Template-Assisted Synthesis of Supramolecular Nanotubes, Anion Receptors, and Molecular Gloves

by

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Supramolecular chemistry has been an exciting branch of organic chemistry during the past decades. Among macrocyclic molecules, macrocyclic arenes are the most well-known and explored type of compounds. In the present thesis, I explored the chemistry of a well-known macrocyclic arene, resorcin[4]arene, as the template to synthesize contorted and strained aromatic compounds, and anion receptors. Chapter 1 provides a general introduction on supramolecular chemistry and has been divided into three sections: 1) macrocyclic molecules, 2) C–H hydrogen bonding architectures, and 3) contorted conjugated macrocycles.

In Chapter 2, I introduce our approach employing derivatized resorcin[4]arenes as templates towards the synthesis of highly strained aromatic molecules. The top rim of these molecules consists of eight para connected phenylenes and resembles the structure of [8]cyclo-para-phenylene. Chapter 3 demonstrates how the same basic template (resorcin[4]arene) can be used towards zigzag tubularenes by incorporating subtle changes in the synthetic approach. The end result is best described as radially-oriented cyclo-meta-phenylenes. The experimental and computational techniques are discussed for these novel species.

Anion recognition molecules are described in Chapter 4. Here, I demonstrate how derivatized resorcin[4]arenes form the basis to create hosts with an unprecedented ability to bind anions via C–H hydrogen bonding. The overall structure is tuned by a late-stage functionalization of the resorcin[4]arene template with a wide range of aromatic building blocks. Our novel
approach demonstrates that by rigidifying and installing electron-withdrawing groups (mainly fluorine atoms), we can produce a new family of anion hosts with highly electropositive hydrogen atoms residing within the cavity of these hosts which are used to sequester non-spherical anions.

Finally, Chapter 5 presents a novel application of resorcin[4]arenes in the gram-scale synthesis of an octa-bromo cavitand, which is used in a two-step synthetic approach towards a rigid basket-like molecule that we colloquially refer to as “nanoglove”, since it is able to host or “catch” fullerenes with high affinity. In contrast to the conjugated systems reported in Chapters 2 and 3, the top rim of this molecule is made of twelve conjugated phenylenes producing an aperture suitable for fullerene binding.
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PREFACE

My Lord! Enrich me with knowledge… (Quran, 20:114)

At first, all the praises and thanks be to Allah (God) who showed us the straight path by sending his messengers and prophets. The profound influence of his commands and legislation within the Holy Quran and the legacy of his last prophet, Mohammad (may peace be upon him), to pursuing knowledge and finding the logic of the astonishing disciples in the world is the main source of inspiration behind my endeavors pursuing doctoral degree.

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تقرير به بابا و مامان

ربِ ارحمهما كما رَبَّيَانِي صَغِيرًا...
1.0 SUPRAMOLECULAR CHEMISTRY: A BACKGROUND

Section 1.3 of this chapter is adapted in part with permission from: Saber Mirzaei; Edison Castro; Raúl Hernández Sánchez*. Conjugated Molecular Nanotubes. *Chemistry–A European Journal* 2021, 27, 8642.

The past century witnessed numerous ways of controlling the synthesis of desired molecules with high precision. However, after decades of covalent chemistry developments, scientists started to focus on targets establishing non-covalent bonds; we can qualitatively mark this ill-defined transition as the birth of supramolecular chemistry, as it shifted the attention of a significant number of chemists all over the globe.1,2 Supramolecular chemistry concerns the study of weak and reversible non-covalent interactions, e.g., hydrogen bonding, π–π stacking, wherein macrocyclic molecules are archetypical species displaying these type of interactions. Macrocycles gained scientific attention due to their high-yielding and straightforward synthesis as well as their host-guest interaction properties, sensing and self-assembling, to name a few. In the first part of this chapter, I will cover some of the most studied macrocyclic molecules and describe their applications.

Among macrocyclic molecules, macrocyclic arenes, e.g., pillarenes, calixarenes, are quintessential compounds in the development of host-guest chemistry, due to their simple and straightforward syntheses and purification. Guests are usually hosted within the inner space or cavity of the macrocycle, where the host provides guest accommodation and stabilization originating from non-covalent interactions. Among these non-covalent interactions, hydrogen bonding is the strongest one,3 especially when considering electronegative atoms like oxygen and
nitrogen, where the difference in Pauling electronegativity with hydrogen ($\Delta \chi$) is 1.24 and 0.84, respectively. Note that the $\Delta \chi$ for C and H is just 0.35 and due to the relatively weak binding affinities ($K_a < 10^4 \text{ M}^{-1}$) resulting from the small $\Delta \chi$, C-H hydrogen bonding has been marginalized in supramolecular host-guest chemistry. In the second part of this chapter, I will cover host-guest chemistry with an emphasis on C-H hydrogen bonding.

In the last part of chapter 1, I will cover bottom-up approaches to prepare strained $\pi$-conjugated systems representing a segment of carbon nanotubes. Note that many hypothetical fully conjugated carbon allotropes have been predicted. However, just a few of them have been discovered experimentally. They can be divided into molecular (e.g., fullerenes) and non-molecular compounds (e.g., carbon nanotubes, CNTs). In addition to fullerenes, the synthesis of carbon nanorings, i.e., cyclo[18]carbon, has been recently reported as the latest molecular carbon allotrope. However, this molecule is not stable at ambient temperature. The discovery of CNTs, around three decades ago, lead to a tremendous impact as a composite material within fields such as supercapacitors, batteries, actuators, coatings, and lightweight electromagnetic shields. In order to control and predict CNT properties, the scientific community has dedicated much effort to the development of synthetic protocols that provide monodisperse products, single-wall CNTs with controllable diameter, and tubes with well-defined chirality. At the same time, scientists around the world have been trying to develop synthetic pathways to realize $[n]$cyclo-para-phenylenes – which are the smallest arm-chair benzenoid CNT segments – until 2008 when Jasti et al. reported the first successful synthesis. Subsequently, by using cutting-edge synthetic methodologies to bend aromatic surfaces, large opportunities in synthesis, property discovery, and applications are expected to emerge from new families of conjugated molecular nanotubes.
1.1 Macro cyclic molecules

1.1.1 Cyclodextrins

Villiers and co-workers were the first group to report cyclodextrins (CDs) as cyclic oligosaccharides in 1891. CDs are accessible in different sizes depending on the number of glucose units: α-, β-, and γ-CD for six, seven, and eight units, respectively (Figure 1.1). Note that all three different sizes are commercially available on large scale, and they are produced using environmentally friendly technologies and renewable natural materials, like starch through an enzymatic conversion. The presence of several hydroxyl groups makes the outer sphere of these toroidal shaped molecules hydrophilic. On the other hand, the internal cavity mostly contains C-C and C-H bonds which generates a hydrophobic internal space/cavity. This hydrophobic nature provides a cavity for hydrophobic guests, or the hydrophobic part of a guest molecule, to reside within the CD when in polar media. However, the strong binding affinity displayed by CDs has been attributed to the unfavorable interactions of water with hydrophobic species, rather than the hydrophobic cavity drawing in molecules. The repulsion of water from the hydrophobic cavity and hydrophobic-hydrophobic interactions leads to the formation of strong host-guest complexes. The cavity within CDs control the size, orientation, and number of guests that can be accommodated.
Host-guest interactions can improve the solubility of hydrophobic compounds in polar solvents, e.g., water and methanol. In essence, the encapsulated molecules are protected from the surrounding environment and are also blocked from undergoing transformations that would otherwise take place in the absence of CDs. However, the slow hydrolysis of CDs can be a major drawback of these hosts which restricts their application as a long-term storage material. It should be noted that longer guests can enforce CD’s homodimerization. In addition to hydrophobic species, Stoddard and coworkers recently showed that α-CD can sequester the AuBr$_4^-$ and Au(CN)$_2^-$ anions, which are critical intermediates in the gold-mining industry, selectively in aqueous media. Using CDs in Au refining can potentially reduce mining costs, energy consumption, and environmental impact.

Despite the several examples of organic molecule encapsulation by CDs, there are just a few reported examples of cyclodextrin-organometallic host-guest adducts. Takahashi reported the CD-ferrocene inclusion complexes with various cyclodextrins (Figure 1.2). Ferrocene and its substituted analogues serve as guests in α-, β-, and γ-CD in different patterns. The small size of α-CD prevents the disubstituted ferrocenes to bind within its cavity. However, it can accommodate

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**Figure 1.1** (Left) Structural formulae of cyclodextrins. (Right) 3-D representation of α-CD; C-H bonds are deleted for clarity.
monosubstituted and unsubstituted ferrocenes in a 2:1 ratio. The binding constant of these ferrocene-containing complexes are highly correlated to the oxidation state of the guest molecule. While ferrocene has a strong binding constant with CDs, the oxidized species, ferrocenium, has a marginal interaction which leads to the dissociation of the whole complex. 

![Diagram](image_url)

**Figure 1.2** Host-guest adducts of ferrocene with *(left) α*, *(middle) β*, and *(right) γ*-CDs.

In addition to host-guest complexation, cyclodextrin-based molecular machines have been reported by Harada and co-workers. In these systems, a CD moves back and forth along a polymer. Moreover, several different groups accomplished syntheses of cyclodextrin-based metal-organic frameworks (CD-MOFs). The first CD-MOF was reported by Yaghi and Stoddart in 2010. In that report, the use of γ-cyclodextrin solved the lack of inherent asymmetry of the natural product building blocks in preparing MOFs by providing highly symmetrical organic linkers. Following this seminal report, other groups described syntheses and applications for other cyclodextrin-based MOFs (α- and β-CD-MOFs).
1.1.2 Crown ethers

Pedersen accidentally discovered the first crown ethers in 1967, which earned him a Nobel prize in 1987.26, 27 Crown ethers – cyclic polyethers with \(-\text{CH}_2\text{CH}_2\text{O}\)- repeating units – rapidly gained popularity among the scientific community. Crown ethers can be obtained in different sizes; thus, a general nomenclature rule has been applied to these unique species: \(m\)-crown-\(n\), where \(m\) represents the number of all atoms (except hydrogens), and \(n\) represents the number of oxygen atoms (Figure 1.3).

As it is obvious from the structures, the lone pairs of the oxygen atoms are readily accessible and can bind to positively charged species. Experimental data proved that these molecules are very good host/ligands for alkali metals. 28, 29 However, due to the different atomic radii of alkali metals, their binding affinity varies depending on the crown ether, where in general the best size match results in the strongest binding. This feature pushed chemists to synthesize different sizes of crown ethers and test them for their sequestration selectivity over a wide range of metal cations. 30, 31 For instance, 12-crown-4, 15-crown-5, 18-crown-6, and 21-crown-7 have high affinity for \(\text{Li}^+\), \(\text{Na}^+\), \(\text{K}^+\), and \(\text{Rb}^+\) ions, respectively (Figure 1.3). 29
Figure 1.3 Chemical structure of common crown ethers and their specificity towards alkali metals.

Crown ethers are soluble in a wide range of organic solvents with different polarity and hydrogen-bonding capabilities. This unique feature can be attributed to the lone pairs of oxygens which play an important role in polar solvents. On the other hand, the presence of several hydrophobic CH$_2$ groups improves the crown’s solubility in non-polar solvents. This unique feature brings water-soluble salts into organic solvents, e.g., KF, by encapsulation of K$^+$ within the crown ether, effectively enhancing the reactivity of the now free fluoride anion (F$^-$). Thus, crown ethers have been employed extensively as an integral part in phase transfer catalysis.

In addition to interacting with protic solvents and acting as ligands for positively charged alkali metals, the lone pairs of the oxygen atoms can engage in strong complexation with other molecules through non-covalent interactions, e.g., hydrogen bonding. For example, 18-crown-6 can accommodate the ammonium ion and protonated primary amines both in solution and gas phase. This complexation leads to the synthesis of a series of mechanically interlocked molecules with...
controllable molecular motions based on the protonation of the amine group.\textsuperscript{38, 39} For example, Stoddart’s group employed this feature for the synthesis of molecular machines, specifically this compound was named “molecular elevator” (Figure 1.4).\textsuperscript{40}

![Figure 1.4](image)

**Figure 1.4** Application of crown ethers in a molecular elevator. The picture was adopted from Ref. 40.

### 1.1.3 Cucurbiturils

Behrend et al. reported for the first time the condensation reaction of formaldehyde and glycouril in 1905.\textsuperscript{41} However, due to the very low solubility of the product and lack of instrumentation, the product was not elucidated until 1981 when Freeman et al. repeated the reaction and obtained the crystal structure of the molecule which showed six glycouril units linked by twelve methylene bridges (CB[6], Figure 1.5).\textsuperscript{42} The similarity of this macrocycle to a pumpkin
(i.e., *cucurbitaceae* family of plants) was the reason behind the name of cucurbit[\(n\)]urils (CB[\(n\]), Figure 1.6).\(^{42,43}\)

For two decades, CB[6] was the only well-characterized molecule within this family of macrocycles. However, later on, different groups employing novel synthetic approaches obtained the smaller \((n = 5)\) and larger \((n > 6)\) members of the CB[\(n\)] family.\(^{44-46}\) The other sizes were accessible when researchers found the importance that temperature had in the synthetic protocol. Running the condensation reaction at temperatures in the range 75 to 90 °C leads to CB[\(n\)] with different sizes.\(^{46}\) The crystal structures of CB[\(n\)] and the computationally simulated structures showed the same depth (~9 Å) for all CBs despite the different diameters. Note that the small diameter of the smallest synthesized cucurbit[\(n\)]uril \((n = 5)\) allows it to fit perfectly inside the cavity of CB[10], leading to a cucurbituril-based gyroscane.\(^{46}\) The largest cucurbit[\(n\)]uril, namely, CB[14], has been synthesized by Tao’s group.\(^{47}\) However, due to the presence of a huge twist (360°) and figure-of-eight conformation, they called the molecule twisted cucurbit[14]uril, tQ[14]. Thus, it does not follow the normal trend for the cavity size of CBs.\(^{47}\)

During the past two decades, several review articles covered the CBs and their applications.\(^{48-54}\) This ever-growing interest and the emerging applications of CBs are due to several factors, including: cheap and commercially available starting materials, one-pot synthesis, possibility of generating different sizes, solubility in aqueous media and complexation with a wide verity of molecules.
The repeating glycouril units of CBs generate a macrocycle through the bridging of two methylene (CH$_2$) groups which results in high conformational rigidity. This rigidity decreases the host-guest entropic penalty upon complexation. Moreover, the symmetrical and barrel-shaped geometry creates similar rims on both sides of the molecule. This feature allows the CBs to be used in interlocked molecules like rotaxanes.$^{55-57}$ Also, functionalizing the threaded guest at the caps with appropriate moieties (e.g., benzoates) can be used to synthesize metal organic frameworks (MOFs).$^{58,59}$
1.1.4 Macrocyclic arenes

The chemistry of macrocyclic arenes dates back more than a century, when in 1872 Adolf von Baeyer mixed different phenols with formaldehyde in acidic media.\textsuperscript{60} However, similar to cucurbiturils, they were not able to characterize the product. Later, in 1952, Zinke and coworkers repeated the same reaction, but in strong basic media, to obtain the cyclic tetramers which Gutsche named calixarenes in the late 1970s.\textsuperscript{61,62} The reaction is based on the electron-rich phenolic units which go through the condensation reactions at the meta-positions. Calix[4]arene is the smallest identified calixarene, and recently Huc and coworkers reported the synthesis of giant calixarenes with up to 90 phenolic subunits.\textsuperscript{63} Calix[4]arenes keep attracting interest due to the wide spectrum of applications. The four meta-connected phenylene units can show four different conformers in solution: 1,3-alternate, partial-cone (paco), cone/boat and 1,2-alternate (Figure 1.7). The substituents control the conformational flexibility and separability of the targeted compound.

\textbf{Figure 1.7} Chemdraw representation of the four different conformers of unsubstituted calix[4]arene.
The presence of the phenylene units and their positions raised the question of whether non-covalent interactions (e.g., \(\pi-\pi\) and \(\pi\)-cation) could be used to encapsulate small molecules/gases. Disproportionation of colorless \(\text{NO}_2\) dimer can generate the nitrosyl ion, \(\text{NO}^+\), which is a good oxidant for the electron-rich aromatic systems of calixarenes. The colorless dimer of nitrogen dioxide (\(\text{NO}_2\)) can undergo disproportionation upon reaction with calixarenes to form a \(\pi\)-cation (\(\text{NO}^+\)) interaction which leads to the color change.\(^{64-66}\) In order to investigate \(\text{NO}^+\) interaction with calixarenes, several group investigated the host-guest interaction with commercially available oxidizers (e.g., \(\text{NOBF}_4\) or \(\text{NOSbCl}_6\) salts) which generate nitric oxide.\(^{67,68}\) Moreover, a variety of calixarenes have been synthesized by Rathore and co-workers to improve their binding constants for their use as nitrogen oxide (NO) detector or storage materials.\(^{69-72}\)

In addition of \(\text{NO}^+\)⋯\(\pi\) interactions, calix[4]arenes are well known hosts for ionic metals. Radioactive nuclear reaction byproducts (e.g., \(\text{Cs}^+\) and \(\text{Sr}^{+2}\)),\(^{73}\) hazardous materials (e.g., mercury)\(^{74}\) and precious metal adsorption\(^{75}\) are just a few examples that have attracted chemists to utilize the supramolecular chemistry of calixarenes.

Since the discovery of calixarene and the optimization of its synthesis, several other aromatic units (especially hydroxy and alkoxy substituted) have been employed to make methylene (CH\(_2\)) or methine (CH) bridged macrocyclic molecules, termed macrocyclic arenes.\(^{76-79}\) calix\([n]\)furans,\(^{78}\) calix\([n]\)carbazoles,\(^{79}\) asar\([n]\)arenes,\(^{80}\) calix\([n]\)pyridines,\(^{81}\) calix\([n]\)pyrroles,\(^{82}\) calix\([n]\)indoles,\(^{83}\) calix\([n]\)naphthalenes,\(^{84}\) resorcin\([n]\)arene,\(^{85}\) pillar\([n]\)arenes,\(^{86}\) pyrogallol\([n]\)arenes,\(^{87}\) and oxatub\([n]\)arenes\(^{88}\) are some of the reported macrocyclic arenes (Figure 1.8). The xanthene\([n]\)arene and acridane\([n]\)arene are two building blocks that have been reported recently by Tiefenbacher’s group.\(^{89,90}\) Note that the combination of two different alkoxybenzene units (hybrid\([n]\)arenes) also has been reported by Szumna’s group.\(^{91-93}\)
The smallest units (i.e., hydroxyl/alkoxy substituted benzene) of these ever-growing families keep attracting scientist’s attention. Their structures can be easily divided in three: ortho-, meta-, and para-methylene-bridged systems. Here, I will cover briefly the chemistry of the most investigated ortho- (cyclo[\(n\)]veratrylenes), meta- (resorcin[\(n\)]arenes), and para-connected (pillar[\(n\)]arenes) macrocycles. It should be noted that Chapters 2 through 5 are relying on the chemistry of resorcin[4]arenes as the template for any subsequent step.

**Figure 1.8** General building blocks for making macrocyclic arenes. The reactive sites are shown with red circles.

**Cyclo[\(n\)]veratrylenes:** The reaction of 1,2-Dimethoxybenzene (veratrole) and paraformaldehyde yields the cyclo[\(n\)]veratrylenes. The regioselectivity of the reaction is governed
by the methoxy groups which install the \( \text{CH}_2 \) bridges \textit{para} to the \text{OMe} groups and \textit{meta} compared to each other in the acidic media. The smallest size of this family is the cyclo\text[triveratrylene (}\( n = 3 \), CTV) which has a crown shape geometry.\textsuperscript{94} In addition to the mentioned reaction, the same product can be obtained using the condensation of veratrole alcohol under acidic condition (Figure 1.9).\textsuperscript{95-97} Note that CTV is the most studied member of the cyclo\text[\text{n}][n]veratrylene family as it is the most thermodynamically stable product, and can be synthesized in grams scale in a one-pot reaction.\textsuperscript{96} The supramolecular chemistry of CTV and its derivatives has been investigated extensively.\textsuperscript{98-101} Despite the small size of CTV, the shape and conformational rigidity of this molecule makes it a good host for fullerenes. The interaction between CTV and fullerenes can be attributed mostly to non-covalent \( \pi-\pi \) interactions. The experimental results revealed that the bigger fullerenes can make better interactions with CTV (\( \text{C}_84 > \text{C}_70 > \text{C}_60 \)).\textsuperscript{102}

Opposite to CTV (}\( n = 3 \), the larger size cyclo\text[4][4]veratrylene (cyclotetraveratrilene, CTTV) showed conformational flexibility in solution. The X-ray and dynamic \( ^1\text{H-NMR} \) studies showed that the sofa-shaped (opened) conformer is the most stable conformer for CTTV in its neutral form.\textsuperscript{103} Rathore and coworkers utilized this conformational flexibility to make a redox-induced molecular actuator.\textsuperscript{96} However, their results showed that the one-electron oxidized CTTV is not
stable, even at low temperature. Later, they accomplished the synthesis of a novel hybrid-bridge macrocyclic molecule (i.e., oxy-alternate-bridged cyclotetraveratrylene, $O^{al}r$CTTV) and showed its robust and reversible switching between open (neutral) and closed (cation radical) conformations under redox condition (Figure 1.10).

![Figure 1.10](image-url)  
**Figure 1.10** Cyclotetraveratrylene-based redox-induced molecular actuators: R = CH$_2$ (CTTV) and R = O ($O^{al}r$CTTV).

**Resorcin[n]arenes**: Niederl and Vogel reported a cyclic tetrameric geometry for the aldehyde-resorcinol condensation reaction for the first time in 1940. This structure was confirmed 28 years later by single-crystal X-ray diffraction structure. The chemistry of resorcin[n]arenes rapidly developed as the product can be obtained on very large scale (>200 g) in a one-pot synthesis using aliphatic or aromatic aldehydes (Figure 1.11). Regardless of the employed aldehyde and the alkoxy substituents, the four-membered macrocycle (resorcin[4]arenes) is either the only or the dominant product. The synthesis of resorcin[6]arene has been reported by Rebek’s group as the by-product (yield < 5%) of resorcin[4]arene. Recently, Chwastek and Szumna reported the synthesis and purification of resorcin[n]arenes ($n =$
5 and 7) with a yield of $< 5\%$.\textsuperscript{109} The relatively low yield and tedious purifications restricted the further developments of the higher analogous ($n > 4$) of resorcin[$n$]arene.

\textbf{Figure 1.11} The general structural formula of resorcin[4]arene and its side view.

