to the poor signal/noise ratio of their ^{13}C NMR spectrum, which led them to incorrectly identify their product as **3b** rather than **4b**. Notably, a resonance is observed at ~60 ppm in their ^{13}C NMR supporting information, which is also coupled to the aromatic methine proton in the HMBC spectrum. The MALDI-TOF mass spectrum (see Figure 2-2b) of **4b** shows a molecular ion [M+H] at m/z 985.9, while a molecular ion at m/z 940 is not present in the report by Yang and coworkers, a discrepancy we cannot account for. The IR absorption at 1724 cm^{-1} also shows the presence of lactone. The ^{13}C NMR resonances of the carbonyl carbon at 161.7 ppm and the aromatic quaternary carbons at 174.5 ppm, 130.3 ppm, 149.5 ppm, and 155.1 ppm are in almost the same positions as those reported by Yang and coworkers. The HMQC spectrum of **4b** shows ^{13}C NMR resonances at 112.7 ppm and 113.6 ppm, assigned to two the aromatic methine carbons (see Figure 2-4 and supporting information). The HMBC spectrum of **4b** shows that two the aromatic methine protons are coupled to the carbonyl carbon at 161.7 ppm and the C_{60} sp^3 carbon at 58.4 ppm.

The structure of **3a,b** having been reformulated, the thermal and photochemical extrusion of CO_2 from **4a,b** was expected to generate **3a,b** via the three-step pathway shown in Scheme 2-3. That is, CO_2 extrusion and a 1-5 shift should be followed by valence isomerization of the [5,6] closed isomer (**6a,b**). In fact, both thermolysis of **4a,b** (reflux in ODCB, 30 min) and irradiation with a high pressure Hg lamp (>300 nm) in degassed ODCB for 40 h resulted in the recovery of **4a,b**. The [5,6] closed isomers (**6a,b**) can plausibly be used as hypothetical intermediates in the thermal and photochemical isomerization of the [6,6] closed isomers (**2a,b**) to the [5,6] open isomers (**3a,b**).[11a,b] The relative energies of these structures were calculated, and are shown in Table 1 together with the corresponding of CH_2- and NH-bridged isomers. The stability order of the CH_2- and NH- bridged isomers is compatible with the hypothesis, wherein the [5,6] open CH_2- and NH-bridged isomers are more stable than the [5,6] closed isomers. This has been explained by avoiding locating any double bonds within the five-membered rings of C_{60}.[11a,b] The [5,6] closed structures as well as the [6,6] open structures of C_{60} derivatives have several experimental precedents, e.g. a valence isomer of a [6,6] open isomer, which involve the absence of a theoretical local minimum.[11c-f] However the data

in Table 1 reveal that the benzyne linkage forming the [5,6] open isomers (**3a,b**) is less stable than the [5,6] closed isomers, both at the HF and DFT levels of theory. Since the instability of double bonds in five-membered rings is greater than that of bridgehead olefins (anti-Bredt's rule), the [5,6] open isomer forms. The benzyne pushes out the bridgehead atoms, and this strained modification makes **3a,b** unstable and prevents their syntheses.

Table 2-1. Relative energies and trans-annular bond distances for the isomerization of [6,6] closed isomers to [5,6] fulleroids proceeding via [5,6] closed valence isomers.

| | [6,6] closed (**2a,b**) | | 1,5-shifts → | [5,6] closed (**6a,b**) | | Valence isomerization → | [5,6] open (**3a,b**) |

X	[6,6] closed		[5,6] closed		[5,6] open	
	Relative energy[a] (kcalmol^{-1})	Trans-annulene distance (Å)	Relative energy[a] (kcalmol^{-1})	Trans-annulene distance (Å)	Relative energy[a] (kcalmol^{-1})	Trans-annulene distance (Å)
R = Me	0	1.65	4.9	1.69	25.0	2.43
^{n}Bu	(0)	(1.61)	(36.6)	(1.69)	(67.7)	(2.47)
CH_2[b]	0	1.55	21	1.62	6	2.21
NH_3[c]	0	1.559	9.4 ~ 21.6	1.62	-1.1 ~ -2.5	2.174 ~ 2.175

a) Calculations at B3LYP/6-31G** (and HF/STO-3G in parentheses). Values are relative to each [6,6] closed isomer (0.0 kcal/mol). b) see ref 11a. c) see ref 11b.
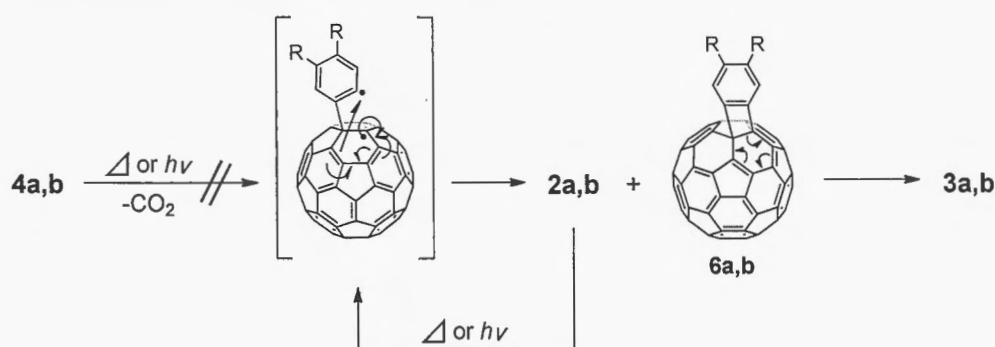
Scheme 2-3

2.3 Conclusion

In conclusion, **4a,b** can be obtained via both thermal and/or amine-promoted reaction as reported by Wang and coworkers. A comparison of the data reported for **4b** by Yang and coworkers and ourselves reveals that, although mass spectral data are different, the ^{1}H and ^{13}C NMR spectra are

strikingly similar. Further structural assignment of **4a,b** via HMBC spectra confirmed the [6,6] closed C_{60}-fused δ lactone structure. This analysis demonstrates that the previously reported [5,6] open fulleroid (**3a,b**) formed via direct benzyne C_{60} addition was misassigned, and that the [6,6] closed C_{60}-fused δ lactone (**4a,b**) is the correct assignment. Theoretical considerations suggest that the [5,6] open valence isomer (**3a,b**) is less stable than the rare [5,6] closed isomer (**6a,b**), although it is possible to prepare the latter.

2.4 Experimental section

Amine-promoted reaction of C_{60} with 2-amino-4,5-dimethoxyanthranilic acid

C_{60} (0.5 mmol), 2-amino-4,5-dimethoxyanthranilic acid (2.50 mmol) (**1a**) isoamyl nitrite (3.00 mmol) and Et_3N (1.00 mmol) were dissolved in 80 mL chlorobenzene, then heated with stirring for 1.5 h at 60 °C. After the reaction mixture was allowed to cool, the solvent was removed under reduced pressure. The residue was purified via silica gel column chromatography, eluting with CS_2 and CH_2Cl_2. Collection and concentration of the 2nd brown fraction gave 106 mg (23.4 %) of **4a** as a dark brown solid.

^1H NMR (400 MHz, CS_2:$CDCl_3$ = 4:1): δ 3.97 (s, 3H), 4.13 (s, 3H), 7.98 (s, 1H), 8.00 (s, 1H); ^{13}C NMR (150 MHz, CS_2 : $CDCl_3$ = 4 : 1): δ 55.67 (OMe), 55.79 (OMe), 58.01 (sp^3-C of C_{60}), 95.05 (sp^3-C of C_{60}), 111.05 (aryl C), 112.10 (aryl C), 115.14 (aryl C), 129.95 (aryl C), 134.35 (2C), 135.20 (2C), 139.61 (2C), 139.80 (2C), 140.87 (2C), 141.00 (2C), 141.78 (2C), 141.92 (2C), 142.28 (2C), 142.35 (2C), 142.52 (2C), 142.56 (2C), 142.80 (2C), 144.24 (4C), 144.66 (2C), 145.05 (2C), 145.12 (2C), 145.15 (2C), 145.49 (2C), 146.02 (2C), 146.06 (2C), 146.11 (2C), 146.38 (2C), 146.41 (2C), 147.88 (2C), 148.36 (3C), 149.39 (aryl C), 153.11 (2C), 154.60 (aryl C), 160.02 (CO) (27 signals observed for C_{60} cage); IR: 525, 771, 1068, 1246, 1277, 1516, 1597, 1728 (CO), 2927 cm^{-1}; HRMS APCI (negative): m/z calcd for $C_{69}H_9O_4$ [M]$^-$ 900.0423, found 900.0473.

Thermal reaction of C_{60} with 2-amino-4,5-dibutoxy-anthranilic acid

C_{60} (0.833 mmol), 2-amino-4,5-dibutoxyanthranilic acid (0.833 mmol) (**1b**) and isoamyl nitrite (0.853 mmol) were dissolved in 60 mL o-dichlorobenzene, then heated with stirring for 24 h at 100 °C. After the reaction mixture was allowed to cool, the solvent was removed under reduced pressure. The residue was purified via silica gel column chromatography, eluting with benzene/AcOEt (1:4). Collection and concentration of the 3rd brown fraction gave 28.3 mg (3.0 %) of **4b** as a brown solid.

^1H NMR (500 MHz, CS_2:$CDCl_3$ = 4:1): δ 0.94 (t, J = 7.4 Hz, 3H), 1.06 (t, J = 7.4 Hz, 3H), 1.49 (sext, J = 7.4 and 7.4 Hz, 2H), 1.60 (sext, J = 7.7 and 7.4 Hz, 2H), 1.82 (quint, J = 7.4 and 6.4 Hz, 2H), 1.95 (quint, J = 7.7 and 6.6 Hz, 2H), 4.09 (t, J = 6.4 Hz, 3H), 4.27 (t, J = 6.6 Hz, 3H), 7.98 (s, 1H), 8.03 (s, 1H); ^{13}C NMR (125 MHz, CS_2:$CDCl_3$ = 4:1): δ 13.84 (CH_3), 13.89 (CH_3), 19.20 (CH_2),

19.27 (CH$_2$), 30.86 (CH$_2$), 31.07 (CH$_2$), 58.47 (C, sp^3-C of C$_{60}$), 69.18 (CH$_2$), 69.20 (CH$_2$), 95.71 (C, sp^3-C of C$_{60}$), 112.80 (aryl C), 113.68 (aryl C), 114.61 (aryl C), 130.39 (aryl C), 134.53 (2C), 135.71 (2C), 139.89 (2C), 139.99 (2C), 141.16 (2C), 141.22 (2C), 142.04 (2C), 142.23 (2C), 142.54 (2C), 142.60 (2C), 142.80 (2C), 142.84 (2C), 143.06 (2C), 144.58 (2C), 144.59 (2C), 144.90 (2C), 145.01 (2C), 145.35 (2C), 145.40 (2C), 145.48 (2C), 145.83 (2C), 146.34 (2C), 146.36 (2C), 146.41 (2C), 146.66 (2C), 146.75 (2C), 148.21 (C), 148.54 (2C), 148.73 (C), 149.53 (aryl C), 153.44 (2C), 155.15 (aryl C), 161.79 (CO) (29 signals observed for C$_{60}$ cage).

Amine-promoted reaction of C$_{60}$ with 2-amino-4,5-dibutoxy-anthranilic acid

C$_{60}$ (0.5 mmol), 2-amino-4,5-dibutoxyanthranilic acid (2.5 mmol), isoamyl nitrite (3.0 mmol) and Et$_3$N (1.0 mmol) were dissolved in 80 mL chlorobenzene, then heated with stirring for 1.5 h at 60 °C. After the reaction mixture was allowed to cool, the solvent was removed under reduced pressure. The residue was purified via silica gel column chromatography eluting with CS$_2$/CH$_2$Cl$_2$ (3:1). Collection and concentration of the 2nd brown fraction gave 105 mg (21.4 %) of **4b** as a brown solid. ^{1}H NMR (400 MHz, CS$_2$:CDCl$_3$ = 4:1): δ 0.99 (t, J = 7.4 Hz, 3H), 1.09 (t, J = 7.4 Hz, 3H), 1.52 (sext, J = 7.4 and 7.2 Hz, 2H), 1.63 (sext, J = 7.4 and 7.2 Hz, 2H), 1.83 (quint, J = 7.2 and 6.3 Hz, 2H), 1.95 (quint, J = 7.2 and 6.4 Hz, 2H), 4.07 (t, J = 6.3 Hz, 2H), 4.24 (t, J = 6.4 Hz, 2H), 7.94 (s, 1H), 7.96 (s, 1H); ^{13}C NMR (150 MHz, CS$_2$:CDCl$_3$ = 4:1): δ 13.84 (CH$_3$), 13.90 (CH$_3$), 19.20 (CH$_2$), 19.26 (CH$_2$), 30.84 (CH$_2$), 31.06 (CH$_2$), 58.44 (C, sp^3-C of C$_{60}$), 69.16 (CH$_2$), 69.18 (CH$_2$), 95.70 (C, sp^3-C of C$_{60}$), 112.76 (aryl C), 113.64 (aryl C), 114.58 (aryl C), 130.36 (aryl C), 134.52 (2C), 135.70 (2C), 139.88 (2C), 139.97 (2C), 141.16 (2C), 141.20 (2C), 142.03 (2C), 142.22 (2C), 142.52 (2C), 142.58 (2C), 142.79 (2C), 142.82 (2C), 143.05 (2C), 144.57 (2C), 144.88 (2C), 144.99 (2C), 145.33 (2C), 145.39 (2C), 145.46 (2C), 145.81 (2C), 146.33 (2C), 146.35 (2C), 146.40 (2C), 146.64 (2C), 146.74 (2C), 148.19 (C), 148.51 (2C), 148.72 (C), 149.51 (aryl C), 153.41 (2C), 155.14 (aryl C), 161.78 (CO) (29 signals observed for C$_{60}$ cage); IR: 498, 667, 748, 872, 1065, 1265, 1404, 1523, 1724 (CO), 2939, 3614, 3741, 3822 cm^{-1}; HRMS APCI (negative): m/z calcd for C$_{75}$H$_{21}$O$_4$ [M]$^-$ 984.1362 found 984.1371.

2.5 Computational studies

Calculations were carried out on an HPC-5000-XH216R2 and HPC-5000-XH218R2S workstation provided by HPC Inc. of Japan. Ab initio calculations were performed using the Gaussian 03 computer program. The initial geometries of the fullerene derivatives were constructed using the Winmostar graphical interface. All geometry optimizations were performed on Cartesian coordinates using the energy gradient minimization method.

Reference

1. Reviews of open-cage fullerenes: (a) Y. Rubin, *Chem. Eur. J.*, **1997**, *3*, 1009. (b) Y. Rubin, *Top. Curr. Chem.*, **1999**, *199*, 67. (c) S.-I. Iwamatsu and S. Murata, *Synlett*, **2005**, 2117. (d) M. Murata, Y. Murata and K. Komatsu, *Chem. Commun.*, **2008**, 6083. (e) G. C. Vougioukalakis, M. M. Roubelakis and M. Orfanopaulos, *Chem. Soc. Rev.*, **2010**, 39, 817. (f) L. Gan, D. Yang, Q. Zhang and H. Huang, *Adv. Mater.*, **2010**, *22*, 1498. (g) L. Shi and L. Gan, *J. Phys. Org. Chem.*, **2013**, *26*, 766.

2. Fulleroid-based open-cage fullerenes: (a) J. C. Hummelen, M. Prato and F. Wudl, *J. Am. Chem. Soc.*, **1995**, *117*, 7003. (b) G. Schick, T. Jarrosson and Y. Rubin, *Angew. Chem. Int. Ed.*, **1999**, *38*, 2360. (c) Y. Rubin, T. Jarroson, G.-W. Wang, M. D. Bartberger, K. N. Houk, G. Schick, M. Saunders and R. J. Cross, *Angew. Chem. Int. Ed.*, **2001**, *40*, 1543. (d) Y. Murata, N. Kato and K. Komatsu, *J. Org. Chem.*, **2001**, *66*, 7235. (e) Y. Murata and K. Komatsu, *Chem. Lett.*, **2001**, 896. (f) Y. Murata, M. Murata and K. Komatsu, *Chem. Eur. J.*, **2003**, *9*, 1600. (g) H. Inoue, H. Yamaguchi, S.-I. Iwamatsu, T. Uozaki, T. Suzuki, T. Akasaka, S. Nagase and S. Murata, *Tetrahedron Lett.*, **2001**, *42*, 895. (h) Y. Murata, M. Murata and K. Komatsu, *J. Am. Chem. Soc.*, **2003**, *125*, 7152. (i) H. Hachiya and K. Kabe, *Chem. Lett.*, **2009**, *38*, 372. (j) Y. Kabe, H. Hachiya, T. Saito, D. Shimizu, M. Ishiwata, K. Suzuki, Y. Yakushigawa and W. Ando, *J. Organometall Chem.*, **2009**, *694*, 1988. (k) M. R. Cerón, M. Izquierdo, A. Aghabali, J. A. Valdez, K. B. Ghiassi, M. M. Olmstead, A. L. Balch, F. Wudl and L. Echegoyen, *J. Am. Chem. Soc.*, **2015**, *137*, 7502. (l) M. Chen, L. Bao, P. Peng, S. Zheng, Y. Xie and X. Lu, *Angew. Chem. Int. Ed.*, **2016**, *55*, 11887.

3. Synthesis of endohedral fullerenes by molecular surgery: (a) K. Komatsu, M. Murata and Y. Murata. *Science*, **2005**, *307*, 238. (b) M. Murata, Y. Murata and K. Komatsu, *J. Am. Chem. Soc.*, **2006**, *128*, 8024. (c) M. Murata, S. Murata, Y. Morinaka, Y. Murata and K. Komatsu, *J. Am. Chem. Soc.*, **2008**, *130*, 15800. (d) K. Kurotobi and Y. Murata, *Science*, **2011**, *333*, 613. (e) Y. Morinaka, F. Tanabe, M. Murata, Y. Murata and K, Komatsu, *Chem. Comm.*, **2010**, *46*, 4532. (f) A. Krachmalnicoff, M. H. Levitt and R. J. Whitby, *Chem. Comm.*, **2014**, *50*, 13037. (g) Y. Hashikawa, M. Murata, A. Wakamiya and Y. Murata, *J. Am. Chem. Soc.*, **2016**, *138*, 4096. (h) A. Krachmalnicoff, R. Bounds, S. Manone, S. Alom, M. Concistrè, B. Meier, K. Kouřil, M. E. Light, M. R. Johnson, S. Rols, A. J. Horsewill, A. Shugai, U. Nagel, T. Rõõm, M. Carravetta, M. H. Levitt, R. J. Whitby, *Nature Chem.*, **2016**, *8*, 953.

