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Self-Assembly, Templation and Biomimetics

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SELF-ASSEMBLY, TEMPLATION AND BIOMIMETICS

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ABSTRACT

Self-assembly, templation and biomimetics are three important, overlapping areas in supramolecular chemistry. Some contributions to these three areas are introduced.

Novel substituted trispyridylmethanol derived ligands were synthesized to mimic the active site of carbonic anhydrase. The key two-step process in constructing the trispyridylmethanol core structure is proven to be more efficient than the traditional one-step synthesis.

Self-assembly is a very efficient way to form nanoscale structure from relatively simple subunits. Tetraphenylmethane-based subunits were synthesized. The result of self-assembly reactions demonstrated the formation of 1~3 nm sized molecules in one step. Potential multi-generation self-assembly on this subunit is also discussed.

A novel and efficient approach for the synthesis of large aromatic crown ethers, using resorcinarenes as templates, has been developed. This simple three-step process generated a new family of aromatic crown ethers in up to 50% overall yield. As intermediates from these three-step syntheses, a large variety of molecular "baskets", which have been shown to be excellent hosts for adamantanes, have also been obtained.

ABBREVIATIONS

Ac	Acetate
aq.	Aqueous
n-BuLi	*n*-Butyllithium
°C	Degrees Celsius
d	Day, days
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCC	Deep cavity cavitand
DMA	N,N'-Dimethylacetamide
DMF	N,N'-Dimethylformamide
DMSO	Dimethylsulfoxide
Et	Ethyl
h	Hour, hours
HMPA	Hexamethylphosphoramide
MALDI	Matrix-assisted laser desorption ionization
Me	Methyl
MOE	Ethoxymethyl
Ph	Phenyl
i-Pr	Isopropyl

rt	Room temperature
SEM	Trimethylsilylethoxymethyl
TBAF	Tetrabutylamonium fluoride
TBDPS	*t*-Butyldiphenylsilyl
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMEDA	N,N,N',N'-Tetramethylenediamine
TMS	Trimethylsilyl
TOF	Time-of-flight
Ts	Tosyl (p-Toluenesulfonyl)

I. INTRODUCTION

1.1 Supramolecular Chemistry

The term "supramolecular chemistry" was introduced in 1969 by Jean-Marie Lehn as "chemistry beyond the molecule".[1] The 1987 Nobel Prize in Chemistry awarded to Pedersen, Cram and Lehn signified the formal arrival of this field of chemistry.

For a long time chemists have tried to understand *Nature* at a purely molecular level, *i.e*., they considered structures and functions involving only covalent bonds. However, many of the most important biological phenomena do not involve breaking and forming covalent bonds. Biological structures are usually made from loose aggregates that are held together by weak, non-covalent interactions. These interactions are responsible for most processes in the living system.

It was not until the end of the 19th century that chemists began to recognize this new, non-covalent facet of chemistry. In 1894, Emil Fischer proposed that an enzyme interacts with its substrate as a key does with its lock.[2] This concept laid the basis for *molecular recognition*, the discrimination by a host between a number of guests. However, supramolecular chemistry remained under-developed for a long time because of the lack of powerful tools to identify the weak interactions

between molecules. Over the past 30 years, with the development of modern technology such as NMR spectroscopy, mass spectroscopy, X-ray diffraction, etc., this area has undergone enormous development. On the other hand, supramolecular chemistry is still in its forming stage. A systematic structure to the various subfields that make up supramolecular chemistry is still not available. Thus, many concepts in this area are overlapping with each other; complete isolation of these concepts is not always possible.

1.2 Molecular Recognition

Molecular recognition is defined by Lehn as "the energy and information involved in the binding and selection of substrate(s) by a given receptor molecule; it may also involve a specific function."[1] Recognition implies the geometrical and interactional complementarity between the associating receptors and substrates. Molecular recognition lies at the core of the so-called "host-guest chemistry" (see section **1.6**).

One of the earliest examples of molecular recognition was the *clathrates* described by Powell.[3] These inclusion compounds were formed when small "guest" molecules such as methanol, hydrogen sulphide or sulphur dioxide, were completely enclosed in cavities formed by a "host" such as a hydroquinone network (Figure 1.1). The host was formed by intermolecular hydrogen bonds of hydroquinones and there was no covalent interaction between the host and the guest. One of the oldest uses of clathrate was in crude oil refining, in which the

undesirable paraffins were removed from gasoline by trapping in a clathrate lattice.

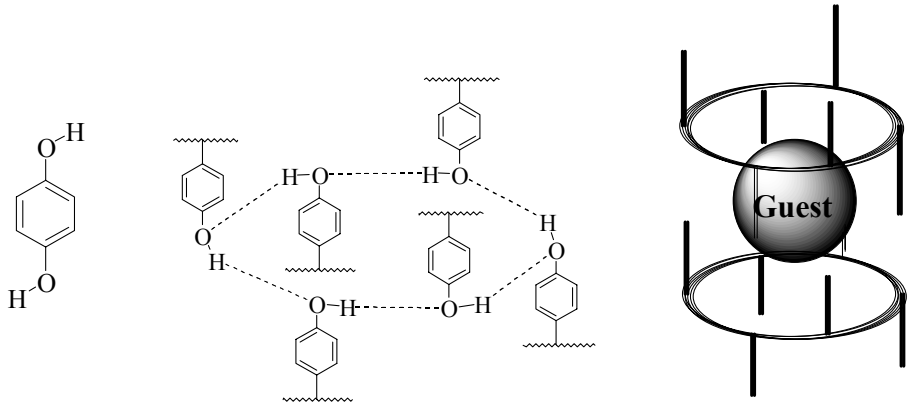
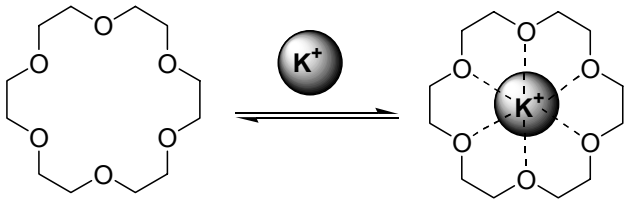


Figure 1.1 Hydroquinone and "guests" molecules assembled into a clathrate.

Another example of molecular recognition is the ability of crown ethers to selectively bind metal cations. 18-Crown-6, which has a diameter of 260-320 pm (depending on the conformation), binds K^+ strongly (Scheme 1.1). Larger sized Cs^+ fits in 21-crown-7, while smaller Na^+ fits in 15-crown-5 and Li^+ fits in 12-crown-4.



Scheme 1.1 18-Crown-6 and its K^+ complex.

1.3 Enzyme Mimicry

The initial motivation behind supramolecular chemistry was to design chemical systems that mimic biological processes. This gradually lead to the formation of biomimetic chemistry; the mimicry of nature. Enzyme mimicry has drawn much attention in the past forty years. In nature, enzymes (usually protein molecules) are the key elements in performing chemical reactions within cells. The active site of an enzyme is usually a three-dimensional entity formed by groups that come from different parts of the linear amino acid sequence. It takes up a relatively small part of the total volume of an enzyme and substrates are bound to enzymes by multiple weak interactions.[4]

1.3.1 Carbonic Anhydrase

A considerable number of enzymes require a metal ion for catalytic activity. One of these elements, zinc, is known to be functional in almost 300 enzymes representing all subgroups of the enzyme classification.[5] Of these enzymes, carbonic anhydrase (CA), a family of enzymes responsible for the hydration of carbon dioxide, are probably the most studied.[6] In addition to its biological role, CA has also been shown to catalyze the hydration of acetaldehyde and carboxylate esters small enough to fit within the active site.[7-10] The three-dimensional structure of carbonic anhydrase II (CAII), an isozyme found in human red blood cells,[11] revealed the active site as shown in Figure 1.2. The essential zinc cofactor is coordinated to three histidine residues (His 94, His 96, and His 119) and a solvent molecule (H_2O) in an approximately tetrahedral arrangement. The most striking feature of this active site is that the pK_a of the

water molecule coordinated to the zinc center has a value of *ca*. 7.5.[12,13] At physiological pH, it is a hydroxide ion that is bound to zinc. It is this species that nucleophilically attacks electron deficient carbon atoms, such as those in carbon dioxide and carboxylate esters, resulting in the hydration or cleavage of the respective molecules. The exact geometry of the active site is determined by the surrounding hydrogen bond network. The zinc ligands are fully saturated by hydrogen bond networks within second shell residues, which are referred as "indirect" zinc ligand (Figure 1.2).[14,15]

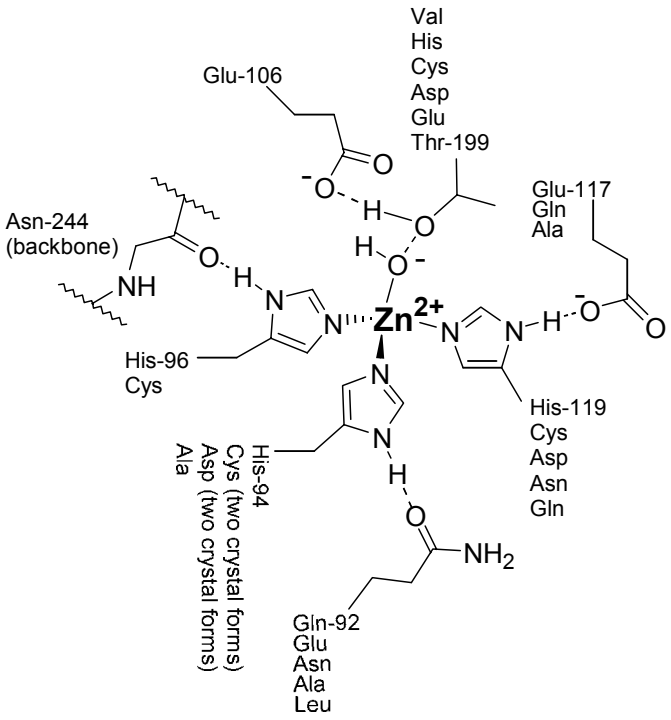
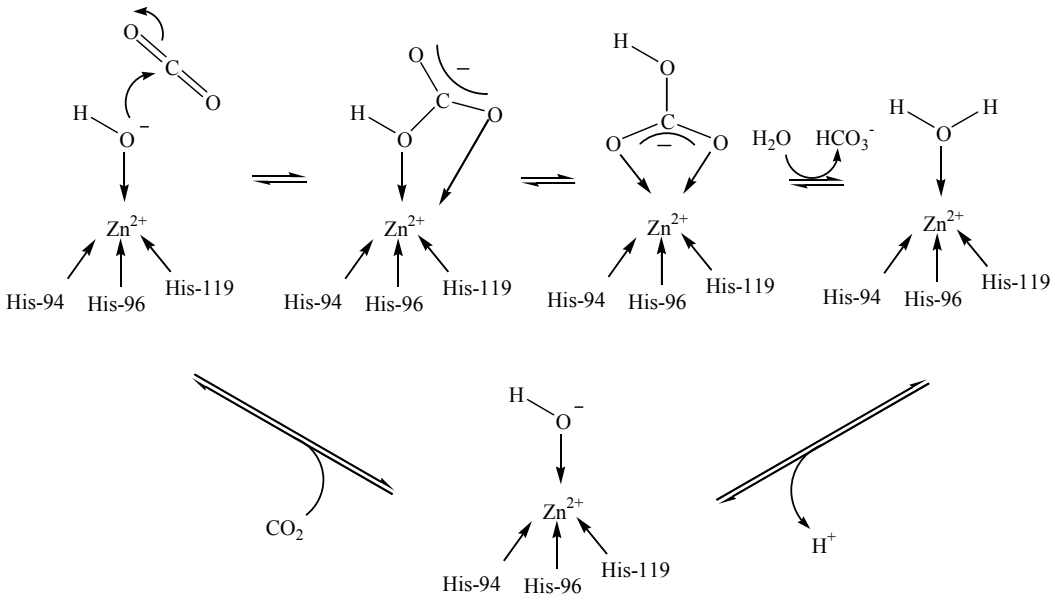


Figure 1.2 The active site of carbonic anhydrase II (CAII).

Scheme 1.2 illustrates the mechanism of hydration of CO_2 by CAII.[6] Zinc-bound hydroxide attacks the carbon atom of CO_2 to form zinc-bound bicarbonate. Isomerization of the bicarbonate, followed by the exchange of water molecule for zinc-bound bicarbonate generates the zinc-bound water species and releases the bicarbonate. Under the physiological environment, the zinc-bound water is deprotonated and regenerates the zinc-bound hydroxide.



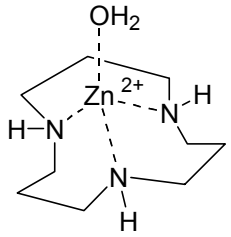
Scheme 1.2 Mechanism of hydration of CO_2 by CAII.

In attempting to elucidate the carbonic anhydrase enzyme mechanism, biomimetic approaches have been widely pursued. In essence, a macromolecule possessing some of the essential functional moieties is synthesized and studied to

establish how, and why, the chemistry of zinc is modulated by its coordination environment.

1.3.2 Polyamine Ligands

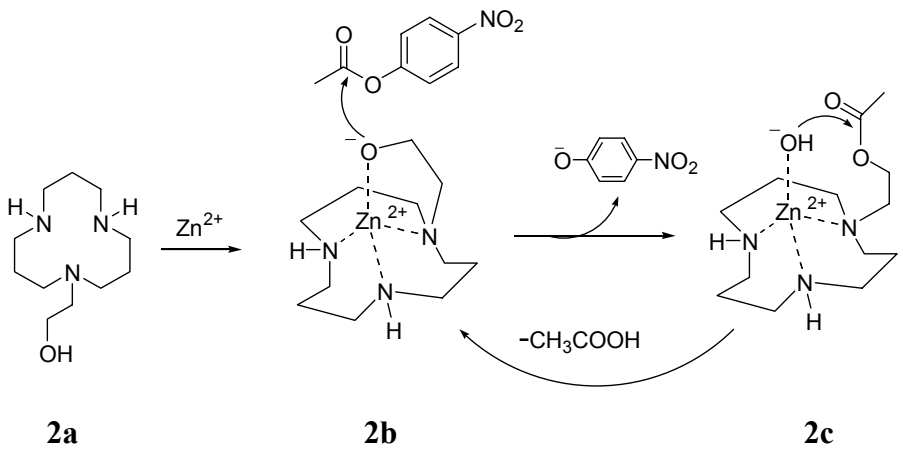
One approach, used by Kimura *et. al*, was to utilize a number of macrocyclic polyamines ligands.[16,17] For examples, the zinc aquo complex of triamine, [12]ane N_3 (**1**) has been shown to possess a pK_a value of 7.3, very similar to CA.[18]



zinc aquo complex of **1**

The alcohol-pendant cyclen (**2a**) has been shown to possess considerable esterase activity (Scheme 1.3).[19] The tethered alcoholic OH of **2a** deprotonated with a pK_a of 7.4 to yield an alkoxide RO^-—Zn^{2+} complex **2b**. The zinc-bound alkoxide anion directly attacked electrophilic ester carbonyls such as those in 4-nitrophenyl acetate, to yield an acyl-intermediate **2c**. It was then quickly hydrolyzed, possibly by the intramolecular zinc-bound water (or ^-OH), to complete the hydrolysis and regenerate the initial alkoxide complex **2b**. However, for these molecules, a note of caution is required: more recent results

indicate that the noted similarity in pK_a between CA and such zinc complex, may be more coincidence than an accurate representation of the active site.[20]



2a **2b** **2c**

Scheme 1.3 Catalytic carboxyester hydrolysis by Zn^{2+} complex of **2a**.

1.3.3 Tripodal Ligands

Another approach towards CA mimicry features the synthetic "tripodal" ligands.[21] Compared to the aforementioned cyclic polyamine ligands, the tripodal ligands have the following advantages: (1) the rigid tripodal ligands are well pre-organized to enforce the "facial" binding that is required to create a tetrahedral metal center (Figure 1.3); (2) the tripodal ligands typically possess only a single relevant binding conformation whereas macrocyclic ligands are more conformational flexible; (3) the directional nature of the tripodal ligands makes it possible to incorporate substituents that directly influence the steric environment around the metal center, while macrocyclic ligands are not suitably placed to have profound impact on the sterics of the coordination pocket.

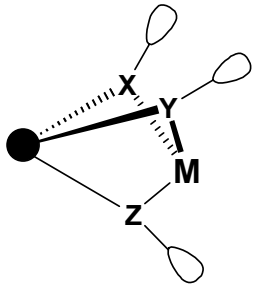
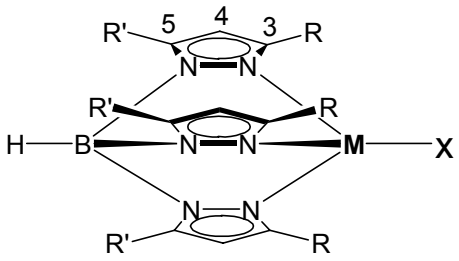


Figure 1.3 “Facial” binding of a tripodal ligand.

An example that illustrated the above virtues was the tris(pyrazolyl)borate ligand syetem, [$Tp^{RR'}$] **(3)**. With bulky *tert*-butyl substituents on the 3-position of the pyrazolyl groups (R = *t*-Bu), the ligand has been referred as a “tetrahedral enforcer”, due to its tendency to favor tetrahedral coordination.[22] Not only could the substituents at the 3-position be used to modify the size of the coordination pocket, they may also be used to influence the electronic properties of the metal center, such as the incorporation of perfluoroalkyl groups.[23,24]



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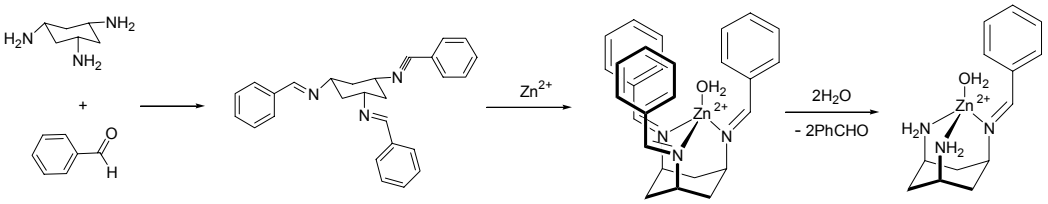
1.3.4 *Tach*-based Ligands

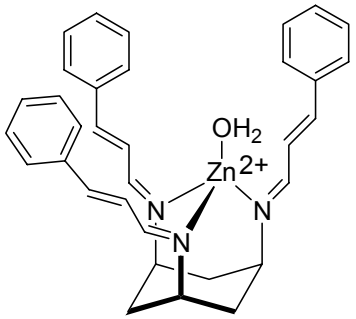
Despite the excellent work done based on the above two systems, neither of them contained a hydrophobic cavity, which is one of the most important

aspects of the enzyme's high acidity and nucleophilicity. In order to incorporate this feature, a new family of versatile *cis*-, *cis*-1,3,5-triaminocyclohexane (*tach*) based face-capping N_3 ligands have caught chemists' attention recently. Ligand **4** was synthesized by the condensation of *tach* with benzaldehyde using Schiff's base chemistry. Upon addition of coordination metals, the ligand adopted a face-capping N_3 geometry (**5**) with the metal cation situated in the bottom of the cavity. However, due to a destabilizing steric effect, the complex underwent a spontaneous hydrolysis of two out of the three imine groups, to form the mono-substituted complex (**6**), with the "cavity" essentially destroyed (Scheme 1.4).[25-27] This problem was overcome by adding an additional ethylene group on the "arm", *i.e.*, the novel metal-ligand complex **7** provided a basis for the modeling of the coordination environment of cabonic anhydrase.[28]



4 **5** **6**

Scheme 1.4 Formation and decomposition of ligand **4**



7

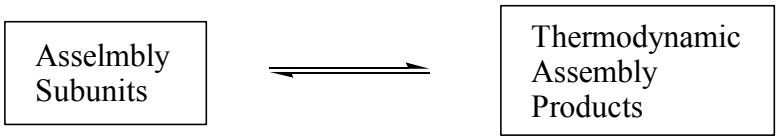
1.4 Self-assembly

Lehn defined self-assembly as, "the evolution towards spatial confinement through spontaneous connection of a few/many components, resulting in the formation of discrete/extended entities at either the molecular, covalent or the supramolecular, non-covalent level."[1] Nature offers the most spectacular examples of discrete molecular assemblies, such as the protein quaternary structure and DNA duplex formation. For synthetic chemists, self-assembly represents a powerful methodology in the creation of large, discrete, ordered structures from relatively simple subunits. Self-assembly can be divided into two categories: strict self-assembly and self-assembly with covalent modification.

1.4.1 Strict Self-assembly

All self-assemblies utilize non-covalent interactions as the driving force to establish an equilibrium between subunits and assembled products. As opposed to self-assemblies with covalent modifications (see section **1.4.2**), self-assembly using pure non-covalent forces are classed as "strict self-assemblies". The final product is produced spontaneously when the components are mixed together in

correct ratios under specific conditions. Because of the nature of non-covalent interactions, these processes are always reversible. The final product represents the thermodynamic minimum for the system (Scheme 1.5), and is produced 'error free'.



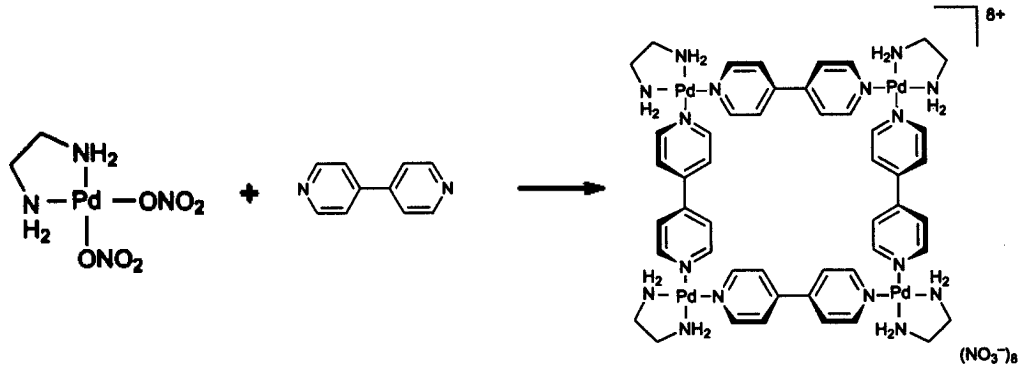
Scheme 1.5 Cartoon representation of strict self-assembly.

1.4.1.1 Metal Coordination Directed Self-assembly

One approach for the formation of supramolecular species *via* spontaneous self-assembly of precursor building blocks is the use of metal ions and coordination bond formation.[29-35] With carefully designed metal and ligand building blocks, discrete products of different symmetry can be obtained depending on the specific assembly information stored in the subunits.

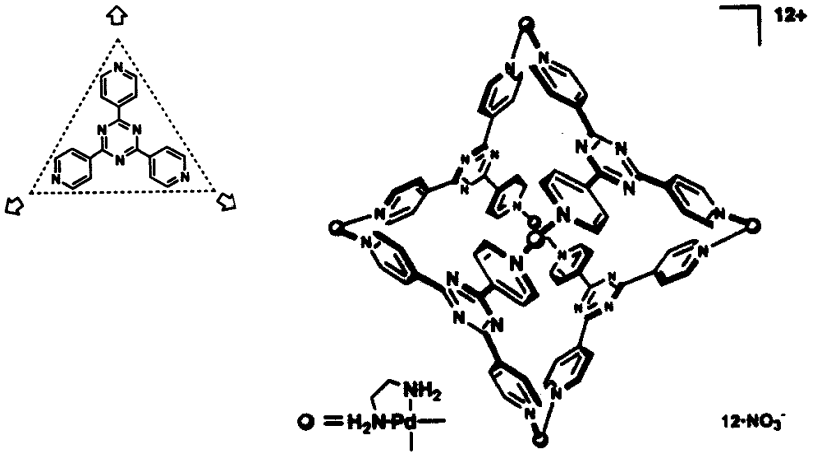
As an elegant example, Fujita and coworkers designed the *cis*-protected square-planar Pd (II) complex **8** and successfully used it as a building block in the self-assembly with different ligands to form a series of cage compounds, which had shown interesting host-guest properties. With the simple linear 4,4'-bipyridine ligand **9**, the square planar framework **10** was formed quantitatively (Scheme 1.6).[36] The molecular design was later extended to the construction of 3D structures by involving 2D building blocks. Namely, the triangular

exotridentate ligand **11** self-assembled with **8** in a 2:3 ratio to generate the M_6L_4 octahedral cage **12** in quantitative yield (Scheme 1.7).[37] Ligand **13**, which had different placement of N atoms, was used to assemble a bowl-like M_6L_4 square-pyramidal cone **14** (Scheme 1.8).[38] As another example, the exohexadentate ligand **15**, when treated with **8**, gave the $M_{18}L_6$ hexahedron **16** (Scheme 1.9).[39]



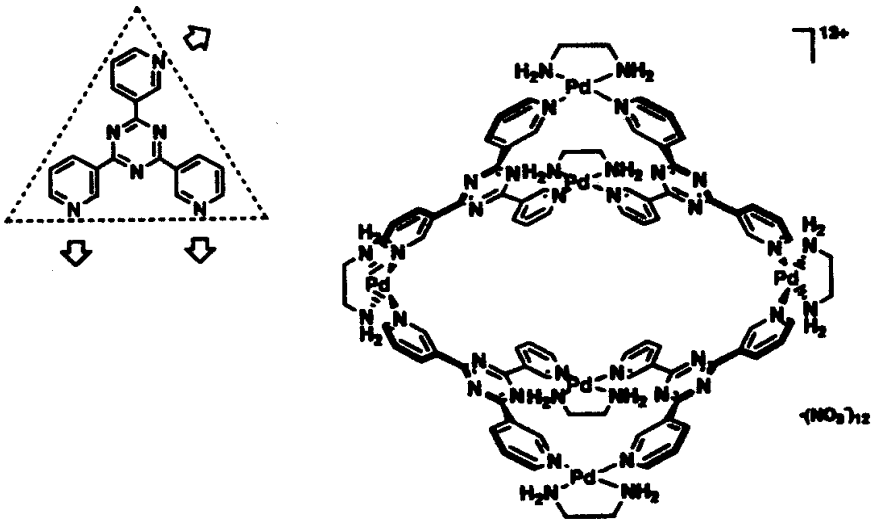
8 **9** **10**

Scheme 1.6 Self-assembly of **8** and **9** to form **10**



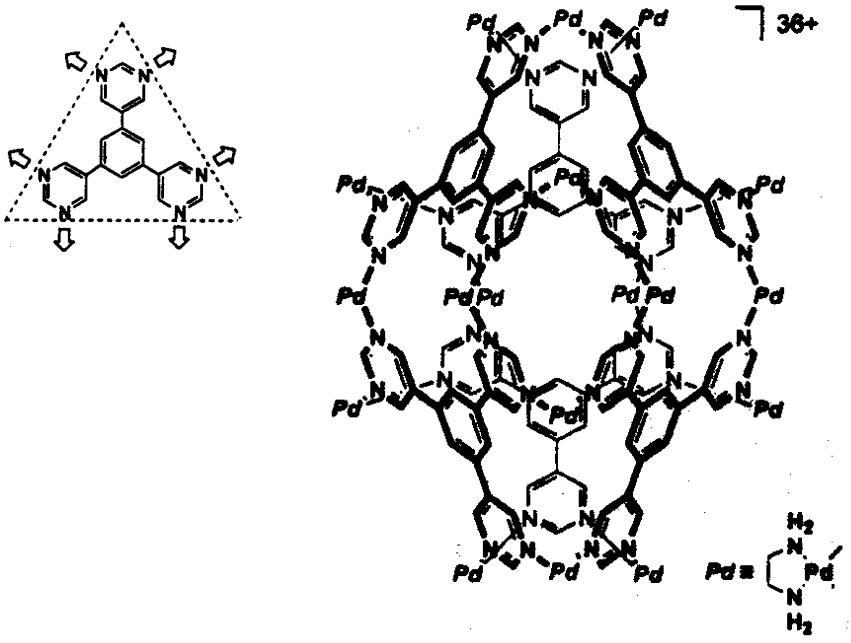
11 **12**

Scheme 1.7 Formation of an M_6L_4 octahedral cage **12**



13 **14**

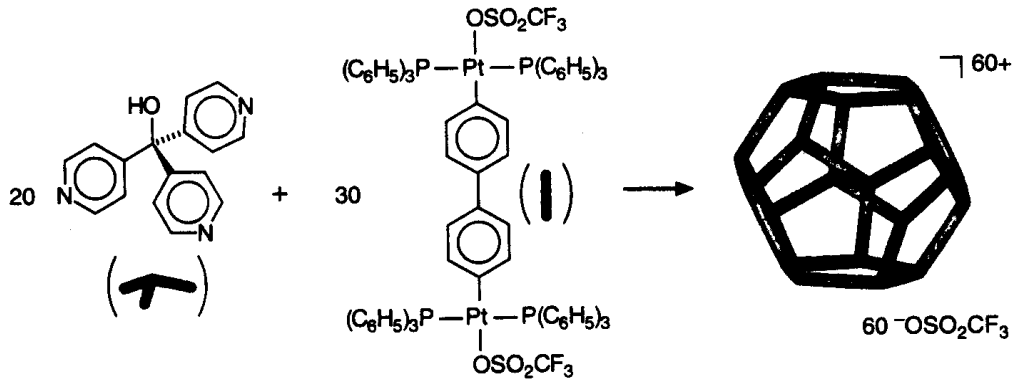
Scheme 1.8 Formation of an M_6L_4 square-pyramidal cone **14**.