A survey of the literature indicates that resorcin[4]arene, similar to calix[4]arene, can ideally show four different conformers. To the contrary of the hydroxyl substituted calix[4]arenes, where the intramolecular hydrogen bonding determines the most stable conformer (cone), other substituents can show conformational flexibility in solution and solid state.\textsuperscript{110-112} This intramolecular hydrogen bonding results naturally in the larger upper rim, as depicted in Figure 1.11 side view. Octa-hydroxyl resorcin[4]arene can go through a self-assembly process to make a hexameric capsule which is connected via eight water molecules.\textsuperscript{113}

In addition to hydrogen bonding, these Ar-OH groups can be easily functionalized. This feature has been used by Cram,\textsuperscript{114} Rebek,\textsuperscript{115} and Gibb\textsuperscript{116} to make different types of cavitands (Figure 1.12). The Gibb cavitands have more conformational rigidity due to the different connectivity pattern. On the other hand, both Cram and Rebek cavitands can show two different conformers: $C_{4V}$ symmetric vase and the $C_{2V}$ symmetric kite conformation.\textsuperscript{117} Note that this conformational flexibility is more restricted in Rebek’s cavitands due to several intramolecular hydrogen bonds present in the vase conformer (Figure 1.12).
In addition to these aromatic-wall containing cavitands, the space between two adjacent resorcinol moieties can be functionalized with methylene, ethylene and propylene groups to rigidify the whole structure.\textsuperscript{118} Moreover, the aromatic carbon atom between the two hydroxyl groups can be easily functionalized. Later work showed that proper substitution and subsequent reactions yields a new family of molecules covalently linking two cavitands from their upper rim to create what the authors described as carcerands.\textsuperscript{119,120} Additionally, Haino’s group showed that

\textbf{Figure 1.12} Resorcin[4]arene-based cavitands.
using bisdimethoxyacetals instead of aldehyde in the reaction with resorcinol can accomplish the synthesis of feet-to-feet connected bisresorcinarenes.\textsuperscript{121,122}

**Pillar[\textit{n}]arenes:** Ogoshi and coworkers were the first group who reported the serendipitous discovery of pillar[5]arene in 2008.\textsuperscript{123} This molecule and the other sizes (especially pillar[6]arene) represents one of the most investigated macrocyclic arenes. A novel CH\textsubscript{2}-bridging pattern (\textit{para} or 1,4), one-pot synthesis, possibility of functionalization, and symmetrical/tubular geometry are some of the features that made the pillar[\textit{n}]arenes popular. Note that the purpose of the first reaction by Ogoshi’s group was a polymer; however, they were able to characterize the methoxy-substituted pillar[5]arene as the byproduct (Figure 1.13).\textsuperscript{123}

\begin{center}
\textbf{Figure 1.13} The first reported synthesis of pillar[\textit{n}]arenes.
\end{center}

Optimization of the original reaction has been carried out by different groups. For example, Ogoshi and coworkers increased their yield form 26\% to around 73\%;\textsuperscript{124} Szumna et al. showed that 1,2-dichloroethane (DCE) is the best solvent for the synthesis of pillar[5]arene and that other solvents (e.g., chloroform) can yield pillar[\textit{n}]arenes with \textit{n} > 5;\textsuperscript{125} Hou and coworkers accomplished the synthesis of higher pillar[\textit{n}]arenes (\textit{n} = 6-10) under kinetically controlled condition despite a low yield of < 3\% for \textit{n} = 7-9.\textsuperscript{126}
The Ogoshi and Rathore groups reported separately the importance of solvent for the selective synthesis of pillar\([n]\)arene \((n = 5, 6)\). Ogoshi and coworkers showed that chlorocyclohexane (ClCy) was a very good solvent for the selective synthesis of pillar\([6]\)arene.\(^{127}\) Their discovery revealed the templating-effect of the solvent during the synthesis of pillar\([n]\)arenes \((n = 5, 6)\), effectively serving as solvent and guest or temple in pillarene formation. For example, ClCy and DCE are good guests for pillar\([6]\)arene and pillar\([5]\)arene, respectively (Figure 1.14). The low yield of cyclohexylmethyl substituted pillar\([5]\)arene \((\text{CH}_2\text{Cy})\) has been attributed to the bulkiness of this group. Following this method, Wilson et al. reported a gram-scale synthesis of ethoxypillar\([6]\)arene.\(^{128}\) Note that pillar\([n]\)arenes \((n = 5, 6)\) are interconvertible utilizing the proper solvents, which indicates the dynamic bond formation/cleavage of the CH\(_2\)-bridges.\(^{127,129}\) Rathore and coworkers showed the same templating effect using different solvents and catalysts (Figure 1.14).\(^{130}\)

![Figure 1.14](image-url)

**Figure 1.14** Solvent effects on the synthesis of pillar\([n]\)arenes \((n = 5\) and 6). One of the main reasons for the huge development of pillarenes is related to the facile synthesis of differently substituted and functionalized species. These accomplishments are in part
boosted by the easy access of the OH group after ether deprotection. The presence of hydroxyl groups allows the synthesis of several different derivatives of this macrocyclic arene family. For example, Isaacs and coworkers reported a water-soluble pillar[n]arene \((n = 5-7)\), dubbed pillar[n]MaxQ with high affinity towards quaternary (di)ammonium ions and methylated amino acids.\(^{131, 132}\)

Pillar[n]arene’s cavity (i.e., 4.7 vs. 6.7 Å for \(n = 5\) and 6, respectively) binding profile has been optimized for the separation of industrially relevant chemicals. For instance, the bigger cavity size of pillar[6]arene can be used to separate \(\text{para-xylene}\) from its structural isomers, \(\text{meta-}\) and \(\text{ortho-}\), with high efficiency (>90%).\(^{133}\) On the other hand, the smaller cavity of pillar[5]arene makes it a perfect host for linear \(n\)-alkanes.\(^{134}\) In addition to a wide-range of host-guest chemistry investigations,\(^{51, 86, 135}\) pillararenes have been used in mechanically interlocked systems,\(^{136}\) metal-organic frameworks,\(^{137}\) and metal-organic pillars.\(^{138}\)

### 1.2 C-H hydrogen bonding

Removing contaminants from the environment is becoming an increasingly challenging task. In recent years, various types of water-soluble anions have been identified as environmental contaminants whose remediation has caught the attention of chemists and environmental scientists. Sulphate from acid rain, nitrate from fertilizers, and pertechnetate from nuclear fuels are just some examples of harmful anions. Within the family of organic anions and with the advent of higher performing polymers for stain- and grease-resistant coatings, more and more per- and polyfluoroalkyl substances (PFAS) – known as “forever chemicals” due to their high persistence in the environment – are found in the environment, especially in drinking water. In all cases,
anionic PFAS contain at least an acetate or sulfonate group. Unfortunately, PFAS presence in drinking water sources is well documented, and coupled with their health-related problems their persistence in the environment makes them a pressing problem for society to solve.\textsuperscript{139} However, the field of anion-based PFAS sequestration is in its infancy and much work is yet to be done. In general, anion sequestration is not trivial as targeting different anions selectively may require different hosts and thus complete synthetic redesign of the anion receptor.\textsuperscript{140-145}

Guests are usually hosted within the inner space or cavity of macrocycles, where the host provides guest accommodation and stabilization originating from non-covalent interactions, e.g. hydrogen bonding, $\pi\cdots\pi$ stacking, and C-H⋯π interactions. Among these non-covalent interactions, hydrogen bonding is the strongest one,\textsuperscript{3} especially when considering electronegative atoms like oxygen and nitrogen, where the difference in Pauling electronegativity with hydrogen ($\Delta\chi$) is 1.24 and 0.84, respectively (Figure 1.15). On the other hand, the $\Delta\chi$ for C and H is just 0.35 which makes it very weak for hydrogen bonding; however, the advantage of C-H bonds is their widespread presence in aliphatic or aromatic compounds.\textsuperscript{146} Thus, understanding this ubiquitous bond and its potential for anion recognition has seen renewed interest among supramolecular chemists.\textsuperscript{147}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure1.15.png}
\caption{Pauling electronegativity difference ($\Delta\chi$) of O, N and C with hydrogen.}
\end{figure}
In 1990, Dixon and coworkers showed that a fluorinated macrocyclic ether can act as a fluoride ion host purely through the C-H⋯F⁻ hydrogen bonding.\textsuperscript{148} The electron withdrawing fluorine atoms are the main source creating a polarized C-H bond therby increasing the electropositivity at the hydrogen atom. Almost a decade later, a comprehensive computational investigation by Scheiner and coworkers showed the strong effects of installing fluorine atoms on the strength of C-H hydrogen bonding. Their results revealed that the interaction between F\textsubscript{n}H\textsubscript{3}.\textsubscript{n}CH as a proton donor is very weak in CH\textsubscript{4} molecule, but increases by 1 kcal/mol with each F that is added to the system.\textsuperscript{149} In addition to Dixon’s fluorinated macrocyclic ether, in 2004, Steed and coworkers reported a preorganized macrobicyclic receptor which uses three N-H and three C-H hydrogen bond donors to encapsulate the fluoride and chloride anions.\textsuperscript{150} More recently, in 2008, Schalley and coworkers employed a rigidified methylene-bridged resorcin[4]arene-based cavitand to investigate its aliphatic C-H hydrogen bonding with a series of anions (Figure 1.16).\textsuperscript{151} Their mass spectrometric experiments confirmed the presence of host-anion adducts in the gas phase which they attributed to the weak aliphatic C-H⋯anion interactions.

![Figure 1.16](image1.png)

**Figure 1.16** (Left) the Chemdraw structure of fluorinated macrocyclic ether. (Middle) the Chemdraw and (3D adopted from ref. 150) structure of macrobicyclic receptor. (Right) the Chemdraw structure of methylene-bridged resorcin[4]arene-based cavitand, effective hydrogens are shown in purple.
Despite a few reports on the aliphatic C-H hydrogen bonding, a range of hosts were reported relying solely on ArC-H hydrogen bonding. The increased attraction towards the aromatic C-H hydrogen bond donor can be attributed to the increased acidity of its aromatic proton compared to the aliphatic C-H, and can be further amplified by the installation of electron withdrawing groups that effectively increase the acid strength of the desired proton. Indeed, Bryantsev et al., showed that electron withdrawing groups can make aryl ArC-H hydrogen bonds as strong as the conventional O−H and N−H groups. Johnson and coworkers utilized this finding and synthesized a series of tripodal receptors with electron-withdrawing substituted aromatic rings (Figure 1.17). Despite the significant increase in the binding of NO2-substituted compounds, compared to phenyl, the association constants ($K_a$) remained relatively small ($> 53 \text{ M}^{-1}$). Due to its weak association constants, the C-H hydrogen bond has been marginalized for several years within the supramolecular chemistry community. Recently, Flood et al. challenged this notion by introducing a cage-like 3-dimensional macrocycle (Figure 1.17) which can bind the chloride ion with exceptional selectivity and affinity ($K_a = 10^{17} \text{ M}^{-1}$). Note that the one-pot synthesis of cyanostar was reported by same group in 2013. This molecule stabilizes the anion inside its cavity with ten protons: five from the aromatic moieties and five from the olefinic C-Hs.
1.3 Conjugated molecular nanotubes

Tubular species, akin to carbon nanotubes (CNTs), have attracted the attention of scientists even before the discovery of CNTs. Selective bottom up syntheses of CNTs are the bottleneck in their application development. In the pursuit to develop this bottom up chemistry (Figure 1.18), the field of contorted aromatics has grown significantly since the report by Jasti et al. in 2008 on the synthesis of \([n]\)cyclo-para-phenylenes, where \(n = 9, 12, \) and 18. Jasti’s seminal contribution, along with others, paved the way for the construction of a wide range of molecules with radially-oriented \(\pi\)-systems. In this section, I start by providing an overview of the synthesis of conjugated molecular nanorings (CMRs), later I describe the field of conjugated molecular nanobelts (CMBs), and finally I focus on the end-capped and phenine nanotubes as the examples for (CMTs). In the coming years, I expect a large number of CMTs to appear in the
literature as a result of the combination of current synthetic methodologies taming the large strain energies required to bend the aromatic system and known macromolecular structures that will serve to template the construction of these CMTs.

![Diagram](image)

**Figure 1.18** Hypothetical armchair CNT retrosynthesis starting from an (a) (8,8)CNT, to (b) a benzene edge-fused nanobelt, and last (c) to its shortest benzenoid segment, an [8]cyclo-para-phenylene.

### 1.3.1 Conjugated molecular nanorings (CMRs)

Bending aromatic systems has been a topic of interest even before fullerenes\(^{161}\) and carbon nanotubes,\(^{156,157}\) two quintessential classes of contorted aromatic compounds, were discovered.\(^{162,163}\) The heart of the synthetic challenge lies in the steep increase of strain energy (SE) when distorting the system.\(^{164,165}\) Strategies to overcome this strain usually revolve around establishing the connectivity of the molecule first, involving sp\(^3\) carbon atoms to provide the angular requirement, prior to aromatization in the last step.\(^{166}\) This strategy has been particularly successful in the development of conjugated molecular nanorings (CMRs) – macrocycles comprised of
polyaromatic hydrocarbon units linked together by single covalent bonds maintaining π-conjugation and connected in a way that orients their π-system radially. Note that \([n]\text{cyclo-para-phenylacetylenes, first synthesized in 1996,}^{167}\) are also regarded as CMRs, although I refer the reader to other more in-depth reviews for additional information.\(^{168}\) In this section, I describe the strategies reported up to now and the current aromatic landscape of molecular variability afforded by these novel methods.
Macrocycles formed by connecting phenylene rings through their 1,4 positions represent the shortest benzenoid segment of an armchair CNT and are known in the literature as \([n]\)cyclo-para-phenylenes (\([n]\)CPPs). These were first reported in 2008 by Jasti et al., and since then the field has grown exponentially, where \([n]\)CPPs are now used in luminescent solar concentrators.
as bioimaging tracers, ligands for metal coordination, various host-guest studies, and several other applications in supramolecular chemistry. The breakthrough in the synthesis of \([n]\)CPPs was possible by using a masked aromatic ring in the form of a \(\text{syn-dimethoxy cyclohexa-1,4-diene intermediate} \) (Figure 1.19a). These cyclohexadiene units were incorporated into a strain-free macrocycle, which then was subsequently reductively aromatized in the last step to form the \([n]\)CPP. Shortly after, Itami and coworkers reported an alternative methodology following an oxidative aromatization synthesis of \([12]\)CPP using cyclohexane as part of the strain-free macrocycle (Figure 1.19b). A different approach to form \([n]\)CPPs was reported by Yamago et al. in 2010, where reductive elimination was forced upon a square-shaped tetranuclear platinum macrocycle for the synthesis of \([8]\)CPP (Figure 1.19c). More recently, five more methods have been reported for the synthesis of \([n]\)CPPs, the first of these was reported in 2014 by Wang and coworkers and include the formation of dimethoxynaphth-1,4-diyl units that are used in \([\text{Ni}]\)-mediated homocoupling reactions to form a strain-free macrocycle, which is oxidatively aromatized with DDQ to form the corresponding \([n]\)CPP (Figure 1.19d). Also in 2014, Wegner et al. reported the use of cyclohexane- and diyne-containing strain-free macrocycles that were treated under \([\text{Rh}]\)-catalyzed cycloaddition conditions to form a functionalized \(\text{para-terphenyl moiety, this cyclohexane-para-terphenyl macrocycle was oxidatively aromatized under air to form [8]CPP.} \) Note how their methodology is able to introduce late-stage functionalization into the nascent \([n]\)CPP (Figure 1.19e). In late 2015, Tanaka et al. reported the synthesis of carboxylate-containing \([12]\)CPP obtained by a \([\text{Rh}]\)-mediated intermolecular cross-cyclotrimerization followed by reductive aromatization (Figure 1.19f). The same group reported in 2019 an approach to the formation of \([8]\)CPP following a \([\text{Rh}]\)-catalyzed intramolecular cyclotrimerizations of a cyclic dodecayne (Figure 1.19g). Most recently, Tsuchido et al. reported the formation of \([6]\)CPP in
69% yield from digold(I) complexes forming a triangular intermediate, as depicted in Figure 1.19h, through an oxidative chlorination using PhICl₂. Overall, these synthetic approaches have provided scientists with a wide range of plain and functionalized [n]CPPs (n = 5–16, and 18). With the advent of [n]CPPs, strategies were simultaneously developed to incorporate larger polyaromatic hydrocarbons (PAHs) into the conjugated nanoring. Two general research avenues have been developed, the first in which a single foreign PAH is incorporated into the [n]CPP, and a second approach where the entire nanoring is composed of a repetitive number of the larger aromatic building block. In this section, I summarize the known building blocks that have been used, and the connectivity enforced within these PAHs, in the formation of nanorings (Figure 1.20).
After phenylene-based nanorings, naphthalene and anthracene follow as the most studied building blocks in the formation of CMRs. Work by Itami, Du, and Isobe, have incorporated naphthalene into CMRs by linking it through its 1,4 and 2,6 positions. This latter linkage imparts chirality to the nanoring, where a rotational barrier of 16 kcal/mol has been determined experimentally for [6]cyclo-2,6-naphthylene. Reports by Jasti, Cong, and Gaeta, on
using anthracene to construct CMRs establish three different connectivity modes: 1,4, 2,6, and 9,10. As in naphthalene, the 2,6-linked anthracenyl CMR provides chiral moieties that interconvert readily since the rotational barrier is just 8.6 kcal/mol.

Using functionalized phenanthrene through a [Pt]-mediated macrocyclization gave rise to [8]cyclo-3,9-phenanthrenylene, a complex case of cyclostereoisomerism. Variable temperature circular dichroism of pure stereoisomers revealed isomerization barriers around 25 kcal/mol. Rotamers of cyclic fluorene, reported by Yamago et al., connected at the 2,7 positions have an even higher calculated rotational barrier of 58.3 kcal/mol, preventing interconversion even at 180 °C for 24 h. Pyrene has also been used in the formation of CMRs. The four-member pyrene-containing nanoring, [4]cyclo-2,7-pyrenylene, has the same circumference as [8]CPP, although its SE is significantly higher at 93.7 versus 72.2 kcal/mol, respectively.

Reports by Isobe et al., show that linking chrysene through its 2,8 or 3,9 positions gives rise to a range of atropisomers with remarkably persistent belt shapes. Esser and coworkers described the first CMR incorporating an anti-aromatic PAH, where two units of dibenzo[a,e]pentalene were incorporated into a [n]CPP. In certain cases, incorporation of a larger aromatic building block occurs in situ. This is the case of dibenz[a,h]anthracene and dibenzo[c,m]pentaphene, connected at positions 3,10 and 2,11, respectively, which were synthesized into an existing [n]CPP by iterative ring-closing metathesis/reductive aromatization steps.

Perylene, a building block extensively used in PAH chemistry, has been incorporated into a nanoring through its 3,9 positions. In fact, this CMR reported by Jasti has been used for in situ growth of 4,10-linked benzo[ghi]perylene with inconclusive results. π-Extended CMRs have been synthesized as 2,8-anthanthrene-only and 4,10-anthanthrene-phenyl systems.
Interestingly, the rotational barrier for the 2,8-linked nanoring is only 21 kcal/mol. Another large PAH that has made it into a CMR is dibenzo[g,p]chrysene.208 [Pt]-mediated macrocyclization of dibenzo[g,p]chrysene, borylated in the 3,11 positions, gives almost exclusively the three-membered CMR in 23% yield.

The first CMR containing five-member rings was synthesized by Isobe et al. out of 5,12-diborylated rubicene.209 These rubicene CMRs stereoisomers do not interconvert at room temperature and have onsets of light absorption around 650 nm. Finally, work by the groups of Du and Mullen reported tribenzo[b,n,pqr]perylene210 and hexa-peri-hexabenzocoronene CMRs,210-216 the largest PAHs forming part of a nanoring, where the smallest nanorings feature SEs of ~80 kcal/mol.

1.3.2 Conjugated molecular nanobelts

During the past sixty years the structure of numerous carbon nanobelts have been proposed theoretically but experimentally unsuccessful.217 The first radially conjugated molecular nanobelt (CMB) was reported by Gleiter et al. in 2008 and it features a [6.8]3cyclacene (1.1 in Figure 1.21).218 Prior DFT studies indicated that 1.1 was thermodynamically feasible.219 The anticipated $D_{3h}$ structure was confirmed by its symmetrical $^1$H NMR and single crystal X-ray structure. CMB 1.1 features an absorption band at $\lambda_{\text{max}}$ of 220 nm, with shoulders at 278 and 290 nm, and emission at $\lambda_{\text{em}} = 370$ nm. Most recently, N-containing belts related to 1.1 appeared in the literature.220

While 1.1 features a radially conjugated system, it does not present “a closed loop of fully fused edge-sharing benzene rings”, akin to [n]cyclacenes. This latter definition was realized for the first time in 2017, when Itami and co-workers reported CMB 1.2 (Figure 1.21).221 The feat was accomplished by sequential Witting reactions followed by intramolecular Yamamoto
couplings providing 1.2 in low yields. The final compound resembles a slice of (6,6)CNT and is a structural isomer of [12]cyclophenacene (not synthesized yet). The diameter of 1.2 is around 0.2 Å larger than that of [6]CPP (~8.1 Å).\(^{222}\) However, due to the less degrees of freedom, the SE of 1.2 is around 23 kcal/mol higher than [6]CPP at 96 kcal/mol.\(^{199,223}\) The frontier molecular orbitals of 1.2 are evenly distributed over the whole structure. Its large radial π-system has lowest energy absorption band centered around 400 nm and a weakly absorbing region extending up to ~500 nm. Also, in contrast to [6]CPP, 1.2 has an appreciable fluorescence with the main emission band centered at ~635 nm.

![Figure 1.21 Conjugated molecular nanobelts.](image)

Follow up work by the same group established the synthesis of carbon nanobelts containing 16 and 24 fused benzene rings.\(^{224}\) In contrast to the ring size-independent absorption of [\(n\)]CPPs at \(\lambda_{\text{max}}\) of ~350 nm, the absorption of these CMBs red shifts with increasing size. Interestingly, their emission behavior has an opposite trend displaying a monotonic blue shift as the size
increases. Finally, although counterintuitive, the HOMO-LUMO gap of these carbon nanobelts, as in \([n]\)CPPs,\textsuperscript{225} becomes larger as the ring size goes up.

Shortly after the publication of carbon nanobelt \textbf{1.2}, Miao and coworkers\textsuperscript{226} reported larger (\textbf{1.3}) and chiral (\textbf{1.4}) nanobelts (\textbf{Figure 1.21}), thus opening the door to extend the family to more CMBs. First thing to note in compounds \textbf{1.3} and \textbf{1.4} is their rigid structure comprising a short segment of a (12,12) and (18,12)CNT, respectively, and concomitantly a larger effective radial \(\pi\) surface. These compounds were synthesized by \(\pi\)-expansion of the corresponding polyarylated nanorings through Scholl reactions. The precursor to \textbf{1.3} comprises the backbone of a [12]CPP, while for \textbf{1.4} is a nanoring comprised of alternating 1,4-phenylene and 2,6-naphthylene units. In cyclizing these nanorings to form \textbf{1.3} and \textbf{1.4} there is a change in the DFT calculated SE of 45.8 to 54.2 kcal/mol and 39.1 to 28.2 kcal/mol, respectively. This is remarkable since it demonstrates that depending on the nanoring, the belt-forming reactions may relieve strain as opposed to the general notion expecting an increase. In fact, the 66\% yield of \textbf{1.4} is attributed to the strain relieving effect.

The absorption properties of the precursors to \textbf{1.3} and \textbf{1.4} are almost identical with \(\lambda_{\text{max}}\) and \(\lambda_{\text{em}}\) of \(\sim310\) and 450 nm, respectively. Upon formation of \textbf{1.3} and \textbf{1.4}, all bands red shift. Specifically, \textbf{1.3} and \textbf{1.4} display lowest energy absorption bands at 466 and 427 nm. Similarly, \textbf{1.2} emits at 498 and 532 nm, while \textbf{1.3} does it at 464 and 492 nm. Visually, \textbf{1.3} and \textbf{1.4} have green and blue luminescence, respectively. The electrochemical HOMO level was determined to be \(-5.69\) and \(-6.04\) eV for \textbf{1.3} and \textbf{1.4}, respectively.

In early 2019, Yamada et al. published the first metal-containing CMB \textbf{1.5} (\textbf{Figure 1.21}),\textsuperscript{227} and similar to \textbf{1.1}, it also presents \(D_{3h}\) symmetry. The nickel porphyrin-based structure of \textbf{5} confers electrochemical activity, shown by its ability to accept and deliver up to five electrons,
as demonstrated from cyclic and differential pulse voltammetry. It was also demonstrated by UV-vis titration and DFT studies that the top and bottom concave structure in 1.5 serves to host two C\textsubscript{60} molecules. As described by the authors, future studies aim to incorporate other transition metals and the synthesis of larger porphyrinoid CMBs.

Most recently, the challenge to synthesize zigzag fused nanobelts, historically called [n]cyclacenes\textsuperscript{163, 218, 228-231} has been accomplished and adds into the growing family of conjugated molecular nanobelts. To this end, early in 2020 Wang and coworkers reported for the first time the detection of an eight-member zigzag carbon nanobelt by MALDI-TOF\textsuperscript{232} [n]Cyclacenes are expected to be reactive as a result of the synergistic effect of its electronic state and strain energy.\textsuperscript{223} Shortly after Wang’s report, two research teams, Segawa, Itami and coworkers,\textsuperscript{233, 234} and simultaneously Chi et al.,\textsuperscript{235} reported the successful synthesis, isolation, and characterization of a zigzag 18- (1.6) and 12-member (1.7) zigzag carbon nanobelts, respectively (Figure 1.2). As determined by X-ray crystallography, compound 1.6 exhibits the sidewall segment of a zigzag (18,0)CNT, while 1.7 matches that of a (12,0)CNT. The calculated SE of the unfunctionalized compound 1.6 (R = H) is 63.3 kcal/mol. Optically, 1.6 displays a strong absorption band at 336 nm with an extended absorption tail until ~410 nm. Moreover, it exhibits blue fluorescence upon irradiation with UV light with two major peaks at 407 and 432 nm. Using this data, an optical band gap of ~3 eV is estimated. Interestingly, CMB 1.7 possess very similar absorption properties to 1.6, except its fluorescence is red shifted to major emission peaks located at 422 and 442 nm. This breakthrough opens the door to fundamental discoveries and potentially new properties in this class of CMBs. We refer the reader to other reviews in the literature with an extended discussion on CMBs.\textsuperscript{231, 236, 237}
1.3.3 End-caped nanotubes

In 2015 Stępień et al. reported the synthesis of highly strained nonclassical nanotube end-caps obtained from strain-free tricarbazole-based precursors via one-step Yamamoto coupling (Figure 1.22). Compound 1.8 is a tubular macrocycle capped on one side with a benzene moiety forming an internal accessible cavity. It was obtained in a 7% yield from the hexabromo species shown in Figure 1.22 using Ni(cod)$_2$ in excess. The DFT-calculated SE of 1.8 is 144 kcal/mol. In contrast to [n]CPPs, which exhibit a single absorption band in the UV region, compound 1.8 shows an intense band at 319 nm and an extended low intensity absorption until about 520 nm, producing an orange coloration when 1.8 is in solution. Emission from 1.8 is centered at $\lambda_{em}$ of ~430 nm showing three overlapping peaks and a low energy low intensity emission band at 630 nm. Overall, this templated approach demonstrates how highly strained architectures can be achieved from strain-free precursors.

