

# Diphenylanthracene Macrocycles from Reductive Zirconocene Coupling: On the Edge of Steric Overload

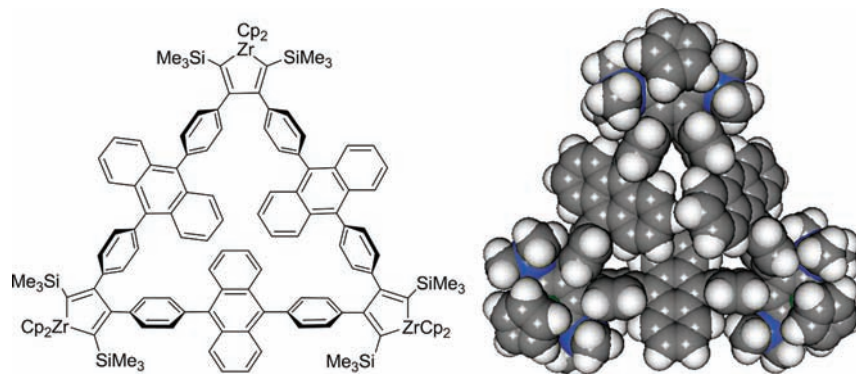
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## ABSTRACT



Trimeric diphenylanthracene macrocycles were synthesized via the zirconocene-mediated coupling of 9,10-bis-[4-trimethylsilyl(ethynyl)phenyl]anthracene. The macrocycles feature a strained architecture due to orientation of the anthracene units into the plane of the macrocycle. The demetalated cyclophane exhibits a considerably higher flexibility in solution, while the zirconocene-containing macrocycle is quite rigid.

Macrocycles are desirable synthetic targets due to various applications such as catalysis,<sup>1</sup> molecular recognition and sensing,<sup>2</sup> and host–guest chemistry.<sup>3</sup> However, macrocycle syntheses often require high-dilution conditions and multiple purification steps, resulting in a limited amount of the desired product.<sup>4</sup> In recent years, this laboratory has developed zirconocene-mediated couplings of dialkynes as an efficient, alternative route to macrocycles. Due to the reversibility of this macrocyclization process, high yields of the thermodynamically most stable product are often obtained. Thus,

macrocycles of different sizes and shapes,<sup>5</sup> incorporating functionalities<sup>6</sup> and chirality,<sup>7</sup> have been synthesized. Of further interest is expansion of this methodology to the preparation of tube-shaped molecules by use of dialkynes with spatially expanded moieties to shield off the sides of the macrocycles. Due to their synthetic availability, an initial effort began with anthracene-based dialkynyl compounds.

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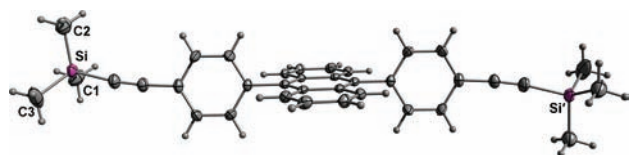
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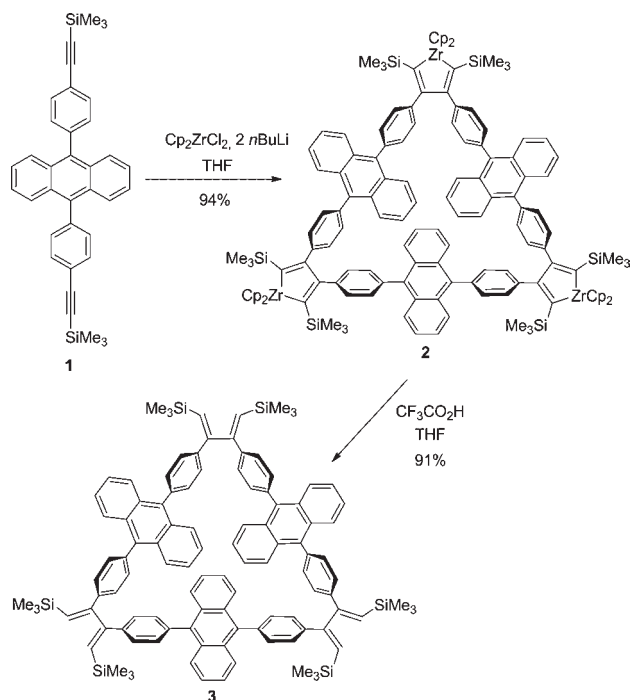