15 **16**

Scheme 1.9 Formation of an $M_{18}L_6$ hexahedron **16**.

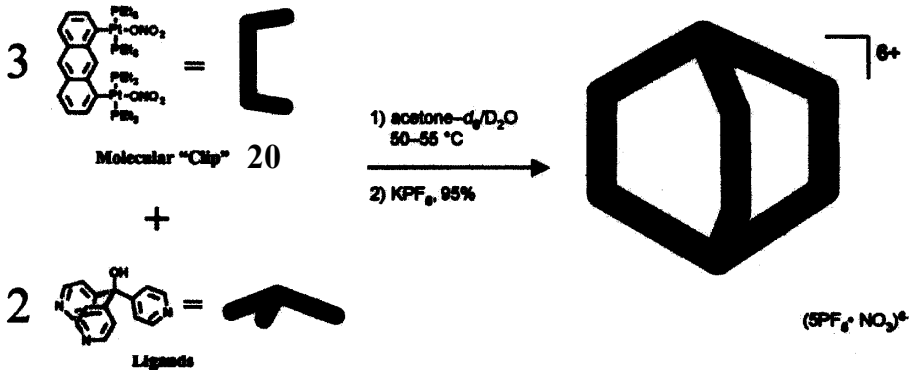
Another series of examples that showed how rational design of subunits could affect the outcome of the assembly products was given by Stang and co-workers. Tri(4'-pyridyl)methanol **17**, a tridentate molecule, served as the vertex unit, while a rod-like bidentate diplatinum complex **18** served as the edge unit. When these were dissolved in an organic solvent, metal-ligand interactions drove twenty vertex units and thirty edge units to assemble into the dodecahedral structure **20** (Scheme 1.10) in 99% yield, with a formula of $C_{2900}H_{2300}N_{60}P_{120}$-$S_{60}O_{200}F_{180}Pt_{60}$.[40,41] This represents the largest so far abiological system that has been made by self-assembly process.



17 **18** **19**

Scheme 1.10 Fifty molecules assemble to form a supramolecular dodecahedron.

With the same vertex unit **17**, but changing the edge unit to the rigid molecular "clip" **20**, a much simpler D_{3h} cage **21** is obtained (Scheme 1.11).[42]



21

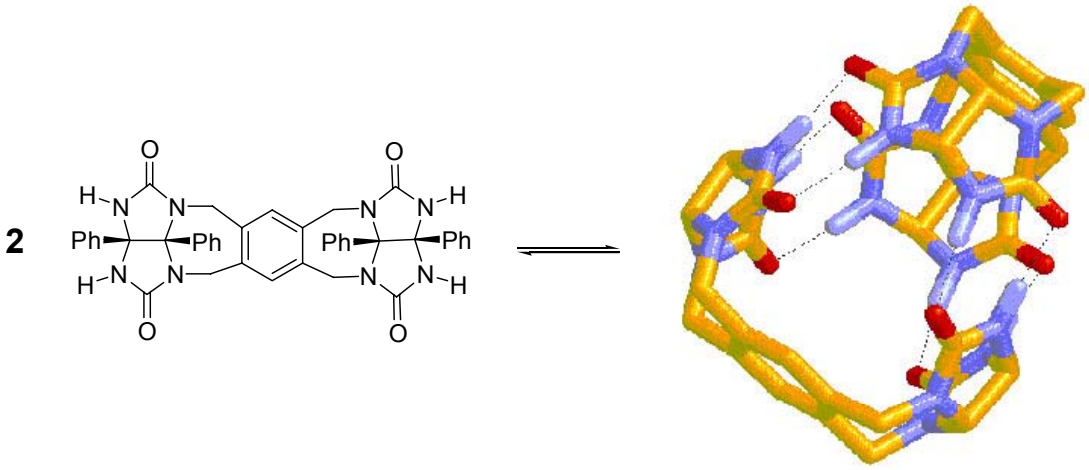
Scheme 1.11 Self-assembly of coordination D_{3h} cage **21**.

1.4.1.2 Hydrogen-Bonding Directed Self-Assembly

The second commonly used approach for self-assembly utilizes hydrogen bonding as the driving force to form the structurally ordered species.[43-46] Compared to the force involved in metal coordination interactions, hydrogen bonding is much weaker and more representative to those found in nature.

Considerable efforts in hydrogen-bonded self-assembly have focused on the design and formation of "self-assembling capsules", *i.e.*, "receptors with enclosed cavities that are formed by the reversible noncovalent interaction of two or more, not necessarily identical, subunits."[43] The aggregates so formed should have a well-defined structure in solution and be capable of binding behavior that none of its individual components displays alone.

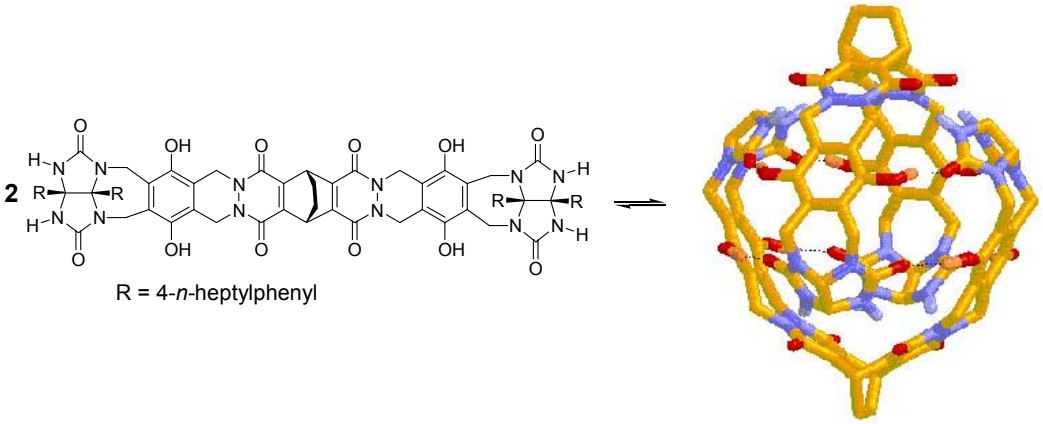
Rebek *et. al.* have utilized glycouril derivatives to form a series of self-assembling capsules that have demonstrated great potential as hosts and reaction vessels. The first studied in this series was the famous "tennis ball" (**23**).[47] The subunit **22** consisted of two diphenylglycouril units linked by a durene spacer. In both solution and the solid state, the two subunits self-assembled spontaneously to produce the tennis ball-shaped dimer, in which the two subunits were seamed together by eight hydrogen bonds (Scheme 1.12). This was supported by ^{1}H NMR spectroscopy study, mass spectrometry, vapor pressure osomometry, and X-ray crystallography analysis.[48]



22 "tennis ball" **23**

Scheme 1.12 Formation of a "Tennis Ball" **23**. (the phenyl substituents are ommited for simplicity.) Picture adapted from Professor Julius Rebek's website http://www.scripps.edu/rebek. Molecular modelers: Arash Rebek and Lubomir Sebo.

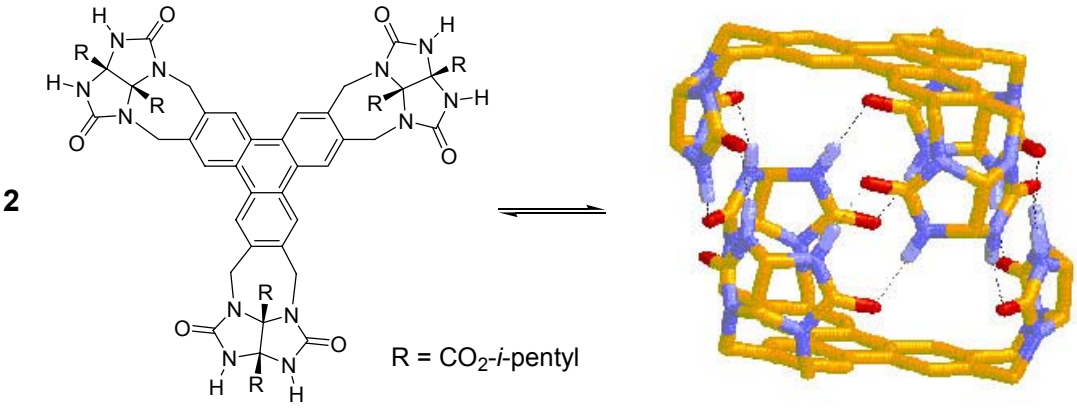
The "tennis ball" had an internal volumn of about 60 $Å^3$ and is capable of encapsulating small guest molecules such as methane or ethane.[49] In an effort to develop self-assembling capsules capable of recognizing and binding larger molecules, Rebek and co-workers further expanded the size of the spacer between the two glycouril units, while still keeping an appropriate shape to allow the dimerization to occur.[50] Thus, the much larger "softball" **25** which showed binding affinities toward larger guest molecules such as 1-adamantanecarboxylic acid and 1-ferrocenecarboxylic acid was developed. The two subunits **24** were "zippered" by a series of hydrogen bonds along the rim (Scheme 1.13).[51]



24 "softball" **25**

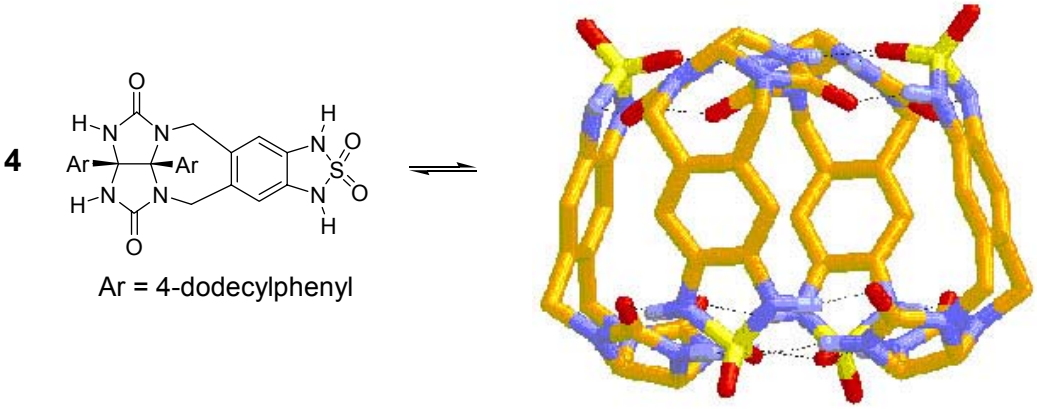
Scheme 1.13 Formation of a "softball" **25**. (R substituents are omitted for simplicity) Picture adapted from Professor Julius Rebek's website http://www.scripps.edu/rebek.
Molecular modelers: Arash Rebek and Lubomir Sebo.

Other glycouril-based hydrogen-bonded self-assembling capsules developed by Rebek's group included the "jelly-doughnut" **27**[52] assembled from tri-glycouril derived subunit **26** (Scheme 1.14) and "tetramer" **29**[53] assembled by four molecules of **28** (Scheme 1.15). A cylindrical capsule **31** has also been formed by the dimerization of tetraimide cavitand **30** (Scheme 1.16).[54]



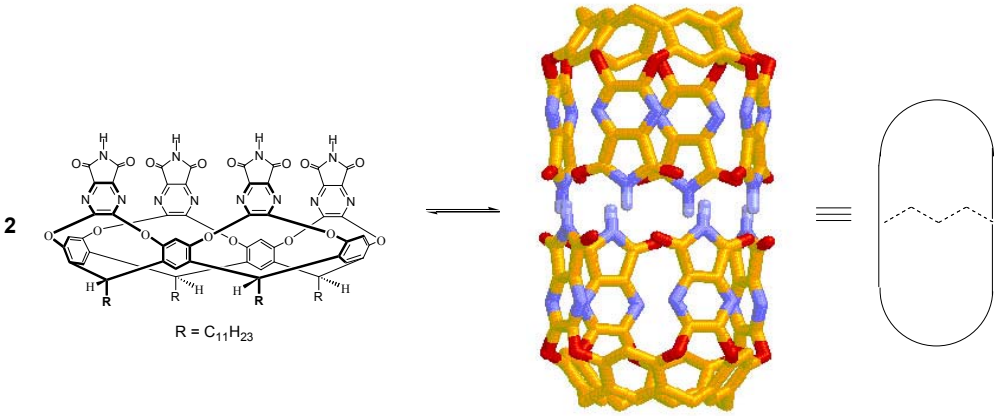
26 "jelly doughnut" **27**

Scheme 1.14 Formation of a "Jelly Doughnut" **27**.(R substituents omitted for simplicity) Picture adapted from Professor Julius Rebek's website http://www.scripps.edu/rebek.
Molecular modelers: Arash Rebek and Lubomir Sebo.



28 "tetramer" **29**

Scheme 1.15 Formation of a "Tetramer" **29**. (Ar substituents omitted for simplicity) Picture adapted from Professor Julius Rebek's website http://www.scripps.edu/rebek.
Molecular modelers: Arash Rebek and Lubomir Sebo.



30 **31**

Scheme 1.16 Formation of a cylindrical capsule **31**. (R groups omitted for simplicity) Picture adapted from Professor Julius Rebek's website http://www.scripps.edu/rebek.
Molecular modelers: Arash Rebek and Lubomir Sebo.

While Rebek's group uses hydrogen-bonded self-assembly to form discrete structured species, others are using this methodology to form essentially infinite lattices.[45,55,56] However, due to the difficulty of analysis, the latter is far less investigated than the former, and none of them has yet been used as receptors.

Organic tubular assemblies are of interest due to their numerous applications such as transmembrane ion channels and closed reaction chambers.[45] In 1993, Ghadiri and co-workers generated peptide nanotubes by the stacking of D,L-octapeptide rings (Figure 1.4).[55] The hydrogen bonds driving the formation of the assembly products were perpendicular to the plane of individual ring, as in a β-sheet. All the amino acid side shains (R groups) lied on the outer surface of

the tube. The peptide nanotube was obtained as microcrystalline aggregates that was examined by electron microscopy, electron diffraction, FT-IR spectroscopy, and crystal modeling. The van der Waals internal diameter is approximately 7 Å. The size of the nanotube could be controlled by varying the size of peptide rings. A dodecapeptide was shown to undergo an assembly in a similar manner, and the resulting micro-crystalline aggregates displayed an expanded van der Waals internal diameter of 13Å.[56]

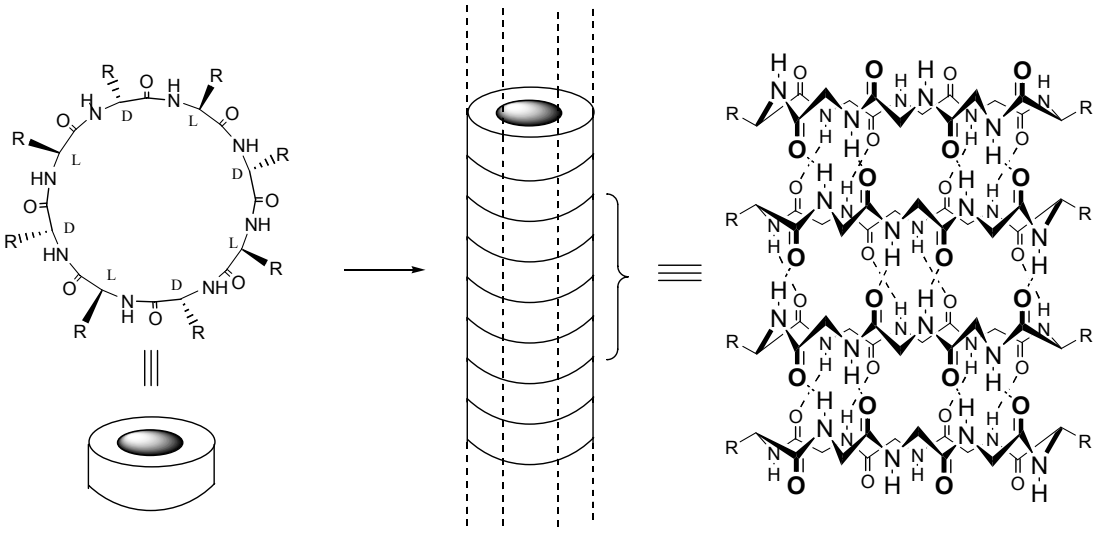
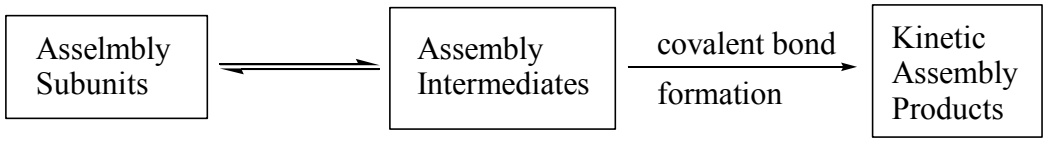


Figure 1.4. Schematic diagram of peptide nanotube formation from cyclic D,L-peptides. For clarity, most of the peptide side-chains have been omitted.

1.4.2 Self-assembly with covalent modification

In contrast to strict self-assembly, self-assembly with covalent modification involves a post-assembly covalent bond formation process (Scheme 1.17). This type of self-assembly generates products that are not necessarily the

thermodynamically minimum. Since the irreversible covalent bonds formation is an essential part of the self-assembly process, kinetic products are isolated. Self-assembly with covalent modification is a relatively poorly investigated area, primarily because of the lower efficiency of kinetic assemblies and the lack of knowledge to control kinetic self-assembly. The syntheses of catananes/rotaxanes[57-59] and carceplexes[60,61] are prominent examples in this area.



Scheme 1.17 Cartoon representation of self-assembly with covalent modification.

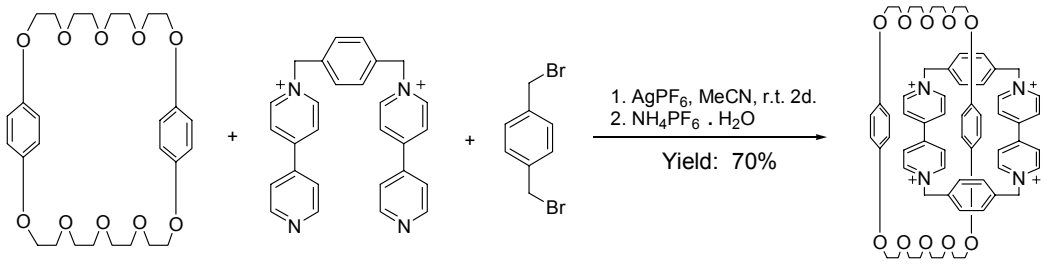
1.4.2.1 Catenanes and Rotaxanes

As illustrated by the cartoon below (Figure 1.5), a catenane is a compound consisting of two or more rings that are interlocked mechanically, while a rotaxane consists of a long, fairly linear molecule threaded through a macrocyclic ring. Generally, the rings or the chain cannot be separated without breaking a chemical bond.

Catananes Rotaxanes

Figure 1.5 Cartoon representation of catenanes and rotaxanes.

The discovery of catenanes and rotaxanes relied on the very small chance that a linear precursor threaded through a macrocyclic component may cyclize (to form a catenane) or "stoppered" by other bulky components (to form a rotaxane). It naturally resulted in extremely low yields. To improve yields, one strategy was to promote the threading (association) of the reactants by non-covalent forces, followed by the covalent bonds formation to cyclize or stopper the threading. Scheme 1.18 illustrates one example to synthesize [2]catenane **35**.[62] Thus, the electron-rich bis-paraphenylene-34-crown-10 **32** acted as a template to direct the threading of the electron-deficient bis-paraquat **33**, which is then cyclized with α,α'-dibromo-*p*-xylene **34**. The [2]catenane **35** was prepared at 70% yield. This tetracationic catenane was stabilized by π-π stacking and charge-transfer interactions between the aryl rings, the solvation of the positive charge by the crown oxygen atoms, and the C—H···O hydrogen bonds from the relatively acidic aryl C-H proton to the crown oxygen atoms.[63,64] Similar to this strategy, a common feature of the vast majority of catenane and rotaxane syntheses is the kinetically controlled final post-assembly modification step.



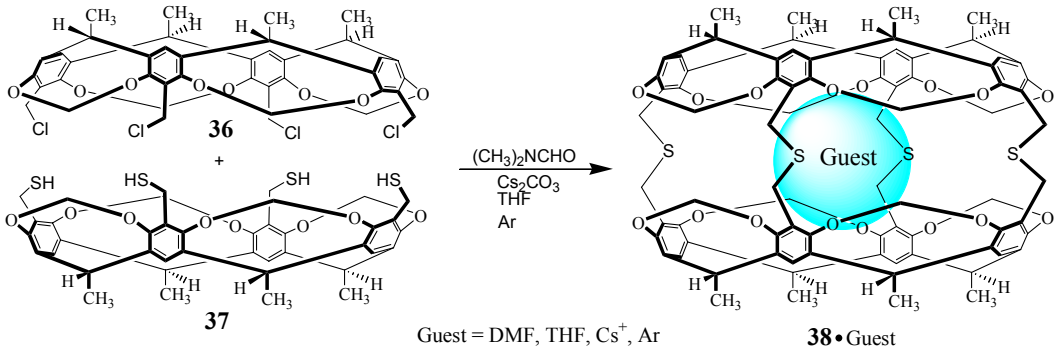
32 **33** **34** **35**

Scheme 1.18 Formation of [2]catenane **35** by the assembly of a bis-paraquat moiety **33** and bis-paraphenylene 34-crown-10 **32**.

1.4.2.2 Carceplexes

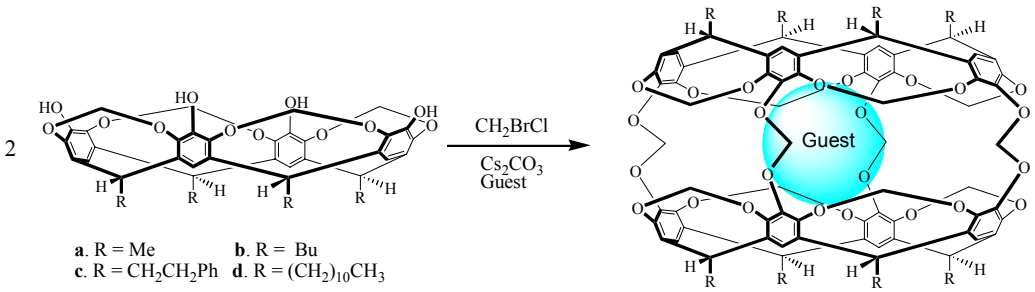
In 1983, Cram introduced the concept of a "carcerand", which is defined as a "closed-surface, global-shaped molecule with an enforced internal cavity within which small molecules, ion, or both could be incarcerated."[61] Carcerands with permanent imprisoned guests are called "carceplexes".

The first carceplex was reported by Cram's group in 1985.[65,66] This was achieved by the coupling of two bowl-shaped cavitands (defined as "macrocyclic molecules with an enforced cavity"[61]) **36** and **37** to form the closed capsule molecule **38** (Scheme 1.19). It was found that the carcerand encapsulated almost every small-sized species in the reaction solution. Hence, MS analysis revealed the presence of carceplexes containing solvent molecules (DMF and THF), Cs^+ from the base used, and the noble gas Ar under which the reaction was conducted.



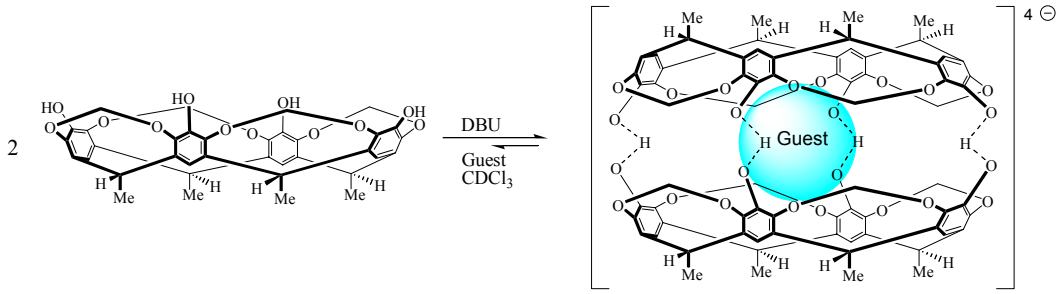
Scheme 1.19 The first synthesis of carceplex **38** by Cram, *et. al*.

An even more remarkable success in carceplex formation was achieved by Sherman *et. al*.[67-71] For example, the acetal-bridged carceplexes **40** were prepared in excellent yields (up to 87%) from tetrol **39** by bridging the two bowls with bromochloromethane in the presence of a suitable guest (Scheme 1.20). The presence of a suitable guest in the reaction mixture was critical in the formation of the desired carceplex. It was elucidated that the guest molecule acted as a template in the formation of the carcerand and ultimately, it was trapped inside the cavity.[71]



Scheme 1.20 Formation of a tetra acetal-bridged carceplex **40**·Guest.

So, what makes this process so efficient? What is the driving force behind it? Further study by Sherman's group revealed that an important intermediate was the novel ternary complex **41**·Guest (Scheme 1.21).[72-74] Formation of this complex was driven by the formation of charged hydrogen bonds between the two cavitands and the maximum possible favorable van der Waals interactions between the forming host's cavity and the guest molecule. The self-assembled structure is well preorganized for the subsequent bridging by bromochloromethane.

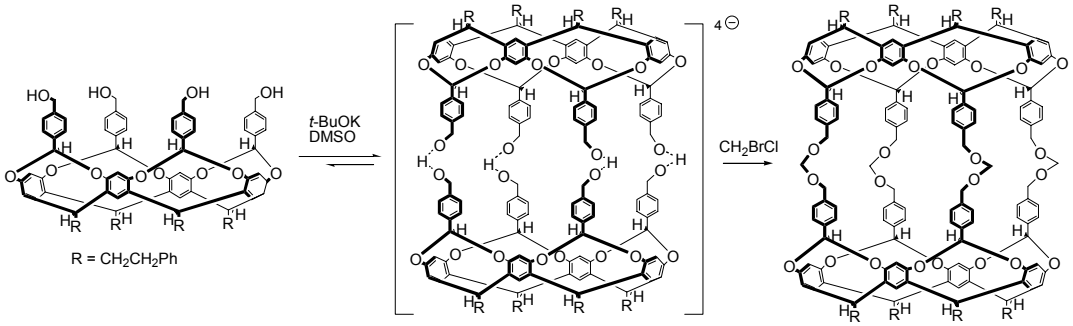


39 **41**·Guest

Scheme 1.21 Two tetrol bowls self-assemble into charged hydrogen-bonded complex **41**·Guest.

More recently, Gibb *et. al*. reported the synthesis of novel hemicarcerand **44** with an extended internal cavity (Scheme 1.22).[75] In contrast to Sherman's carce-plex formation, this process did not involve an apparent (single) template. As a possible explanation, they suggested an efficient self-assembly of **35** through charged hydrogen bonds (CHBs) between the poorly acidic benzyl alcohol groups

and their conjugated bases. Such CHBs were stronger than those in **41**. The resulting dimeric species **43** was then bridged by CH_2BrCl to form **44** in a remarkable 80% yield. This was an excellent example of self-assembly with covalent modifications.



