PRF#: 58919-ND
Project Title: Cyclobenzoins: Hosts for Small Gases and Precursors to Curved Aromatics
PI: Ognjen Š. Miljanić, Professor of Chemistry, University of Houston

Objectives and New Results

The objective of research supported by this ACS Petroleum Research Fund grant is to study **cyclobenzoins**: organic macrocycles made by the cyclooligomerization of aromatic dialdehydes via benzoin condensation. Acyclic analogs known as benzoins have a rich and well-developed chemistry, whose exploration in the context of cyclobenzoins can lead to the facile syntheses of useful and fundamentally interesting curved aromatics. The nonpolar cavity of cyclobenzoins and their polar external functionalities bode well for their use as supramolecular hosts. Our progress during the past project year is described below, organized along the four specific objectives originally proposed.

Synthesis of New Cyclobenzoins. Preparation of new cyclobenzoins was initially challenging because of their low solubility, which made the synthetic manipulations and purification of crude cyclobenzoins difficult. During the past year, we have made a major improvement in this isolation procedure: after the synthesis, acetylation of the crude mixture provided acetic esters of cyclobenzoins. These compounds were characterized by much improved solubility, which allowed their facile purification and the study of their properties as supramolecular hosts (see below). This methodology allowed the preparation of two cyclobenzoins with enlarged pores, based on the 4,4'-biphenyldialdehyde and 3,7-naphthalenedialdehyde (Figure 1) as starting materials. Work on even larger cyclobenzoins is in progress, with the specific targets including cyclobenzoins derived from terphenyl and fluorescent anthracenyl linkers. These new macrocycles will present larger pores which will be utilized as hosts in the solution state and also explored as precursors for larger pores in the solid-state structures. With fluorescent hosts, we anticipate changed in fluorescence properties with the guest encapsulation.

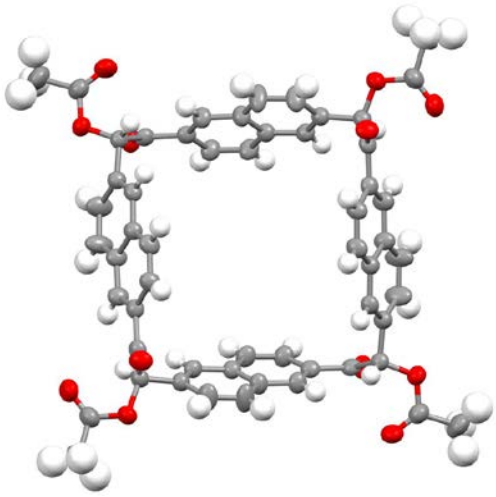

Figure 1. An example of a larger cyclobenzoin synthesized in this project.

Preparation of Curved Aromatics from Cyclobenzoins. Relatively minimal progress has been made in this research direction. In collaboration with the group of Prof. Uwe Bunz at the University of Heidelberg (Germany), we have prepared several condensation conjugates of oxidized cyclobenzoins with a variety of 1,2-phenylenediamines. However, their oxidative cyclization under the Scholl (or related) conditions failed to produce cyclized aromatized product. The reasons for this observation are most likely traced to the presence of nitrogen atoms; synthesis of all-carbon precursors for School cyclization is currently underway.

Use of Cyclobenzoins as Supramolecular Hosts. Existing cyclobenzoin derivatives have narrow cavities. A hypothetical aromatic guest residing the middle of the cyclotetrabenzoin host could establish idealized 3.4 Å [π···π] stacking interactions with the top and bottom benzene wall, but it could not fit sideways—the cavity is too narrow. However, during the past project year, we have identified a number of "thin" guests that can fit within the cavity. For example, the crystal structure of cyclotetrabenzoin,

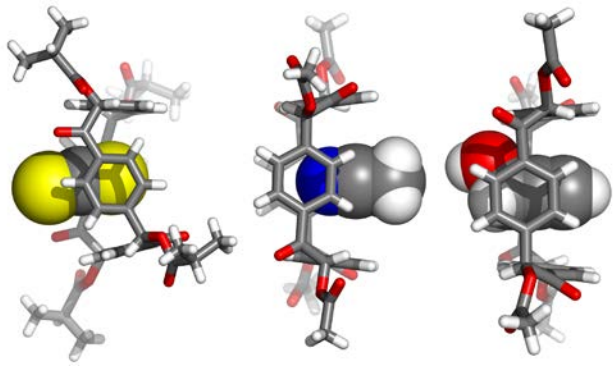

Figure 2. Thin guests such as carbon disulfide (left) are fully included into the narrow central cyclotetrabenzoin cavity. So are the linear fragments of larger molecules, such as the CN functionality of nitriles (center) and CCH terminal triple bond of alkynes (right).

obtained by crystallization from chloroform, shows a single Cl atom included into the cavity. We have also obtained crystal structures with CS_2 as the guest—fully included into the central cavity. Even more broadly, linear fragments of larger molecules—such as the nitrile functionality or the terminal triple bond—are also included into the cavity. A selection of crystal structures of such "thin guests" included in the cavity of cyclotetrabenzoin esters is shown in Figure 2.

These initial discoveries are currently being extended by (a) NMR experiments aimed at elucidating the extent of encapsulation in solution; (b) calculations aimed at extracting binding energies for encapsulation in the gas phase, and (c) the studies of the scope and limitations of this encapsulation behavior. Preliminary work suggests preferential encapsulation of aliphatic vs. aromatic guests.

Assembly of Reduced Cyclobenzoins into "Superhosts". A reduced cyclotribenzoin derivative forms hexameric "superhosts" in the solid state. These oligomers have a nonpolar exterior and a polar interior, within which a pentameric water cluster is found. We are currently exploring methods to observe this behavior in other media—solution and the gas phase. For the former, we are looking at NMR spectroscopic signatures in very nonpolar solvents such as pentane, which we hope will preserve the nonpolar outer shell organization. For the latter, we are collaborating with the group of Prof. Chris Schalley at the Freie Universität in Berlin; they specialize in mass spectrometry using "soft" ionization techniques and their applications in supramolecular chemistry. The objective of this collaboration is to ionize the hexameric superhost cluster without decomposing it and to then detect its behavior and dynamics in the gas phase with a mass spectrometer.

Impact on the Careers of the PI and Students Involved in the Project

Based on the support from the PRF, the PI has published one article, with three more in preparation. Work supported by this grant was presented at five international conferences and four universities in Europe, Asia, and America. During the proposal period, the PI received fellowships from the Max Kade and Alexander von Humboldt Foundations, which supported his stay in Germany and the establishment of several collaborations described above. In addition, the PI was elected Fellow of the Royal Society of Chemistry, and—very recently—promoted to Full Professor in Chemistry at the University of Houston.

The two students that were involved in the project during the first year were Corie McHale (nee Peterson) and Andrew Eisterhold. They are both on track for achieving their career goals—Andrew is scheduled to graduate with a MS degree later this semester and Corie with a PhD by May 2020. Corie has published a paper related to this work and has two more in preparation, while Andrew also has a paper about to be submitted. Thamon Puangsamlee also contributed to parts of this project and has started preparing her first publication. Maymounah Alrayyani worked on cyclobenzoins (even though she was not supported by PRF) and has published a review article on this chemistry earlier in 2019.