**Figure 1.** Molecular structure of **1** with thermal displacement parameters drawn at 50% probability (for crystallographic details, see Supporting Information).

The readily available 9,10-bis(trimethylsilylethynyl)anthracene was prepared from lithiated trimethylsilylacetylene and anthraquinone.<sup>8</sup> However, all attempts to couple this diyne into a macrocycle—using either the Negishi protocol for *in situ* generation of the zirconocene reagent from  $\text{Cp}_2\text{ZrCl}_2/n\text{BuLi}$ <sup>9</sup> or Rosenthal's  $\text{Cp}_2\text{Zr}(\text{py})(\text{Me}_3\text{SiCCSiMe}_3)$ <sup>10</sup>—resulted in the formation of complex product mixtures. Presumably, this outcome results from steric congestions that prevent selective formation of one macrocyclic product. Thus, it was assumed that this limitation might be overcome by elongation of the diyne spacer groups, by incorporation of phenylene groups into the 9- and 10-positions of the anthracene derivative. 9,10-Bis-[4-(trimethylsilylethynyl)phenyl]anthracene (**1**) was prepared by lithiation of 4-bromo-1-(trimethylsilylethynyl)benzene with *n*BuLi at low temperature and subsequent reaction with 9,10-anthraquinone followed by rearomatization with tin(II) chloride (Supporting Information). Figure 1 depicts the molecular structure of the  $C_7$  symmetric dialkyne, which features the expected pseudoperpendicular arrangement of the anthracene moiety relative to the adjacent phenylene groups. The angle between the least-squares planes of the phenylene and anthracene groups is  $84.19(4)^\circ$ , which is in the range of values reported for analogous compounds.<sup>11</sup>

For macrocyclization the dialkyne **1** was used in a previously established zirconocene coupling protocol using the Negishi reagent.<sup>9</sup> Heating the reaction mixture for 20 h at  $60^\circ\text{C}$  and subsequent aqueous workup generated the corresponding metal-containing macrocycle **2** as a yellow powder in excellent yield (94%, Scheme 1). Compound **2** is stable as a solid in the glovebox for weeks but decomposes in solution within hours. Unfortunately, various attempts to crystallize **2** failed and mass spectrometry showed only fragments of the expected<sup>5d</sup> trimeric macrocycle. To verify the trimeric nature of the macrocycle, **2** was converted to the corresponding cyclophane **3**. Treatment

**Scheme 1**



of **2** with trifluoroacetic acid in THF afforded the demetallated macrocycle **3** as a colorless solid in 91% yield. The trimeric structure of the cyclophane and thus of the zirconacycle **2** was confirmed by mass spectrometry and X-ray diffraction analysis. Single crystals were grown by slow concentration of a hexane/THF solution of **3**.