42 **43** **44**

Scheme 1.22 Formation of hemicarcerand **44** from DCC **42**.

1.5 Templation

Stoddart's [2]catenane **35** and Sherman's carceplex **40** are just two examples of classical template effect being used in organic synthesis. Template-controlled reactions allow the synthesis of complex molecules which could hardly been achievable through classic methods.[76] Located at the borderline between supramolecular chemistry and molecular chemistry, templation has become an important research area in recent years.

The term "template" originated from mediaeval craftsmen. They used templates, usually full-scale patterns or molds, to cut stones, molding plasters, or

building archways. Figure 1.6 shows an example of using template to build a stone arch. The template (in black) is used to hold the stone blocks in place while they are cemented together; the template is removed from the finished archway to leave the free-standing structure.

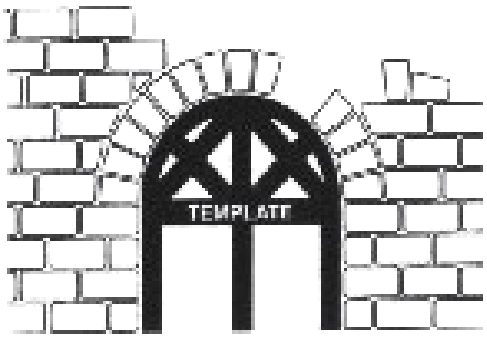
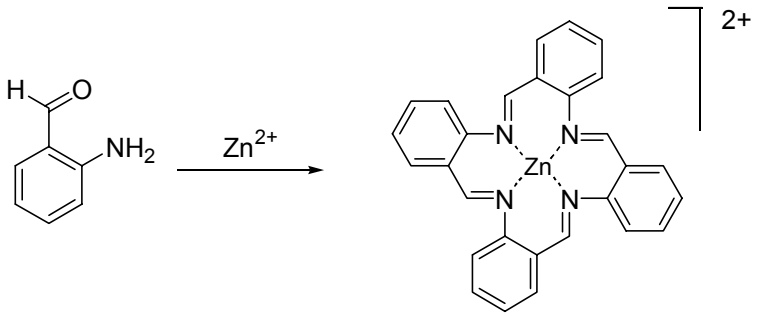


Figure 1.6 Template used in building archways. (reproduced from "*Templated Organic Synthesis*" Diederich, F.; Stang, P.J. *Ed*. **2000**, Wiley-VCH)

Down at the molecular level, template effects are ubiquitous in nature. DNA is a template for RNA, which is in turn a template for protein synthesis. Inspired by the application of molecular templates in biochemistry, synthetic chemists have made tremendous efforts in utilizing template effects to construct complex molecules. As early as in 1926, Seidel reacted 2-aminobenzaldehyde **45** with anhydrous $ZnCl_2$ (Scheme 1.23), but did not recognize that he had prepared the macrocycle **46**.[77] It was not until 40 years later that Busch and co-workers elucidated the structure of the product and investigated how metal cations templated its formation.[78,79]



45 **46**

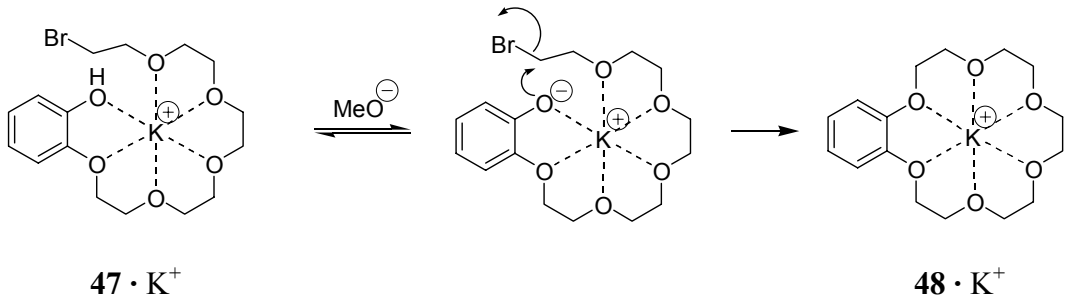
Scheme 1.23 Condensation of 2-aminobenzaldehyde in the presence of zinc (II) chloride leads to the tetrameric macrocycle **46**.

So what do we mean by "template" in a chemical sense? Busch gave a very general definition of a template as "a chemical template organizes an assembly of atoms with respect to one or more geometric *loci*, in order to achieve a particular linking of atoms."[80,81] A template organizes an assembly of atoms in a specific spatial arrangement and favors the formation of a single product where the possibility of forming more than one theoretically exists. Templates can be classified as non-covalent and covalent according to the strength of the template-substrate interaction.[76]

1.5.1 Non-covalent tempation

Most classical templates bind non-covalently to their substrate, and assist in the formation of covalent bond. One celebrated example is the synthesis of crown ethers. Crown ethers were first synthesized by Pederson in 1967. In his seminal publication,[82] Pederson reported the synthesis and metal ion complex-ation properties of a large number of macrocyclic polyethers. The unusual ligation

properties of crown ethers stimulated great interest in the scientific community. Great efforts have been made to improve the yields of crown ethers. Mandolini and co-workers have made a detailed study of the influence of alkali and alkaline earth metal cations on the cyclization of 2-hydroxyphenyl-3.6.9.12-tetraoxa-14-bromotetradecyl ether **47** in methanol and dimethylsulfoxide.[83-85] It was found that when potassium ion was used as the template, the formation of benzo-18-crown-6 **48** was 1500 times more efficient than the non-templated process. It is clear that the potassium ion pre-organizes the linear backbone in a position favorable for the nucleophilic attack to occur (Scheme 1.24).

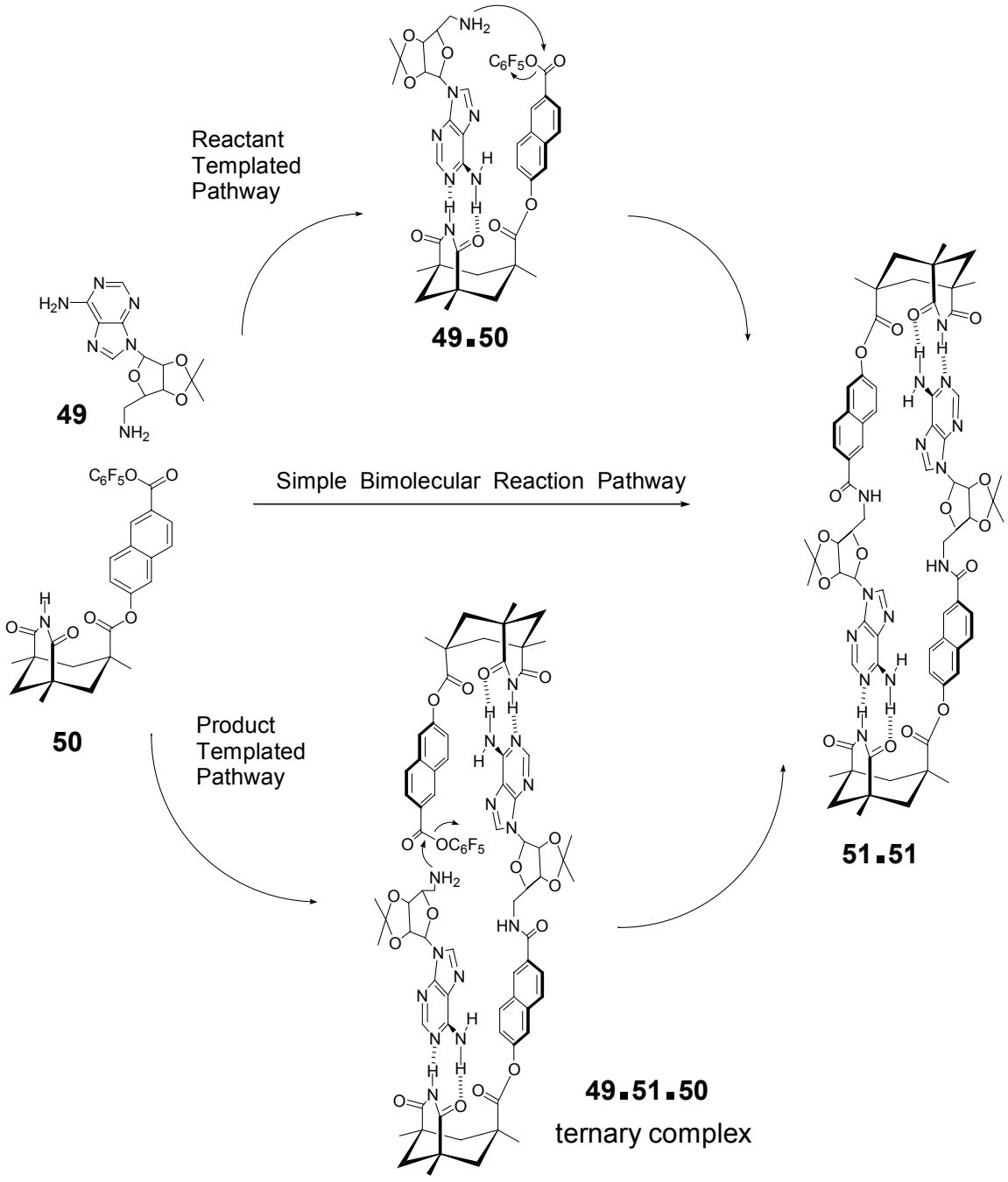


47 · K^+ **48** · K^+

Scheme 1.24 Potassium ion template directed formation of benzo[18]crown-6.

The power of templation can be further demonstrated by Rebek's self-replication system outlined in Scheme 1.25.[86-90] Molecule **49** and **50** could bind *via* double N—H···O hydrogen bonds to form the bimolecular complex **49·50**. This brought the reacting groups into close proximity, hence the product **51** could be generated through this reagent templated pathway. Once **51** was formed, it itself could serve as a linear template to bind **49** and **50** to form the **49·51·50**

ternary complex. Reaction between the template bound substrates was favored over reaction in free solution, to yield the dimerized template **51·51**. Dissociation of this complex released two template molecules for further reactions. The reaction was autocatalytic; seeding the reaction with its product leads to a rate enhancement.

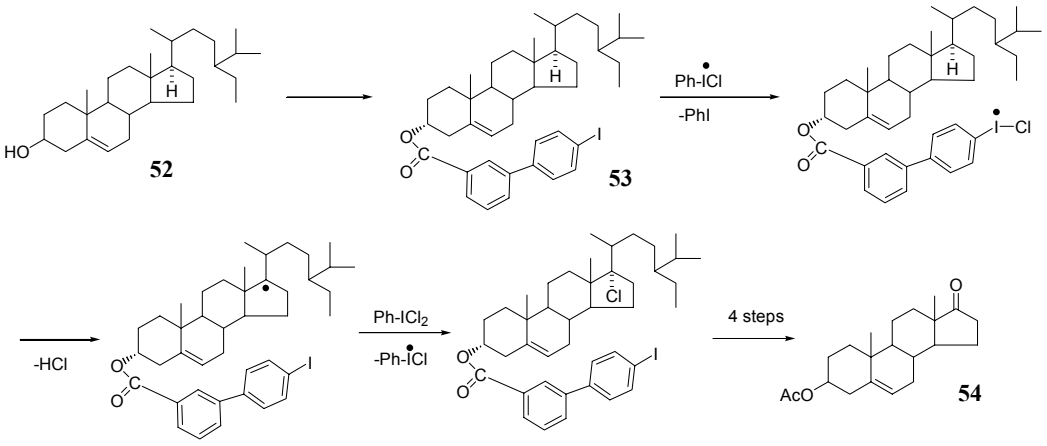


Scheme 1.25 Self-replicating system designed by Rebek and co-workers.

1.5.2 Covalent Templation

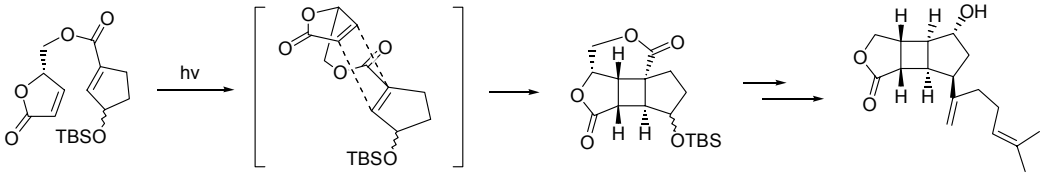
Covalent templates promote the desired reaction of a substrate by temporarily joining the substrate to a template. The template is then removed to release the desired product.

Breslow and co-workers have utilized covalent templated methods to perform a variety of biomemetic controlled reactions, mimicking enzyme-catalyzed processes.[91-95] One example was the template controlled synthesis of androsterone acetate **54** from readily available sitosterol **52** *via* a radical-relay process.[96,97] As shown in Scheme 1.26, a biphenyl derived template was added to the alcohol group on **52**. It was then treated under standard "radical-relay" conditions. The suitable length of the template ensured the selective chlorination on C-17. A short sequence of further chemical steps completed the side-chain removal to produce **54** in good yield. Without the aid of a suitable template, chlorination at this specific position was very difficult to obtain.



Scheme 1.26 Radical-relay chlorination under template control.

Covalent template strategy has also been shown to affect the regio- and stereochemical outcome in cycloaddition reactions. In the first asymmetric synthesis of stoechospermol **57**, Koga and co-workers utilized this strategy to control the absolute stereochemical outcome of the key [2+2] photocycloaddition, which installed the correct stereochemistry at the two ring junction (Scheme 1.27).[98] The ester precursor **55** was readily achieved as a 1:1 mixture of diastereoisomers. Upon irradiation, it afforded 1:1 mixture of cyclobutanes **56** differing only in the stereochemistry of the siloxy substituent. Subsequent manipulation afforded the desired stoechospermol **57**. Therefore, the temporary connection of the two cyclization precursors had controlled both the regio- and stereoselectivity of the cycloaddition event.



55 **56** **57**

Scheme 1.27 Template-controlled [2+2] cycloaddition in Koga's synthesis of Stoechospermol **57**.

1.6 Host-Guest Chemistry

Supramolecular chemistry deals with the interactions between molecules. Put in another way, it involves some kind of (non-covalent) binding or complexation event. The term "host-guest chemistry" was introduced by Cram in 1970's to

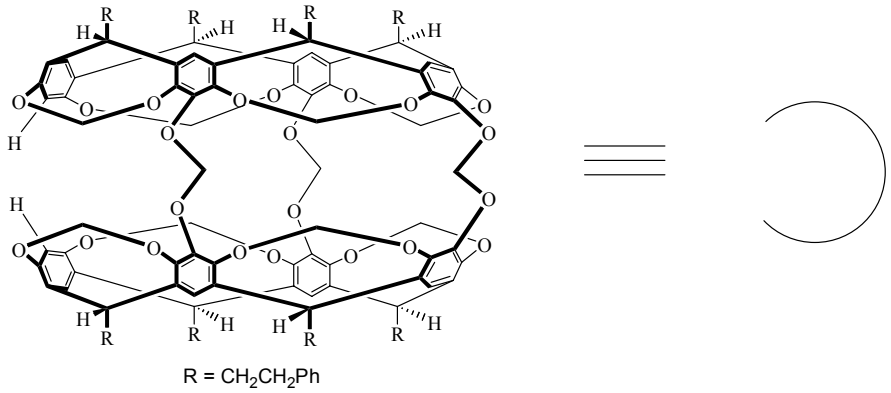
describe this type of events.[99-101] One molecule (a 'host') binds another molecule (a 'guest') to produce a 'host-guest' complex. Formally, a host is defined as a molecular entity possessing convergent binding sites, and a guest is a molecular or ionic entity possessing divergent binding sites.[99-101] Commonly a host is a large molecule or aggregate such as enzyme or synthetic cyclic compound possessing a sizable, central hole or cavity; a guest may be a monoatomic species, or a more sophiscated molecule such as hormone, pheromone or neuro-transmitter.[102] The forces that drive the binding between host and guest could be ion-ion interac-tions, ion-dipole interactions, dipole-dipole interactions, hydrogen bonding, cation-π interactions, π-π stacking, van der Waals forces, hydrophobic effects, or combinations of these interactions.

Pederson's study on metal and crown ether complexation represents one of the earliest host-guest systems studied.[82] Sherman's carceplex formation is another well-studied host-guest system.[67,68,70,71] In this system, the guest molecule acts as a template to promote the assembly of the host molecule, and is itself trapped inside the host during the synthesis. In this case, the incarcerated guest is rather a "prisoner". To date, many host-guest complex systems have been designed and studied in detail. Many work in this area have demonstrated the capability of host molecules to stabilize short-lived reactive intermediates and direct reactions inside the cavity of hosts.

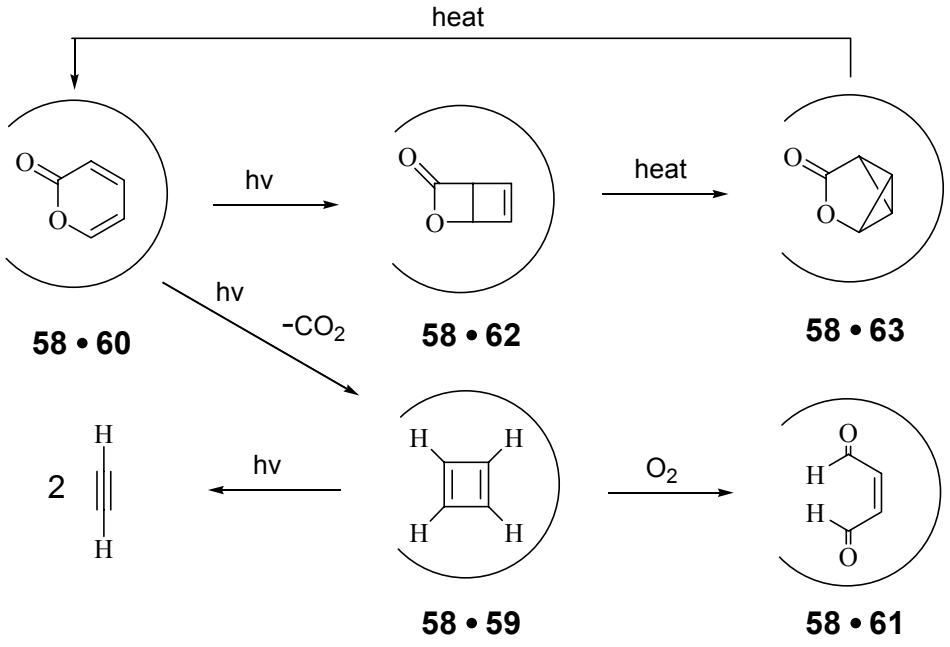
1.6.1 Stabilization of Reactive Intermediates

One ingenious application of host-guest chemistry is the stablization of short-lived reaction intermediates as guests, protected from destruction by the constrictive binding of the surrounding host.

Cram *et. al*. first stabilized the highly reactive cyclobutadiene **59** inside a hemicarcerand **58**, the "Mona Lisa of Organic Chemistry" (Scheme 1.28).[103] They generated **59** photochemically from α-pyrone **60** inside the host **58**. Prior to this inner-phase isolation, cyclobutadiene had been made and studied only in cryogenic matrixes below 8 K.[104] However, the inner-phase stabilized cyclobutadiene was stable up to 60ºC in the absence of oxygen. When a solution of **58·59** is oxygenated, inner-phase maleic aldehyde **61** was produced. Prolonged photolysis split incarcerated **59** into two acetylene molecules, which escaped into the bulk phase. A reaction cycle of reactive intermediates was completed inside the inner phase of the host: photolysis at 300 nm convert **58·60** into photopyrone **58·62**, which rearranged at 90ºC to **58·63**. Upon heating **58·63** reverted quantitatively to **58·60**.

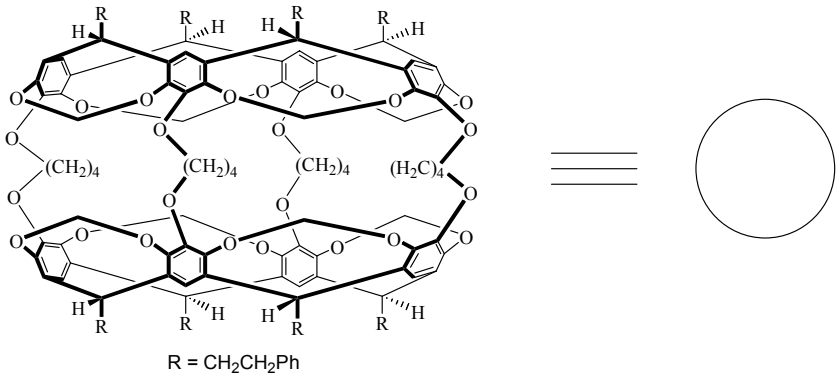


58

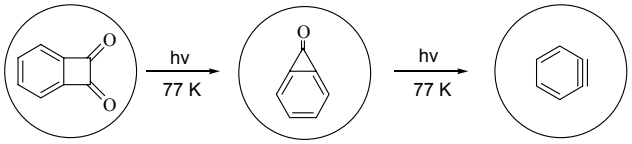


Scheme 1.28 Photochemical generation of cyclobutadiene.

Recently, Warmuth reported the isolation of hemicarceplex **64**·*o*-benzyne, albeit at -75ºC (Scheme 1.29).[105] Heating empty host **64** in molten benzocyclobutenedione **65** provided the corresponding hemicarceplex **64·65** (30-35%);



64

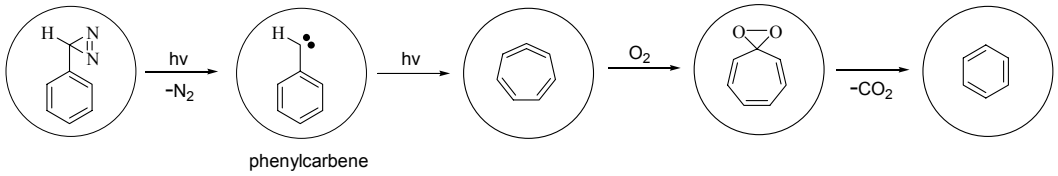


64·65 **64·66** **64·***o*-benzyne

Scheme 1.29 *o*-benzyne stabilized by hemicarcerand host **64**.

subsequent photolysis in $CDCl_3$ at 77K furnished the benzocyclopropenone complex **64·66**. Further irradiation (280 nm) in THF-d_8 at 77K provided **58·***o*-benzyne. Evidence for the formation of this complex came from ^{1}H and ^{13}C NMR at -75ºC and -98ºC respectively. Warmuth had also demonstrated the stabilization of highly strained cycloheptatetraene **67** by incarceration in **64**.[106,107] Scheme 1.30 summerizes the formations carried out within the cavity of **64**. Photolysis of **64·**phenyldiazirine lead to **64·67** *via* a photochemical phenylcarbene rearrangement. Although free **67** had fleeting existence in solution, **64·67** was stable at 60ºC in the absence of oxygen. Surprisingly, incarcerated **67** did not

react with bulk phase water or methanol, despite their ability to enter the inner phase through a portal in the host shell. Very unexpected was the quantitative formation of **64**·benzene if **64·67** was exposed to oxygen. Low temperature NMR studies uncovered the formation of intermediate dioxirane **68**, which decarboxylates after a cycloheptetriene-norcaradiene shift.



64·phenyldiazirine **64·67** **64·68**

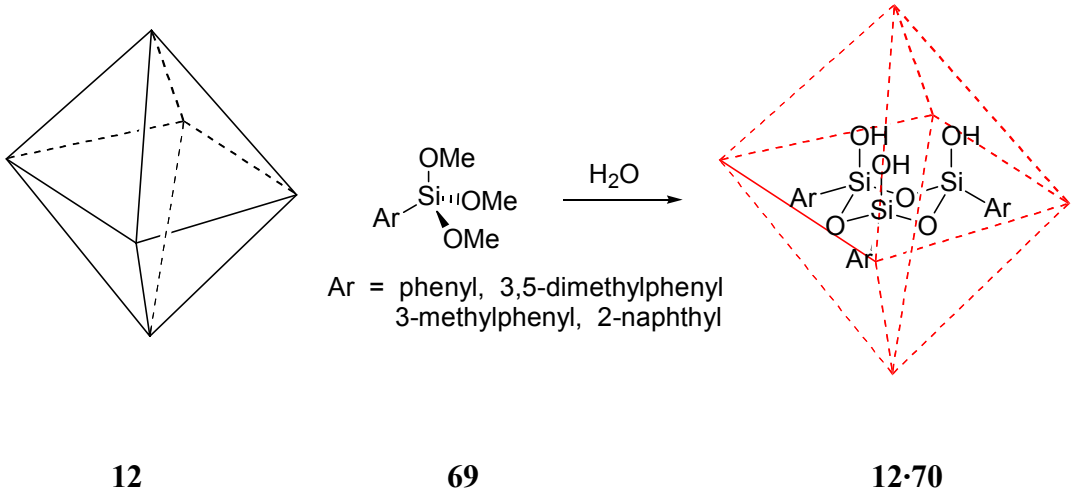
Scheme 1.30 Inner-phase phenylcarbene rearrangement inside hemicarcerand **56**.

1.6.2 Promotion of Reactions Inside Hosts

Encapsulation complexes have been used to accelerate, even catalyze, chemical reactions within their cavities.

The polycondensation of alkoxysilanes is a well-known method for the low-temperature fabification of silica-based materials (so-called sol-gel condensation).[108-110] However, the regulation of the degree of oligomerization, especially at an early stage of the process, is very difficult because of rapid condensation leading to siloxane networks. However, Fujita and co-workers demonstrated that in the presence of octahedral cage **12** (discussed in section **1.4.1.1**), the process was halted after the formation of cyclic trimer **69** within the cavity of the capsule.[111-113] Thus, arylthrimethoxysilanes **69** was suspended in an

aqueous solution of **12** (for structure see page 41) and the mixture was stirred at 100ºC for 5 hours. The **12·70** complex was obtained at 90% yield (Scheme 1.31).

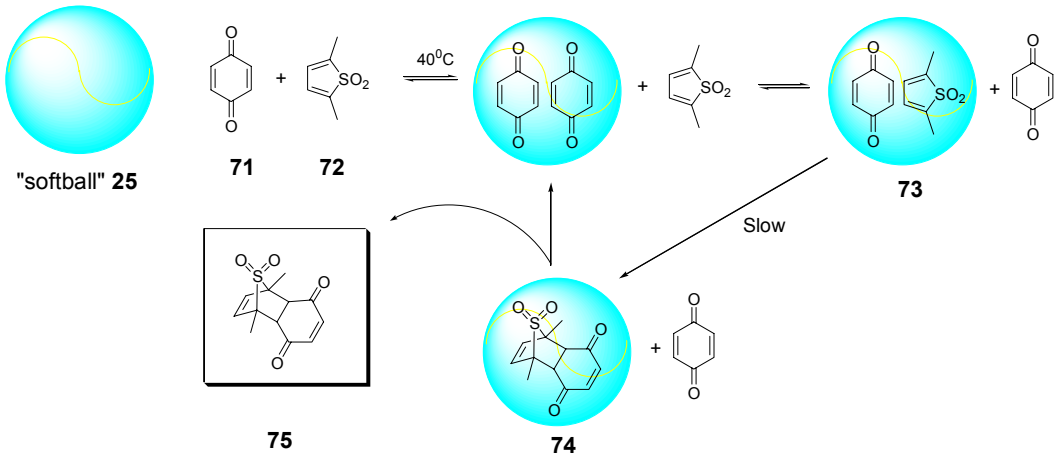


12 **69** **12·70**

Scheme 1.31 Cavity-directed synthesis of cyclic silanol trimer **70**.

