

Paracyclophane Self-Assembly Promoted by Transannular Hydrogen Bonding
Ronald K. Castellano, Professor, University of Florida

Background and significance

[*n.n*]Paracyclophanes (**pCps**, where *n* = 2 or 3) have been the subject of fundamental research for decades due to their unique reactivity, stereochemistry, and optical properties.^[1] Differences in these **pCp** scaffolds have been exploited to design multilayered architectures including through-space donor-acceptor molecules, conjugated polymers, and charge-transfer complexes. We recently reported (Fig. 1) the [2.2]**pCpTA** scaffold and confirmed formation of its designed 1-D self-assembly. This award explores and expands this system, specifically seeking to understand the effects of transannular hydrogen bonding on structure, stability, and optical properties, and factors governing assembly thermodynamics and kinetics. In addition, fundamental aspects of **pCpTA** self-assembly, such as stereospecific self-sorting, and the impact of relative amide conformation on assembly macrodipole, remain of interest. From a functional perspective, the overlapped, multi-tiered aromatic core of the suprastructure is attractive for materials science applications involving charge transport and can be viewed as a non-covalent analog to the multitered paracyclophanes (Figure 1).

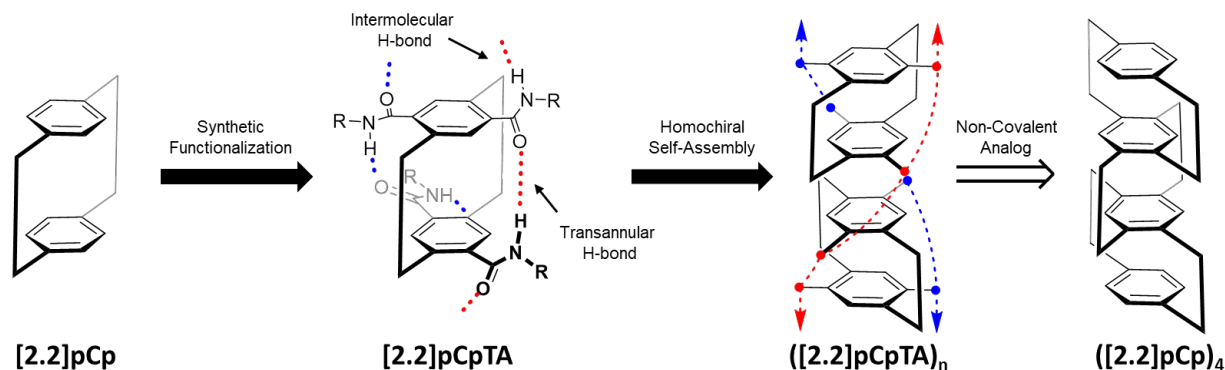


Figure 1. The parent [2.2]**pCp** is functionalized with four amides to form [2.2]**pCpTA**, which self-assembles via synergistic transannular and intermolecular hydrogen bonding.

[3.3]Paracyclophane: A strain-relieved scaffold

Due to the reduction in strain-energy (ca. 20 kcal/mol^[3]), increased planarity of the phenyl rings, and increase in conformational freedom (*chair/boat* isomerism^[4]) associated with the addition of a single bridge carbon, [3.3]paracyclophane-5,8,14,17-tetracarboxamide (**[3.3]pCpTA**) was chosen as a suitable comparator to examine structural factors that affect the assembly of **pCpTAs**. Single-crystal X-ray analysis has now confirmed the intended design, and proved the wider applicability of the **pCpTA** assembly motif, while IR, NMR, and UV-vis solution studies have been used to identify spectroscopic signatures of assembly similar to [2.2]**pCpTA** (Figure 2).

