Carbon Nanorings

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A Modular and Size-Selective Synthesis of [*n*]Cycloparaphenylenes: A Step toward the Selective Synthesis of [*n*,*n*] Single-Walled Carbon Nanotubes**

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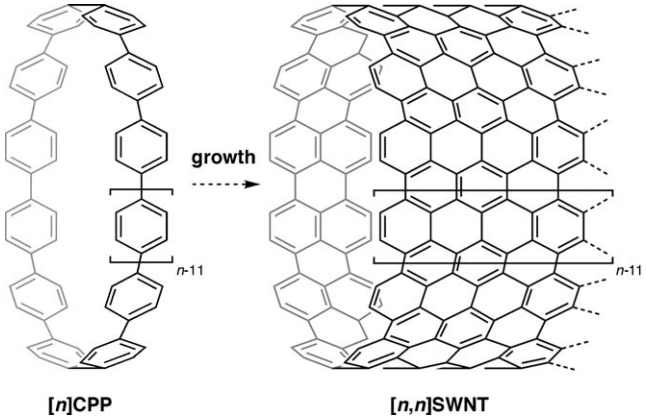
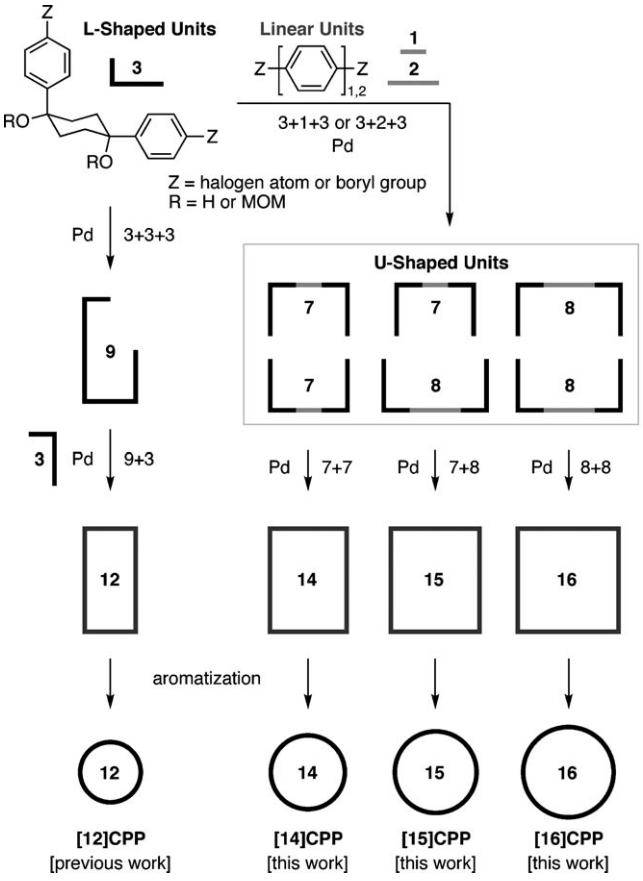
For nearly one century, cycloparaphenylene (CPP), a simple string of benzene rings, has captivated scientists for many reasons.[1,2] Adding to their sheer aesthetic appeal and unique curved conjugation, CPPs represent the shortest sidewall segment of armchair carbon nanotube structures (Scheme 1).[1,3] After extensive trials by numerous chemists,[4] the groups led by Bertozzi,[5] Itami,[6,7] and Yamago[8] have finally accomplished the bottom-up organic synthesis of some [*n*]CPPs ($n = 8$, 9, 12, 18). Although several possible routes toward CPP structures have been identified in these studies, a uniform strategy allowing the flexible and size-selective synthesis of a range of [*n*]CPPs has yet to be developed.



Scheme 1. [*n*]CPPs as possible precursors or seeds for [*n*,*n*] single-walled carbon nanotubes.

Devising such a strategy is important in view of the expectation that CPP could serve as a precursor or seed in the preparation of structurally uniform armchair single-walled carbon nanotubes (SWNTs) (Scheme 1).[1,9] As proposed and demonstrated by others,[10] the amplification growth strategy using a relatively short hydrocarbon template such as CPP holds the promise of a long-awaited selective synthesis of SWNTs. In such a strategy, a modular and size-selective synthesis of [*n*]CPPs would be critically important in providing [*n*,*n*]SWNTs in a controlled and selective fashion. We now describe a modular and size-selective synthetic approach to [*n*]CPPs ($n \geq 14$) and report the synthesis of [14]-, [15]-, and [16]CPP as a proof-of-principle of our new strategy.