Rebek's group has been successful in utilizing the glycouril-based "softball" **25** (discussed in section **1.4.1.2**) as a reaction vessel and catalyst to promote cycloaddition reaction between *p*-benzoquinone **71** and thiophene dioxide derivative **72**.[114-116] In their experiments, the solution of **72** (10 mM) and **71** (10 mM) in *p*-xylene-d_{10} was added to a "softball" solution (1 mM). The reaction was monitored by NMR and showed 55% conversion after two days and 75% conversion after 4 days. In the absence of the "softball", only 10% and 17% conversions were obtained respectively. The catalytical cycle is shown in Scheme 1.32. In a mixture of **71**, **72** and "softball" **25**, the resting state of the capsule contains two benzoquinone, one of which is occasionally displaced by the

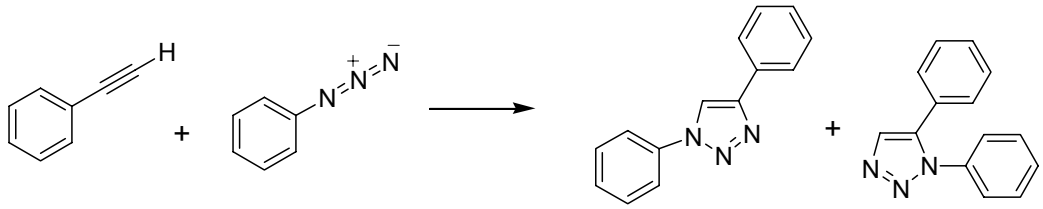
thiophene dioxide to give the fully loaded "Michaelis" complex **73**.[117] A moderate enhanced cycloaddition ensues, followed by the displacement of the adduct **74** by two molecules of **71**, which released the desired product **75** and regenerate the catalyst. The exchange of the different encapsulated species in and out of the "softball" is fast compared to the chemical step, the formation of **74**.



Scheme 1.32 Catalytical cycle of cycloaddition of **71** and **72** with a "softball" **25** as catalyst.

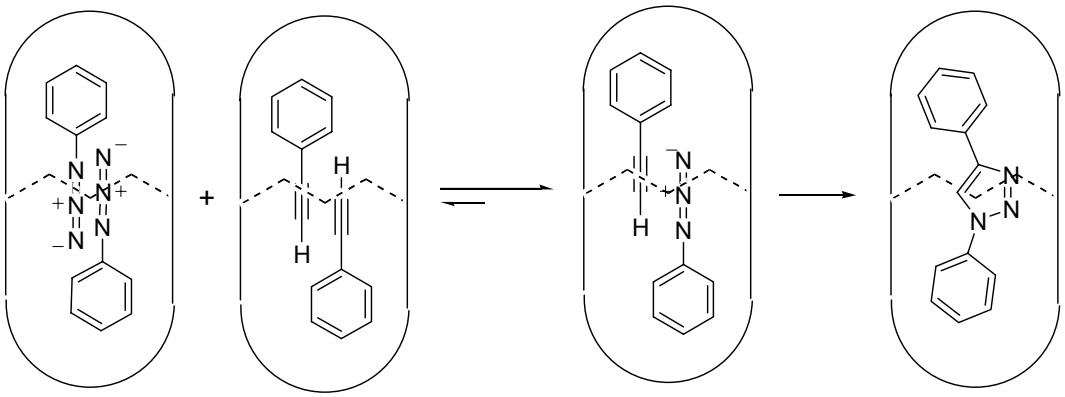
In a related ongoing research from the Rebek group, it has also been shown that host **31** (for structure see page 21) could be used to control the absolute regioselectivity of cycloaddition reactants. Thus, the cylindrical capsule **31** has been used as a reaction vessel to control the outcome of the products of the cycloaddition between phenylacety-lene **76** and phenyl azide **77** (Scheme 1.33).[117] In free solution, these two compounds react very slowly (corresponds to a half-

life of several years at 1 M) to give roughly equal amounts of two regioisomeric triazoles **78** and **79**. However, in the presence of 5 mM of the cylindrical host, a solution of **76** (50 mM) and **77** (25 mM) shows the encapsulated product within a few days. Isomer **78** is the only product observed, and is liberated upon addition of dimethylformamide. NMR studies has shown that the "Michaelis complex" **80** (Scheme 1.34) is the most abundant species in solution. It is this complex that accelerates the rate of the reaction and defines **78** as the only product.



76 **77** **78** **79**

Scheme 1.33 The reaction of **76** and **77** gives comparable amounts of the two regioisomers.



80

Scheme 1.34 The disproportionation equilibria of encapsulated reactants.

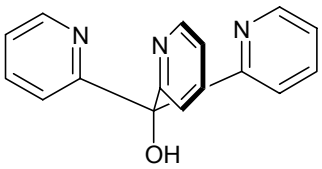
II. NOVEL LIGANDS FOR CARBONIC ANHYDRASE MIMICRY

The successful modeling of the active site of carbonic anhydrase (CA) relies on a combination of a highly Lewis acidic metal ion, and sufficient steric bulk to prevent the deleterious formation of $[ML_2]$ sandwich complexes (Scheme 2.1).

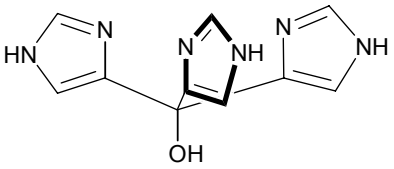
$$M^{n+} + 2L \rightarrow [M^{n+}L_2]$$

Scheme 2.1 ML_2 sandwich complex formation.

In considering ligands candidates to mimic carbonic anhydrase (CA), three specific criteria were taken into account. First, to closely replicate the zinc binding site of CA, the ligands should consist of three sp^2 hybridized nitrogen donors in a trigonal planar array. Second, the ligands should share a common functionality that allows the construction of a bulky hydrophobic environment around the proposed active site. Finally, the ligands should be sufficiently robust to allow full evaluation of their physicochemical properties.

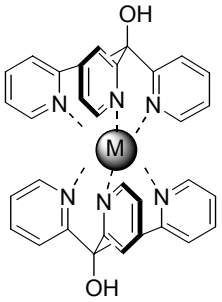


81

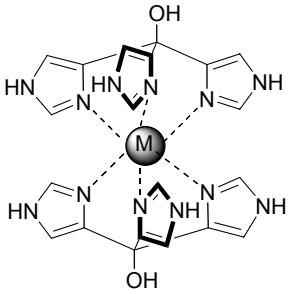


82

Ligands **81** and **82** closely replicate the three imidazole groups in CA, however, without the steric bulk, they have a stong tendency to form catalytically inactive sandwich [ML_2] complexes (Figure 2.1).[118-122]



M•(81)$_2$



M•(82)$_2$

Figure 2.1 ML_2 complexes **M•(81)$_2$** and **M•(82)$_2$**.

Although **82** mimics the actual CA active site more closely, ligands trispyridylmethanol **81** system was chosen to serve as CA mimic, primarily due to complications arising from the possibility of the sp^3 nitrogen atoms of **82** participating in the metal binding.

Tris(2-pyridyl)methanol **81** was first reported in 1951 by Wibaut and co-workers as an analogue to triphenylmethanol.[123] Later, Brown and co-workers indicated the potential use of **81** as a model for the enzyme carbonic anhydrase.[124] To minimize the formation of aforementioned ML_2 complex, a natural thought is the addition of sufficient bulky groups on the pyridine rings. However, work relating to the synthesis of substituted tris-pyridyl methanol ligand derivatives is rare.[120,125,126] It is noteworthy that, recently, Hannon *et. al*. have demonstrated an elegant approach in tailoring the hydrophobic environment around tris-(2-pyridyl) methanol ligands by attching them to dendimeric clefts (Figure 2.2).[127] The resulting ligand efficiently forms the $[Zn^{II}L]$ species by eliminating the sandwich complex formation process.

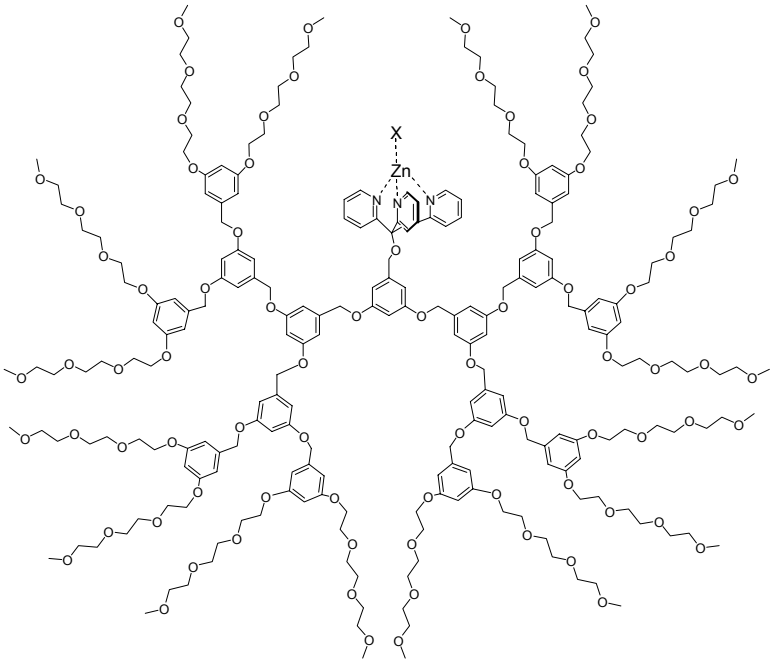
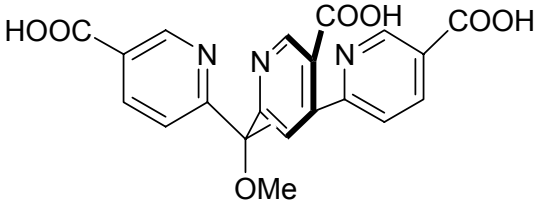
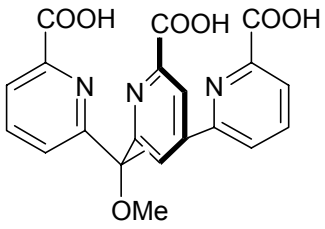


Figure 2.2 A dendritic structure containing a designed cleft to control the ligand coordination behavior.

Efforts from this laboratory towards the CA mimicry have been based on the synthesis of trisnicotinic acid and trispicolinic acid ligands **83** and **84**.[128] It was anticipated that by attaching bulky amino acids or peptide chains to the acid groups with the aid of standard peptide coupling technologies, hydrophobic pockets which isolated the active site from the surrounding environment could be created; a key factor in mimicking CA functionality. Substituting on the 5- or 6-position on the pyridine rings would vary the micro-environment of the pockets significantly. Also, attaching different fragments onto the three sites of the ligands, would provide ready access to a range of chiral ligands which will engender structure-activity information pertinent to both CA and metallo enzyme mimics in general.



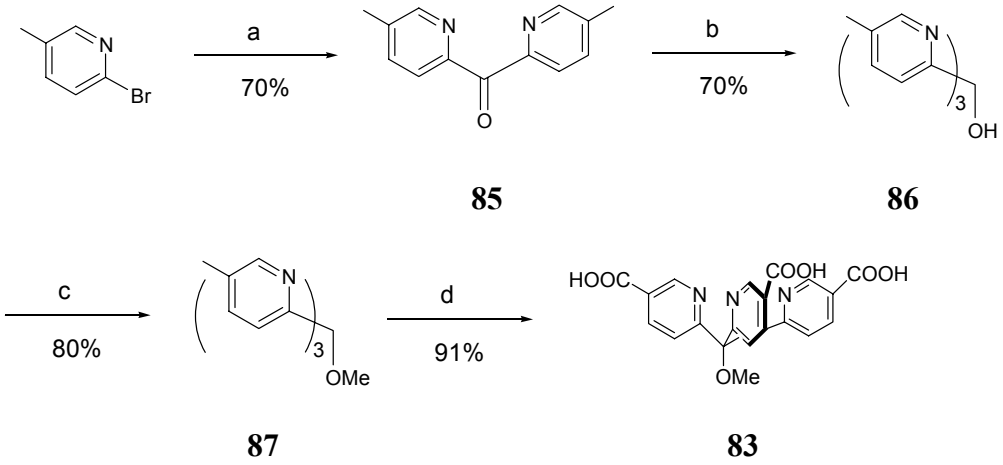
83



84

2.1 Trisnicotinic Acid Ligand 83[¶]

The synthesis of trisnicotinic acid ligand **83** started with the commercially available 2-bromo-5-methyl pyridine (Scheme 2.2). Formation of the corresponding lithiate *via* metal-halogen exchange with *n*-BuLi followed by the slow addition of diethyl carbonate gave the expected ketone **85** in 70% yield. Compound **85** was then treated with the aforementioned litiate to generate the trisnicotine ligand **86**. Alkylation of the tertiary hydroxy group of **86** was then readily accomplished with the combination of sodium hydride and methyl iodide. Although the ligand contains three nitrogen atoms that can potentially undergo alkylation, the 80% yield of **87** indicated that despite being relatively hindered, attack by the alkoxide was the kinetically favored reaction. Finally, oxidation of the methyl groups of **87** with potassium permanganate afforded ligand **83** in good yield.

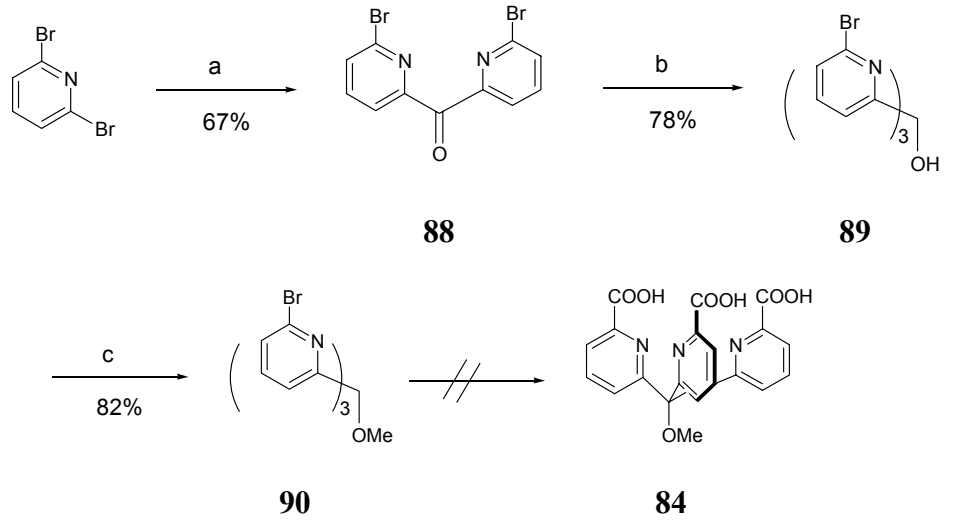


Scheme 2.2 Key: (a) (i) *n*-BuLi, ether. (ii) $(EtO)_2CO$. (b) 2-lithio-5-methyl-pyridine, THF. (c) NaH, MeI, THF. (d) $KMnO_4$, water.

[¶] This part of work was carried out by C.L.D. Gibb and M.E.Kuebel from this laboratory.

2.2 Trispicolinic Acid Ligand 84

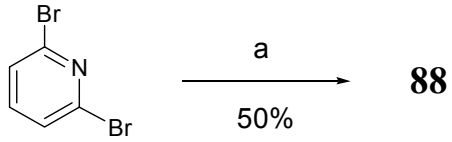
The synthesis of the trispicolinic acid ligand **84** proved more problematic. The investigation of an analogous process to that shown in the synthesis of ligand **83** was avoided, primarily because the greater acidity of the methyl group of 2-bromo-6-methyl pyridine (pKa = 29.5)[129] was expected to interfere with the two lithiation steps. Consequently, the first attempt centered around the synthesis of tribromide **90** (Scheme 2.3). Thus, mono-lithiation of 2,6-bromopyridine followed by the quenching with diethyl carbonate gave the dibromo ketone **88** in good yield.



Scheme 2.3 Key: (a) (i) *n*-BuLi, ether. (ii) $(EtO)_2CO$. (b) 2-bromo-6-Lithiopyridine, THF. (c) NaH, MeI, THF.

Treatment of **88** with mono-lithiated 2,6-dibromopyridine yielded the *tris*(2-(6-bromopyridyl)-methanol **89**. Methylation of the hydroxy group was readily achieved to give **90**, in a similar manner to the formation of **87**. Unfortunately, attempts to react the corresponding tris-lithiated species with dimethylformamide

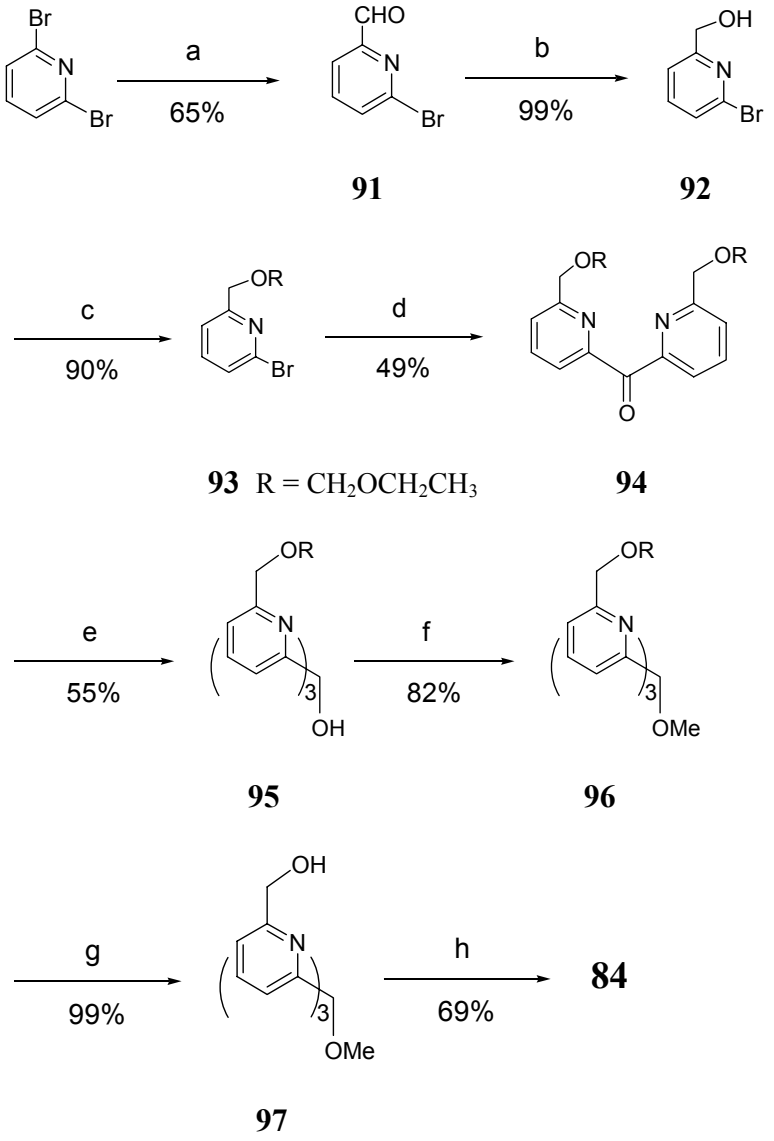
(to form the corresponding *tris*aldehyde) were unsuccessful over a range of reactions that considered solvent (THF, ether, and CH_2Cl_2), concentration (5 mM ~ 15 mM), temperature (-78 °C, -42 °C, and –15 °C), or additives (HMPA and TMEDA) to break up the anticipated lithiate aggregates.[130] Only intractable mixtures of compounds were obtained. In addition, attempts to directly form the tris-carboxylic acid by quenching with CO_2 resulted in further complications with the apparent alkylation of the newly formed carboxy groups. Although a full identification of the reaction mixtures was not achieved, a model reaction of quenching the mono-lithiated 2,6-dibromopyridine with CO_2 resulted in the formation of ketone **88** in 50% yield (Scheme 2.4).



Scheme 2.4 Key: (a) (i) *n*-BuLi, ether. (ii) CO_2.

Consequently, a successful alternative route to ligand **84** was devised (Scheme 2.5). Mono-lithiation of 2,6-dibromopyridine and quenching with DMF afforded aldehyde **91** in 65% yield. Reduction of **91** with $NaBH_4$ gave alcohol **92**, which was protected as the ethoxymethyl ether (**93**). The bromide **93** then served as the building block for the construction of the *tris*-pyridyl framework. Thus, formation of the corresponding lithiate of **93** and quenching with diethyl carbonate, resulted in the expected ketone **94**. Correspondingly, reacting the aforementioned lithiate with **94** gave the anticipated alcohol **95**. As was observed

in the previous cases, protection of the alcohol as its methyl ether (**96**) proceed smoothly. Finally, removal of the ethoxymethyl ether protecting groups with dilute HCl in methanol, and oxidation of the resulting triol **97** with potassium permanganate, gave the desired ligand **84** in reasonable yield.



Scheme 2.5 Key: (a) (i) *n*-BuLi, ether. (ii) DMF. (iii) H_3O^+. (b) $NaBH_4$, MeOH. (c) $^iPr_2NEt$, $CH_3CH_2OCH_2Cl$, DMF. (d) (i) *n*-BuLi, THF. (ii) $(EtO)_2CO$. (e) lithiate derived from **92** + *n*-BuLi, ether. (f) NaH, MeI, THF. (g) HCl, MeOH. (h) $KMnO_4$, water.

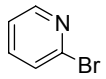
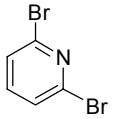
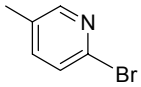
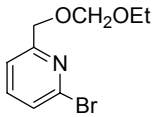
2. 3 Discussion

Previously, Hannon *et. al*.[126] observed that the direct (one pot) formation of *tris*-pyridylmethanol derivatives from the constituent pyridine derivatives was a rather ineffective process. Yields of the *tris*(2-pyridyl)methanol ligands ranged from 12% to 24%. In most cases, the major side products (20-61%) were noted to be the corresponding *bis*(2-pyridyl) ketone. Our results indicated that the two-step synthesis of *tris*(2-pyridyl)methanol derivartives was a much more successful strategy to construct these *tris*(2-pyridyl)methanol ligands. The overall yields over the two steps were as high as 50%. Re-investigation of the synthesis of the unsubstituted ligand **81**, allowed a comparison of the one or two-step approach to *tris*pyridyl ligands. Our results (Table 2.1) indicated that a two-step process, which also opens the way to non-C_{3v} ligands, gave higher yields of the targets.

Thorough examination on these reactions allows the following observations which may explain the low yields often associated with these types of reactions. For both the ketone and trispyridyl methanol reactions investigated, a significant interdependence between scale and yield was noted. Thus, on a small scale yields were generally poor unless an excess of lithiate was used. It was also noted that the temperature of small scale reactions was difficult to control. As pyridyl lithiates are known to rapidly decompose at temperature above -20°C, it is assumed that an excess of lithiate was required to compensate for the decomposition process arising from the poor temperature control. On the larger scale, where temperature control was straightforward, the equivalents of

lithiate could be kept to a minimum. This was essential in large-scale ketone syntheses where an excess of lithiate resulted in the alkylation of the ketone to give (poor yields of) *tris*pyridyl and *bis*pyridylbutyl alcohols side products. Consequently, both ketone and *tris*pyridyl methanol formation were undertaken on the large scale with careful control of the reagent stoichiometry.

Table 2.1 Formation of C_{2v} bis-pryidylketones and C_{3v} tris-pyridylmethanols

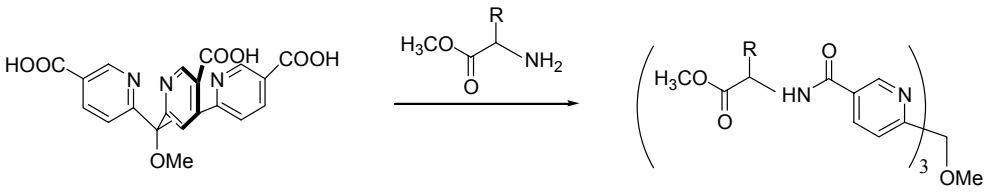
Pyridine building block	Yield of ketone[a]	Solvent system	Yield of trispyridyl methanols[b]	Solvent system
	- [c]		78 (38)[d]	Et_2O
	67	Et_2O	78	Et_2O/THF
	70	THF	70 (24)[d]	THF
	49	THF	55	Et_2O

[a] By formation of lithiate (-78°C) and reaction with diethyl carbonate.
[b] By formation of pyridyl-lithiate (-78°C) and reaction with the corresponding ketone.
[c] Commerically available ketone was used for the second lithiation.
[d] In brackets: yields reported by Hannon[126](one-step synthesis from the correcponding pyridine building blocks).

The effect of adding specific additives[130] known to break up lithiate aggregates, and considered how reaction temperature might influence reaction outcome. Briefly, no improvement in yields observe if TMEDA (N,N,N',N'-tetramethylethylenediamine) or HMPA (hexamethylphosphoramide) were added to the lithiation reactions. Likewise, with respect to reaction temperature, -78°C

struck a fine balance between lithiate stability and the solubility of the various species. Finally, it should be noted that there was no clear choice in whether to use diethyl ether or THF as solvent. Thus, bearing in mind the previously noted preference for performing the mono-lithiation of 2,6-dibromopyridine in diethyl ether,[131] solvent choice was dictated by solubility concerns.

Base on this work, amino acids (protected as methyl esters) were later coupled to ligand **83** with the aid of standard peptide coupling techniques and a variety of new ligands with a general structure of **98** were synthesized (Scheme 2.6).[132] It has been demonstrated that with the bulky amino residues on the ligands, the ZnL_2 sandwich complex formation was efficiently eliminated. However, the binding of Zn^{2+} to these ligands became much weaker than the unsubstituted trispyridyl ligands.[132]



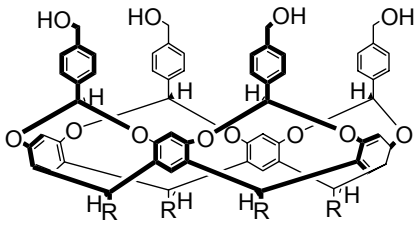
83 **98**

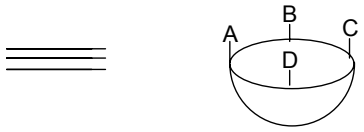
Scheme 2.6 Formation of new ligands **98**.

III. Synthesis and Assembly of Tetraphenylmethane-based Subunits

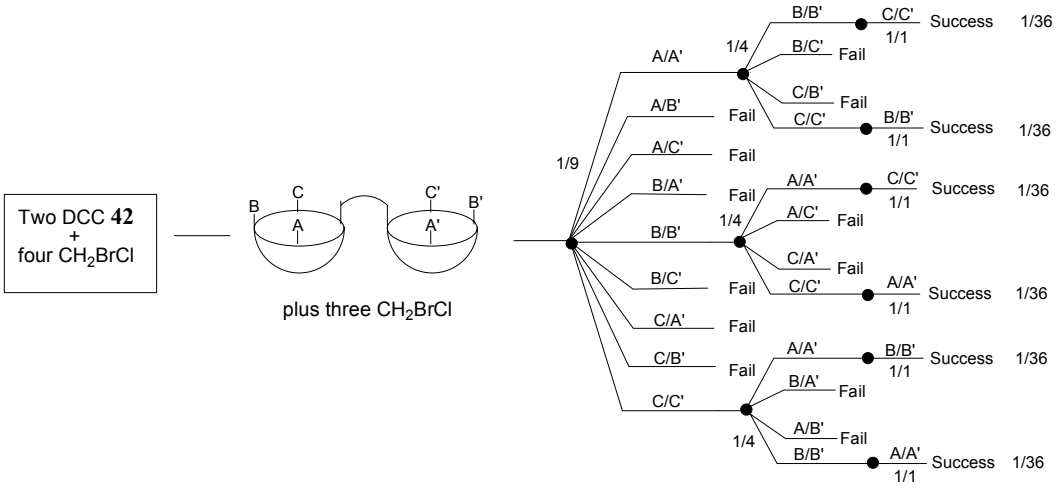
Previous results from this laboratory have identified the benzyl alcohol group as a useful functional group for self-assembly with covalent modification.[75] The utility of this group allows the access to highly efficient assemblies; even in the absence of molecular templates (see Section **1.4.2.2**). As shown in Scheme 1.22, two molecules of deep-cavity cavitand **42** were linked by four molecules of CH_2BrCl, and resulted in an 80% yield of cage molecule **44**.[75] In order to better explain the efficiency of the process, the ideas of "assembly number" and "assembly tree" were introduced.[134] The "assembly number" (AN) is defined as the quotient of the actual yield over the theoretical yield of the product. When the AN of one process is greater than one, it can then be defined as a self-assembly one.[134] In order to determine the theoretical yield, the drawing of an "assembly tree" is needed. Scheme 3.1 shows the assembly tree of the aforementioned reaction. Assume the first acetal is formed quantitatively between the two DCC. The six remaining benzyl alcohols on the intermediate have a total of nine possible reactions to form the second actal, six of which result in non-product. The three remaining reactions give the *bis*-linked intermediate. Accordingly, the *bis*-linked intermediate has 50% chance of forming the right product. The theoretical yield of the whole process will be $\rho = [1/9 \times 1/4 \times 1/1] \times 6 = 1/6$, which

corresponds to a 16.7% yield. Thus, the AN of this process is 80 / 16.7 = 4.8. This is a very good example of self-assembly.





