



# A Modular Synthesis of Substituted Cycloparaphenylenes

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**Abstract:** Herein, we report a modular synthesis providing access to substituted cycloparaphenylenes (CPPs) of different sizes. A key synthon introducing two geminal ester units was efficiently prepared by [2 + 2 + 2] cycloaddition. This building block can be conveniently converted to macrocyclic precursors controlling the ring size of the final CPP. Efficient reductive aromatization through single-electron transfer

provided the substituted nanohoops in a straightforward manner. The *t*Bu ester substitution pattern enables a tube-like arrangement in the solid-state governed by van der Waals interactions that exhibits one of the tightest packings of CPPs in tube direction, thus opening new avenues in the crystal design of CPPs.

## Introduction

With their cyclic arrangement of *para*-connected phenyl subunits, CPPs represent the smallest repeatable section of armchair carbon nanotubes. The first synthesis reported by Jasti and Bertozzi opened a new research area around this carbon allotrope.<sup>[1]</sup> Analogous to ground-breaking studies by Vögtle,<sup>[2]</sup> the synthesis of an angulated macrocyclic precursor is key to success in tackling the strained nature of the cyclic arrangement of planar phenyl subunits. A variety of ring sizes was realized based on this strategy to build a library of CPPs.<sup>[3,4]</sup> Thereby, the CPPs can be accessed in a combinatorial fashion from a small number of crucial key compounds by cross-coupling followed by aromatization, thus enabling the preparation of different CPPs. For example, [5]-,<sup>[5]</sup> [6]-,<sup>[6]</sup> [8]- and [10]CPP<sup>[7]</sup> were synthesised from the same five-membered building block. Besides these efforts on the parent CPPs, substituted derivatives were targeted early on, permitting a greater structural diversity, which is of special interest in view of materials applications. Examples include substituted CPPs mimicking larger CNTs cutouts,<sup>[8]</sup> indeno-fluorene substituted CPPs prepared by intramolecular Friedel-Crafts reactions,<sup>[9]</sup> or polyfluorinated CPPs reported by the groups of Yamago ([6]- and [9]CPP) and Jasti

([10]CPP).<sup>[10]</sup> Chiral nanohoops were reported either by an asymmetric synthesis of an helical CPP,<sup>[11]</sup> or chiral resolution of an racemic precursor,<sup>[12]</sup> giving an enantiopure CPP derivative. Tetraalkoxy-substituted [10]CPP analogues were synthesized by the group of Yamago by employing the corresponding substituted benzoquinone as a building block.<sup>[13]</sup> A porphyrin substituted CPP was presented by an analogues approach, introducing a TMS group at an early stage and converting it after CPP formation into an iodo-substituted CPP to which the porphyrin unit was connected by Sonogashira coupling.<sup>[14]</sup> Our group relied on the [2 + 2 + 2] cycloaddition as an efficient method for the introduction of substituents.<sup>[15]</sup> Strain-reduced macrocycles were accessed by Sonogashira coupling, which incorporated alkynes for a subsequent [2 + 2 + 2] cycloaddition, conceding structural alteration on a rather late state. The strategy of [2 + 2 + 2] cycloaddition was also adapted by the group of Tanaka for the introduction of *t*Bu esters.<sup>[16]</sup> Here, in the [2 + 2 + 2] cycloaddition not only the substituents are introduced, but also the square-shaped macrocyclic ring is formed. Interestingly, this substituted CPP arranged in a tube-like fashion in the solid-state in contrast to the basket-weaver structure usually found for unsubstituted CPPs. This feature was also observed for [6]- and [8]CPP derivatives decorated with *t*Bu esters.<sup>[17]</sup> Besides *t*Bu ester substituted CPPs, a carbon nanocage<sup>[18]</sup> as well as a Möbius-belt shaped [10]CPP<sup>[19]</sup> derivative were prepared using this method. Employing the [2 + 2 + 2] cycloaddition as the macrocyclization step reduces the overall reaction steps but also has a drawback: To access a different sized substituted CPP derivative, a complete new synthetic route needs to be designed.