4. Reviews and selected papers of azafullerenes: (a) O. Vostrowsky and A. Hirsch, *Chem. Rev.*, **2006**, *106*, 5191. (b) G. Rotas and N. Tagmatarchis, *Chem. Eur. J*, **2016**, *22*, 1206. (c) J. C. Hummelen, B. Kinght, J. Pavlorich, R. González and F. Wudl, *Science*, **1995**, *269*, 1554. (d) M. Keshavarz-K, R. González, R. G. Hicks, G. Srdanov, V. I. Srdanov, T. G. Collins, J. C. Hummelen, C. Bellavia-Lund, J. Pavlovich, F. Wudl and K. Holczer, *Nature*, **1996**, *383*, 147. (e)

B. Nuber and A. Hirsch, *Chem. Comm.*, **1996**, 1421. (f) K.-C. Kim, F. Hauke, A. Hirsch, P. D. W. Boyd, E. Carter, R. S. Armstrong, P. A. Lay and C. A. Reed, *J. Am. Chem. Soc.*, **2003**, *125*, 4024. (g) N. Xin, H. Huang, J. Zhang, Z. Dai and L. Gan, *Angew. Chem. Int. Ed.* **2012**, *51*, 6163.

5. (a) M. Prato, Q. C. Li, F. Wudl and V. Lucchini, *J. Am. Chem. Soc.*, **1993**, *113*, 1148. (b) T. Suzuki, Q. Li, K. C. Khemani, F. Wudl and O. Almarsson, *Science*, **1991**, 1186.

6. (a) M. J. Arce, A. L. Viado, Y. Z. An, S. I. Khan and Y. Rubin, *J. Am. Chem. Soc.*, **1996**, *118*, 3775. (b) H. Inoue, H. Yamaguchi, T. Suzuki, T. Akasaka and S. Murata, *Synlett*, **2000**, 1178.

7. (a) S. H. Hoke II, J. Molstad, D. Dilettato, M. J. Jay, D. Carlson, B. Kahr and R. G. Cooks, *J. Org. Chem.*, **1992**, *57*, 5069. (b) M. Tsuda, T. Ishida, T. Nogami, S. Kurono and M. Ohashi, *Chem. Lett.*, **1992**, *21*, 2333. (c) T. Nogami, M. Tsuda, T. Ishida, S. Kurono and M. Ohashi, *Fullerene Sci. Technol.*, **1993**, *1*, 275. (d) A. D. Darwish, A. K. Abdul-Sada, G. J. Langley, H. W. Kroto, R. Taylor and D. R. M. Walton, *J. Chem. Soc., Chem. Commun.*, **1994**, 2133. (e) T. Ishida, K. Shinozuka, T. Nogami, S. Sasaki and M. Iyoda, *Chem. Lett.*, **1995**, *24*, 317. (f) A. D. Darwish, A. G. Avent, R. Taylor and D. R. M. Walton, *J. Chem. Soc., Perkin Trans. 2*, **1996**, 2079. (g) M. S. Meier, G.-W. Wang, R. C. Haddon, C. P. Brock, M. A. Lloyd and J. P. Selegue, *J. Am. Chem. Soc.*, **1998**, *120*, 2337. (h) Y. Nakamura, N. Takano, T. Nishimura, E. Yashima, M. Sato, T. Kudo and J. Nishimura, *Org. Lett.*, **2001**, *3*, 1193.

8. G. Kim, K. C. Lee, J. Kim, J. Lee, S.-M. Lee, J.-C. Lee, J.-H. Seo, W.-Y. Choi and C. Yang, *Tetrahedron*, **2013**, *69*, 7354.

9. G.-W. Wang and B. Zhu, *Chem. Comm.*, **2009**, 1769.

10. (a) G.-W. Wang, F.-B. Li and T.-H. Zhang, *Org. Lett.*, **2006**, *8*, 1355. (b) F.-B. Li, T.-X. Liu and G.-W. Wang, *J. Org. Chem.*, **2008**, *73*, 6417. (c) T.-X. Liu, F.-B. Li, and G.-W. Wang, *Org. Lett.*, **2011**, *13*, 6130.

11. For calculation and syntheses of [5,6] closed and [6,6] open isomers of C_{60}: (a) F. Diederich, L. Isaccs and D. J. Philp, *J. Chem. Soc., Perkin Trans. 2*, **1994**, 391. (b) M. Cases, M. Duran, J. Mestres, N. Martin and M. Sola, *J. Org. Chem.*, **2001**, *66*, 433. (c) V. V. Zverev, V. I. Kovalenko, I. P. Romanova and O. G. Sinyashin, *Int. J. Quantum Chem.*, **2007**, *107*, 2442. (d) O. G. Sinyashin, I. P. Romanova, G. G. Yusupova, V. I. Kovalenko, V. V. Yanilkin, and N. M. Azancheev, *Mendeleev Commun.*, **2000**, 96. (e) Y. Kabe, H. Ohgaki, T. Yamagaki, H. Nakanishi and W. Ando, *J. Organomet. Chem.*, **2001**, *636*, 82. (f) J. Nagatsuka, S. Sugitani, M. Kako, T. Nakahodo, N. Mizorogi, M. O. Ishitsuka, Y. Maeda, T. Tsuchiya, T. Akasaka, X. Gao and S. Nagase, *J. Am. Chem. Soc.*, **2010**, *132*, 12106. (g) A. S. Pimenova, A. A. Kozlov, A. A. Goryunkov, V. Yu. Markov, P. A. Khavrel, S. M. Avdoshenko, I. N. Ioffe, S. G. Sakharov, S. I. Troyanova and L. N. Sidorov, *Chem. Comm.*, **2007**, 374.

Chapter 3

Regioselective Diels–Alder reaction
to open-cage ketolactam derivatives of C$_{60}$

3. Regioselective Diels-Alder Reaction to Open-cage Ketolactam Derivatives of C_{60}

3.1 Introduction

Open-cage fullerenes[1] allow atoms and small molecules to be encapsulated in a molecular container, and are also key intermediates in the production of endohedral[2] and azafullerenes.[3] In the preparation of open-cage fullerenes.[4] Diels-Alder reactions, 1,3-dipolar additions, and other cycloadditions have played an important role. For example, 1,3-butadines,[5] 1,2-diazine,[4e] 3,4-triazine,[4f] azide compounds,[4a-c,h,k,6a] and diazo compounds,[4i,j,6b] have been added to C_{60} to form cyclohexadiene, azacyclohexadiene, pyrazoline, and triazoline intermediates, which rearrange to form open-cage mono- and bis-fulleroids under [4+4] or retro [2+2+2][5] reactions followed by N_2 extrusion.[6] Singlet oxygenation of these fulleroids results in open-cage fullerenes possessing an orifice large enough for small atoms or molecules to pass through.[4a] Several strategies have been developed in order to expand the orifice of open-cage fullerenes including hydroamination,[7] sulfur or selenium atom insertion,[8] and oxidation with *N*-oxide.[9] An entirely different approach to open-cage fullerenes involving a peroxide-mediated pathway was reported by Gan and coworkers.[10] In their study, a Diels-Alder reaction with 1,4-diphenylbutadiene on the rim of an open-cage fullerene occurred first.[3g,10i-k] The regioselective addition takes place on α,β-unsaturated ketones and not α,β-unsaturated[3g,10j] lactones to afford the Diels-Alder adducts (I and II) shown in Figure 1. This is due to the stronger electron-withdrawing effect of ketones vs. lactones. In contrast, both Diels-Alder adduct CO@IIIa and CO@IIIb (Figure 3-1) were obtained from the addition of 1,4-diphenyl butadiene to CO-encapsulated open-cage fullerenes.[10k] The regioselectivity of the fullerene-fused cyclohexadiene rings was unequivocally confirmed via X-ray crystallography.[10j,k] However, the cause of the stereoselectivity remained a mystery. Herein we report regioselective Diels-Alder reactions on the rims of open-cage ketolactam derivatives **2a-e** (Scheme 3-1). The structures of the Diels-Alder adducts were confirmed via 2D INADEQUATE NMR spectra of the ^{13}C–highly enriched ketolactam derivatives of C_{60} as well as agreement of the experimental ^1H NMR spectra with those obtained via DFT-GIAO calculations. The regioselectivity around the unsaturated ketone structure and the endo stereoselectivity were elucidated in terms of an orbital-controlled reaction based on theoretical calculations.
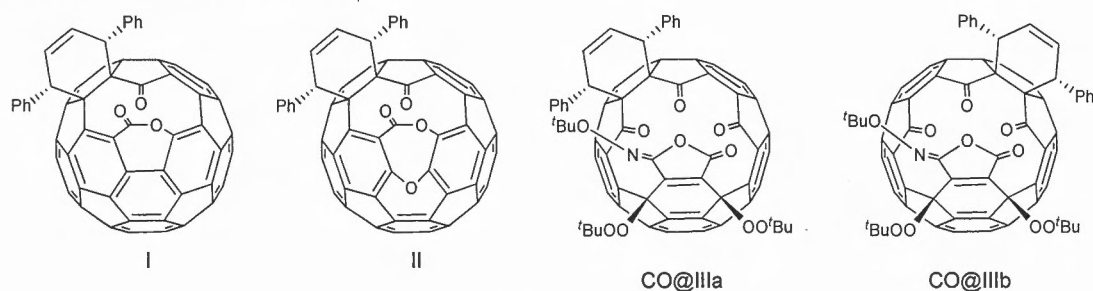

Figure 3-1.

3.2 Synthesis of Azafulleroids 1a-e and Open-cage Fullerenes 2a-e

The syntheses of azafulleroids **1a-c** having acyl or tosyl substituents was accomplished via the *N*-iodosuccinimide (NIS)-mediated reaction of C_{60} with the corresponding carbamate or sulfone amide (Scheme 3-1, method A).[11d,e,g] On the other hand, azafulleroids **1d** and **1e**, having silylmethyl groups, required the 1,3-dipolar cycloaddition of an azide to C_{60} followed by thermal N_2 extrusion without solvent (Scheme 3-1, method B and Table 3-1).[11c,g] Whereas [5,6]-open azafulleroids have been known to isomerize readily giving [6,6]-closed aziridinofullerenes in the azide addition reaction, method A can be selectively controlled to synthesize azafulleroids. Even in the azide addition reaction, aziridinofullerenes bearing electron withdrawing groups such as sulfonyl groups can isomerize to azafulleroids thermodynamically.[11b] However, azafulleroids bearing electron donating groups such as silylmethyl groups do not undergo this isomerization. Thus, a solvent-free thermal reaction was also applied to the synthesis of azafulleroids **1d** and **1e** in order to limit the formation of aziridinofullerene byproducts.[11c,h] Fortunately, purple 60π azafulleroid is easily separated from brown 58π aziridinofullerene via silica gel column chromatography. Azafullerroids **1a-e** were prepared in moderate yields as shown in Table 3-1, and were fully characterized based on the ^1H and ^{13}C NMR spectra and MALDI-TOF mass spectra observed. In the fullerene skeleton regions of the ^{13}C NMR spectra about 30 signals were observed, indicating C_s symmetry for **1a-e**.

Scheme 3-1.

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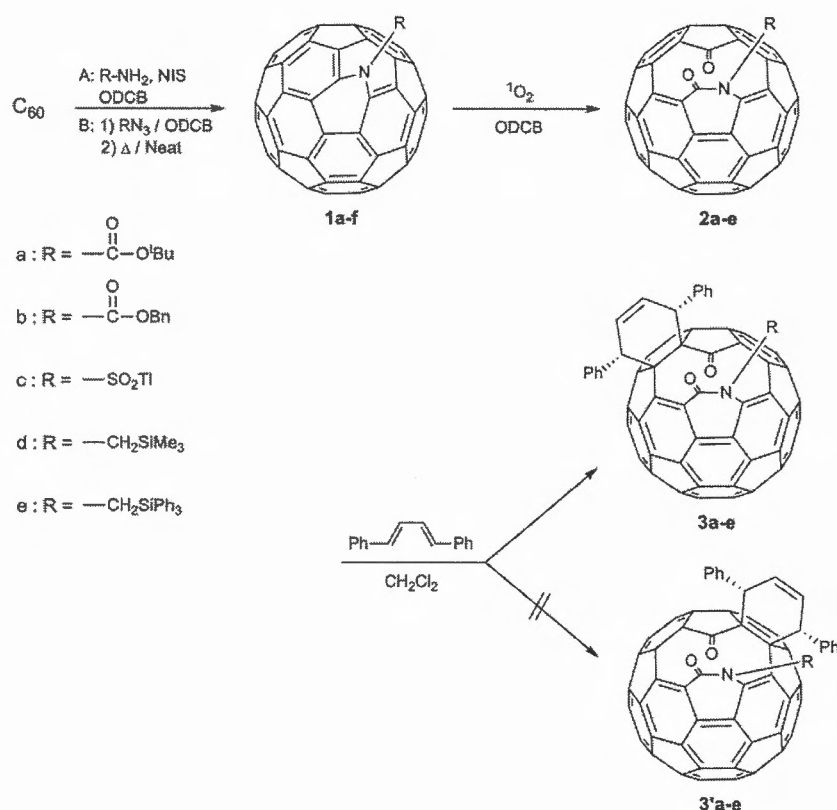
Table 3-1. Diels-Alder cycloadditon of 1,4-diphenylbutadiene to open-cage ketolactam fullerenes (2a-e)

R	Synthetic method of 1a-e	1a-e Yield (%)	2a-e Yield (%)	3a-e Yield (%)
—COtBu(1a)	A[a)]	28.9	25.2	9.9
—COCH$_2$Ph(1b)	A	29.2	6.8	37.8
—SO$_2$Tol(1c)	A	48.0	72.6	44.7
—CH$_2$SiMe$_3$(1d)	B[b)]	19.0[c)]	70.0[c)]	17.6
—CH$_2$SiPh$_3$(1e)	B	40.1[c)]	85.0[c)]	16.9

a) Method A is the reaction of C$_{60}$, RNH$_2$ and N-iodosuccinimide (NIS) in o-dichlorobenzene (ODCB).[11d] b) Method B is the reaction of C$_{60}$ and RN$_3$ in ODCB followed by thermolysis without solvent.[11c] c) References.[11c,h]

Although singlet oxygenation of an azafulleroid bearing a methoxyethoxymethyl group has often been reported as an intermediate step in the synthesis of an azafullerene,[3] singlet oxygenation of azafullerois having other substituents is limited to our previous research.[11c] Thus, we carried out the singlet oxygenation of five azafulleroids having N-alkoxy carbonyl (1a,b), tosyl (1c) or silylmethyl (1d,e) substituents as shown in Scheme 3-1 and Table 3-1. Since silylmethyl-substituted azafulleroids 1d,e are electron-donating, they exhibited the highest reactivity, with high yields as noted in our preliminary report.[11c] Alkoxycarbonyl- and tosyl-substituted azafulleroids (1a,b and 1c, respectively) required a longer reaction time. The former gave lower yields due to the electron-withdrawing effect toward electrophilic singlet oxygen, while the later unexpectedly afforded the product in moderate yield. The MALDI-TOF mass spectra of 2a-e show molecular ion peaks, indicating that the products were formed by addition of O$_2$ to azafulleroids 1a-e. The ^{13}C NMR spectra as well as the IR spectra of 2a-e display the two carbonyl carbons from ketolactam moiety. In the fullerene skeleton regions, about 60 signals were observed, indicating C_1 symmetry for 2a-e. It is noteworthy that the symmetry of the azafulleroid (C_s) and the open-cage fullerene (C_1) can easily be distinguished by the characteristic ^{1}H NMR spectra of the CH$_2$SiR$_3$[11h] and OCH$_2$Ph

methylene protons, which appear as singlets and a pair of doublets, respectively.

3.3 Diels-Alder Reaction of Open-cage Ketolactam Fullerenes 2a-e

Treatment of the open-cage ketolactam fullerenes **2a-e** with 1,4-diphenylbutadiene at room temperature allowed for formation of moderate yields of adducts **3a-e**, as shown in Scheme 3-1 and Table 3-1. Only one stereoisomer was obtained in all reactions. In contrast to the formation of **2a-e**, the yields of **3b** and **3c** (with electron withdrawing groups) are greater than those of **3d** and **3e** (with electron donating groups). Synthesis of **3a** is an exception. Structural assignments of the cycloaddition products **3a-e** were made based on spectroscopic data. There is a clear molecular ion peak in the ESI mass spectra, representing the sum of **2a-e** and 1,4-diphenylbutadiene. The ^{1}H NMR and ^{13}C NMR spectra show the expected protons and carbons for the dienyl moieties. Two allylic and two olefinic methine protons are observed for dienyl adducts **3a-e** at 5.66-5.71 and 6.70-6.92 ppm, respectively (Figure 3-2). The ^{1}H NMR chemical shifts are shifted slightly downfield compared to I (5.40, 5.46, 6.64 and 6.73 ppm)[10j] and II (5.12, 5.23, 6.59 and 6.73 ppm).[3g] Similarly, two sp^3 fullerenyl and two allylic methine carbons of **3a-e** appear at 51.20-53.70 and 65.15-83.05 ppm, respectively (Figure 3-3). These ^{13}C signals are essentially the same as those reported I (51.99, 53.94, 65.70 and 82.62 ppm)[10j] and II (52.17, 53.97, 63.63 and 80.11 ppm).[3g] These data strongly suggest that the regio- and stereoselectivity of the Diels-Alder addition is in good agreement with Gan's work.[3g,10j] Further evidence is provided by the heteronuculear multiple bond correlation (HMBC) spectra which indicate three-bond ^{1}H-^{13}C correlations between the allylic methine (H) and ketone carbonyl carbon (CO) as shown in Figure 3-4. These observations indicate that addition of 1,3-diphenylbutadiene to provide adducts **3a** and **3'a** occurs at one of the two double bonds next to the ketone groups, as shown also in Figure 3-4. The endo stereochemistry was determined by comparison of the observed ^{1}H NMR chemical shift of the allylic methine with those obtained via DFT-GIAO calculations (see below). It was not possible to grow single crystals of Diels-Alder adducts **3a-e** in order to obtain more conclusive data about these structural assignments, thus 2D INADEQUATE spectroscopy of a highly ^{13}C-enriched ketolactam fullerene derivative was utilized to assign the structure conclusively.
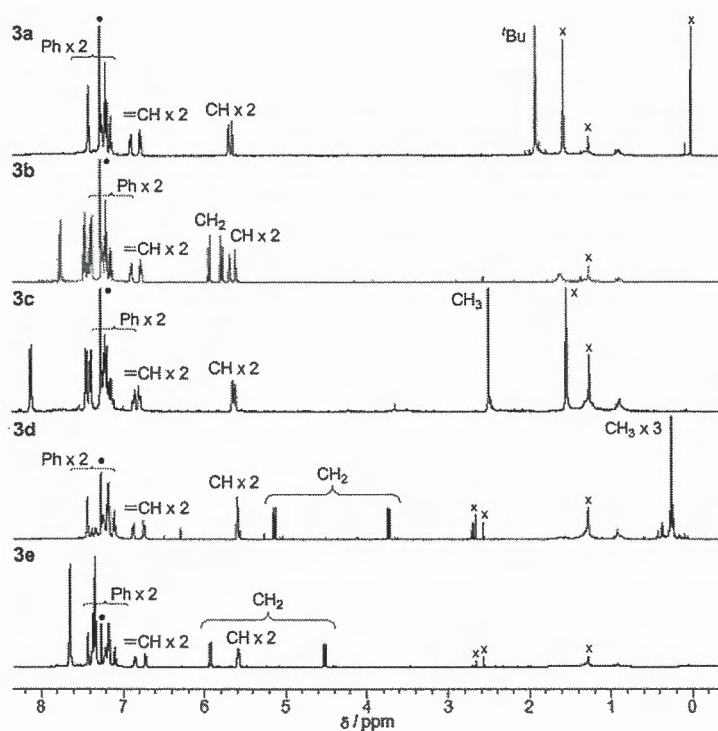
Figure 3-2. ^{1}H-NMR spectra of **3a-e** (600/500 MHz, CDCl$_3$). Solvent and impurities are denoted by filled circles (•) and hatches (×), respectively.