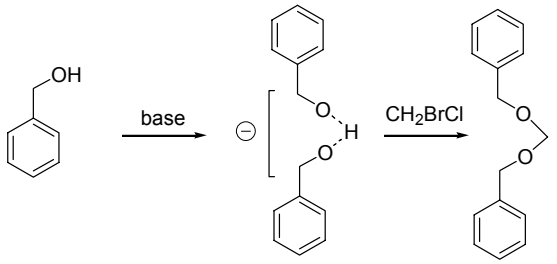
42



Scheme 3.1 Assembly tree of the assembly of DCC **42**.[134]

It is believed that the formation of a charged hydrogen bonding (CHB) complex intermediate is an important driving force of the assembly process mentioned above (Scheme 3.2). Thus, under the standard condition (*t*-BuOK/DMSO/CH_2BrCl), the alcohol groups are deprotonated and associated into dimeric species *via* a charged hydrogen bond. The intermediate is then trapped by CH_2BrCl. It has also been demonstrated that instead of using CH_2BrCl, CH_2Cl_2

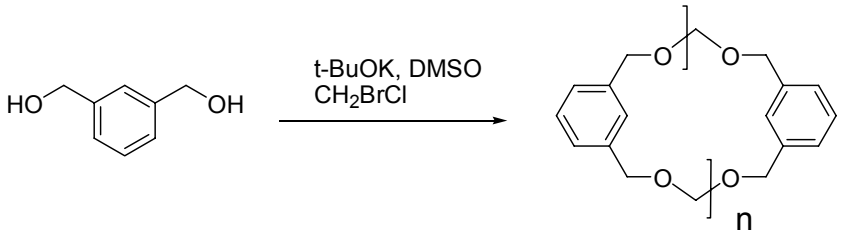
also worked, but with lower yield; CH_2Br_2, CH_2BrI, or CH_2I_2 did not give trace of desired product.[75] Changing the solvent to DMF also gave low yield of the desired product.[75] The non-corrective manner of this process allows the isolation of kinetic products rather than the thermodynamic products. This assembly is an example of self-assembly with covalent modification.[102]



Scheme 3.2 Acetal formation *via* a Charged Hydrogen Bond (CHB) complex.

The combination of benzyl alcohol moieties to form the acetal under the standard reaction condition, provides a very efficient methodology for self-assembly. However, it should be pointed out that not all processes that involve the use of this methodology can be classified as self-assembly. For example, recent results[133] from this laboratory had demonstrated that under the standard conditions (*t*-BuOK / CH_2BrCl / DMSO), 1,3-benzenedimethanol was capable of forming a range of cyclic crown ether compounds (Scheme 3.3). Thus, treatment of a DMSO solution of 1,3-benzenedimethanol with *t*-BuOK, followed by the addition of CH_2BrCl resulted in a mixture of products dominated by three components, which accounted for 70% of the mass. These three compounds were characterized as the cyclic 'dimer', 'trimer' and 'tetramer' **99** (n = 1, 2, and 3

respectively). It is obvious that, the 120º angle between the two benzyl alcohol groups reduces the propensity of the subunits to 'dimerize' and allowed the proportions of the alternative products to rise. The yields of individual species depended upon the concentration of the reactions. Studies at the range from 2.5 mM to 100 mM revealed that at low concentration the 'dimer' predominanted, while at higher concentration, the proportion of higher oligmers arised.[133] For example, at 2.5 mM, the 'dimer' was obtained at 47% yield; at 50 mM, it was obtained at 33%; at 100 mM, the 'dimer' was isolated at 26% yield.[133] This one-pot reaction provides an easy access to a series of cyclic crown ether type compounds.

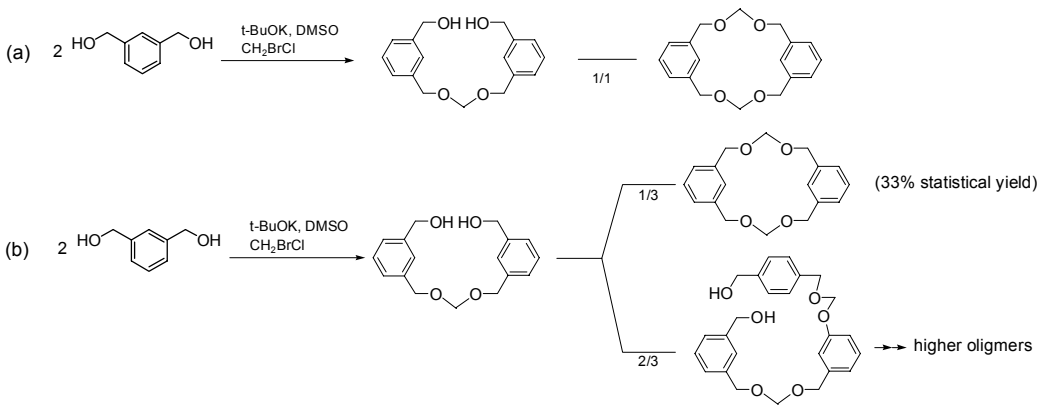


99

Scheme 3.3 Assembly of 1,3-benzenedimethanol.[133]

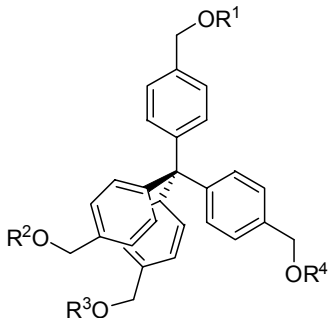
However, this reaction cannot be regarded as a self-assembly. The assembly tree of the coupling of 1,3-benzenedimethanol is drawn in Scheme 3.4(a) according to the literature procedure.[134] The theoretical yield of 'dimer' is 100%. It is obvious that this process is not a self-assembly one. Alternatively, the statistical yield of the 'dimer' can be calculated as shown in Scheme 3.4 (b). After the initial acetal formation, the remaining two benzyl alcohol groups have 1 : 2 chance to cyclize or react with the third benzenedimethanol molecule to lead to

higher oligmers. The 47% yield of 'dimer' at 2.5 mM can be interpreted as an assembly with AN = 47/33 = 1.4.



Scheme 3.4 The assembly tree (a) and 'probability tree' (b) of the assembly of 1,3-benzenedimethaol to form the 'dimer'

To expand the knowledge of self-assembly, and to synthesize unusual nano-scale molecules as possible hosts and catalysts, the synthesis and coupling of tetraphenylmethane derivative **100** were proposed. It was believed that, due to its tetrahedral geometry and the presence of four benzyl alcohol groups, this compound could form an infinite diamaondiod network.[135-139] However, the analysis of the resulting infinite network is difficult. In order to avoid the infinite polymerization, tetrol **100** can be partial protected to generate two new subunits, the *mono*-protected subunit **100a** and *bis*-protected **100b**. It is expected that under the same conditions, **100a** would form the tetrahedral cage compound **101** because of the symmetry of the three benzyl alcohols on subunit **100a** (Scheme 3.5). This could be an excellent example of self-assembly.

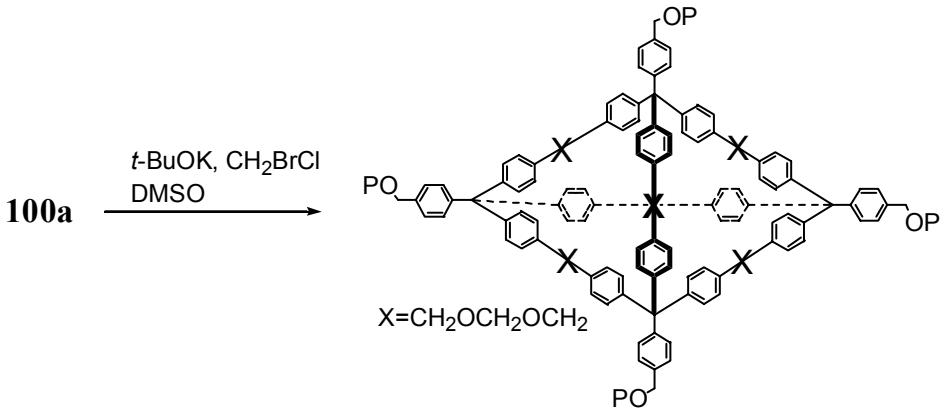


100 $R^1 = R^2 = R^3 = R^4 = H$

100a $R^1 = H, R^2 = R^3 = R^4 = P$

100b $R^1 = R^2 = H, R^3 = R^4 = P$

(**P** = protecting group)



101

Scheme 3.5 Proposed self-assembly of subunit **100a**.

Before the extensive investigation on the assembly of **100a**, the *bis*-protected subunit **100b** was studied. The study on this subunit will provide very important information for the assembly of **100a**, such as the protecting group selection. It is expected that, similar to 1,3-benzendimethanol, this new subunit, whose two benzyl alcohol groups define an angle of *ca*. 109.5°, would also form a range of macrocyclic compounds. Figure 3.1 shows some of the possible products derived from the coupling of this subunit. It is therefore relatively straightforward to construct nanoscale molecules with this approach.

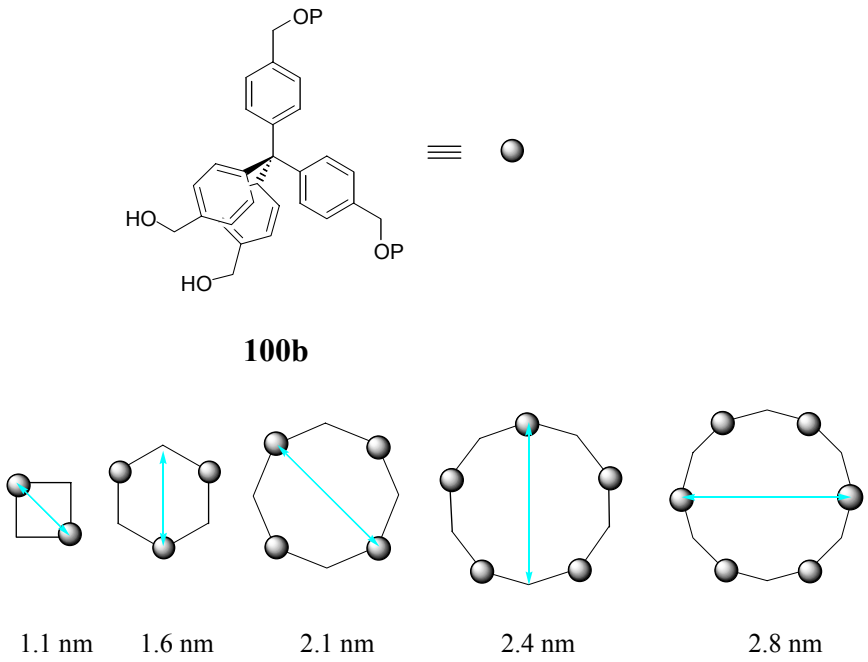
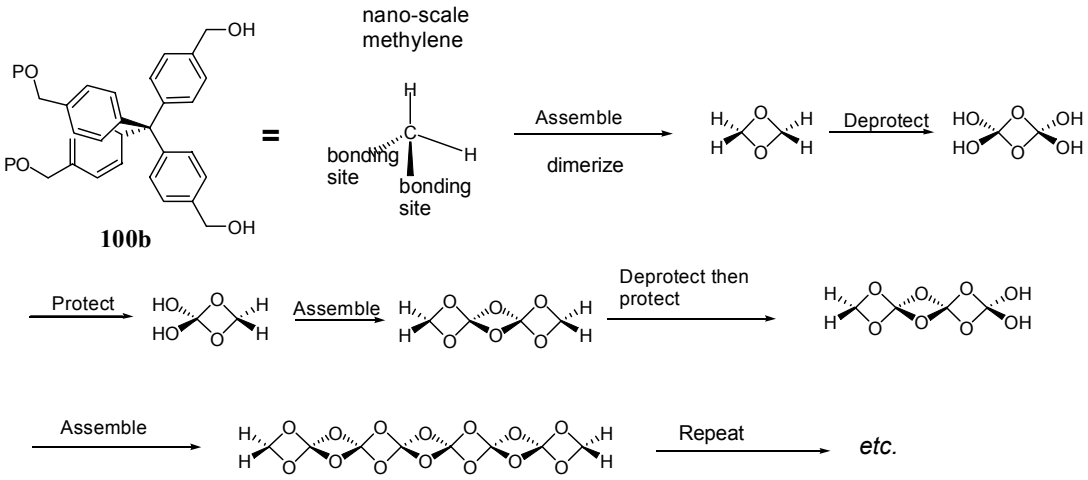


Figure 3.1 Some of the possible products derived from the coupling of **101**, and the approximate sizes of different products.

Another advantage of this approach, is the possibility of performing multi-generation coupling. It is convenient to view the *bis*-protected species **101** as a nano-scale "methylene" group; a species capable of forming two bonds to other subunits while the other two sites in the tetrahedral array have been blocked by a terminating group (a nanoscale "Hydogen" atom). Scheme 3.6 shows how this subunit can be viewed as the nanoscale methylene and how it is possible to perform multi-generation coupling reactions. Thus, after the first generation assembly, the 'dimer' product, which has a cross distance of *ca*. 1.1 nm, can be isolated. Deprotection of this 'dimer' releases four new bonding sites (benzyl alcohol groups). Selective *bis*-protection of the tetrol gives the second generation coupling subunit, whose two benzyl alcohol groups also define a 109.5° angle. Under the same conditions, this new subunit is expected to form similar products

as the first generation coupling, with the size of the resulting molecules literally doubled. The new 'dimer' (*ca*. 3.3 nm) can then be isolated and undergoes the third generation coupling. Up to three generations of the repetitive couplings are shown, with the resulting product having a length exceeding 7.7 nm. To our awareness, such a strategy, has never yet been reported.

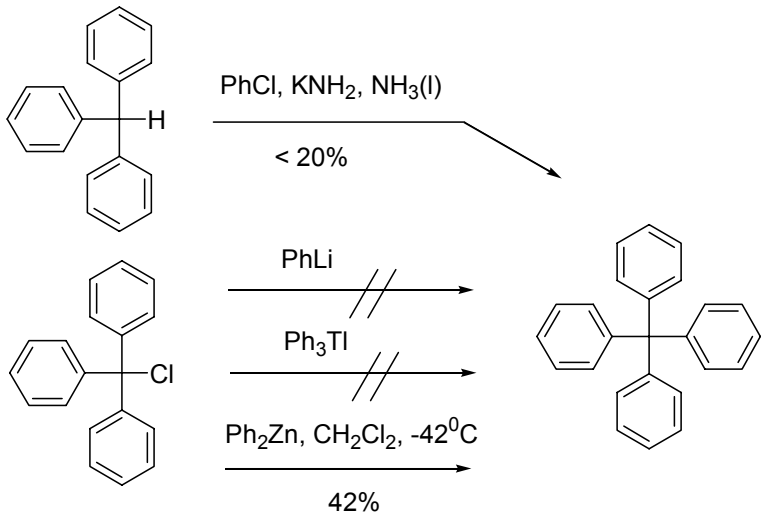


Scheme 3.6 Multi-generation coupling of proposed subunit **100b**.

3.1 Synthesis of Tetraphenylmethane-based Subunit 100

The synthesis of **100** began with the construction of the tetraphenyl-methane core (Scheme 3.7). Although tetraphenylmethane has been known for almost a century,[140] the synthesis has proven to be very difficult and inefficient. Traditionally, tetraphenylmethane was obtained by coupling triphenylmethane with chlorobenzene in the presence of KNH_2 and liquid ammonia solvent.[141,142] However, the laborious procedure of the experiments, the use of potentially hazardous ammonia and potassium metal, and the low yield (less than 20% in the

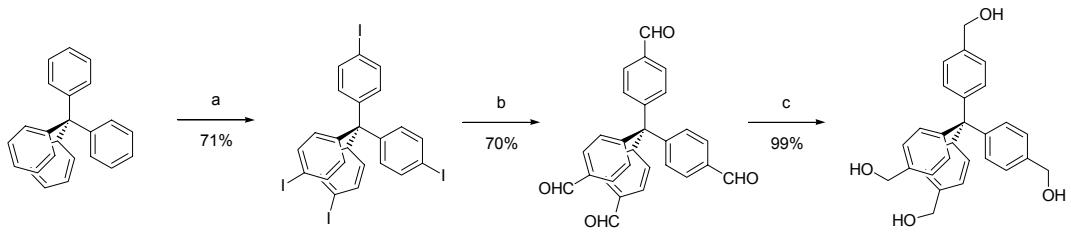
author's hands) of the desired product discouraged the use of this method. Thus, extensive efforts were made to seek alternative methods which would give higher yields of tetraphenylmethane, and require less efforts in setting up and working up the experiments. The first attempt focused on the coupling of phenyllithium with trityl chloride. Despite an extensive probe on solvents (THF, ether, CH_2Cl_2, benzene), temperature (ranging from -78ºC to 60ºC), and time (ranging from 1 h to 24 h), no trace of desired product was found. As an alternative, organothallium chemistry was turned to. Marko *et. al*. reported an 80% yield of tetraphenyl-methane by reacting trityl chloride with triphenylthallium.[143] However, it was not possible to reproduce this result. Only unidentified mixtures were obtained in these reactions. Finally, success came from the coupling reaction of trityl chloride with diphenylzinc (Ph_2Zn).[144] Although Ph_2Zn was commercially available, it was more economical and convenient to generate it *in situ* by mixing PhLi and anhydrous $ZnCl_2$ in dry diethyl ether. After removing the ether and the addition of dichloromethane, the coupling reaction was then carried out by the addition of a solution of trityl chloride at -42°C. Tetraphenylmethane could be easily isolated by washing the crude product with ethyl ether and recrystalizing from hot $CHCl_3$. By this approach it was possible to obtain a moderate 42% yield in this one pot synthesis. Consider the ease of carrying out the reaction, this is a superior method in preparing tetraphenylmethane.



Scheme 3.7 Formation of tetraphenylmethane.

Once the tetraphenylmethane core was set in place, the functionalization at the 4- positions was relatively straightforward (Scheme 3.8). Tetraiodination of tetraphenylmethane was accomplished with a combination of I_2 and bis(trifluoro-acetoxy)-iodobenzene in CCl_4,[145] and the tetraiodide **102** obtained in 71% yield. Tetraiodide **102** was then treated with *n*-BuLi and quenched with DMF to give the tetraaldehyde **103**. This reaction was complicated by the poor solubility of both the starting tetraiodide and the corresponding lithiates. Initial attempts on this reaction under the standard condition (-78°C, *n*-BuLi, then DMF) yielded a mixture of *mono*-, *bis*-, *tris*-, and *tetra*-aldehyde. The desired tetraaldehyde was isolated in only *ca*. 35% yield. For the intermediate *mono*- *bis*- and *tris*-aldehydes, the presence of unexchanged iodide was evidenced from NMR spectra. No improvement was made despite efforts to vary the reaction temperature (-78ºC, -42ºC, and -15ºC), time (from 2 h to 5 h) and concentration (from 1 mM to

5 mM). Obviously, a solubility problem of the lithiates was encountered. In contrast it was found that by warming up the lithiate to *ca*. -30°C after the lithium-halogen exchange, the yield of the desired tetraaldehyde was increased to 70%. Finally, the tetraaldehyde **103** was converted into tetrol **100** with $NaBH_4$ without difficulty.



102 **103** **100**

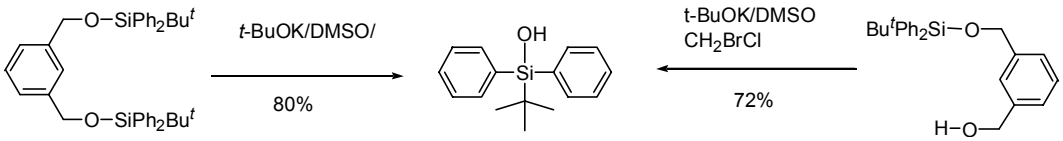
Scheme 3.8 *Key*: (a) I_2, $PhI(CF_3CO_2)_2$, CCl_4. (b) i. *n*-BuLi, THF; ii. DMF; iii. H_3O^+. (c) $NaBH_4$, THF/MeOH.

3.2 Selection of Protecting Group

In selecting suitable protecting groups for the purpose of multi-generation couplings, three criteria were taken into account. First, the protection and deprotection should be efficient enough to allow reasonable yields throughout the multi-site, multi-generation processes. Second, both the aforementioned steps should not require acidic conditions, as the acetal groups used to connect the subunits are extremely sensitive to acid. Third, the protecting group should be stable to strong basic conditions as the coupling reactions involve the use of *t*-BuOK and DMSO. After careful survey of protecting groups for alcohols,[146]

silicon protecting groups were chosen to be investigated; primarily because of the general high efficiency of protection and their ability to be removed by fluoride ion under neutral conditions.

Silyl ethers are among the most frequently used protecting groups for alcohols, of which the *t*-butyldiphenylsilyl (TBDPS) group is one of the most stable due to the steric bulk around the silicon atom. To determine the suitability of TBDPS group for the proposed couplings, the *bis*- and *mono*-protected benzenedimethanol model compounds **104** and **105** were synthesized. Unfortunately, treatment of these two compounds with *t*-BuOK/DMSO/CH_2BrCl resulted in the generation of *t*-butyldiphenylsilanol **106** in high yield (Scheme 3.9). It was proposed that this compound was the result of nucleophilic attacks on the benzyl carbon by methylsulfinyl carbanion (CH_3-SO-CH_2^-)[147] generated by mixing *t*-BuOK with DMSO. However, this proposal was not confirmed since all attempts to isolate the corresponding sulfoxide products were unsuccessful.

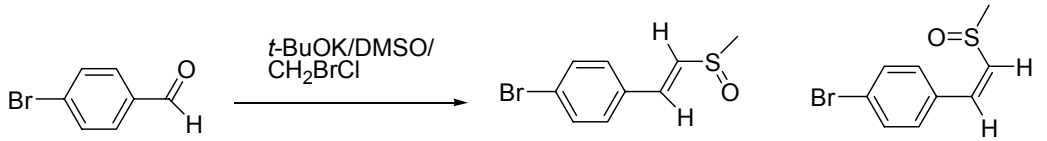


104 **106** **105**

Scheme 3.9 Model study on the stability of TBDPS.

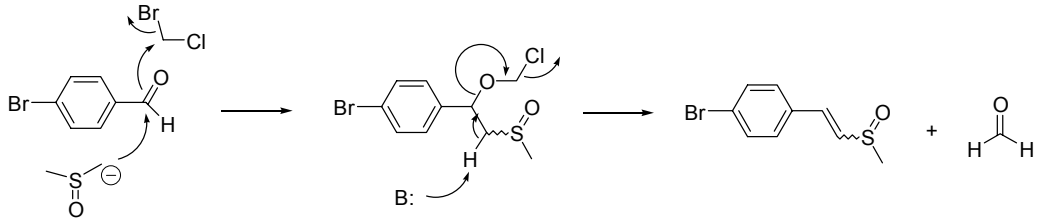
The methylsulfinyl carbanion has been known to be a strong nucleophile to attack electrophilic centers such as esters[148] and aldehydes.[149] Indeed, the treatment of 4-bromobenzaldehyde to the standard assembly conditions gave 4-

bromophenylethenyl methyl sulfoxide in 70% yield. The *trans* (**107**) : *cis* (**108**) ratio was 6:1. The mechanism of this reaction was suggested as shown in Scheme 3.10. Thus, nucleophilic attack of the carbonyl by CH_3-SO-CH_2^-, followed by the eliminiation of formaldehyde and HCl, resulted in the formation of the *trans*/*cis* diastereomers.



trans **107** (60%) *cis* **108** (10%)

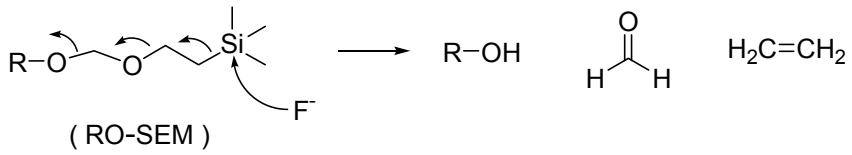
Proposed mechanism:



Scheme 3.10 Nucleophilic attack of $CH_3SOCH_2^-$ on the aldehyde group.

The potent nucleophilicity of the methylsulfinyl carbanion made the silyl ethers protecting groups unsuitable for the coupling reaction conditions. Consequently, the 2-(trimethylsilyl)ethoxymethyl (SEM) group[150] was investigated as an alternative. This protective group is connected to the alcohol *via* a C-O bond, which was expected to be more stable under the strong basic

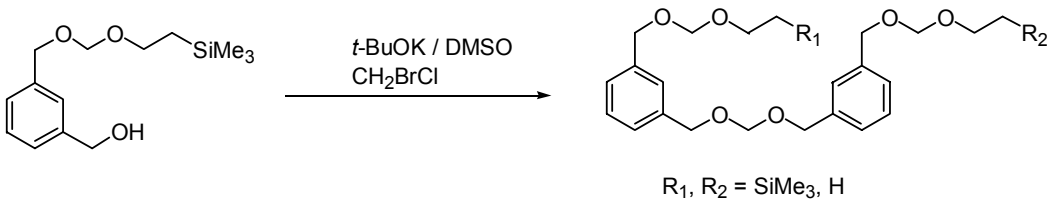
conditions. However, it can also be cleaved by F^- *via* a concerted elimination of ethylene and formaldehyde, to reveal the hydroxy group (Scheme 3.11).



Scheme 3.11 Deprotection of RO-SEM.

The model compound, mono-protected benzenedimethanol **109**, was initially prepared. It was then treated under the standard reaction conditions. Initially, it was believed the coupling process went smoothly, giving moderate yields of the dimeric species. However, close scrutinization revealed that an inseparable mixture of three possible products **110a-c** (**a**: R_1=R_2=$SiMe_3$; **b**: R_1=H, R_2=$SiMe_3$; **c**: R_1=R_2=H) had been obtained, *i.e.*, a fraction of the SEM protecting groups (-CH_2O-$CH_2CH_2SiMe_3$) had decomposed to MOE groups (-$CH_2OCH_2CH_3$) (Scheme 3.12). The percentage of the decomposition depended upon the equivalents of *t*-BuOK used. Table 3.1 summarized the results of a series of reactions carried out with varying equivalents of base. The more *t*-BuOK used, the greater the degree of decomposition. Hence, the use of 5 equivalent of *t*-BuOK allowed the isolation and fully characterization of **110c**. On the other hand, when less equivalents of *t*-BuOK were employed, considerable quantities of starting material were recovered. Varying the reaction time (from 1 h to 24 h) made no significant difference to the reaction. Thus, it was concluded

that SEM protecting groups were not compatible with the standard reaction conditions. The coupling process and the decomposition of SEM were not kinetically separable.



109

110a $R_1 = R_2 = SiMe_3$
110b $R_1 = SiMe_3$, $R_2 = H$
110c $R_1 = R_2 = H$

Scheme 3.12 Model reaction of compound **109**.

Table 3.1 Model reactions of compound **109**[a]

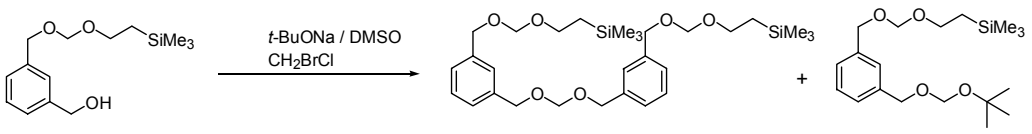
Entry	t-BuOK (e.q.)	CH_2BrCl (e.q.)	Left over **109**	Yield of **110a-c**[b]	Decomposition[c]
1	5.0	4.0	0	58%	70%
2	2.5	2.0	0	71%	26%
3	1.2	1.1	25%	64%	13%
4	0.6	1.1	15%	55%	13%

a. All reactions were carried out at 5 mM in DMSO, room temperature, 5 hours.
b. Obtained as a mixture of the three products.
c. Calculated from integration from NMRs of the mixture.

