A Journal of the Gesellschaft Deutscher Chemiker
Angewandte Chemie
International Edition
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Accepted Article

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To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201903422
Angew. Chem. 10.1002/ange.201903422

Link to VoR: http://dx.doi.org/10.1002/anie.201903422
http://dx.doi.org/10.1002/ange.201903422

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Angewandte Chemie International Edition
10.1002/anie.201903422

Synthesis of a Strained Spherical Carbon Nanocage by Regioselective Alkyne Cyclotrimerization

Norihiko Hayase,[a] Juntaro Nogami,[a] Yu Shibata,[a] and Ken Tanaka*[a]

Abstract: The smallest spherical carbon nanocage so far, [2.2.2]carbon nanocage, has been synthesized via the cationic rhodium(I)/H_8-binap complex-catalyzed regioselective intermolecular cyclotrimerization of a *cis*-1-ethynyl-4-arylcyclohexadiene derivative followed by the triple Suzuki-Miyaura cross-couplings with 1,3,5-triborylbenzene and reductive aromatization. This cage molecule is highly strained, and its ring strain is between those of [6] and [5]cycloparaphenylenes. A significant red-shift of an emission maximum was observed, compared with that of known [4.4.4]carbon nanocage. The sequential cyclotrimerizations of a *cis*-1,4-diethynylcyclohexadiene derivative with the same rhodium(I) catalyst followed by reductive aromatization failed to afford [1.1.1]carbon nanocage; instead, a β-graph-shaped cage molecule was generated.

The synthesis of highly strained cyclic π-conjugated molecules, possessing bent benzene rings, has been attracting much attention as a challenging target in organic synthesis.[1] In order to achieve this synthesis, overcoming molecular strain is crucial. In 2008, Jasti reported the elegant synthesis of cyclic paraphenylene rings, [9], [12], and [18]cycloparaphenylenes (CPPs), via the multiple coupling reactions followed by reductive aromatization of cyclohexadiene template **A** (R = Me).[2] In this synthesis, the reductive aromatization can overcome the molecular strain to produce CPPs. Independently, Itami reported the synthesis of [12]CPP via the multiple coupling reactions followed by oxidative aromatization of cyclohexane template **B**.[3] Subsequently, Yamago reported a different route to CPPs via the formation of cyclic platinum complexes followed by reductive elimination.[4] Following these pioneering works, [6]–[16] and [18]CPPs were synthesized until 2012.[5,6] Finally, more strained [5]CPP was synthesized by Jasti in 2014.[7] This synthesis consists of the intramolecular boronate homocoupling and stepwise reductive aromatization of template **A** (R = Me) by treatment with sodium naphthalenide, methanol, and lithium diisopropyl amide. Independently, Yamago also reported the synthesis of [5]CPP, which employs the $SnCl_2$/HCl-mediated reductive aromatization of template **A** (R = H).[8] This molecule is a fragment of C_{60}, and its calculated strain energy is significantly larger (119 kcal•mol^{-1}) than that of [6]CPP (96 kcal•mol^{-1}).[7,8]