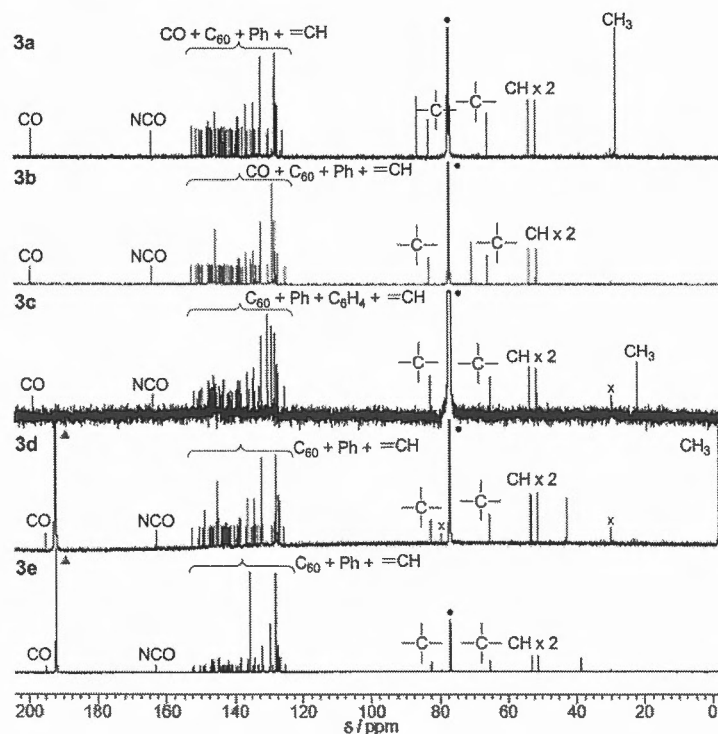Figure 3-3. ^{13}C-NMR spectra of **3a-e** (150/125 MHz, CDCl$_3$ or CDCl$_3$/CS$_2$). Solvent and impurity are denoted by filled circles (•), triangles(▲) and hatches (×), respectively.
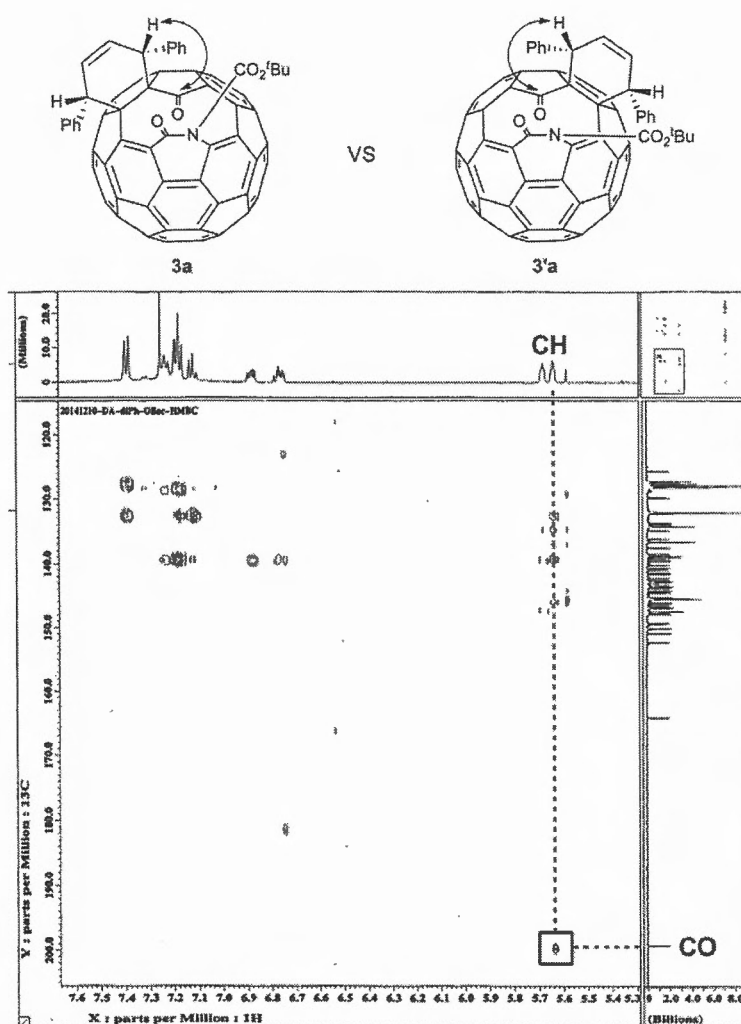
Figure 3-4. HMBC (500 MHz, CDCl₃) expansion spectrum of **3a**

3.4 2D INADEQUATE ^{13}C NMR Spectrum of 3a

To confirm the regiochemistry, compound **3a** was synthesized from a 30% ^{13}C-enriched fullerene, and 2D INADEQUATE experiments were carried out.[12] The ^{13}C NMR spectrum of **3a** show 56 fullerenyl carbons together with two sp^3 and two carbonyl carbons, indicating C_1 symmetry as shown in Figure 3-5. The spectrum reveals 5-bond connectivity, noted with bold lines, between the amide carbonyl carbon (C1) and the ketone carbonyl carbon (C6), providing unequivocal evidence that the structure is **3a** and not **3'a**. Starting from C1, a correlation is observed to highest-field fullerenyl carbon (C2). C2 is correlated with the lowest-field fullerenyl carbon (C3), which in turn is correlated with an sp^3 carbon (C4), unequivocally confirming the position of the 1,4-diphenyl butadiene addition. C4 is correlated with another sp^3 carbon (C5), which exhibits a correlation with a ketone carbonyl carbon (C6). These and four o ther correlations (C2-C12, C4-C17, C5-C20 and C6-C7) were identified and allowed for subsequent analysis of the fullerenyl carbons corresponding

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to the carbon sphere shown in the Schlegel diagram (Figure 3-6).

In evaluating the carbon (sp^2) – carbon (sp^2) connectivity of the carbon sphere, the ^{13}C NMR chemical shifts in the F2 direction were not helpful since 56 peaks are observed very close to each other. This assignment difficulty was reduced by using both relatively higher ^{13}C enrichment (30% compared to the normal 10-15%) and non-uniform sampling (NUS)[14] which allowed for assignment of more than half of the ^{13}C-^{13}C correlation peaks in the carbon sphere (Figure 3-6).[14]
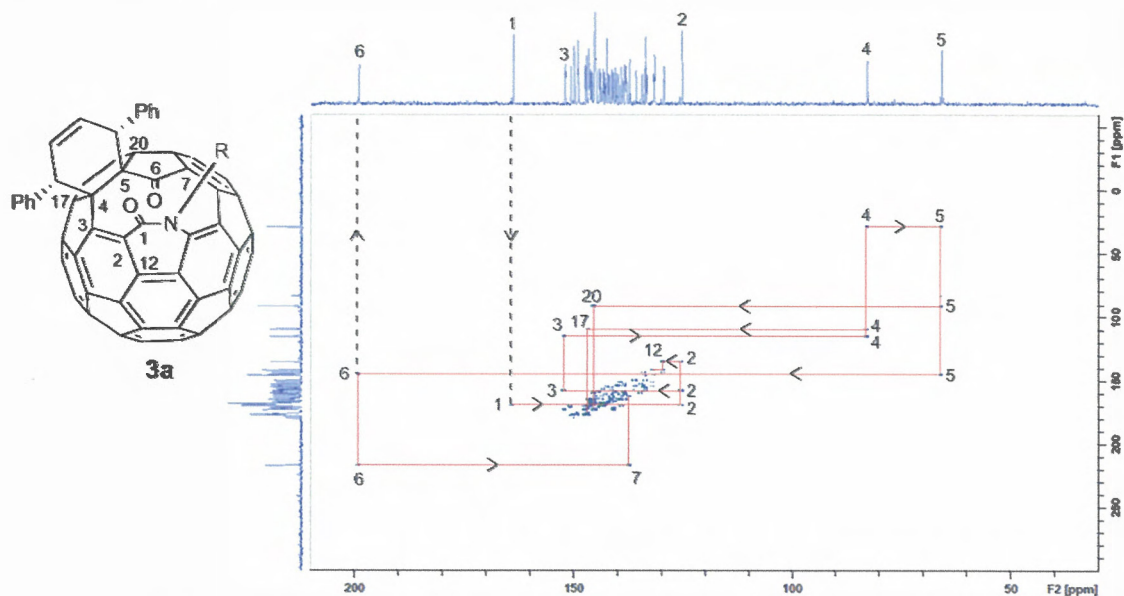

Figure 3-5. ^{13}C 2D INADEQUATE NMR spectrum of **3a** (100 MHz, CDCl$_3$)
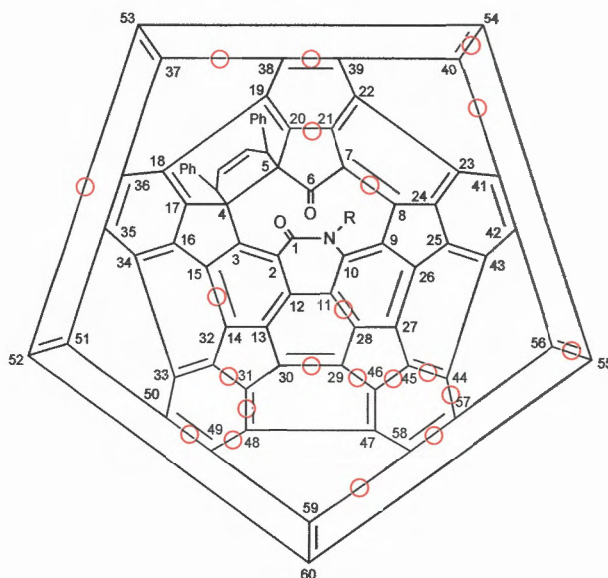

Figure 3-6. Schlegel diagram of the correlation of **3a** in the ^{13}C 2D INADEQUATE NMR spectrum (R = CO$_2$^{t}Bu). With the exception of the bonds maked by a circyle, correlation peaks between carbons appeared in the spectrum. The diagram is numbered according to reference.

3.5 Theoretical Study of the Diels-Alder Reaction on the Rim of Open-cage Fullerenes 2a-e

Based on the results of the 2D INADEQUATE ^{13}C NMR spectrum of **3a** described above, two stereoisomeric adducts (**3a$_{exo}$** and **3a$_{endo}$**) remain possible as shown in Table 3-2. To distinguish between the two isomers, a comparison of the experimental and calculated ^{1}H NMR spectra was conducted using gauge-independent atomic orbital (GIAO)[15] calculations based on structures optimized at the B3LYP/6-31G** level of theory. As shown in Figure 3-7a, the experimentally observed spectrum of **3a** is characterized by two allylic methine protons. The GIAO calculations of **3a$_{endo}$** shown in Figure 3-7b reproduced the experimental chemical shifts of the allylic methine fairly well. The calculated chemical shifts of the allylic methine protons of **3a$_{endo}$** are more downfield than those of **3a$_{exo}$** as shown in Figure 3-7c. A similar trend was also observed in the calculated ^{1}H NMR shifts on adducts **3a-f** (Table 3-2). The endo geometry of compounds I[10j] and II[3g] was unambiguously confirmed via X-ray analysis, in which similar downfield shifts of the allylic methine protons were also observed. In the structure of Figure 3-8a optimized at the B3LYP/6-31G** level, the deshielded allylic methine protons are oriented toward the rim of the orifice. On the other hand, the structure in Figure 3-8b shows the deshielded allylic methine protons pointing toward the fullerene core. These findings suggest the diamagnetic effect of the rim of the orifice in the open-cage fullerene might be greater than that of the fullerene coreconsisting of 6- and 5-membered rings.[16] All endo adducts **3a-f$_{endo}$** are also energetically favored over exo adducts **3a-e$_{exo}$**. Even unobserved adducts **3'a-e** follow the same endo- stereochemistry as that of **3a-e** as shown in Table 3-2. Upon inspection of Table 3-2, **3a$_{endo}$** and **3a$_{exo}$** are exothermic by -10.1 and -7.0 kcal/mol, respectively, and slightly endothermic for **3'a$_{endo}$** and **3'a$_{exo}$** by 0.12 and 1.7 kcal/mol. This gradual increase in endothermicity reflects the fact that the reaction is hindered by a repulsive steric interaction between substituents the nitrogen substituents and the dienyl. However, these steric preferences do not necessarily explain the predicted regiochemistry and endoselectivity. As seen in Table 3-2, even hydrogen on the nitrogen atom (**3f**) undergoes a similar regio- and endo-selective addition. This calculated result for **3f** means that the predicted regiochemistry is mainly attributable to an electronic effect and not the steric effect of substituents on the nitrogen atom or the dienyl.
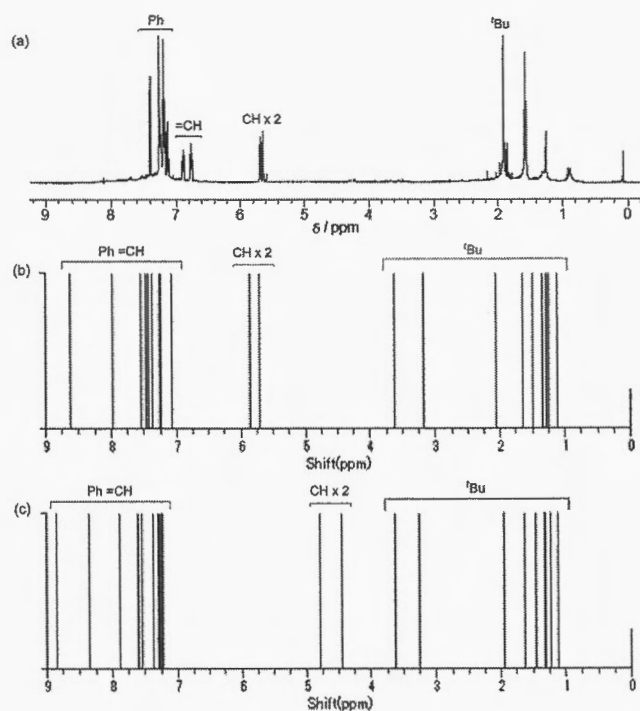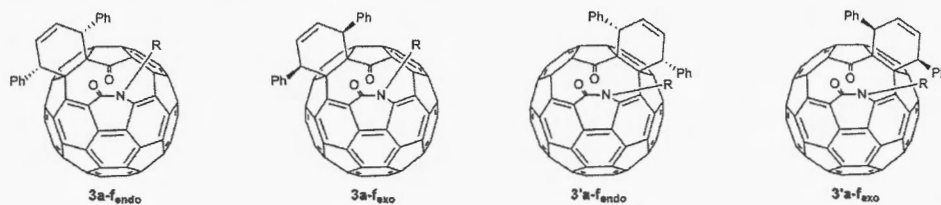
Figure 3-7. (a) Experimental ^{1}H NMR spectrum of **3a**. GIAO calculated spectrum of (b) **3a$_{endo}$** and (c) **3a$_{exo}$** at B3LYP/6-31G** level.

Table 3-2. Relative heats of formation of the adduct formed by 1,4-diphenylbutadiene and **2a-f** and GIAO calculated chemical shifts of allylic methine of **3a-f**

R	3a-f$_{endo}$			3a-f$_{exo}$		3'a-f$_{endo}$	3'a-f$_{exo}$
	Experimental chemical shifts (ppm)	Calculated[a] chemical shifts (ppm)	Relative energy[b] (kcal/mol)	Calculated[a] chemical shifts (ppm)	Relative energy[b] (kcal/mol)	Relative energy[b] (kcal/mol)	Relative energy[b] (kcal/mol)
$-\overset{\overset{O}{\|\|}}{C}-O^tBu$ (3a)	5.65, 5.69	5.71, 5.86	−10.1	4.45, 4.79	−7.0	0.12	1.7
$-\overset{\overset{O}{\|\|}}{C}-OBn$ (3b)	5.61, 5.68	5.80, 5.91	−10.9	4.51, 4.82	−8.0	−2.2	−0.7
$-SO_2Tl$ (3c)	5.62, 5.65	5.72, 5.76	−9.8	4.39, 4.79	−7.1	−5.6	−3.1
$-CH_2SiMe_3$ (3d)	5.64, 5.68	5.77, 5.80	−8.1	4.22, 4.57	−5.9	−1.1	1.7
$-CH_2SiPh_3$ (3e)	5.56, 5.61	5.81, 5.88	−8.4	4.13, 4.28	−5.4	−0.64	2.4
$-H$ (3f)	—	5.71, 5.75	−9.6	4.41, 4.81	−6.7	−2.5	−1.9

a) Calculations at B3LYP/6-31G** level.

b) Values are relative to sum of 1,4-dipnenylbutadiene and **2a-f** set as 0.0 kcal/mol.
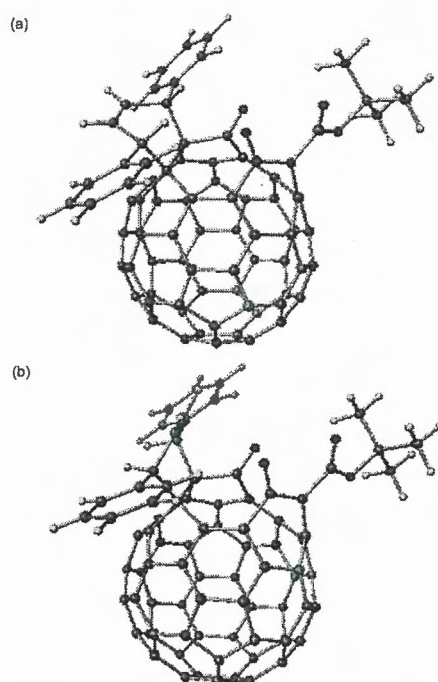
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Figure 3-7. Optimized structures of (a) **3a_endo** and (b) **3a_exo** at the B3LYP/6-31G** level.