The decomposition process is literally the displacement of trimethylsilyl group (TMS) by a H atom. In organic synthesis, the TMS group is often refered as "bulky proton".[151] When it is bonded to a carbon, it is also referred as "super proton" and the silicon-carbon bond usually breaks more easily than the corresponding hydrogen-carbon bond.[152] Thus, under the strong basic condition

(*t*-BuOK in DMSO) the "super protons" were "deprotonated" and protonated by hydogen in the subsequent workup. Hence, the base used in the process was varied. Although a number of alkoxides proved ineffective in driving the reaction, the use of *t*-BuONa as the base lead to no decompostion of the protecting groups and the efficient synthesis of **110a**. Table 3.2 lists some results of the model reactions with **109** under the modified conditions. Too much *t*-BuONa resulted in a lower yield of desired dimer **110a**, and the committant formation of byproduct **111**. Clearly, the *tert*-butoxide anion can act as a nucleophile and attack the reaction intermediate in the reaction. As observed previously, less equivalents of base reduced the efficiency of the reaction. The best conditions discovered required 2.5 equivalents of base, and seemed to strike a near perfect balance; the desired dimer was isolated in 93% yield, and no byproduct was observed. The reason why changing the counterion of the *t*-butoxide base from potassium to sodium affected the outcome of the reactions is unclear. Presumably the metal ions could coordinate with the series of oxygen atoms of the intermediates and affect the products formation.

Table 3.2 Model reactions of **109** under modified conditions[a]



109 **110a** **111**

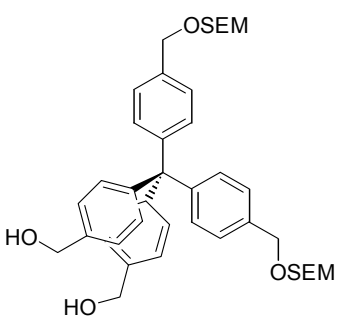
Entry	*t*-BuONa (e.q.)	CH_2BrCl (e.q.)	Left over **109**	Yield of **110a**	Yield of **111**[b]
1	5.0	4.0	0	68%	16%
2	2.5	2.0	0	93%	0
3	1.5	1.1	38%	55%	0

a. All reactions were carried out at 5 mM in DMSO, room temperature, 3.5 hours.
b. Calculated from the integration from NMR spectra of the mixture **110a** + **111**.

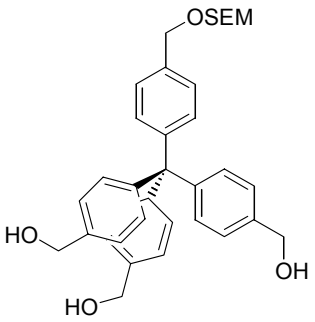
Based on the above model studies, the coupling under the slightly modified condition (*t*-BuONa / DMSO / CH_2BrCl), with SEM as a suitable protective group, is a suitable strategy for future self-assembly reactions.

3.3 Coupling of Subunit 112

The successful selection of a protective group allowed us to synthesize the the *bis*-protected tetrol **101** (P = SEM). Because of the poor selectivity of this protection, the desired *bis*-protected subunit **112** was obtained in low yield. Thus, treating **100** with SEM-Cl gave **112** in 41% isolated yield, along with 26% mono-protected species **113** and a mixture of *tris*- and fully protected species. Fortunately, all other byproducts could be deprotected to regenerate the starting material. Thus, despite the inefficient *bis*-protection, quantities of **112** could be obtain without too much difficulty.

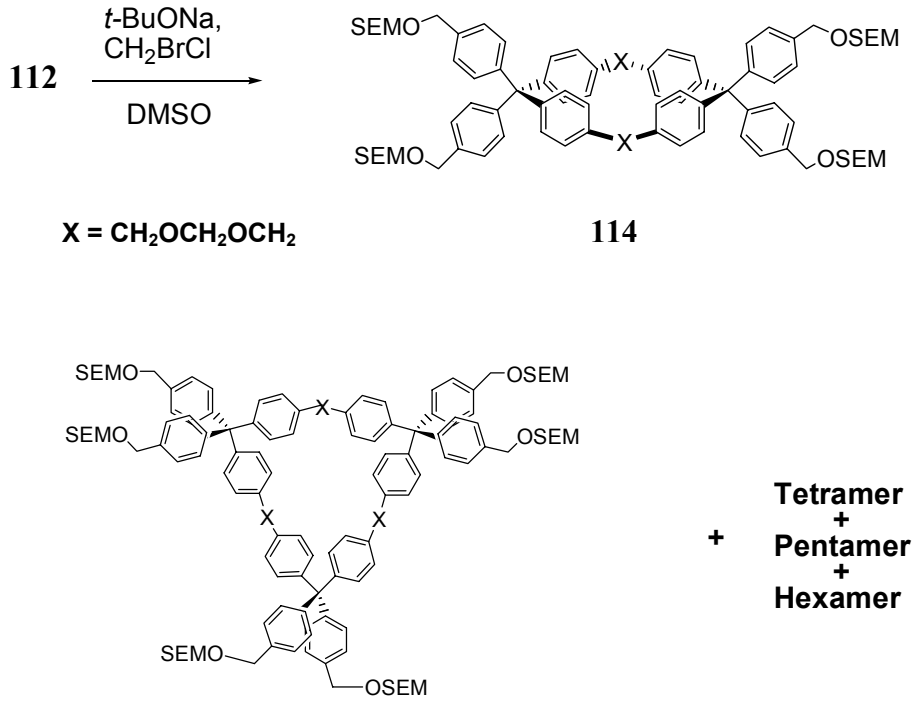


112



113

The modified reaction condition was then applied to this subunit. Treating the DMSO solution of **112** with *t*-BuONa, followed by the immediate addition of CH_2BrCl, yielded a mixture of the expected 'dimer' **114**, 'trimer' **115**, and other cyclic products from 'tetramer' to 'hexamer' (Scheme 3.13). The 'dimer' and 'trimer' were readily separable by routine column chromatography. The ^{1}H NMR spectrum of the 'dimer' **114** and the peak assignments are shown in Figure 3.2. The two types of acetal protons (a,d) are at 5.0 and 4.8 ppm respectively, with a ratio of 1:2. Compared to the two types of benzyl protons (b,c), which are at *ca*. 4.5 ppm, they are shifted downfield because of the combined deshielding effects of the adjacent oxygen atoms. The ^{1}H NMR spectrum of the 'trimer' **115** (Figure 3.3) has exactly the same pattern as **114** because of the similar symmetry. The other oligmers were obtained as a mixture, and were characterized by mass spectrometry. The MALDI-TOF mass spectrum of the mixture (Figure 3.4) showed the presence of 'tetramer' (2959, $[M+Ag]^+$), 'pentamer' (3630, $[M+Ag]^+$), and 'hexamer' (4387, $[M+Ag]^+$).



Scheme 3.13 Coupling of subunit **112**.

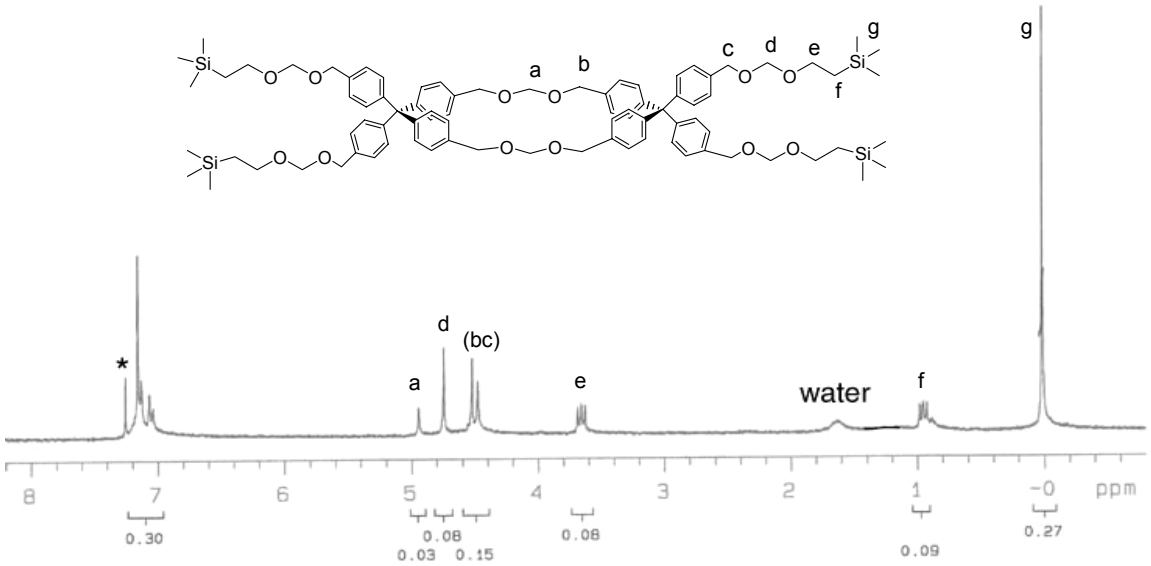


Figure 3.2 ^{1}H NMR spectrum of 'dimer' **114** (400 MHz, ∗ : solvent $CDCl_3$ peak)

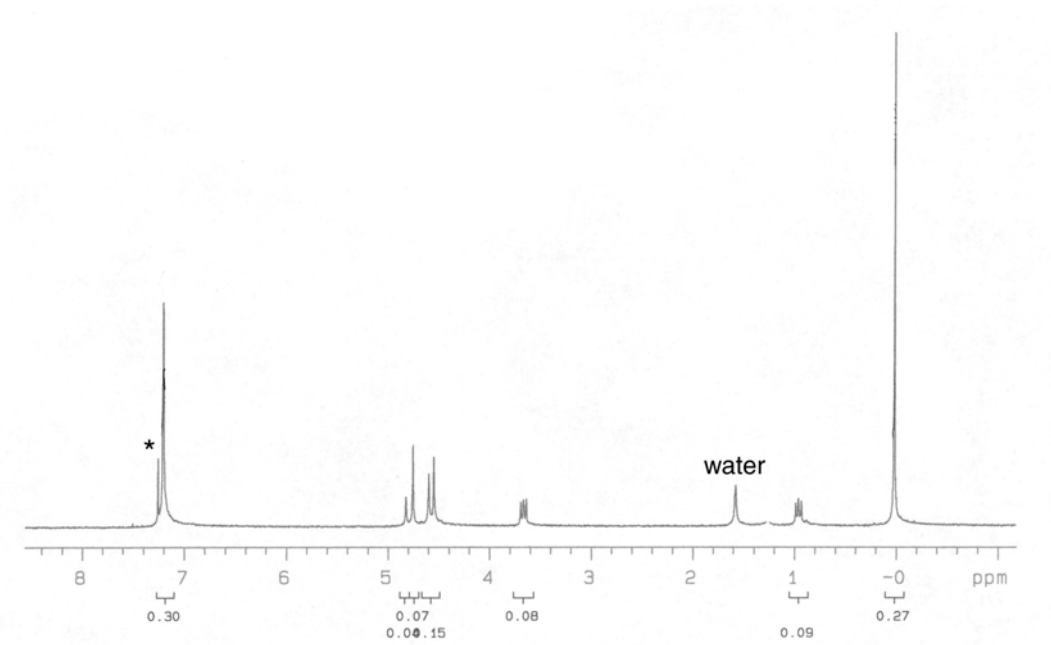


Figure 3.3 ^{1}H NMR spectrum of 'trimer' **115** (400 MHz, ∗ : solvent $CDCl_3$ peak)

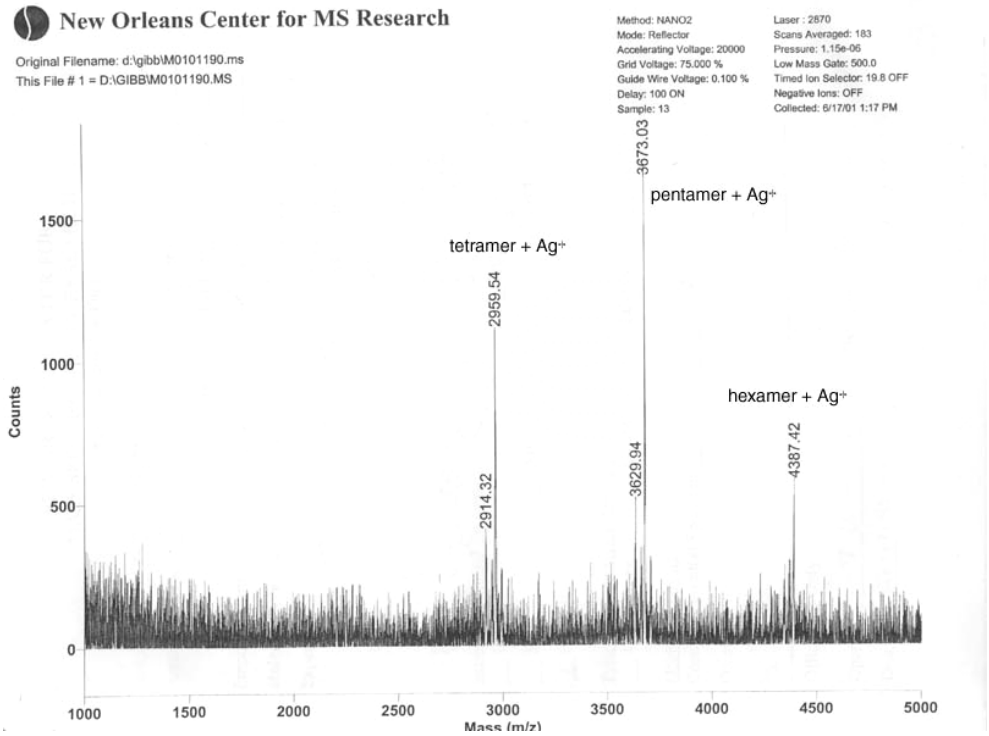


Figure 3.4 MALDI-TOF mass spectrum of the mixture of 'tetramer' through 'hexamer'.

Table 3.3 showed some results of reactions carried out under different concentrations. Reaction concentration (from 2.5 mM to 100 mM) had been shown to greatly affect the distribution of the products on 1,3-benzenedimethanol.[133] However, for diol **112**, concentrations from 2.5 mM to 10 mM made little difference in the product composition: the 'dimer', 'trimer', and other cyclic products ('tetramer', 'pentamer' and 'hexamer') were formed in >50% overall yield, with an approximately ratio of 4:2:1. When the concentration was higher than 10 mM, solubility problem were encountered, and decreased yields of the corresponding products were obtained.

Table 3.3 Coupling reactions of **112** at different concentrations[a]

Entry	Concentraion (nM)	Yield of dimer **114**	Yield of trimer **115**	Tetramer~ Hexamer[b]
1	2.5	33%	15%	8%
2	5.0	29%	12%	8%
3	10.0	33%	15%	10%
4	15.0[c]	20%	10%	0

a : all reactions conditions were: 5 eq. *t*-BuONa, 4 eq. CH_2BrCl, DMSO, 3.5h.
b : obtained as mixtures.
c : significant amount of precipitate formed during the reaction.

Despite the low yields of individual species, this coupling process represents an efficient way to prepare nanoscale molecules. Figure 3.5 showed a CPK model of the 'hexamer', the diameter of this macrocycle is approximately 3 nm.

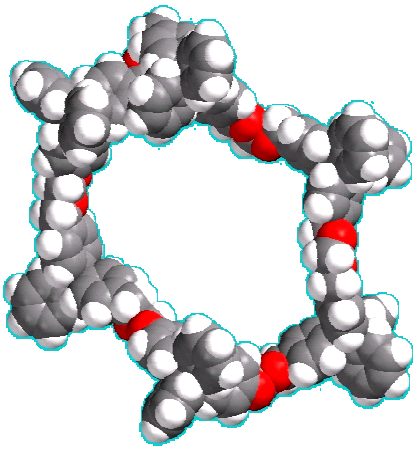
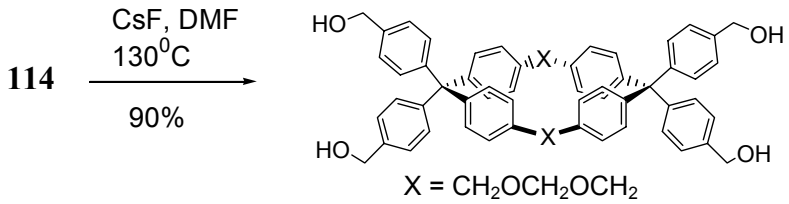


Figure 3.5 Space filling model of the 'hexamer' (protecting groups omitted for clarity)

As the most abundant product from this process, 'dimer' **114** was deprotected to generate the new tetrol **116** for the use of potential multi-generation self-assemblies. The SEM protective group turned out to be very stable. Commonly used fluoride source TBAF (tetrabutylamonium fluoride) in THF failed to remove the protecting group. Instead, more vigorous condition had to be employed. Thus, heating **114** with CsF in DMF at 130ºC for 2 days gave the desired tetrol **116** in 90% yield (Scheme 3.14).



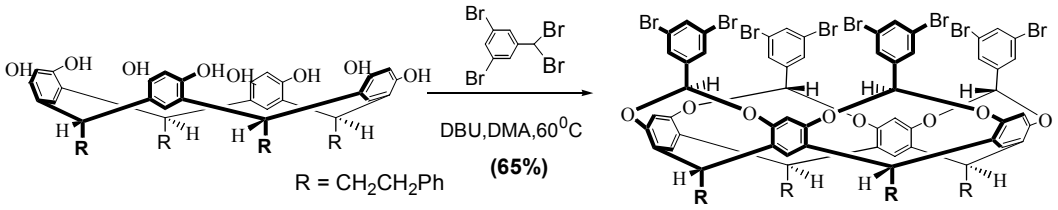
116

Scheme 3.14 Deprotection of the 'dimer' **114**.

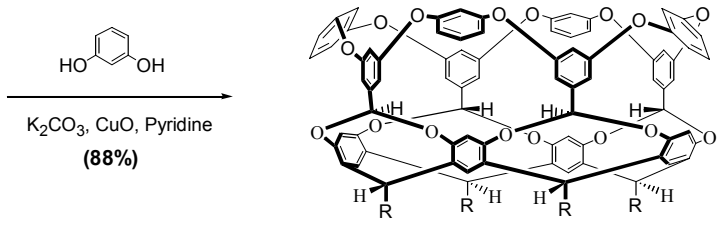
Thus, the first generation of coupling based on the tetraphenylmethane derived subunit **112** has been completed. It has been demonstrated that SEM is a suitable protecting group under the slightly modified conditions (*t*-BuONa / CH_2BrCl / DMSO). It provided very important information for the potential self-assembly of subunit **100a**. Base on this knowledge, the proposed second generation coupling on the new subunit **116** is currently underway in this laboratory.

IV. NOVEL MOLECULAR "BASKETS"

The construction of host molecules with large cavities is a challenging task in supramolecular chemistry. Recently, molecular "basket" **119**, which has an enforced cavity size of *ca.* 10 Å × 6 Å, has been synthesized from this laboratory *via* a two-step process (Scheme 4.1).[153] Based on this result, a series of molecular baskets have been synthesized.[154] Their syntheses will be described in the following sections.



117 **118**

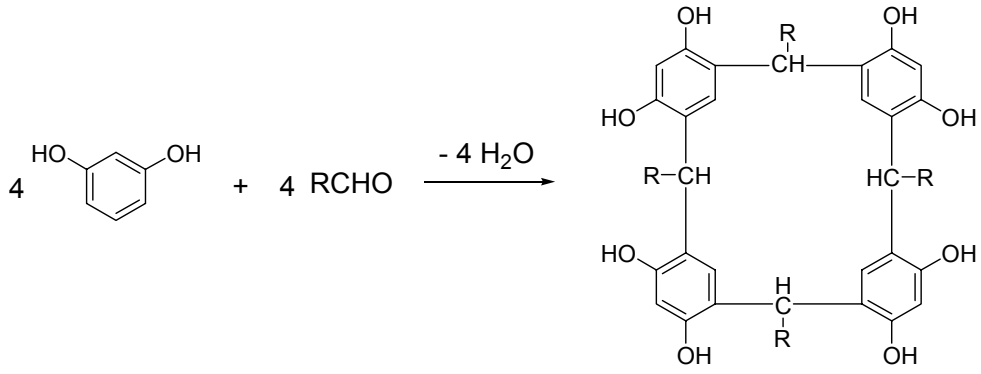


119

Scheme 4.1 Synthesis of basket **119**.

4.1 Formation of Deep-cavity Cavitand 118

The synthesis of deep-cavity cavitand (octabromide) **118** starts with the synthesis of resorcinarene (octol) **117**. It has long been observed that crystaline products are formed from the condensation of resorcinol with aldehydes.[155-157] It wasn't until 1940 that Niederl and Vogel proposed the structure of the resulting products as cyclic "resocinol-hydrins" (Scheme 4.2).[158] This hypothesis was finally proved by Nilsson and co-workers in 1968 when they obtained a single crystal X-ray crystallography structure.[159,160] The resorcinol-aldehyde condensation is a reversible process. In solution, a mixture of a series of resorcin[n]arenes (n = 3, 4, 5, 6,…) is obtained. However, resorcin[4]arenes[161], such as **117**, are usually the most insoluble products and so precipitate out during the reaction. Thus, by le Chateliers principle, the equilibrium is driven towards the formation of resorcin[4]arene (octol) and high yields are usually obtained.

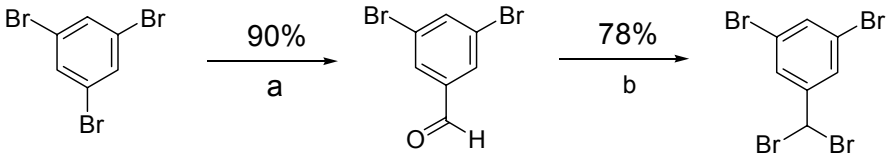


117

Scheme 4.2 Structure of resorcinarene **117** proposed by Niederl and Vogel.[135]

The synthesis of the new family of molecular "baskets" such as **119** was based on the phenethyl footed resorcinarene (octol) **117**. It was formed in 80% yield by treating resorcinol with hydrocinnamonaldehyde in the presence of ethanol and aqueous HCl.[162,163] This compound adopts a bowl-shaped conformation due to the hydrogen bondings between the hydroxy groups on the upper rim, while the bulky phenethyl feet preventing ring-flipping. This helps to keep the adjacent hydroxy groups in close proximity for bridging with 3,5-dibromobenzal bromide to give the deep-cavity cavitand (DCC) **118**. The bridging material (3,5-dibromobenzal bromide) itself was prepared in large scales from 1,3,5-tribromobenzene (Scheme 4.3). Thus, monolithation follwed by quenching with DMF and acidic workup affored 3,5-dibromobenzaldehyde in high yield. Treating the aldehyde with BBr_3 gave the bridging material in 78% yield.

The bridging reaction [164-166] involves the formation of eight new covalent bonds and four stereogenic centers. For each of the bridges, the newly added aromatic ring could adopt two possible configurations at 1 : 1 chance: pointing up to form the "wall" of the DCC, or pointing down to fill in the cavity of the DCC. By slow addition of a DMA solution of octol to a DMA solution of 3,5-dibromobenzal bromide and DBU (1,8-diazabicyclo[5,4,0]undec-7-ene), the desired octabromide **118** was obtained in 65% yiled. This is much higher than the statistical yield of 6.25% (ρ = 50%*50%*50%*50%). It corresponds to a 95% efficiency of each bond, and over 90% diastereoselectivity for each stereogenic center.

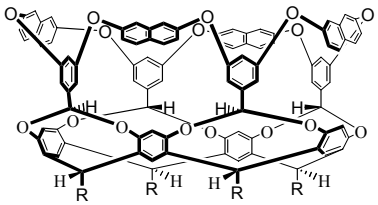


Scheme 4.3 Key: (a) i. *n*-BuLi, ether; ii. DMF.; iii. H_3O^+. (b) BBr_3, CH_2Cl_2.

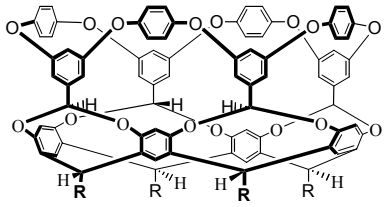
4.2 Formation of Molecular Baskets

The overall result of the aforementioned DCC formation is to position the four aromatic rings at set distances from each other; well pre-organized for the subsequent eight-fold Ullman ether reactions to form the molecular baskets. Thus, refluxing a mixture of octabromide **118**, resorcinol, K_2CO_3, and CuO in pyridine for one week gave basket **119** in a remarkable 88% yield (Scheme 4.1).[153] This corresponds to a greater than 98% yield for each bond being formed.

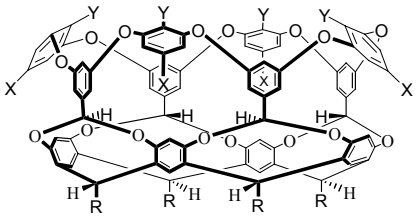
The formation of the basket from octabromide **118** is a general process that can be expanded to include the syntheses of a series of molecular baskets **120**-**124** (R = CH_2CH_2Ph) by reacting the octabromide **118** with 2,7-dihydroxy-naphthalene, hydroquinone, 2-methyl-resorcinol, 5-methyl-resorcinol, 3,5-dihydroxybenzyl alcohol in 70%, 45%, 80%, 88%, and 60% yields respectively. Compound **123**, **124** were synthesized previously in this laboratory.[167] We have also tried this reaction with catechol. As a result, an intractable polymeric mixtrue was obtained.



120 (70%)



121 (45%)



122 X = H, Y = Me (80%)

123 X = Me, Y = H (88%)

124 X = CH_2OH, Y = H (60%)

For all these successful syntheses of baskets, the yields were generally high. One exception was the synthesis of basket **121**. In the literature, hydroquinone was reportedly to give low yields upon performing Ullman ether synthesis on it.[168] The authors proposed the reason to be the ready oxidation of dianions from hydroquinone by cupric ion from the catalyst. However, the 45% yield of **121** still represents a 90% yield of each Ullman ether reaction. Although we had no success using 3,5-dihydroxybenzoic acid and 3,5-dihydroxy benzaldehyde (the former gave no reaction, and the latter gave a small amount of partly bridged material; presumably, the electron-withdrawing substituents on resorcinol decreased the nucleophilicity of the phenoxide moiety), 3,5-dihydroxybenzyl alcohol when treated under the reaction condition, furnished basket **124** smoothly in a moderate 60% yield. This reaction required more

concentrated conditions than those used in the synthesis of **119-123**. As a result, the amount of intractable polymer increased, at the expense of **124**.