![Diagram of compound 1.8](image)

Figure 1.22 Carbazole-derived end-capped nanotubes.
CNTs early synthesis experiments were carried out at elevated temperatures (arc discharge, >1700 °C) and later substituted for lower temperature chemical vapor deposition (CVD, <800 °C) techniques. Nonetheless, temperatures in the hundreds of degrees Celsius are normally used in CNT preparation, likely to be able to overcome the large reaction barriers to bend the π-surface. By performing “stitching reactions” on aromatic precursors with inherent curvature, Scott and co-workers were able to transform the functionalized corannulene, shown in Figure 1.23, under flash vacuum pyrolysis (FVP) to a short (5,5)CNT end-cap with formula C_{50}H_{10} (1.9). Compound 1.9 can be regarded as an axially extended corannulene. FVP provides the required energy to twist and bring the transient radicals into bonding conformations. Following this approach, corannulene bowl’s shape is transformed into a cylindrical structure (Figure 1.23). Conjugated molecular nanotubes (CMT) 1.9 was obtained in ~3% yield, the small conversion to 1.9 likely reflects the large strain energy induced in this structural transformation. Compound 1.9 is soluble in organic solvents such as dichloromethane, chloroform, benzene, and carbon disulfide. Similar to C_{60}, 1.9 exhibits λ_{max} at 268 and 308 nm, and a long absorption tail extending into the visible producing a red-orange powder in the solid state.
1.3.4 Phenine nanotubes

Nanotubes with periodic vacancies were reported by Isobe and coworkers as models of discrete CNTs. These are rigid cylindrical nanotubes formed by connecting benzene rings at their 1, 3, and 5 positions, as shown in Figure 1.24. Their synthesis involves the [Ni]-mediated homocoupling of $\text{I.10}$ to provide a [6]CMP derivative $\text{I.11}$. Iridium C-H borylation of $\text{I.11}$ provides $\text{I.12}$, with pinacol boronic esters at the $\text{para}$ positions ($\text{R}^2$). Following Yamago’s [Pt]-macrocyclization affords floppy macrocycle $\text{I.13}$, where tri, tetra and pentameric [6]CMP-containing macrocycles were isolated in 3, 6 and 3% yield, respectively. These motifs were then iododesilylated with ICl and subsequently coupled with 3-$\text{tert}$-butyl-5-chlorophenylboronic acid pinacol ester to provide the axially-extended macrocycles $\text{I.14}$. Finally, intramolecular Yamamoto coupling provided the target phenine nanotubes $\text{I.15}$. Tetrameric $\text{I.15a}$ was confirmed by MALDI-TOF, NMR and X-ray single crystal diffraction. Despite characterization of the
trimeric and pentameric phenine tubes by MALDI-TOF and NMR, these did not yield crystals. Tetrameric 1.15a fits almost within a cube since its diameter (1.65 nm) is only slightly shorter than its height (1.71 nm). To put it in perspective, it is large enough to encapsulate C\textsubscript{70}, as demonstrated from a second crystal structure.

![Chemical structures](image)

**Figure 1.24** Synthesis of phenine nanotubes.

Follow up work demonstrated how a slight modification in starting compound 1.10 (E = N) renders the nitrogen containing tetrameric phenine nanotube 1.15b\textsuperscript{243}. The X-ray molecular crystal structure of 1.15b is isostructural to tetrameric 1.15a, except with E = N. The optical and DFT data revealed a smaller optical band gap of 3.28 eV for 1.15b in comparison to 3.59 eV for tetrameric 1.15a. DFT calculations showed that this band gap narrowing effect upon nitrogen incorporation is due to LUMO rather than HOMO stabilization, similar to the what is observed in N-doped acenes\textsuperscript{244, 245}. Finally, trifluoroacetic acid protonates the pyridine rings in 1.15b and
concomitantly red-shifts its fluorescence with reduction of its quantum yield from 16% (non-protonated) to 8% (protonated).

1.4 Perspective and outlook

In recent years, scientists around the globe have embraced the challenging synthesis and development of rigid tubular architectures with radial π-systems. One of the major challenges to overcome in all these radially oriented π-systems is the build-up of strain energy in the final molecule. Utilizing non-aromatic intermediates to form a strain-free macrocycle, followed by the aromatization of the system in the final step, is one of the most prevalent methods to mitigate this build-up of strain. Another solution is to use organometallic macrocyclic intermediates (especially Pt and Au) to solve the uphill energy battle of the final product. Here, we describe an alternative solution making use of supramolecular chemistry, which has witnessed tremendous progress over the past decades, especially after Pedersen’s famous report on the macrocyclic molecules he coined as “crown ethers”. Since then, macrocyclic molecules have been at the center of supramolecular chemistry. Despite the vast progress in this field, a survey of the literature indicates that utilizing macrocyclic compounds, especially macrocyclic arenes, as templates for making shape-persistent conjugated systems is extremely rare. Although, it should be noted that utilizing these compounds can address some of the limitations of previous methodologies such as shorter synthetic routes and large modularity of the basic scaffold. Previous work on both rigid tubular architectures with radial π-systems and macrocyclic arenes inspired us to close the gap between these two branches of chemistry. Thus, in the following chapters, I will present the early attempts of our research group
towards the development of an alternative method to overcome the large penalty of building up strain.

This method will expand the access to novel conjugated molecular nanotubes in a few synthetic steps and is amenable to a variety of building blocks. My goal is to develop a short and general method that bridges the gap between contorted aromatics and macrocyclic arenes based on a scaffolding approach. The results outlined in the following chapters indicate that this approach can generate unprecedented properties such as permanent porosity, tubular rigidity, and optical and electrochemical activity. Moreover, the final structure can offer unprecedented hosts for large molecules, e.g., fullerenes. Most importantly, with the development of novel protocols to bend aromatic systems, I foresee many compounds forming part of the tubularene family. I expect a vast landscape of novel properties and fundamental discoveries to be reported as the field evolves.

It should be noted that the relatively low yields and tedious purifications of higher analogous \((n > 4)\) of resorcin\([n]\)arene is at present the main limitation of the approach outlined in this thesis. The lack of access to larger scaffolds restricts a direct way to modulate the diameter of the final compound. Thus, I believe that further investigations to facilitate the large-scale synthesis of resorcin\([n]\)arene with \(n > 4\), or other similar macrocycles, is an inevitable task required to access a larger arsenal of nanotubes. As hinted above, an alternative solution to this problem is the utilization of other macrocyclic arenes accessible in different sizes, e.g., calix\([n]\)arenes.
2.0 TEMPLATE-ASSISTED SYNTHESIS OF SUPRAMOLECULAR NANOTUBES: ARMCHAIR MOLECULAR NANOTUBE

This chapter is adapted in part with permission from: Saber Mirzaei; Edison Castro; Raúl Hernández Sánchez. Tubularenes. Chemical Science 2020, 11, 8089-8094. Equal contribution.

In this chapter, I report the synthesis and characterization of conjugated, conformationally rigid, and electroactive carbon-based nanotubes that we term tubularenes. These structures are constructed from a resorcin[mb]arene base. Cyclization of the conjugated aromatic nanotube is achieved in one-pot eight-fold C–C bond formation via Suzuki-Miyaura cross-coupling. DFT calculations indicate a buildup of strain energy in excess of 90 kcal/mol. The resulting architectures contain large internal void spaces >260 Å³, are fluorescent, and able to accept up to 4 electrons. This represents the first scaffolding approach that provides conjugated nanotube architectures.

2.1 Introduction

Macromolecules in the nanosize regime with host-guest capabilities offer opportunities to develop novel applications in electronic devices, purification systems, and sensing. Frequently, their preparation involves the bending of aromatic systems, further increasing their strain and complexity. As a result, overcoming the build-up of strain energy has to be carefully considered during their design process. The syntheses reported
for \([n]\)cyclo-\textit{para}-phenylenes (CPPs) – the smallest circular segment forming an armchair carbon nanotube (CNT) – elegantly showcases the importance of this design process.\textsuperscript{159, 160, 267} These \([n]\)CPPs or nanorings, with sizable strain energies (<120 kcal/mol), were first\textsuperscript{267} synthesized by exploiting non-aromatic intermediates with \(sp^3\) carbon atoms to facilitate establishing the overall connectivity before re-aromatizing the nanoring in the last step. This synthetic breakthrough gave access to CPPs of varying sizes and concomitantly uncovered unexpected structure-function relationships,\textsuperscript{268} while also developing novel applications.\textsuperscript{176} Despite these advances, streamlined synthesis to extend the nanoring along its main axis to yield tubular systems comprised of contorted aromatic species are exceedingly rare.\textsuperscript{212, 215, 238, 262, 269, 270}

To expand current approaches, our group started exploring the possibility of using macrocycles to template the synthesis of strained conjugated aromatics, with the ultimate goal of extending this methodology to longer and more complex nanotube structures. Herein, I describe the first members of this class of highly-strained aromatic architectures having a tubular shape – that we have termed \textit{tubularenes}.

These macromolecules bottom-up approach starts from resorcin\([nb]\)arenes – macrocycles resulting from the acid-catalysed condensation of resorcinol and an aldehyde – as templates.\textsuperscript{107, 271} Given the resulting shape and templated origin of the molecules reported herein, we decided to term these \textit{tubular}\([nb,n,m,r]\)arenes (\textit{tubularenes} for short), where \(nb\) (b stands for basal) comes from the resorcin\([nb]\)arene parent, \(n\) and \(m\) are the CNT chiral indices, and \(r\) corresponds to the number of aromatic rings making up the armchair nanoring in the upper termini (disregarding the pyrazininc ring). In this report we describe the synthesis and characterization of tubular\([4,8,8,8]\)arene (\textbf{2.1}) and tubular\([4,8,8,12]\)arene (\textbf{2.2}), as shown in \textbf{Figure 2.2}.
2.2 Results and discussion

2.2.1 Armchair tubularenes construction

Starting materials 2.4 and 2.5 can be synthesized on a multigram scale. Reaction between 2.4 and 2.5 under basic conditions using triethylamine (TEA) in acetonitrile under reflux produces octabromo-derivative 2.3 in 57% yield. Under similar reaction conditions, Suzuki-Miyaura cross coupling of 2.3 with either 1,4-benzenediboronic or 1,4-naphthalenediboronic acid bis(pinacol) ester affords 2.1 and 2.2 (Figure 2.2), respectively, after an eight-fold C–C bond formation. The isolated yield after the cross-coupling step to give 2.1 is ~1.3% (0.8% for 2.2). Similarly, other contorted aromatics initially reporting low yields have been optimized up to seven-fold.221,224 The cross-coupling cyclization step provides rigidity and aromatic conjugation to 2.1 and 2.2, much like the walls of CNTs. In 2.1, this newly formed upper nanoring resembles [8]CPP,160 although with fewer degrees of freedom since only four phenyl rings may rotate as opposed to eight in [8]CPP. We hypothesize this rigid conformation is vital to maintaining electron or hole delocalization across the conjugated framework, especially since it is known that departure from the radially oriented π system breaks the spin density distribution in radical monocationic CPPs.272

![Figure 2.1 Synthesis of compound 2.5](image_url)
2.2.2 Armchair tubularenes structure

MALDI-TOF MS of tubularenes 2.1 and 2.2 display matching simulated values and isotopic distributions as shown in Figure 2.3a. In solution, $^1$H NMR of 2.1 and 2.2 is readily assigned indicating $C_{4v}$ symmetry (Figure 2.3b). To our delight, slow evaporation of a dichloromethane/acetonitrile solution of 2.1 at room temperature affords high quality yellow-green crystals. In contrast, crystals of 2.2 are needle-like and weakly diffracting. The rigid framework expected for 2.1 is observed in its molecular crystal structure shown in Figure 2.3c. In the same figure, its internal cavity is readily apparent from the top view of the sphere packing model. To determine the size of this cavity, we obtain a volume of $\sim 360 \, \text{Å}^3$, if we consider the average
diameter of 2.1 as ~10 Å, and having a height of ~4.6 Å (as described in Figure 2.4). Alternatively, by employing the solvent accessible calculator in Olex2\textsuperscript{273} we find a volume of ~266 Å\textsuperscript{3}.

**Figure 2.3** (a) Experimental MALDI-TOF MS molecular ion peaks of 2.1 (blue trace) and 2.2 (red trace). Black traces represent the simulated [M+H]\textsuperscript{+} isotopic distributions. (b) \textsuperscript{1}H NMR of (top) 2.1 and (bottom) 2.2 in CD\textsubscript{2}Cl\textsubscript{2} at 20 °C. Proton labels according to Figure 2.2. (c) Molecular crystal structure of 2.1 obtained at 150 K. Thermal ellipsoids are set at 50% probability level. The C, N, and O atoms are colored grey, blue, and red, respectively. The H atoms are omitted for clarity. Bottom: top view of the sphere packing model (van der Waals radii) of 2.1. (d) DFT calculated barrier for ring flipping. Rotation of the phenyl moiety was followed by tracking the dihedral angle between the highlighted carbon atoms in orange.
Figure 2.4 Interior cavity measurements of tubularene 2.1. Calculated volume ≈ 360 Å³. Left: Diameter (10.044 Å). Defined as the distance from centroid-to-centroid of two opposing pyrazinic rings. Right: Height (4.626 Å). Defined as the distance between i) centroid 1 (resulting from the four top carbon atoms of each of the aromatic rings making up the resorcin[4]arene fragment), and ii) centroid 2 (resulting from the para carbons in the top eight-member aromatic ring).

The upper nanoring of 2.1 resembles [8]CPP, albeit with fewer degrees of freedom. The strain energy reported by Itami et al. for [8]CPP is 72.2 kcal/mol, obtained by DFT at the B3LYP/6-31G(d) level of theory, considering a homodesmotic reaction (Figure 2.5). Following a similar approach at the same level of theory, we determine the strain energy of 2.1 to be 92.4 kcal/mol. DFT calculations at different levels of theory produced consistent values around 89 ± 3 kcal/mol (Table 1.1). This larger value for tubularene 2.1 relative to [8]CPP is expected, especially since 2.1 has only four out of eight phenyl rings that can freely rotate. In fact, free rotation is hampered at room temperature as observed in the vastly different chemical environments of a versus b protons at 6.8 and 8.7 ppm (Figure 2.3b), respectively.
Figure 2.5 Homodesmotic reactions for the calculation of strain energies of a) tubularene 2.1 and 2.2 and b) [8]CPP.

Table 2.1 Strain energies (ΔH, in kcal/mol) of 2.1, 2.2, and [8]CPP calculated at DFT/6-31G* level of theory based on homodesmotic reactions as described in Figure 2.5.

<table>
<thead>
<tr>
<th></th>
<th>B3LYP</th>
<th>B3LYP-D3BJ</th>
<th>M062X</th>
<th>MN15</th>
<th>ωB97XD</th>
</tr>
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<tbody>
<tr>
<td>2.1</td>
<td>92.4</td>
<td>86.6</td>
<td>89.2</td>
<td>86.4</td>
<td>90.5</td>
</tr>
<tr>
<td>2.2</td>
<td>87.4</td>
<td>76.7</td>
<td>81.6</td>
<td>78.1</td>
<td>81.4</td>
</tr>
<tr>
<td>[8]CPP</td>
<td>71.9</td>
<td>69.3</td>
<td>72.7</td>
<td>70.9</td>
<td>72.4</td>
</tr>
</tbody>
</table>

DFT-calculated nucleus-independent chemical shifts (NICS) establish a shielding effect at the interior of the tubularene (Figure 2.6).\(^{274}\) We find by DFT analysis a rotational barrier of \(~29 ± 1\) kcal/mol for this phenyl group (Figure 2.3d) Comparing to other highly strained molecules,
this barrier is similar in magnitude to several others where temperatures well above 150 °C are required for rotation of the aromatic group or inversion of stereochemistry.\textsuperscript{185, 188-190, 201, 275-277} Note that in the latter examples DFT calculations reproduce closely the experimental rotational barriers. In contrast, similar phenyl rotation in [8]CPP is lower than 4 kcal/mol. We hypothesize the locked conformation in 2.1 to be particularly relevant to maintaining conjugation across the tubularene. Indeed, DFT calculations show the HOMO density evenly distributed across the upper rim of 2.1, whereas the LUMO has significant orbital density at the pyrazinic fragments (Figure 2.7a).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure26.png}
\caption{Nucleus-independent chemical shifts (NICS) in 2.1. The origin of the grid shown in the left hand side starts at the geometric center of the [8]CPP-like nanoring in 2.1. At the origin, NICS = $-3.87$ ppm. NCIS were calculated at the MN15/6-31G*+PCM(CH$_2$Cl$_2$) level of theory.}
\end{figure}

The 1,4-naphthylene fragments in tubularene 2.2 are significantly more restricted to rotation. In fact, due to steric clashing of the naphthylene moiety with the resorcin[4]arene base we were not able to calculate the rotational barrier via DFT. At room temperature, there is a single resonance for protons a', b', and c' (Figure 2.3b). Furthermore, we determine by DFT the strain
energy in \textbf{2.2} to be $\sim 81 \pm 5$ kcal/mol. The magnitude of this strain energy is substantially higher than that of the similar nanoring [8]cyclo-1,4-naphthylene ([8]CN) at 50.6 kcal/mol.\textsuperscript{278} Looking at the DFT optimized structure of \textbf{2.2}, we note it converges to a conformation where all naphthylene units are almost horizontally aligned pointing away from the tubularene. This naphthylene bending results in large dihedral angles ($\sim 55$ degrees) and is likely the reason of the increased strain.\textsuperscript{199}

\textbf{2.2.3 Armchair tubularenes optoelectronic properties}

Species \textbf{2.1} and \textbf{2.2} display lowest energy absorption bands at $\lambda_{\text{max}}$ of 394 ($\epsilon = 31380$ L/mol·cm) and 402 ($\epsilon = 12970$ L/mol·cm) nm, respectively. These bands are red-shifted in comparison to the lowest energy transition of precursor \textbf{2.3} at $\lambda_{\text{max}} = 338$ ($\epsilon = 42030$ L/mol·cm) nm (Figure 2.7c). Regarding emission, the fluorescence envelope of \textbf{2.1} and \textbf{2.2} is also red-shifted in comparison to precursor \textbf{2.3} ($\lambda_{\text{em}} = 435$ nm). Emission bands of \textbf{2.1} and \textbf{2.2} are almost identical to each other only slightly shifted in $\lambda_{\text{em}}$ from 546 to 542 nm, respectively. Using these data we extracted the optical band gap ($E_{\text{gap}}$)\textsuperscript{279} for both tubularenes. $E_{\text{gap}}$ for \textbf{2.1} and \textbf{2.2} is 2.57 and 2.64 eV, respectively.

To gain further insight of the photophysical properties of \textbf{2.1} and \textbf{2.2} we performed time-dependent (TD) DFT calculations at various levels of theory. For both tubularenes, we found that the HOMO-to-LUMO transition is forbidden, as in [n]CPPs.\textsuperscript{280} Du et al. established a structure-function relationship between octamethoxy-[8]CPP ($\lambda_{\text{em}} = 458$ nm) and [8]CPP ($\lambda_{\text{em}} = 535$ nm) indicating that a bathochromic shift in emission corresponds to increased radial $\pi$-conjugation.\textsuperscript{281} Extrapolating this correlation to the emissive properties of \textbf{2.1} and \textbf{2.2} supports our claim that
tubularene’s rigidity assists to maintain a large $\pi$-conjugated surface, although not as much as [8]CN ($\lambda_{em} = 570$ nm).\textsuperscript{278}

Electrochemically, tubularenes 2.1 and 2.2 display a rich series of reductive events in ortho-dichlorobenzene. Cyclic voltammograms (CVs) exhibit onset of reduction at around $-1.95$ and $-2.05$ V vs Fc/Fc$^+$ for 2.1 and 2.2 (Figure 2.7d,e), respectively. Initially, these values are counterintuitive since we expect the LUMO of 2.1 to be more accessible and lower in energy than 2.1 due to the larger $\pi$ surface of 2.2. Inspection of the DFT optimized structure of 2.2, and its LUMO density plot shown in Figure 2.7b, provides an explanation for this unexpected behavior. As a result of the naphthylene fragments bending outwards as shown in Figure 2.7b these are devoid of LUMO density, hence effectively reducing the extent of conjugation of the $\pi$ surface in 2.2.
Figure 2.7 HOMO and LUMO density plots (±0.02 au) of (a) 2.1, and (b) 2.2. (c) UV-Vis absorption (solid trace) and emission spectra (dotted trace) of 2.1, 2.2, and 2.3, collected in CH₂Cl₂ at room temperature. Cyclic (CV) and differential pulse voltammetry (DPV) for (d) 2.1, and (e) 2.2 in ortho-dichlorobenzene at room temperature. CV scan rate: (d) 100 mV/s, and (e) 50 mV s⁻¹. A 0.1 M [n-Bu₄N][PF₆] solution was used as supporting electrolyte. The labels on italics correspond to the oxidation level q represented as: (d) [2.1]q and (e) [2.2]q. The E₁/₂ potentials were obtained from the DPV data. DPV traces are shifted down for better visualization of the data. (f) Experimentally determined HOMO-LUMO energy levels of 2.1, 2.2, and [8]CPP.

The CV of 2.1 displays four reduction events on the cathodic scan, but since these are clustered together, it is not possible to extract the half-wave potentials (E₁/₂) from the CV alone. Fortunately, by differential pulse voltammetry (DPV, orange trace in Figure 2.7d) we observe
four peak maximums at −2.01, −2.13, −2.31, and −2.45 V vs Fc/Fc⁺, each corresponding to a reduction event. In contrast to [8]CPP, oxidation events for 2.1 or 2.2 are not observed up to ca. +0.8 V vs Fc/Fc⁺. Similar to 2.1, tubularene 2.2 displays an equally crowded CV (Figure 2.7e). As in tubularene 2.1, DPV of 2.2 is well-resolved and shows three reduction peaks at −2.17, −2.25, and −2.41 V vs Fc/Fc⁺ (purple trace in Figure 2.7e). The fourth reduction of 2.2 is presumed to occur concomitant with solvent reduction based on the shoulder observed at around −2.65 V vs Fc/Fc⁺ (marked with an asterisk in Figure 2.7e). Note however how for the same number of electrons added (q), the $E_{1/2}$ for 2.2 is 100 to 150 mV more cathodic relative to 2.1, indicating that 2.2 is harder to reduce than 2.1.

We calculated the electrochemical LUMO levels ($E_{\text{LUMO}}$) for 2.1 and 2.2 by employing $E_{1/2}$ of the first reduction event according to $E_{\text{LUMO}} = -[E_{1/2} + 4.80] \text{ eV}$. Additionally, the HOMO energy level is obtained by subtracting $E_{\text{gap}}$ from $E_{\text{LUMO}}$. HOMO and LUMO levels for 2.1 and 2.2 are plotted in Figure 2.7f. For comparison, the computed HOMO and LUMO positions for [8]CPP are −5.16 and −1.92 eV, respectively. Therefore, by extending the conjugation to the quinoxaline walls, while maintaining a radial orientation of the π surface, tubularene 2.1 and 2.2 are able to bring down the LUMO energy level. In contrast, HOMO-LUMO levels in [n]CPPs are determined by the number of 1,4-phenylene units making up the nanoring.

Last, to gain further insight into the rigidity effect of tubularene 2.1 into electron delocalization across the aromatic framework, we performed DFT calculations on the radicals formed in 2.1 after removing an electron from the HOMO ($2.1^+/•$) and adding an electron to the LUMO ($2.1^-•$). Results show the spin density of the radical completely delocalized across the conjugated backbone of 2.1 (Figure 2.8), in stark contrast to [8]CPP and other similar contorted aromatics, where the radical is mostly localized into a portion of the molecule.
Figure 2.8 Spin density distribution plots (±0.0004 au) in the ground state of radical monocation and monoanion of tubularene 2.1 calculated by DFT at the ωB97XD/6-31G**+PCM(CH₂Cl₂) level of theory.
2.3 Conclusions

Herein we describe the synthesis of a new family of compounds that we have termed tubularenes. These offer a wide range of potential applications given their permanent internal void space, tubular rigidity, conjugation, and electrochemical activity. Tubularene's overall architecture is highly modular and tunable. For example, modifications to the “wall” (compound 2.5), diboronate coupling partner, or the basal resorcin[6]arene are envisioned as the tuning knobs of tubularene solubility profile (hydrophobic vs. hydrophilic), diameter, and overall electronic properties. Expansion of the tubularene family will open a new landscape for discovery of novel properties and applications of contorted aromatic systems with potential in host-guest chemistry or taking advantage of their unique optoelectronic features to fabricate electronic devices.
This chapter is adapted in part with permission from: Edison Castro;§ Saber Mirzaei;§ Raúl Hernández Sánchez*. Radially Oriented \([n]\)Cyclo-meta-phenylenes. *Organic Letters* 2021, 23, 1, 87–92. §Equal contribution.

Molecular compounds with zigzag carbon nanotube geometries are exceedingly rare. Here we report the synthesis and characterization of carbon-based nanotubes with zigzag geometry, best described as radially oriented \([n]\)cyclo-meta-phenylenes, extending the tubularene family of compounds. By the incorporation of edge-sharing benzene rings into the tubularene’s radial \(\pi\)-surface, we have uncovered the first step to give rise to the emergence of radial orbital distribution in zigzag nanorings.

### 3.1 Introduction

Carbon nanotubes (CNTs)\(^{156, 157}\) matchless feature is their permanently oriented radial \(\pi\)-system.\(^{287}\) Molecules with a rigid conformation able to display an electron cloud in this geometry were, until recently, unprecedented in the literature. The first molecule of this kind, referred to as a carbon nanobelt (CNB), comprises a “closed loop of [twelve] fully fused edge-sharing benzene rings” in an armchair\(^{288}\) CNT geometry.\(^{221}\) To date, few other fully fused compounds have been reported, including chiral species.\(^{238, 240, 263}\) All reported CNBs thus far are obtained by first
establishing the overall backbone connectivity in the form of an arene-alkene macrocycle or \([n]\text{cyclo-para-phenylene ([n]CPP),}\)\textsuperscript{175, 176} which in turn are closed into a CNB by inducing a cascade of nickel-mediated aryl-aryl\textsuperscript{221, 224} or Scholl cyclohydrogenation\textsuperscript{263} reactions, respectively. Most importantly, extrapolating a similar stepwise design logic to zigzag CNTs has not been successful (Figure 3.1a), although, by following other synthetic routes zigzag CNBs have been reported.\textsuperscript{235, 289} While \([n]\text{CPPs serve as nanobelt precursors for armchair geometries,}\)\textsuperscript{263} related \([n]\text{cyclo-meta-phenylenes ([n]CMPs)}\textsuperscript{290-295} could hypothetically serve similarly to synthesize zigzag-type CNBs, also termed \([n]\text{cyclacenes. However, [n]CMPs lack a radial }\pi\text{-system since their 1,3 connectivity favors flat-like macrocycles.}\)\textsuperscript{296} Aside from one previous report,\textsuperscript{297} the synthesis and characterization of radially oriented \([n]\text{CMPs remain largely unknown.}\)
In the previous chapter, I reported the synthesis of tubularenes by following an approach that facilitates the formation of the strained aromatic, the bottleneck step, in a one-pot eight-fold C–C bond formation via Suzuki-Miyaura cross-coupling. The upper rim of Chapter 2 tubularenes follows an armchair CNT geometry. Taking advantage of our modular strategy, we were able to almost double the height of these new tubularenes relative to the previous ones, and at the same time allowing us to switch to a zigzag-like geometry.
that resembles a radially oriented \([n]\)CMP. Herein I report tubular\([4,12,0,8]\)arene (3.1) and tubular\([4,16,0,12]\)arene (3.2), building on our prior strategy by introducing a belt of hydrogen bonds\(^{299, 300}\) to maintain the aryl reacting fragments close to each other, and demonstrating the modularity of our templated approach to both armchair and zigzag CNT geometries.