In this study, we combined the [2 + 2 + 2] cycloaddition for an efficient introduction of *t*Bu esters with the modularity of cross-coupling chemistry to provide a modular access to different sized substituted CPPs (Scheme 1).

## Results and Discussion

Our synthetic strategy is centred around the building block **10** containing five ring units, half of a [10]CPP (Scheme 2). Suzuki

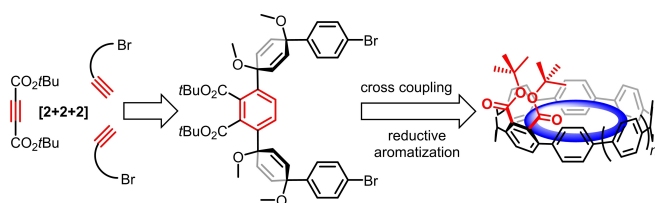
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Scheme 1. Synthetic strategy for CPPs decorated with *t*Bu ester.

cross-coupling reaction of such an intermediate as **10** with itself after conversion to the boronic ester or with an unsubstituted intermediate **12** will provide access to two different macrocyclic [10]CPP derivative precursors.<sup>[7]</sup> The possibility to combine **10** with other building blocks offers a highly modular approach to various substituted CPPs. To showcase the flexibility of our approach an [8]CPP derivative was also targeted.

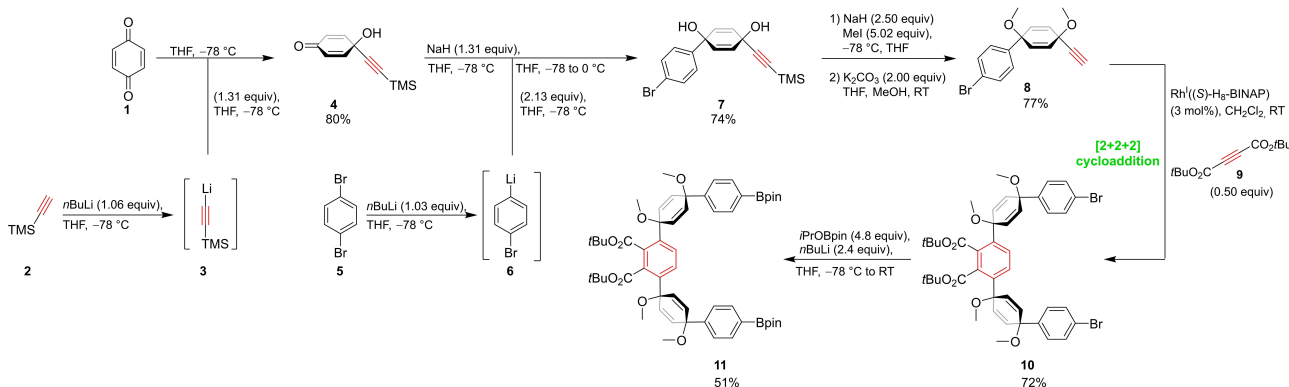
The synthesis commences with the addition of lithium (trimethylsilyl)acetylide (**3**) and (4-bromophenyl)lithium (**6**) to benzoquinone (**1**) in two sequential steps providing **7** in 59% (Scheme 2). This intermediate was recently reported by the group of Tanaka in their synthesis of a nanocage by a strategy relying on a [2+2+2] cycloaddition.<sup>[18]</sup> Deviating from their strategy we performed the synthesis by two sequential nucleophilic additions, which improved the overall yield by more than 10% and facilitated the separation. The following cleavage of the silyl protection group and the formation of the methoxy-ethers provided the [2+2+2] cycloaddition precursor **8** in 77%. Building block **8** features the cyclohexadiene unit as angulated phenyl surrogate as well as the alkyne functionality for the subsequent [2+2+2] cycloaddition. For this key step, a catalytic system consisting of a  $\text{Rh}^{\text{I}}/(\text{S})\text{-H}_8\text{-BINAP}$  complex, developed by the group of Tanaka for such [2+2+2] cycloadditions, was applied.<sup>[20]</sup> The catalyst loading could be reduced to 3% with respect to alkyne **8** providing the product in 72% on a gram scale. The boronic esters **12** and **13**, necessary for the cross-coupling reaction, were prepared according to a literature protocol.<sup>[7]</sup> The combination of the two entities **10** and **12** in the cross-coupling macrocyclization was realized in 17% yield with  $\text{Pd}^{\text{II}}/\text{SPHOS}$  as the catalytic system.<sup>[7]</sup> In this