An x-ray structure analysis was performed on basket **124**. The crystal was obtained from the slow evaporation of a solution of **124** in THF / $CHCl_3$. Figure 4.1 showed the crystal structure of this compound. The third-row aromatic rings adopt an "open" conformation; similar to those found in other baskets such as **119**, **122**, and **123**.[153,169] A guest $CHCl_3$ molecule is situated inside the cavity. One of the chlorine atoms of $CHCl_3$ is located at the near bottom of the cavity, aligned with the benzal crown of the host molecule. Presumably, this complexation is driven by the C-H···Cl···R hydrogen bonds, similar to those investigated in basket **119**.[153]

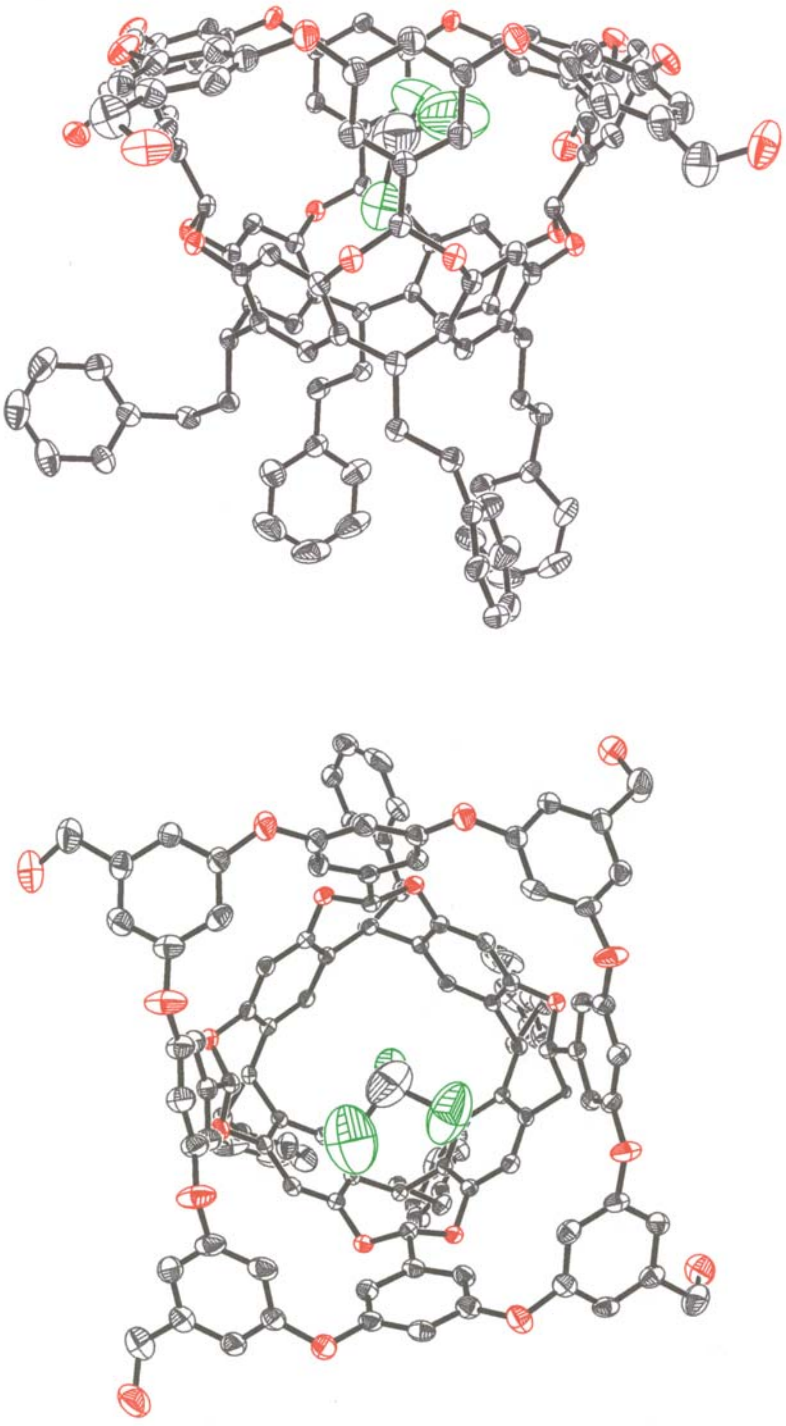


Figure 4.1 ORTEP view of basket **124**. A solvent $CHCl_3$ molecule is inside the cavity. Thermal ellipsoids are plotted at the 50% probability level. (Above: side view; Below: top view) Structure solved by Prof. Edwin Stevens at the University of New Orleans.

The NMR spectrum of **124** in DMSO-d_6 is shown in Figure 4.2. At room temperature, the spectrum gave broad peaks, due to the aggregation of the hydroxy groups on the rim of the molecule. The spectrum became well-resolved at elevated temperature. The aggregation was further confirmed by the dilution experiment. Diluting the NMR sample resulted in better resolution of the spectrum.

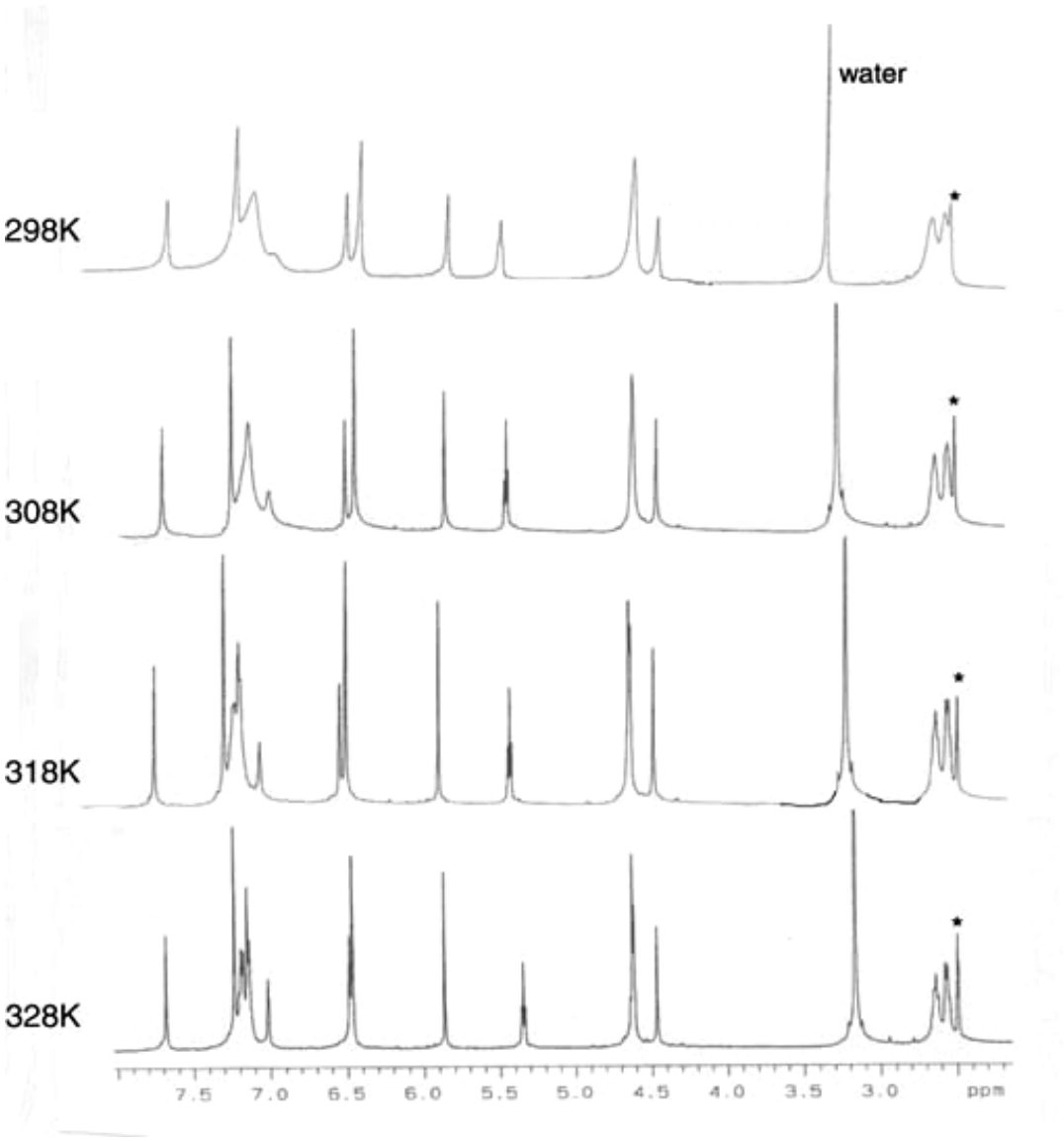
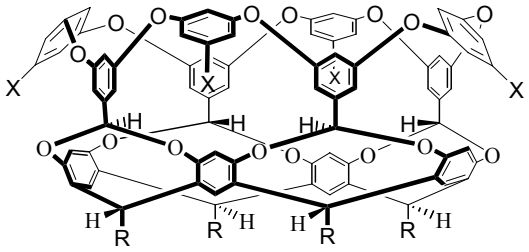


Figure 4.2 VT NMR of **124** in DMSO-d_6 (500 MHz, ∗ : solvent DMSO-d_6)

Compared to the other baskets, **124** has four benzyl alcohol groups on the upper rim which are easily functionalizable to allow the addition of new functional groups on the basket. For instance, treating **124** with *p*-toluenesulfonyl chloride (TsCl) gave basket **125** in almost quantitative yield. This simple step transformed the benzyl alcohol groups into excellent leaving groups. Thus, four elctrophilic centers were created and the way to a wide variety of functionalized molecular baskets was open. An example was the preparation of the fluorine-tagged basket **126**.[¶] Thus, refluxing **125** with "anhydrous"[170] TBAF (tetrabutylamonium fluoride) in THF yielded the desired product at 53% yield (Scheme 4.4). It is noted that in order to obtain a reasonable yield, commercially available hydrated TBAF had to be pre-treated (heat at 40-50ºC at 0.1 mmHg) to remove most of the water.



Scheme 4.4 Key: a. TsCl, KOH, THF (97%). b. TBAF, THF, heat (53%).

[¶] This compound was synthesized for a collaboration with Professor V. Rotello in University of Massachusett, Amherst to conduct surface, self-assembly studies of the baskets.

The NMR of **126** is shown in Figure 4.3. The most characteristic peak is the doublet at *ca*. 5.5 ppm. It corresponds to the benzyl protons at the upper rim of the basket. They are coupled to the adjacent F atom, with a coupling constant of 46.8 Hz.

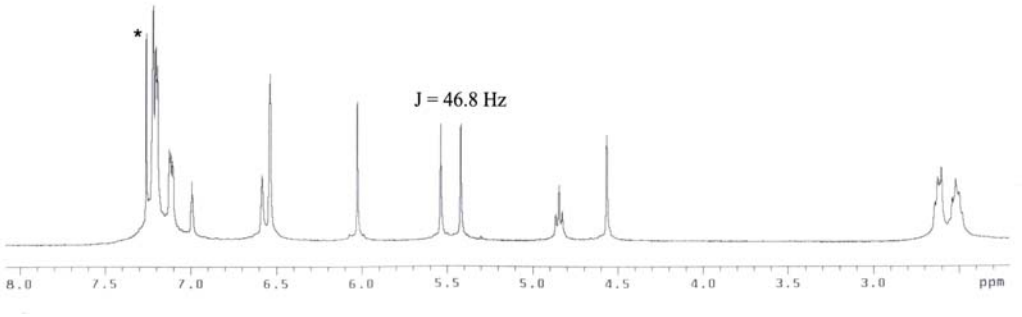


Figure 4.3 ^{1}H NMR spectrum of **126**. (400 MHz, ∗ : solvent $CDCl_3$)

Earlier results from this laboratory have demonstrated that these basket-shaped compounds are good hosts for adamantanes.[153,169,171] For example, basket **119** binds to a variety of adamatane derivatives. Although adamantane and most substituted adamantanes bind weakly, halogenated substituted adamantanes bind to the basket very strongly.[153] Generally, halogen adamantanes bind to **119** with the halogen atom down into the base of the cavity.[153] It is believed that the binding occurs *via* a C-H···X interaction between the benzal crown inside the cavity, and the halogen atom of the guest. Basket **123**, with methyl substituents on the 5- position of the third-row aromatic rings, has similar binding affinity towards the adamatoid guests. The substituted adamantane guests predominately adopt the orientation with the functional groups down within the cavity in non-

polar solvents which are not capable of forming hydrogen bonds with the guest molecule or competing with the binding of the guest (Figure 4.4).[169] However, basket **122**, in which case the methyl groups are on the 2- position, the binding towards adamantanes is completely shut down.[169] Obviously, the four methyl groups at the portal of the cavity reduce the size of the entrance and thus inhibit the complexation.

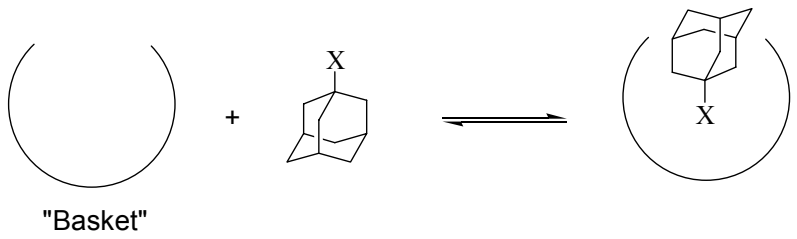
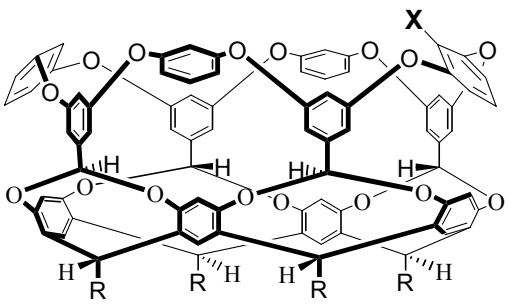


Figure 4.4 Cartoon representation of guest orientation within the cavity of the baskets.

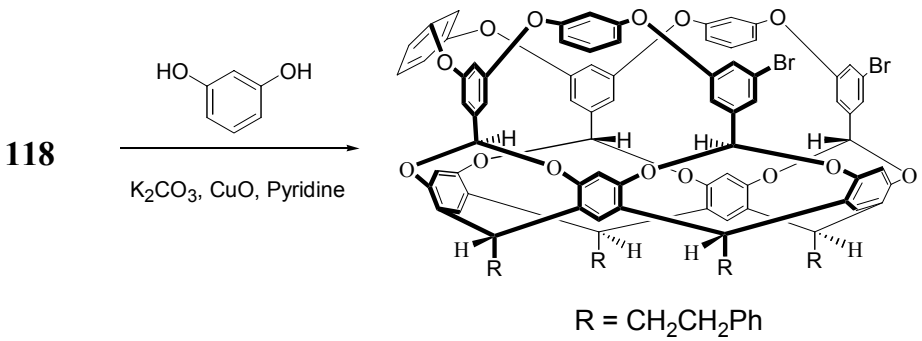
As an extension of this work, the synthesis and binding properties study of relatively low symmetry baskets were carried out. More specifically, the synthesis of mono-functionalized baskets with a general structure shown in Figure 4.5 was proposed. The substituent X group at the entrance of the cavity should alter the complexation rate and the orientation of the guests. Two successful examples were mono-functionalized baskets **127** and **128**.[172] Compound **130**, which has a methyl substituent, is expected to slow down the complexation rate; while basket **132**, which possess an electron-rich hydroxy group, is expected to also affect the orientation of suitably functionalized guests by hydrogen bonding.



127 X = Me; **128** X = OH

Figure 4.5 Mono-functionalized baskets.

Key to the synthesis of these mono-functionalized baskets is the dibromide **129**.[171] It was formed by a combination of three molecules of resorcinol and one molecule of octabromide **118**, using a six-fold Ullman ether reaction (Scheme 4.5). Efforts were made to optimize the yield of **129** by changing reaction



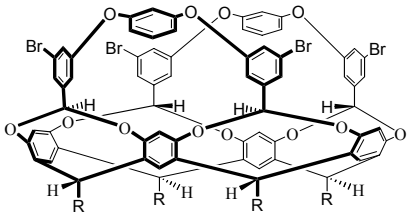
129

Scheme 4.5 Synthesis of key intermediate **129**.

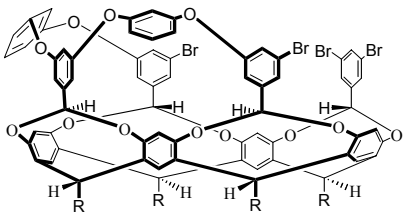
variables such as the equivalents of the reagents, the reaction time and temperature, *etc*. in turn. However, the best yield obtained was 35%.[¶] Quantities of bis-bridged cavitand and tetra-bridged (basket) **119** (18% and 25% respectively) were also obtained in these reactions. Varying the equivalents of the reagents from 150% to 250% of stochiometry made little difference on outcome of the reactions. A vigorous reflux of the reactions was required. Changing the temperature to less than the boiling point of the pyridine solvent completely shut down the reactions. Only starting materials were recovered. The reaction time had a significant effect on the reaction outcome. Refluxing the mixture for two days gave only trace of tris-bridged intermediate **129**, along with sizable quantities of bis- and mono-bridged cavitands, and the starting material **119**. Keeping the reaction under reflux for three days gave the highest yield of the tris-bridged cavitand **129**. More than three days drove the reaction to near completion, *i.e*., after four days the fully bridged product **119** was obtained at 50% and the desired **129** was obtained at only 7%.

Interestingly, of the two possible bis-bridged species (Figure 4.6), it was only the A/C isomer (**130a**) that was obtained in sizable quantities. Despite the fact that statistics suggest that the A/B : A/C isomers ratio should be formed in *ca.* 2:1, only traces of A/B isomer (**130b**) was ever observed in these reactions.

[¶] The optimization of this reaction was carried out in collaboration with Gibb, C.L.D., Upton, T.G., and Ugbema, M. from this laboratory.



A/C Bis-bridged cavitand (130a)



A/B Bis-bridged cavitand (130b)

Figure 4.6 The two bis-bridged cavitand isomers.

The reason for the preference of the formation of **130a** over **130b** is tentatively illustrated below. The insertion of the first resorcinol moiety gave mono-bridged compound **131a**, whose CPK model is shown in Figure 4.7. As indicated, the two bromine atoms on the bridged aromatic rings were splayed open, creating a large distance between the remaining bromine atoms on the bridged aromatic rings and the bromine atoms on the free aromatic rings. On compound **131a**, the bridging of the adjacent aromatic rings stopped the free rotation around the two bonds shown in **131b** (Scheme 4.6). It may be much easier for the second resorcinol moiety to bridge between the remaining two free aromatic rings. This results in the predominant formation of A/C isomer **130a**.

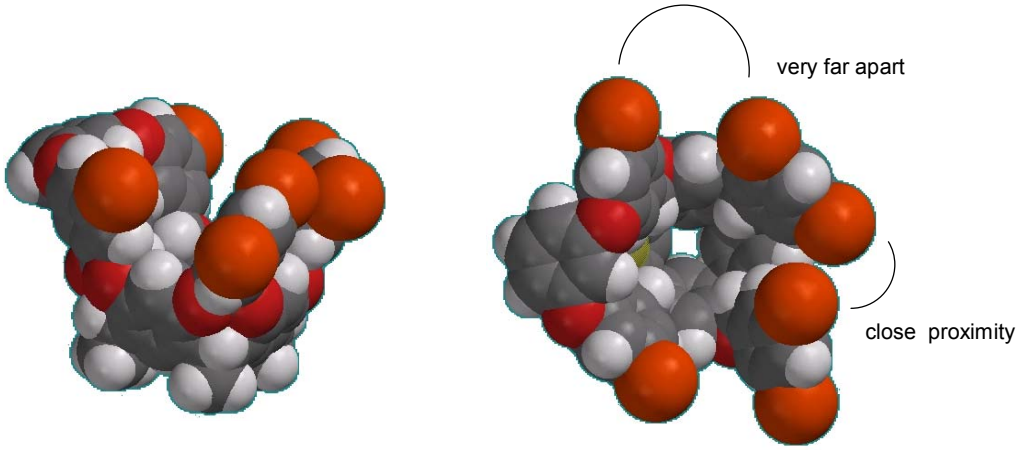
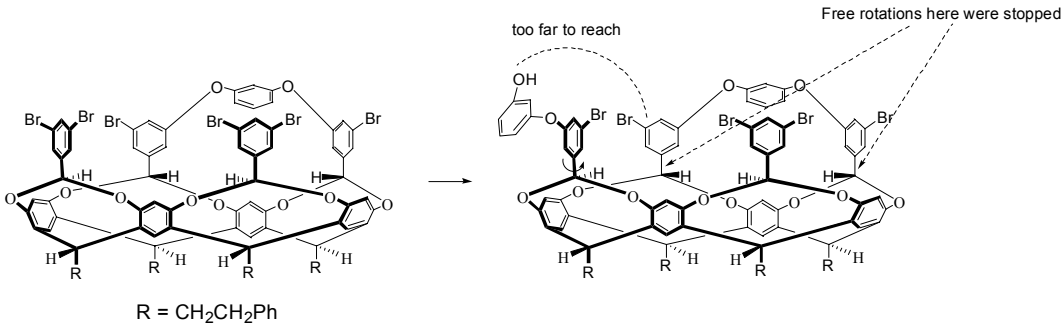
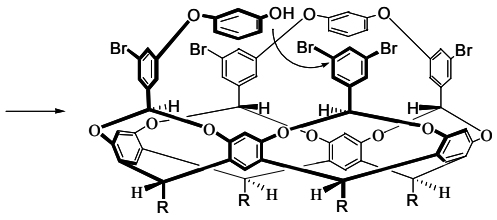


Figure 4.7 CPK model of mono-bridged species **131a**. (left: side view; right: top view)



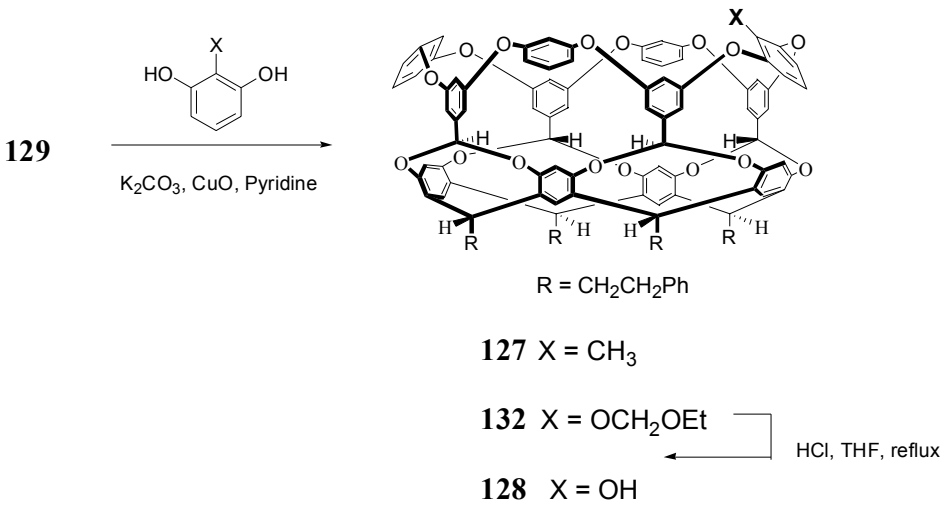
131a **131b**



130a

Scheme 4.6 Preference of the formation of A/C isomer **130a**.

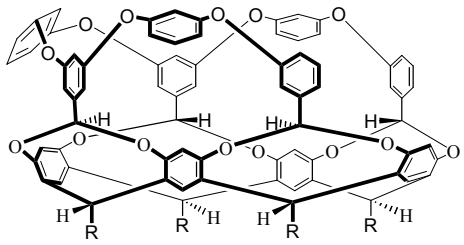
With quantities of **129** in hand, it was relatively straightforward to react it with 2-methyl resorcinol and form the monomethyl derivative **127** in 90% yield (Scheme 4.7).



Scheme 4.7 Formation of mono-functionalized baskets.

The formation of monophenol derivative **132** (Scheme 4.7), however, was slightly more problematic. Direct reaction between **127** and pyrogallol (1,2,3-trihydroxy benzene) gave a new compound in near quantitative yield. It was identified as the debrominated species **133**. Presumable, the 1,2-diol moiety of pyragallol was acting as a reductant and reductively debrominating the starting material via a $Cu^{+} \rightarrow Cu^{0}$ process. Thus, the pyragallol reactant was mono-protected ($X = OCH_2OEt$) at the 2-position. This product did not possess the requisite H atom that must be lost during the oxidation of pyragallol. Indeed, this mono-protected pyragallol reacted smoothly with **129** to give basket **132**. Normal

conditions (2% HCl in THF, room temperature) did not result in the removal of the protecting group. Apparently, the protecting group is itself protected within the confined cavity. However, by using more vigorous condition (HCl, THF, reflux), the protecting group was removed to give the desired monophenol basket **128** in quantitative yield.

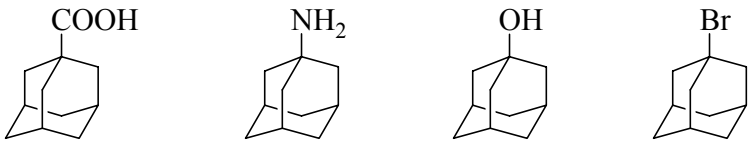


R = CH_2CH_2Ph

133

The reaction between **129** and 2-amino-resorcinol was also attempted. Unfortunately, a debromination process similar to that of pyragallol occurred. As a result, **133** was obtained in over 50% yield. Protecting the amino group with acetate and react the resulting product (X = NHAc) with **129** gave a intractable polymeric mixture. The reactions of **129** with 2,6-dihydroxybenzoic acid (X = COOH) and 2,6-dihydroxybenzyl alcohol (X = CH_2OH) were also attempted. The former gave 80% yield of **119**, and the latter gave 20% of **119** along with 80% starting material. Clearly, under the vigorous reaction conditions, oxidation of benzyl alcohol and decarboxylation of carboxylic acid occurs. We were also unsuccessful with 2,6-dihydroxybenzoic methyl ester. An intractable mixture was again obtained.

The binding behavior of **127**, **128** along with that of **119** were studied in detail.[¶] Table 4.1 listed a few examples of binding constants of these three hosts towards four different adamatanoid guests **G1**-**G4**. Compared to **119**, host **127**, which has a methyl group at the entrance, significantly reduced the binding affinity towards the admantane derivatives guests. Host **128**, which has a hydroxyl group located at the entrance, increased the binding of the guests which were potentially capable of forming hydrogen bonds with the hydroxy group. This was especially true for binding with 1-amino-adamantane (**G2**). The presence of one hydroxyl group increased the association constant by more than nine fold. Presumably, **G2** binds to **128** through a salt bridge interaction.[172]



G1 **G2** **G3** **G4**

Table 4.1 Selected data of association constants between guests **G1**-**G4** and the hosts **119**, **127**, **128** in toluene-d_8 at 298K (unless otherwise noted)

Guest	Host **111**	Host **127**	Host **128**
G1	18[a]	0[a]	46[a]
G2	120[a]	23[a]	10,000[b]
G3	77[a]	14[a]	930[a]
G4	1,700	190	1,100

a : Associate constants determined at 248K.
b : Determined by competition experiments with 1-bromoadamantane (**G4**).

[¶] This part of work was done by Corinne L.D. Gibb from this laboratory.

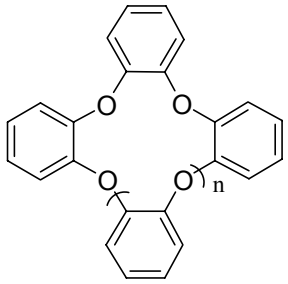
The presence of OH group in **128** can also affect the orientation of the guests. For examples, **G2** bound to baskets **119**, **127** with the functional group (NH_2) down, while it bound to **128** with the functional group exclusively up, due to the hydrogen bonding between OH and NH_2. Similarly, **119** bound **G1** with no preferential orientation of the functional group (COOH), *i.e*., the two possible isomers $\mathbf{G1}_{COOH\downarrow}$ and $\mathbf{G1}_{COOH\uparrow}$ are formed at *ca.* 1:1 ratio. However, when **G1** bound to **128**, the COOH group was exclusively pointing up and forming hydrogen bond with the hydroxyl group of the host. These observations demonstrated how subtle change in these hosts could dramatically alter their binding behaviors.

