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Selective Synthesis of [6]-, [8]-, and [10]Cycloparaphenylenes

Eiichi Kayahara,[1,2] Takahiro Iwamoto,[1] Toshiyasu Suzuki,[2,3] and Shigeru Yamago*[1,2]
[1]*Institute for Chemical Research, Kyoto University, Kyoto 611-0011*
[2]*CREST, Japan Science and Technology Agency, Tokyo 102-0076*
[3]*Institute for Molecular Science, Myodaiji, Okazaki, Aichi 444-8787*

(Received March 5, 2013; CL-130188; E-mail: yamago@scl.kyoto-u.ac.jp)

The selective synthesis of [6]-, [8]-, and [10]cycloparaphenylenes (CPPs) was achieved by a new synthetic route involving Ni(0)-mediated coupling of bis(*para*-haloaryl)dinuclear arylplatinum complexes and the reductive elimination of the complexes. Importantly, the highly strained [6]CPP was prepared in good overall yield.

Cycloparaphenylenes (CPPs; Figure 1a), being hoop-shaped π-conjugated molecules consisting of *para*-linked phenylene rings, have recently gained much attention from a variety of disciplines, which, besides their structural beauty, is mostly associated with the topologically unique array of π-orbitals.[1–5] Since CPPs are the smallest structural units of armchair carbon nanotubes (CNTs; Figure 1b), their application in electronic and optoelectronic devices[6–9] and their use as a seed compound for the synthesis of structurally uniform CNTs have been suggested.[2,5,10] In addition, the cavity of CPPs offers a unique opportunity in supramolecular chemistry to study concave–convex π–π interactions and fabricate hierarchically ordered π materials.[11,12] Despite their simple structure, however, the synthesis of CPPs was only recently achieved by three groups including our own despite intensive efforts that spanned more than half a century.

Bertozzi and Jasti were the first to synthesize [9]-, [12]-, and [18]CPPs utilizing *cis*-cyclohexa-2,5-diene-1,4-diyl as the key precursor (Scheme 1a).[13] The subsequent extension of this synthetic strategy by Jasti realized the selective synthesis of a series of [6]–[12]CPPs,[14–16] as well as the gram-scale synthesis of [8]- and [10]CPPs.[17] So far, the smallest CPP synthesized is [6]CPP. Jasti also reported the synthesis of substituted CPPs,[18] including CPP-dimers,[19] based on the same synthetic strategy. Itami used *cis*-cyclohexan-2,5-diol as a key precursor (Scheme 1b) and succeeded in the size-selective synthesis of a series of [9]–[16]CPPs.[20–24] Several derivatives have furthermore been synthesized via this route.[25–29]

We have utilized cyclic *cis*-bisarylplatinum complexes prepared by transmetallation of bismetallated aryls and platinum dihalides, as the key precursor (Scheme 1c). Once formed, reductive elimination of Pt affords the CPPs,[30,31] allowing the selective synthesis of [8]- and [12]CPPs, as well as the random synthesis of [8]–[13]CPPs. At that time (2010), [8]CPP was the smallest CPP reported. As the CPPs could be obtained in high overall yield, the isolation of CPPs with different ring sizes enabled us to study the size-dependency of their physical properties and size-selective host–guest chemistry between CPPs and fullerenes.[12] Isobe applied our method to the synthesis of the shortest sidewall segments of helical CNTs.[32,33] Very recently, we reported the selective synthesis of [10]CPP through an L-shaped *cis*-substituted bis(*para*-haloaryl)platinum complex.[34]