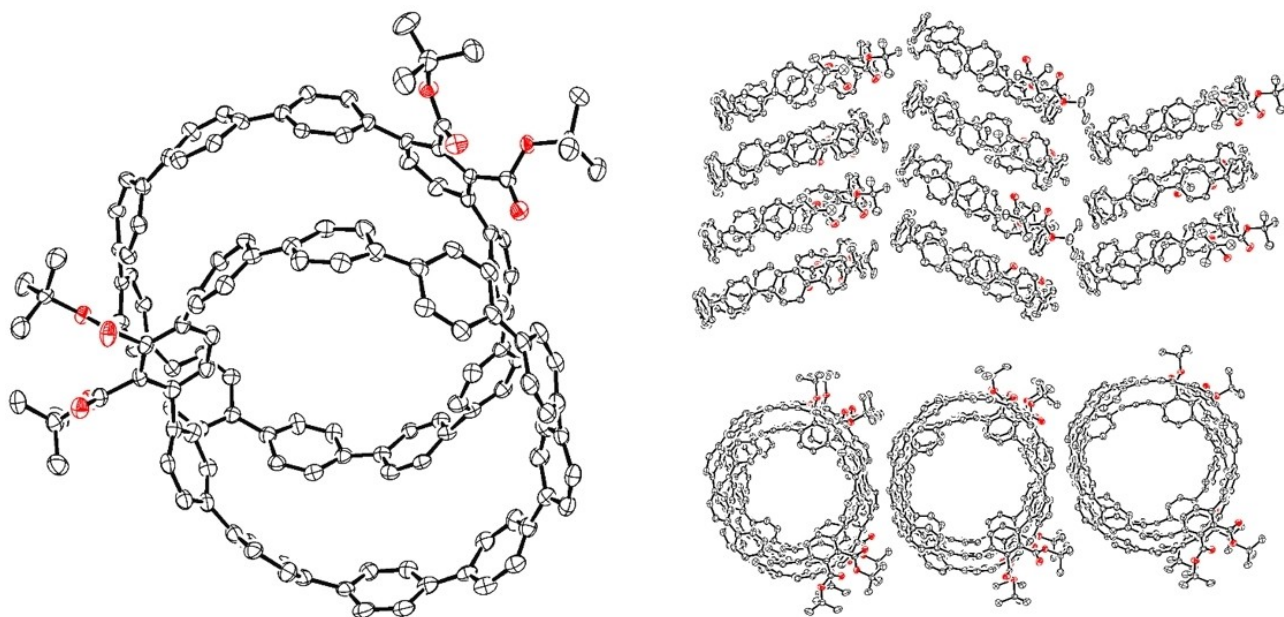
reaction the formation of a five-membered macrocycle could be detected as a side product originating from an intramolecular homo-coupling of the bis-boronic ester.<sup>[5]</sup> Finally, the desired di-substituted [10]CPP **18**, which forms a tubular packing in the solid state (Figure 1), could be obtained in 42% isolated yield by aromatization with sodium naphthalide. This flexible approach also provides access to the tetra-substituted CPP **17**, where the two bis-(*t*Bu)-functionalized phenyl rings are positioned vis-à-vis within the nanohoop (Scheme 3). For this purpose, substituted boronic ester **11** was synthesized from key compound **10** by lithium-halogen exchange and quenching with *i*PrOBpin. The same cross-coupling/aromatization sequence gave the desired CPP **17**. As in the previous case, a five-membered macrocycle was observed as side product in the Suzuki cross-coupling macrocyclization. Finally, the reductive aromatization, with sodium naphthalide led to the tetra-substituted CPP **17** in 35% isolated yield.