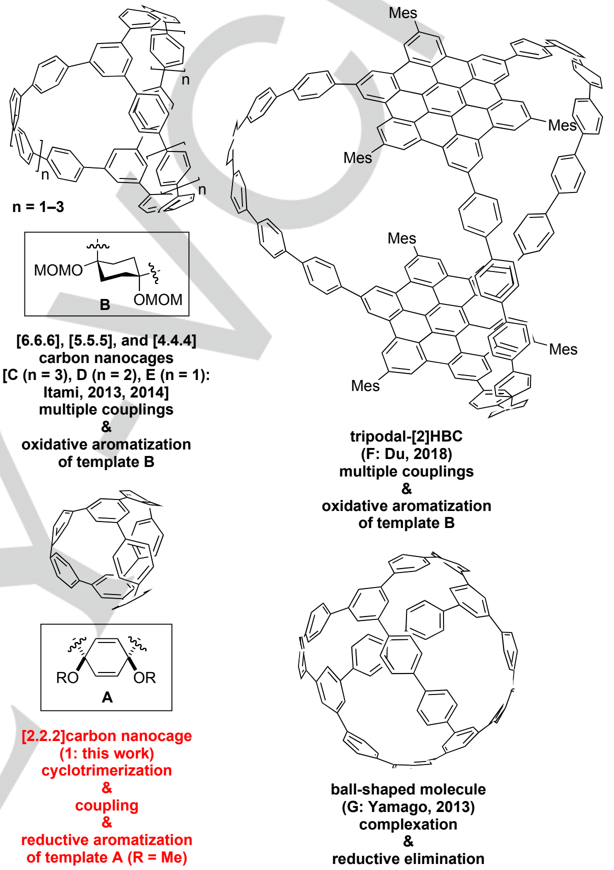

Figure 1. Spherical carbon nanocages **C**–**G** and **1.** MOM = methoxymethyl. Mes = mesityl.

Following the successful synthesis of CPPs, three-dimensional spherical carbon nanocages have been synthesized. In 2013, Itami reported the synthesis of cage **C,** possessing two trisubstituted benzene units, via the multiple coupling reactions followed by oxidative aromatization of template **B** (Figure 1, top left).[9a] The cage **C** is a junction unit of branched carbon nanotubes and named as [6.6.6]carbon nanocage, in which “6” is the number of benzene rings between the two trisubstituted benzenes. High conformational flexibility of template **B** allowed the size-selective synthesis of [6.6.6], [5.5.5], and [4.4.4]carbon nanocages **C**–**E**,[9b] and additionally large cage **F,** possessing two hexabenzocoronene units (Figure 1, top right).[10] Independently, Yamago reported the synthesis of cage **G**, possessing four trisubstituted benzene units, via the formation of an octahedral platinum complex followed by reductive elimination (Figure 1, bottom right).[11] However, smaller and more strained cages have not been synthesized presumably due to the difficulty of aromatization of template **B** with the large strain energy.[12]

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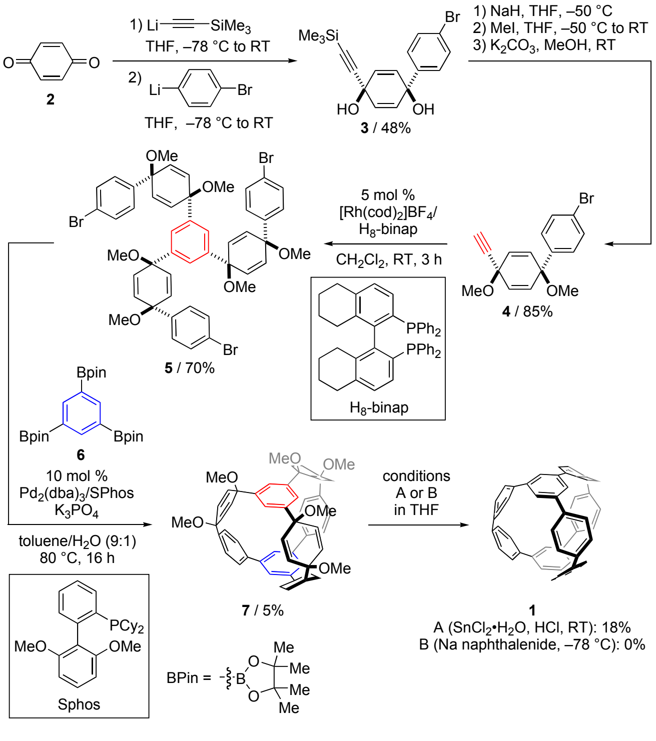
10.1002/anie.201903422

In this paper, we disclose the synthesis of the smallest spherical carbon nanocage so far, [2.2.2]carbon nanocage **1**, via the cationic rhodium(I)/H_8-binap complex-catalyzed regioselective intermolecular homo-cyclotrimerization of terminal alkynes[13–15] followed by the triple Suzuki-Miyaura cross-couplings with 1,3,5-triborylbenzene and reductive aromatization of template **A** (Figure 1, bottom left). Properties of this highly strained cage molecule **1** and the unexpected synthesis of a β-graph-shaped cage molecule are also disclosed.

