ORGANIC LETTERS

2004
Vol. 6, No. 25
4667−4670

Novel π-Expanded Radialene Macrocycles with Inner Cavity

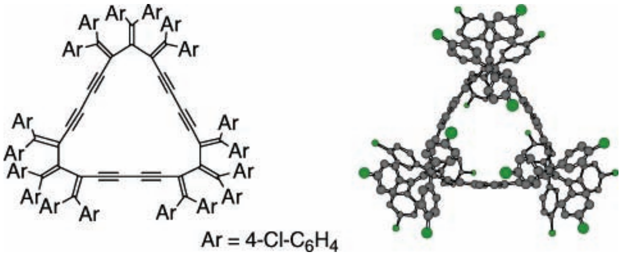
Masahiko Iyoda,*,[†] Yoshiyuki Kuwatani,[†] Sachiko Yamagata,[†] Nobuko Nakamura,[†] Mie Todaka,[†] and Gaku Yamamoto[‡]

Department of Chemistry, Graduate School of Science, Tokyo Metropolitan University, Hachioji, Tokyo 192-0397, Japan, and Department of Chemistry, School of Science, Kitasato University, Sagamihara, Kanagawa 228-8555, Japan

iyoda-masahiko@c.metro-u.ac.jp

Received September 14, 2004

ABSTRACT



Polyenyne macrocycles with π-extended [9]- and [12]radialene frameworks have been synthesized. These radialenes exhibit restricted rotation of the aromatic rings, and the D_3- and D_4-symmetric structures in solutions have been determined by dynamic NMR. The macrocyclic radialenes bear small to medium inner cavities, and the small cavity of the π-extended [9]radialene can incorporate a silver cation.

Polyenyne macrocycles have attracted considerable attention because of their π-conjugation, all-carbon networks, formation of unusual metal complexes, self-association, and inclusion properties.[1,2] Among them, cylindrical π-systems with a shape-persistent macrocyclic structure[3] can be regarded as π-cavitands and are expected to show unique structures, host/guest interactions, and interesting electronic properties.[4] Although these molecules do not exhibit perfect cyclic conjugation, fully unsaturated macrocycles form a π-cavity with a concave−convex nature. We report here the synthesis of π-extended [9]- and [12]radialenes starting from the [3]dendralene precursor, together with their unique structural properties.

Although [3]- to [6]radialenes have been synthesized and fully characterized,[5,6] larger [7]- and [8]radialenes were previously unknown, mainly because the steric repulsion between the neighboring exocyclic methylene groups may destabilize the large-numbered radialenes. One possible

---

[†] Tokyo Metropolitan University.

[‡] Kitasato University.

(1) For reviews, see: (a) Marsden, J. A.; Palmer, G. J.; Haley, M. M. *Eur. J. Org. Chem.* **2003**, 2355. (b) Hopf, H. In *Modern Arene Chemistry*; Astruc, D., Ed.; Wiley-VCH: Weinheim, 2002; pp 169−195. (c) Wan, W. B.; Brand, S. C.; Pak, J. J.; Haley, M. M. *Chem. Eur. J.* **2000**, *6*, 2044. (d) Bunz, U. H. F.; Rubin, Y.; Tobe, Y. *Chem. Soc. Rev.* **1999**, *28*, 107.

(2) For recent examples, see: (a) Mitzel, F.; Boudon, C.; Gisselbrecht, J.-P.; Seiler, P.; Gross, M.; Diederich, F. *Chem. Commun.* **2003**, 1634. (b) Tobe, Y.; Ohki, I.; Sonoda, M.; Niino, H.; Sato, T.; Wakabayashi, T. *J. Am. Chem. Soc.* **2003**, *125*, 5614. (c) Heuft, M. A.; Collins, S. K. Fallis, A. G. *Org. Lett.* **2003**, *5*, 1911. (d) Campbell, K.; Kuehl, C. R.; Ferguson, M. J.; Stang, P. J.; Tykwinski, R. R. *J. Am. Chem. Soc.* **2002**, *124*, 7266.

(3) For reviews, see: (a) Scott, L. T. *Angew. Chem., Int. Ed.* **2003**, *42*, 4133. (b) Zhao, D.; Moore, J. S. *Chem. Commun.* **2003**, 807. (c) Yamaguchi, Y.; Yoshida, Z. *Chem. Eur. J.* **2003**, *9*, 5430. (d) Höger, S. *Chem. Eur. J.* **2004**, *10*, 1320.