Due to the electron deficient nature of fullerenes, the unsaturated ketone of open-cage fullerenes **2a-e** acts as a 2π electron electrophile (LUMO), while 1,4-diphenyl butadiene acts as a 4π electron nucleophile (HOMO).[17] The LUMOs of **2a-f** are shown in Figures 3-9a-f. These LUMOs are antisymmetric in the same way as the HOMO of s-*cis*-1,4-diphenyl butadiene as shown in Figure 3-9g. Thus, concerted thermal [4+2] cycloadditions should be symmetry allowed. A closer look at the LUMOs of **2a-f** shows that the LUMOs are concentrated on one side of the unsaturated ketones as shown in Figures 3-9a-f. This MO symmetry (as well as larger LUMO coefficients) should make the Diels-Alder cycloaddition easier, which correlates exactly with the predicted regiochemistry. In Figure 3-9g, the primary and secondary orbital interactions are shown by dashed and dotted lines, respectively. The primary bonding interaction leads directly to new bonds. The secondary interaction is thought to be important role in the endo stereo selectivity of the Diels-Alder reaction, although it does not lead to a new bond.[18] A pair of dashed lines for **2a-f** and 1,4-diphenyl butadiene identifies bonding interactions, while one of two pairs of dotted lines is for a bonding and the other is for an antibonding interaction. The negligibly-small HOMO coefficients and nonplanarity of α,β-unsaturated ketones shown in Figures 3-8a-f seems to prevent effective secondary orbital interactions between **2a-f** and 1,4-diphenyl butadiene. As a result, the repulsive steric interaction between **2a-f** and 1,4-diphenyl butadiene prevails, resulting in a weak antibonding interaction.
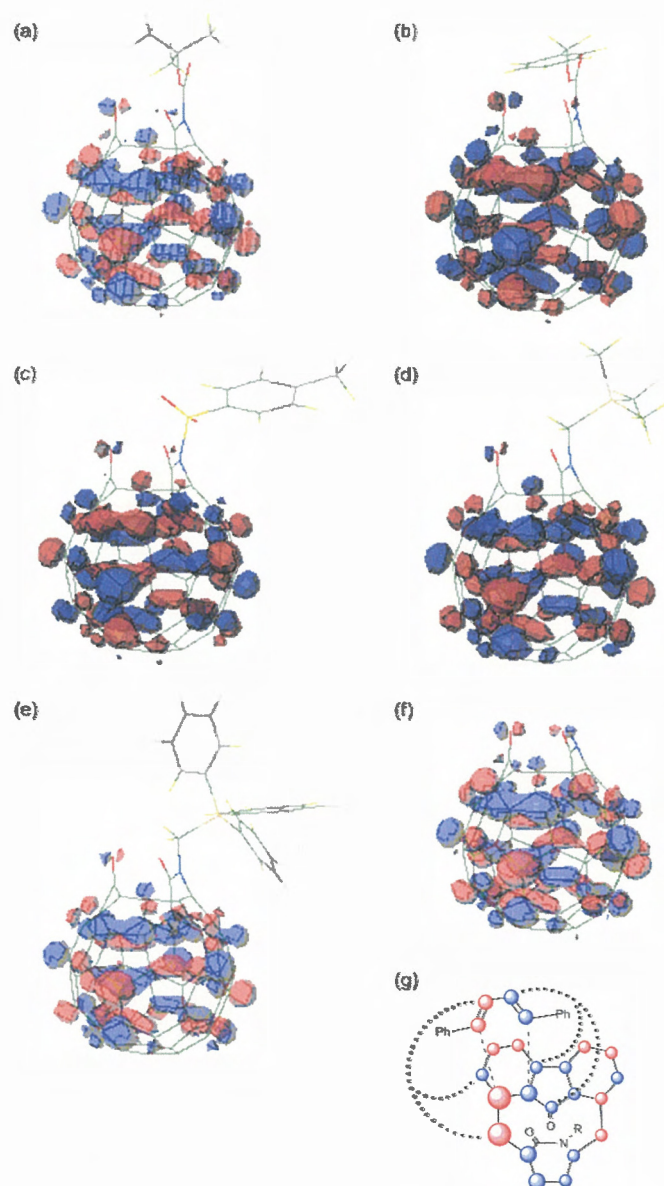
Figure 3-9. Map of the LUMO of (a) **2a**, (b) **2b**, (c) **2c**, (d) **2d**, (e) **2e**, and (f) **2f**. (g) Sign and magnitude of the LUMO coefficients for 1,4-diphenylbutadiene (HOMO) and rim of the open-cage fullerenes **2a-f** (LUMO). The dashed and dotted lines show primary and secondary orbtal interactions, respectively.

3.6 Conclusions

Singlet oxygenation of azafulleroids affords open-cage ketolactam fullerenes. The yields depend on the nitrogen substituents. A regio- and stereo-selective Diels-Alder reaction on the rim of an open-cage ketolactam derivative of fullerene with 1,4-diphenylbutadiene takes place. All adducts were fully characterized by ^{1}H- and ^{13}C NMR spectroscopy as well as the MALDI-TOF mass spectra. The regioselectivity was unequivocally determined from HMBC spectrum and

INADEQUATE experiment on a 30% ^{13}C enriched sample, eliminating the need for X-ray crystallography to determine the structure. The endo stereoselectivity was estimated by comparison of the observed ^{1}H NMR spectra and those obtained by DFT-GIAO calculations. The origin of the regio- and endo stereoselectivity is explained first in terms of an orbital-controlled reaction, and second by the repulsive steric interaction between the substituents on the nitrogen atom and diene based on theoretical calculations.

3.7 Experimental Section

Typical procedure for synthesis of azafulleroids (1a-b)

C_{60} (1.00 mmol), t-butyl carbamate (1.00 mmol) and N-iodosuccinimide (NIS) (1.99 mmol) were dissolved in 18 mL of o-dichlorobenzene (ODCB), then heated with stirring for 6 hours at 80 □C. After the reaction mixture was allowed to cool, the solvent was removed under vacuum at 50 °C. The residue was purified via silica gel column chromatography, eluting with CS_2. Collection and concentration of the 3rd purple fraction gave 241 mg (28.9 %) of Boc-substituted azafulleroid (1a) as a brown solid.

1a: ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.67 (s, 9H); ^{13}C NMR (125 MHz, CS$_2$: CDCl$_3$ = 4 : 1) δ 28.03 (CH$_3$), 82.80 (1C), 134.50 (2C), 135.09 (2C), 136.05 (2C), 137.10 (1C), 137.38 (2C), 138.25 (2C), 138.31 (2C), 138.96 (2C), 139.11 (2C), 139.55 (2C), 141.20 (2C), 141.63 (2C), 142.55 (2C), 142.66 (2C), 142.72 (2C), 142.95 (2C), 143.01 (2C), 143.21 (3C), 143.39 (2C), 143.72 (2C), 143.75 (2C), 143.82 (2C), 143.93 (3C), 144.01 (2C), 144.20 (2C), 144.31 (2C), 144.58 (2C), 144.83 (1C), 147.24 (2C), 153.22 (C=O); IR (KBr) : 1733 cm^{-1} (C=O); MS (MALDI-TOF MASS; negative) m/z calcd for C$_{65}$H$_8$NO$_2$ ([M-H]$^-$) 834, found, 834.

1b: 185 mg (29.2 %) as brown solid. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.44 (s, 2H), 7.34-7.41 (m, 3H), 7.44-7.47 (m, 2H); ^{13}C NMR (125 MHz, CS$_2$: CDCl$_3$ = 4 : 1) δ 68.42 (CH$_2$), 128.17 (Ph), 128.38 (Ph), 128.46 (Ph), 133.75 (2C), 134.40 (2C), 135.05 (2C), 135.83 (2C), 137.04 (2C), 137.42 (2C), 138.23 (2C), 138.36 (2C), 138.97 (2C), 139.03 (2C), 139.56 (2C), 141.21 (2C), 141.50 (2C), 142.51 (2C), 142.61 (2C), 142.72 (2C), 142.90 (2C), 142.93 (2C), 143.19 (2C), 143.21 (1C), 143.38 (2C), 143.69 (1C), 143.73 (3C), 143.90 (2C), 143.99 (2C), 144.00 (2C), 144.14 (2C), 144.23 (2C), 144.63 (2C), 145.39 (1C), 147.15 (2C), 154.09 (C=O); IR (KBr) 1735 cm^{-1} (C=O); MS (MALDI-TOF MASS, negative) m/z calcd for C$_{68}$H$_7$NO$_2$ ([M]$^-$) 869, found, 869.

Synthesis of azafulleroids 1c-e

Other azafulleroids **1c**[11d] and **1d,e**[11c,h] were prepared via literature methods. The spectral data were identical to those in the literature.

Typical procedure for synthesis of open-cage fullerenes (2a-c)

A 50 mL o-dichlorobenzene (ODCB) solution of Boc-substitued azafulleroid (1a) (0.111 mmol) in a Pyrex® tube was irradiated with a halogen lamp under bubbling oxygen for 30 hours. After the solvent was removed under vacuum at 50 °C, the residue was purified via silica gel column chromatography, eluting with $CHCl_3$. Collection and concentration of the 2nd brown fraction gave 25.1 mg (25.2 %) of **2a** as a brown solid.

2a: ^1H NMR (500 MHz, $CDCl_3$) δ 1.98 (s, 9H); ^{13}C NMR (125 MHz, CS_2 : $CDCl_3$ = 4 : 1) δ 27.89 (CH$_3$), 86.39 (1C), 128.48 (1C), 128.78 (1C), 130.32 (1C), 132.17 (1C), 132.29 (1C), 132.55 (1C), 132.59 (1C), 132.64 (1C), 133.13 (1C), 135.75 (1C), 135.93 (1C), 136.04 (1C), 136.21 (1C), 136.40 (1C), 137.79 (1C), 138.18 (1C), 138.49 (1C), 138.53 (1C), 139.42 (1C), 139.53 (1C), 139.58 (1C), 140.07 (1C), 140.40 (1C), 140.64 (1C), 141.08 (1C), 142.72 (1C), 143.08 (1C), 143.27 (1C),143.32 (1C), 143.54 (1C), 143.67 (1C), 143.78 (1C), 143.82 (1C), 143.86 (1C), 143.90 (1C), 144.08 (1C), 144.27 (1C), 144.31 (1C), 144.51 (1C), 144.88 (1C), 145.06 (1C), 145.20 (1C), 145.42 (1C), 145.46 (1C), 145.49 (1C), 145.70 (1C), 145.77 (1C), 145.83 (1C), 145.89 (1C), 146.04 (1C), 146.07 (1C), 146.09 (1C), 146.60 (1C), 146.89 (1C), 146.92 (1C), 147.34 (1C), 147.35 (1C), 149.19 (1C), 150.23(C=O), 160.15(C=O), 197.59(C=O); IR (KBr) 1733 (C=O), 1752 cm^{-1} (C=O); MS (MALDI-TOF MASS; negative) m/z calcd for $C_{65}H_8NO_2$ ([M-H]$^-$) 866, found, 866.

2b: 11.8 mg (6.8 %) as brown solid. ^1H NMR (500 MHz, $CDCl_3$) δ 5.80 (d, J = 12.2 Hz, 1H), 5.89 (d, J = 12.2 Hz, 1H), 7.39-7.44 (m, 1H), 7.47-7.52 (m, 2H), 7.78-7.82 (m, 2H); ^{13}C NMR (125 MHz, CS_2 : $CDCl_3$ = 4 : 1) δ 70.79 (CH$_2$), 128.23 (1C), 128.28 (Ph), 128.44 (Ph), 128.51 (Ph), 132.08 (1C), 132.13 (1C), 132.55 (1C), 132.71 (1C), 133.07 (1C), 134.39 (1C), 135.83 (1C), 136.00 (1C), 136.21 (1C), 136.25 (1C), 136.37 (1C), 137.80 (1C), 138.15 (1C), 138.20 (1C), 138.36 (1C), 139.34 (1C), 139.55 (1C), 139.61 (1C), 140.03 (1C), 140.32 (1C), 140.54 (1C), 141.22 (1C), 142.70 (1C), 143.10 (1C), 143.28 (1C), 143.32 (1C), 143.53 (1C), 143.67 (1C), 143.72 (1C), 143.79 (1C), 143.86 (2C), 144.07 (1C), 144.12 (1C), 144.24 (1C), 144.41 (2C), 144.90 (1C), 145.08 (1C), 145.22 (1C), 145.43 (1C), 145.43 (1C), 145.49 (1C), 145.53 (1C), 145.68 (1C), 145.75 (1C), 145.76 (1C), 145.85 (1C), 145.90 (1C), 146.05 (1C), 146.06 (2C), 146.56 (1C), 146.76 (1C), 146.90 (1C), 147.28 (1C), 149.20 (1C), 150.32 (1C), 160.06 (C=O), 197.84 (C=O); IR (KBr) 1735 (C=O), 1791 cm^{-1} (C=O); MS (MALDI-TOF MASS; negative) m/z calcd for $C_{68}H_7NO_4$ ([M]$^-$) 901, found, 901.

2c: 41.6 mg (72.6 %) as brown solid. ^1H NMR (600 MHz, $CDCl_3$) δ 2.58 (s, 3H), 7.42 (d, J = 8.4 Hz, 2H), 8.11(d, J = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, CS_2 : $CDCl_3$ = 4 : 1) δ 21.77(CH$_3$), 128.08(1C), 129.12(Ph), 129.32(1C), 129.56(1C), 129.73(Ph), 129.79(1C), 132.47(2C), 133.16(1C), 133.37(1C), 134.33(1C), 135.12(1C), 135.82(1C), 136.04(Ph), 136.18(1C), 136.20(1C), 137.50(1C), 137.93(1C), 138.31(1C), 138.66(2C), 138.87(2C), 138.96(1C), 139.60(1C), 139.62(1C), 140.31(1C), 140.36(1C),

141.40(1C), 142.12(1C), 142.72(1C), 143.25(1C), 143.35(1C), 143.41(1C), 143.45(1C), 143.69(1C), 143.74(1C), 143.79(1C), 143.92(1C), 143.97(1C), 144.11(1C), 144.19(1C), 144.61(1C), 145.14(1C), 145.42(1C), 145.47(1C), 145.49(1C), 145.66(2C), 145.80(1C), 145.84(1C), 145.96(1C), 146.00(2C), 146.08(Ph), 146.22(1C), 146.55(1C), 146.88(1C), 146.97(1C), 147.11(1C), 149.33(1C), 150.70(1C), 161.35(C=O), 196.12(C=O); IR (KBr) 1710 (C=O), 1740 (C=O) cm^{-1}; MS (MALDI-TOF MASS; negative) m/z calcd for $C_{60}NO_2$ ([M-$C_7H_7O_2S$]$^-$), 766, found, 766.

Synthesis of open-cage fullerenes 2d-e

Open-cage fullerenes **2d-e** were prepared via the literature method.[11h]

Typical procedure for syntheses of Diels-Alder adducts (3a-e)

Open-cage fullerene **2a** (0.185 mmol) and 1,4-diphenylbutadiene (0.926 mmol) were dissolved in 20 mL of dichloromethane, then stirred for 3 hours at room temperature. After the solvent was removed under vacuum, the residue was purified via silica gel column chromatography, eluting with CS_2 and CH_2Cl_2. Collection and concentration of the 3rd brown fraction gave 19.7 mg (9.9 %) of Diels-Alder adduct **3a** as a brown solid.

3a: ^{1}H NMR (500 MHz, CDCl$_3$) δ 1.91 (s, 9H), 5.63-5.66 (m, 1H), 5.67-5.71 (m, 1H), 6.74-6.79 (m, 1H), 6.86-6.91 (m, 1H), 7.10-7.15 (m, 1H), 7.16-7.27 (m, 7H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 28.13 (CH$_3$), 51.43 (1C), 53.68 (1C), 65.99 (1C), 83.06 (1C), 86.38 (1C), 125.63 (1C), 127.18 (1C), 127.58 (1C), 127.91 (Ph), 128.13 (Ph), 129.74 (1C), 131.99 (1C), 132.04 (Ph), 132.21 (1C), 133.64 (1C), 133.83 (1C), 134.12 (1C), 134.21 (1C), 134.81 (1C), 136.14 (1C), 136.54 (1C), 137.51 (1C), 138.42 (1C), 138.67 (1C), 138.75 (1C), 138.93 (1C), 139.13 (1C), 139.49 (1C), 140.14 (1C), 140.64 (1C), 140.92 (1C), 141.37 (1C), 141.57 (1C), 142.15 (1C), 142.51 (1C), 142.73 (1C), 142.79 (1C), 142.85 (1C), 143.17 (1C), 143.39 (1C), 143.55 (1C), 143.59 (1C), 143.72 (1C), 144.07 (1C), 144.31 (1C), 144.47 (1C), 145.20 (1C), 145.30 (1C), 145.36 (1C), 145.40 (1C), 145.49 (1C), 145.50 (1C), 145.54 (1C), 146.08 (1C), 146.39 (1C), 146.68 (1C), 146.77 (1C), 146.86 (1C), 146.92 (1C), 147.40 (1C), 147.41 (1C), 147.64 (1C), 147.81 (1C), 149.23 (1C), 149.37 (1C), 150.06 (1C), 150.11 (1C), 150.88 (1C), 152.28 (1C), 164.08 (C=O), 199.21 (C=O); IR (KBr) 1720 (C=O), 1781 cm^{-1} (C=O); HRMS (ESI) m/z calcd for $C_{81}H_{23}NNaO_4$ ([M+Na]$^+$) 1096.1525, found, 1096.1525.

3b: 33.9 mg (37.8 %) as brown solid. ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.59-5.63 (m, 1H), 5.66-5.70 (m, 1H), 5.78 (d, J = 12.3 Hz, 1H), 5.93 (d, J = 12.3 Hz, 1H), 6.74-6.79 (m, 1H), 6.86-6.91 (m, 1H), 7.11-7.27 (m, 8H), 7.35-7.47 (m, 5H), 7.73-7.77 (m, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 51.36 (1C), 53.70 (1C), 65.71 (1C), 70.45 (CH$_2$), 83.05 (1C), 125.14 (1C), 127.20 (1C), 127.62 (1C), 127.99 (Ph), 128.16 (1C), 128.58 (Ph), 128.60 (Ph), 128.67 (Ph), 129.76 (1C), 131.99 (Ph), 132.09 (1C), 132.30 (1C), 133.11 (1C), 133.70 (1C), 134.17 (1C), 134.22 (1C), 134.71 (1C), 135.01 (1C), 136.37

(1C), 136.53 (1C), 137.57 (1C), 138.23 (1C), 138.44 (1C), 138.57 (1C), 138.86 (1C), 139.12 (1C), 139.12 (1C), 139.48 (1C), 140.20 (1C), 140.57 (1C), 140.78 (1C), 141.41 (1C), 141.51 (1C), 142.12 (1C), 142.63 (1C), 142.65 (1C), 142.78 (1C), 142.85 (1C), 143.15 (1C), 143.36 (1C), 143.52 (1C), 143.58 (1C), 143.74 (1C), 144.07 (1C), 144.28 (1C), 144.42 (1C), 145.03 (1C), 145.31 (1C), 145.32 (1C), 145.43 (1C), 145.46 (Ph), 145.53 (1C), 145.99 (1C), 146.38 (1C), 146.49 (1C), 146.76 (1C), 146.85 (1C), 146.92 (1C), 147.36 (1C), 147.44 (1C), 147.62 (1C), 149.21 (1C), 149.37 (1C), 150.04 (1C), 150.16 (1C), 150.28 (1C), 150.83 (1C), 152.40 (1C), 163.97 (C=O), 199.57 (C=O); IR (KBr) 1727 (C=O), 1786 cm^{-1} (C=O); HRMS (ESI) m/z calcd for $C_{84}H_{21}KNO_4$ ([M+K]$^+$) 1146.1108, found, 1146.1108.