Scheme 1 displays the synthesis of [2.2.2]carbon nanocage **1**. The stepwise 1,2-additions of lithium (trimethylsilyl)acetylide and (4-bromophenyl)lithium to 1,4-benzoquinone (**2**) afforded *cis*-diol **3** in good yield. Dimethylation followed by desilylation afforded terminal alkyne **4** in high yield. The intermolecular homo-cyclotrimerization of **4** proceeded in the presence of a cationic rhodium(I)/H_8-binap complex (5 mol %) at room temperature to give tribromide **5** in good yield as a single regio- and stereoisomer.[16] The triple Suzuki-Miyaura cross-couplings of **5** with 1,3,5-triborylbenzene **6** afforded cage molecule **7**, although the yield was low. Finally, the Yamago's reductive aromatization of **7** with $SnCl_2$/HCl[8,17] proceeded at room temperature to give **1** in 18% yield. Importantly, the $SnCl_2$/HCl-mediated reduction is crucial to obtaining **1**. The treatment of **7** with sodium naphthalenide did not afford **1** at all and led to an unidentified complex mixture.



Scheme 1. Synthesis of [2.2.2]carbon nanocage **1**. THF = tetrahydrofuran. cod = 1,5-cyclooctadiene. dba = dibenzylideneacetone.

Compound **1** was identified by ^{1}H, ^{13}C, and 2D-NMR spectroscopy, and HRMS (high-resolution mass spectrometry). The ^{1}H NMR signals of aromatic protons appeared at 7.32 (d, 12H), 7.26 (d, 12H), and 7.06 (s, 6H) ppm. In the ^{13}C NMR spectrum, six aromatic carbons appeared at 142.8, 137.2, 136.8, 128.1, 127.4, 127.2 ppm. These data are consistent with the D_3 symmetric structure of **1**. In the APCI-TOF mass spectrum, $[M+H]^+$ was clearly observed at m/z = 607.2430 (calcd value = 607.2420) with an isotopic distribution pattern identical to the theoretical pattern (Figure S1). As with [5]CPP,[7] this cage **1** is air-sensitive and decomposed into an insoluble white solid compound presumably by oxidation. Although we failed to obtain a single crystal of **1** due to its poor crystallizability and instability, the structure of **7** (precursor to cage **1**) was confirmed by an X-ray crystallographic analysis (Figure S2).[18]

The UV/Vis absorption and fluorescence spectra of **1** are shown in Figure 2. The absorption maximum (302 nm) is blue-shifted, compared to [4.4.4]carbon nanocage **E** (316 nm).[9b] On the contrary, the emission maximum (499 nm) is red-shifted, compared to **E** (427 nm).[9b] These observations are the same as previously reported [6.6.6], [5.5.5], and [4.4.4]carbon nanocages **C**–**E**, in which as the cage size becomes smaller, the absorption and emission maxima become shorter and longer, respectively. The maximum absolute fluorescence quantum yield (Φ_F) of **1** was 5%, which is significantly smaller than that of **E** (66%),[9b] but it is important to note that [6] and [5]CPPs show no fluorescence despite their comparable degree of strain energies to cage **1**.[5e,7]

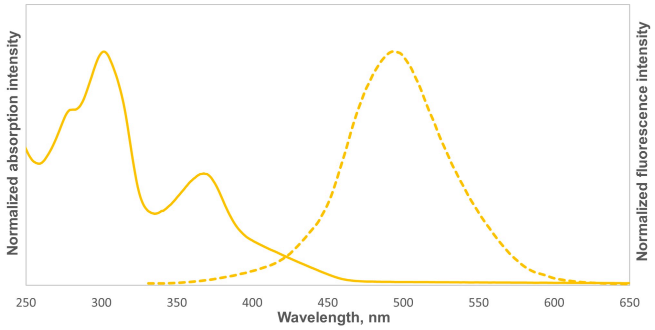


Figure 2. UV/Vis absorption (in $CHCl_3$; solid line) and fluorescence (excited at 302 nm in $CHCl_3$; broken line) spectra of **1**.