(4) For recent examples, see: (a) Kawase, T.; Tanaka, K.; Shiono, N.; Seirai, Y.; Oda, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 1722. (b) Kuwatani, Y.; Igarashi, J.; Iyoda, M. *Tetrahedron Lett.* **2004**, *45*, 359. (c) Srinivasan, M.; Sankararaman, S.; Hopf, H.; Varghese, B. *Eur. J. Org. Chem.* **2003**, 660. (d) Kawase, T.; Tanaka, K.; Seirai, Y.; Shiono, N.; Oda, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 5597.

(5) For a review, see: Hopf, H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 931.

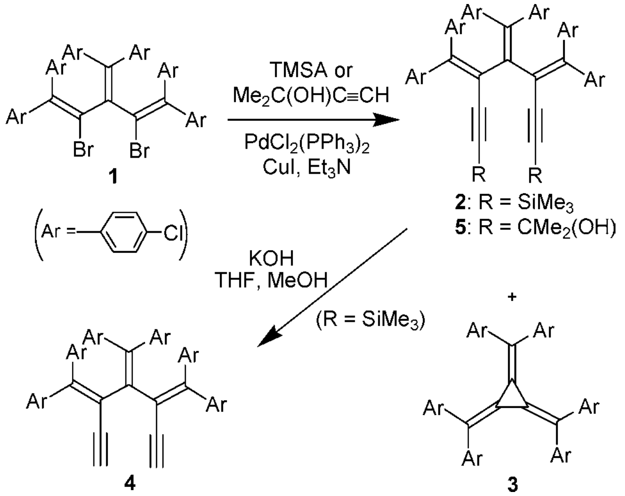
(6) For recent examples, see: (a) Eisler, S.; Tykwinski, R. R. *Angew. Chem., Int. Ed.* **1999**, *38*, 1940. (b) Nielsen, M. B.; Schreiber, M.; Baek, Y. G.; Seiler, P.; Lecomte, S.; Boudon, C.; Tykwinski, R. R.; Gisselbrecht, J.-P.; Gramlich, V.; Skinner, P. J.; Bosshard, C.; Günter, P.; Goss, M.; Diederich, F. *Chem. Eur. J.* **2001**, *7*, 3263. (c) Höpfner, T.; Jones, P. G.; Ahrens, B.; Dix, I.; Ernst, L.; Hopf, H. *Eur. J. Org. Chem.* **2003**, 2596. (d) Tobe, Y.; Umeda, R.; Iwasa, N.; Sonoda, M. *Chem. Eur. J.* **2003**, *9*, 5549. (e) Kuwatani, Y.; Yamamoto, G.; Iyoda, M. *Org. Lett.* **2003**, *5*, 3371.

10.1021/ol048146g CCC: \$27.50

approach to large-numbered radialenes is π-extension of *exo*-methylene groups by insertion of double or triple bonds.[6] However, no π-extended large-numbered radialene has been synthesized, mainly due to synthetic reasons, i.e., the lack of suitable dendralene precursors. We recently reported the synthesis of hexaaryl[3]radialenes (aryl = phenyl or *p*-chlorophenyl) starting from dibromohexaaryl[3]dendralenes.[7,8] On the basis of these results, we designed the synthesis of π-extended large-numbered radialenes with an inner cavity.

The Sonogashira reaction of dibromo[3]dendralene **1**[8] with trimethylsilylacetylene (TMSA) produced the bis(trimethylsilylethynyl)[3]dendralene **2** (55%), together with the [3]radialene **3** (12%). Since the two bromine atoms in **1** are located close to each other (Br···Br: 3.95 Å), the formation of **3** took place simultaneously. Deprotection of **2** with KOH in methanol–THF afforded bis(ethynyl)[3]dendralene **4** in 77% yield (Scheme 1). The dendralene **4** in solution gradually decomposed at room temperature on standing under air for a long time. However, **4** in the crystalline state is very stable and can be stored at room temperature without decomposition.