3.2 Results and discussion

3.2.1 Zigzag tubularenes construction

Abundant literature exists on the synthesis of species similar to 3.4.\(^{301}\) Treatment of 3.4 with 3,5-dibromobenzaldehyde in 4:1 EtOH:H\(_2\)O and excess NaHSO\(_3\) under reflux for 2 days affords 3.3 in 70\% yield (>2.5 g, Figure 3.2). Suzuki-Miyaura cross-coupling of 3.3 with 1,3-phenyldiboronic acid bis(pinacol) ester in 10:1:1 THF:H\(_2\)O:EtOH at 70 °C, with excess K\(_2\)CO\(_3\) and using Pd(PPh\(_3\))\(_4\) as catalyst, affords 3.1 in 3.3\% yield. Under similar reaction conditions, cross-coupling of 3.3 with 2,7-naphthalenediboronic acid bis(pinacol) ester provides 3.2 in 2.5\% yield. Unassigned \(^1\)H NMR resonances in 3.1 and 3.2 may indicate trapping of molecules in their cavities. Analogous tubularene wall structures 3.5a and 3.5b (Figure 3.2) were synthesized in order to gain more insight into the effects of rigidifying the overall architecture while maintaining the \(\pi\)-system radially oriented.
3.2.2 Zigzag tubularenes structure

Compounds 3.1 – 3.3 have poor solubility in standard organic solvents, but upon the addition of a small alcohol, e.g. MeOH or EtOH, these species readily go into solution. Vapor diffusion of Et$_2$O into a solution of 3.3 in MeOH:DCM formed colorless block-shaped crystals. The molecular crystal structure of 3.3, shown in Figure 3.3a, confirms our hypothesis in which a belt of hydrogen bonds is formed by the benzimidazole fragments and an external hydrogen bond donor-acceptor. Crystals of two different adducts have been obtained: 3.3·2H$_2$O·2MeOH (Figure
3.2a) and 3.3·H₂O·3MeOH. Density functional theory (DFT) optimized structures of tubularenes 3.1 and 3.2 at the MN15/6-31G*+PCM(CH₂Cl₂) level of theory are shown in Figure 3.2b and c, respectively. Attempts to grow crystals of 3.1 and 3.2 have only produced microcrystals with extremely weak X-ray diffraction. The structural information suggests that compounds 3.1 – 3.3 should be C₄-symmetric in solution. Indeed, ¹H NMR indicates a symmetric environment in all three cases (Figure 3.3d). From compound 3.3 we expect six unique chemical aromatic environments, all integrating for one hydrogen, except one, e” expected for two H. The single resonance for e” at 7.82 ppm demonstrates that at room temperature there is no steric hindrance for free rotation of the 1,3-dibromophenyl fragment as shown in Figure 3.2d. Note however that the tubular conformer is maintained in solution as indicated from the chemical shift of i” (>5.5 ppm, independent of the solvent system used). Following a similar analysis, under C₄ symmetry we expect ten aromatic resonances for tubularene 3.1 (Figure 3.1c). Indeed, all resonances are observed and assigned based on comparisons to 3.3, DFT calculated ¹H NMR, and their splitting pattern, e.g., a and b. Also, MALDI-TOF MS for 3.1 – 3.3 display a single ion in each case across a wide range in m/z (Figure 3.3e). Upon close inspection, the observed mass spectra match the simulated [M+H]⁺ isotopic distribution patterns for 3.1 – 3.3, as indicated in Figure 3.3 e1-e3.

Tubularene’s rigidity is particularly relevant to maintain the radial orientation of the π-system, and it also creates a permanent cavity. Octabromo species 3.3 maintains its tubular shape thanks to its belt of hydrogen bonds (Figure 3.3e inset). Closely related cavitands are known to flip between open (kite) and closed (vase) conformers depending on the guest and/or temperature,¹¹⁷ and in some the closed conformer has been enforced by intramolecular hydrogen bonding. Octabromo species 3.3 has eight hydrogen bonds formed between N and O atoms at an average distance of 2.77(1) Å, which is relatively short and likely provides a significant
energetic stabilization to the tubular form of 3.3. In the absence of the hydrogen bond donor-acceptor interaction, compound 3.3 lacks any significant solubility, presumably forming aggregates without an internal cavity. This is not the case in 3.1 and 3.2, where covalent bonding rigidifies the overall structure creating pores along the walls and permanent internal void spaces (Figure 3.3e inset). The diameters of 3.1 and 3.2 are ~9.5 and ~12.7 Å, respectively. These are remarkably larger than initially reported porous organic cages and on par with state-of-the-art organic moisture-stable porphyrin box cages with permanent porosity. The calculated internal volume of 3.1 and 3.2 are ~620 and ~910 Å³, respectively, and were obtained in a similar way to tubular[4,8,8,8]arene in the previous chapter. Tubularene’s internal cavity and rigidity makes them ideal candidates for novel porous organic solids.
Figure 3.3 Characterization of 3.1, 3.2 and 3.3. (a) Molecular crystal structure of 3.3, obtained at 150 K. Thermal ellipsoids set at 50% probability level. Hydrogen bonds shown in stripes of white and grey. (b, c) DFT optimized structures of 3.1 and 3.2 at the MN15/6-31G*+PCM(CH2Cl2). (d) 1H NMR of 3.1, 3.2, and 3.3 in selected solvent systems. Symbol * indicates residual solvent signals from 1,2-C6D4Cl2. (e) Experimental MALDI-TOF MS and isotope patterns of (e1) 3.3, (e2) 3.1, and (e3) 3.2. [M+H]+ simulated traces shown in black. Insets: top view of the structures of 3.1, 3.2, and 3.3, with their corresponding internal diameters.
Radially bending the aromatic π-system in 3.1 and 3.2 inherently builds strain. DFT calculations employing the homodesmotic reactions described in Figure 3.4, at different levels of theory, provide average strain energies (SEs) for 3.1 and 3.2 of 42.2 and 61.9 kcal/mol (Table 3.1), respectively. These are significantly lower in comparison to the average SEs of tubular[4,8,8,8]arene and tubular[4,8,8,12]arene at 89 and 81 kcal/mol, respectively, and substantially higher than those reported for [n]CMPs (≤23 kcal/mol) and [n]cyclo-2,7-naphthylens (≤19 kcal/mol). The obtained SEs are counterintuitive, since to a first approximation one would expect 3.2 to have less strain than 3.1 based on its larger diameter. In fact, while the top nanoring in 3.1 resembles a radial [n]CMP, the analogous nanoring in 3.2 with its 2,7-naphthylene moieties can be devised as a partial [n]cyclacene since it has conjugated edge-sharing benzene rings – a feature extensively investigated and until very recently unprecedented in the literature.
Figure 3.4 Homodesmotic reactions for the calculation of strain energies of tubularenes 3.1 and 3.2.

Table 3.1 Strain energies (ΔH, in kcal/mol) of 3.1 and 3.2 calculated at DFT/6-31G* level of theory based on homodesmotic reactions as described in Figure 3.4.

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<td>42.9</td>
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<td>45.0</td>
<td>66.2</td>
<td>58.9</td>
<td>58.1</td>
<td>64.3</td>
</tr>
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3.2.3 Zigzag tubularenes optoelectronic properties

Tubularene 3.2 can be regarded as an intermediate between a fully fused zigzag nanoring – [\textit{n}]cyclacene – and a non-fused radially oriented \([\textit{n}]\)CMP, just like the upper terminus in 3.1 (Figure 3.1a,c). UV-vis absorption and emission spectra of 3.1 – 3.3, 3.5a, and 3.5b were collected to gain further insight into their electronic structure. Absorption bands of 3.1 and 3.2 are clearly sharper than their precursor 3.3, and analogous wall building block compounds 3.5a and 3.5b (Figure 3.5a). From 300 to 340 nm, an almost identical peak progression is observed with \(\lambda_{\text{max}}\) at [306, 317, 334] versus [305, 318, 335] nm for 3.1 and 3.2, respectively. Note that the strong band at \(\lambda_{\text{max}} = 280\) nm in 3.2 is the only marked difference since this is not present in 3.1. Also, the absorption spectra of 3.1 and 3.2 depart significantly from \([8]\)CMP\(^{291, 296}\) (\(\lambda_{\text{max}} \approx 245\) nm) and \([\textit{n}]\)CNAP\(^{311}\) (size-independent \(\lambda_{\text{max}} \approx 270\) nm for \(\textit{n} = 5–7\)), which only have a single broad absorption band. Time-dependent (TD) DFT calculations establish the HOMO-to-LUMO transition in 3.1 and 3.2 to be forbidden, akin to previous chapter’s tubularenes\(^{208}\) and other radially conjugated compounds.\(^{166, 221}\) Most importantly, absorption band sharpening is a signature of tubularene’s rigidity, similar to the effects of rigidifying linear polymers,\(^{316}\) and akin to single-wall CNT.\(^{317, 318}\)

Non-contorted compounds 3.5a and 3.5b, analogues of the tubular walls of 3.1 and 3.2, respectively, display distinctive two sets of two emission transitions around 370 and 470 nm (Figure 3.5b). Surprisingly the low energy bands \(\sim 470\) nm are not present in 3.1 and 3.2, where only two peaks are observed at \(\lambda_{\text{em}}\) of [364, 376] nm for 3.1 and [365, 405] nm for 3.2. Notice how the high energy emission line is independent of the size of the zigzag nanoring in 3.1 and 3.2, while the low energy emission band red-shifts in 3.2, likely related to its larger radial \(\pi\)-surface.
From this optical data an identical Stokes shift of \( \sim 2460 \text{ cm}^{-1} \) is observed for tubularenes 3.1 and 3.2. This is in stark contrast to the Stokes shifts of 7065 and 6425 cm\(^{-1}\) observed in the previously chapter armchair tubular[4,8,8,8]arene and tubular[4,8,8,12]arene,\(^{298}\) respectively. Compounds having large Stokes shifts, e.g. \( >7000 \text{ cm}^{-1} \), are exceedingly rare,\(^{319-322}\) and highly desired to prevent self-quenching of fluorophores in materials and biologically relevant applications.\(^{169,323}\) Interestingly, when comparing zigzag to armchair tubularenes of the same diameter (~1 nm), e.g. 3.1 and tubular[4,8,8,8]arene, we observe a remarkable three-fold increase in Stokes shift. Optical gaps (\( E_{\text{gap}} \))\(^{279}\) are similarly tuned between zigzag and armchair tubularenes, whereas for 3.1 and 3.2 we obtain 3.58 and 3.52 eV, respectively, armchair tubularenes in Figure 3.1b have \( E_{\text{gap}} \)s significantly smaller at \( \sim 2.6 \text{ eV} \). The larger \( E_{\text{gap}} \)s in zigzag 3.1 and 3.2, or cross-conjugated systems,\(^{324}\) is attributed to their lack of global conjugation and inherent destructive quantum interference.\(^{325,326}\) The modularity of the synthetic approach developed here, and combined with chapter 2,\(^{298}\) demonstrate its remarkable capability to fine tune the Stokes shifts in comparatively similar conjugated molecular nanotubes, while maintaining their emissive properties as determined from their fluorescence quantum yields (\( \phi_{\text{fl}} \)) of 35, 39, 40 and 38 for compounds 3.1, 3.2, tubular[4,8,8,8]arene, and tubular[4,8,8,12]arene (using anthracene as standard\(^{127}\)), respectively. In comparison, note that [8]CPP and [6]CMP have poor \( \phi_{\text{fl}} \) of 0.084\(^{268}\) and 6%,\(^{328}\) respectively.
Figure 3.5 Electronic structure of tubularenes 3.1 and 3.2. (a) UV-Vis absorption and (b) emission spectra collected in CH₂Cl₂/MeOH (9:1) at room temperature. Emission data was collected by light excitation at 305 nm. Side and top views of LUMO density plots (±0.02 au) of tubularene (c) 3.1 and (d) 3.2, calculated at the MN15/6-31G*+PCM(CH₂Cl₂) level of theory.

DFT calculations at different levels of theory were carried out to support the electronic structure of tubularenes 3.1 and 3.2. Extending the radial π-surface area has a profound effect on the HOMO-LUMO density in these tubularenes; in fact, it is particularly evident in the LUMOs as shown in Figure 3.5c and d, whereas in 3.1 the orbital density is located along its tubular walls, in 3.2 the LUMO is distributed exclusively across its upper nanoring. This dramatic shift of the location of the LUMO density is also reflected in its DFT calculated energy level values, where the radially distributed LUMO of 3.2 is lower in energy than that of 3.1 across all theory levels. Finally, the electronic structure evolution from 3.1 to 3.2 demonstrates the fundamental effect of
the stepwise incorporation of edge-sharing benzene rings into zigzag nanorings en route to a fully fused system, akin to \([n]\)cyclacenes.

### 3.3 Conclusions

Here I demonstrated how tubularenes of zigzag geometry can be synthesized with just a minor perturbation of our initial strategy for armchair tubularenes. This expansion significantly increases the number of potentially new species within the tubularene family of compounds, and therefore widens the landscape for new discoveries. Tubularenes 3.1 and 3.2 establish an unprecedented fundamental electronic structure-function relationship demonstrating how orbital delocalization is shifted radially by incorporation of edge-sharing benzene rings into the radial zigzag nanoring. These findings can be extrapolated to provide an understanding of the evolution of the electronic structure of carbon nanotubes early in their formation.
4.0 TEMPLATE-ASSISTED SYNTHESIS OF SUPRAMOLECULAR ANION RECEPTORS

This chapter is adapted in part with permission from: Saber Mirzaei; Victor M. Espinoza Castro; Raúl Hernández Sánchez*. Nonspherical Anion Sequestration By C-H Hydrogen Bonding. Chemical Science 2022, 13, 2026–2032.

Macrocyclic arenes laid the foundations of supramolecular chemistry and their study established the fundamentals of noncovalent interactions. Advancing their frontier, here I designed rigidified resorcin[4]arenes that serve as hosts for large nonspherical anions. In one synthetic step, I vary the host's anion affinity properties by more than seven orders of magnitude. This is possible by engineering electropositive aromatic C–H bond donors in an idealized square planar geometry embedded within the host's inner cavity. The hydrogen atom's electropositivity is tuned by introducing fluorine atoms as electron withdrawing groups. These novel macrocycles, termed fluorocages, are engineered to sequester large anions. Indeed, experimental data shows an increase in the anion association constant ($K_a$) as the number of F atoms increase. The observed trend is rationalized by DFT calculations of Hirshfeld Charges (HCs). Most importantly, fluorocages in solution showed weak-to-medium binding affinity for large anions like $\text{[PF}_6^-$ ($10^2 < K_a < 10^4 \text{ M}^{-1}$), and high affinity for $\text{[MeSO}_3^- (K_a > 10^6$).
4.1 Introduction

Macrocyclic arenes are quintessential compounds in the development of host-guest chemistry. Guests are usually hosted within the inner cavity of the macrocycle through non-covalent interactions, e.g., hydrogen bonding, \( \pi \cdots \pi \) stacking, and C-H-\( \pi \) interactions. Among these non-covalent interactions, hydrogen bonding is the strongest one, especially when considering oxygen and nitrogen, where the difference in Pauling electronegativity with hydrogen (\( \Delta \chi \)) is 1.24 and 0.84, respectively. Lehn et al. recognized in 1976 that incorporating hydrogen bonding capabilities (N-H bonds) within cryptands resulted in weak-to-medium affinity for spherical anions (e.g., halides), this realization opened the door to “anion coordination chemistry”. Later reports demonstrated fluorinated macrocycles hosting fluoride ion purely through C-H-\( \cdots \)F\(^-\) hydrogen bonding, which is remarkable noting that \( \Delta \chi \) for C and H is just 0.35. However, due to the relatively weak binding affinities, molecular designs for anion binding based solely on C-H hydrogen bonding were marginalized in supramolecular host-guest chemistry. This notion has been challenged, and in the past few decades a range of hosts with remarkable affinities towards spherical anions (\( K_a > 10^6 \) M\(^{-1}\)) have been reported by J. Sessler, P.A. Gale, A. P. Davis, B. D. Smith, A. Flood, V. Sindelar, J. Yoon, J. You, M. Pittelkow, H. Jinag, M. Stępień, and others.

Molecular recognition of nonspherical anions have transformed the design of rotaxanes assemblies, advanced novel catalytic processes by stabilization of in situ generated anions, laid the ground work supporting anion-anion stabilization theories, facilitate ion pair dissociation in battery electrolytes, and provided systems of remarkable selectivity towards the recognition of bifluoride, organophosphates, dicarboxylates, the biologically relevant GTP
anion, nitrate anion, and sulfate. Despite these noteworthy advances, hosts capable of binding nonspherical anions with high affinity are rare and usually lack synthetic tunability requiring a complete host redesign to tune binding affinities, therefore efforts to develop hosts for nonspherical anions remains a challenge. Herein, I report a strategy to create novel supramolecular anion cages through a straightforward and versatile synthetic procedure in which we discovered binding preferences for nonspherical anions.

4.2 Results and discussion

4.2.1 Host-guest design

Fluorocages, as we refer to these supramolecular hosts, were conceived by trying to maximize the host-guest properties of resorcin[4]arenes towards anionic species. Note that while their host-guest capabilities for neutral guests are well-established, their anion hosting abilities are not nearly as developed. Towards this goal, we designed and synthesized a modular family of resorcin[4]arene-based cages, 4.1 – 4.8 (Figure 4.1), all having the same binding cage geometry capable of accommodating large guests, and also able to tune the overall framework to systematically and monotonically increase the anion binding affinity.
4.2.2 Fluorocages structure

Fluorocages 4.1 – 4.8 were synthesized from 4.81 or 4.82 through Suzuki-Miyaura cross-coupling reactions with the corresponding aromatic flanking unit, $F_n$, as described in Figure 4.1, in yields ranging from 38 to 53%. All hosts define a cavity comprised of eight C-H donors, four aromatic colored in blue (C$_{Ar}$-H) and four aliphatic colored in dark purple (C$_{CH2}$-H). Our hypothesis is that by installing electron withdrawing groups (EWGs) on the aromatic flanking units...
would produce sufficiently high electropositive hydrogen atoms in C_Ar-H capable of binding anionic species with high affinity. Moreover, fluorocages 4.1 – 4.8 are designed as rigid scaffolds to minimize entropic penalties that may arise from conformational flexibility and host rearrangement upon guest binding.\textsuperscript{370, 371}

$^1$H, $^{13}$C, and $^{19}$F NMR spectra in CDCl$_3$ of 4.1 – 4.4, 4.6, and 4.8 reveals their expected ideal $C_{4v}$ molecular symmetry in solution. Fluorocages 4.5 and 4.7 display a more complex behavior, however in-depth analysis of their $^1$H NMR spectra corroborates their assignment. High quality crystals for single-crystal X-ray diffraction for 4.1 – 4.8 provided further confirmation of their molecular structure (Figure 4.2). Crystals of 4.1 – 4.8 were all obtained by slow evaporation of a MeCN:CH$_2$Cl$_2$ solution at room temperature. Note that all fluorocage structures display one molecule of MeCN bound within their inner cavity, except 4.7 which displayed heavy disorder that prevented correct modeling of the MeCN molecule. The molecular structures of 4.3, 4.5, and 4.7 displayed rotational disorder around their aromatic flanking units. For example, fluorocage 4.3 displays in the major occupancy structure three F atoms pointing into the inner cavity while one F atom is pointing away. Nonetheless, this behavior is not manifest in solution, as the NMR data indicates a fully $C_4$-symmetric structure.
Figure 4.2 Molecular crystal structures of fluorocages 4.1 – 4.8. Thermal ellipsoids are set at 50% probability level (except for 4.6 which are at 30%). The R groups (n-pentyl) and H atoms are omitted for clarity, except those H atoms within the fluorocage’s inner cavity. The C, N, O, F, and H atoms are colored grey, blue, red, green, and white, respectively.

In contrast, 4.5 and 4.7 display solid state major occupancy structures with idealized $C_s$ and $C_{2v}$ point group symmetries, respectively, which is reconciled with their complex solution behavior indicating that rotation around the biaryl moiety is hampered and that all possible rotational isomers coexist in solution, even at 100 °C. Up to six different rotamers are possible for 4.5 and 4.7 (Figures 4.3 and 4.4). DFT calculations at the M06-2X/6-311++G(3df,2p)+CP/M06-2X/6-31+G(d,p) level of theory, where solvent = CHCl$_3$ or DMSO, showed that these rotamers are relatively close in energy, thus supporting the experimental observations in solution (Tables 4.1 and 4.2).
**Figure 4.3** six possible rotamers of 4.5.

**Table 4.1** DFT calculated conformational energies of the six possible rotamers of 4.5 at the M062X/6-311++G(3df,2p)+CPM(solvent)/M062X/6-31+G(d,p) level of theory, where solvent = CHCl₃ or DMSO. Provided in this table are the relative Gibbs free energy (ΔG) for these rotamers.

<table>
<thead>
<tr>
<th>Conformational energies in kcal/mol</th>
<th>CHCl₃</th>
<th>DMSO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.5</td>
<td>4.5-1in</td>
</tr>
<tr>
<td>ΔG</td>
<td>0.0</td>
<td>−1.8</td>
</tr>
<tr>
<td>DMSO</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 4.4 six possible rotamers of 4.7.

Table 4.2 DFT calculated conformational energies of the six possible rotamers of 4.7 at the M062X/6-311++G(3df,2p)+CP3CM(solvent)/M062X/6-31+G(d,p) level of theory, where solvent = CHCl₃ or DMSO. Provided in this table are the relative Gibbs free energy (ΔG) for these rotamers.

<table>
<thead>
<tr>
<th>Conformational energies in kcal/mol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>CHCl₃</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>ΔG</td>
</tr>
<tr>
<td>4.7</td>
</tr>
<tr>
<td>4.7-1ln</td>
</tr>
<tr>
<td>4.7-2syn-in</td>
</tr>
<tr>
<td>4.7-2anti-in</td>
</tr>
<tr>
<td>4.7-3ln</td>
</tr>
<tr>
<td>4.7-4ln</td>
</tr>
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<td>0.0</td>
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<tr>
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</tr>
<tr>
<td>−0.3</td>
</tr>
<tr>
<td>−2.0</td>
</tr>
<tr>
<td>−0.8</td>
</tr>
<tr>
<td>−0.4</td>
</tr>
<tr>
<td>DMSO</td>
</tr>
<tr>
<td>ΔG</td>
</tr>
<tr>
<td>0.0</td>
</tr>
<tr>
<td>−1.4</td>
</tr>
<tr>
<td>0.5</td>
</tr>
<tr>
<td>−1.2</td>
</tr>
<tr>
<td>0.3</td>
</tr>
<tr>
<td>0.9</td>
</tr>
</tbody>
</table>

77
4.2.3 Anion affinity towards square planar electropositive cavity

The design and engineering of the electropositive cavity within 4.1 – 4.8 is best exemplified by the hosted MeCN molecule, which has its electronegative N atom residing in the same plane as the cavity’s electropositive H atoms (colored in blue in Figure 4.1). The average C-to-N distances (C$_{Ar}$-H and N$_{MeCN}$) for all fluorocages is 4.0 ± 0.2 Å [4.0(2) Å (number in parenthesis indicates the estimated standard deviation in the final digit)], while the average C-to-π system centroid (C$_{MeCN}$ and centroid of each aromatic ring comprising the resorcin[4]arene base) is 3.55(4) Å.

Anion sequestration was first tested by $^1$H NMR titration experiments adding [n-Bu$_4$N][PF$_6$] to 4.2 – 4.8 in CDCl$_3$ (solvent dielectric constant, $\varepsilon_r = 4.7$) at 20 °C. There is negligible affinity for [PF$_6$]$^-$ by 4.1 – 4.3, however 4.4, 4.6, and 4.8 display weak-to-medium binding peaking at 4.6 with $K_a$ of $1.510(1) \times 10^4$ M$^{-1}$, while 4.4 and 4.8 display $K_a$ of 84(12) and 280(15) M$^{-1}$, respectively (Table 4.3). To our surprise, 4.5 displays no binding of [PF$_6$]$^-$, while 4.7 only reaches $K_a = 1.64(11) \times 10^3$ M$^{-1}$, likely as a result of the energetic penalty involved in rearranging their initial conformational distribution. Note that only a few synthetic hosts are known to bind large anions such as [PF$_6$]$^-$. Overall, the adduct [PF$_6$$\subset$4.6]$^-$ demonstrates that the square planar arrangement of electropositive H atoms serves to sequester large anionic species.
Table 4.3 Anion association constants ($K_a$, M$^{-1}$) of [PF6]$^-$ and [MeSO$_3$]$^-$ to fluorocages 4.1 – 4.8.