The electronic structure of **1** was examined by DFT and time-dependent DFT (TD-DFT) calculations using Gaussian 09 at the B3LYP/6-31G(d) level. In order to compare with previously reported [6.6.6], [5.5.5], and [4.4.4] carbon nanocages **C**–**E** of which the calculations were carried out with structures fixed in D_3 symmetry,[9b] the calculations of **1** were also carried out with a structure fixed in D_3 symmetry. The frontier molecular orbitals (MOs) of **1** are depicted in Figure 3. The orbitals of HOMO and HOMO–1 as well as those of LUMO and LUMO+1 are degenerate (Figure 3, right). The energy diagram of **1** was compared with **E** (Figure 3, left). The HOMO energy of **1** is calculated to be higher in energy than that of **E**, on the contrary, the LUMO energy of **1** is calculated to be lower in energy than that of **E**. Thus, the HOMO–LUMO energy gap of **1** (3.43 eV) is smaller than that of **E** (3.78 eV). A TD-DFT calculation revealed the origin of the UV/Vis absorption bands. The strongest absorption peak (302 nm) is assigned to the following transition: HOMO–2 → LUMO+2, and the second strongest absorption peak (369 nm) is assigned to the following transitions: HOMO → LUMO and HOMO–1 → LUMO+1.

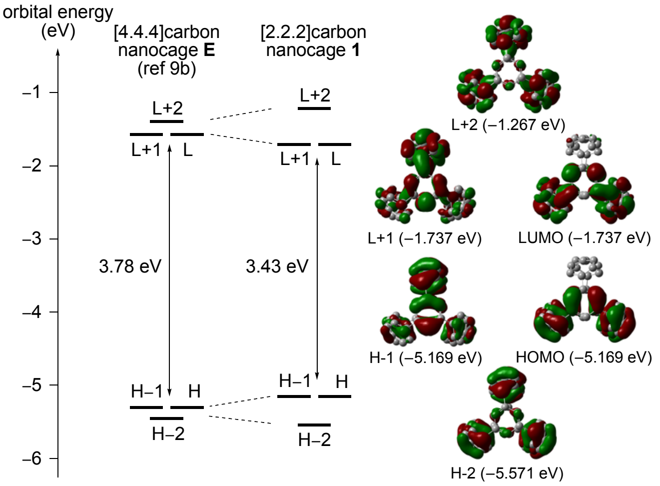
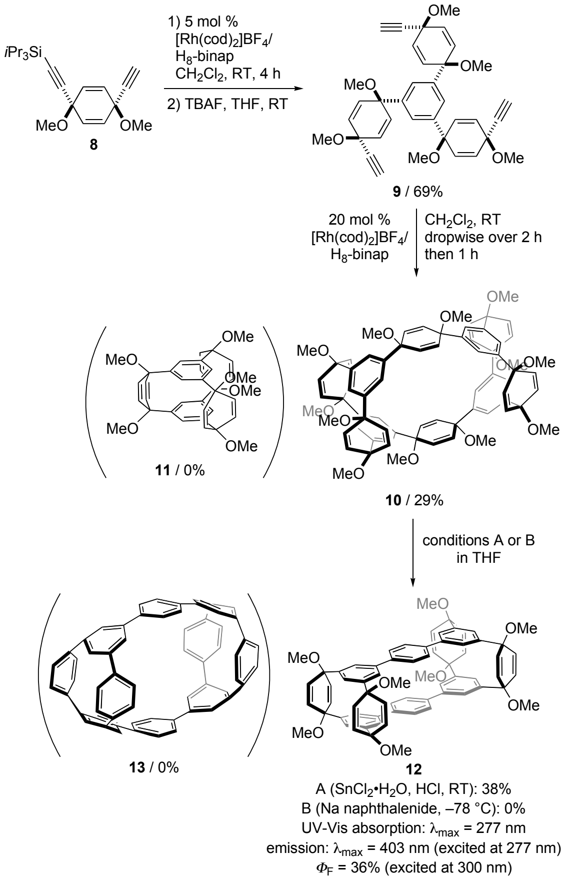


Figure 3. Energy diagrams of the frontier MOs of [4.4.4] and [2.2.2]carbon nanocages **E** (ref 9b) and **1** (left and middle, respectively). Two-way arrows represent HOMO–LUMO gaps. H = HOMO, L = LUMO. Pictorial representations of the frontier MOs of **1** (right).