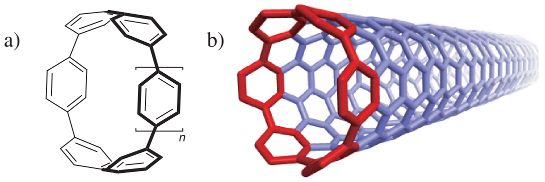
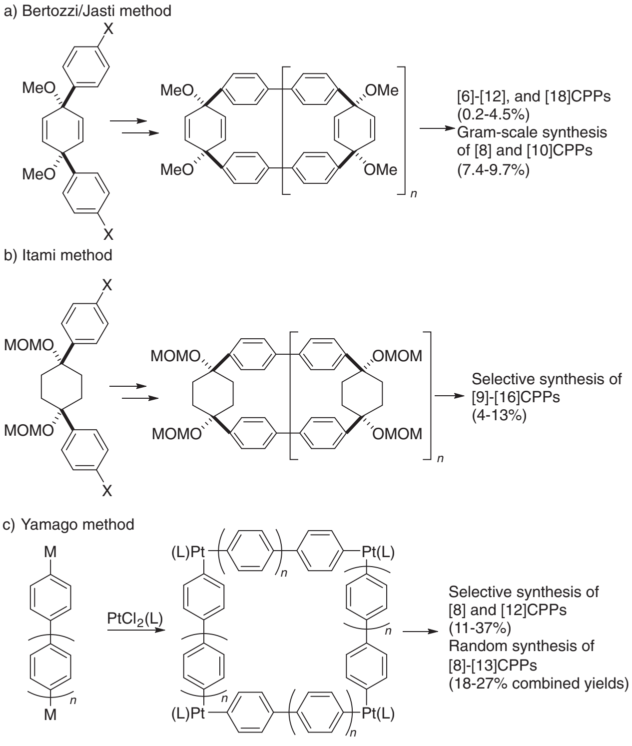
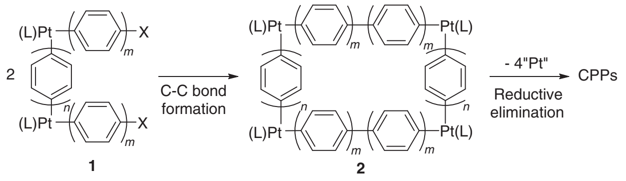


Figure 1. Structure of a) $[n + 5]$cycloparaphenylene (CPP) and b) armchair CNT. The constituting [6]CPP unit of the armchair CNT is highlighted in red.



Scheme 1. Previously reported synthetic routes to CPPs.

Theoretical studies by our group have suggested that,[31] in sharp contrast to linear oligoparaphenylenes, the gap between the highest-occupied and lowest-unoccupied molecular orbital (HOMO–LUMO gap) of CPPs becomes narrower as the number of phenylene rings decreases, which is due to increasing and decreasing HOMO and LUMO energies, respectively. As a result, compared to larger CPPs, CPPs of small ring size should display a range of intriguing properties, including a higher redox activity. Unfortunately, despite recent developments, the synthesis of small CPPs still poses serious synthetic difficulties; the



Scheme 2. The proposed new synthetic route to CPPs via platinum squares.

synthesis of [6]CPP as reported by Jasti requires long reaction steps in a low overall yield (0.7% over 8 steps).[15] So far, our own investigations on the synthesis of CPPs smaller than [8]CPP have been unsuccessful. Therefore, a new and high-yielding synthetic route for small CPPs is highly anticipated.

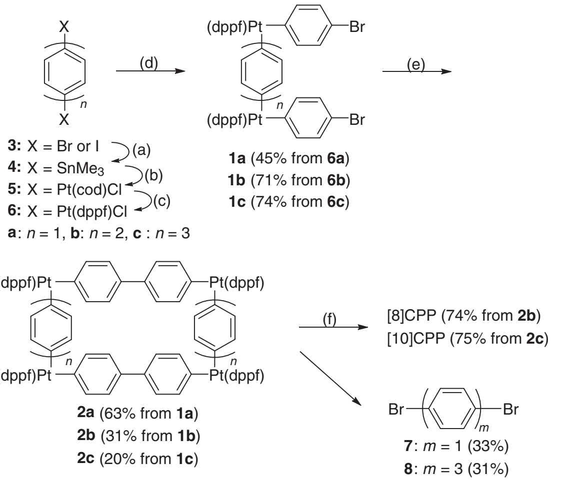
We envisioned that *para*-haloaryl-substituted dinuclear platinum complex **1** could serve as a precursor for tetranuclear platinum complex **2** through double carbon–carbon bond formation mediated by the carbon–halogen functionality (Scheme 2). Reductive elimination by platinum in **2** should then give the CPP. We here report the selective synthesis of [6]CPP by this route, in which a Ni(0)-mediated Yamamoto coupling[35,36] was utilized as the key step for the synthesis of **2**. We further report an improved reductive elimination of **2** to yield [6]CPP, as previously reported conditions did not give the desired compound, probably because of the high ring strain. To clarify the scope of this new route, we also report the selective synthesis of [8]- and [10]CPPs.