As a third derivative, [8]CPP derivative **19** was targeted to also showcase the flexibility in ring-size of this approach (Scheme 3). The cross-coupling reaction of **10** and **13** provided the macrocyclic precursor **16** in higher yields compared to the ten-membered derivatives **14** and **15**. This can be rationalized by the absence of a possible intramolecular homo-coupling of the boronic ester. The aromatization delivered the final product in 58% isolated yield. The decreased number of cyclohexadiene moieties, which have to be converted to phenyl rings, combined with the larger scale on which the reaction was performed might be the main reasons for the increased yield.

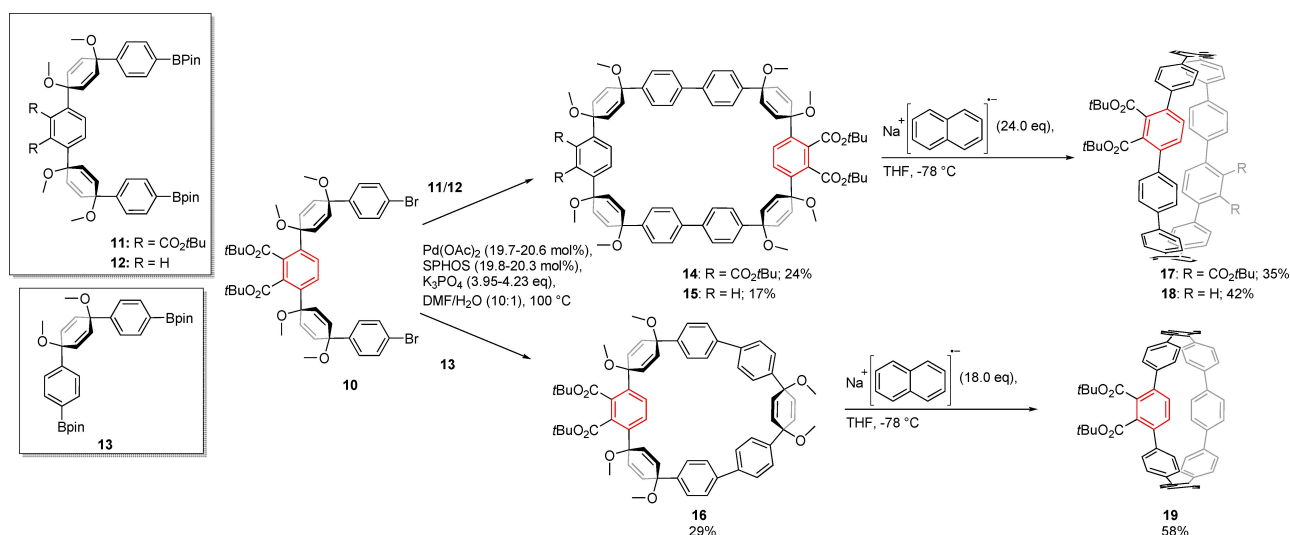
For the cross-coupling reactions of **10** with **11–13**, a C-shape arrangement, as shown in Scheme 3, is necessary. This conformation, however, could be disfavoured by repulsive interactions between the *t*Bu groups from the ester functionalities and methoxy ethers on the  $\text{sp}^3$ -hybridized positions in the neighbored cyclohexadiene moieties. Single crystals suitable for X-ray analysis of key compound **10** were obtained, which support the desired conformation of this key building block (Figure 2).