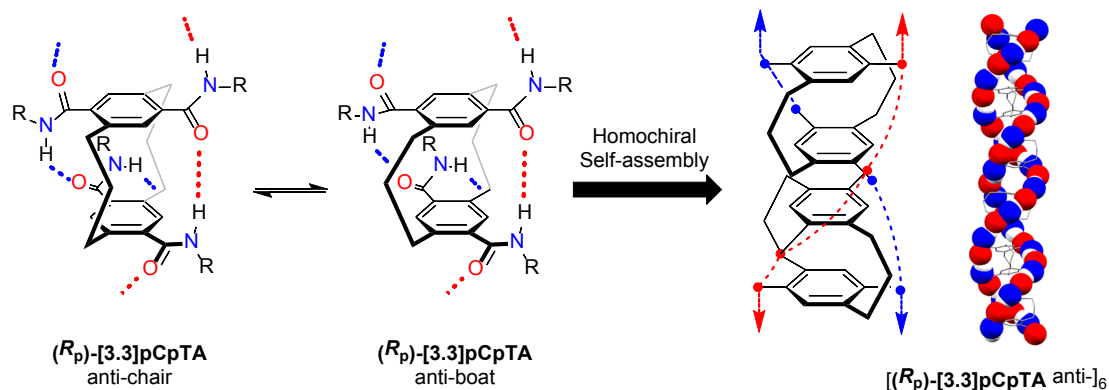
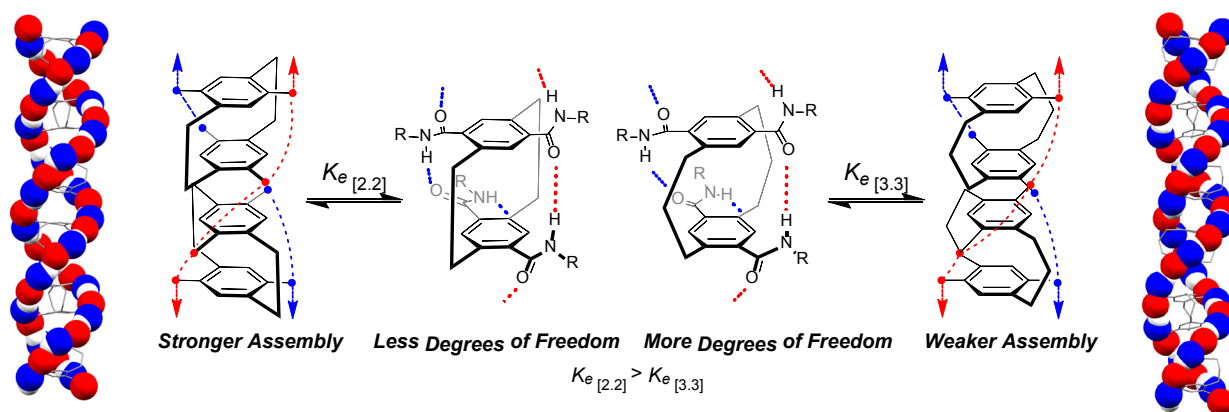


Figure 2. Conformational flexibility introduced in [3.3]**pCpTA** and its corresponding assembly. *Far right:* A hexameric arrangement observed by single crystal X-ray diffraction.

Determination of pCpTA self-assembly mechanism and structure-property relationships

Variable temperature UV-vis spectroscopy was used to monitor the transition from the molecularly dissolved to the assembled state in dilute nonpolar solutions (methylcyclohexane) that feature persistent aggregates at concentrations needed for IR or NMR spectroscopy. Both [3.3]pCpTA and [2.2]pCpTA exhibit similar hypsochromic shifts of the π - π^* transition upon cooling, and the data can be described by an isodesmic model^[5]. By van't Hoff analysis and isodesmic fitting of the degree of aggregation data, it was found that the assembly of [2.2]pCpTA is more exergonic than that of [3.3]pCpTA by ca. 2 kcal/mol at 298 K. This is believed to be a result, in part, of entropic effects associated with the increased conformational dynamics of [3.3]pCpTA (Figure 3).



Research and award impact

This award has supported the development of two families of pCps that are capable of one-dimensional self-assembly in solution and the solid state. Two manuscripts are in preparation along these lines. The supramolecular platform is robust, presents unique features, and we anticipate that the results generated thus far will help to secure federal funding in the near future. For the PI, the award has strengthened a promotion packet. One graduate student working on the project has successfully earned her Ph.D. (May 2018) based on a portion of this work and is now pursuing postdoctoral studies at the University of Michigan.

References:

- [1] D. J. Cram, J. M. Cram, "Cyclophane chemistry: bent and battered benzene rings", *Accounts of Chemical Research* **1971**, *4*, 204-213.
- [2] D. E. Fagnani, M. J. Meese, Jr., K. A. Abboud, R. K. Castellano, "Homochiral [2.2]Paracyclophane Self-Assembly Promoted by Transannular Hydrogen Bonding", *Angewandte Chemie, International Edition* **2016**, *55*, 10726-10731.
- [3] C.-F. Shieh, D. McNally, R. H. Boyd, "The heats of combustion and strain energies of some cyclophanes", *Tetrahedron* **1969**, *25*, 3653-3665.
- [4] H. Dodziuk, S. Szymański, J. Jąźwiński, M. E. Marchwiany, H. Hopf, "Structure and Dynamics of [3.3]Paracyclophane As Studied by Nuclear Magnetic Resonance and Density Functional Theory Calculations", *The Journal of Physical Chemistry A* **2010**, *114*, 10467-10473.
- [5] M. M. J. Smulders, M. M. L. Nieuwenhuizen, T. F. A. de Greef, P. van der Schoot, A. P. H. J. Schenning, E. W. Meijer, "How to Distinguish Isodesmic from Cooperative Supramolecular Polymerisation", *Chemistry - A European Journal* **2010**, *16*, 362-367, S362/361-S362/315.