<table>
<thead>
<tr>
<th>Salt</th>
<th>[n-Bu$_4$N][PF$_6$]</th>
<th>[n-Bu$_4$N][MeSO$_3$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent</td>
<td>CDCl$_3$</td>
<td>DMSO-$d_6$</td>
</tr>
<tr>
<td>4.1</td>
<td>0</td>
<td>ND$^a$</td>
</tr>
<tr>
<td>4.2</td>
<td>0</td>
<td>ND$^a$</td>
</tr>
<tr>
<td>4.3</td>
<td>0</td>
<td>ND$^a$</td>
</tr>
<tr>
<td>4.4</td>
<td>84(12)</td>
<td>$&gt;10^6$ $^b$</td>
</tr>
<tr>
<td>4.5</td>
<td>0</td>
<td>$&gt;10^6$ $^b$</td>
</tr>
<tr>
<td>4.6</td>
<td>$1.510(1) \times 10^4$</td>
<td>$&gt;10^6$ $^b$</td>
</tr>
<tr>
<td>4.7</td>
<td>$1.64(11) \times 10^3$</td>
<td>$&gt;10^6$ $^b$</td>
</tr>
<tr>
<td>4.8</td>
<td>280(15)</td>
<td>ND$^c$</td>
</tr>
</tbody>
</table>

$^a$ ND = Not determined. $^b$ Strong binding that prevents direct titration via $^1$H NMR, even at 100°C the anion remains bound. $10^6$ M$^{-1}$ is taken as the maximum reliable limit for NMR titration experiments.$^{373}$ Not soluble in DMSO-$d_6$ even at 100°C.
Table 4.4 Anion association constants ($K_a$, M$^{-1}$) of [n-Bu$_4$N][anion] to fluorocage 4.6. Thermochemical radii ($r$) in parenthesis.

<table>
<thead>
<tr>
<th>Host</th>
<th>4.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent</td>
<td>CDCl$_3$</td>
</tr>
<tr>
<td>I$^-$ / Br$^-$</td>
<td>161(19) / 0</td>
</tr>
<tr>
<td>[NO$_2$]$^-$ / [NO$_3$]$^-$</td>
<td>40(40) / 76(6)</td>
</tr>
<tr>
<td>[BF$_4$]$^-$ (2.05)</td>
<td>990(23)</td>
</tr>
<tr>
<td>[HSO$_4$]$^-$ (2.21)</td>
<td>$7(3) \times 10^4$</td>
</tr>
<tr>
<td>[ClO$_4$]$^-$ (2.25) / [ReO$_4$]$^-$ (2.27)</td>
<td>$7.91(9) \times 10^3$ / $1.08(2) \times 10^3$</td>
</tr>
<tr>
<td>[IO$_4$]$^-$ (2.31)</td>
<td>$1.00(3) \times 10^3$</td>
</tr>
<tr>
<td>[PF$_6$]$^-$ (2.42) / [SbF$_6$]$^-$ (2.52)</td>
<td>$1.510(1) \times 10^4$ / 230(20)</td>
</tr>
<tr>
<td>[MeCO$_2$]$^-$ / [MeSO$_3$]$^-$</td>
<td>$4.8(3) \times 10^3$ / $&gt;10^6$</td>
</tr>
<tr>
<td>[$p$TsO]$^-$$^a$</td>
<td>$1.88(4) \times 10^3$</td>
</tr>
</tbody>
</table>

$^a$ $p$Ts = $p$-toluenesulfonyl.

Encouraged by the binding results of [PF$_6$]$^-$, we tested the ability of fluorocage 4.6 to bind other noncoordinating nonspherical anions. For reference, the large iodide anion, with a thermochemical radii ($r$)$^{374}$ of 2.11(19) Å displays a $K_a = 161(19)$ M$^{-1}$; and as the spherical anion shrinks, e.g. Br$^-$ ($r = 1.90(19)$ Å), the observed $K_a$ goes to zero. Linear [N$_3$]$^-$ and [SCN]$^-$, bent [NO$_2$]$^-$, and trigonal planar [NO$_3$]$^-$ have negligible-to-weak binding affinities (Table 4.4), likely resulting from their size mismatch with the host’s cavity. However, strong binding is observed as the anion’s size reaches a radius of $\sim 2.2$ Å juding from the series [BF$_4$]$^-$ ($r = 2.05(19)$ Å), [HSO$_4$]$^-$
$(r = 2.21(19) \text{ Å}), [\text{ClO}_4]^− (r = 2.25(19) \text{ Å}), [\text{ReO}_4]^− (r = 2.27(19) \text{ Å}), [\text{IO}_4]^− (r = 2.31(19) \text{ Å}), \text{and } [\text{SbF}_6]^ − (r = 2.52(19) \text{ Å}).$ Note that anion binding affinity decreases by about two orders of magnitude when the anion’s size surpass $[\text{PF}_6]^ −$, as observed in $[\text{SbF}_6]^ −$ which is only $\sim 4\%$ larger than $[\text{PF}_6]^ −$. Thus, we establish that the optimum anion’s size fitting in the host’s cavity must be $2.2 < r < 2.4 \text{ Å}$. Other nonspherical anions, as acetate, $[\text{MeCO}_2]^−$, also binds to $4.6 \left( K_a = 4.8(3) \times 10^3 \text{ M}^{−1} \right)$, however the closely related $[\text{MeSO}_3]^−$ binds so strongly to $4.6$ in CDCl$_3$ that its affinity falls beyond the reliable measurable limit via $^1\text{H NMR} \left( 10^6 \text{ M}^{−1} \right)$, see Figure 4.5a.$^{373}$ Note that a marked downfield complexation-induced chemical shift occurs for protons “a” $(\Delta \delta \approx 0.57 \text{ ppm})$ and “b$_{in}$” $(\Delta \delta \approx 0.69 \text{ ppm})$ as established for H atoms involved in direct hydrogen bonding with the bound anion (Figure 4.5a). In contrast, proton “b$_{out}$“ shifts upfield as a result of increased electron density on the C atom (methylene) due to anion binding.$^{375}$ We conclude that sulfonate’s structure is better poised to interact with the four electropositive H atoms as opposed to the flat structure of carboxylate. Note that $p$-toluenesulfonate, $[p\text{TsO}]^−$, with its much larger organic group, also binds to $4.6$ displaying a $K_a$ of $1.88(4) \times 10^3 \text{ M}^{−1}$, where its $p$-toluene fragment points away from the fluorocage’s cavity.
Figure 4.5 Equilibrium between 4.6 and [MeSO₃]⁻. (a) ¹H NMR titration of [n-Bu₄N][MeSO₃] into 4.6 in CDCl₃ at 20 °C. (b) ¹H NMR of 4.6 (bottom) and [n-Bu₄N][MeSO₃⊂4.6] (top) in DMSO-d₆ at 100 °C. Circular symbols correspond to the blue and dark purple hydrogen atoms in the scheme above. Open symbols indicate free host 4.6, while solid symbols correspond to the adduct [n-Bu₄N][MeSO₃⊂4.6]. Relevant H atoms are labeled a, b_{in}, and b_{out}. 
Sulfonate anion appears to have the optimum size to fit in the cavity described by the four electropositive H atoms in C$_A$-H. Intrigued by this observation, I decided to expand our efforts and investigate the binding properties of $[\text{MeSO}_3^-]$ towards 4.1 – 4.5 and 4.7 – 4.8 in CDCl$_3$ at 20 °C. Host 4.1 failed to bind $[\text{MeSO}_3^-]$. Fluorocages 4.2 and 4.3 displayed binding of $[\text{MeSO}_3^-]$ with $K_a$ of 22(4) and 667(38) M$^{-1}$, respectively, while host 4.8 exhibited slow exchange$^{376,377}$ in the NMR time scale with $K_a \approx 2.5(2) \times 10^3$ M$^{-1}$. In contrast, fluorocages 4.4 and 4.7, similar to 4.6, revealed binding affinities well-above $10^6$ M$^{-1}$. Note that 4.5 displayed no binding of $[\text{MeSO}_3^-]$ in CDCl$_3$. To our surprise, NMR experiments in the much more polar solvent DMSO ($\varepsilon_r = 46.8$) display 4.4 – 4.7 strongly binding $[\text{MeSO}_3^-]$, even when the solution is heated to 100 °C (in situ $^1$H NMR, Figure 4.5b). This finding led us to conclude that binding of $[\text{MeSO}_3^-]$ to hosts 4.4 – 4.7 in DMSO-$d_6$ exceeds $K_a$ of $10^6$ M$^{-1}$. Assuming the general anion binding in solution model put forward by Flood et al.$^{378}$ holds true for $[\text{MeSO}_3^-]$, we expect $K_a$ for $[\text{MeSO}_3^-]$ binding to hosts 4.4 – 4.7 in CDCl$_3$ to surpass by several orders of magnitude $10^6$ M$^{-1}$. We note that binding is mostly driven by interaction with the four electropositive H atoms in C$_A$-H and not by C-H⋯π interactions found between the Me group in MeSO$_3^-$ and the π system centroids since the average C-to-π distance for $[\text{MeSO}_3\subset\text{host}]$, where host = 4.4, and 4.6 – 4.8, is 3.62(3) Å; which is larger than that found in the neutral adduct $[\text{MeCN}\subset\text{host}]$, for host = 4.1 – 4.6, and 4.8 (vide supra). Altogether, the qualitative picture portrayed by this NMR data reveals that the equilibrium between host + $[\text{MeSO}_3^-]$ and $[\text{MeSO}_3\subset\text{host}]$, for hosts 4.4 – 4.7, is strongly displaced towards the host-guest adduct.

The strong interaction with methanesulfonate allowed us to isolate and crystallize the adducts $[n\text{-Bu}_4\text{N}][\text{MeSO}_3\subset\text{host}]$, for host = 4.4, and 4.6 – 4.8. Shown in Figure 4.6a is the molecular structure and relevant distances for $[\text{MeSO}_3\subset\text{4.6}]^-$. Note how the three O atoms from
the sulfonate group reside in the square plane described by the four electropositive H1X atoms, X = A – D (colored in blue in Figure 4.1). This sulfonate anion accommodation maximizes the CAr-H⋯OMeSO3- hydrogen bonding, with remarkably short C-to-O average distances of 3.31(4), 3.24(3), 3.18(7), and 3.34(6) Å for 4.4, 4.6, 4.7, and 4.8 (Figure 4.6b), respectively.379 Note that the sum of the van der Waals radius for C and O is 3.22 Å.380 Fluorocages adopt a cone-shaped structure; to determine the expansion of this cone, we measured the distances between rigid carbon atoms C6X (Figure 4.6a), X = A – D, which define an almost ideal square (C–C\text{square}). Plotting these data together, we observe a V-shaped trend in the C-to-O distance, with 4.7 at the minimum, and no discernable correlation in C–C\text{square} distances (Figure 4.6b), meaning that strengthening of the hydrogen bonds within the host’s cavity only requires rotational movement of the aromatic flanking units as opposed to a breathing in or out distortion.

Figure 4.6 (a) Side and top view of the molecular crystal structure of [MeSO\textsubscript{3}⊂\textit{4.6}]\textsuperscript{-} obtained at 220 K. Thermal ellipsoids are set at 50% probability level. The [n-Bu\textsubscript{4}N]\textsuperscript{+}, R groups (n-pentyl), and H atoms are omitted for clarity, except those H atoms within the inner cavity. (b) Comparison of structural molecular metrics. Average C–C\text{square} (red and maroon) and C⋯O (green) distances. Open symbols correspond to 4.1 – 4.8, and filled symbols to [MeSO\textsubscript{3}⊂\textit{host}]\textsuperscript{-}, for host = 4.4, and 4.6 – 4.8.
4.2.4 DFT-supported structure-function relationship

To gain insight into the trends observed in this family of fluorocages, we performed DFT calculations (M06-2X/6-31+G(d,p) level of theory) in 4.1 – 4.8 to obtain their Hirshfeld charges (HCs) in an effort to access quantitative data about the electropositivity of the H atoms involved in hydrogen bonding (Figure 4.7). Note that HCs are recommended as they yield chemically meaningful partial charges. Following the series from 4.1 to 4.7, we observe a monotonic increase in HC at the H atoms in C_{Ar}-H (blue). Unexpectedly, the calculated HCs for fluorocage 4.8 reside in between those of 4.3 and 4.4. Notably, HCs for 4.8 explain its weaker binding of [MeSO_3]^- compared to 4.4 – 4.7. The HC values for the hydrogen atoms in C_{CH2}-H (dark purple) are provided in Figure 4.7 as control since these should not be affected by the nature of the EWG in the aromatic flanking unit. Overall, this trend correlates well with the binding affinity studies of 4.1 – 4.8, and with the metrics observed in the host-guest adducts [n-Bu_4N][MeSO_3⊂host], for host = 4.4, and 4.6 – 4.8 (Figure 4.7b). Note that the HCs on 4.5 and 4.7 does not correlate well with their binding properties, which we attribute to the conformational distribution observed in the as-synthesized hosts and the large aromatic flanking unit rotational barrier (biaryl bond) of ~22 kcal/mol, compared to ~12 kcal/mol for all other hosts (Table 4.5).
Figure 4.7 DFT-calculated Hirshfeld charges for 4.1 – 4.10 (M06-2X/6-31+G(d,p) level of theory). Blue C<sub>Ar</sub>-H, dark purple C<sub>CH2</sub>-H, pink C<sub>CC</sub>-H, and red Ctriazole-H hydrogen atoms correspond to those shown in Figure 4.1 or in the chemdraw drawings in this figure.
Table 4.5 DFT calculated rotational barriers of biaryl bonds for hosts 4.1 – 4.7 at the M062X/6-311++G(3df,2p)+CPCM(solvent)//M062X/6-31+G(d,p) level of theory, where solvent = CHCl$_3$ or DMSO. Provided in this table are the relative Gibbs free energy (ΔG) for the rotation of one of the aromatic flanking units around the biaryl bond. Data for host 4.5 was calculated starting from the rotamer 4.5-4in. Data for host 4.7 was calculated starting from the rotamer 4.7-4in.

<table>
<thead>
<tr>
<th>Rotational barrier in kcal/mol</th>
<th>CHCl$_3$</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</tr>
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<tbody>
<tr>
<td></td>
<td>4.1</td>
<td>4.2</td>
<td>4.3</td>
<td>4.4</td>
<td>4.5</td>
<td>4.6</td>
<td>4.7</td>
</tr>
<tr>
<td>ΔG</td>
<td>12.6</td>
<td>12.5</td>
<td>13.1</td>
<td>13.1</td>
<td>22.7</td>
<td>12.6</td>
<td>22.6</td>
</tr>
</tbody>
</table>

| DMSO                          |   |   |   |   |   |   |   |
|-------------------------------|---|---|---|---|---|---|
| ΔG                            | 12.8 | 12.7 |13.4 |13.3 |22.8|12.8|22.6|13.0 |

In an effort to compare hosting capabilities of fluorocages with other rigid anion-binding hosts operating solely by C-H hydrogen bonding, we analyzed two recent macrocyclic hosts reported in the literature: 1) pentagonal cyanostar 4.9, capable of forming a strong 2:1 host:guest adduct with Cl$^-$ (40% MeOH/CDCl$_3$, β ≈ 10$^8$ M$^{-2}$),$^{155}$ and 2) cryptand-like triazole cage 4.10,$^{382}$ which binds Cl$^-$ remarkably strong (CDCl$_3$, $K_a$ ≈ 10$^{17}$ M$^{-1}$).$^{154}$ HCs of the H atoms involved in C-H hydrogen bonding increase from 4.9 to 4.10, as shown in Figure 4.7, supporting the relative trend observed in their anion binding properties. Furthermore, in the case of 4.10, the most electropositive H atoms reside in C$_\text{triazole}$-H and are on par to those found in fluorocage 4.4. However, while 4.4 has four of these electropositive H atoms, 4.10 has six of them making its internal cavity more electropositive. Most importantly, 4.5 – 4.7 display higher HCs relative to 4.10 suggesting that further exploration of these fluorocages have the potential to uncover strong
affinities for anions of appropriate size to fit in the square planar geometry defined by the blue electropositive H atoms.

4.3 Conclusions

Herein I described a family of anion hosts – termed fluorocages – sharing the same overall structure, however with anion affinities tuned by several orders of magnitude through a straightforward single four-fold Suzuki-Miyaura cross-coupling synthetic step. These fluorocages are able to bind nonspherical anions, such as sulfonate groups, which display remarkable affinity and size complementarity to their cavity. Further development of this general strategy, and based on the structure-function relationship reported herein, will guide the development of novel, more potent, and selective hosts for anion sequestration from polluted ecosystems, e.g., sulfonate-based PFAS,\textsuperscript{383-385} currently an unmet pressing challenge.
5.0 TEMPLATE-ASSISTED SYNTHESIS OF MOLECULAR GLOVES

Macrocyclic arenes are one of the cornerstones of supramolecular chemistry and have seen continued growth over the past decades. Herein, I employ a decades-old macrocyclic arene (i.e., resorcin[4]arene) to synthesize a novel series of rigid and conjugated deep-cavity cavitands, termed nanogloves. To obtain these compounds, a two-step synthetic approach was developed. First, chlorobenzene moieties were installed onto an octabromo-cavitand via a one-pot eight-fold Suzuki-Miyaura cross-coupling reaction. Second, macrocyclization was carried out executing a one-pot Ni-mediated Yamamoto coupling to form the final four C-C bonds, which rigidify the overall system. The top rim is composed of twelve conjugated phenylenes that are connected to the resorcin[4]arene scaffold via four acetal bonds. These compounds were characterized using NMR, UV-vis, emission, and single-crystal X-ray diffraction methods and further analyzed using DFT calculations. Structural calculations suggested that the deep cavity of our novel compounds was the proper size for fullerene encapsulation. In fact, NMR and emission titration experiments demonstrated strong binding affinities ($K_a \sim 10^7$) of $C_{60}$ and $C_{70}$ towards these molecular nanogloves.

5.1 Introduction

Conjugated macrocycles\textsuperscript{386} with well-defined shapes have attracted scientists from many different fields, and have led to their applications in organic nanodevices,\textsuperscript{387} host-guest chemistry,\textsuperscript{176, 388} and optoelectronic materials,\textsuperscript{389} to name a few. Among conjugated macrocycles,
cyclic oligophenylenes stand out, and are categorized into three general groups based on their connectivity patterns (i.e., ortho-phenylenes, cyclo-meta-phenylenes, and cyclo-para-phenylenes). Note that the combination of these patterns has also been reported. Despite advancements in the precise organic synthesis of highly strained conjugated macrocycles, and the emergence of innovative approaches to obtain challenging compounds like carbon nanobelts (CNB) and analogous structures; templating methods that circumvent product mixtures, and selectively give the target macrocycle in an atomically precise fashion are rare.

Macrocyclic arenes (e.g., calixarenes, pillararenes, etc.) established the basics of supramolecular chemistry. Converting these non-conjugated arenes to the conjugated macrocycles has been reported by Itami, Chen, Wang, and Lucas. Another approach uses macrocyclic arenes as scaffold in the bottom-up synthesis of radially-conjugated macrocycles. Huc and coworkers were the first to employ calix[n]arenes as scaffolds in the synthesis of radially oriented cyclo-meta-phenylenes (Figure 5.1). More recently, our group developed bottom-up approaches to obtain armchair (Chapter 2) and zigzag (Chapter 3) tubularenes. As depicted in Figure 5.1, our modular system uses a resorcin[4]arene base which is built up via the installation of different groups that results in fully conjugated macrocycles. Advancing our previous work, herein I report a series of cup-like conjugated resorcin[4]arene-based macrocycles. The final compounds are totally rigid despite the presence of several Ar-Ar single bonds. In contrast to previous methods, this novel two-step synthetic approach improves the yield by >15 times with Ni-mediated macrocyclization as the final step. Most importantly, the cavity of these systems is large enough to host C_{60} and C_{70}, the two most accessible fullerenes.
5.2 Results and discussion

5.2.1 Synthesis of molecular gloves

The construction of the molecular nanogloves reported herein start with the multigram scale synthesis of 9-n-pentyl resorcin[4]arene (5.S1)\textsuperscript{271} or 9-n-undecyl resorcin[4]arene (5.S2)\textsuperscript{409} tail, and 3,5-dibromo benzal bromide (5.S3).\textsuperscript{410} Reaction of 5.S1 or 5.S2 with 5.S3 in anhydrous dimethylacetamide (DMA) under basic condition using DBU (1,8-Diazabicyclo[5.4.0]undec-7-
ene) affords the octa-bromo cavitands 5.3 and 5.54; note that the gram-scale synthesis of octa-Br compound 5.54 has been reported by Gibb et al. in 2007.41 The full characterization of compound 5.3 (1H and 13C NMR and single-crystal structure) can be found in the experimental information. Suzuki–Miyaura cross coupling of 5.3 or 5.54 with ten equivalents of 3-chlorophenyl boronic acid 5.55a (R’ = H) results in an eight-fold C–C bond formation. The isolated yield of this step is >80% for both compounds 5.5C5 and 5.5a. The final macrocyclization of the 5.5C5 and 5.5a were carried out in a nitrogen filled glovebox using Ni-mediated Yamamoto reaction conditions. The reaction was performed using a 1:1 solvent mixture of toluene:DMF, 2,2′-bipyridine as supporting ligand, and Ni(cod)2 as Ni(0) source at 80 °C. The yield of the final product is ~32% and ~59% for 5.1C5 and 5.1a, respectively. We observed poor solubility of 5.1C5 in common organic solvents like CHCl3 and CH2Cl2; this lower solubility complicates column purification which results in lower yield.

Moreover, to investigate the substituent effects on the electronic properties of our compounds, and to better assign the 1H NMR data, we carried out syntheses starting from 5.54 and 3-chloro-5-methylphenylboronic acid pinacol ester (5.55b), and 5.54 with 3-chloro-5-methoxyphenylboronic acid pinacol ester (5.55c). The isolated yield for 5.1b (R’ = Me) and 5.1c (R’ = OMe) is 62% and 62%, respectively. Similar yield demonstrates the reliability of this approach for the different substituents (H, Me and OMe) in this study. Additionally, I investigated the direct formation of nanoglove 5.1a starting from 5.54. Carrying out the Suzuki–Miyaura cross coupling of 5.54 with 3,3′-bis(Bpin)-1,1′-biphenyl compound under diluted conditions. The yield of the product is ~3%, which reveals that the formation of octa-Cl and subsequent Yamamoto coupling provide a better synthetic route for these compounds.
5.2.2 Structural analysis

The $^1$H NMR of molecules 5.1C$^5$ in 1,1,2,2-tetrachloroethane-$d_2$ (TCE-$d_2$) and 5.1a-c in chloroform-$d_1$ (CDCl$_3$) revealed their $C_{4v}$ symmetry in solution (Figure 5.3). Note that TCE was used due to the poor solubility of 5.1C$^5$ in common organic solvents. It should be noted that this symmetry group is enforced by the template (resorcin[4]arene) and is the same as previously...
reported species in Figure 5.1. Moreover, the MALDI-TOF mass spectroscopy showed good agreement with the expected values and isotopic distribution patterns. Fortunately, we have been able to grow high-quality crystals of 5.1c5 and 5.1c using slow diffusion of MeCN into their chlorobenzene solution at room temperature. The single-crystal molecular structures unambiguously prove the successful synthesis of these target molecules.

The biphenyl moieties are in different dihedral angles with respect to their single bond (rings A and A’). However, the largest dihedral angle is ~23.3° and ~30.0° (the average of four dihedral angles is 14.3° and 12.1°) for 5.1c5 and 5.1c, respectively, which shows the highly restricted rotational freedom of them. There are no significant structural changes due to the different substituents (H vs. OMe). The average diagonal acetal-carbon (carbon i) distance in octa-Br compound crystal structure is ~8.7 Å; this value is 8.5 Å for both 5.1c5 and 5.1c nanogloves which shows the small contraction due to the macrocyclization and rigidification. This small contraction resembles itself in small strain energy of ~9 kcal/mol (obtained by DFT at the B3LYP/6-31G(d) level of theory) considering a homodesmotic reaction. Note that this strain energy was as high as 90 kcal/mol for the tubularenes in Chapter 2.407

The packing pattern of the 5.1c5 molecule shows a pseudo-capsule formation through homodimerization. The CH⋯π interactions are the dominant noncovalent interaction between these homo species in the solid state. As illustrated in the Figure 5.4, the 5.1c molecule exhibits a different packing pattern, and the dimerization of the molecules does not form a capsule shaped structure.
Figure 5.3 (a) $^1$H NMR of 5.1a (R’ = H), 5.1b (R’ = Me) and 5.1c (R’ = OMe) in CDCl$_3$ at 20 °C. Proton labels according to Figure 5.2.

Figure 5.4 Molecular crystal structure of 5.1c and 5.1c obtained at 150 K. Thermal ellipsoids are set at 50% probability level. The C and O atoms are colored grey, and red, respectively. The H atoms are omitted for clarity.
To better understand the electronic structure of these novel compounds, the absorption and emission spectra were collected in CH$_2$Cl$_2$ (Figure 5.5). The $\lambda_{\text{max}}$ of 5.1a-c are 254, 259, and a low-intensity broad peak around 320 nm, respectively. The absorption spectrum is red-shifted, as expected, and is attributed to the different electron-donating abilities of the substituents. However, this shift is not significant when moving from H to Me ($\sim$5 nm). Note that the $\lambda_{\text{max}}$ for benzene is $\sim$255 nm, this reveals the destructive quantum interference that results from the cross-conjugated nature of the twelve phenylene rings. The emission spectra showed $\lambda_{\text{em}}$ is 344, 343, and 342/354 for H, Me and OMe, respectively.