To address our hypothesis, **1** was first synthesized from the commercially available dibromo (or diiodo) biaryls **3a**–**3c** (Scheme 3). The halogens in **3a**–**3c** were transmetallated to a trimethylstannyl group by treatment with BuLi or Mg (2.5 equiv) in THF at −78 °C, followed by reaction with Me_3SnCl (3.0 equiv), giving **4a**–**4c** in 75–94% yield. Compound **4** was then reacted with 2 equiv of [Pt(cod)Cl_2] (cod: 1,5-cyclooctadiene) giving bisplatinum complexes **5a**–**5c** in 87–94% yield, which were subsequently treated with 1,1′-bis(diphenylphosphino)ferrocene (dppf) to give **6a**–**6c** in 87–92% yield. Treatment of **6a**–**6c** with in situ generated 4-bromophenyllithium afforded **1a**–**1c** in 45–74% yield. The structure of **1** was characterized by ^{1}H and ^{31}P NMR and ESI-TOF mass spectrometry.

Homocoupling of **1** was then attempted under Yamamoto coupling conditions.[35] Treatment of 5 mM **1a**–**1c** in THF with [Ni$(cod)_2$] (2.0 equiv) and dppf (2.0 equiv) at 50 °C for 12–18 h gave **2a**–**2c** in 20–63% yield. A highly diluted solution of **1** and a low temperature were required to achieve these high yields. [8]- and [10]CPPs were obtained in 74 and 75% yield from **2b** and **2c**, respectively, using the Br_2-induced reductive elimination adopted from previous studies.[30] The yields were significantly improved by careful adjustment of the amount of added Br_2 vs. **2**.

In contrast, treatment of **2a** with Br_2 did not afford [6]CPP at all. Careful analysis revealed that the major side products formed were *p*-dibromobenzene (**7**) and *p*-dibromoterphenyl (**8**) in 33 and 31% yield, respectively. The formation of **7** and **8** must be the result of undesirable C–Br reductive elimination from Pt(IV) complex **9**, formed by oxidation of **2** by Br_2 (Figure 2).[37,38]

Since C–F reductive elimination requires higher activation energy than C–Br reductive elimination, we anticipated that the desired reductive C–C bond coupling reaction could take place when **2a** was oxidized by a fluorine-based reagent.[39,40] Indeed, treatment of **2a** with XeF_2 (4 equiv) at 90 °C afforded [6]CPP in 47% yield (as determined by NMR, isolated yield: 40% (Table 1, Entry 1)). AgF was also found to be effective, giving [6]CPP in moderate yield (Entry 2). Surprisingly, tetrabutylammonium fluoride (TBAF), which does not act as an oxidant but rather is a fluorine anion source, was equally effective in inducing the reductive elimination of **2a** to give [6]CPP in 44%



Scheme 3. Synthesis of [8]- and [10]CPPs. Reagents and conditions: a) 1) BuLi (2.0 equiv), THF, −78 °C, 1 h or Mg (2.5 equiv), THF, reflux, overnight; 2) Me_3SnCl (2.5–3.0 equiv), room temperature (rt), 3–6 h, 75–94%; b) [Pt(cod)Cl_2] (2.0 equiv), THF or THF/toluene, 60 °C, 8–12 h, 87–94%; c) dppf (2.0 equiv), CH_2Cl_2, rt, 6–8 h, 87–92%; d) LiC_6H_4Br (3.0–5.0 equiv), THF, −78 °C to rt, 12 h, 45–74%; e) [Ni$(cod)_2$] (2.0 equiv), dppf (2.0 equiv), THF, 50 °C, 12–18 h, 20–63%; f) Br_2 (4.0 equiv), toluene, 90 °C, 12 h.