Our CPP synthesis is very flexible, assembling bent and linear building blocks in a controlled and programmable manner. In essence, we previously synthesized [12]CPP in a 3+3+3+3 mode using a terphenyl-equivalent L-shaped diphenylcyclohexane unit; Pd-catalyzed stepwise formation of a "box" (3+3+3 and then 9+3), followed by aromatization (Scheme 2).[6] By strategically varying the number of bent



Scheme 2. A modular and size-selective synthetic strategy for [*n*]CPPs.

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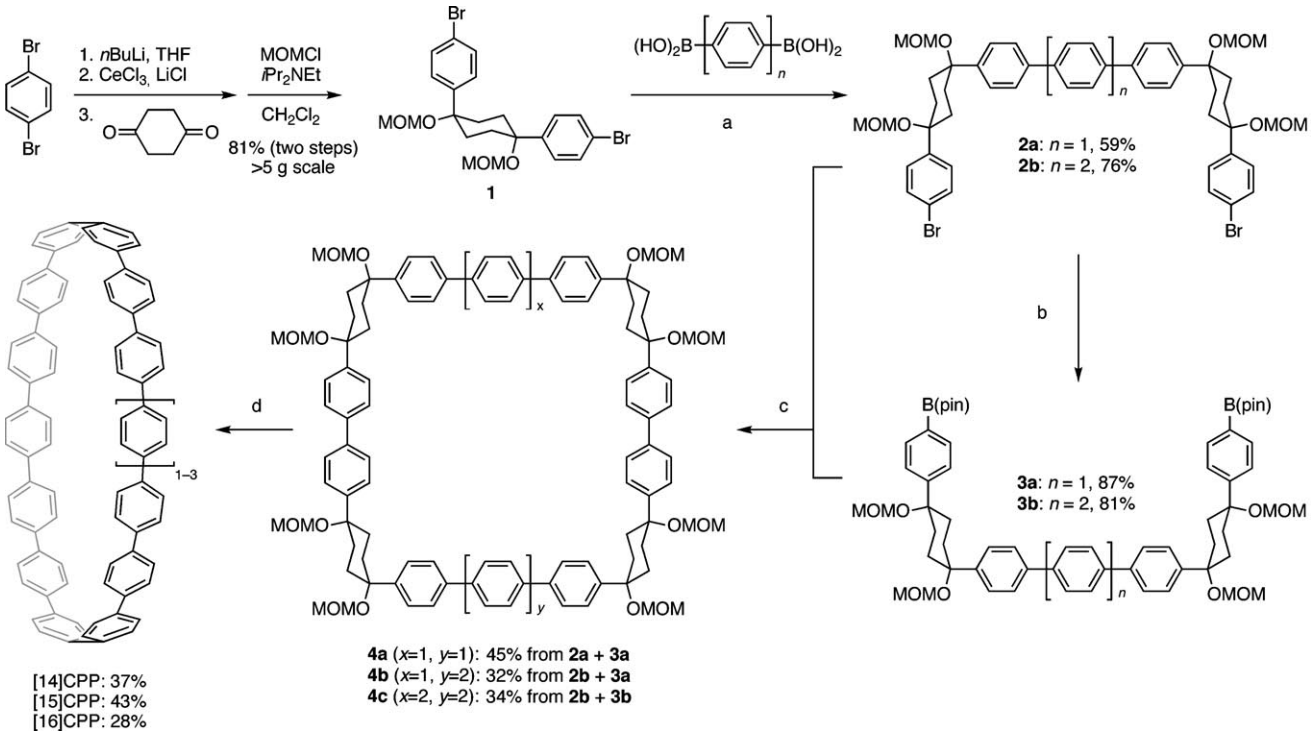
(cyclohexane) and linear (benzene) building blocks, a range of [*n*]CPPs should be accessible. For example, the assembly of an L-shaped diphenylcyclohexane unit and a linear benzene/biphenyl unit in a 3+1+3 or 3+2+3 mode should give a U-shaped septi- or octiphenyl unit (Scheme 2). The cyclizative dimerization of these U-shaped units and subsequent aromatization would lead to [14]CPP (7+7) and [16]CPP (8+8). Through a "hetero" coupling of these units, odd-numbered [*n*]CPPs such as [15]CPP (7+8) should also be accessible. Although all the reported strategies including our previous one[5,6,8] are not designed for the synthesis of odd-numbered [*n*]CPPs, our new approach makes it possible to access these CPPs in a strategic way (see below). In addition, as the number of benzene rings in these U-shaped units can be easily increased, this method can be a uniform synthetic strategy for [*n*]CPPs ($n \geq 14$).