Time-dependent calculations (TD-DFT) were used to investigate the nature of these electronic transitions. The major features are reproduced with acceptable accuracy, however, with some overestimation. The major transition is around 282 nm (oscillator strength $\approx$ 0.27), 285 nm (oscillator strength $\approx$ 0.33), and 314 nm (oscillator strength $\approx$ 0.51) for H, Me, and OMe, respectively. Note that none of these transitions come from the HOMO-to-LUMO transition. Opposite to our previous reports and cyclo-para-phenylenes, the HOMO-to-LUMO transition is not forbidden for the nanogloves of this study. For example, for the H substituted nanoglove, the transition around 288 nm (oscillator strength $\approx$ 0.04) mostly ($\sim$55%) originates from the HOMO-to-LUMO transition.

To understand the origin of these differences with previous conjugated macrocycles, we evaluated the frontier molecular orbitals (FMOs). As depicted in Figure 5.5, the HOMO and LUMO are mostly delocalized over the top twelve phenylene rings. However, opposite to [n]CPPs this distribution is not equal over all phenyl rings; this unequal distribution is more obvious when increasing the electron donation ability of the substituent. This lack of the equal FMOs delocalization can be attributed to the feasibility of the HOMO-to-LUMO transition of these
species. In addition to the substituents effect on the unequal distribution of FMOs, they also have a significant effect on their shape; while the HOMO of H and Me are in benzenoid shape, the HOMO of OMe reveals the quinoid shape on the biphenyl moieties. Opposite to the HOMO, similar pattern of LUMO is observed for all substituents.

![Figure 5.5](image.png)

**Figure 5.5** (left) UV-Vis absorption and emission spectra of H, Me and OMe, collected in CH$_2$Cl$_2$ at room temperature. (Right) HOMO and LUMO density plots (+0.02 au) of H, Me and OMe calculated at B3LYP-D3BJ/6-31G(d)+PCM(DCM).

### 5.2.3 Catching fullerenes

The discovery of fullerenes, curved and fully conjugated molecules which resemble a ball of $\pi$ electrons, opened a new door for host-guest chemistry. Thus, so many different types of hosts are designed and/or evaluated for encapsulation of fullerenes. Molecular tweezers, carbon nanohoops, phenine nanotubes, metallosupramolecular receptors, and molecular organic cages are just few examples of the sea of hosts; most of these hosts stabilize fullerenes trough concave-convex $\pi$-$\pi$ interactions. In addition, several groups reported the encapsulation of fullerenes by macrocyclic arenes; for example, cyclotrimeratrylene (CTV), calixarenes,
and pillararenes.\textsuperscript{430} Though the binding constant of these molecules are weak (<10\textsuperscript{3})\textsuperscript{430} in the solution or just observed in the solid state\textsuperscript{431,432} which can be attributed to the shallow cavity and weak noncovalent interactions of these molecules. Note that molecules with bowl-shaped geometry and proper size to encapsulate and cover a significant amount C\textsubscript{60}’s surface are very rare.\textsuperscript{433} Recently, Tiefenbacher’s group reported acridane[4]arene-based cavitand, termed megalocavitand, which can bind the C\textsubscript{60} and C\textsubscript{70} with $K_a$ of 10\textsuperscript{6} and 10\textsuperscript{4} M\textsuperscript{-1}, respectively.\textsuperscript{86} To evaluate the binding of most abundant fullerenes (C\textsubscript{60} and C\textsubscript{70}), I performed the $^1$H NMR titration in TCE-$d_2$ at room temperature (Figure 5.6). As expected, encapsulation of fullerenes significantly affects the acetal proton ‘i’; gradual disappearance of this peak and formation of a new upfield resonance for C\textsubscript{60} (blue peak in Figure 5.6) indicates strong binding which is out of the range of NMR direct titration measurement ability.\textsuperscript{373} The emission-quenching titration revealed a binding around 10\textsuperscript{7} M\textsuperscript{-1} for both C\textsubscript{60} and C\textsubscript{70} (Figure 5.7). Moreover, opposite to C\textsubscript{70}, the C\textsubscript{60} encapsulation can be readily detected with the naked eye as the colorless host solution changes to brown with incremental addition of purple C\textsubscript{60} solution (Figure 5.7).
Figure 5.6 (Left) $^1$H NMR titration of C$_{60}$ into 5.1 in TCE-d$_2$ at 20 °C. (right) schematic representation of H interaction with C$_{60}$. \[ K_a > 10^6 \text{ M}^{-1} \]
Figure 5.7 (Left) Color change of 5.1 molecules upon the addition of C$_{60}$. (Right) Fluorescence titration plot of incremental addition of C$_{60}$ to 5.1a in C$_2$H$_2$Cl$_2$ (TCE).

Fortunately, high-quality crystals (dark brown) were obtained by slow diffusion of MeCN into the C$_{60}$⊂5.1$^{c5}$ solution in 1-chloronaphthalene. As illustrated in Figure 5.8, the single molecular crystal structure revealed the 1:1 binding of C$_{60}$ inside the deep cavity of 5.1$^{c5}$. The C$_{60}$ molecule is highly disordered which shows its free rotation inside the cavity. The general geometry of the host does not change upon host-guest complexation which indicates very low conformational flexibility of these novel species; such rigidity decreases the reorganization energy penalties which can have negative effects on the binding constants.$^{370,371}$ The guest is stabilized inside the cavity by several CH⋯π and π⋯π interactions. The acetal phenyl rings (rings B) are the source of all π⋯π interactions. The average distance from the least-squares-fit planes of rings B to nearest C$_{60}$ carbons is $\sim$3.4 Å, which is in the range of acceptable π⋯π interactions (3.4–3.8 Å)$^{434}$ On the other hand, the biphenyl moieties (rings A and A’) and acetal hydrogens are the source of CH⋯π interactions. The average distance of acetal protons ($i$) to the nearest C$_{60}$ carbons is $\sim$3.1 Å; this value is $\sim$3.1 Å for biphenyl protons ($b$, see Figure 5.2).
Figure 5.8 Space-filing model of molecular crystal structure of C$_{60}$⊂C$_5$ obtained at 150 K. The C and O atoms are colored grey, and red, respectively. The H atoms are omitted for clarity.

Besides the experimental data, the DFT calculations revealed the presence of these interactions (CH⋯π and π⋯π) by plotting the noncovalent interactions generated by independent gradient model based on Hirshfeld partition of molecular density (IGMH, Figure 5.9). In order to measure the amount of the C$_{60}$’s surface that has been masked by the nanogloves, we calculated the least-squares-fit planes of a and c carbons (see Scheme 2) and the centroid of the bottom ring of C$_{60}$; the distance between these two (i.e., plane and centroid) is ~2.6 Å. Considering that the distance between the top and bottom centroids of C$_{60}$ is ~6.6 Å, less than 39% of C$_{60}$’s surface is masked by our novel molecules. This value is important in controlling the regioselectivity and amount of functionalization of fullerenes.
5.3 Conclusions

Herein, we developed a two-step synthetic approach using a bottom-up synthesis strategy to make a series of top rim fully conjugated deep-cavity molecules termed nanogloves. This approach employs resorcin[4]arene as the scaffold to obtain the octa-Br, and subsequent octa-Cl species using a one-pot eight-fold Suzuki-Miyaura cross-coupling reaction. These octa-Cl compounds with three different substituents (H, Me and OMe) are amenable to macrocyclization using Ni-mediated Yamamoto coupling. The final step forms four C-C bonds which rigidify the whole molecule. The size of these nanoglove’s cavity allows them to host fullerenes. Indeed, NMR and emission titration data revealed the high binding affinity ($K_a \sim 10^7$) for both $C_{60}$ and $C_{70}$. This high binding constant can be attributed to the presence of several CH⋯π, π⋯π interactions, and the absence of host’s conformational flexibility. The X-ray single crystal data unambiguously
revealed the 1:1 binding of C_{60}:nanoglove, and showed that \sim 40\% of C_{60}’s surface is masked by the host. These findings open a new door for macrocyclic arenes and conjugated macrocycles that benefit the different fields (i.e., applications, purifications, functionalization, etc.) of fullerene chemistry.
6.0 EXPERIMENTAL AND COMPUTATIONAL DETAILS

6.1 General experimental information

All reactions were performed in oven-dried or flame-dried round bottom flasks, unless otherwise noted. The flasks were fitted with Teflon magnetic stir bar, rubber septa and/or reflux condenser, under a positive pressure of nitrogen, unless otherwise noted. Anhydrous and anaerobic THF, diethyl ether, hexane, dichloromethane, and benzene were dried and deoxygenated on dual high-performance columns within a Glass Contour 800L Solvent Purification System. Anhydrous and anaerobic ortho-dichlorobenzene was purchased from Sigma Aldrich (sure-seal bottle).

$^1$H and $^{13}$C NMR spectra were recorded on Bruker Avance III 400 MHz or Bruker Avance III 600 MHz. Chemical shifts for protons are reported in parts per million (ppm) downfield from tetramethysilane (TMS) and are reference to residual protium in the NMR solvent (CHCl$_3$: δ 7.26; CH$_2$Cl$_2$: δ 5.32; (CH$_3$)$_2$SO: δ 2.50; and CH$_3$OH: δ 4.78, 3.31). Chemical shifts for carbon are reported in ppm downfield from TMS and are referenced to the carbon resonances of the solvent (CHCl$_3$: δ 77.0; CH$_2$Cl$_2$: δ 54.0; (CH$_3$)$_2$SO: δ 39.51; and CH$_3$OH: δ 49.1. Data is presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants in Hertz, and integration. Some $^1$H NMR and $^{13}$C NMR were recorded at high temperatures to enhance signal resolution in the aromatic region. Resonances corresponding to the numerous aromatic carbon atoms in the reported compounds sometimes overlap, thereby reducing the number of observed resonances.

High-resolution mass spectrometry (HRMS) was performed on a (1) Thermo Scientific Q-Exactive Orbitrap instrument equipped with a Dionex Ultimate 3000 (RSLC) inlet system, and
electrospray (ESI) and atmospheric pressure chemical (APCI) ionization sources; or (2) a Bruker Daltonics UltrafleXtreme MALDI TOF/TOF MS instrument using dithranol (DIT) matrix.

Absorption spectra were obtained on a Cary 60 UV-Vis spectrophotometer and emission spectra were recorded in a HORIBA Jobin Yvon Fluoromax-3 spectrofluorometer.

Electrochemical data (cyclic voltammetry and differential pulse voltammetry) were recorded on a CHI760E bipotentiostat using a three-electrode cell setup with a 1 mm diameter glassy carbon working electrode, Pt wire counter electrode, and Ag wire as reference electrode. All measurements were done under a dinitrogen atmosphere and at room temperature. A 0.1 M solution of tetrabutylammonium hexafluorophosphate, \([n-\text{Bu}_4\text{N}][\text{PF}_6]\), in ortho-dichlorobenzene was used as the supporting electrolyte. Data was referenced to Fc/Fc\(^+\) by introducing ferrocene in the same solution. The energy level values of the lowest unoccupied molecular orbitals (LUMO) were calculated according to the following equation: 

\[
E_{\text{LUMO}} = [E_{1/2}(\text{first reduction}) - 4.80] \text{ eV.}
\]

Single crystal data for tubular[4,8,8,8]arene (2.1) was collected on a Bruker X8 Prospector Ultra diffractometer equipped with an APEX II CCD detector and an I\(\mu\)S microfocus Cu K\(\alpha\) X-ray source (\(\lambda = 1.54178 \text{ Å}\)). Temperature was maintained using an Oxford Cryosystem nitrogen flow apparatus. Single crystals of 2.1 suitable for X-ray structure analysis were coated with Paratone N-oil and mounted on MiTeGen Kapton loops (polyimide). Data for compound 2.1 was collected at 150 K. Raw data were integrated and corrected for Lorentz and polarization effects using Bruker APEX3.\(^{437}\) Absorption corrections were applied using SADABS.\(^{438}\) Space group assignments were determined by examination of systematic absences, E-statistics, and successive refinement of the structures. The program PLATON\(^{439,440}\) was employed to confirm the absence of higher symmetry for any of the crystals. The positions of the heavy atoms were determined using intrinsic phasing methods using the program SHELXT\(^{441}\) and SHELXL\(^{442}\) with Olex2\(^{273}\)
interface. Successive cycles of least-square refinement followed by difference Fourier syntheses revealed the positions of the remaining non-hydrogen atoms. Non-hydrogen atoms were refined with anisotropic displacement parameters, and hydrogen atoms were added in idealized positions. The cavity size of 2.1 was calculated from the solvent accessible volume calculator in Olex2. By employing this functionality, we found a discrete pocket within the interior of 2.1 of 265.9 Å³ (Probe 1.2 Å, grid 0.25 Å).

Fluorescence quantum yield were calculated following the comparative method described by Williams et al.\textsuperscript{327} using the following equation:

\[
\phi_x = \phi_{ST} \left( \frac{Grad_x}{Grad_{ST}} \right) \left( \frac{\eta_x^2}{\eta_{ST}^2} \right)
\]

where the subscripts ST and x denote standard sample (anthracene in our case) and sample under analysis, \( \phi \) is the fluorescence quantum yield, Grad is the gradient from the plot of integrated fluorescence intensity vs absorbance, and \( \eta \) the refractive index of the solvent (cyclohexane for anthracene and dichloromethane for the tubularene samples).

All titrations with different anions in the form of tetra-\(n\)-butylammonium ([\(n\)-Bu\(4\)N]\textsuperscript{+} or TBA) salts were carried out using \( ^1\)H NMR spectroscopy on a Bruker Avance 400 MHz spectrometer at room temperature (293 K) unless otherwise noted. 0.5 mL of receptor solutions (~0.0298 M) were prepared in NMR tubes and aliquots of concentrated salt (0.2 mL, 7-10 eq) solutions in screw-cap scintillation vials were prepared and added using micro-syringes. The titration started with 5 μL of the salt and after the first titration the desired amount (0.2 eq of the salt relative to host) has been determined using the integration of the TBA vs host protons. To determine the exact host:guest equivalence, the relative integration of proton e (for host) and N(CH\(2\))\(_4\) of tetra-\(n\)-butylammonium salts (TBA) have been used. Following the integration of these protons shows a 1:1 stoichiometry for all examined anions especially those with strong binding
constant (e.g., 4.6 with TBAMeSO₃). The titration has been stopped when the H NMR of the tracking protons (a, bᵢₙ and bₒᵤᵗ) did not show further shifts. The ¹H NMR binding constant have been determined using Bindfit online software. NMR 1:1 fitting method with Nelder–Mead algorithm has been used for calculating the binding constants using non-linear regression method. The excel input files are prepared where the first row has the headers, the first two columns are the host and guest concentrations, and the rest three columns represent the proton resonances (in ppm) for protons a, bₒᵤᵗ and bᵢₙ. The calculated errors are based on so-called "asymptotic standard error" at the 95% confidence interval level.

The titration of 4.7 with [n-Bu₄N][PF₆], 4.6 with [n-Bu₄N][pTsO], and 4.8 with [n-Bu₄N][MeSO₃] have shown a slow exchange on the ¹H NMR time scale. In these cases, we used the ¹H NMR single-point method to determine the binding constant (Kₐ) at different concentrations using the following equation, where I(Hₑ) and I(H) are the integrals of a specific proton in the host-guest adduct (Hₑ) and free host (H), respectively, and c(H) and c(G) are the initial molar concentrations of host and guest, respectively.

\[
K_a = \frac{I(H_e)}{I(H) \left( c(G) - \frac{I(H_e)}{I(H) + I(H_e)} c(H) \right)}
\]
6.1.1 Experimental data for chapter 2


![Compound 2.S3](image)

Compound 2.S3.

A 500 mL round bottom flask was loaded with 10.0 g (37.6 mmol) of 2.S2 in 150 mL of 4 N HCl. The first portion of oxalic acid (2.5 g, 27.8 mmol) was added, and the reaction mixture was refluxed for 6 h. Then a second portion of oxalic acid (2.5 g, 27.8 mmol) was added, and the mixture refluxed overnight (~12 h). The solution mixture was cooled down to room temperature and vacuum filtered. The filtrate was washed several times with copious amounts of deionized water and dried in air to obtain a brown solid. The product was used in the next step without further purifications. Yield: 52% (6.3 g, 19.7 mmol). $^1$H NMR (400 MHz, DMSO-$d_6$, 20 °C): 7.32 (2H, s), 11.03 (2H, s).
Compound 2.5.

A 500 mL flask was loaded with 5.0 g (15.6 mmol) of 2. S3 in 100 mL of thionyl chloride. After stirring for 5 min at room temperature, 1 mL of dimethyl formamide (DMF) was added dropwise. The reaction mixture was refluxed for 5 h and then cooled down to room temperature. The reaction mixture was dried under vacuum (caution: thionyl chloride has a very strong odor, consider setting up the rotary evaporator in a well-ventilated hood). The solid was washed several times with copious amounts of deionized water and 100 mL of MeOH, subsequently it was dried in air. The pure product (pale yellow solid) was obtained by flash column using a pure DCM. Yield: 63% (3.5 g, 9.9 mmol). 1H NMR (400 MHz, DMSO-d6, 20 °C): 8.20. 13C NMR (100 MHz, DMSO-d6, 20 °C): 121.3, 135.0, 138.7, 146.9. C8H3N2Br2Cl2, HRMS (calculated): 354.8036, HRMS (exp.): 354.8028.
Compound 2.3.

A 500 mL round bottom flask was loaded with 1.5 g of 2.4 (2 mmol) and 2.9 g of 2.5 (8.2 mmol, 4.1 eq) in 100 mL of acetonitrile. Triethylamine (TEA, 5.6 mL, 40 mmol, 20 eq) was added to the latter solution dropwise over 10 min. The reaction mixture was refluxed overnight (~12 h). The reaction mixture was cooled down to room temperature followed by removal of solvent under vacuum. A brown solid was obtained and washed with 200 mL of MeOH. This brown solid was dried in air. The pure product (beige powder) is obtained after passing the crude product through a flash column starting with DCM/Hexanes (1:1) and moving to pure DCM as the eluent. Yield: 57% (2.17 g, 1.14 mmol). $^1$H NMR (400 MHz, DMSO-$d_6$, 100 °C): 0.67 (12H, broad), 1.07 (24H, broad), 2.10 (8H, broad), 3.63 (4H, t), 7.05 (4H, s), 7.42 (4H, s), 7.84 (8H, s). $^{13}$C NMR (100 MHz, DMSO-$d_6$, 100 °C): 12.9, 21.2, 25.5, 29.9, 30.1, 36.4, 112.9, 119.8, 124.4, 130.9, 132.2, 135.8, 148.3, 151.7. C$_{80}$H$_{64}$Br$_8$N$_8$O$_8$, HRMS ([M+H]/z$^+$ calculated): 1904.8305, HRMS (exp.): 1904.8298.
Tubular[4,8,8,8]arene (2.1).

A Pyrex Schlenk flask was loaded with 0.3 g of 2.3 (0.16 mmol), 0.3 g of 1,4-benzenediboronic acid bis(pinacol) ester (0.9 mmol, 5.6 eq), and 1.2 g of K$_2$CO$_3$ in 250 mL of toluene, 25 mL of water and 25 mL of EtOH. The reaction mixture was degassed for 30 min while stirring vigorously at room temperature. To this mixture, 0.18 g of Pd(PPh$_3$)$_4$ (0.16 mmol, 1 eq) was added. This amount of catalyst forms 8 C-C bonds, thus representing ~0.12 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. Then, the reaction mixture was refluxed under N$_2$ atmosphere overnight (~12 h). This reaction was repeated three times. The solvent was removed under vacuum and the resulting dark black solid passed through a flash column using 70% DCM in hexanes. The final product was purified using 40% DCM in hexanes by preparatory TLC. Yield: 1.3% (0.011 g, 0.006 mmol). High quality crystals were grown by slow evaporation of a DCM/MeCN (1:1) solution of 2.1. $^1$H NMR (400 MHz, CD$_2$Cl$_2$, 20 °C): 0.96 (12H, t), 1.41 (24H, m), 2.34 (8H, q), 5.80 (4H, t), 6.78 (8H, s), 7.40 (4H, s), 7.74 (4H, s), 8.11 (8H, s), 8.75 (8H, s). $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 20 °C): 14.5, 23.3, 28.3, 30.3, 32.5, 34.5, 117.4, 124.3, 128.3, 129.4, 134.6, 136.1, 137.1, 139.2, 139.8, 150.2, 152.0. C$_{104}$H$_{80}$N$_8$O$_8$, HRMS ([M/z]$^+$ calculated): 1569.6172, HRMS (exp.): 1569.6179.
Tubular[4,8,8,12]arene (2.2).

A Pyrex Schlenk flask was loaded with 0.3 g of 2.3 (0.16 mmol), 0.34 g of 1,4-naphthalenediboronic acid bis(pinacol) ester (0.9 mmol, 5.6 eq), and 1.2 g of K$_2$CO$_3$ in 250 mL of toluene, 25 mL of water and 25 mL of EtOH. The reaction mixture was degassed for 30 min while stirring vigorously at room temperature. To this mixture, 0.18 g of Pd(PPh$_3$)$_4$ (0.16 mmol, 1 eq) was added. This amount of catalyst forms 8 C-C bonds, thus representing ~0.12 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. Then, the reaction mixture was refluxed under N$_2$ atmosphere overnight (~12 h). This reaction was repeated three times. The solvent was removed under vacuum and the resulting dark black solid passed through a flash column using 70% DCM in hexanes. The final product was purified using 50% DCM in hexanes by preparatory TLC. Yield: 0.8% (0.007 g, 0.004 mmol). $^1$H NMR (400 MHz, CD$_2$Cl$_2$, 20 °C): 0.88 (24H, t), 2.08 (16H, q), 5.45 (4H, t), 5.98 (4H, s), 6.55 (8H, s), 7.07 (4H, s), 7.62 (8H, m), 8.30 (8H, s), 8.41 (8H, m). $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 20 °C): 14.4, 23.2, 28.1, 30.2, 32.3, 32.5, 116.5, 123.8, 125.1, 130.2, 133.1, 133.4, 136.6, 138.3, 139.5, 141.3, 150.1, 151.5. C$_{120}$H$_{88}$N$_8$O$_8$, HRMS ([M/z]$^+$ calculated): 1769.6798, HRMS (exp.): 1769.6634.
6.1.2 Experimental data for chapter 3


Compound 3.4.

A 1 L flask was loaded with 3.S2 (7.13 g, 5 mmol) and EtOH (500 mL) under vigorously stirring at room temperature. Anhydrous tin (II) chloride (70 g, 370 mmol) was added to the suspension followed by the addition of HCl (37%, 200 mL). The reaction was refluxed overnight under N2 atmosphere. Heating was carried out through a bath of stainless-steel beads sitting on top of a hot plate. The solvent was removed under vacuum and HCl (3 N, 200 mL) was added and sonicated for 10 min. The pure product was filtrated and washed several times with HCl (3 N), and finally dried under vacuum at room temperature overnight. Compound 4 was obtained as a pale yellow amorphous solid at an 80% purity, the remaining 20% may correspond to the tin salts according to literature on similar compounds. $^1$H NMR (500 MHz, DMSO-d$_6$, 25 °C): δ 7.75 (s, 1H), 7.57 (s, 2H), 7.19 (s, 1H), 5.54 (br, 1H), 2.33 (q, $J$ = 4.0 Hz, 2H), 1.37 (m, 2H), 1.28 (m, 4H) and 0.86 (t, $J$ = 8.0 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, DMSO-d$_6$, 25 °C): δ 155.2, 155.2, 141.6,
136.0, 126.1, 121.5, 116.3, 33.5, 32.2, 31.7, 27.8, 22.7 and 14.4 ppm. C$_{72}$H$_{80}$N$_8$O$_8$ (free amines), MALDI-TOF-MS [M+]$^+$ calc.: 1185.6172, exp.: 1185.6185.

**Compound 3.3.**

In a 500 mL flask compound 3.4 (2.5 g, 1.7 mmol) and 3,5-dibromobenzaldehyde (2.5 g, 9.5 mmol) were dissolved in an EtOH:H$_2$O (4:1) mixture (300 mL). Sodium bisulfite (NaHSO$_3$) (5 g, 48 mmol) was added, and the reaction was refluxed over 2 days. Heating was carried out through a bath of stainless-steel beads sitting on top of a hot plate. The reaction mixture was cooled down to room temperature, filtered under vacuum, and washed with water and MeOH several times. After column purification on silica gel using a DCM:MeOH mixture (15:1) compound 3.3 was obtained as a white amorphous solid. Yield 70% (2.57 g). Single crystals were grown from diffusion of ether in a dichloromethane:methanol (10:1) mixture. $^1$H NMR (400 MHz, CD$_2$Cl$_2$:CD$_3$OD, 25 °C): δ 7.81 (d, $J = 2.5$ Hz, 2H), 7.64 (t, $J = 2.4$ Hz, 1H), 7.64 (br, 1H), 7.51 (s, 1H), 7.51 (br, 1H), 7.30 (s, 1H), 5.73 (t, $J = 8.2$ Hz, 1H), 2.29 (m, 2H), 1.45 (m, 2H), 1.39 (m, 4H) and 0.94 (t, $J = 7.2$ Hz, 3H) ppm. $^1$H NMR (600 MHz, TCE:CD$_3$OD, 25 °C): δ 7.82 (s, 2H), 7.66 (s, 1H), 7.65 (s, 1H), 7.54 (s, 1H), 7.31 (s, 1H), 5.83 (t, $J = 7.8$ Hz, 1H), 2.31 (q, $J = 4.1$ Hz, 2H), 1.46 (m, 6H), and 1.00 (t, $J = 7.9$ Hz, 3H) ppm. $^{13}$C NMR (150 MHz, TCE:CD$_3$OD, 25 °C):
δ 155.9, 155.6, 150.7, 150.1, 139.6, 135.5, 135.3, 135.0, 132.7, 131.7, 128.1, 123.9, 123.1, 116.6, 112.7, 106.3, 33.3, 32.7, 32.2, 27.9, 23.0 and 14.2 ppm. C_{100}H_{80}Br_{8}N_{8}O_{8}, HRMS (ESI) [M+2H]^{2+} \text{calc.:} 1076.9856; \text{exp.:} 1076.9856.

