Highlights

Cyclophanes

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New Strategies for Synthesizing Short Sections of Carbon Nanotubes**

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aromatic hydrocarbons · cyclophanes · macrocycles · strained molecules · synthetic methods

Dedicated to Professor Julius Rebek, Jr. on the occasion of his 65th birthday

"Bent and battered benzene rings" have captivated organic chemists since the middle of the last century.[1] Most commonly, the bending is enforced by bridging the *para* (or *meta*) positions of benzene with short chains of atoms to produce "cyclophanes".[1,2] The degree of bending depends inversely on the length of the tether, and these strained macrocycles sometimes contain more than one bridged benzene ring. Cyclophanes incorporating bent naphthalene units or even larger polyarenes have also been prepared. In recent months, one of the highest unclimbed pinnacles in this field was finally conquered, and shortly thereafter, the impressive record for bending was resoundingly shattered. Figure 1 depicts the new cyclophanes that have recently rocked this venerable branch of chemistry. The scientists responsible for their synthesis have noted the structural features that these compounds share with carbon nanotubes (Figure 1), and they are already contemplating ways to extend their successes toward the rational, chemical synthesis of carbon nanotubes.

The first of these recent breakthroughs was reported in late 2008 by Bertozzi and co-workers.[3] As newcomers to cyclophane chemistry, this creative team conceived a fresh strategy for synthesizing macrocycles composed entirely of *para*-substituted benzene rings. Implementing the plan required a novel solution to one particularly challenging late-stage transformation, but, ultimately, they prepared and spectroscopically characterized three members of the previously unknown family of [*N*]cycloparaphenylenes (**CPP-9**, **CPP-12**, and **CPP-18**; $N = 9$, 12, and 18, respectively).[4]

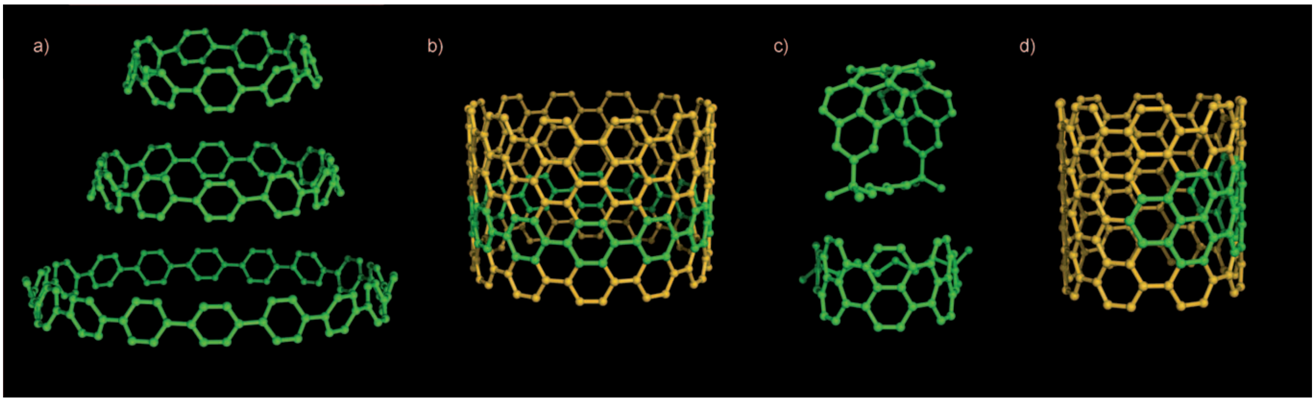

Figure 1. a) [*N*]cycloparaphenylenes (**CPP-9**, **CPP-12**, and **CPP-18**, respectively); b) mapping of **CPP-12** onto a section of a [12,12]carbon nanotube; c) 1,1,8,8-tetramethyl[8](2,11)teropyrenophane (**4**); d) mapping of the teropyrene unit in **4** onto a section of an [8,8]carbon nanotube.