Also, the solid-state structure of CPP **18** was obtained by X-ray analysis. Interestingly, it exhibits stacking of the molecules in the [100] direction, forming infinite tubes with slightly shifted entities relative to each other. The rings are tilted towards the

Scheme 2. Synthesis of key building block **10** and its corresponding boronic ester.



**Figure 1.** Left: ORTEP plot of the asymmetric unit of the crystal structure of substituted CPP **18**. Solvent molecules and hydrogen atoms are omitted for clarity, thermal ellipsoid are shown at 50% probability. Top right: Columnar packing of bis-substituted CPP **18**; view along the *c*-axis. Bottom: columnar packing of di-substituted CPP **18**; view along the *a*-axis.

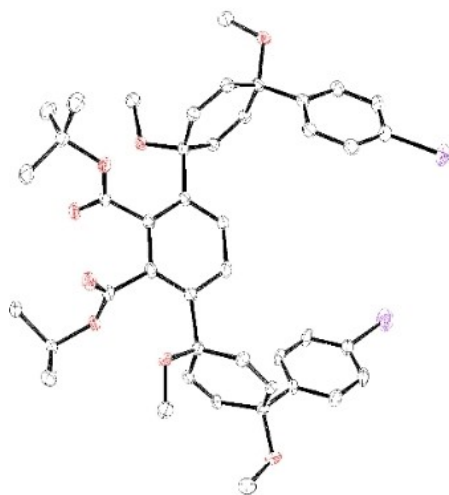


**Scheme 3.** Synthesis of substituted [8]- and [10]CPPs. The key intermediate **10** was prepared by a [2 + 2 + 2] cycloaddition.

2<sub>1</sub> screw axis causing alternating tube directions (Figure 1). In contrast, for unsubstituted CPPs basket-weaver-type packing is typically observed.<sup>[4,7,21]</sup> The preferred basket-weaver packing of the unsubstituted CPPs can be rationalized by maximizing CH- $\pi$  interactions. The tubular arrangement is stabilized by van der Waals interactions between *t*Bu groups and phenyl rings, though. With the introduction of the substitution, the formation of CH- $\pi$  interactions of the CPP core is reduced and the tubular-type packing is more favorable. Additionally, a contribution of weak CH-O hydrogen bonds could play a role. With an average ring to parallel ring distance of about 4.9 Å, the substituted

[10]CPP **18** represents one of the tightest packed (in the direction of the tube) CPP structures reported so far. As a side effect, the torsion angles of the substituted aromatic ring with its neighbors are significantly increased, allowing for a flat arrangement of the bulky *t*Bu groups within the plane of the macrocycle.

Optoelectronic properties of the prepared CPPs were investigated by measuring UV/vis absorption spectra and fluorescence spectra (Figure 3). Only small deviations from the absorption maxima of the parent CPPs (340 nm independent of the ring size)<sup>[22]</sup> were found. Substituted [10]CPP **17** revealed a



**Figure 2.** ORTEP plot of *t*Bu ester-substituted dibromide **10**. Hydrogen atoms are omitted for clarity, thermal ellipsoids are shown at 50 % probability.

single maximum in its fluorescence spectrum, which is in accordance with our previous reported results on substituted [8]CPPs.<sup>[15]</sup> In contrast to this, both CPP derivatives substituted at only one phenyl unit show two maxima within their emission spectra. This can be attributed to the change in dihedral angle due to the large substituents influencing the dynamic behavior in the excited state, which has been calculated to be the crucial factor.<sup>[23]</sup> Additionally, the substituted [8]CPP derivative has a larger Stoke's shift compared to the [10]CPP derivatives and the emission is broader, which is in accordance with results reported for the corresponding unsubstituted CPPs.<sup>[22]</sup>