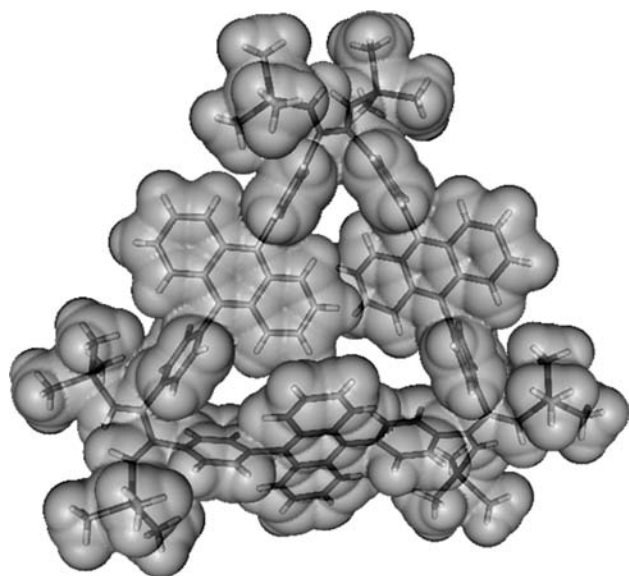
Figure 2 depicts the molecular structure of the trimeric cyclophane **3**. Analogous to the starting diyne, the anthracene units adopt a nearly perpendicular arrangement relative to the phenylene substituents. However, due to steric congestion within the macrocycle the angles between the least-squares planes of adjacent anthracene and phenylene groups deviate considerably from  $90^\circ$  and range between  $61.5^\circ$  and  $83.0^\circ$  ( $84.2^\circ$  in dialkyne **1**) such that the three anthracenes adopt a helical arrangement.<sup>11</sup> Because the phenylene substituents are roughly perpendicular to the cyclophane plane, the anthracene moieties are forced to adopt orientations that leave them substantially tilted into the plane of the macrocycle, such that the “wings” of each anthracene point into and away from the center of the macrocycle. The butadiene units exhibit torsion angles ranging from  $39^\circ$  to  $46^\circ$ , which are slightly larger than corresponding values observed for similar cyclophanes,<sup>5d</sup> implying significant steric pressure in the macrocycle. Steric congestion in **3** is apparent in a plot of the van der Waals radii (Figure 2). Note also that steric congestion in macrocycle **3** appears to lead to decomposition in solution within days. Attempts to extend this macrocyclization to the pentacene analogue of **2**, under the same reaction conditions, failed (see Supporting Information). As with 9,10-bis(trimethylsilylethynyl)anthracene, this is probably

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(11) Angles between  $68^\circ$  and  $90^\circ$  are usually observed in diphenylanthracene compounds, depending on the substitution pattern and solvents used. For examples, see: (a) Iida, A.; Yamaguchi, S. *Chem. Commun.* **2009**, 3002. (b) Adams, J. M.; Ramdas, S. *Acta Crystallogr., Sect. B* **1979**, *35*, 679. (c) Brownstein, S. K.; Ding, J.; Robertson, G.; Roovers, J.; Enright, G. *J. Org. Chem.* **2002**, *67*, 663. (d) Tanaka, T.; Tasaki, T.; Aoyama, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12453. (e) Wagner, G.; Herrmann, R.; Scherer, W. *J. Organomet. Chem.* **1996**, *516*, 225.



**Figure 2.** Molecular structure of cyclophane **3** (for crystallographic details, see the Supporting Information) including van der Waals radii.

due to unfavorable steric interactions which prevent the selective formation of one macrocyclic product.

Interestingly, the  $^1\text{H}$  NMR spectra of macrocycles **2** and **3** exhibit key differences in the region associated with the anthracene protons (Supporting Information). Thus, the zirconocene macrocycle **2** exhibits four clearly resolved signals for the anthracene protons at 20 °C, as expected for a structure with the three anthracene groups strongly leaning toward the center of the macrocycle. In addition, one proton resonance is significantly shifted upfield and appears at 6.21 ppm in chloroform-*d* and at 6.51 ppm in toluene-*d*<sub>8</sub>.<sup>12</sup> This apparently reflects a stacking of the anthrylene units in solution, in the manner observed for **3** in the crystal. Thus, the 2,3-anthrylene protons oriented toward the macrocycle center experience ring currents that lead to the observed upfield shift.<sup>13</sup> In contrast to **2**, the demetalated compound **3** exhibits only two  $^1\text{H}$  NMR signals for the anthracene protons at room temperature, which indicates a dynamic process that exchanges the outer rings of the anthracene groups, and increased flexibility of