Scheme 1. Synthesis of Bis(ethynyl)[3]dendralenes **2**, **4**, and **5**



The molecular structure of **4** obtained by X-ray crystallography is shown in Figure 1.[9] Due to the steric repulsion among 4-chlorophenyl groups, the molecule is significantly distorted and adopts a twisted chiral conformation with approximate C_2 symmetry. The planes of the two outer $C=C$ bonds are twisted by 60.6 and 49.3° from the plane of the inner $C=C$ bond, and thus, the two ethynyl groups are oriented with a dihedral angle of 96° and the intramolecular distances between the acetylene carbons are 3.50 and 4.82 Å for C(8)···C(10) and C(7)···C(9), respectively. The aryl rings are twisted from the attaching $C=C$ planes by 41.1–65.0° (average: 50.0°) and the rings **a** and **b** are stacked face-to-face with a distance of 3.20 Å.

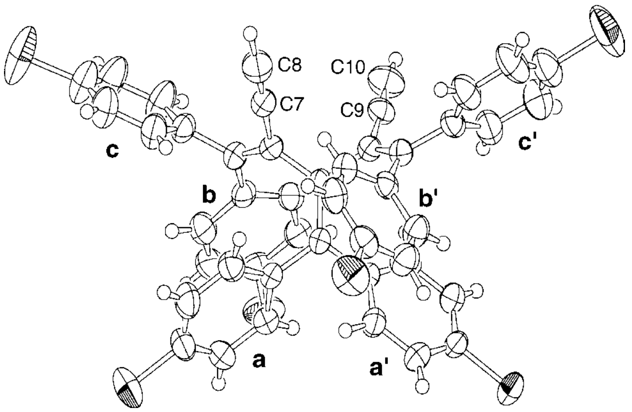


Figure 1. ORTEP view of the bis(ethynyl)[3]dendralene **4**. The twist angles (deg) of the aryl rings **a**, **b**, **c**, **a′**, **b′**, and **c′** from the $C=C$ planes are 46.8(6), 65.0(6), 48.1(7), 49.8(6), 41.1(7), and 49.0(7). See the Supporting Information for bond lengths and angles of **4**.

The ^1H NMR spectrum of **4** is highly dependent on temperature as shown in Figure 2. The signals ascribed to the **c** rings are almost temperature independent and appear as a single sharp AB quartet (AA′BB′, strictly), indicating that the rotation of these rings is fast on the NMR time scale throughout the temperature range examined. The signals due to the **b** rings are sharp at high temperatures but significantly broadened at −50 °C although no splitting was observed at low temperatures. The signals due to the **a** rings are broadened and buried under the baseline at 10 °C and appear as four separate signals at −50 °C, indicating the retarded rotation of the aryl groups [*o*-H: δ 7.44 and 5.37 (■ in Figure 2c); *m*-H: δ 7.33 and 6.74 (● in Figure 2c)]. Quantitative saturation transfer experiments gave $\Delta G^\ddagger = 12.4$ kcal mol^{-1} at 200 K for the ring **a** rotation.[10]

Judging from the chiral nature of **4** (Figure 1), it is reasonable to assume that **4** adopts a chiral conformation in solution and that enantiomerization takes place. The observed barrier to ring **a** rotation, $\Delta G^\ddagger = 12.2$ kcal mol^{-1}, affords the lower limit of the enantiomerization barrier, but the exact value cannot be elucidated. Thus, we studied the dendralene **5** carrying 1-hydroxy-1-methylethyl groups as a chirality

---

[7] For dendralenes, see: (a) Hopf, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 948. (b) Norinder, V. J. *THEOCHEM* **1987**, *150*, 85. (c) Cadogan, J. I. G.; Cradock, S.; Gillam, S.; Gosney, I. *J. Chem. Soc., Chem. Commun.* **1991**, 114. (d) Fielder, S.; Rowan, D. D.; Sherburn, M. S. *Angew. Chem., Int. Ed.* **2000**, *39*, 4331. (e) Hopf, H. *Angew. Chem., Int. Ed.* **2001**, *40*, 705.

[8] Iyoda, M.; Nakamura, N.; Todaka, M.; Ohtsu, S.; Hara, K.; Kuwatani, Y.; Yoshida, M.; Matsuyama, H.; Sugita, M.; Tachibana, H.; Inoue, H. *Tetrahedron Lett.* **2000**, *41*, 7059.