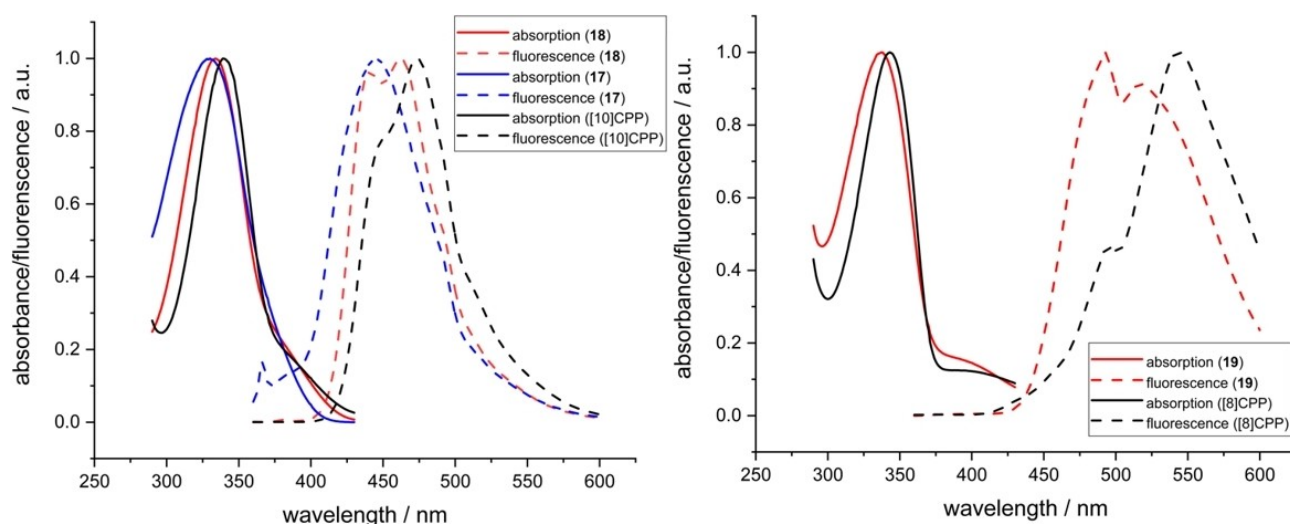
## Conclusion

In conclusion, a modular synthetic strategy has been developed allowing the flexible introduction of substituents and control of the CPP ring size. The approach features access to CPPs with *t*Bu ester as substituents in different positions and various ring sizes. As examples, two different [10]CPP derivatives and one [8]CPP derivative were prepared by choosing a different cross-coupling partner followed by a reductive aromatization as the final step. The solid-state structure of [10]CPP **18** was studied by X-ray single crystal analysis. A tube-like arrangement was found that exhibits the tightest packing in the tube direction of any CPP known. The higher substituted derivatives reported in the literature have a tubular arrangement governed by substituent–substituent interactions that results in a larger ring-to-ring distance. In contrast, interactions between *t*Bu groups and the unsubstituted phenyl rings of the neighboring CPP are the main reason for the tubular arrangement in our case. Hence, this strategy can serve as general concept for crystal engineering of molecular carbon allotropes.

## Experimental Section

Experimental procedures, analytical data of new compounds and details for X-ray crystallographic data are described in the Supporting Information.

Deposition Numbers 2122351 (for **10**), 1996824 (for **18**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.



**Figure 3.** Normalized UV/vis absorption (solid lines) and fluorescence spectra (dashed lines) of left: substituted [10]CPPs **17** (blue,  $1.12 \times 10^{-5}$  M for absorption,  $1.12 \times 10^{-6}$  M for fluorescence), **18** (red,  $1.00 \times 10^{-5}$  M for absorption,  $1.00 \times 10^{-6}$  M for fluorescence) and [10]CPP (black,  $1.29 \times 10^{-5}$  M for absorption and fluorescence; for reference). Right: substituted [8]CPP **19** (red,  $2.05 \times 10^{-5}$  M for absorption and fluorescence) and [8]CPP (black,  $1.12 \times 10^{-5}$  M for absorption and fluorescence; for reference). All solutions in toluene.



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## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

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