(12) For examples of NMR studies on 9,10-substituted anthracenes, see: (a) Nikitin, K.; Müller-Bunz, H.; Ortin, Y.; Muldoon, J.; McGlinchey, M. *Org. Lett.* **2011**, *13*, 256. (b) Zehm, D.; Fudickar, W.; Hans, M.; Schilde, U.; Kelling, A.; Linker, T. *Chem.—Eur. J.* **2008**, *14*, 11429. (c) Fairfull-Smith, K. E.; Bottle, S. E. *Eur. J. Org. Chem.* **2008**, 5391. (d) Nakatsuji, S.; Matsuda, K.; Uesugi, Y.; Nakashima, K.; Akiyama, S.; Fabian, W. *J. Chem. Soc., Perkin Trans. 1* **1992**, 755. (e) Schmidt, R.; Göttling, S.; Leusser, D.; Stalke, D.; Krause, A.-M.; Würthner, F. *J. Mater. Chem.* **2006**, *16*, 3708. (f) Valentini, L.; Bagnis, D.; Marrocchi, A.; Seri, M.; Taticchi, A.; Kenny, J. M. *Chem. Mater.* **2008**, *20*, 32.

(13) For other examples of molecules exhibiting resonance upfield shifting in  $^1\text{H}$  NMR spectra due to intramolecular  $\pi$ - $\pi$  stacking and/or ring current shielding effects in constrained structures, see: (a) Ting, Y.; Lai, Y. H. *J. Am. Chem. Soc.* **2004**, *126*, 909. (b) Mei, X.; Wolf, C. *J. Org. Chem.* **2005**, *70*, 2299. (c) Nandy, R.; Subramoni, M.; Varghese, B.; Sankararaman, S. *J. Org. Chem.* **2007**, *72*, 938.

the diene units relative to the zirconacyclopentadiene rings of **3**. Related dynamic behavior was observed for a trimeric 9,10-anthrylene ethynylene macrocycle.<sup>14</sup>

To further probe conformational changes in macrocycles **2** and **3**, VT-NMR studies were performed. High temperature NMR studies of **2** revealed only decomposition of the macrocycle at temperatures above 40 °C. This suggests that decoupling of the zirconocene-containing macrocycle requires less energy than rotation of the anthracene moieties. This lability is consistent with the observed, facile fragmentation of the macrocycle observed by mass spectrometry. Interestingly, low-temperature NMR spectra of cyclophane **3** in dichloromethane-*d*<sub>2</sub> feature only insignificant chemical shift changes from 20 to –80 °C. This suggests that, despite the common, trimeric nature of **2** and **3**, these macrocycles feature significant structural differences.

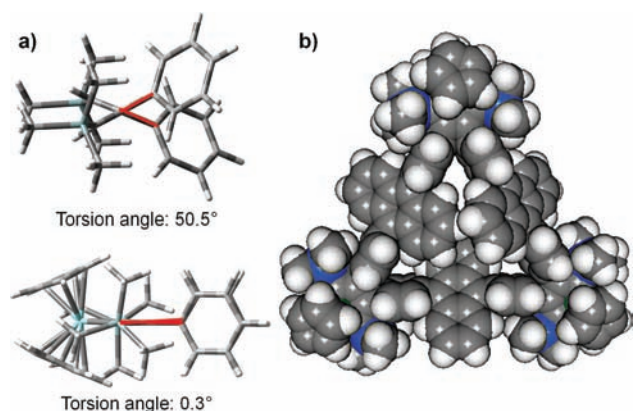
Comparisons with analogous macrocycles, in metalated and demetalated forms, indicate that the most dramatic structural change associated with hydrolytic removal of the zirconocene units is reflected in differences in torsion angles about the butadiene/zirconacyclopentadiene “corners” of the macrocycles. For example, in the zirconocene-based macrocycle resulting from cyclization of 4,4′-bis-(trimethylsilylethynyl)biphenyl, the phenylene substituents are highly eclipsed as reflected in a  $(\text{C}_6\text{H}_4)\text{C}-\text{C}-\text{C}(\text{C}_6\text{H}_4)$  torsion angle of only 2° for the zirconacyclopentadiene units. The corresponding cyclophane is considerably twisted at the butadiene groups (analogous torsion angle of 37.0°).<sup>5a</sup> Similar structural differences were observed by DFT studies of the simple (*1E,3E*)-1,4-bis(trimethylsilyl)-2,3-diphenylbuta-1,3-diene and its corresponding zirconacycle, in which no ring strain influences the arrangement of the phenyl substituents (for computational details, see Supporting Information).<sup>15</sup> The optimized structures (Figure 3a) feature torsion angles of 0.3° and 50.5°, respectively. Due to steric pressure in the cyclic structures, this difference is less pronounced in **2** and **3**. The average torsion angle for the optimized structure of **2** was found to be 9.66°, whereas the analogous torsion angle in the crystal structure of **3** is 43.7°.