[9] Crystallographic data for **4**: $C_{46}H_{26}Cl_6$, MW = 791.41, triclinic, space group *P*-1 (No. 2), $a = 11.766(2)$ Å, $b = 16.768(3)$ Å, $c = 10.475(1)$ Å, $\alpha = 91.42(1)°$, $\beta = 93.51(1)°$, $\gamma = 109.86(1)°$, $V = 1937.7(5)$ Å^3, $Z = 2$, $D_c = 1.356$ g/cm^3, $F(000) = 808$, μ(Mo Kα) = 4.75 cm^{-1}, $R = 0.071$, $R_w = 0.129$, GOF = 1.949. All measurements were performed on a Rigaku AFC7R diffractometer with graphite monochromated Mo Kα ($\lambda = 0.710\,69$ Å) radiation at 23 °C. Among a total of 9375 reflections measured, 8893 were unique and the observed ($I > 3.00\sigma(I)$) 3986 reflections were used for the refinement. The crystal structure was solved by a direct method and refined by the full-matrix least-squares method.

[10] (a) Sandström, J. *Dynamic NMR Spectroscopy*; Academic Press: London, 1982; Chapter 4. (b) Yamamoto, G. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1967.

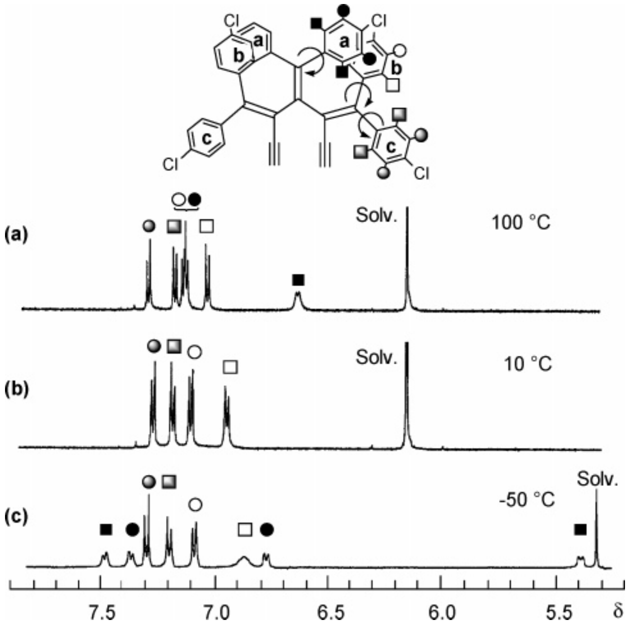


Figure 2. Temperature-dependent ^{1}H NMR spectra (500 MHz) of **4** at (a) 100 °C in $C_2D_2Cl_4$, (b) 10 °C in $C_2D_2Cl_4$, and (c) −50 °C in CD_2Cl_2. See the Supporting Information for further details.

probe, this was similarly prepared from **1** (Scheme 1). The *gem*-dimethyl groups are diastereotopic at room temperature, and the two singlets at δ 1.41 and 1.38 ($CDCl_3$) coalesced into a single peak at 43 °C. Total line shape analysis afforded $\Delta G^{\ddagger} = 17.1$ kcal mol^{-1} at 300 K for the enantiomerization. Meanwhile, saturation transfer experiments for the ring **a** signals of **5** gave $\Delta G^{\ddagger} = 13.5$ kcal mol^{-1} at 250 K for the ring **a** rotation (Figure 3).

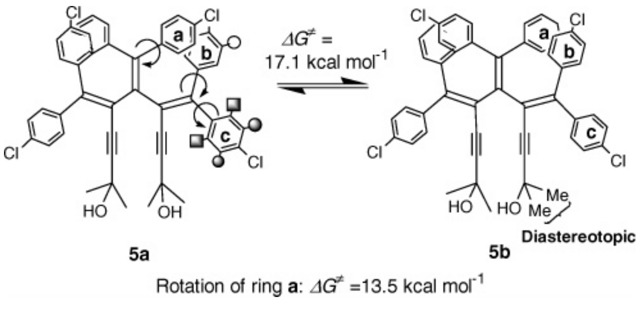
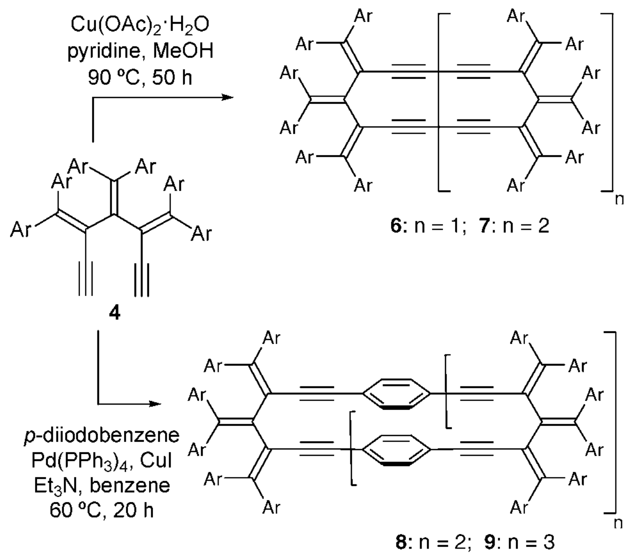


Figure 3. Conformational mobility of **5** and activation energies for the two restricted movements in **5**.