The realization of our synthesis required a new L-shaped unit **1** (Scheme 3). Our previous L-shaped unit (the iodo analogue of **1**)[6] proved to be problematic in the synthesis of U-shaped units. As significant homocoupling of the L-shaped diiodide was observed during the Pd-catalyzed synthesis of U-shaped unit, we changed our monomer unit to the corresponding dibromide **1** expecting high selectivity for cross-coupling. Accordingly, we developed a high-yielding synthesis of L-shaped dibromide **1**: the addition of two equivalents of a 4-bromophenylcerium reagent[11] to cyclohexane-1,4-dione was followed by protection of the hydroxy groups with methoxymethyl (MOM) units (81% overall yield of **1** from 1,4-dibromobenzene). Unlike our previous organolithium method, this Ce-based protocol provided the L-shaped unit with virtually complete *cis* stereoselectivity; the formation of the unfavorable *trans* isomer and the monoaddition product were both suppressed.[12] Notably, the L-shaped dibromide **1** can be prepared on a multigram scale.

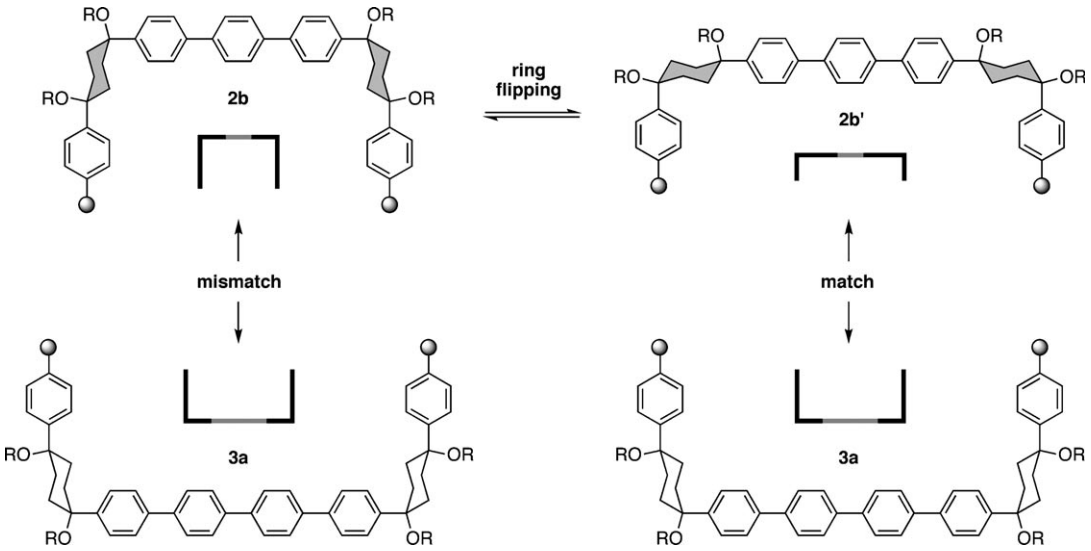
The U-shaped dibromides **2** were then prepared by the Suzuki–Miyaura coupling of benzene- or biphenyldiboronic acids with excess **1** under the catalytic influence of [Pd(PPh_3)$_4$] (**2a**: 59%, **2b**: 76%). After the reaction, most of unreacted **1** could be recovered. The treatment of **2** with (pin)BB(pin)[13] in the presence of [$Pd_2(dba)_3$]/X-Phos[13] catalyst and KOAc afforded the U-shaped diboronates **3** (**3a**: 87%, **3b**: 81%).[14]

With the requisite U-shaped units (**2** and **3**) in hand, we next investigated the macrocyclization (Scheme 3). Under somewhat dilute conditions (2 mM **2**), a cyclizative Suzuki–Miyaura coupling of **2a** and **3a** took place in the presence of $Pd(OAc)_2$/X-Phos[15] to provide the macrocycle **4a** in 45% yield. The macrocycle **4c** was similarly obtained by the coupling of **2b** and **3b**. Gratifyingly, the "hetero" coupling of **2b** and **3a** also took place to afford **4b**.

Finally, we examined the aromatization of macrocycles **4** to produce the corresponding CPPs. We previously reported that the treatment of a cyclohexane-inserted macrocycle (analogue of **4**) with *p*-toluenesulfonic acid in *m*-xylene under microwave irradiation afforded [12]CPP.[6] However, we had difficulty in adjusting the reaction parameters under these microwave conditions. After extensive screening of non-microwave conditions, we finally found that the treatment of macrocycles **4** with $NaHSO_4 \cdot H_2O$ in refluxing *m*-xylene/DMSO under air yielded [14]-, [15]-, and [16]CPP



Scheme 3. Synthesis of [14]-, [15]-, and [16]CPP. Conditions and reagents: a) [Pd(PPh_3)$_4$], Na_2CO_3, nBu_4NBr, H_2O, THF, 60°C; b) (pin)BB(pin), [$Pd_2(dba)_3$], X-Phos, KOAc, 1,4-dioxane, 90°C; c) $Pd(OAc)_2$, X-Phos, NaOH, H_2O, 1,4-dioxane, 80°C; d) $NaHSO_4 \cdot H_2O$, *m*-xylene, DMSO, reflux, under air.