The increased torsion angles associated with demetalation result in a conformationally less rigid macrocycle. In the case of compounds **2** and **3** this may explain the observed differences in the  $^1\text{H}$  NMR spectra. In **3**, the phenylene substituents have more freedom of motion with respect to one another, via lower rotational barriers about the  $(\text{C}_6\text{H}_4)\text{C}-\text{C}(\text{diene})$  and  $(\text{C}_6\text{H}_4)\text{C}-\text{C}(\text{C}_6\text{H}_4)$  bonds. The rather bulky silyl groups also appear to play a role in determining the conformational rigidity of the macrocycles. In particular, these groups should hinder rotation about the  $(\text{C}_6\text{H}_4)\text{C}-\text{C}(\text{zirconacycle})$  bonds of **2**. This is apparent from a space-filling model of the optimized structure of **2** (Figure 3b) and from distances between adjacent phenylene and silyl groups in **2** and **3**. The distance between

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**Figure 3.** (a) Different torsional angles of the phenylene substituents on (1*E*,3*E*)-1,4-bis(trimethylsilyl)-2,3-diphenylbuta-1,3-diene (top) and its corresponding zirconocycle (bottom) groups; (b) space-filling model of an energy-optimized structure of **2** (Supporting Information).

the center of the phenylene group and the carbon atom of the closest methyl group average to 3.98 Å (crystal structure) and 3.99 Å (DFT calculations) in **3** and only 3.49 Å in **2**.

Thus, conformational changes in the more rigid macrocycle **2** appear to largely be the result of restricted rotations

(16) The planar arrangement of the phenylene and anthrylene groups is not a minimum on the potential energy surface. Both structures are transition states for rotation about the phenylene–anthrylene bond. Deviations of 30° from the ideal perpendicular arrangement have only small influences on the energy of the system (Supporting Information).

about the zirconacyclopentadiene–phenylene–anthracene linkages. This is partially supported by DFT studies on the model system 9,10-diphenylanthracene, which reveal a rather high barrier for rotation in this molecule (Supporting Information). The perpendicular arrangement of the phenyl groups with respect to the anthracene is considerably favored compared to the planar,  $D_{2h}$ -symmetric structure ( $\Delta H = 93$  kcal/mol) and to a  $C_{2v}$ -symmetric isomer with one phenyl ring coplanar to the anthracene ( $\Delta H = 40$  kcal/mol).<sup>16</sup> These considerations indicate that restricted rotations in macrocycle **2** result in a persistent conformation with the anthrylene groups tilted toward the inside of the macrocyclic ring.

In conclusion, the trimeric 9,10-anthrylene phenylene macrocycles **2** and **3** are highly strained due to steric pressure which forces the anthracene moieties into the plane of the macrocycle. This arrangement of one ring of each anthrylene group outside of the macrocyclic core should allow for the introduction of substituents on these “outer” rings to create unusual molecular shapes. The results reported here should also be of use in the design of new nanoscopic organic structures via zirconocene-coupling routes.

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**Supporting Information Available.** Experimental, spectroscopic, computational, and crystallographic details of the presented compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.