3c: 34.3 mg (44.7 %) as brown solid. ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.50 (s, 3H), 5.62-5.65 (d, 2H), 6.80-6.85 (m, 2H), 7.13-7.26(m, 14H), 7.37-7.45 (d, 4H), 8.11-8.13 (d, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 21.89 (CH$_3$), 51.39 (1C), 53.61 (1C), 65.15 (CH), 82.69 (CH), 125.37 (1C), 127.23 (Ph), 127.57 (Ph), 127.77 (1C), 128.07 (Ph), 128.17 (Ph), 128.87 (Ph), 129.00 (1C), 129.11 (Ph), 130.00 (1C), 130.05 (1C), 130.12 (Ph), 131.83 (1C), 131.95 (Ph), 132.57 (1C), 133.91 (1C), 134.09 (1C), 134.22 (1C), 134.31 (Ph), 134.51 (1C), 135.69 (2C), 136.41 (Ph), 138.18 (1C), 138.43 (1C), 138.47 (1C), 138.54 (1C), 138.61 (1C), 138.66 (1C), 138.90 (1C), 139.07 (1C), 139.39 (1C), 139.78 (1C), 140.71 (1C), 141.08 (1C), 141.59 (1C), 141.75 (1C), 142.04 (1C), 142.23 (1C), 142.94 (1C), 143.00 (1C), 143.02 (1C), 143.18 (1C), 143.40 (1C), 143.59 (Ph), 143.87 (Ph), 144.14 (1C), 144.31 (1C), 144.34 (1C), 145.18 (1C), 145.35 (CH), 145.39 (CH), 145.46 (1C), 145.50 (1C), 145.57 (1C), 145.66 (1C), 145.85 (1C), 145.91 (1C), 145.99 (1C), 146.45 (1C), 146.68 (1C), 146.92 (1C), 147.04 (1C), 147.25 (1C), 147.68 (1C), 149.29 (1C), 149.46 (1C), 150.07 (1C), 150.36 (1C), 150.80 (1C), 151.88 (1C), 163.85 (C=O), 198.73 (C=O); IR (KBr) 1713 (C=O), 1733 cm^{-1} (C=O); HRMS (ESI) m/z calcd for $C_{83}H_{21}NNaO_4S$ ([M+Na]$^+$) 1150.1089, found, 1150.1089.

3d: 8.9 mg (17.6 %) as dark brown solid. ^{1}H NMR(400 MHz, CDCl$_3$); δ 0.21 (s, 9H), 3.80 (d, J = 15.5 Hz, 1H), 5.13 (d, J = 15.5 Hz, 1H), 5.64-5.68 (m, 2H), 6.73-6.78 (m, 1H), 6.86-6.92 (m, 1H), 7.10-7.30 (m, 8H), 7.46-7.51 (m, 2H); ^{13}C NMR(150 MHz, CS$_2$: CHCl$_3$ = 4 : 1); δ -1.85 (CH$_3$), 42.75 (CH$_2$), 51.30 (CH), 53.21 (CH), 65.57 (1C), 82.62 (1C), 125.56 (1C), 126.88 (Ph), 127.26 (Ph), 127.64 (Ph), 127.90 (Ph), 128.07 (1C), 128.25 (1C), 128.36 (1C), 129.07 (1C), 131.86 (1C), 132.01 (1C), 132.07 (Ph), 132.42 (1C), 133.27 (1C), 133.89 (1C), 134.17 (3C), 134.49 (1C), 135.05 (1C), 136.38 (Ph), 136.92 (1C), 138.43 (1C), 138.58 (1C), 138.72 (1C), 138.77 (1C), 138.90 (1C), 139.49 (1C), 140.26 (1C), 141.15 (1C), 141.63 (1C), 141.86 (1C), 141.92 (1C), 142.20 (1C), 142.50 (1C), 142.59 (2C), 142.70 (1C), 142.77 (1C), 142.91 (1C), 142.96 (1C), 143.33 (1C), 143.47 (1C), 143.82 (1C), 143.87 (1C), 144.05 (1C), 144.77 (1C), 144.89 (2C), 145.07 (Ph), 145.18 (1C), 145.35 (2C), 146.21 (1C), 146.43 (1C), 146.59 (1C), 146.62 (1C), 146.95 (1C), 147.02 (1C), 147.19 (1C), 147.60

(1C), 148.88 (2C), 149.17 (1C),149.52 (1C), 150.46 (1C), 152.50 (1C), 162.97 (C=O), 195.08 (C=O); IR (KBr) 1675 (C=O), 1723 cm^{-1} (C=O); HRMS (ESI) m/z calcd for $C_{80}H_{25}NNaO_2Si$ ([M+Na]$^+$) 1082.1552, found, 1082.1552.

3e: 17.2 mg (16.9 %) as brown solid. ^{1}H NMR (600 MHz, CDCl$_3$) δ 4.52 (d, J = 16.1 Hz, 1H), 5.56-5.61 (m, 2H), 5.93 (d, J = 16.1 Hz, 1H), 6.70-6.74 (m, 1H), 6.83-6.87 (m, 1H), 7.08-7.12 (m, 1H), 7.14-7.24 (m, 3H), 7.30-7.39 (m, 6H), 7.40-7.44 (m, 1H), 7.62-7.67 (m, 4H); ^{13}C NMR (150 MHz, CS$_2$: CDCl$_3$ = 4 : 1) δ 38.76 (CH$_2$), 51.25 (1C), 53.10 (1C), 65.44 (1C), 82.48 (1C), 125.20 (1C), 126.82 (1C), 127.13 (1C), 127.60 (1C), 127.82 (1C), 127.94 (Ph), 128.91 (1C), 129.72 (Ph), 131.73 (1C), 131.93 (1C), 131.96 (1C), 132.02 (1C), 132.13 (1C), 133.07 (1C), 133.38 (1C), 134.13 (1C), 134.37 (1C), 134.87 (1C), 135.63 (Ph), 136.32 (1C), 136.56 (1C), 138.31 (1C), 138.52 (1C), 138.66 (1C), 138.75 (1C), 139.29 (1C), 139.97 (1C), 140.80 (1C), 141.22 (1C), 141.65 (1C), 141.87 (1C), 141.89 (1C), 142.03 (1C), 142.42 (1C), 142.51 (1C), 142.60 (1C), 142.63 (1C), 142.85 (1C), 143.18 (1C), 143.34 (1C), 143.59 (1C), 143.71 (1C), 143.90 (1C), 144.60 (1C), 144.73 (1C), 144.78 (1C), 144.91 (1C), 144.95 (1C), 144.96 (1C), 145.20 (1C), 146.08 (1C), 146.33 (1C), 146.43 (1C), 146.82 (1C), 147.03 (1C), 147.40 (1C), 148.70 (1C), 148.72 (1C), 149.03 (1C), 149.38 (1C), 150.35 (1C), 152.31 (1C), 163.07 (C=O), 195.04 (C=O); IR (KBr) 1672 (C=O), 1725 cm^{-1} (C=O); HRMS (ESI) m/z calcd for $C_{95}H_{31}KNO_2Si$ ([M+K]$^+$) 1284.1761, found, 1284.1761.

3.8 2D INADEQUATE ^{13}C NMR of 3a

30% ^{13}C-enriched fullerenes were purchased from MER Corp and used to prepare **3a** according to preceding experimentals without any further purification. Measurements were performed on a Bruker AVANCE III 400 MHz NMR spectrometer. The standard, phase-sensitive 4-pulse program, which is pre-installed on the TOPSPIN 3.5 software, was used for all of the 2D experiments. The demanded parameter $^1J_{CC}$ was set to 60 Hz. The 2D data were acquired via States-TPPI for avoiding axial peaks F1-axis center. 25% over all of the t1 data points were acquired employing NUS.[12f] 32 scans of FID data were accumulated using phase cycling for each t1 point. After acquiring all of the FID data, a standard data reconstruction process for a 2D spectrum based on the compressed sensing (CS) algorithm[12g] was performed automatically by the software prior to the 2D Fourier transformation.

3.9 Computational Studies

Calculations were carried out on an HPC-5000-XH216R2 and HPC-5000-XH218R2S workstation provided by HPC Inc. of Japan. Ab initio calculations were preformed using the Gaussian 03 computer program.[19] The initial geometries of the fullerene derivatives were constructed using the Winmostar graphical interface.[20] All geometry optimizations were performed on Cartesian

coordinates using the energy gradient minimization method. DFT-GIAO calculations were performed using the program installed in Gaussian 03.

Reference

1. Reviews of open-cage fullerenes: (a) Y. Rubin, *Chem. Eur. J.*, 1997, *3*, 1009. (b) Y. Rubin, *Top. Curr. Chem.*, 1999, *199*, 67. (c) S.-I. Iwamatsu and S. Murata, *Synlett*, 2005, 2117. (d) M. Murata, Y. Murata and K. Komatsu, *Chem. Commun.*, 2008, 6083. (e) G. -C. Vougioukalakis, M. M. Roubelakis and M. Orfanopaulos, *Chem. Soc.v Rev.*, 2010, 39, 817. (f) L. Gan, D. Yang, Q. Zhang and H. Huang, *Adv. Mater.*, 2010, *22*, 1498. (g) L. Shi and L. Gan, *J. Phys. Org. Chem.*, 2013, *26*, 766.

2. Synthesis of endohedral fullerenes by molecular surgery: (a) K. Komatsu, M. Murata and Y. Murata. *Science*, 2005, *307*, 238. (b) M. Murata, Y. Murata and K. Komatsu, *J. Am. Chem. Soc.*, 2006, *128*, 8024. (c) M. Murata, S. Murata, Y. Morinaka, Y. Murata and K. Komatsu, *J. Am. Chem. Soc.*, 2008, *130*, 15800. (d) K. Kurotobi and Y. Murata, *Science*, 2011, *333*, 613. (e) Y. Morinaka, F. Tanabe, M. Murata, Y. Murata and K, Komatsu, *Chem. Comm.*, 2010, *46*, 4532. (f) A. Krachmalnicoff, M. H. Levitt and R. J. Whitby, *Chem. Comm.*, 2014, *50*, 13037. (g) Y. Hashikawa, M. Murata, A. Wakamiya and Y. Murata, *J. Am. Chem. Soc.*, 2016, *138*, 4096. (h) A. Krachmalnicoff, R. Bounds, S. Manone, S. Alom, M. Concistrè, B. Meier, K. Kouřil, M. E. Light, M. R. Johnson, S. Rols, A. J. Horsewill, A. Shugai, U. Nagel, T. Rõõm, M. Carravetta, M. H. Levitt, R. J. Whitby, *Nature Chem.*, 2016, *8*, 953.

3. Reviews and selected papers of azafullerenes: (a) O. Vostrowsky and A. Hirsch, *Chem. Rev.*, 2006, *106*, 5191. (b) G. Rotas and N. Tagmatarchis, *Chem. Eur. J*, 2016, *22*, 1206. (c) J. C. Hummelen, B. Kinght, J. Pavlorich, R. González and F. Wudl, *Science*, 1995, *269*, 1554. (d) M. Keshavarz-K, R. González, R. G. Hicks, G. Srdanov, V. I. Srdanov, T. G. Collins, J. C. Hummelen, C. Bellavia-Lund, J. Pavlovich, F. Wudl and K. Holczer, *Nature*, 1996, *383*, 147. (e) B. Nuber and A. Hirsch, *Chem. Comm.*, 1996, 1421. (f) K.-C. Kim, F. Hauke, A. Hirsch, P. D. W. Boyd, E. Carter, R. S. Armstrong, P. A. Lay and C. A. Reed, *J. Am. Chem. Soc.*, 2003, *125*, 4024. (g) N. Xin, H. Huang, J. Zhang, Z. Dai and L. Gan, *Angew. Chem. Int. Ed.* 2012, *51*, 6163.

4. Open-cage fullerenes: (a) J. C. Hummelen, M. Prato and F. Wudl, *J. Am. Chem. Soc.*, 1995, *117*, 7003. (b) G. Schick, T. Jarrosson and Y. Rubin, *Angew. Chem. Int. Ed.*, 1999, *38*, 2360. (c) Y. Rubin, T. Jarroson, G.-W. Wang, M. D. Bartberger, K. N. Houk, G. Schick, M. Saunders and R. J. Cross, *Angew. Chem. Int. Ed.*, 2001, *40*, 1543. (d) Y. Murata, N. Kato and K. Komatsu, *J. Org. Chem.*, 2001, *66*, 7235. (e) Y. Murata and K. Komatsu, *Chem. Lett.*, 2001, 896. (f) Y. Murata, M. Murata and K. Komatsu, *Chem. -Eur. J.*, 2003, *9*, 1600. (h) H. Inoue, H. Yamaguchi, S.-I. Iwamatsu, T. Uozaki, T. Suzuki, T. Akasaka, S. Nagase and S. Murata, *Tetrahedron Lett.*, 2001,

42, 895. (g) Y. Murata, M. Murata and K. Komatsu, *J. Am. Chem. Soc.*, 2003, *125*, 7152. (h) H. Hachiya and K. Kabe, *Chem. Lett.*, 2009, *38*, 372. (i) Y. Kabe, H. Hachiya, T. Saito, D. Shimizu, M. Ishiwata, K. Suzuki, Y. Yakushigawa and W. Ando, *J. Organometall Chem.*, 2009, *694*, 1988. (j) M. R. Cerón, M. Izquierdo, A. Aghabali, J. A. Valdez, K. B. Ghiassi, M. M. Olmstead, A. L. Balch, F. Wudl and L. Echegoyen, *J. Am. Chem. Soc.*, 2015, *137*, 7502. (k) M. Chen, L. Bao, P. Peng, S. Zheng, Y. Xie and X. Lu, *Angew. Chem. Int. Ed.*, 2016, *55*, 11887.

5. (a) M. J. Arce, A. L. Viado, Y. Z. An, S. I. Khan and Y. Rubin, *J. Am. Chem. Soc.*, 1996, *118*, 3775. (b) H. Inoue, H. Yamaguchi, T. Suzuki, T. Akasaka and S. Murata, *Synlett*, 2000, 1178.

6. (a) M. Prato, Q. C. Li, F. Wudl and V. Lucchini, *J. Am. Chem. Soc.*, 1993, *113*, 1148. (b) T. Suzuki, Q. Li, K. C. Khemani, F. Wudl and O. Almarsson, *Science*, 1991, 1186.

7. Hydroamination of open-cage fullerenes: (a) S.-I. Iwamatsu, F. Ono and S. Murata, *Chem. Lett.*, 2003, *7*, 614. (b) S.-I. Iwamatsu, F. Ono and S. Murata, *Chem. Commun.,* 2003, 1268. (c) G. C. Vougioukalakis, K. Prassides, J. M. Campanera, M. I. Heggie and M. Orfanopoulos, *J. Org. Chem.*, 2004, *69*, 4524. (d) S.-I. Iwamatsu, T. Uozaki, K. Kobayashi, R. Suyong, S. Nagase and S. Murata, *J. Am. Chem. Soc.*, 2004, *126*, 2668. (e) S.-I. Iwamatsu and S. Murata, *Tetrahedron Lett.*, 2004, *45*, 6391. (f) S. -I. Iwamatsu, S. Murata, Y. Andoh, M. Minoura, K. Kobayashi, N. Mizorogi and S. Nagase, *J. Org. Chem.*, 2005, *70*, 4820. (g) S.-I. Iwamatsu, C. M. Stanisky, R. J. Cross, M. Saunders, N. Mizorogi, S. Nagase and S. Murata, *Angew. Chem. Int. Ed.*, 2006, *45*, 5337. (h) M. M. Roubelakis Y. Murata, K. Komatsu and M. Orfanopoulos, *J. Org. Chem.*, 2007, *72*, 7042. (i) K. E. Whitener. Jr, M. Frunzi, S.-I. Iwamatsu, S. Murata, R. J. Cross and M. Saunders, *J. Am. Chem. Soc.*, 2008, *130*, 13996. (j) C. M. Stanisky, R. J. Cross, M. Saunders, *J. Am. Chem. Soc.*, 2009, *131*, 3392. (k) K. E. Whitener. Jr, R. J. Cross, M. Saunders, S.-I. Iwamatsu, S. Murata, N. Mizorogi and S. Nagase, *J. Am. Chem. Soc.*, 2009, *131*, 6338. (l) M. Frunzi, A. M. Baldwin, N. Shibata, S.-I. Iwamatsu, R. G. Lawler and N. J. Turro, *J. Phys. Chem. A*, 2011, *115*, 735. (m) Z. Xiao, G. Ye, Y. Liu, S. Chen, Q. Peng, Q. Zuo and L. Ding, *Angew. Chem. Int. Ed.*, 2012, *51*, 9038. (n) Y. Yu, L. Xu, X. Huang and L. Gan, *J. Org. Chem.* 2014, *79*, 2156. (o) L. Xu, S. Liang, J. Sun and L. Gan, *Org. Chem. Front.*, 2015, *2*, 1504. (p) C.-S. Chen, T.-S. Kuo and W.-Y. Yeh, *Angew. Chem. int. Ed.*, 2016, *22*, 8733. (q) C.-S. Chen and W.-Y. Yeh, *Chem. Eur. J.*, 2016, *22*, 16425.

8. Sulfur and selenium atom insertion of open-cage fullerene: (a) G. C. Vougionkalakis, K. Prassidies and M. O. Orfunopoulas, *Org. Lett.*, 2004, *6*, 1245. (b) S.-C. Chuang, Y. Murata, M. Murata, S. Mori, S. Maeda, F. Tanabe and K. Komatsu, *Chem. Commun.*, 2007, 1278. (c) M. Murata, Y. Morinaka, K. Kurotobi, K. Komatsu and Y. Murata, *Chem. Lett.*, 2010, *39*, 298. (d) T. Futagoishi, M. Murata, A. Wakamiya, T. Sasamori and Y. Murata, *Org. Lett.*, 2013, 2750. (e) R. Zhang, T. Futagoishi, M. Murata, A. Wakamiya and Y. Murata, *J. Am. Chem. Soc.*, 2014, *136*, 8193. (f) T. Futagoishi, M. Murata, A. Wakamiya and Y. Murata, *Angew. Chem. Int. Ed.*, 2015,

54, 14791. and 2(a-c), 2(e,f).

9. Oxidation of open-cage fullerenes with *N*-oxide: (a) Y. Hashikawa, M. Murata, A. Wakamiya and Y. Murata, *Org. Lett.*, 2014, *16*, 2970. (b) A. Krachmalnicoff, R. Bounds, S. Mamone, M. H. Levit, M. Carravetta and R. J. Whitby, *Chem. Commun.*, 2015, *51*, 4993. and 2(d), 2(f-h).