As shown in Figure 1, the conformation of **4** is favorable for intermolecular coupling reactions because the two ethynyl groups are located in the same direction. Thus, homocoupling of the acetylene units in **4** and Sonogashira coupling of **4** with *p*-diiodobenzene would form the corresponding cyclic oligomers (Scheme 2). Reaction of **4** with $Cu(OAc)_2 \cdot 2H_2O$ in pyridine−methanol under Eglinton−Glaser conditions[11]

Scheme 2. Synthesis of the Extended Radialenes **6**−**9**



afforded the corresponding cyclic trimer **7** in 23% yield, together with a small amount of the cyclic dimer **6**. The trimer **7** was isolated as yellow fine crystals and characterized by spectroscopic analysis, whereas **6** was only detected by TOF-MS.

The Sonogashira reaction of **4** with *p*-diiodobenzene was carried out using $Pd(PPh_3)_4$ and CuI in triethylamine−benzene at 60 °C for 20 h. Although the reaction produced a complex mixture of cyclic and acyclic oligomers, the cyclic trimer **8** (27%) and the cyclic tetramer **9** (11%) were isolated by gel-permeation liquid chromatography (GPLC), followed by column chromatography on alumina. The trimer and tetramer **8** and **9** were obtained as yellow prisms and the structures were fully characterized.

The ^{1}H and ^{13}C NMR spectra of the cyclic trimer **7** are rather simple, reflecting its highly symmetric structure with D_3 symmetry on the NMR time scale, where the three dendralene moieties have the same sense of chirality. Semiempirical MO calculations (AM1) support the structure with a 3-fold axis as the most stable conformation (see the Abstract graphic), and the C_2 conformer, in which one of the dedralene unit has the opposite sense of chirality, is 6.5 kcal mol^{-1} less stable than the one at the global minimum. The rotation of rings **b** and **c** is fast and that of the **a** rings is slow on the NMR time scale at 30 °C in CD_2Cl_2, and $\Delta G^{\ddagger} = 15.5$ kcal mol^{-1} at 300 K was obtained for the rotation of the **a** rings, which is higher than in **4** and **5**. No information is available for the enantiomerization in **7**, but an energy barrier significantly higher than 15.5 kcal mol^{-1} is expected, judging from the data for **5**. The AM1 calculations suggest that **7** has an inner cavity of 2.6 Å, by considering the van der Waals radii. Interestingly, **7** forms a silver complex on mixing with an excess amount of $Ag(OCOCF_3)$ or $AgClO_4$.[12] The complex formation was

---

(11) Behr, O. M.; Eglington, G.; Galbraith, A. R.; Raphael, R. A. *J. Chem. Soc.* **1960**, 3614.

determined by ^{1}H NMR (Supporting Information) and MALDI TOF-MS (Figure 4) spectra, the latter showing a molecular ion corresponding to **7·Ag**$^+$ at *m/z* 2474.8, together with a molecular ion of **7** at *m/z* 2368.2.

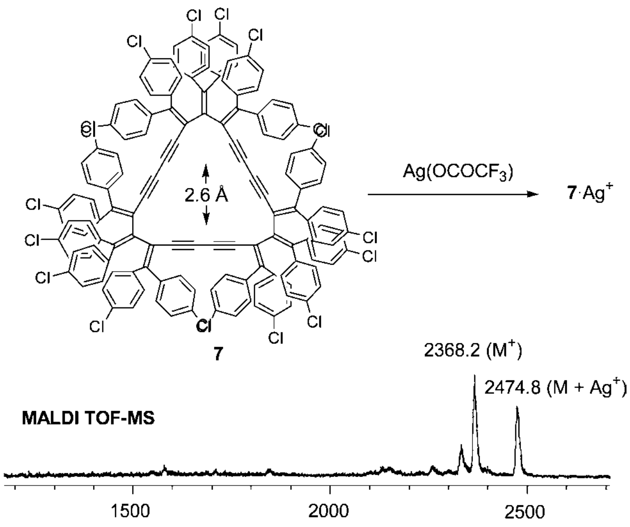


Figure 4. Formation of the silver complex **7**·Ag$^+$.