The synthesis of an ultimately small spherical carbon nanocage, [1.1.1]carbon nanocage,[19] was attempted as shown in Scheme 2. The intermolecular cyclotrimerization of known diyne **8** in the presence of the cationic rhodium(I)/H$_8$-binap catalyst followed by desilylation afforded terminal triyne **9** in good yield as a single regio- and stereoisomer. We expected that the subsequent intramolecular cyclotrimerization of **9** in the presence of the same rhodium catalyst would afford cage molecule **11** that is a precursor of [1.1.1]carbon nanocage. Unexpectedly, the intermolecular cyclotrimerization of two molecules of **9** proceeded to give cage molecule **10** in 29% yield. Partial reductive aromatization of **10** proceeded by using SnCl$_2$/HCl as a reducing reagent to give β-graph-shaped[20] cage molecule **12** in 38% yield, although fully aromatized cage molecule **13**[21] was not obtained. Also in this reduction, the use of sodium naphthalenide did not afford **12** and **13** at all, and led to an unidentified complex mixture. The structures of **10** and **12** were unambiguously determined by X-ray crystallographic analyses (Figures S3 and S4).[18] The thus obtained cage molecule **12** is a fluorescent compound (Φ_F = 36%). The emission maximum (403 nm) of **12** is markedly longer than that (338 nm[22]) of *p*-terphenyl presumably due to the presence of excimer emission of two *p*-terphenyl cores.

In summary, we have achieved the synthesis of the smallest spherical carbon nanocage so far, [2.2.2]carbon nanocage, via the rhodium-catalyzed regioselective intermolecular cyclotrimerization, the triple Suzuki-Miyaura cross-couplings, and reductive aromatization. This cage molecule is highly strained, and its ring strain is between those of [6] and [5]CPPs. A significant bathochromic shift of an emission maximum was observed, compared with that of known [4.4.4]carbon nanocage. We have also achieved the synthesis of a unique β-graph-shaped cage molecule via the rhodium-catalyzed sequential regioselective cyclotrimerizations followed by reductive aromatization, although we failed to synthesize an ultimately small spherical carbon nanocage, [1.1.1]carbon nanocage.



8

9 / 69%

11 / 0%

10 / 29%

13 / 0%

12

A (SnCl$_2$•H$_2$O, HCl, RT): 38%
B (Na naphthalenide, −78 °C): 0%
UV-Vis absorption: λ_{max} = 277 nm
emission: λ_{max} = 403 nm (excited at 277 nm)
Φ_F = 36% (excited at 300 nm)

Scheme 2. Attempted synthesis of [1.1.1]carbon nanocage, which affords β-graph-shaped cage **12**. TBAF = tetrabutylammonium fluoride.

Acknowledgements

This research was supported partly by a Grant-in-Aid for Scientific Research on Innovative Areas "π-System Figuration: Control of Electron and Structural Dynamism for Innovative Functions" (No. JP26102004) from the Japan Society for the Promotion of Science (JSPS, Japan), and ACT-C (No. JPMJCR1122YR) from the Japan Science and Technology Agency (JST, Japan). We thank Takasago International Corporation for the gift of H$_8$-binap, and Umicore for generous support in supplying the palladium and rhodium complexes.

Keywords: alkyne cyclotrimerization • carbon nanocages • molecular strain • reductive aromatization • rhodium

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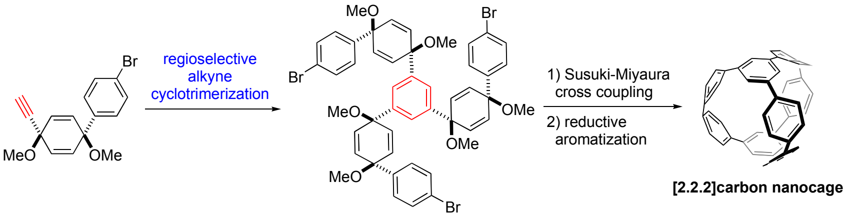

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