10. Peroxide-mediated syntheses of open-cage fullerenes: (a) L. Gan, *Pure Appl. Chem.*, 2006, *78*, 841. (b) Z. Xiao, J. Yao, D. Yang, F. Wang, S. Huang. L. Gan, Z. Jia, Z. Jiang, X. Yang, B. Zheng, G. Yuan, S. Zhang and Z. Wang, *J. Am. Chem. Soc.*, 2007, *129*, 16149. (c) Q. Zhang, Z. Jia, S. Liu, G. Zhang, Z. Xiao, D. Yang, L. Gan, Z. Wang and Y. Li, Org. Lett., 2009, *11*, 2772. (d) Q. Zhang, T. Pankewitz, S. Liu, W. Klapper and L. Gan, *Angew. Chem. Int. Ed.*, 2010, *49*, 9935. (e) Y. Yu, X. Xie, T. Zhang, S, Liu, Y. Shao, L. Gan and Y. Li, *J. Org. Chem.*, 2011, *76*, 10148. (f) J. Zhang, F. Wang, N. Xin, D. Yang and L. Gan, *Eur. J. Org. Chem.*, 2011, 5366. (g) G. Zhang, Q. Zhang, Z. Jia, S. Liang, L. Gan and Y. Li, *J. Org. Chem.*, 2011, *76*, 6743. (h) S. Liu, Q. Zhang, Y. Yu and L. Gan, *Org. Lett.*, 2012, *14*, 4002. (i) L. Xu, Q. Zhang, G. Zhang, S. Liang, Y. Yu and L. Gan, *Eur. J. Org. Chem.*, 2013, 7272. (j) N. Xin, X. Yang, Z. Zhou, J. Zhang, S. Zhang and L. Gan, *J. Org. Chem.*, 2013, *78*, 1157. (k) L. Shi, D. Yang, F. Colombo, Y. Yu, W.-X. Zhang and L. Gan, *Chem. Eur. J.*, 2013, *19*, 16545. (l) Y. Yu, L. Shi, D. Yang and L. Gan, *Chem. Sci.*, 2013, *4*, 814. (m) L. Xu, H. Ren, S. Liang, J. Sun, Y. Liu and L. Gan, *Chem. Eur. J.*, 2015, *21*, 13539.

11. Syntheses and reactions of azafulleroids: (a) M. Prato, Q. C. Li, F. Wudl and V. Lucchini, *J. Am. Chem. Soc.*, 1993, *115*, 1148. (b) T. Nakahodo, M. Okada, H. Morita, T. Yoshimura, M. O. Ishitsuka, T. Tsuchiya, Y. Maeda, H. Fujihara, T. Akasaka, X. Gao and S. Nagase, *Angew. Chem. Int. Ed.*, 2008, *47*, 1298. (c) H. Hachiya, T. Kakuta, M. Takami and Y. Kabe, *J. Organometallic Chem.*, 2009, *694*, 630. (d) T. Nagamachi, Y. Takeda, K. Nakayama and S. Minakata, *Chem. Eur. J.*, 2012, *18*, 12035. (e) C.-B. Miao, X.-W. Lu, P. Wu, J. Li, W.-L. Ren, M.-L. Xing, X.-Q. Sun and H.-T. Yang, *J. Org. Chem.*, 2013, *78*, 12257. (f) N. Ikuma, Y. Doi, K. Fujioka, T. Mikie, K. Kokubo and T. Oshima, *Chem. Asian J.*, 2014, *9*, 3084. (g) N. Ikuma, K. Fujioka, Y. Misawa, K. Kokubo and T. Oshima, *Org. Biomol. Chem.*, 2015, *13*, 5038. (h) H. Hachiya and Y. Kabe, *Chem. Lett.*, 2009, *38*, 372.

12. (a) J. M. Hawkins, S. Loren, A. Meyer and R. Nunlist, *J. Am. Chem. Soc.*, 1991, *113*, 7770. (b) J. M. Hawkins, *Acc. Chem. Res.*, 1992, *25*, 150. (c) J. M. Hawkins, A. Meyer, T. A. Lewis, U. Bunz, R. Nunlist, G. E. Ball, T. W. Ebbesen and K. Tanigaki, *J. Am. Chem. Soc.*, 1992, *114*, 7954. (d) G. A. Burley, P. A. Keller, S. G. Pyne and G. E. Ball, *Magn, Reson. Chem.*, 2001, *39*, 466. (e) L. Chaker, G. E. Ball, J. R. Williams, G. A. Burley, B. C. Hawkins, P. A. Keller and S. G. Pyne, *Eur. J. Org. Chem.*, 2005, *24*, 5158. (f) S. G. Hyberts, H. Arthanari and G. Wagner, *Topics of Current Chemistry*, 2011, *316*, 125, and references therein. (g) D. J. Holland, M. J. Bostock, L. F. Gladden and D. Nietlispach, *Angew. Chem. Int. Ed.*, 2011, *50*, 6548.

13. (a) R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1993, 813. (b) E. W. Godly and R. Taylor, *Pure Appl. Chem.*, 1997, *69*, 1411.

14. Details of the NUS-modified 2D INADEQUATE ^{13}C NMR and ^{13}C-^{13}C connectivity of the carbon sphere of 3a will be given elsewhere.

15. (a) K. Wolinski, J. F. Hilton and P. Pulay, *J. Am. Chem. Soc.*, 1990, *112*, 8251. (b) T. Helgaker, M. Jaszuński and K. Ruud, *Chem. Rev.*, 1999, *99*, 293.

16. (a) M. Prato, T. Suzuki, F. Wudl, V. Lucchini and M. Maggini, *J. Am. Chem. Soc.*, 1993, *115*, 7876. (b) M. Bühl and A. Hirsch, *Chem. Rev.*, 2001, *101*, 1153.

17. Selected papers concerning the reaction mechanism of Diels-Alder reactions of C$_{60}$ derivatives: (a) K. Mikami, S. Matsumoto, Y. Okubo, M. Fujitsuka, O. Ito, T. Suenobu and S. Fukuzumi, *J. Am. Chem. Soc.*, 2000, *122*, 2236. (b) N. Chronakis and M. Orfanopoulos, *Org. Lett.*, 2001, *3*, 545. (c) N. Chronakis and M. Orfanopoulos, *Tetrahedron Lett.*, 2001, *42*, 1201. (d) N. Chronakis, G. Froudakis and M. Orfanopoulos, *J. Org. Chem.*, 2002, *69*, 4284. (e) N. Ikuma, Y. Susami and T. Oshima, *Org. Biomol. Chem.*, 2010, *8*, 1394. (f) N. Ikuma, Y. Susami and T. Oshima, *Eur. J. Org. Chem.*, 2011, 6452. (g) T. Oshima, T. Mikie, N. Ikuma and H. Yakuma, *Org. Biomol. Chem.*, 2012, *10*, 1730. (h) H. Kawakami, H. Okada and Y. Matsuo, *Org. Lett.*, 2013, *15*, 4466. (i) H. Ueno, H. Kawakami, K. Nkagawa, H. Okada, N. Ikuma, S. Aoyagi, K. Kokubo, Y. Matsuo and T. Oshima, *J. Am. Chem. Soc.*, 2014, *136*, 11162. (j) S. Osuna, M. Swart and M. Solà, *J. Phys. Chem. A*, 2011, *115*, 3491. (k) Y. García-Rodeja, M. Solà, and I. Fernández, *J. Org. Chem.*, 2017, *82*, 754. (l) C.-X. Cui, Y.-J. Liu, Y.-P. Zhang, L.-B. Qu and Z.-P. Zhang, *J. Phys. Chem. A*, 2017, *121*, 523.

18. Secondary effect of frontier molecular orbitals: (a) R. B. Woodward and R. Hoffmann, *Angew. Chem.*, 1969, *81*, 797. (b) R. B. Woodward and R. Hoffmann, in "The Conservation of Orbital Symmetry", *Academic Press*, New York, 1969. (c) I. Fleming, in "Frontier Orbitals and Organic Chemical Reactions", *Wiley*, New York, 1976.

19. Gaussian 03 (Revision C.02): M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Natatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P.

M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, Gaussian, Inc., Wallingford CT, 2004.

20. http://winmostar.com/.

Chapter 4

Regioselective hydroamination of open-cage ketolactam derivatives of C_{60} with phenylhydrazine and water encapsulation

4. Regioselective Hydroamination of Open-Cage Ketolactam Derivatives of C_{60} with Phenylhydrazine and Water Encapsulation

4.1 Introduction

Open-cage fullerenes (**1a**)[1,2] have attracted interest in the production of endohedral fullerenes via organic reactions involving the "molecular surgery method."[3] This approach consists of ring opening of the fullerene cage, i.e. photooxygenation of the azafulleroids[2a-c,i,j,4a] and bisfulleroids[2d-h] formed by [2+3] and [4+4] cycloadditions of azide[4] and cyclohexadiene fullerene derivatives, followed by rearrangement reactions.[5] However, the ring-openings in these open-cage fullerenes are not large enough to pass a small atom or molecule through.[2a] In order to expand the orifice of such open-cage fullerenes, several strategies have been developed including hydroamination with aromatic hydrazines,[6a-c,g,i] hydrazone,[6e] 1,2-phenylenediamine,[6d,f,h,j-r] sulfur or selenium atom insertion,[2f,3a-c,3e,f,7] and oxidation with N-oxide.[3a,3f-h,8] An entirely different approach to open-cage fullerenes through peroxide-mediated chemical transformation has also been developed.[9] Recently, we reported regioselective Diels-Alder (DA) reactions on the rim of open-cage ketolactam derivatives (**1b,c**), and the structures of the Diels-Alder adducts were confirmed via the 2D INADEQUATE NMR spectra of the ^{13}C-highly-enriched (30%) ketolactam derivatives of C_{60} using non-uniform sampling (NUS).[10] The LUMO of the open-cage ketolactam derivatives (**1a**) shown in Figure 4-1 are concentrated on one side of the unsaturated ketone, which causes the regioselective reactions. Hydroamination of the N-MEM-ketolactam open-cage fullerene (**1a**) with phenylhydrazine is also known to proceed regioselectively. However, different structures for the orifice-expanded open-cage fullerene (**2a** and **2a'**) were proposed by two groups (Scheme 4-1).[6a,c] Herein we report the structure of the product of regioselective mono hydroamination, as confirmed by 2D INADEQUATE NMR spectra of the ^{13}C-highly-enriched product (**2a**).
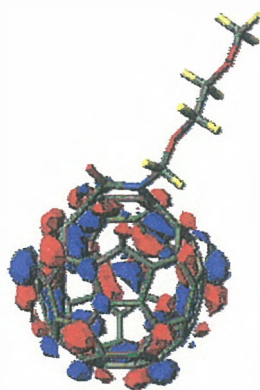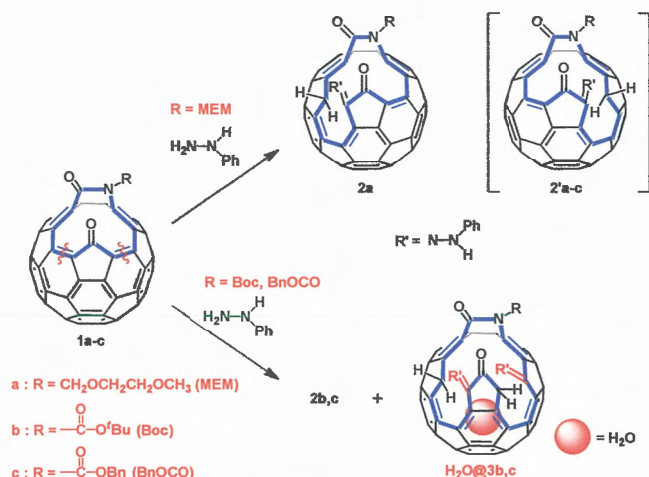

Figure 4-1.

Scheme 4-1.

4.2 Results and Discussion

N-electron withdrawing group substituted open-cage fullerenes (**1b,c**) undergo double hydroamination of the open-cage ketolactam derivatives of C_{60}, as shown in Scheme 4-1. The resulting 19-membered orifice allowed for the concomitant encapsulation of one water molecule. Compound **2a** was synthesized according to the literature[6] from 30% ^{13}C-enriched fullerene, and 2D INADEQATE experiments using non-uniform sampling (NUS)[10] were carried out. The resulting spectrum reveals 9-bond connectivity (noted with bold lines) between the ketone carbonyl carbon (C2) and the amide carbonyl carbon (C7) via the methylene carbon (C10), providing unequivocal evidence that the structure is **2a** and not **2a'** (Figure 4-2).
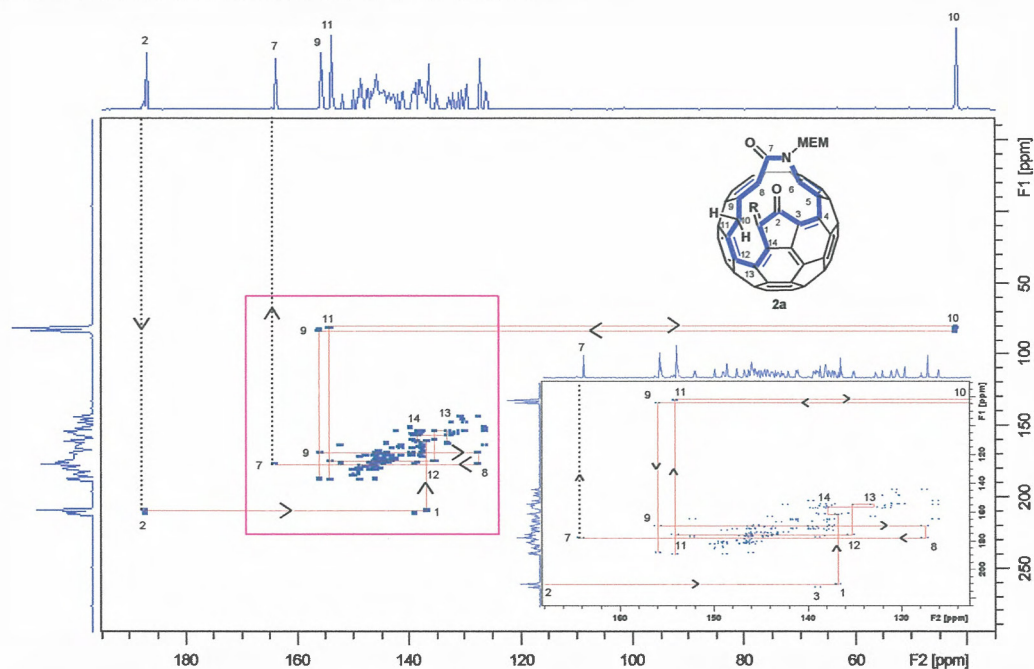
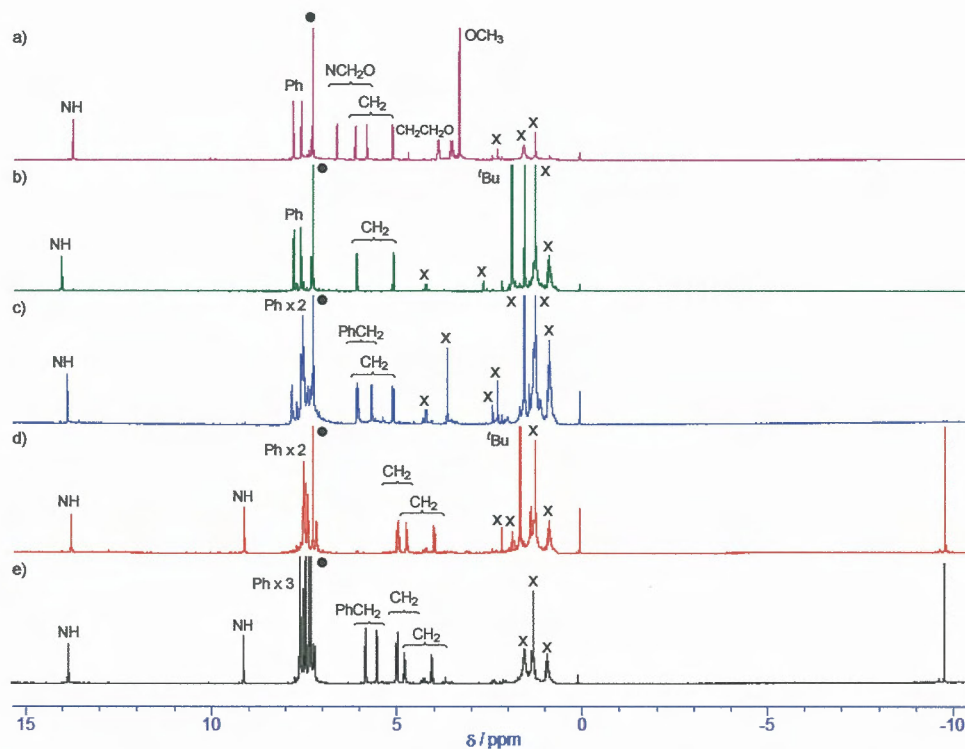Figure 4-2. 2D INADEQUATE ^{13}C NMR spectrum of **2a** (100 MHz, CDCl₃).

Figure 4-3. ^{1}H NMR spectra of (a) **2a**, (b) **2b**, (c) **2c**, (d) H$_2$O@**3b** and (e) H$_2$O@**3c** (600 MHz, CDCl$_3$). Solvent and impurities are denoted by filled circles (●) and crosses (×), respectively.
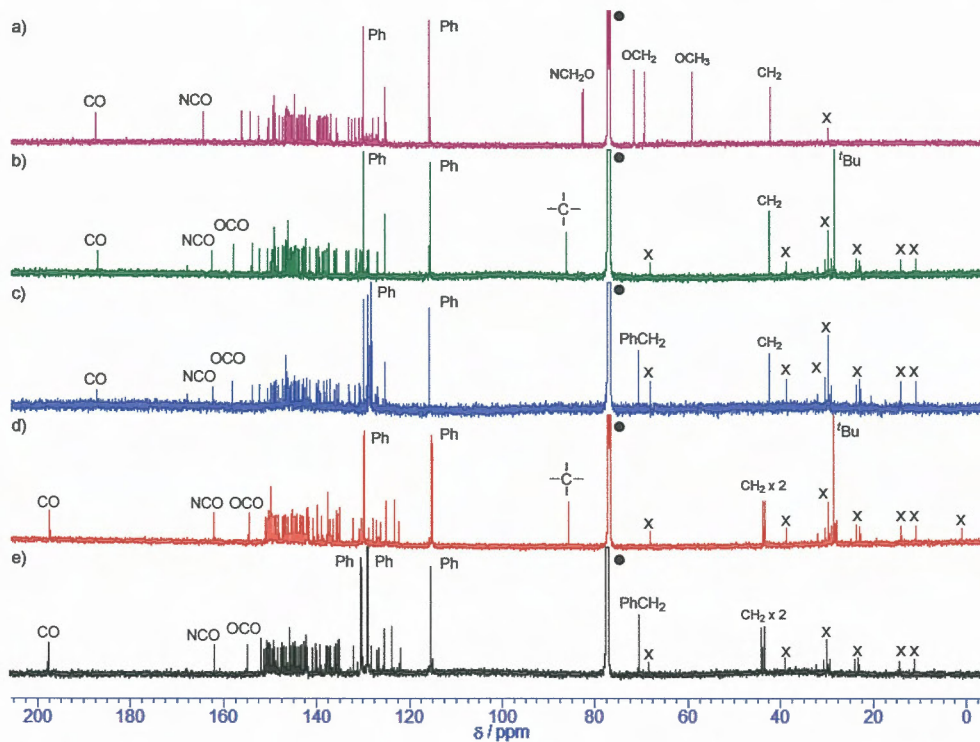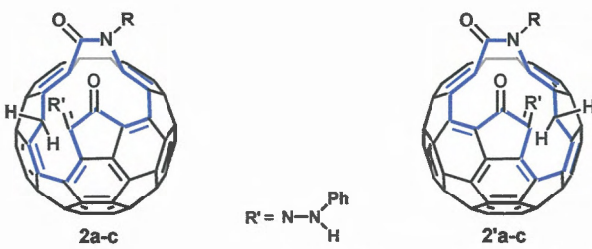
Figure 4-4. ^{13}C NMR spectra of (a) **2a**, (b) **2b**, (c) **2c**, (d) H$_2$O@**3b** and (e) H$_2$O@**3c** (150 MHz, CDCl$_3$). Solvent and impurities are denoted by filled circles (●) and crosses (×), respectively.