The cyclic trimer and tetramer **8** and **9** expanded by 1,4-phenylene-ethynylene bridges show D_3- and D_4-symmetric ^{1}H and ^{13}C NMR signals at room temperature, although the ^{1}H NMR spectra of **8** and **9** exhibit temperature dependence. AM1 calculations suggest that **8** and **9** adopt conformations with the highest symmetry. The activation energy for the rotation of the central benzene ring in **8** is $\Delta G^{\ddagger} = 15.1$ kcal mol^{-1} (quantitative saturation transfer experiments in CDCl$_3$ at −5 °C), which is slightly smaller than that of **7**. However, the activation energy for the rotation of the ring in **9** could not be determined by ^{1}H NMR, because **9** was decomposed at higher temperatures. As shown in Figure 5, AM1 calculations show the unique structures of **8** and **9** with inner cavities. Thus, **8** and **9** have larger inner cavities than **7**, and hence **8** and **9** formed no silver complexes on mixing with Ag(OCOCF$_3$).

UV−vis spectra of the expanded radialenes **7**−**9** exhibited longer wavelength absorptions than [3]dendralene **4**, reflecting either an extension of π-conjugation or an increase of planarity in **7**−**9** (see the Supporting Information). Although **7** possesses a smaller π-conjugated system than **8** and **9**, **7** shows a longer absorption maximum than **8** and **9**. Since the B3LYP/6-31G* calculations of the core radialene frameworks in **7**−**9** exhibit similar structural parameters (bond distances, NAO charges, etc.) except for the ethynylene bridges, all expanded radialenes can be regarded as a similar cross-conjugated system. Thus, the longer absorption maximum in **7** may be attributable to its larger effective conjugation.

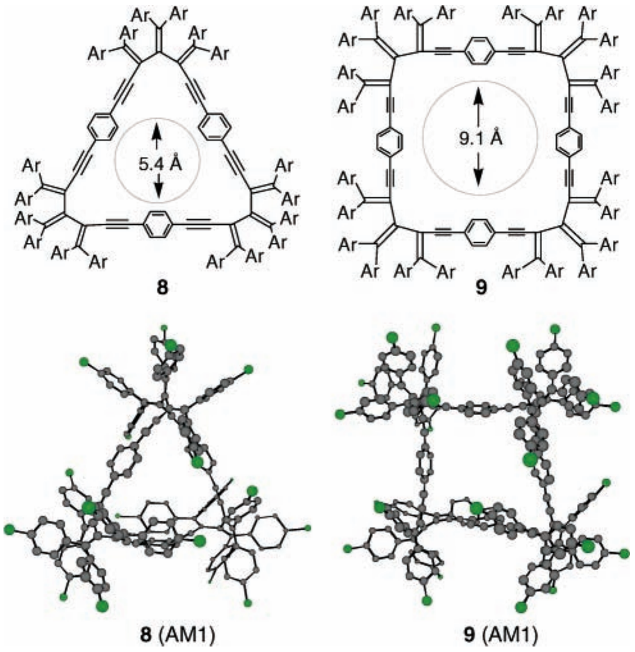


Figure 5. Inner cavities and AM1-calculated structures of **8** and **9**.

Acknowledgment. This work has been supported in part by CREST of JST (Japan Science and Technology Corp.). We thank Dr. Yoshihiro Miyake, Dr. Masato Yoshida, and Prof. Masahiko Hada, Tokyo Metropolitan University, for helpful discussions.

Supporting Information Available: Spectroscopic data of **2**, **4**, **5**, **7**, **7**·Ag$^+$, **8**, and **9** and X-ray data of **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL048146G

---

(12) (a) Yoshida, T.; Kuwatani, Y.; Hara, K.; Yoshida, M.; Matsuyama, H.; Iyoda, M.; Nagase, S. *Tetrahedron Lett.* **2001**, *42*, 53. (b) Iyoda, M.; Horino, T.; Takahashi, F.; Hasegawa, M.; Yoshida, M.; Kuwatani, Y. *Tetrahedron Lett.* **2001**, *42*, 6833.