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Synthesis and Structure of A Triptycene-Based Nanosized Molecular Cage

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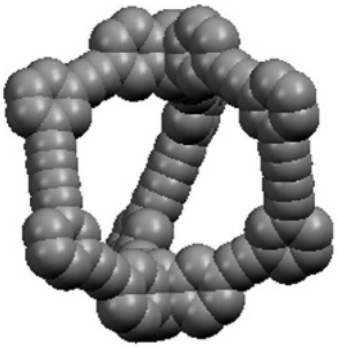

A triptycene-based nanosized molecular cage was designed and efficiently synthesized by Eglington−Glaser coupling reaction, and its structure was determined by NMR, MS spectrometry and X-ray analysis. Moreover, it was found that the cage molecules could pack into a microporous structure in the solid state and 1,3,5-trimethylbenzene molecules were located in the channels.

Inspired by nanosized cage compounds in biological systems,[1] considerable attention has been attracted to prepare synthetic cages for potential applications such as storage,[2] recognition,[3] delivery[4] and catalysis.[5] Different methods have been developed in recent years; however, most of the interests were focused on the construction of self-assembled supramolecular cages using the ability of a coordination bond or a hydrogen bond to direct orientation of the desired components.[6] So far, the covalent synthesis of nanosized cage compounds with high symmetry still remains a challenge in this field for chemists.

It has been proven that a phenyldiacetylenic bridge unit with rigid and directional characteristics is a useful building block for the synthesis of a variety of carbon-rich molecules, which not only show unique properties in supramolecular chemistry and material science[7] but also are regarded as attractive precursors for novel carbon allotropes such as graphite or fullerene.[8] However, the three-dimensional (3D) cages[9] based on phenyldiacetylenic unit are so rare that their chemistry has not been well developed.

Recently, we[10] became interested in the synthesis and properties of novel receptors based on the triptycene with a unique 3D rigid structure, which resulted in the development of some new supramolecular systems. For constructing new receptors with specific structures and properties, we recently synthesized a series of trisubstituted triptycene derivatives.[11] In particular, the synthesis of 2,7,14-trihalotriptycenes could provide us opportunities to construct interesting molecular architectures. As a result, we designed and synthesized a novel nanosized cage with 2,7,14-triiodotriptycene as the starting material. Herein we report the synthesis and structure of the molecular cage.

(1) (a) Johnson, J. E.; Speir, J. A. *J. Mol. Biol.* **1997**, *269*, 665−675. (b) Lin, T.; Chen, Z.; Usha, E.; Stauffacher, C. V.; Dai, J.-B.; Schmidt, T.; Johnson, J. E. *Virology* **1999**, *265*, 20−34. (c) Lawson, D. M.; Artymiuk, P. J.; Yewdall, S. J.; Smith, J. M. A.; Livingstone, J. C.; Treffry, A.; Luzzago, A.; Levi, S.; Arosio, P.; Cesareni, G.; Thomas, C. D.; Shaw, W. V.; Harrison, P. M. *Nature* **1991**, *349*, 541−544. (d) Proulxcurry, P. M.; Chasteen, N. D. *Coord. Chem. Rev.* **1995**, *144*, 347−368.

(2) (a) Martin, T.; Obst, U.; Rebek, J., Jr. *Science* **1998**, *281*, 1842−1845. (b) Davis, A. V.; Raymond, K. N. *J. Am. Chem. Soc.* **2005**, *127*, 7912−7919. (c) Kusukawa, T.; Fujita, M. *J. Am. Chem. Soc.* **2002**, *124*, 13576−13582.

(3) (a) Heinz, T.; Rudkevich, D. M.; Rebek, J., Jr. *Nature* **1998**, *394*, 764−766. (b) Tashiro, S.; Tominaga, M.; Kawano, M.; Therrien, B.; Ozki, T.; Fujita, M. *J. Am. Chem. Soc.* **2005**, *127*, 4546−4547. (c) Kerchoffs, J. M. C. A.; van Leeuwen, F. W. B.; Spek, A. L.; Kooijman, H.; Crego-Calama, M.; Reinhoudt, D. N. *Angew. Chem., Int. Ed.* **2003**, *42*, 5717−5722.

(4) (a) Turner, J. L.; Wooley, K. L. *Nano Lett.* **2004**, *4*, 683−688. (b) Pan, D.; Turner, J. L.; Wooley, K. L. *Chem. Commun.* **2003**, 2400−2401. (c) Perkin, K. K.; Turner, J. L.; Wooley, K. L.; Mann, S. *Nano Lett.* **2005**, *5*, 1457−1461.