Besides solving one of the longest standing problems in cyclophane chemistry, this synthesis is also remarkable for its brevity: only five steps were required to assemble the fully aromatized macrocycles from 1,4-diiodobenzene (Scheme 1). The *syn*-selective addition of 4-iodophenyllithium to *para*-benzoquinone provided the key building block (**1**), from which the final target molecules were all assembled. A portion of **1** was converted into the corresponding diboronate (**2**), and Suzuki coupling of **1** with **2** gave macrocycles **3a**, **3b**, and **3c** in a combined yield of 22%. The smallest of these cyclic oligomers actually appeared as an unexpected bonus and presumably arises from the homocoupling of **2**, which gives an acyclic dimer that then cross-couples with **1**. The syntheses were completed by chromatographic separation of the three macrocycles and then reductive elimination of all the methoxy groups by the action of lithium naphthalenide at

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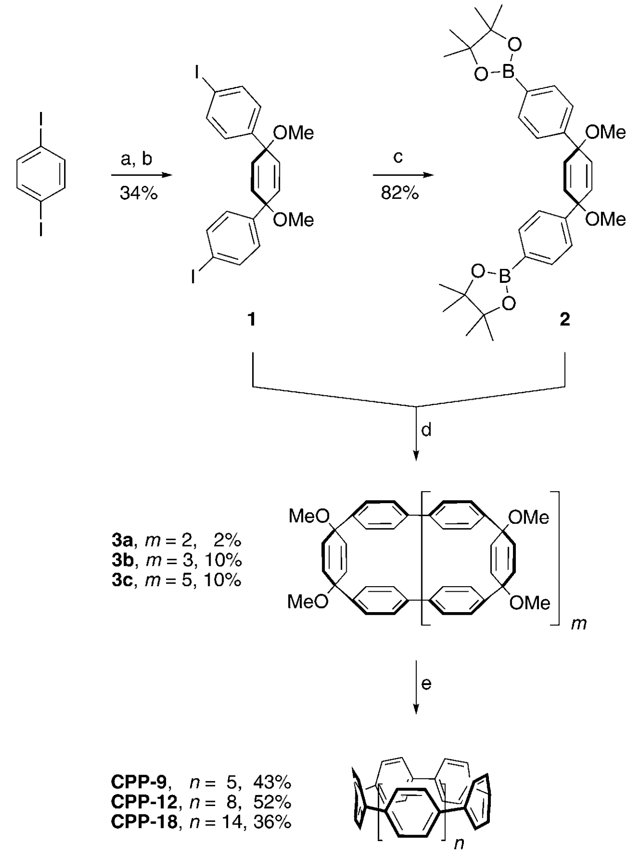


Scheme 1. a) 1. *n*BuLi, THF, −78 °C, 2. benzoquinone; b) 1. NaH, THF, 0 °C, 2. MeI, 0 °C to RT; c) 1. *n*BuLi, THF, −78 °C, 2. isopropyl pinacol borate, −78 °C; d) [Pd(PPh$_3$)$_4$], Cs$_2$CO$_3$, toluene/methanol (10:1), 80 °C; e) lithium naphthalenide, THF, −78 °C.

−78 °C. The known propensity of cyclophanes to suffer skeletal rearrangements under acidic conditions necessitated the development of this clever aromatization protocol.

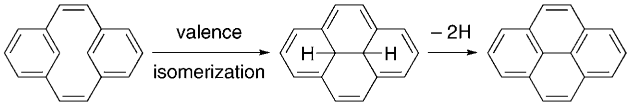
A strain energy of 47 kcal mol^{-1} is calculated for the smallest of these three cyclophanes (**CPP-9**); however, the more gentle curvatures of the larger rings impose less bending on the benzene subunits. The calculated strain energy of **CPP-12** is only 28 kcal mol^{-1}, whereas that of **CPP-18** is just 5 kcal mol^{-1}. Still larger [*N*]cycloparaphenylenes should be virtually strain free.