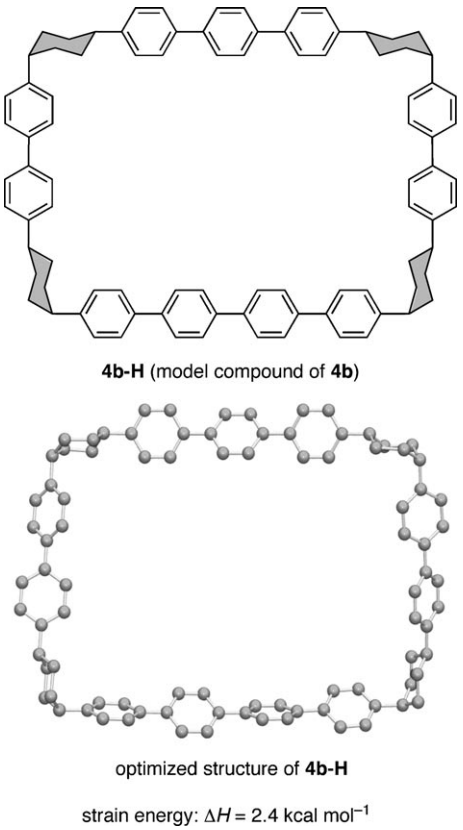


Scheme 4. Flipping of cyclohexane rings in the U-shaped units.

(Scheme 3). We assume that this aromatization consists of a sequence of 1) eightfold removal of MOM groups, 2) eightfold dehydration (dihydroxycyclohexane→cyclohexadiene), and 3) oxidation (cyclohexadiene→benzene). The use of DMSO as a co-solvent is critically important, and we assume that DMSO helps in dissolving highly polar intermediates during the aromatization. In the ^{1}H NMR spectra ($CDCl_3$), only one singlet peak is observed for all CPPs; $\delta =$ 7.65 ([14]CPP), 7.67 ([15]CPP), and 7.68 ppm ([16]CPP). Similarly, only two peaks are observed in the ^{13}C NMR spectra of these CPPs. These data clearly indicate that the benzene rings in these CPPs are rotating rather freely at room temperature, which is in line with our previous DFT studies.[7a]

The successful size-selective synthesis of [15]CPP is particularly noteworthy since none of the reported syntheses is designed for making odd-numbered [*n*]CPPs.[5,6,8] The cyclizative coupling between **2b** and **3a** en route to [15]CPP highlights the important U-shaped design element in our new strategy. From the conformations shown in Scheme 3, the "arch widths" of two U-shaped units (**2b** and **3a**) with different numbers of benzene rings are not suitable for macrocyclization (Scheme 4, left). However, when the two cyclohexane rings in **2b** undergo chair-flipping, the "arch width" of the resulting new conformation **2b′** nicely matches that of **3a** to produce **4b** (Scheme 4, right). Thus, the change in arch width induced by two cyclohexane flips corresponds roughly to the width of one benzene ring.

To increase out our understanding of the ring flipping during the macrocyclization, we optimized the structure of macrocycle **4b-H** (model compound of **4b**) by DFT calculation at the B3LYP/6-31G(d) level (Scheme 5). Gratifyingly, the optimized structure adopts the conformation we predicted in Scheme 4. Moreover, the strain energy of **4b-H** was determined to be 2.4 kcal mol^{-1} by using the hypothetical homodesmotic reaction of **4b-H** and biphenyl forming *p*-terphenyl and *cis*-1,4-diphenylcyclohexane (see the Supporting Information for details). This value is similar to the strain energy of **4a-H** (model compound of **4a**), which was



Scheme 5. Optimized structure and strain energy of **4b-H**.

determined to be 1.5 kcal mol^{-1}. Nevertheless, the use of the cyclohexane unit is extremely important in our CPP synthesis not only because its L-shaped structure attenuates the buildup of strain energy during the macrocyclization but also because the chair-flipping aptitude of cyclohexane provides a strategic basis for accessing odd-numbered [*n*]CPPs.

In summary, a new strategy has been established for the modular and size-selective synthesis of [*n*]CPPs. The ring-

flipping aptitude of cyclohexane ring is an advantage of this strategy, which allows the deliberate construction of odd-numbered [*n*]CPPs. Although the present methodology permits access primarily to all possible [*n*]CPPs ($n \geq 14$), the potential impact of our strategy is unlimited. By simply inserting other functional π systems into the U-shaped units, a range of aromatic carbon nanorings should be available. The selective synthesis of [*n*,*n*]SWNTs using [*n*]CPPs as a template is the subject of ongoing work in our laboratory.

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[13] Abbreviations: pin = pinacolato; dba = dibenzylideneacetone; X-Phos = 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl.

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