(5) (a) Fiedler, D.; Leung, D. H.; Bergman, R. G.; Raymond, K. N. *Acc. Chem. Res.* **2005**, *38*, 351−360. (b) Yoshizawa, M.; Takeyama, Y.; Kusukawa, T.; Fujita, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1347−1349.

(6) (a) Conn, M. M.; Rebek, J., Jr. *Chem. Rev.* **1997**, *97*, 1647−1668. (b) Swiegers, G. F.; Malefetse, T. J. *Chem. Rev.* **2000**, *100*, 3483−3537. (c) Seidel, S.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972−983. (d) Fujita, M.; Tominaga, M.; Hori, A.; Therrien, B. *Acc. Chem. Res.* **2005**, *38*, 371−380.

(7) (a) Moore, J. S. *Acc. Chem. Res.* **1997**, *30*, 402−413. (b) Höger, S. *J. Polym. Sci., Part* A: *Polym. Chem.* **1999**, *37*, 2685−2698. (c) Haley, M. M.; Pak, J. J.; Brand, S. C. *Top. Curr. Chem.* **1999**, *201*, 81−130. (d) Grave, C.; Schlüter, A. D. *Eur. J. Org. Chem.* **2002**, 3075−3098. (e) Zhao, D.; Moore, J. S. *Chem. Commun.* **2003**, 807−818. (f) Yamaguchi, Y.; Yoshida, Z. *Chem.-Eur. J.* **2003**, *9*, 5430−5440. (g) Höger, S. *Chem.-Eur. J.* **2004**, *10*, 1320−1329. (h) Moore, J. S. *Curr. Opin. Colloid Interface Sci.* **1999**, *4*, 108−116. (i) Schmittel, M.; Kalsani, V. *Top. Curr. Chem.* **2005**, *245*, 1−53.

(8) (a) Diederich, F. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, Germany, 1995; Chapter 13, pp 443−471. (b) Diederich, F., Stang, P. J., Tykwinski, R. R., Eds. *Acetylene Chemistry*; Wiley-VCH: Weinheim, Germany, 2004. (c) Rubin, Y.; Diederich, F. In *Stimulating Concepts in Chemistry*; Vögtle, F., Stoddart, J. F., Shibasaki, M., Eds.; Wiley-VCH: Weinheim, Germany 2000; pp 163−186. (d) Scott, L. T.; Cooney, J. M. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, Germany, 1995; Chapter 9, pp 321−351. (e) Bunz, U. H. F.; Rubin, Y.; Tobe, Y. *Chem. Soc. Rev.* **1999**, *28*, 107−119. (f) Nielsen, M. B.; Diederich, F. *Chem. Rev.* **2005**, *105*, 1837−1867.

(9) (a) Wu, Z.; Lee, S.; Moore, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 8730−8732. (b) Rubin, Y.; Parker, T. C.; Khan, S. I.; Holliman, C. L.; McElvany, S. W. *J. Am. Chem. Soc.* **1996**, *118*, 5308−5309. (c) Rubin, Y.; Parker, T. C.; Pastor, S. J.; Jalisatgi, S.; Boulle, C.; Wilkins, C. L. *Angew. Chem., Int. Ed.* **1998**, *37*, 1226−1229. (d) Tobe, Y.; Nakagawa, N.; Naemura, K.; Wakabayashi, T.; Shida, T.; Achiba, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4544−4545. (e) Tobe, Y.; Nakagawa, N.; Kishi, J.; Sonoda, M.; Naemura, K.; Wakabayashi, T.; Shida, T.; Achiba, Y. *Tetrahedron* **2001**, *57*, 3629−3636.

(10) (a) Zhu, X.-Z.; Chen, C.-F. *J. Am. Chem. Soc.* **2005**, *127*, 13158−13159. (b) Zong, Q.-S.; Chen, C.-F. *Org. Lett.* **2006**, *8*, 211−214. (c) Zong, Q.-S.; Zhang, C.; Chen, C.-F. *Org. Lett.* **2006**, *8*, 1859−1862. (d) Zhu, X.-Z.; Chen, C.-F. *Chem. Eur. J.* **2006**, *12*, 5603−5609. (e) Zhang, C.; Chen, C.-F. *J. Org. Chem.* **2007**, *72*, 3880−3888.

(11) Zhang, C.; Chen, C.-F. *J. Org. Chem.* **2006**, *71*, 6626−6629.