**Tubular[4,12,0,8]arene (3.1).**

In a 100 mL round bottom flask compound 3.3 (108 mg, 0.05 mmol), 1,3-phenyldiboronic acid bis(pinacol) ester (82.5 mg, 0.25 mmol) and potassium carbonate (K_{2}CO_{3}) (300 mg, 2.2 mmol) were dissolved in a THF:H_{2}O:EtOH (10:1:1) mixture (50 mL). This solution was degassed with N_{2} for 10 min, then the temperature was increased to 70 °C. Tetrakis(triphenylphosphine)palladium (0) (Pd(PPh_{3})_{4}, 100 mg, 0.087 mmol) was added to the reaction mixture. Temperature and stirring was kept overnight under N_{2} atmosphere. Heating was carried out through a bath of stainless-steel beads sitting on top of a hot plate. The reaction mixture was dried under vacuum, the resulting solid was sonicated with water (20 mL), filtrated and washed several times with water, MeOH, ethyl acetate, hexanes and DCM, in that specific order. The crude product was purified by preparative thin layer chromatography (PTLC) using a DCM:MeOH (15:1) mixture, to obtain 3.1 as a withe amorphous solid. Yield: 3.3% (3 mg, 0.0033
mmol). $^1$H NMR (700 MHz, CD$_2$Cl$_2$:CD$_3$OD, 25 °C): δ 8.32 (s, 1H), 7.99 (s, 1H), 7.72 (s, 1H), 7.59 (s, 1H), 7.53 (m, 2H), 7.50 (s, 1H), 7.48 (m, 1H), 7.39 (s, 1H), 6.91 (s, 1H), 6.48 (s, 1H), 5.83 (t, 1H), 2.34 (m, 2H), 1.50 (m, 2H), 1.42 (m, 4H) and 0.96 (t, 3H) ppm. $^1$H NMR (700 MHz, 1,2-C$_6$D$_4$Cl$_2$:CD$_3$OD, 25 °C): δ 8.27 (s, 1H), 7.94 (s, 1H), 7.66 (s, 1H), 7.50 (s, 1H), 7.49 (s, 1H), 7.38 (m, 3H), 7.30 (t, $J = 7.7$ Hz, 1H), 6.75 (s, 1H), 6.45 (s, 1H), 5.97 (t, $J = 8.0$ Hz, 1H), 2.30 (br, 2H), 1.27 (br, 4H), 1.18 (m, 2H) and 0.72 (t, $J = 7.3$ Hz, 3H) ppm. C$_{124}$H$_{96}$N$_8$O$_8$, HRMS (ESI) [M+H]$^+$ calc.: 1825.7424; exp.: 1825.7477.

**Tubular[4,16,0,12]arene (3.2).**

In a 100 mL round bottom flask compound 3.3 (108 mg, 0.05 mmol), 2,7-naphthalenediboronic acid bis(pinacol) ester (95 mg, 0.25 mmol), and K$_2$CO$_3$ (300 mg, 2.2 mmol) were dissolved in a THF:H$_2$O:EtOH (10:1:1) mixture (50 mL). This solution was degassed with N$_2$ for 10 min, then the temperature was increased to 70 °C. Pd(PPh$_3$)$_4$ (100 mg, 0.087 mmol) was added to the reaction mixture. The reaction mixture was stirred at this temperature overnight under
N₂ atmosphere. Heating was carried out through a bath of stainless-steel beads sitting on top of a hot plate. The reaction flask was dried under vacuum, the resulting solid was sonicated with water (20 mL), filtered and washed several times with water, MeOH, ethyl acetate, hexanes and DCM, in that specific order. The crude product was purified by PTLC using a DCM:MeOH (15:1) mixture, to get a white amorphous solid. Yield: 2.5% (2.5 mg, 0.00125 mmol). ¹H NMR (700 MHz, CD₂Cl₂:CD₃OD, 25 °C): δ 8.76 (s, 1H), 8.51 (s, 1H), 7.85 (d, J = 8.6 Hz, 2H), 7.83 (s, 1H), 7.78 (d, J = 9.0 Hz, 2H), 7.60 (m, 2H), 7.55 (s, 1H), 7.49 (td, J = 8.1 Hz, J = 3.1 Hz, 1H), 7.41 (s, 1H), 7.20 (s, 1H), 6.00 (t, J = 7.9 Hz, 1H), 2.42 (q, J = 6.9 Hz, 2H), 1.46 (m, 6H) and 0.98 (t, J = 7.2 Hz, 3H) ppm. C₁₄₀H₁₀₄N₈O₈, HRMS (ESI) [M+H]⁺ calc.: 2025.8050; exp.: 2025.8132.

**Compound 3.S5.**

In a 500 mL flask compound 3.S4 (8.4 g, 50 mmol) and 3,5-dibromobenzaldehyde (13.12 g, 50 mmol) were dissolved in an EtOH:H₂O (4:1) mixture (300 mL). NaHSO₃ (5g, 48 mmol) was added and the reaction mixture refluxed over 2 days. Heating was carried out through a bath of stainless-steel beads sitting on top of a hot plate. The reaction mixture was cooled down to room temperature and 150 mL of cold water was added and stirred for another 15 min. The precipitate was filtered under vacuum and washed with water several times. This solid was also washed with hexanes until the filtrate came out colorless. Compound 3.S5 was obtained as a white amorphous solid. Yield: 98% (20.2 g, 49 mmol). ¹H NMR (400 MHz, CD₂Cl₂, 25 °C): δ 8.04 (d, J = 1.7 Hz,
2H), 7.61 (t, J = 1.7 Hz, 1H), 7.02 (s, 2H, benzimidazole) and 3.85 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$:CD$_3$OD, 25 °C): δ 148.7, 147.7, 134.9, 134.2, 128.3, 124.1 and 56.9 ppm. C$_{15}$H$_{12}$N$_2$O$_2$Br$_2$, HRMS (ESI) [M+H]$^+$ calc.: 410.9338; exp.: 410.9335.

Compound 3.5a.

In a 100 mL round bottom flask compound 3.S5 (412 mg, 1 mmol), phenylboronic acid pinacol ester (430 mg, 2.1 mmol), and K$_2$CO$_3$ (300 mg, 2.2 mmol) were dissolved in a THF:H$_2$O:EtOH (10:1:1) mixture (50 mL). This solution was degassed with N$_2$ for 10 min before increasing the temperature to 70 °C. Pd(PPh$_3$)$_4$ (100 mg, 0.087 mmol) was added to the reaction. The reaction mixture was kept at 70 °C overnight under N$_2$ atmosphere. Heating was carried out through a bath of stainless-steel beads sitting on top of a hot plate. After this step, it was dried under vacuum, the resulting solid filtrated and washed several times with water and hexanes. The crude product was purified by silica gel column chromatography using hexanes:ethyl acetate (1:1) to obtain a white amorphous solid. Yield: 90% (365 mg, 0.9 mmol). Single crystals were grown from slow evaporation of a dichloromethane:methanol (10:1) mixture. $^1$H NMR (400 MHz, CD$_2$Cl$_2$, 25 °C): δ 10.29 (s, 1H), 8.29 (d, J = 1.0 Hz, 2H), 7.78 (br, 1H), 7.45 (d, J = 6.7 Hz, 4H), 7.23 (m, 8H) and 3.74 (s, 6H) ppm; (400 MHz, CD$_2$Cl$_2$/MeOD, 25 °C): δ 8.26 (d, J = 2.5 Hz, 2H), 7.89 (d, J = 2.5 Hz, 1H), 7.77 (m, 4H), 7.50 (m, 4H), 7.40 (m, 2H), 7.20 (s, 1H), 7.04 (s, 1H) and
3.89 (s, 6H) ppm; (400 MHz, TCE/MeOD, 25 °C): δ 8.29 (s, 2H), 7.84 (s, 1H), 7.75 (d, J = 7.2 Hz, 4H), 7.44 (m, 4H), 7.33 (m, 2H), 7.19 (s, 1H), 6.97 (s, 1H), 3.88 (s, 3H), and 3.84 (s, 3H) ppm.

$^{13}$C NMR (100 MHz, CD$_2$Cl$_2$, 25 °C): δ 151.4, 148.4, 143.3, 141.0, 132.2, 129.6, 128.5, 127.8, 127.6, 124.7 and 56.9. C$_{27}$H$_{22}$N$_2$O$_2$, HRMS (ESI) [M+H]$^+$ calc.: 407.1754; exp.: 407.1746.

**Compound 3.5b.**

In a 100 mL round bottom flask compound 3.5S (412 mg, 1 mmol), naphthalene-2-boronic acid pinacol ester (550 mg, 2.16 mmol), and K$_2$CO$_3$ (300 mg, 2.2 mmol) were dissolved in 50 mL of a THF:H$_2$O:EtOH (10:1:1) mixture. This solution was degassed with N$_2$ for 10 min, and subsequently the temperature increased to 70 °C. Pd(PPh$_3$)$_4$ (100 mg, 0.087 mmol) was added to the reaction mixture, and temperature and N$_2$ atmosphere were kept overnight. Heating was carried out through a bath of stainless-steel beads sitting on top of a hot plate. The reaction mixture was dried under vacuum, filtered, and washed several times with water and hexanes. The crude product was purified by silica gel column chromatography using hexanes:ethyl acetate (1:1) to obtain a white amorphous solid. Yield: 60% (304 mg, 0.6 mmol). Single crystals were grown from slow evaporation of a dichloromethane:methanol (10:1) mixture. $^1$H NMR (400 MHz, DMSO-$d_6$, 25 °C): δ 12.92 (s, 1H), 8.59 (s, 2H), 8.50 (s, 2H), 8.31 (s, 1H), 8.06 (m, 8H), 7.60 (m, 4H), 7.30 (s, 1H), 7.08 (s, 1H), 3.87 (s, 3H), and 3.83 (s, 3H) ppm; (400 MHz, CD$_2$Cl$_2$, 25 °C): δ 11.60 (s, 1H), 8.39 (d, J = 1.5 Hz, 2H), 8.01 (s, 1H), 7.97 (s, 2H), 7.82 (m, 4H), 7.75 (m, 2H), 7.67 (m, 2H), 7.46
(m, 4H), 7.18 (bs, 2H), and 3.79 (s, 6H) ppm; (400 MHz, CD\textsubscript{2}Cl\textsubscript{2}/MeOD, 25 °C): δ 8.41 (d, J = 1.5 Hz, 2H), 8.25 (s, 2H), 8.12 (s, 1H), 7.94 (m, 8H), 7.54 (m, 4H), 7.12 (s, 2H) and 3.88 (s, 6H) ppm; (400 MHz, TCE/MeOD, 25 °C): δ 8.50 (s, 2H), 8.30 (s, 2H), 8.14 (s, 1H), 7.92 (m, 8H), 7.50 (m, 4H), 7.10 (b, 2H) and 3.90 (s, 6H) ppm. \textsuperscript{13}C NMR (100 MHz, DMSO-\textit{d}\textsubscript{6}, 25 °C): δ 149.4, 147.3, 146.4, 141.5, 137.5, 137.0, 133.4, 132.5, 132.0, 128.7, 128.6, 128.3, 127.6, 126.6, 126.4, 126.1, 125.7, 125.3, 123.5, 101.7, 94.4, 56.0 and 55.9 ppm. C\textsubscript{35}H\textsubscript{26}N\textsubscript{2}O\textsubscript{2}, HRMS (ESI) [M+H]\textsuperscript{+} calc.: 507.2067; exp.: 507.2059.
6.1.3 Experimental data for chapter 4

Characterization spectra for Chapter 4 compounds can be viewed in the Supporting Information of: Mirzaei, S; Castro, V. M. E.; Hernández Sánchez, R. Chem. Sci. 2022, 13, 2026–2032.

Compound 4.S2.

The synthesis of 4.S2 has been reported in the literature. However, we have modified the synthetic procedure, as described next, increasing the overall product yield. A 250 mL Schlenk flask was loaded with 4.S1 (4.0 g, 3.53 mmol), sealed with rubber septum and dried at 80 °C for 4 h using high vacuum. The flask was filled with nitrogen and put under a nitrogen flow by placing a needle (0.7 mm×40 mm) through the rubber septum. Dry tetrahydrofuran (THF, 170 mL) was added through the rubber septum using another needle (0.9 mm× 40 mm). The resulting clear solution was cooled down to −78 °C using a dry ice/acetone bath. After stirring for 10 min at this temperature, n-butyllithium (1.6 M in hexanes, 9.24 mL, 14.83 mmol, 4.2 eq) was added dropwise over 5 min, and the mixture was stirred for an additional 0.5 h. The dry ice/acetone bath was replaced with ice/NaCl bath, and the white cloudy mixture was stirred vigorously for 20 min. 2-isoproxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (10 mL, 53.74 mmol, 15.2 eq) was added
dropwise in 5 min. After 30 min the ice/NaCl bath was removed, and the reaction mixture (clean solution) warmed to room temperature. Around 50 mL deionized water was added, and the mixture stirred vigorously for 20 min. The THF was removed under low pressure and the white solid was washed with copious amount of water and 200 mL of acetone to obtain the pure produce (white solid). Yield: 73% (3.40 g, 2.57 mmol). Spectral characterization is in agreement with previous literature.\textsuperscript{368}

\begin{center}
\includegraphics[width=0.5\textwidth]{compound41.png}
\end{center}

**Compound 4.1.**

To a 250 mL Schlenk flask containing 4.S1 (1.00 g, 0.88 mmol) we added phenylboronic acid (0.53 g, 4.41 mmol, 5 eq), K\textsubscript{2}CO\textsubscript{3} (3 g, 21.7 mmol, 24.7 eq), and a mixed solvent of toluene, ethanol, and water (40/30/10, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.4 g of Pd(PPh\textsubscript{3})\textsubscript{4} (0.32 mmol, 0.36 eq) was added. This amount of catalyst forms 4 C-C bonds, thus representing \textasciitilde9 mol\% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was left at reflux and under N\textsubscript{2} atmosphere for three days after which the solvents were removed under reduced pressure. The crude product was purified by column chromatography using DCM/Hexanes (50-60\%, v/v) giving a white solid.
Yield: 53% (0.53 g, 0.48 mmol). Melting pint = 258-260 °C. High quality crystals of 4.1 were grown by slow evaporation of a DCM/MeCN solution. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.34-7.29 (m, 3H), 7.26-7.22 (m, 1H), 7.03 (d, 2H, $J$ = 7.2 Hz), 5.20 (d, 1H, $J$ = 6.8 Hz), 4.87 (t, 1H, $J$ = 7.0 Hz), 4.23 (d, 1H, $J$ = 70 Hz), 2.37 (q, 2H, $J$ = 6.4 Hz), 1.50-1.38 (m, 6H), and 0.96 (t, 3H, $J$ = 7.1 Hz). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 152.7, 138.5, 134.2, 130.0, 129.5, 128.0, 127.2, 120.0, 100.7, 37.3, 32.2, 30.6, 27.8, 22.9, and 14.3 ppm. C$_{76}$H$_{80}$O$_8$, HRMS [M+H]$^+$ calc.: 1121.5926; exp.: 1121.5900.

**Compound 4.2.**

To a 250 mL Schlenk flask containing 4.S1 (1.00 g, 0.88 mmol) we added 4-fluorophenylboronic acid (0.68 g, 4.84 mmol, 5.5 eq), K$_2$CO$_3$ (3 g, 21.7 mmol, 24.7 eq), and a mixed solvent of toluene, ethanol, and water (40/30/10, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.4 g of Pd(PPh$_3$)$_4$ (0.32 mmol, 0.36 eq) was added. This amount of catalyst forms 4 C-C bonds, thus representing ~9 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was left at reflux and under N$_2$ atmosphere for three days after which the solvents were removed under reduced
pressure. The crude product was further purified by column chromatography using DCM/Hexanes (40-50%, v/v) giving a white solid. Yield: 46% (0.48 g, 0.40 mmol). Melting pint = >260 °C. High quality crystals of 4.2 were grown by slow evaporation of a DCM/MeCN solution. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.31 (s, 1H), 7.05-6.98 (m, 4H), 5.25 (d, 1H, $J = 6.8$ Hz), 4.83 (t, 1H, $J = 8.0$ Hz), 4.19 (d, 1H, $J = 7.0$ Hz), 2.33 (q, 2H, $J = 6.6$ Hz), 1.49-1.35 (m, 6H), and 0.95 (t, 3H, $J = 7.1$ Hz). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.3, 160.8, 152.7, 138.5, 131.6, 131.6, 129.8, 129.8, 128.5, 120.1, 115.2, 115.0, 100.6, 32.2, 30.5, 27.8, 22.9, and 14.3 ppm. $^{19}$F NMR (376 MHz, CDCl$_3$): δ –114.91 ppm. C$_{76}$H$_{76}$O$_8$F$_4$, HRMS [M+H]$^+$ calc.: 1193.5549; exp.: 1193.5532.

![Chemical Structure](image)

**Compound 4.3.**

To a 250 mL Schlenk flask containing 4.S1 (1.00 g, 0.88 mmol) we added 3-fluorophenylboronic acid pinacol ester (1.17 g, 5.28 mmol, 6 eq), K$_2$CO$_3$ (3 g, 21.7 mmol, 24.7 eq), and a mixed solvent of toluene, ethanol, and water (40/30/10, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.4 g of Pd(PPh$_3$)$_4$ (0.32 mmol, 0.36 eq) was added. This amount of catalyst forms 4 C-C bonds, thus representing ~9 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was
left at reflux and under N\textsubscript{2} atmosphere for three days after which the solvents were removed under reduced pressure. The crude product was further purified by column chromatography using DCM/Hexanes (50\%, v/v) giving a white solid. Yield: 38\% (0.40 g, 0.33 mmol). Melting pint = 249-251 °C. High quality crystals of 4.3 were grown by slow evaporation of a DCM/MeCN solution. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): δ 7.35 (s, 1H), 7.30 (m, 1H), 6.99 (dt, 1H, \( J = 2.1 \) Hz and \( J = 8.4 \) Hz), 6.80 (t, 2H, \( J = 7.7 \) Hz), 5.26 (d, 1H, \( J = 6.9 \) Hz), 4.85 (t, 1H, \( J = 8.1 \) Hz), 4.20 (d, 1H, \( J = 7.0 \) Hz), 2.35 (q, 2H, \( J = 6.5 \) Hz), 1.50-1.36 (m, 6H), and 0.94 (t, 3H, \( J = 7.1 \) Hz). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) δ 163.7, 161.3, 152.6, 138.5, 136.3, 136.2, 129.6, 129.5, 128.5, 125.6, 120.4, 117.2, 117.0, 114.5, 114.5, 100.6, 37.2, 32.2, 30.5, 27.8, 22.9, and 14.3. \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}): δ –113.45 ppm. C\textsubscript{76}H\textsubscript{76}O\textsubscript{8}F\textsubscript{4}, HRMS [M+H]\textsuperscript{+} calc.: 1193.5549; exp.: 1193.5528.

**Compound 4.4.**

To a 250 mL Schlenk flask containing 4.S1 (1.00 g, 0.88 mmol) we added 3,5-difluorophenylboronic acid pinacol ester (1.27 g, 5.28 mmol, 6 eq), K\textsubscript{2}CO\textsubscript{3} (3 g, 21.7 mmol, 24.7 eq), and a mixed solvent of toluene, ethanol, and water (40/30/10, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.4 g of Pd(PPh\textsubscript{3})\textsubscript{4} (0.32 mmol, 0.36 eq) was added. This amount of catalyst forms 4 C-C bonds,
thus representing ~9 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was left at reflux and under N\textsubscript{2} atmosphere for three days after which the solvents were removed under reduced pressure. The crude product was further purified by column chromatography using DCM/Hexanes (50%, \textit{v/v}) giving a white solid. Yield: 42% (0.47 g, 0.37 mmol). Melting pint = >260 °C. High quality crystals of 4.4 were grown by slow evaporation of a DCM/MeCN solution. 

\( ^1 \text{H NMR (400 MHz, CDCl}_3) \delta 7.34 (s, 1H), 6.68 (b, 1H), 6.56 (d, 2H, \textit{J} = 7.8 \text{ Hz}), 5.30 (d, 1H, \textit{J} = 6.8 \text{ Hz}), 4.83 (t, 1H, \textit{J} = 8.1 \text{ Hz}), 4.13 (d, 1H, \textit{J} = 7.0 \text{ Hz}), 2.33 (q, 2H, \textit{J} = 6.5 \text{ Hz}), 1.49-1.36 (m, 6H), and 0.95 (t, 3H, \textit{J} = 7.1 \text{ Hz}). \) \( ^{13} \text{C NMR (100 MHz, CDCl}_3) \delta 163.9, 163.7, 161.4, 161.3, 152.4, 138.7, 137.3, 137.2, 137.1, 127.8, 120.8, 113.1, 112.9, 103.1, 103.0, 102.8, 100.6, 37.1, 32.2, 30.4, 27.8, 22.9, and 14.3 \text{ ppm.} \) \( ^{19} \text{F NMR (376 MHz, CDCl}_3) \delta –110.27 \text{ ppm.} \) C\textsubscript{76}H\textsubscript{72}O\textsubscript{8}F\textsubscript{8}, HRMS [M+H\textsuperscript{+}] calc.: 1265.5172; exp.: 1265.5130.

**Compound 4.5.**

To a 250 mL Schlenk flask containing 4.S2 (0.5 g, 0.38 mmol) we added 1-bromo-2,3,4-trifluorobenzene (0.4 g, 1.9 mmol, 5 eq), K\textsubscript{2}CO\textsubscript{3} (1.5 g, 10.8 mmol, 28.4 eq), and a mixed solvent
of toluene, ethanol, and water (40/20/20, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.2 g of Pd(PPh$_3$)$_4$ (0.16 mmol, 0.47 eq) was added. This amount of catalyst forms 4 C-C bonds, thus representing ~0.12 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was left at reflux and under N$_2$ atmosphere for 16 h after which the solvents were removed under reduced pressure. The crude product was further purified by column chromatography using DCM/Hexanes (50%, v/v) giving a white solid. Yield: 43% (0.22 g, 0.16 mmol). Melting pint = >260 °C. High quality crystals of 4.5 were grown by slow evaporation of a DCM/MeCN solution. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.37 (s, 1H), 6.90 (b, 1H), 6.52 (b, 0.4), 5.21 (b, 1H), 4.81 (b, 1H), 4.13 (b, 1H), 2.34 (b, 2H), 1.45 (b, 6H), and 0.95 (t, 3H, $J$ = 6.9 Hz). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 37.1, 32.2, 30.4, 27.7, 22.8, 14.3, and several multiplets in 100-160 ppm. $^{19}$F NMR (376 MHz, CDCl$_3$): δ –159.05 to –160.57 (m), and –136.09 to –131.40 (m) ppm. C$_{76}$H$_{88}$O$_8$F$_{12}$, HRMS [M+H]$^+$ calc.: 1337.4795; exp.: 1337.4810.
Compound 4.6 (Method A).

To a 250 mL Schlenk flask containing 4.S1 (1.00 g, 0.88 mmol) we added 3,4,5-trifluorophenylboronic acid pinacol ester (1.83 g, 7.04 mmol, 8 eq), K$_2$CO$_3$ (3 g, 21.7 mmol, 24.7 eq), and a mixed solvent of toluene, ethanol, and water (40/30/10, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.4 g of Pd(PPh$_3$)$_4$ (0.32 mmol, 0.36 eq) was added. This amount of catalyst forms 4 C-C bonds, thus representing ~9 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was left at reflux and under N$_2$ atmosphere for three days after which the solvents were removed under reduced pressure. The crude product was further purified by column chromatography using DCM/Hexanes (50%, v/v) giving a white solid. Yield: 38% (0.45 g, 0.34 mmol). Melting pint = >260 °C. High quality crystals of 6 were grown by slow evaporation of a DCM/MeCN solution.

Compound 4.6 (Method B).

To a 250 mL Schlenk flask containing 4.S2 (1.5 g, 1.14 mmol) we added 1-bromo-3,4,5-trifluorobenzene (1.92 g, 9.1 mmol, 8 eq), K$_2$CO$_3$ (3 g, 21.7 mmol, 19 eq), and a mixed solvent of
toluene, ethanol, and water (40/30/10, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.5 g of Pd(PPh₃)₄ (0.43 mmol, 0.38 eq) was added. This amount of catalyst forms 4 C-C bonds, thus representing ~9 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was left at reflux and under N₂ atmosphere for 16 h after which the solvents were removed under reduced pressure. The crude product was further purified by column chromatography using DCM/Hexanes (50%, v/v) giving a white solid. Yield: 49% (0.74 g, 0.55 mmol). ¹H NMR (400 MHz, CDCl₃): δ 7.35 (s, 1H), 6.61 (b, 1H), 5.35 (d, 1H, J = 6.6 Hz), 4.85 (t, 1H, J = 8.0 Hz), 4.08 (d, 1H, J = 7.0 Hz), 2.34 (q, 2H, J = 6.4 Hz), 1.50-1.39 (m, 6H), and 0.97 (t, 3H, J = 7.1 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 152.4, 151.6, 149.9, 139.7, 138.9, 138.0, 130.1, 127.3, 121.0, 114.3, 100.5, 37.2, 32.1, 30.3, 27.8, 22.9, and 14.3 ppm. ¹⁹F NMR (376 MHz, CDCl₃): δ −135.46 (d), and −162.93 (t). C₇₆H₆₈O₈F₁₂, HRMS [M+H]⁺ calc.: 1337.4795; exp.: 1337.4752.