The previous determination of the structure by Iwamastu[6b] and Orfanopoulos[6c] based on their discussion show that Iwamatsu's structure is correct finally. The reaction of **1a** even with 10 equivalents of phenylhydrazine in toluene under reflux for several hours, gave only product **2a** with 1:1 stoichiometry in 79.4 % yield. Since **1b** and **1c** have electron-withdrawing substituents on the nitrogen atom, they were expected to exhibit higher reactivity toward nucleophilic hydrazine addition. Using 5-10 equivalents of phenylhydrazine, the adducts ($H_2O@3b$ and $H_2O@3c$) with 1:2 stoichiometry were primarily obtained (in 40.1 % and 38.5 % yields, respectively), along with the 1:1 stoichiometric products (**2b** and **2c** in 13.7 % and 11.8 % yields, respectively), as shown in Scheme 4-1. The hydroamination proceeds with migration of two hydrogen atoms from the hydrazine to the α,β-unsaturated carbonyl moiety of the fullerenes, affording methylene protons along the orifices.[6] Although the ^{1}H NMR spectra of **2a-c** have one pair of methylenes each at 5.12 ppm and 6.12 ppm (d, $J = 17.9$ Hz), 5.10 ppm and 6.08 ppm (d, $J = 18.1$ Hz), and 5.11 ppm and 6.07 ppm (d, $J = 18.2$ Hz), respectively, the ^{1}H NMR spectra of $H_2O@3b$ and $H_2O@3c$ show two pairs of methylenes at 4.00 ppm and 4.98 ppm (d, $J = 22.7$ Hz) plus 4.75 ppm and 4.97 ppm (d, $J = 19.5$ Hz), and 4.01 ppm and 4.98 ppm (d, $J = 22.6$ Hz) plus 4.76 ppm and 4.97 ppm (d, $J = 19.4$ Hz), as shown in Figures 4-3. Furthermore, the two NH protons at 9.13 ppm & 13.8 ppm ($H_2O@3b$) and 9.12 ppm & 13.8 ppm ($H_2O@3c$), as well as the two and three phenyl ring protons and carbons, support the reaction stoichiometry in a 1:2 ratio between **1b,c** and phenylhydrazine, as shown in Figures 4-3d,e and Figures 4-4d,e. For 1:1 stoichiometry, the ^{1}H chemical shifts of the methylenes **2b** and **2c** are essentially the same as that of **2a** shown in Figures 4-3. The GIAO-calculated ^{1}H chemical shifts of the methylenes of **2a-c** (5.15-6.49 ppm) are shifted more downfield than those of **2'a-c** (4.53-6.85 ppm). Adducts **2a-c** are also energetically favored over the regioisomeric adducts **2'a-c**, as shown in Table 4-1. These data strongly suggest that regioselective mono-hydroamination of **1b,c** takes place on the same (left) side of the ketone carbonyl group as for **1a**, as shown in Scheme 4-1. Based on the regiochemistry of the 1:1 adducts, the 1:2 stoichiometry indicates that the C-C double bonds next to the ketone of **2b,c** would be cleaved. The HMBC spectra of $H_2O@3b$ and $H_2O@3c$ indicate two-bond ^{1}H-^{13}C correlations between the methylene proton and ketone carbonyl group, leading to one unambiguous structure out of the several possible isomers shown in Scheme 4-1. In the ESI mass spectra, positive ions peaks at 1124.1910 (m/z) [($H_2O@3b$+Na)$^+$] and 1158.1751 (m/z) [($H_2O@3c$+Na)$^+$] confirm the 1:2 stoichiometry for $H_2O@3b$ and $H_2O@3c$ along with water encapsulation.

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Table 4-1. GIAO calculated chemical shifts of methylenes and relative heats of formation of **2a-c** and **2'a-c**

2a-c

R' = N—N$\diagdown$Ph, H

2'a-c

		2a-c			2'a-c	
R		Experimental chemical shifts (ppm)	Calculated[a] chemical shifts (ppm)	Relative energy[b] (kcal/mol)	Calculated[a] chemical shifts (ppm)	Relative energy[b] (kcal/mol)
—MEM	(2a)	5.12, 6.12	5.15, 6.49	-36.5	5.05, 6.65	-28.3
$\overset{O}{\overset{\|}{-C}}$—O^{t}Bu	(2b)	5.10, 6.08	5.15, 6.43	-38.0	4.96, 6.85	-30.9
$\overset{O}{\overset{\|}{-C}}$—OBn	(2c)	5.11, 6.07	5.17, 6.47	-38.7	4.53, 6.48	-32.2

a)Calculation at B3LYP/6-31G** level.

b)Values are relative to the sum of phenylhydazine and **1a-c** set as 0.0 kcal mol^{-1}.

With respect to molecular encapsulation, the ^{1}H NMR spectra of H$_2$O@**3b** and H$_2$O@**3c** show sharp signals at -9.78 ppm and -9.80 ppm (Figures 4-3d,e), which are reasonably assigned to the water molecules inside **3b** and **3c**.[3d,6a,6g,9b] The intensity of these signals at a 82 % encapsulation ratio is diminished slowly by treatment of H$_2$O@**3b** with deuterated water, while the two NH protons disappear very rapidly (Figure 4-5). In spite of the 19-membered ring orifice, this behavior indicates that the trapped water cannot easily escape, in solution. These results indicate that the two hydrazone moieties in compounds H$_2$O@**3b** and H$_2$O@**3c** make it difficult for the trapped water molecule to escape due to the "stopper effect".[1g,9d]
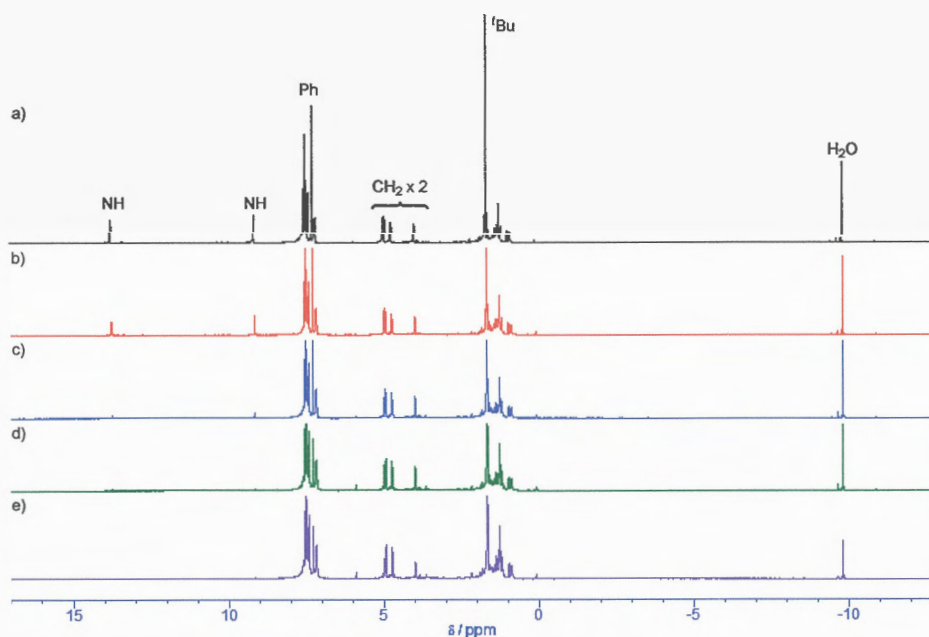
Figure 4-5. ^{1}H NMR monitoring of D$_2$O exchange experiment for H$_2$O@**3b** at (a) 0h, (b) 1h, (c) 3h, (d) 1day and (e) 4days after addition of D$_2$O.

4.3 Conclusion

In conclusion, unequivocal evidence for the structure of the regioselective mono-hydroamination product (**2a**) of the *N*-MEM-ketolactam open-cage fullerene (**1a**) has been provided by 2D INADEQUATE ^{13}C NMR studies on ^{13}C-enriched material. Double hydroamination of the *N*-electron withdrawing group-substituted open-cage ketolactams (**1b,c**) was found to afford open-cage fullerene derivatives H$_2$O@**3b** and H$_2$O@**3c** possessing 19-membered ring orifices with water encapsulation. The mechanism of water encapsulation is currently being studied.

4.4 Experimental Section

Synthesis of MEM-substituted open-cage fullerene (2a).

Phenylhydrazine (0.400 mmol) was add to a solution of open-cage fullerene **1a** (0.0400 mmol) in 10 mL of dry toluene under an argon atmosphere at room temperature and the solution was stirred for 2 hours. After the solvent was purified via silica gel column chromatography and eluted with toluene and AcOEt. Collection and concentration of the 1st brown fraction gave 30.6 mg (79.4 %) of hydroamination adduct **2a** as a brown solid.

2a: ^{1}H NMR (600 MHz, CDCl$_3$) δ 3.32 (s, 3H), 3.48-3.59 (m, 2H), 3.83-3.93 (m, 2H), 5.12 (d, *J* = 17.9 Hz, 1H), 5.81 (d, *J* = 11.3 Hz, 1H), 6.12 (d, *J* = 17.9 Hz, 1H), 6.62 (d, *J* = 11.3 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.59 (t, *J* = 7.4 and 7.9 Hz, 2H), 7.80 (d, *J* = 7.9 Hz, 1H), 13.73 (s, NH); ^{13}C NMR (150 MHz, CDCl$_3$) δ 42.07 (CH$_2$), 59.04 (CH$_3$), 69.33 (CH$_2$), 71.49 (CH$_2$), 82.54 (CH$_2$), 115.66 (Ph),

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125.14 (Ph), 126.58 (1C), 127.72 (1C), 129.92 (Ph), 130.13 (1C), 130.88 (1C), 131.63 (1C), 132.50 (1C), 133.21 (1C), 135.56 (1C), 136.93 (1C), 137.60 (1C), 137.83 (1C), 137.88 (1C), 138.19 (1C), 138.51 (1C), 138.60 (1C), 139.18 (1C), 139.38 (1C), 139.49 (1C), 139.67 (1C), 139.87 (1C), 141.51 (1C), 141.70 (1C), 142.27 (1C), 142.54 (1C), 143.11 (1C), 143.25 (1C), 143.69 (1C), 143.88 (1C), 144.21 (1C), 144.32 (1C), 144.74 (2C), 145.08 (1C), 145.38 (1C), 145.66 (1C), 145.90 (1C), 146.00 (1C), 146.09 (1C), 146.11 (1C), 146.24 (1C), 146.33 (1C), 146.34 (1C), 146.37 (1C), 146.45 (1C), 146.46 (1C), 146.74 (1C), 147.20 (1C), 147.93 (1C), 148.96 (1C), 148.99 (2C), 149.02 (1C), 149.41 (2C), 150.36 (1C), 152.46 (1C), 154.33 (1C), 156.17 (1C), 164.38 (C=O), 187.46 (C=O); IR (KBr) 1670 cm^{-1} (C=O); HRMS (ESI) m/z calcd for $C_{70}H_{17}N_3NaO_4$ ([M+Na]$^+$) 986.1117, found, 986.1086.

Synthesis of *N*-Boc-substituted open-cage fullerene (2b).

Phenylhydrazine (0.167 mmol) was add to a solution of open-cage fullerene **1b** (0.0333 mmol) in 10 mL of dry toluene under an argon atmosphere at room temperature and the solution was stirred for 2 hours. After the solvent was purified via silica gel column chromatography and eluted with toluene and AcOEt. Collection and concentration of the 1st brown fraction was purified via silica gel column chromatography and eluted with CS_2 and $CHCl_3$. Collection and concentration of the 1st brown fraction gave 4.5 mg (13.7 %) of hydroamination adduct **2b** as a brown solid.

2b: ^{1}H NMR (600 MHz, CDCl$_3$) δ 1.90 (s, 9H), 5.10 (d, $J = 18.1$ Hz, 1H), 6.08 (d, $J = 18.1$ Hz, 1H), 7.30 (t, $J = 7.4$ Hz, 1H), 7.59 (t, $J = 7.4$ and 7.9 Hz, 2H), 7.80 (d, $J = 7.9$ Hz, 2H), 14.02 (s, NH); ^{13}C NMR (150 MHz, CDCl$_3$) δ 28.29 (CH$_3$), 42.32 (CH$_2$), 86.04 (1C), 115.61 (Ph), 125.19 (Ph), 126.83 (1C), 128.71 (1C), 129.03 (1C), 129.96 (Ph), 130.64 (1C), 131.51 (1C), 133.16 (1C), 133.61 (1C), 135.58 (1C), 136.01 (1C), 137.22 (1C), 137.77 (1C), 137.82 (1C), 138.22 (1C), 138.29 (1C), 138.63 (1C), 139.48 (1C), 139.56 (1C), 139.62 (1C), 139.99 (1C), 140.06 (1C), 141.42 (1C), 141.54 (1C), 142.30 (1C), 142.52 (1C), 142.95 (1C), 143.09 (1C), 143.73 (1C), 144.09 (1C), 144.37 (1C), 144.42 (1C), 144.57 (1C), 144.74 (1C), 145.04 (1C), 145.33 (1C), 145.69 (1C), 145.98 (2C), 146.00 (2C), 146.08 (1C), 146.37 (1C), 146.42 (1C), 146.45 (1C), 146.49 (1C), 146.53 (1C), 146.71 (1C), 146.76 (1C), 147.28 (1C), 148.10 (1C), 148.76 (1C), 148.94 (1C), 149.02 (2C), 149.35 (1C), 149.66 (1C), 150.41 (1C), 152.35 (1C), 154.05 (1C), 157.84 (1C), 162.49 (C=O), 187.05 (C=O); IR (KBr) 1670 (C=O), 1697 (C=O), 1751 cm^{-1} (C=O); HRMS (ESI) m/z calcd for $C_{71}H_{17}N_3NaO_4$ ([M+Na]$^+$) 998.1117, found, 998.1099.

Synthesis of *N*-BnOCO-substituted open-cage fullerene (2c).

Phenylhydrazine (0.213 mmol) was add to a solution of open-cage fullerene **1c** (0.0439 mmol) in 10 mL of dry toluene under an argon atmosphere at room temperature and the solution was stirred for 2 hours. After the solvent was purified via silica gel column chromatography and eluted with toluene and AcOEt. Collection and concentration of the 1st brown fraction was purified via silica gel

column chromatography and eluted with CHCl₃. Collection and concentration of the 1st brown fraction gave 2.4 mg (11.8 %) of hydroamination adduct **2c** as a brown solid.

2c: ^{1}H NMR (600 MHz, CDCl₃) δ 5.11 (d, J = 18.2 Hz, 1H), 5.67 (d, J = 12.3 Hz, 1H), 6.07 (d, J = 18.2 Hz, 1H), 6.03 (d, J = 12.3 Hz, 1H), 7.20-7.34 (m, 1H), 7.36-7.44 (m, 1H), 7.45-7.63 (m, 7H), 7.80-7.87 (m, 1H) 13.88 (s, NH); ^{13}C NMR (150 MHz, CDCl₃) δ 42.40 (CH₂), 70.58 (CH₂), 115.76 (Ph), 125.26 (Ph), 126.82 (1C), 128.04 (1C), 128.15 (Ph), 128.53 (Ph), 128.80 (1C), 128.89 (Ph), 129.18 (1C), 129.85 (Ph), 130.50 (1C), 130.88 (1C), 131.64 (1C), 132.86 (1C), 133.10 (1C), 135.22 (1C), 135.60 (1C), 136.16 (1C), 137.10 (1C), 137.83 (1C), 137.85 (1C), 138.20 (1C), 138.35 (1C), 138.49 (1C), 139.25 (1C), 139.65 (1C), 139.69 (1C), 139.93 (1C), 140.05 (1C), 141.44 (1C), 141.52 (1C), 142.13 (1C), 142.56 (1C), 142.85 (1C), 143.13 (1C), 143.78 (1C), 144.07 (1C), 144.40 (1C), 144.46 (1C), 144.59 (1C), 144.71 (1C), 145.00 (1C), 145.36 (1C), 145.58 (1C), 145.97 (1C), 145.99 (1C), 146.04 (1C), 146.21 (1C), 146.41 (1C), 146.43 (1C), 146.50 (1C), 146.57 (1C), 146.68 (1C), 146.78 (1C), 147.28 (1C), 148.09 (1C), 148.73 (1C), 148.95 (1C), 149.00 (1C), 149.03 (1C), 149.38 (1C), 149.70 (1C), 150.42 (1C), 152.33 (1C), 153.95 (1C), 158.16 (1C), 162.28 (C=O), 187.31 (C=O); IR (KBr) 1666 (C=O), 1704 (C=O), 1747 cm^{-1} (C=O); HRMS (ESI) m/z calcd for C₇₄H₁₅N₃NaO₄ ([M+Na]$^+$) 1032.0960, found, 1032.0988.

Synthesis of *N*-Boc-substituted endohedral open-cage fullerene (H₂O@3b).

Phenylhydrazine (0.372 mmol) was add to a solution of open-cage fullerene **1b** (0.0372 mmol) in 10 mL of dry toluene under an argon atmosphere at room temperature and the solution was stirred for 2 hours. After the solvent was purified via silica gel column chromatography and eluted with toluene and AcOEt. Collection and concentration of the 1st brown fraction was purified via silica gel column chromatography and eluted with CHCl₃. Collection and concentration of the 1st brown fraction gave 16.4 mg (40.1 %) of hydroamination adduct H₂O@**3b** as a brown solid.