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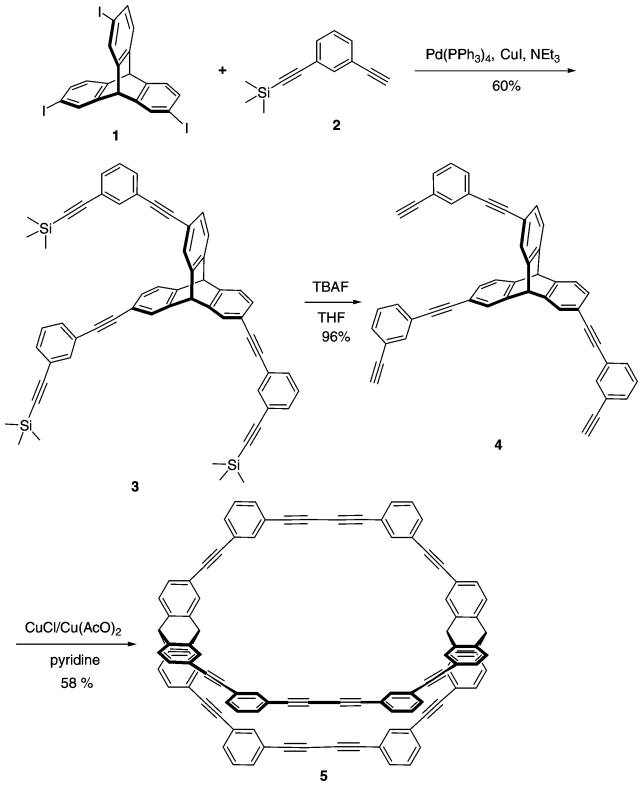
SCHEME 1. Synthesis of Molecular Cage 5



The synthesis of cage **5** was carried out as outlined in Scheme 1. Starting from the 2,7,14-triiodotriptycene **1**,[11] its palladium-catalyzed coupling reaction with the singly protected 1,3-diethynylbenzene **2**[12] afforded triethynylation product **3** in 60% yield, which was then deprotected by tetrabutylammonium fluoride (TBAF) in THF to give the terminal acetylene **4** in 96% yield. By the copper-mediated modified Eglington−Glaser oxidative coupling of **4** with CuCl/Cu(OAc)$_2$ in pyridine, the molecular cage **5** was obtained in 58% yield.

The D_{3h} structure of **5** is evident from its ^{1}H NMR and ^{13}C NMR spectra, which showed only two signals for the bridgehead or methine protons and two signals for the bridgehead carbons. In comparison with the ^{1}H NMR spectra of **3** and **4**, compound **5** showed almost identical shifts for the outer aromatic proton signals but significant downfield shifts for the inner aromatic proton signals (Figure 1). Moreover, the obvious different chemical shifts with $\Delta\delta$ of 0.07 ppm for the two methine protons in the triptycene moiety of **5** were observed, while the ones in **3** and **4** only showed different shifts with $\Delta\delta$ of 0.04 and 0.03 ppm, respectively. These observations may be attributed to the strong shielding effect of the inner protons in the molecular cage **5**. Furthermore, it was found that the MALDI-TOF mass spectrum of compound **5** revealed the peak at *m*/*z* 1247 for M^+, which is consistent with its cage structure. We also found that the peak was isotopically resolved and it agreed very well with the theoretical distribution.[13]

The structure of molecular cage **5** was further determined by its X-ray single-crystal analysis. During the crystallization process, we initially tested many solvent systems such as CH_2Cl_2, $CHCl_3$, CH_2Cl_2/benzene, and CH_2Cl_2/chlorobenzene, but

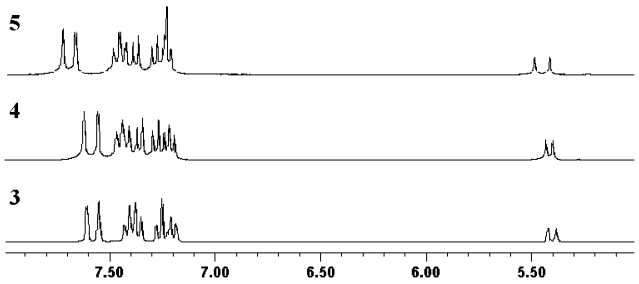


FIGURE 1. ^{1}H NMR spectra of **3**, **4**, and **5** (300 MHz, $CDCl_3$).