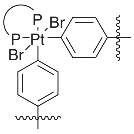


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Figure 2. Structure of proposed intermediate **9**, as formed by treatment of complex **2** with Br_2. DPPF ligand is abbreviated to P–P.

Table 1. Reaction optimization for the synthesis of [6]CPP via reductive elimination of **2a**

Entry	Additive (equiv)	Product (%)[a]
1	XeF_2 (4)	[6]CPP (47) [40][b]
2	AgF (4)	[6]CPP (29)
3	TBAF (4)	[6]CPP (44)
4	$P[OCH(CF_3)_2]_3$ (8)	[6]CPP (37)
5	acrylonitrile (4)	[6]CPP (25)
6	cod (4)	[6]CPP (22)
7	PPh_3 (8)	quaterphenyl (4)

[a]Determined by ^{1}H NMR using 1,1,2,2-tetrachloroethane as the internal standard. [b]Isolated yield.

yield (Entry 3). Several neutral and electron-deficient Pt ligands such as $P[OCH(CF_3)_2]_3$,[41,42] acrylonitrile, and cod, were also effective in forming [6]CPP (Entries 4–6), while the reactions without additive or with PPh_3, dppf, I_2, and tetrabutylammonium bromide (TBABr) were ineffective. Under optimized conditions, [6]CPP was obtained in 8.9% overall yield from commercially available **3a**. Even though the preparation of [6]CPP has already been reported by Jasti, the overall yield was low (0.7%). In contrast, the method reported here opens the way for the production of large-scale quantities of [6]CPP in 8.9% overall yield from commercially available **3a**. The obtained [6]CPP was fully characterized by ^{1}H NMR (7.63 ppm in $CDCl_3$), ^{13}C NMR (127.03 and 134.90 ppm), MALDI-TOF MS (m/z 456.1908 [M^+]), and UV–vis spectroscopy ($\lambda_{max} = 340$ nm, $\varepsilon = 1.0 \times 10^5$ M^{-1} cm^{-1}), which fully agreed with the data reported by Jasti.[15]

However, electrochemical analysis of [6]CPP in 1,1,2,2-tetrachloroethane containing 0.1 mol L^{-1} Bu_4NPF_6 solution (as used in our previous studies) yielded a different result. Although a reversible oxidation of [6]CPP was indeed observed by cyclic voltammetry (CV), the half-wave oxidation potential (${E_{ox}}^{1/2}$) was 0.29 V vs. ferrocene/ferrocenium (Fc/Fc^+) (Figure S2a).[43] Differential pulse voltammetry (DPV) also resulted in a similar oxidation potential (0.30 V vs. Fc/Fc^+) (Figure S2b).[43] These values were considerably smaller than that obtained by Jasti (0.44 V vs. Fc/Fc^+), who conducted the CV analysis using 0.1 mol L^{-1} Bu_4NPF_6 in dichloromethane. When the oxidation potential of the [6]-, [8]-, [10]-, and [12]CPPs, as obtained by our analysis,[31] was plotted against their corresponding HOMO energies, a good linear correlation was observed (Figure S2c).[43] Therefore, the current data appears to be reasonable and suitable for clarifying the size-dependence redox properties of CPPs. We tentatively attribute this difference to an effect of the solvent, as electrochemical measurements are generally sensitive to measurement conditions.

In conclusion, we developed a new and efficient synthetic route to [6]-, [8]-, and [10]CPPs based on cyclic platinum intermediate **2** and subsequent reductive elimination. This new approach is attractive because it gives [6]CPP, which is the most strained CPP so far reported, in high overall yield. Apart from its utility in the synthesis of CPPs, the reported reductive elimination could be applicable in the development of more efficient transition-metal-mediated coupling reactions.

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