## Novel $\pi$ -Expanded Radialene Macrocycles with Inner Cavity

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ABSTRACT



Polyenyne macrocycles with  $\pi$ -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  $\pi$ -extended [9]radialene can incorporate a silver cation.

Polyenyne macrocycles have attracted considerable attention because of their  $\pi$ -conjugation, all-carbon networks, formation of unusual metal complexes, self-association, and inclusion properties.<sup>1,2</sup> Among them, cylindrical  $\pi$ -systems with a shape-persistent macrocyclic structure<sup>3</sup> can be regarded as  $\pi$ -cavitands and are expected to show unique structures, host/guest interactions, and interesting electronic properties.<sup>4</sup> Although these molecules do not exhibit perfect cyclic conjugation, fully unsaturated macrocycles form a  $\pi$ -cavity with a concave—convex nature. We report here the synthesis of  $\pi$ -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,<sup>5,6</sup> 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

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approach to large-numbered radialenes is  $\pi$ -extension of *exo*methylene groups by insertion of double or triple bonds.<sup>6</sup> However, no  $\pi$ -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.<sup>7,8</sup> On the basis of these results, we designed the synthesis of  $\pi$ -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.

The molecular structure of **4** obtained by X-ray crystallography is shown in Figure 1.<sup>9</sup> 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.

The <sup>1</sup>H 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:  $\delta$  7.44 and 5.37 (**1** in Figure 2c); *m*-H:  $\delta$  7.33 and 6.74 (**0** in Figure 2c)]. Quantitative saturation transfer experiments gave  $\Delta G^{\ddagger} = 12.4$  kcal mol<sup>-1</sup> at 200 K for the ring **a** rotation.<sup>10</sup>

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<sup>-1</sup>, 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

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<sup>(9)</sup> 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,  $\alpha = 91.42(1)^\circ$ ,  $\beta = 93.51(1)^\circ$ ,  $\gamma = 109.86(1)^\circ$ , V = 1937.7(5) Å<sup>3</sup>, Z = 2,  $D_c = 1.356$  g/cm<sup>3</sup>, F(000) = 808,  $\mu$ (Mo K $\alpha$ ) = 4.75 cm<sup>-1</sup>, R = 0.071,  $R_w$ = 0.129, GOF = 1.949. All measurements were performed on a Rigaku AFC7R diffractometer with graphite monochromated Mo K $\alpha$  ( $\lambda = 0.716$  69 Å) radiation at 23 °C. Among a total of 9375 reflections measured, 8893 were unique and the observed ( $I \ge 3.00\sigma(I)$ ) 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.

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**Figure 2.** Temperature-dependent <sup>1</sup>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  $\delta$  1.41 and 1.38 (CDCl<sub>3</sub>) coalesced into a single peak at 43 °C. Total line shape analysis afforded  $\Delta G^{\ddagger} = 17.1$  kcal mol<sup>-1</sup> 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<sup>-1</sup> at 250 K for the ring **a** rotation (Figure 3).



Rotation of ring **a**:  $\Delta G^{\neq} = 13.5$  kcal mol<sup>-1</sup>

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  $Cu(OAc)_2$ ·2H<sub>2</sub>O in pyridine—methanol under Eglinton—Glaser conditions<sup>11</sup>



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 <sup>1</sup>H and <sup>13</sup>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<sup>-1</sup> 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<sub>2</sub>Cl<sub>2</sub>, and  $\Delta G^{\ddagger} = 15.5 \text{ kcal mol}^{-1}$  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<sup>-1</sup> 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  $AgClO_4$ .<sup>12</sup> The complex formation was

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



The cyclic trimer and tetramer 8 and 9 expanded by 1,4phenylene-ethynylene bridges show  $D_3$ - and  $D_4$ -symmetric <sup>1</sup>H and <sup>13</sup>C NMR signals at room temperature, although the <sup>1</sup>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  $\Delta G^{\dagger} = 15.1$  kcal mol<sup>-1</sup> (quantitative saturation transfer experiments in CDCl<sub>3</sub> 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 <sup>1</sup>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, reflect-



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

ing either an extension of  $\pi$ -conjugation or an increase of planarity in 7–9 (see the Supporting Information). Although 7 possesses a smaller  $\pi$ -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.

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

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