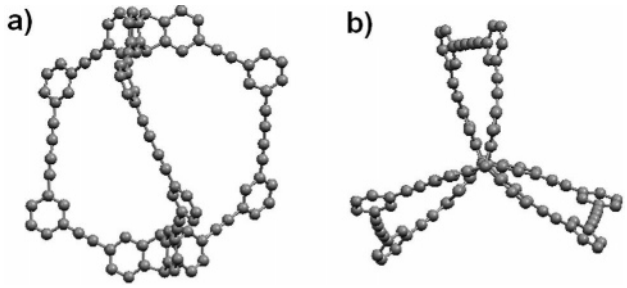


FIGURE 2. (a) Side view and (b) top view of crystal structure of compound **5**. Hydrogen atoms are omitted for clarity.

the crystals in all these systems proved to be fragile and extremely sensitive to solvent loss. Fortunately, we obtained the single crystals of **5** suitable for X-ray diffraction by slow evaporation of a CH_2Cl_2/1,3,5-trimethylbenzene solution. As shown in Figure 2, the crystal structure reveals that the distance between the two bridgehead carbons in the two triptycene moieties of **5** is 13.03 Å, and the distances between the three carbons in the *m*-phenylene units are 12.38, 13.04, and 12.90 Å, respectively. The twist angles of the benzene rings linked by acetylenic units are 24.5°, 35.2°, and 24.5°, respectively. The acetylenic units show deviations from linearity with the C≡C−C angles ranging from 178.0 to 178.8°. The distortion of **5** in the solid state from more energetically favorable structures found by minimization may be due to the relative flexibility of alkynes, which also resulted in a helical chiral feature of the molecular cage.[13]

Furthermore, it was found that by virtue of C−H···π ($d_{C-H\cdots\pi}$ = 2.90 and 2.86 Å) interactions between the homochiral cage molecules, and by virtue of C−H···π ($d_{C-H\cdots\pi}$ = 2.72 and 2.81 Å) interactions between the heterochiral molecules, an interlaced one-dimensional (1D) supramolecular structure was formed in the solid state (Figure 3). Moreover, we also found that by three pairs of C−H···π ($d_{C-H\cdots\pi}$ = 2.84, 2.88, and 2.89 Å) interactions, the adjacent 1D supramolecular structures are connected with each other, which resulted in a 2D-layer structure and a further microporous structure (Figure 3). Interestingly, the 1,3,5-trimethylbenzene molecules were found to be located in the channels, and the multiple C−H···π interactions between the trimethylbenzene molecules and the molecular cage **5** existed.[13] These observations implied that the cage **5** could be utilized as a novel intriguing microporous material for storage and delivery of aromatic compounds.

In conclusion, a triptycene-based nanosized molecular cage has been efficiently synthesized by an Eglington−Glaser coupling reaction, and its structure was determined by NMR, MS spectra, and X-ray analysis. Moreover, we found that the cage molecule could also pack into a microporous structure in

(12) Ohkita, M.; Ando, K.; Suzuki, T.; Tsuji, T. *J. Org. Chem.* **2000**, *65*, 4385−4390.

(13) See Supporting Information.

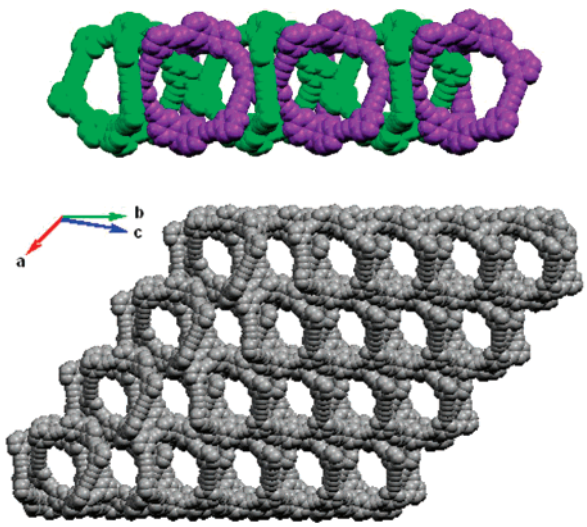


FIGURE 3. Packing of **5**. View of an interlaced 1D supramolecular structure along the *b*-axis (top) and view of a microporous structure (bottom). Hydrogen atoms and solvent molecules are omitted for clarity.

the solid state and the trimethylbenzene molecules were located in the channels. The work described here can provide not only a new approach to the design of molecular architectures based on the triptycene unit but also new opportunities for constructing novel receptors and microporous organic materials with specific properties.