In contrast to the stylized picture of the **CPPs** in Scheme 1, the benzene rings in **CPP-18** are calculated to tilt inwards and outwards around the perimeter, with dihedral angles alternating between +34° and −34° (Figure 1 a), which is close to the dihedral angle found in biphenyl itself.[5] The dihedral angles in **CPP-12** are calculated to alternate between +33° and −33°, whereas the odd number of benzene rings in **CPP-9** necessarily leads to a more complicated assortment of dihedral angles.

The intriguing Möbius conformations of these **CPPs**, with dihedral angles all of the same sign and equal in magnitude to 180°/*N*, are calculated to lie at least 2 kcal mol^{-1} per phenyl ring higher in energy than the minimum-energy conformations. It is interesting to note, however, that dihedral angles of +30° in **CPP-18** would result in an overall one-and-a-half twist (3 × 180°) Möbius conformation, but a full appreciation of the complete conformational landscape available to these fascinating "nanohoops" must await more extensive calculations. No X-ray crystal structures have yet been reported.

While this work was underway, Bodwell and co-workers were completing the synthesis of a cyclophane containing a long polyarene strip that is bent back on itself by nearly 180° (**4**, Figure 1 c).[6] From the X-ray crystal structure, a value of 167° was determined for the end-to-end bending of the 36-carbon teropyrene unit in **4**.[7] With this teropyrenophane, the Bodwell research group has dramatically rewritten the record book in cyclophane chemistry in terms of both the largest bridged polyarene (previous record: 20-carbon corannulene[8]) and the most bent polyarene (previous record: 109.2° for bent pyrene[9]).

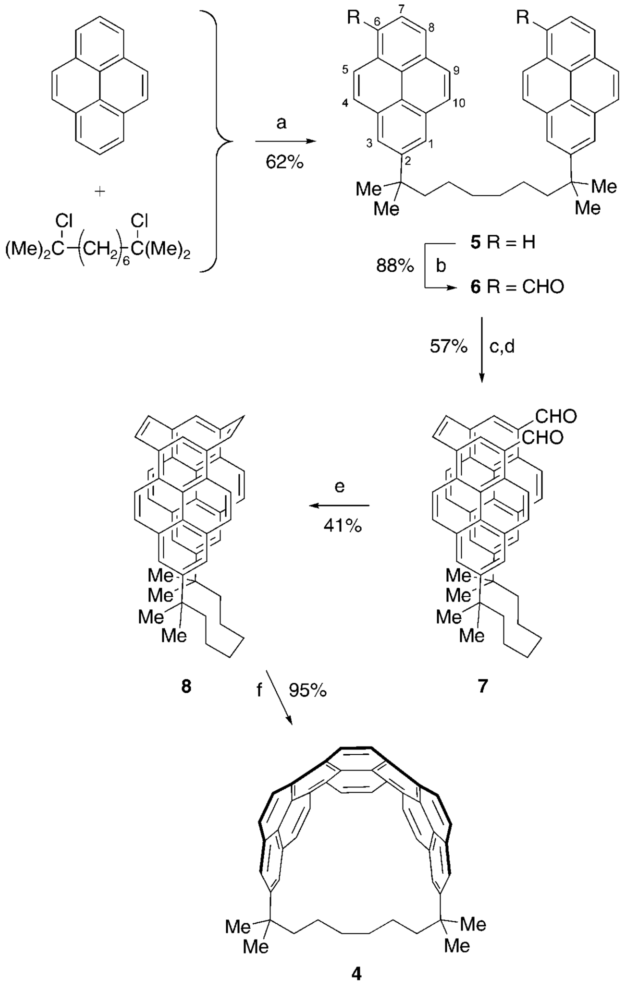
Rather than start from a planar, fully aromatic teropyrene and try to bend it around, Bodwell and co-workers built the long polyarene of **4** in the last step of the synthesis by stitching together the tips of two shorter pyrene units that were already tethered at their other ends. This strategy exploited a valence isomerization/dehydrogenation reaction that had been used before to transform simpler [2.2]metacyclophane dienes into pyrenes (Scheme 2).[9,10]