**Compound 4.7.**

To a 250 mL Schlenk flask containing 4.S2 (0.5 g, 0.37 mmol) we added 1-bromo-2,3,4,5-tetrafluorobenzene (0.52 g, 2.27 mmol, 6 eq), K₂CO₃ (1.5 g, 10.8 mmol, 29 eq), and a mixed
solvent of toluene, ethanol, and water (40/30/10, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.2 g of Pd(PPh3)4 (0.17 mmol, 0.46 eq) was added. This amount of catalyst forms 4 C-C bonds, thus representing ~11 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was left at reflux and under N2 atmosphere for 24 h after which the solvents were removed under reduced pressure. The crude product was further purified by column chromatography using DCM/Hexanes (50%, v/v) giving a white solid. Yield: 53% (0.28 g, 0.20 mmol). Melting pint = >260 °C. High quality crystals of 4.7 were grown by slow evaporation of a DCM/MeCN solution. 1H NMR (400 MHz, CDCl3): δ 7.28 (s, 1H), 6.71 (b, 0.72H), 6.39 (b, 0.3), 5.19 (b, 1H), 4.71 (b, 1H), 4.06 (b, 1H), 2.24 (b, 2H), 1.32 (b, 6H), and 0.85 (t, 3H, J = 7.1 Hz). 13C NMR (100 MHz, CDCl3) δ 37.1, 32.2, 30.3, 27.7, 22.8, 14.3, and several multiplets in 100-160 ppm. 19F NMR (376 MHz, CDCl3): δ –156.01 to –154.65 (m) and –140.86 to –136.03 (m) ppm. C76H64O8F16, HRMS [M+H]+ calc.: 1409.4419; exp.: 1409.4417.
To a 250 mL Schlenk flask containing 4.8 (1.0 g, 0.75 mmol) we added 1-bromo-3,5-bis(trifluoromethyl)benzene (1.32 g, 4.5 mmol, 6 eq), K₂CO₃ (3 g, 21.7 mmol, 28.9 eq), and a mixed solvent of toluene, ethanol, and water (40/30/10, mL/mL/mL). The reaction mixture was degassed for 15 min while stirring vigorously at room temperature. To this mixture, 0.4 g of Pd(PPh₃)₄ (0.34 mmol, 0.46 eq) was added. This amount of catalyst forms 4 C-C bonds, thus representing ~11 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. The reaction mixture was left at reflux and under N₂ atmosphere for 16 h after which the solvents were removed under reduced pressure. The crude product was further purified by column chromatography using DCM/Hexanes (20%, v/v) giving a white solid. Yield: 46% (0.58 g, 0.35 mmol). Melting point = >260 °C. High quality crystals of 4.8 were grown by slow evaporation of a DCM/MeCN solution. ¹H NMR (400 MHz, CDCl₃): δ 7.83 (s, 1H), 7.53 (s, 2H), 7.44 (s, 1H), 5.33 (d, 1H, J = 6.8 Hz), 4.88 (t, 1H, J = 8.0 Hz), 4.29 (d, 1H, J = 6.9 Hz), 2.38 (q, 2H, J = 6.6 Hz), 1.52-1.38 (m, 6H), and 0.98 (t, 3H, J = 7.1 Hz). ¹³C NMR (100 MHz, CDCl₃): δ 152.6, 139.0, 135.7, 132.1, 131.8, 131.4, 131.1, 130.4, 127.3, 126.7, 124.6, 121.9, 121.6, 121.4, 119.2, 100.6, 37.4, 32.2, 30.5, 27.8, 22.9, and 14.3 ppm. ¹⁹F
NMR (376 MHz, CDCl₃): δ −62.94 ppm. C₉₂H₁₀₈N₄O₂₀, HRMS [M+H]+ calc.: 1825.7423; exp.: multiple attempts were carried out, however none of them was successful.

6.1.4 Isolated host-guest adducts for chapter 4

Compound [n-Bu₄N][MeSO₃⊂4.4]

15 mg of compound 4.4 in 0.5 mL of CDCl₃ were titrated with [n-Bu₄N][MeSO₃] up to ~1.1 eq. This solution was transferred to a 20 mL vial. The NMR tube was rinsed with 5-7 mL of DCM, which was combined with the initial solution. Additionally, around 4-5 mL of MeCN were added to the latter solution. The vial was left aside for slow solvent evaporation. Colorless crystals were formed within 12-16 hours.

Compound [n-Bu₄N][MeSO₃⊂4.6]

15 mg of compound 4.6 in 0.5 mL of CDCl₃ were titrated with [n-Bu₄N][MeSO₃] up to ~1.1 eq. This solution was transferred to a 20 mL vial. The NMR tube was rinsed with 5-7 mL of DCM, which was combined with the initial solution. Additionally, around 4-5 mL of MeCN were added to the latter solution. The vial was left aside for slow solvent evaporation. Colorless crystals were formed within 12-16 hours.

Compound [n-Bu₄N][MeSO₃⊂4.7].

15 mg of compound 4.7 in 0.5 mL of CDCl₃ were titrated with [n-Bu₄N][MeSO₃] up to ~1.2 eq. This solution was transferred to a 20 mL vial. The NMR tube was rinsed with 5-7 mL of DCM, which was combined with the initial solution. Additionally, around 4-5 mL of MeCN were
added to the latter solution. The vial was left aside for slow solvent evaporation. Colorless crystals were formed within 12-16 hours.

Compound \([n\text{-Bu}_4\text{N}][\text{MeSO}_3 \subset 4.8]\).

15 mg of compound 4.8 in 0.5 mL of CDCl$_3$ were titrated with \([n\text{-Bu}_4\text{N}][\text{MeSO}_3]\) up to ~4.2 eq. This solution was transferred to a 20 mL vial. The NMR tube was rinsed with 5-7 mL of DCM, which was combined with the initial solution. Additionally, around 4-5 mL of MeCN were added to the latter solution. The vial was left aside for slow solvent evaporation. Colorless crystals were formed within 12-16 hours.
6.1.5 Experimental data for chapter 5

A 500 mL round bottom Schlenk flask was loaded with 3,5-dibromobenzal bromide \textit{5.S3} (14.0 g; 34.3 mmol) and pentyl-footed octol \textit{5.S1} (4.0 g; 5.2 mmol) and left under the high vacuum for \(\sim 5\) h at 60 °C. Degassed DMA (200 mL) and 10 g of activated molecule sieves (4 Å) has been added to the mixture. After 30 min the solution has been cooled down to room temperature and 8 mL of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) has been added. The reaction mixture was stirred at rt for 30 min and then at 80 °C for 3 days. DMA was removed under reduced pressure at 70 C and washed with copious amount of water. The flash column is used first with pure hexane to remove excess 3,5-dibromobenzal bromide and then with 20-30% DCM in hexanes to get the pentyl-footed octabromide \textit{5.3} as a white solid (2.8 g, 1.6 mmol, 31%).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): 7.27 (s, 2H), 7.66 (s, 1H), 7.26 (s, 1H), 5.34 (s, 1H), 4.89 (t, 1H), 2.32 (b, 2H), 1.47 (b, 6H) and 0.96 (t, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\), 20 °C): 154.1, 142.1, 139.4, 134.7, 128.5, 123.2, 121.2, 116.6, 105.8, 36.8, 32.2, 29.9, 27.8, 22.9 and 14.2.
Compound 5.2<sup>cis</sup>.  

A 250 mL Pyrex Schlenk flask was loaded with 0.5 g of 5.3 (0.28 mmol), 0.45 g of 3-Chlorophenylboronic acid (2.8 mmol, 10 eq), and 2 g of K<sub>2</sub>CO<sub>3</sub> in 100 mL of toluene, 25 mL of water and 25 mL of EtOH. The reaction mixture was degassed for 20 min while stirring vigorously at room temperature. To this mixture, 0.25 g of Pd(PPh<sub>3</sub>)<sub>4</sub> (0.21 mmol, 0.75 eq) was added. This amount of catalyst forms 8 C-C bonds, thus representing ~0.09 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. Then, the reaction mixture was refluxed under N<sub>2</sub> atmosphere overnight (~16 h). The solvent was removed under vacuum and the final product (off-white solid) was purified using 30% DCM in hexanes. Yield: 88% (0.5 g, 0.25 mmol).

<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>, 20 °C): 7.85 (s, 2H), 7.73 (s, 1H), 7.60 (s, 2H), 7.47 (d, 2H), 7.35-7.27 (m, 5H), 6.75 (s, 1H), 5.63 (s, 1H), 5.03 (t, 1H), 2.38 (q, 2H), 1.51 (m, 4H), 1.42 (sex, 2H), 0.97 (t, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>, 20 °C): 154.3, 142.4, 141.2, 140.2, 139.3, 135.0, 130.3, 128.0, 127.5, 126.9, 125.5, 124.5, 121.1, 117.0, 107.5, 77.4, 77.2, 76.9, 36.8, 32.3, 30.0, 27.9, 22.9, and 14.3.
Compound 5.1\textsuperscript{c5}.

In a 150 mL pressure tube inside the nitrogen filled glovebox, a mixture of 2,2'-bipyridine (0.4 g, 2.54 mmol), and bis(1,5-cyclooctadiene)nickel(0) (Ni(Cod)\textsubscript{2}, 0.7 g, 2.54 mmol) in a mixture of degassed toluene (30 mL) and DMF (30 mL) was stirred at 80 °C for 1 h. To the mixture at 80 °C was added a solution of 5.2\textsuperscript{c5} (0.2 g, 0.1 mmol) in 1:1 toluene:DMF (20 mL) pipetwise over 1 h, and the mixture was stirred at 80 °C for an additional 12 h. After the reaction mixture was cooled down to ambient temperature. The solvent was removed under vacuum and passed through the flash column with pure DCM. The obtained product has been dissolved in 1,1,2,2-tetrachloroethane (TCE, ~20 mL) and loaded on the silica gel; the silica gel has been dried totally and loaded on the column to purify using 40-50% DCM in hexanes to obtain the white solid as the pure product. Yield: 32% (55 mg, 0.032 mmol). High quality crystals were grown by slow diffusion of a MeCN into a solution of 5.2\textsuperscript{c5} in chlorobenzene (PhCl).

\textsuperscript{1}H NMR (400 MHz, C\textsubscript{2}D\textsubscript{2}Cl\textsubscript{4}, 100 °C): 8.31 (s, 2H), 8.27 (s, 2H), 8.01 (d, 2H), 7.92 (s, 1H), 7.82 (d, 2H), 7.66 (t, 2H), 7.56 (s, 1H), 7.23 (s, 1H), 5.69 (s, 1H), 5.20 (s, 1H), 2.52 (q, 2H), 1.61-1.46 (b, 6H), 1.02 (t, 3H). \textsuperscript{13}C NMR (100 MHz, C\textsubscript{2}D\textsubscript{2}Cl\textsubscript{4}, 100 °C): 154.9, 142.4, 141.4, 138.8,
A 250 mL Pyrex Schlenk flask was loaded with 0.7 g of 5.84 (0.33 mmol), 0.52 g of 3-chlorophenylboronic acid (3.3 mmol, 10 eq), and 3 g of K$_2$CO$_3$ in 100 mL of toluene, 25 mL of water and 25 mL of EtOH. The reaction mixture was degassed for 20 min while stirring vigorously at room temperature. To this mixture, 0.3 g of Pd(PPh$_3$)$_4$ (0.26 mmol, 0.78 eq) was added. This amount of catalyst forms 8 C-C bonds, thus representing ~0.1 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. Then, the reaction mixture was refluxed under N$_2$ atmosphere overnight (~16 h). The solvent was removed under vacuum and the final product (pale yellow solid) was purified using 20-30% DCM in hexanes. Yield: 90% (0.70 g, 0.30 mmol).

$^1$H NMR (400 MHz, CDCl$_3$, 20 °C): 7.86 (s, 2H), 7.74 (s, 1H), 7.60 (s, 2H), 7.48 (d, 2H), 7.35-7.26 (m, 5H), 6.76 (s, 1H), 5.63 (s, 1H), 5.04 (t, 1H), 2.39 (q, 2H), 1.52 (b, 4H), 1.29 (b, 14H)
and 0.90 (t, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$, 20 °C): 154.3, 142.4, 141.2, 140.2, 139.4, 135.0, 130.7, 127.9, 127.5, 126.9, 125.5, 124.5, 121.1, 117.0, 107.5, 36.8, 32.1, 30.2, 30.0, 29.9, 29.6, 28.2, 22.9 and 14.3.

**Compound 5.1a.**

In a 150 mL pressure tube inside the nitrogen filled glovebox, a mixture of 2,2'-bipyridine (0.34 g, 2.18 mmol), 1,5-cyclooctadiene (0.25 mL, 2.0 mmol), and bis(1,5-cyclooctadiene)nickel(0) (Ni(Cod)$_2$, 0.6 g, 2.18 mmol) in a mixture of degassed toluene (30 mL) and DMF (30 mL) was stirred at 80 °C for 1 h. To the mixture at 80 °C was added a solution of 5.2a (0.2 g, 0.085 mmol) in 1:1 toluene:DMF (20 mL) pipetwise over 1 h, and the mixture was stirred at 80 °C for an additional 12 h. After the reaction mixture was cooled down to ambient temperature. The solvent was removed under vacuum. The obtained product has been dissolved in DCM (~30 mL) and loaded on the silica gel; the silica gel has been dried totally and loaded on the column to purify using 30-40% DCM in hexanes to obtain the white solid as the pure product. Yield: 59% (0.103 g, 0.050 mmol).
\(^1\)H NMR (400 MHz, CDCl\(_3\), 20 °C): 8.25 (s, 2H), 8.18 (s, 2H), 7.94 (d, 2H), 7.83 (s, 1H), 7.75 (d, 2H), 7.59 (t, 2H), 7.43 (s, 1H), 7.14 (s, 1H), 5.60 (s, 1H), 5.10 (s, 1H), 2.22 (b, 2H), 1.51 (b, 4H), 1.27 (b, 14H) 0.88 (t, 3H). \(^1^3\)C NMR (100 MHz, CDCl\(_3\), 20 °C): 155.4, 142.7, 141.9, 139.2, 138.7, 138.0, 129.8, 126.7, 126.4, 125.0, 124.9, 124.3, 121.8, 116.4, 108.6, 36.72, 32.10, 31.75, 30.25, 30.03, 29.58, 28.11, 22.86, 14.29, 1.20.

**Compound 5.2b.**

A 250 mL Pyrex Schlenk flask was loaded with 0.7 g of 5.S4 (0.33 mmol), 0.89 g of 3-chloro-5-methylphenylboronic acid (3.3 mmol, 10 eq), and 2.0 g of K\(_2\)CO\(_3\) in 100 mL of toluene, 25 mL of water and 25 mL of EtOH. The reaction mixture was degassed for 20 min while stirring vigorously at room temperature. To this mixture, 0.3 g of Pd(PPh\(_3\))\(_4\) (0.26 mmol, 0.78 eq) was added. This amount of catalyst forms 8 C-C bonds, thus representing ~0.1 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. Then, the reaction mixture was refluxed under N\(_2\) atmosphere overnight.
(~16 h). The solvent was removed under vacuum and the final product (pale yellow solid) was purified using 30-50% gradient of DCM in hexanes. Yield: 92% (0.75 g, 0.30 mmol).

$^1$H NMR (600 MHz, CDCl$_3$, 20 °C): 7.81 (s, 2H), 7.69 (s, 1H), 7.38 (s, 2H), 7.34 (s, 1H), 7.26 (s, 2H), 7.13 (s, 2H), 6.75 (s, 1H), 5.61 (s, 1H), 5.03 (t, 1H), 2.38 (q, 2H), 2.30 (s, 6H), 1.50 (m, 4H), 1.29 (b, 14H) and 0.89 (t, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$, 20 °C): 154.4, 142.2, 141.3, 140.4, 140.1, 139.3, 134.6, 128.5, 126.9, 126.4, 124.6, 124.4, 121.1, 117.0, 107.6, 36.8, 32.1, 30.2, 29.9, 29.6, 28.2, 22.9, 21.4, and 14.3.

**Compound 5.1b.**

In a 150 mL pressure tube inside the nitrogen filled glovebox, a mixture of 2,2'-bipyridine (0.45 g, 2.9 mmol), 1,5-cyclooctadiene (0.25 mL, 2.0 mmol), and bis(1,5-cyclooctadiene)nickel(0) (Ni(Cod)$_2$, 0.8 g, 2.9 mmol) in a mixture of degassed toluene (30 mL) and DMF (30 mL) was stirred at 80 °C for 1 h. To the mixture at 80 °C was added a solution of 5.2b (0.2 g, 0.081 mmol) in 1:1 toluene:DMF (20 mL) pipetwise over 1 h, and the mixture was stirred at 80 °C for an additional 12 h. After the reaction mixture was cooled down to ambient temperature. The solvent
was removed under vacuum. The obtained product has been dissolved in DCM (~30 mL) and loaded on the silica gel; the silica gel has been dried totally and loaded on the column to purify using 40% DCM in hexanes to obtain the white solid as the pure product. Yield: 62% (0.110 g, 0.050 mmol).

$^1$H NMR (600 MHz, CDCl$_3$, 20 °C): 8.21 (s, 2H), 7.98 (s, 2H), 7.81 (s, 1H), 7.77 (s, 2H), 7.57 (s, 2H), 7.42 (s, 1H), 7.13 (s, 1H), 5.57 (s, 1H), 5.07 (t, 1H), 2.58 (s, 6H), 2.41 (b, 2H), 1.50 (b, 4H), 1.27 (b, 14H) and 0.88 (t, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$, 20 °C): 155.5, 142.8, 141.9, 139.3, 139.0, 138.7, 138.0, 127.0, 126.5, 125.0, 124.9, 122.7, 121.8, 116.4, 108.7, 36.7, 32.1, 30.2, 30.0, 30.0, 29.9, 29.9, 29.6, 28.1, 22.9, 22.0, and 14.3.

**Compound 5.2c.**

A 250 mL Pyrex Schlenk flask was loaded with 0.7 g of 5.S4 (0.33 mmol), 0.89 g of 3-Chloro-5-methoxyphenylboronic acid, pinacol ester (3.3 mmol, 10 eq), and 2.0 g of K$_2$CO$_3$ in 100 mL of toluene, 25 mL of water and 25 mL of EtOH. The reaction mixture was degassed for 20 min while stirring vigorously at room temperature. To this mixture, 0.3 g of Pd(PPh$_3$)$_4$ (0.26 mmol,
0.78 eq) was added. This amount of catalyst forms 8 C-C bonds, thus representing ~0.1 mol% for each bond formation. The solution was degassed again for an additional 15 min while gradually increasing the temperature to reflux. Then, the reaction mixture was refluxed under N₂ atmosphere overnight (~16 h). The solvent was removed under vacuum and the final product (yellow solid) was purified using 40-70% gradient of DCM in hexanes. Yield: 86% (0.73 g, 0.28 mmol).

¹H NMR (600 MHz, CDCl₃, 20 °C): 7.80 (s, 2H), 7.66 (s, 1H), 7.33 (s, 1H), 7.14 (s, 2H), 6.96 (s, 2H), 6.83 (s, 2H), 6.74 (s, 1H), 5.60 (s, 1H), 5.01 (t, 1H), 3.73 (s, 6H), 2.38 (q, 2H), 1.50 (m, 4H), 1.29 (b, 14H) and 0.89 (t, 3H). ¹³C NMR (150 MHz, CDCl₃, 20 °C): 160.7, 154.4, 143.2, 141.2, 140.2, 139.4, 135.5, 126.9, 124.6, 121.1, 120.0, 117.0, 113.4, 112.0, 107.6, 55.7, 36.8, 32.1, 30.2, 30.1, 30.0, 29.9, 29.9, 29.9, 29.6, 28.2, 22.9, 14.3.

**Compound 5.1c.**

In a 150 mL pressure tube inside the nitrogen filled glovebox, a mixture of 2,2'-bipyridine (0.34 g, 2.18 mmol), 1,5-cyclooctadiene (0.25 mL, 2.0 mmol), and bis(1,5-cyclooctadiene)nickel(0) (Ni(Cod)₂, 0.6 g, 2.18 mmol) in a mixture of degassed toluene (30 mL)
and DMF (30 mL) was stirred at 80 °C for 1 h. To the mixture at 80 °C was added a solution of 5.2c (0.2 g, 0.077 mmol) in 1:1 toluene:DMF (20 mL) pipetwise over 1 h, and the mixture was stirred at 80 °C for an additional 12 h. After the reaction mixture was cooled down to ambient temperature. The solvent was removed under vacuum. The obtained product has been dissolved in DCM (~30 mL) and loaded on the silica gel; the silica gel has been dried totally and loaded on the column to purify using 25-50% gradient ethyl acetate in hexanes to obtain the white solid as the pure product. The product has been washed with 15 mL of MeOH and 15 mL of EtOH. Yield: 0.62% (0.110 g, 0.048 mmol). High quality crystals were grown by slow diffusion of a MeCN into a solution of 5.1c in chlorobenzene (PhCl).

$^1$H NMR (600 MHz, CDCl$_3$, 20 °C): 8.22 (s, 2H), 7.79 (s, 1H), 7.76 (s, 2H), 7.44 (s, 2H), 7.41 (s, 1H), 7.28 (s, 2H), 7.11 (s, 1H), 5.55 (s, 1H), 5.06 (t, 1H), 4.01 (s, 6H), 2.41 (b, 2H), 1.49 (b, 4H), 1.26 (b, 14H) and 0.87 (t, 3H). $^{13}$C NMR (150 MHz, CDCl$_3$, 20 °C): 161.0, 155.4, 143.1, 142.6, 139.3, 139.1, 138.8, 126.4, 125.2, 121.8, 118.4, 116.4, 112.0, 110.1, 108.6, 55.9, 36.7, 32.1, 30.2, 29.9, 29.9, 29.6, 28.1, 22.8 and 14.3.
### 6.2 Crystallographic tables

#### 6.2.1 Crystallographic data for chapter 2

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### 6.2.2 Crystallographic data for chapter 3

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<td>C\textsubscript{68}H\textsubscript{48}F\textsubscript{16}O\textsubscript{8}</td>
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6.3 General computational information

6.3.1 Computational details for chapters 2, 3 and 5

All calculations were carried out using Gaussian 16 software package. Four different hybrid functionals, long-range corrected (ωB97XD), meta-GGA (M06-2X), meta-NGA (MN15), and GGA (B3LYP) of density functional theory (DFT) were used for all optimizations and subsequent studies. The frequency calculations were carried out for all optimized structures to ensure the absence of any imaginary frequencies for the ground state molecules. The intrinsic reaction coordinate (IRC) calculation is carried out, in addition to the presence of one imaginary frequency, for the transition state structures. In order to include the dispersion effects, the D3 version of Grimme with Becke-Johnson damping factors (D3BJ) were used for the B3LYP functional. The double-zeta quality basis set (6-31G*) was used for all calculations. The implicit solvation effects were included using the integral equation formalism variant of the polarizable continuum model (IEF-PCM) with standard parameters of dichloromethane (CH₂Cl₂). The gauge-independent atomic orbital (GIAO) method was used for ¹H NMR chemical shift calculations. The calculated chemical shieldings were scaled with ¹H NMR chemical shift of tetramethylsilane (TMS) calculated at the same level of theory. The DFT calculated ¹H NMR chemical shifts assisted in assigning the experimental spectra. The analysis of TD-DFT studies was carried out using GaussSum 3.0 software.
6.3.2 Computational details for chapter 4

All calculations were carried out using Gaussian 16 software package.\textsuperscript{444} The M06-2X\textsuperscript{446} functional was used for all optimizations and subsequent studies. The frequency calculations were carried out for all optimized structures to ensure the absence of any imaginary frequencies for the ground state molecules. The intrinsic reaction coordinate (IRC) calculation is carried out, in addition to the presence of one imaginary frequency, for the transition state structures. The double-zeta quality basis set (6-31+G(d,p)) was used for all calculations. For the sake of accuracy, the single point energies were calculated using 6-311++G(3df,2p) basis set. The implicit solvation effects were included using the CPCM solvation model with standard parameters of chloroform (CHCl\textsubscript{3}) and dimethyl sulfoxide (DMSO).\textsuperscript{453, 454} This method [M062X/6-311++G(3df,2p)+CPCM(solvent)//M062X/6-31+G(d,p)] showed reliable results in the previous study.\textsuperscript{378} The quantitative charge distributions are calculated using Hirshfeld method at 6-31+G(d,p) level.\textsuperscript{455} This method showed the lowest basis set dependency for population analysis.\textsuperscript{456}


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166. Lewis, S. E., Cycloparaphenylenes and related nanohoops. Chem. Soc. Rev. 2015, 44 (8), 2221-2304.


302. Roncucci, P.; Pirondini, L.; Paderni, G.; Massera, C.; Dalcanale, E.; Azov, V. A.; Diederich, F., Conformational Behavior of Pyrazine-Bridged and Mixed-Bridged


310. The B3LYP functional without dispersion correction factors showed totally different values compared with other functionals, e.g. M062X, MN15 and ωB97XD, and its own dispersion corrected version B3LYP-D3BJ (see Supporting Information). This relatively large discrepancy can be attributed to the poor simulation capabilities of B3LYP regarding non-covalent interactions (e.g. CH–π and π-π) that are important in flexible molecules like 3.


377. The exchange barrier for anion binding likely results from steric impediment of the CF3 groups in 8, as shown in Figure S12.


379. The H-to-O distance comprising formally the hydrogen bonds seen here are remarkably short. However, since the H atoms are not refined (they are simply fixed to the structure through AFIX commands), we decided not to relay on those figures and instead use the more reliable C-to-O distances.


382. Host 11 has been reported with R = -CONCy2, however to reduce computational costs, Cy was truncated to Me.


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443. Bindfit software can be found here: [http://supramolecular.org](http://supramolecular.org)