Experimental Section

Synthesis of 3. To a suspension of **1** (63 mg, 0.1 mmol), Pd(PPh$_3$)$_4$ (8 mg, 0.007 mmol), and CuI (2 mg, 0.007 mmol) in dry triethylamine (10 mL) was added a solution of **2** (60 mg, 0.3 mmol) in triethylamine (5 mL). The mixture was stirred at 70 °C under argon for 12 h, cooled, evaporated to remove triethylamine, taken up in ether (50 mL), and washed with 1 M aqueous HCl (3 × 30 mL). The aqueous solution was extracted with ether (2 × 50 mL). The organic extracts were combined, washed successively with aqueous $NaHCO_3$ (2 × 50 mL) and brine (2 × 50 mL), dried over anhydrous Na_2SO_4, concentrated, and chromatographed on silica gel eluted with 1:10 (v:v) CH_2Cl_2/petroleum ether to give 51 mg (60%) of **3** as white solid. Mp 110−112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.25 (s, 27H), 5.40 (s, 1H), 5.44 (s, 1H), 7.20 (d, J = 7.6 Hz, 3H), 7.26 (t, J = 7.9 Hz, 3H), 7.36 (d, J = 7.9 Hz, 3H), 7.41 (t, J = 7.9 Hz, 6H), 7.55 (s, 3H), 7.61 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.00, 53.4, 53.7, 77.3, 88.0, 90.0, 95.0, 104.3, 120.3, 123.6, 123.6, 123.9, 127.0, 128.4, 129.3, 131.6, 135.1, 144.6, 144.7. MALDI TOF-MS: m/z 842.7 (M^+). Anal. Calcd for $C_{59}H_{50}Si_3$: C, 84.03; H, 5.98. Found: C, 84.21; H, 6.03.

Synthesis of 4. To a suspension of **3** (41 mg, 0.05 mmol) in THF (7 mL) was added Bu_4NF (50 mg, 0.18 mmol) solution in THF (1 mL) dropwise, and the reaction was stirred at room temperature for 30 min. The mixture was evaporated to remove THF, taken up in ether (50 mL), washed successively with water (30 mL) and brine (30 mL), dried with Na_2SO_4, concentrated, and chromatographed on silica gel eluted with CH_2Cl_2/petroleum ether (1:8) to give 30 mg (96%) of colorless amorphous **4**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.08 (s, 3H), 5.40 (s, 1H), 5.44 (s, 1H), 7.20 (dd, J = 7.6, 1.4 Hz, 3H), 7.27 (t, J = 7.7 Hz, 3H), 7.34 (d, J = 7.6 Hz, 3H), 7.44 (dt, J = 7.7, 1.4 Hz, 6H), 7.55 (d, J = 1.1 Hz, 3H), 7.62 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.3, 53.6, 77.8, 82.8, 87.8, 90.1, 120.6, 122.5, 123.7, 123.8, 127.0, 128.4, 129.3, 131.7, 131.8, 135.1, 144.5, 144.6. MALDI TOF-MS: m/z 626.4 (M^+). Anal. Calcd for $C_{50}H_{26}$: C, 95.82; H, 4.18. Found: C, 95.68; H, 4.21.

Synthesis of 5. To a slurry of CuCl (223 mg, 2.25 mmol) and $Cu(OAc)_2$ (546 mg, 3.0 mmol) in dry pyridine (15 mL) was added dropwise a solution of **4** (30 mg, 0.05 mmol) in dry pyridine (5 mL) at 60 °C. The mixture was stirred for an additional 2 h at the same temperature, cooled, evaporated to remove pyridine, taken up in CH_2Cl_2 (50 mL), and washed with 1 M aqueous HCl (3 × 30 mL). The aqueous solution was extracted with CH_2Cl_2 (2 × 30 mL). The organic extracts were combined, washed successively with aqueous $NaHCO_3$ (2 × 50 mL) and brine (2 × 50 mL), dried with Na_2SO_4, concentrated, and chromatographed on silica gel eluted with CH_2Cl_2 and petroleum ether (1:5) to give 17 mg (58%) of white solid **5**. Mp 257−259 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.47 (s, 2H), 5.55 (s, 2H), 7.25 (dd, J = 7.6, 1.4 Hz, 6H), 7.30 (t, J = 7.8 Hz, 6H), 7.40 (d, J = 7.6 Hz, 6H), 7.47 (dt, J = 7.8, 1.3 Hz, 12H), 7.68 (d, J = 1.1 Hz, 6H), 7.74 (t, J = 1.4 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.3, 53.7, 74.3, 80.8, 87.8, 90.6, 120.1, 122.1, 123.9, 123.9, 127.3, 128.6, 129.1, 131.8, 131.1, 135.5, 144.6, 144.7. HRMS calcd for $C_{100}H_{46}$: $[M]^+$ 1247.4352, found: 1247.4355.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for compounds **3**, **4**, and **5**; X-ray crystallographic file (CIF) for molecular cage **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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