Scheme 2. The valence isomerization/dehydrogenation method for converting [2.2]metacyclophane dienes into longer polyarenes

In just five steps, the tethered [2.2]metapyrenophane diene **8**, with two pyrenes units held in a face-to-face arrangement, was efficiently synthesized from a readily accessible dichloroalkane (Scheme 3). The known selectivity of tertiary carbocations to attack the 2-position of pyrene in Friedel–Crafts alkylations conveniently provided a method for linking the tip of one pyrene to the tip of another through an alkyl chain (**5**). Most other electrophiles attack the intrinsically more reactive 1-, 3-, 6-, and 8-positions of pyrene, and formylation of **5** gave, as expected, the unhindered dialdehyde **6** in 88 % yield. McMurry coupling of the two aldehydes in **6** and a second formylation gave the unsaturated (2,6)pyrenophane **7**, and another McMurry coupling gave the (2,6,8)pyrenophane diene **8**.[11] Valence isomerization/dehydrogenation to give teropyrenophane **4** was achieved in 95 % yield by heating **8** in *m*-xylene at reflux (145 °C) with DDQ for two days.

Historically, the strain energy in cyclophanes has been introduced most often by ring contraction reactions that progressively shorten the bridges.[1,2] The strategies employed by the research groups of Bertozzi and Bodwell for preparing their new cyclophanes (Figure 1), on the other hand, both relied on the aromatization of less-strained dihydroaromatic ring systems in the last step to build in the strain. This tactic of drawing on the energetic benefits of aromatization to pay for the energetic cost of introducing additional strain has previously been exploited to synthesize other classes of



Scheme 3. a) $AlCl_3$, CH_2Cl_2, 0 °C to RT, 4 h; b) Cl_2CHOCH_3, $TiCl_4$, CH_2Cl_2, 0 °C to RT, 2 h; c) $TiCl_4$, Zn, pyridine, THF, 0 °C to reflux, 5 h; d) Cl_2CHOCH_3, $TiCl_4$, CH_2Cl_2, 0 °C to RT, 2 h; e) $TiCl_4$, Zn, pyridine, THF, 0 °C to reflux, 4 h; f) DDQ, *m*-xylene, 145 °C, 48 h. DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

nonplanar aromatic compounds, such as the bowl-shaped polyarenes corannulene[12] and sumanene,[13] and further applications in cyclophane chemistry are bound to follow.

The ^{1}H NMR spectra of **CPP-9**, **CPP-12**, **CPP-18**, and **4** reveal substantial deshielding of the hydrogen atoms attached to the aromatic rings by strong, induced diamagnetic ring currents ($\delta = 7.53$ ppm for **CPP-9**, 7.62 ppm for **CPP-12**, 7.71 ppm for **CPP-18**, and 7.42–8.62 ppm for **4**). The strengths of these ring currents attest to the persistence of good cyclic conjugation within the aromatic rings of all four cyclophanes, despite their nonplanarity. UV/Vis absorption and fluorescence spectra are also reported for all four cyclophanes: **CPP-9** is described as "yellowish-white", whereas **CPP-12** and **CPP-18** are colorless, and **4** is orange.

The **CPP** nanohoops synthesized by Bertozzi and co-workers can be viewed as ultrashort sections of "armchair" carbon nanotubes of various diameters (Figure 1 b). The curved teropyrene (**4**) synthesized by Bodwell and co-workers, on the other hand, makes up approximately half of a wider section (an aromatic belt) of an [8,8]nanotube (Figure 1 d). Both research groups allude to the enticing prospect of using armchair nanohoops or nanobelts as templates from which to grow long, open-ended, armchair carbon nanotubes of predefined diameter. The same growth process has been envisioned as a route to nanotubes that are closed at one end, starting from hemispherical polyarenes with armchair rims;[14] however, the chemistry to enable the growth of such armchair nanotubes from small-molecule templates remains to be worked out. These recent triumphs by the research groups of Bertozzi and Bodwell instill confidence that, in time, we will see even this final obstacle overcome.

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