H₂O@**3b**: ^{1}H NMR (600 MHz, CDCl₃) δ -9.78 (s, H₂O), 1.67 (s, 9H), 4.00 (d, J = 22.7 Hz, 1H), 4.75 (d, J = 19.5 Hz, 1H), 4.97 (d, J = 19.5 Hz, 1H), 4.98 (d, J = 22.7 Hz, 1H), 7.13-7.20 (m, 2H), 7.38-7.42 (m, 2H), 7.45-7.55 (m, 6H), 9.13 (s, NH), 13.78 (s, NH); ^{13}C NMR (150 MHz, CDCl₃) δ 28.43 (CH₃), 43.34 (CH₂), 43.68 (CH₂), 85.61 (1C), 115.06 (Ph), 115.28 (Ph), 122.30 (1C), 123.16 (Ph), 125.02 (Ph), 126.27 (1C), 127.01 (1C), 127.74 (1C), 129.70 (Ph), 129.78 (Ph), 130.26 (1C), 132.15 (1C), 135.03 (1C), 135.46 (1C), 135.58 (1C), 136.32 (1C), 136.96 (1C), 137.47 (1C), 137.53 (1C), 137.55 (1C), 138.81 (1C), 139.74 (1C), 139.86 (1C), 140.69 (1C), 141.70 (1C), 141.81 (1C), 141.86 (1C), 141.94 (1C), 142.04 (1C), 142.21 (1C), 142.82 (1C), 143.04 (1C), 143.37 (1C), 143.50 (1C), 144.12 (1C), 144.29 (1C), 144.32 (1C), 144.35 (1C), 144.67 (1C), 145.15 (1C), 145.22 (1C), 145.28 (1C), 146.07 (1C), 146.60 (1C), 146.72 (1C), 146.92 (1C), 146.96 (1C), 147.05 (1C), 147.31 (1C), 148.09 (1C), 148.54 (1C), 148.69 (1C), 148.86 (1C), 148.92 (1C), 149.18 (1C), 149.65 (1C), 149.75 (2C), 150.01 (1C), 150.19 (1C), 150.21 (1C), 150.28 (1C), 150.48 (1C), 150.86 (1C), 154.62

(1C), 162.12 (C=O), 197.36 (C=O); IR (KBr) 1685 (C=O), 1743 (C=O), 1766 (C=O), 3263 cm^{-1} (NH); HRMS (ESI) m/z calcd for $C_{77}H_{27}N_5NaO_5$ ([M+Na]$^+$) 1124.1910, found, 1124.1910.

Synthesis of N-BnOCO-substituted endohedral open-cage fullerene (H$_2$O@3c).

Phenylhydrazine (0.417 mmol) was add to a solution of open-cage fullerene **1c** (0.0418 mmol) in 10 mL of dry toluene under an argon atmosphere at room temperature and the solution was stirred for 2 hours. After the solvent was purified via silica gel column chromatography and eluted with toluene and AcOEt. Collection and concentration of the 1st brown fraction was purified via silica gel column chromatography and eluted with CHCl$_3$. Collection and concentration of the 1st brown fraction gave 10.6 mg (38.5 %) of hydroamination adduct H$_2$O@**3c** as a brown solid.

H$_2$O@**3c**: ^{1}H NMR (600 MHz, CDCl$_3$) δ -9.80 (s, H$_2$O), 4.01 (d, J = 22.6 Hz, 1H), 4.76 (d, J = 19.4 Hz, 1H), 4.97 (d, J = 19.4 Hz, 1H), 4.98 (d, J = 22.6 Hz, 1H), 7.14-7.24 (m, 2H), 7.29-7.34 (m, 3H), 7.38-7.44 (m, 4H),7.47-7.51 (m, 2H), 7.55-7.60 (m, 4H), 9.12 (s, NH), 13.81 (s, NH); ^{13}C NMR (150 MHz, CDCl$_3$) δ 43.09 (CH$_2$), 43.67 (CH$_2$), 70.22 (CH$_2$), 114.99 (Ph), 115.10 (Ph), 121.65 (1C), 123.36 (Ph), 125.09 (Ph), 126.23 (1C), 126.56 (1C), 127.79 (1C), 128.59 (Ph), 128.70 (Ph), 129.80 (Ph), 129.96 (1C), 130.02 (Ph), 131.79 (1C), 134.66 (1C), 135.02 (1C), 135.34 (1C), 135.42 (1C), 135.64 (1C), 136.58 (1C), 136.94 (1C), 137.17 (1C), 137.47 (1C), 137.50 (1C), 137.62 (1C), 138.85 (1C), 139.62 (1C), 139.84 (1C), 140.51 (1C), 141.61 (1C), 141.82 (1C), 142.01 (1C), 142.15 (1C), 142.33 (1C), 142.82 (1C), 143.11 (1C), 143.52 (1C), 143.60 (1C), 144.07 (1C), 144.33 (1C), 144.38 (1C), 144.67 (1C), 145.20 (1C), 145.31 (2C), 146.08 (1C), 146.63 (1C), 146.82 (1C), 146.92 (1C), 147.00 (1C), 147.29 (1C), 148.00 (1C), 148.52 (1C), 148.74 (1C), 148.83 (1C), 148.88 (1C), 149.16 (1C), 149.63 (1C), 149.84 (1C), 150.01 (1C), 150.14 (1C), 150.22 (1C), 150.31 (1C), 150.47 (1C), 150.86 (1C), 151.59 (1C), 154.74 (1C), 161.66 (C=O), 197.33 (C=O); IR (KBr) 1685 (C=O), 1770 (C=O), 3275 cm^{-1} (NH); HRMS (ESI) m/z calcd for $C_{80}H_{25}N_5NaO_5$ ([M+Na]$^+$) 1158.1753, found, 1158.1751.

4.5 Computational Studies

Calculations were carried out on an HPC-5000-XH216R2 and HPC-5000-XH218R2S workstation provided by HPC Inc. of Japan. Ab initio calculations were performed using the Gaussian 03 computer program. The initial geometries of the fullerene derivatives were constructed using the Winmostar graphical interface. All geometry optimizations were performed on Cartesian coordinates using the energy gradient minimization method.

Reference

1. Reviews of open-cage fullerenes: (a) Y. Rubin, *Chem. -Eur. J.*, **1997**, *3*, 1009. (b) Y. Rubin, *Top. Curr. Chem.*, **1999**, *199*, 67. (c) S.-I. Iwamatsu and S. Murata, *Synlett*, **2005**, 2117. (d) M. Murata, Y. Murata and K. Komatsu, *Chem. Commun.*, **2008**, 6083. (e) G.-C. Vougioukalakis, M. M. Roubelakis and M. Orfanopoulos, *Chem. Soc. Rev.*, **2010**, 39, 817. (f) L. Gan, D. Yang, Q. Zhang and H. Huang, *Adv. Mater.*, **2010**, *22*, 1498. (g) L. Shi and L. Gan, *J. Phys. Org. Chem.*, **2013**, *26*, 766.

2. Fulleroid-based open-cage fullerenes: (a) J. C. Hummelen, M. Prato and F. Wudl, *J. Am. Chem. Soc.*, **1995**, *117*, 7003. (b) G. Schick, T. Jarrosson and Y. Rubin, *Angew. Chem. Int. Ed.*, **1999**, *38*, 2360. (c) Y. Rubin, T. Jarroson, G.-W. Wang, M. D. Bartberger, K. N. Houk, G. Schick, M. Saunders and R. J. Cross, *Angew. Chem. Int. Ed.*, **2001**, *40*, 1543. (d) Y. Murata, N. Kato and K. Komatsu, *J. Org. Chem.*, **2001**, *66*, 7235. (e) Y. Murata and K. Komatsu, *Chem. Lett.*, **2001**, 896. (f) Y. Murata, M. Murata and K. Komatsu, *Chem. -Eur. J.*, **2003**, *9*, 1600. (g) H. Inoue, H. Yamaguchi, S.-I. Iwamatsu, T. Uozaki, T. Suzuki, T. Akasaka, S. Nagase and S. Murata, *Tetrahedron Lett.*, **2001**, *42*, 895. (h) Y. Murata, M. Murata and K. Komatsu, *J. Am. Chem. Soc.*, **2003**, *125*, 7152. (i) H. Hachiya and K. Kabe, *Chem. Lett.*, **2009**, *38*, 372. (j) Y. Kabe, H. Hachiya, T. Saito, D. Shimizu, M. Ishiwata, K. Suzuki, Y. Yakushigawa and W. Ando, *J. Organometall Chem.*, **2009**, *694*, 1988. (k) M. R. Cerón, M. Izquierdo, A. Aghabali, J. A. Valdez, K. B. Ghiassi, M. M. Olmstead, A. L. Balch, F. Wudl and L. Echegoyen, *J. Am. Chem. Soc.*, **2015**, *137*, 7502. (l) M. Chen, L. Bao, P. Peng, S. Zheng, Y. Xie and X. Lu, *Angew. Chem. Int. Ed.*, **2016**, *55*, 11887.

3. Synthesis of endohedral fullerenes by molecular surgery: (a) K. Komatsu, M. Murata and Y. Murata. *Science*, **2005**, *307*, 238. (b) M. Murata, Y. Murata and K. Komatsu, *J. Am. Chem. Soc.*, **2006**, *128*, 8024. (c) M. Murata, S. Murata, Y. Morinaka, Y. Murata and K. Komatsu, *J. Am. Chem. Soc.*, **2008**, *130*, 15800. (d) K. Kurotobi and Y. Murata, *Science*, **2011**, *333*, 613. (e) Y. Morinaka, F. Tanabe, M. Murata, Y. Murata and K, Komatsu, *Chem. Comm.*, **2010**, *46*, 4532. (f) A. Krachmalnicoff, M. H. Levitt and R. J. Whitby, *Chem. Comm.*, **2014**, *50*, 13037. (g) Y. Hashikawa, M. Murata, A. Wakamiya and Y. Murata, *J. Am. Chem. Soc.*, **2016**, *138*, 4096. (h) A. Krachmalnicoff, R. Bounds, S. Manone, S. Alom, M. Concistrè, B. Meier, K. Kouřil, M. E. Light, M. R. Johnson, S. Rols, A. J. Horsewill, A. Shugai, U. Nagel, T. Rõõm, M. Carravetta, M. H. Levitt, R. J. Whitby, *Nat. Chem.*, **2016**, *8*, 953. (i) R. Zhang, M. Murata, T. Aharen, A. Wakamiya, T. Shimoaka T. Hasegawa and Y. Murata, *Nat. Chem.*, **2016**, *8*, 435. (j) R. Zhang, M. Murata, A. Wakamiya, T. Shimoaka, T. Hasegawa and Y. Murata, *Sci. Ad.*, **2017**, *3*, 4.

4. (a) M. Prato, Q. C. Li, F. Wudl and V. Lucchini, *J. Am. Chem. Soc.*, **1993**, *113*, 1148. (b) T. Suzuki, Q. Li, K. C. Khemani, F. Wudl and O. Almarsson, *Science*, **1991**, 1186.

5. (a) M. J. Arce, A. L. Viado, Y. Z. An, S. I. Khan and Y. Rubin, *J. Am. Chem. Soc.*, **1996**, *118*,

3775. (b) H. Inoue, H. Yamaguchi, T. Suzuki, T. Akasaka and S. Murata, *Synlett*, **2000**, 1178.

6. Hydroamination of open-cage fullerenes: (a) S.-I. Iwamatsu, F. Ono and S. Murata, *Chem. Lett.*, **2003**, *7*, 614. (b) S.-I. Iwamatsu, F. Ono and S. Murata, *Chem. Commun.*, **2003**, 1268. (c) G. C. Vougioukalakis, K. Prassides, J. M. Campanera, M. I. Heggie and M. Orfanopoulos, *J. Org. Chem.*, **2004**, *69*, 4524. (d) S.-I. Iwamatsu, T. Uozaki, K. Kobayashi, R. Suyong, S. Nagase and S. Murata, *J. Am. Chem. Soc.*, **2004**, *126*, 2668. (e) S.-I. Iwamatsu, T. Kuwayama, K. Kobayashi, S. Nagase and S. Murata, *Synthesis*, **2004**, 2962. (f) S.-I. Iwamatsu and S. Murata, *Tetrahedron Lett.*, **2004**, *45*, 6391. (g) S. -I. Iwamatsu, S. Murata, Y. Andoh, M. Minoura, K. Kobayashi, N. Mizorogi and S. Nagase, *J. Org. Chem.*, **2005**, *70*, 4820. (h) S.-I. Iwamatsu, C. M. Stanisky, R. J. Cross, M. Saunders, N. Mizorogi, S. Nagase and S. Murata, *Angew. Chem. Int. Ed.*, **2006**, *45*, 5337. (i) M. M. Roubelakis Y. Murata, K. Komatsu and M. Orfanopoulos, *J. Org. Chem.*, **2007**, *72*, 7042. (j) K. E. Whitener. Jr, M. Frunzi, S.-I. Iwamatsu, S. Murata, R. J. Cross and M. Saunders, *J. Am. Chem. Soc.*, **2008**, *130*, 13996. (k) C. M. Stanisky, R. J. Cross, M. Saunders, *J. Am. Chem. Soc.*, **2009**, *131*, 3392. (l) K. E. Whitener. Jr, R. J. Cross, M. Saunders, S.-I. Iwamatsu, S. Murata, N. Mizorogi and S. Nagase, *J. Am. Chem. Soc.*, **2009**, *131*, 6338.   (m) M. Frunzi, A. M. Baldwin, N. Shibata, S.-I. Iwamatsu, R. G. Lawler and N. J. Turro, *J. Phys. Chem. A*, **2011**, *115*, 735. (n) Z. Xiao, G. Ye, Y. Liu, S. Chen, Q. Peng, Q. Zuo and L. Ding, *Angew. Chem. Int. Ed.*, **2012**, *51*, 9038. (o) Y. Yu, L. Xu, X. Huang and L. Gan, *J. Org. Chem.* **2014**, *79*, 2156. (p) L. Xu, S. Liang, J. Sun and L. Gan, *Org. Chem. Front.*, **2015**, *2*, 1504. (q) C.-S. Chen, T.-S. Kuo and W.-Y. Yeh, *Chem. -Eur. J.*, **2016**, *22*, 8773. (r) C.-S. Chen and W.-Y. Yeh, *Chem. -Eur. J.*, **2016**, *22*, 16425.

7. Sulfur and selenium atom insertion of open-cage fullerene: (a) G. C. Vougionkalakis, K. Prassidies and M. O. Orfanopoulos, *Org. Lett.*, **2004**, *6*, 1245. (b) S.-C. Chuang, Y. Murata, M. Murata, S. Mori, S. Maeda, F. Tanabe and K. Komatsu, *Chem. Commun.*, **2007**, 1278. (c) M. Murata, Y. Morinaka, K. Kurotobi, K. Komatsu and Y. Murata, *Chem. Lett.*, **2010**, *39*, 298. (d) T. Futagoishi, M. Murata, A. Wakamiya, T. Sasamori and Y. Murata, *Org. Lett.*, **2013**, 2750. (e) R. Zhang, T. Futagoishi, M. Murata, A. Wakamiya and Y. Murata, *J. Am. Chem. Soc.*, **2014**, *136*, 8193. (f) T. Futagoishi, M. Murata, A. Wakamiya and Y. Murata, *Angew. Chem. Int. Ed.*, **2015**, *54*, 14791.

8. Oxidation of open-cage fullerenes with *N*-oxide: (a) Y. Hashikawa, M. Murata, A. Wakamiya and Y. Murata, *Org. Lett.*, **2014**, *16*, 2970. (b) A. Krachmalnicoff, R. Bounds, S. Mamone, M. H. Levit, M. Carravetta and R. J. Whitby, *Chem. Commun.*, **2015**, *51*, 4993.

9. Peroxide-mediated syntheses of open-cage fullerenes: (a) L. Gan, *Pure Appl. Chem.*, **2006**, *78*, 841. (b) Z. Xiao, J. Yao, D. Yang, F. Wang, S. Huang. L. Gan, Z. Jia, Z. Jiang, X. Yang, B. Zheng, G. Yuan, S. Zhang and Z. Wang, *J. Am. Chem. Soc.*, **2007**, *129*, 16149. (c) Q. Zhang, Z. Jia, S. Liu, G. Zhang, Z. Xiao, D. Yang, L. Gan, Z. Wang and Y. Li, *Org. Lett.*, **2009**, *11*, 2772.

(d) Q. Zhang, T. Pankewitz, S. Liu, W. Klapper and L. Gan, *Angew. Chem. Int. Ed.*, **2010**, *49*, 9935. (e) Y. Yu, X. Xie, T. Zhang, S, Liu, Y. Shao, L. Gan and Y. Li, *J. Org. Chem.*, **2011**, *76*, 10148. (f) J. Zhang, F. Wang, N. Xin, D. Yang and L. Gan, *Eur. J. Org. Chem.*, **2011**, 5366. (g) G. Zhang, Q. Zhang, Z. Jia, S. Liang, L. Gan and Y. Li, *J. Org. Chem.*, **2011**, *76*, 6743. (h) S. Liu, Q. Zhang, Y. Yu and L. Gan, *Org. Lett.*, **2012**, *14*, 4002. (i) L. Xu, Q. Zhang, G. Zhang, S. Liang, Y. Yu and L. Gan, *Eur. J. Org. Chem.*, **2013**, 7272. (j) N. Xin, X. Yang, Z. Zhou, J. Zhang, S. Zhang and L. Gan, *J. Org. Chem.*, **2013**, *78*, 1157. (k) L. Shi, D. Yang, F. Colombo, Y. Yu, W.-X. Zhang and L. Gan, *Chem. -Eur. J.*, **2013**, *19*, 16545. (l) Y. Yu, L. Shi, D. Yang and L. Gan, *Chem. Sci.*, **2013**, *4*, 814. (m) L. Xu, H. Ren, S. Liang, J. Sun, Y. Liu and L. Gan, *Chem. -Eur. J.*, **2015**, *21*, 13539.

10. T. Tanaka, R. Nojiri, Y. Sugiyama, R. Sawai, T. Takahashi, N. Fukaya, J.-C. Choi, Y. Kabe, *Org. Biomol. Chem.*, **2017**, *15*, 6136.

Acknowledgment

Teruhiko TANAKA

Kanagawa University

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List of Publications

Publications for This Thesis

1. R. Mizunuma, T. Tanaka, Y. Nakamura, Y. Kamijima, Y. Kabe, "Direct benzyne-C_{60} addition does not generate a [5,6] open fulleroid." *Tetrahedron*, in press.

2. T. Tanaka, R. Nojiri, Y. Sugiyama, R. Sawai, T. Takahashi, N. Fukaya, J.-C. Choi, Y. Kabe, "Regioselective Diels–Alder reaction to open-cage ketolactam derivatives of C_{60}." *Org. Biomol. Chem.*, **2017**, *15*, 6136.

3. T. Tanaka, K. Morimoto, T. Ishida, T. Takahashi, N. Fukaya, J.-C. Choi, Y. Kabe, "Regioselective Hydroamination of Open-Cage Ketolactam Derivatives of C_{60} with Phenylhydrazine and Water Encapsulation." *Chem., Lett.*, **2018**, in submission (minor revision).

Other Publications

4. N. Watanabe, K. Matsumoto, T. Tanaka, H. Suzuki, H. K. Ijuin, M. Matsumoto, "*N*-Acyl group-directed color modulation in the *t*-BuOK-mediated chemiluminescent decomposition of hydroxyaryl-substituted dioxetanes fused with a pyrrolidine ring." *Tetrahedron Lett.*, **2012**, *53* 5309.