V. TEMPLATED SYNTHESIS OF LARGE CROWN ETHERS

The use of the templation effect has become an increasingly important aspect of supramolecular chemistry.[76] Templates provide instructions for the formation of a single product from a substrate, or substrates, which otherwise have the potential to assemble and react in different ways to give different products. Crown ethers [173-177] are a class of compounds whose synthesis predominantly relies on templation.[82,85,178-180] Usual metal ions, that the resulting crown ethers will bind to, are used as templates. In these cases, the template ions are coordinated with the donor atoms on the cyclic backbone of the substrates *via* ion-dipole interactions (see Scheme 1.24). However, templation is less useful for the synthesis of crown ethers possessing more than approximately twenty-four atoms in their macrocyclic chain. Hence, these are usually synthesized in a stepwise manner. Low yields are usually associated with large crown ethers synthesized in this fashion due to the long synthetic routes, often slow cyclization step, and general purification difficulties.[181-183]

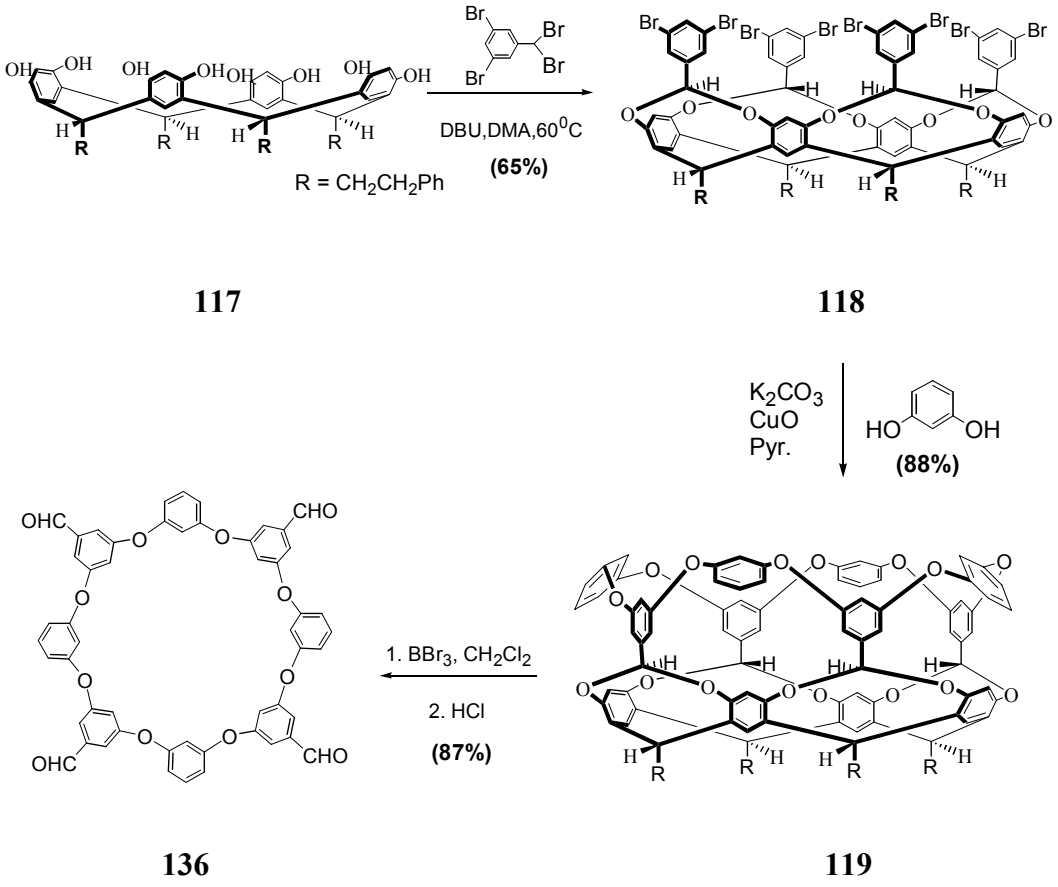
Because of the aforementioned difficulties, large, fully aromatic crown ethers are rare. The only two examples that have been reported, are hexabenzo-

18-crown-6 **134** and heptabenzo-21-crown-7 **135**.[184] Both were synthesized in low yield (<0.1%) using multiple Ullman ether reactions. The general difficulty in accessing these compounds prevented thorough investigation of their properties. Described here is a novel approach to synthesizing this type of compounds, using resorcinarenes as templates.



134 (n = 1) **135** (n = 2)

In the previous chapter, the syntheses of a variety of molecular baskets was described. This process can be viewed as the addition of two rows of aromatic rings onto the resorcinarene (octol) **117** template. Removal of this template generates the fully aromatic crown ethers (Scheme 5.1). Following this general route, a large variety fully aromatic crown ether compounds have been synthesized.



Scheme 5.1 Template assisted synthesis of crown ether **136**.

In order to remove the template, four acetals need to be broken. Initially, removal of the template was attempted by treating the basket with dilute, aqueous HCl in THF. Only starting material was recovered. Indeed, only starting meterial was recovered even after refluxing **119** in 1:1 sulfric acid and ethanol for a week. Presumably, due to the reversible nature of the reaction (Figure 5.1), each acetal group that had been cleaved has the chance to reform before a second acetal can be broken.

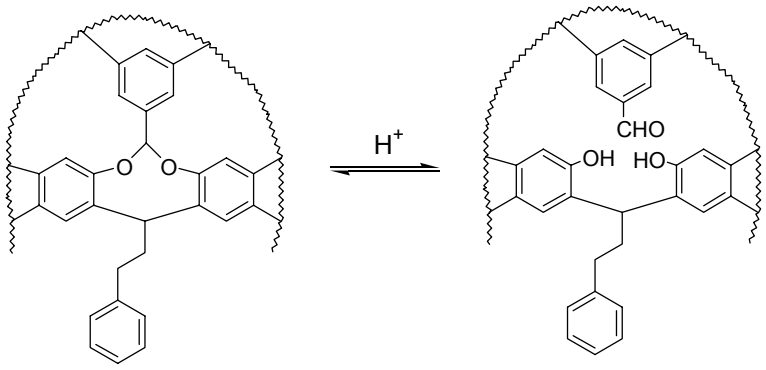


Figure 5.1 Reversible acetal cleavage and formation.

Fortunately, a stronger Lewis acid, BBr_3, furnished the removal of the template smoothly (Scheme 5.1) *via* an irreversible mechanism. Thus, treatment of a CH_2Cl_2 solution of **119** with BBr_3 at room temperature for one hour, removed the resorcinarene (octol) template efficiently. The template could be readily recovered in near quantitatively yield by column chromatography. However, although the resulting crude product showed primarily a single spot by TLC, it gave very complex NMR pattern (Figure 5.2a). This problem was soon overcome by adding a hydrolysis step to the reaction. After hydrolysis, the crude NMR showed essentially the desired product (Figure 5.2b). The fully aromatic crown ether **136** was isolated in 87% yield. Presumably, the complex NMR pattern arised because of the heterogenious substituents (presumably, the substituents may include aldehydes, benzal bromides, boronic ester derivatives, *etc*.) on the aromatic rings. An effective hydrolysis converted all substituents into aldehyde groups. The exact composition of the crude product before hydrolysis, and the mechanism of this hydrolysis step, were not determined. It was observed that

whereas HCl, HBr were effective in promoting the hydrolysis, H_2SO_4 failed to convert the mixture to clean desired product. A slightly weaker Lewis acid BCl_3 also furnished the removal of the template, but lower yields were obtained. Weaker Lewis acid such as $AlCl_3$ failed to remove the template.

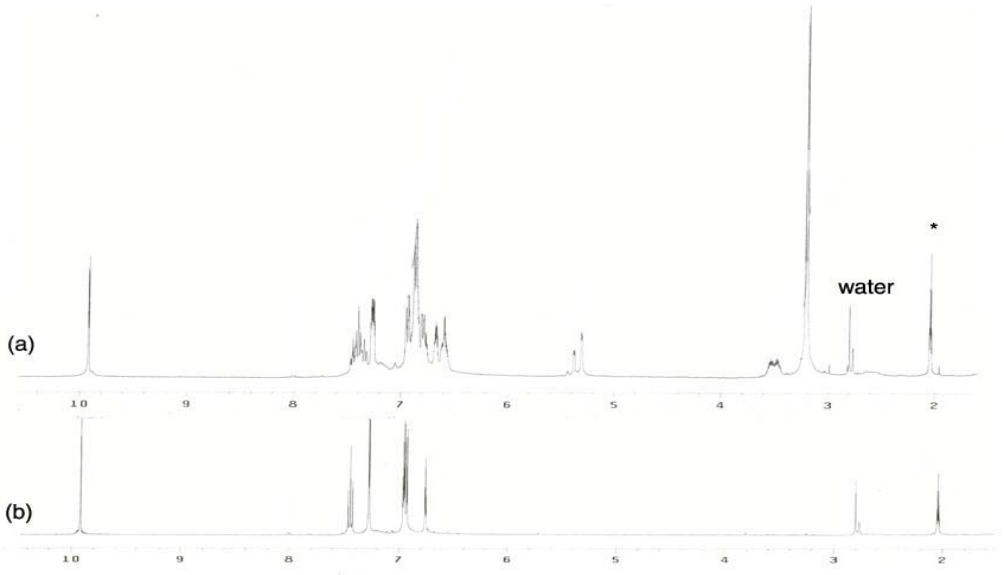
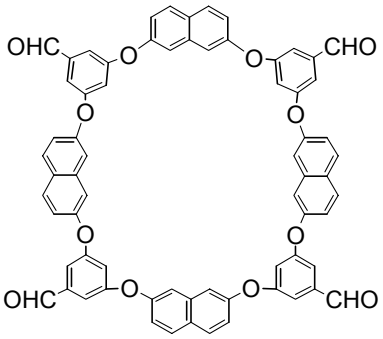


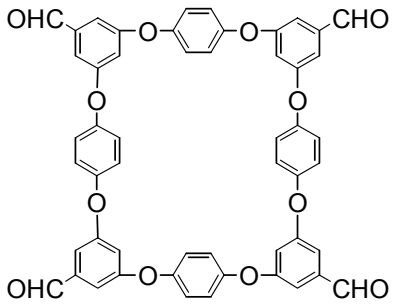
Figure 5.2 NMR spectra (a) before and (b) after the hydrolysis of the crude product from the reaction between **119** and BBr_3. (400 MHz, * : solvent CD_3COCD_3 peaks)

Exposing **120**, **121**, **122**, and **123** to BBr_3 under similar conditions gave the corresponding 40-crown-8 **137**, 36-crown-8 **138**, and 32-crown-8 ethers **139**, **140** in 85-95% yields. The same conditions failed to lead to the clean cleavage of **124**, presumably due to the extremely low solubility of **124** in CH_2Cl_2. Fortunately, it was discovered that using $SOCl_2$ as a solvent and BCl_3 as the Lewis acid, removed the template efficiently. In this process, the benzyl alcohol

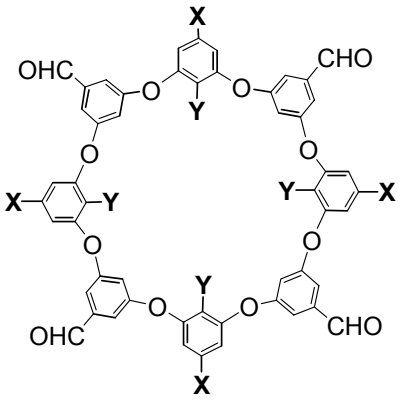
groups were converted into benzyl chlorides. The highly functionalized **141** was produced in 71% yield. This compound is of particular interest because each aromatic ring possesses a readily functionalizable substituent. However, using the combination of $BBr_3/SOCl_2$ resulted in the formation of an inseparable mixture of macrocycles arising from Br/Cl exchange.



137

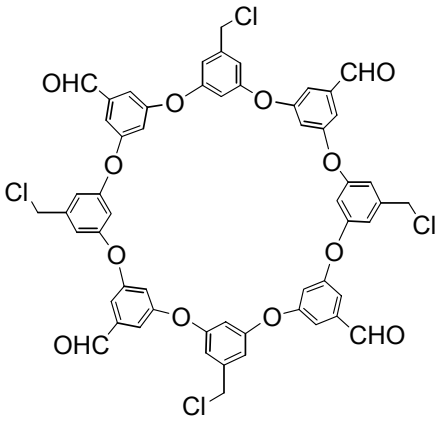


138



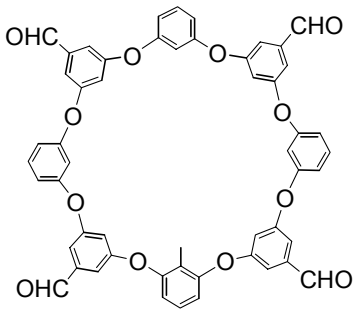
139 X = H, Y = Me

140 X = Me, Y = H



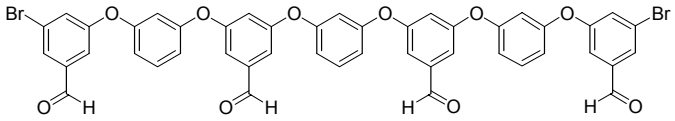
141

Additionally it is worth mentioning that the less symmetric basket **127**, when treated under the same condition, underwent a clean cleavage and generated the lower symmetry, 32-crown-8 **142**.



142

Finally, partially bridged cavitands such as **129** lead to acyclic derivative **143**. Such derivatives may find utility as subunits for the synthesis of larger macrocycles, or as components in co-block polymers.



143

In summary, an effective method in synthesizing aromatic crown ethers using resorcin[4]arene as a template has been demonstrated. A simple three steps process gives the products at up to 50% overall yields. To the author's best knowledge, this is the first example of covalent template assisted synthesis of crown ether compounds. This process may be a general strategy to synthesize

large macrocycles. By varying the reaction conditions, it is possible to bridge non-aromatic components onto the template, which will lead to large macrocycles with aliphatic fragments in the backbones. Furthermore, with the development of expanded [n]cavitands, where n is greater than 4,[185] access to even larger sized macrocycles is also possible with this methodology.

VI. CONCLUSION

Novel ligands for carbonic anhydrase mimicry have been synthesized. The general strategy to synthesize these trispyridylmethanol derived ligands are described. The two-step synthesis towards such structure gives the desired products in higher overall yields than the traditional one step synthesis. This also opens a way to less symmetry trispyridyl ligands.

The synthesis and assembly of tetraphenylmethane based subunits has been described. This relatively straightforward method generates a variety of macrocycles with size as large as 3 nm. The potentially multi-generation coupling of this subunit is also discussed. For the purpose of multi-generation coupling, the suitable protecting group and the compatible self-assembly condition are illustrated.

A new, efficient covalent template assisted synthesis of fully aromatic crown ethers is shown. The simple three-step process induces over a thousand folds increase in yields compared to similar compounds synthesized by conventional means. As intermediates from this process, a variety of molecular "baskets" which can be used in carceplex formation are obtained.

VII. EXPERIMENTAL SECTION

7.1 General

All reagents were purchased from Aldrich Chemical Company and were used as received without further purification (unless otherwise noted). Melting points were determined using a hot-stage apparatus and are uncorrected. ^{1}H NMR was performed at either 400 MHz or 500 MHz. ^{13}C NMR was performed at 75 MHz. Mass spectra were obtained with CI, ESI or MALDI technique. Elemental analyses were conducted by Atlantic Microlab. Column chromatography was performed using Natland® International 200 – 400 mesh silica gel. Diethyl ether, THF were distilled over sodium benzophenone ketyl. All other organic solvents for reactions were stored over molecular sieves. dimethylformamide, dimethyl-acetamide, and dimethylsulfoxide were degassed before use. All reactions were carried out under nitrogen atmosphere.

7.2 Synthesized Compounds

Bis(2-(6-bromopyridyl)ketone 88

A solution of of 2,6-dibromo-pyridine (5.0 g, 21mmol) in 150 mL diethyl ether was cooled down to -78°C. To this stirred solution was added dropwise *n*-

BuLi (19 ml, 1.2 M solution in hexanes, 23 mmol), followed by the slow addition of a solution of diethyl carbonate (1.2 ml, 9.5 mmol) in 20 mL diethyl ether. The reaction was left to react at –78°C for 2 h. After this time, it was allowed to warm up to *ca*. 0°C and then quenched with 10% aqueous HCl until acidic. The mixture was then basified with 10% K_2CO_3 and the mixture was partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4, after the addition of some decolorizing carbon the solution was filtered and the solvent removed under reduced pressure. Rerystallization from acetone / hexanes afforded the ketone **88** (2.4 g, 7.0 mmol, 67%) as colorless needles. Mp. 155-156 °C (Lit.[186] 155-156.5ºC). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.70 (dd, *J* = 8.0 Hz, 0.8 Hz, 2H), 7.76 (pseudo t, *J* = 8.0 Hz, 2H), 8.09 (dd, *J* = 8.0 Hz, 0.8 Hz, 2H).

Tris(2-(6-bromopyridyl)methanol 89

A solution of 2,6-dibromopyridine (1.09g, 4.62 mmole) in 46 mL diethyl ether was cooled down to –78^{0}C. To this solution was added *n*-BuLi (4.20 mL, 1.2 M solution in hexanes, 5.06 mmol) dropwise. Then a solution of ketone **88** (1.43 g , 4.20 mmole) in 14 mL THF was added to the lithiated solution dropwise. The stirred solution was left to react at -78°C for 2 h and then allowed to warm up to *ca*. 0°C and quenched with 10% HCl until acidic. The resulting mixture was basified with 10% aqueous K_2CO_3 solution. The biphasic mixture was partitioned between $CHCl_3$ and water three times. The organic layer were combined, dried with anhydrous Na_2SO_4 and salts filtered off. Removal of the solvent under

reduced pressure gave the crude product as a yellowish solid. Column chromatography with a mobile phase of 1% acetone in hexanes gave the alcohol **89** (1.64 g, 3.28 mmol, 78%) as a white solid. Mp. 146-147ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.59 (s, 1H), δ 7.39 (d, J = 7.3 Hz, 3H), 7.56 (pseudo t, J = 8.1 Hz, 7.3 Hz, 3H), 7.71 (d, J = 8.1 Hz, 3H). ^{13}C NMR (75 mHz, $CDCl_3$) δ (ppm) 80.4, 122.2, 127.4, 139.1, 140.3, 162.9. IR (film) cm^{-1} 3406, 1591, 1566, 1436, 1412, 1168, 1143, 993, 808, 759. MS m/z 500 M^+, 422 $[M\text{-}Br]^+$. Anal. Calcd. for $C_{16}H_{10}N_3Br_3O$: C, 38.44; H, 2.02. Found: C, 38.70; H, 2.01.

Tris(2-(6-bromopyridyl)methanol methyl ether 90

The 60% oil suspension of NaH (0.62 g, 16 mmol) was washed twice with pentane and added to 104 mL THF. To this stirred mixture was added the alcohol **89** (1.56 g, 3.11 mmol) and iodomethane (0.97 mL, 17 mmol). The mixture was stirred at 60°C for 16h. After cooling to rt, the mixture was quenched with an excess of 10% aqueous HCl until acidic, and then basified with 10% aqueous K_2CO_3 solution. The mixture was then partitioned between $CHCl_3$ and water three times. The organic layers were combined and dried with anhydrous Na_2SO_4, and salts filtered off. Removal of the solvent under reduced pressure gave the crude product as a yellowish solid. Column chromatography with a mobile phase of 10% acetone in hexanes gave the desired product **90** (1.3 g, 2.6 mmol, 82%) as a white solid. Mp. 128^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.31 (s, 3H), 7.37 (d, J = 7.3 Hz, 3H), 7.54 (pseudo t, J = 7.3 Hz, 8.1 Hz, 3H), 7.61 (d, J = 7.3 Hz, 3H). ^{13}C NMR (75 mHz, $CDCl_3$) δ (ppm) 53.5, 87.4, 123.6, 127.2, 138.6, 140.5,

161.8. IR (film) cm^{-1} 2957, 2837, 1601, 1576, 1437, 1412, 1168, 1143, 998, 804, 759, 709. MS m/z 514 M^+, 436 $[M\text{-}Br]^+$. Anal. Calcd. for $C_{17}H_{12}N_3Br_3O$: C, 39.72; H, 2.35. Found: C, 39.92; H, 2.37.

2-Bromo-6-pyridinecarboxaldehyde 91

A sloution of 2,6-dibromopyridine (10.0 g, 42.2 mmol) in 200 mL diethyl ether was cooled down to -78ºC. To this stirred solution was added *n*-BuLi (16.9 mL, 2.5 M solution in hexanes, 42.2 mmol) dropwise. After stirring the lithiate for 5 min, an solution of *ca*. 4 mL DMF in 20 mL diethyl ether was added over 10 min. The reaction was then allowed to warm up to *ca*. –10°C. At this point, an excess of 5% aqueous HCl was added to quench the reaction until acidic and the resulting biphasic mixture was stirred for an additional 10 min. The mixture was then basified with 10% aqueous K_2CO_3 and partitioned between ether and water three times. The organic layers were combined and dried with anhydrous Na_2SO_4 and salts filtered off. Removal of the solvent under reduced pressure gave the crude product as a yellowish oil. Column chromatography with a mobile phase of 2% acetone in hexanes gave the 2-bromo-6-pyridinecarboxaldehyde **91** (5.10 g, 27.4 mmol, 65%) as a white solid. Mp. 78.5-79ºC (Lit.[187] 77-78ºC). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72~7.78 (m, 2H), 7.93 (dd, J = 6.4 Hz, 2.4 Hz, 1H), 10.0 (s, 1H).

2-Bromo-6-pyridylcarbinol 92

To a solution of the aldehyde **91** (6.55g, 34.2 mmol) in 150 mL methanol was added solid $NaBH_4$ (1.29 g, 34.2 mmol). The reaction was stirred for 1 h at rt. After this time the reaction was quenched with 5% aqueous HCl and then concentrated under reduced pressure. The solution was then basified with 5% aqueous K_2CO_3 and partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. Removal of the solvent under reduced pressure gave the crude product as a yellowish oil. Column chromatography with a mobile phase of 8% ethyl acetate in $CHCl_3$ gave the alcohol **92** (6.37 g, 33.9 mmol, 99%) as a viscous oil which solidified on standing. Mp. 36-37ºC (Lit.[188] 36-37ºC). ^{1}H NMR (400 MHz, Acetonitrile-d_3) δ (ppm) 3.53 (t, J = 5.8 Hz, 1H), 4.61 (d, J = 5.9 Hz, 2H), 7.41~7.42 (m, 1H), 7.44~7.46 (m, 1H), 7.66 (dd, J = 7.7 Hz, 7.7 Hz, 1H).

2-Bromo-6-pyridylcarbinol ethoxymethyl ether 93

To a stirred solution of the alcohol **92** (9g, 48.2 mmol) in 35 mL DMF was added diisopropylethyl amine (8.39 mL, 121 mmol) and chloromethyl ethyl ether (6.71 mL, 72.3 mmol). After stirring at rt for 16 h, the solvent was removed under reduced pressure. The mixture was partitioned between $CHCl_3$ and water three times. The organic layer were combined, dried with anhydrous Na_2SO_4, and salts filtered off. Removal of the solvent under reduced pressure gave the crude product as a yellowish oil. Distillation of the crude material gave **93** (10.7 g, 43.4 mmol, 90%) as a colorless oil. Bp. 113^{0}C (0.6 mmHg). ^{1}H NMR (400 MHz,

$CDCl_3$) δ (ppm) 1.22 (t, *J* = 7.3 Hz, 3H), 3.65 (q, *J* = 7.3 Hz, 2H), 4.70 (s, 2H), 4.82 (s, 2H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.56 (pseudo t, *J* = 7.3 Hz, 8.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 15.3, 63.8, 69.6, 95.2, 120.1, 126.8, 139.1, 141.5, 160.2. IR (film) cm^{-1} 2937, 2851, 1601, 1576, 1451, 1422, 1133, 1053, 799. MS m/z 247 $[M+H]^+$. Anal. Calcd. for $C_9H_{12}NBrO_2$: C, 43.92; H, 4.91. Found: C, 44.04; H, 4.90.

Bis(2-(6-pyridylcabinol ethoxymethyl ether)ketone 94

A solution of **93** (2.35g, 9.55 mmol) in 40 mL THF was cooled down to -78ºC. To the stirred solution was added *n*-BuLi (8.75 mL, 1.2 M solution in hexanes, 10.5 mmol) dropwise. This was followed by the slow addition of a solution of diethyl carbonate (0.58 mL, 4.8 mmol) in 16 mL THF. The mixture was left to react at -78ºC for 2 h and then allowed to warm up to *ca.* 0°C. At this point water was added to the solution to quench the reaction and it was then basified with 10% aqueous K_2CO_3 solution. The mixture was then partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4, and salts filtered off. Removal of the solvent under reduced pressure gave the crude product as a yellowish oil. Column chromatography with a mobil phase of 4% acetone in hexanes gave the ketone **94** (0.84g, 2.3 mmol, 49%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.22 (t, *J* = 7.0 Hz, 6H), 3.65 (q, *J* = 7.0 Hz, 4H), 4.79 (s, 4H), 4.84 (s, 4H), 7.66 (d, *J* = 7.8 Hz, 2H) 7.87 (pseudo t, *J* = 7.8 Hz, 7.8 Hz, 2H), 8.00 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 15.1, 63.6, 70.1, 95.1, 123.9, 124.3; 137.1,

153.4, 158.4, 192.6. IR (film) cm^{-1} 2997, 2947, 2897, 1696, 1596, 1457, 1402, 1372, 1337, 1237, 1197, 1168, 1128, 1058, 854, 814, 764. MS m/z 361 $[M+H]^+$. Anal. Calcd. for $C_{19}H_{24}N_2O_5$: C, 63.32; H, 6.71. Found: C, 63.30; H, 6.77.

1

Tris(2-(6-pyridylcarbinol ethoxymethyl ether)-methanol 95

A solution of **93** (0.26g, 1.1 mmol) in 10 mL diethyl ether was cooled down to -78ºC. To this stirred solution was added dropwise *n*-BuLi (0.98 mL, 1.2 M solution in hexanes, 1.2 mmol), followed by the slow addition of a solution of ketone **94** (0.34g, 0.95 mmol) in 5 mL diehtyl ether. The mixture was then left to react for 2 h and then allowed to warm up to *ca*. 0°C. Water was then added to quench the reaction and the mixture was basified with 10% aqueous K_2CO_3. The biphasic mixture was partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4, and salts filter off. Removal of the solvent under reduced pressure gave the crude product as a yellowish oil. Gradient column chromatography with a mobil phase varying from hexanes to $CHCl_3$ gave the product **95** (0.28g, 0.52 mmol, 55%) as a colorless oil. ^{1}H NMR (400 MHz, acetonitril-d_3) δ (ppm) 1.11 (t, J = 7.0 Hz, 9H) 3.55 (q, J = 7.0 Hz, 6H) 4.55 (s, 6H), 4.71 (s, 6H), 7.08 (s, 1H), 7.33 (d, J = 7.3 Hz, 3H), 7.54 (d, J = 7.3 Hz, 3H), 7.72 (pseudo t, J = 7.3 Hz, 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 15.4, 63.7, 70.3, 81.1, 95.1, 119.8, 122.0, 137.0, 156.4, 162.2. IR (film) cm^{-1} 3326, 3007, 2947, 2907, 1606, 1586, 1472, 1407, 1377, 1197, 1163, 1113, 1058, 794, 769. MS m/z 528 $[M+H]^+$. Anal. Calcd. for $C_{28}H_{37}N_3O_7$: C, 63.74; H, 7.07. Found: C, 63.46; H, 7.10.

Tris(2-(6-pyridylcarbinol ethoxymethyl ether)-methanol methyl ether 96

The 60% oil suspension of NaH (0.31g, 7.8 mmol) was washed twice with pentane and added to 60 mL THF. To this stirred mixture was added the alcohol **95** (0.82 g, 1.6 mmol) and CH_3I (0.49 mL, 7.8 mmol). The mixture was stirred at 60°C for 16 h. After cooling to rt, the mixture was quenched with water and then basify with 10% aqueous K_2CO_3 solution. The mixture was then partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4, and salts filtered off. The solvent was then removed under reduced pressure. Column chromatography with a mobile phase of 10% acetone in hexanes gave **96** (0.69 g, 1.3 mmol, 82%) as a colorless oil. ^{1}H NMR (400 MHz, Acetonitrile-d_3) δ (ppm) 1.10 (t, J = 7.0 Hz, 9H), 3.17 (s, 3H), 3.53 (q, J = 7.0 Hz, 6H), 4.50 (s, 6H), 4.69 (s, 6H), 7.29 (d, J = 7.3 Hz, 3H), 7.49 (d, J = 7.3 Hz, 3H), 7.69 (pseudo t, J = 7.3 Hz, 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 15.3, 53.3, 63.6, 70.6, 88.6, 95.1, 119.4, 123.2, 136.3, 157.0, 161.0. IR (film) cm^{-1} 2997, 2947, 2887, 1606, 1581, 1462, 1407, 1372, 1193, 1158, 1118, 1068, 799, 764. MS m/z 542 $[M+H]^+$. Anal. Calcd. for $C_{29}H_{39}N_3O_7$: C, 64.31; H, 7.26. Found: C, 64.28; H, 7.35.

Tris(2-(6-pyridylcarbinol)-methanol methyl ether 97

To a soultion of **96** (0.50g, 0.92 mmol) in 30 mL MeOH was added *ca.* 1 mL 30% aqueous HCl. The stirred mixture was warmed up to 60°C for 15 min. After cooling to rt, the mixture was partitioned between $CHCl_3$ and water three

times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. Removal of the solvent gave the essentially pure product **97** (0.33 g, 0.91 mmol, 99%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.26 (s, 3H), 4.2~3.8 (s, 3H), 4.64 (s, 6H), 7.09 (d, *J* = 7.3 Hz, 3H), 7.54 (d, *J* = 7.3 Hz, 3H), 7.67 (pseudo t, *J* = 7.3 Hz, 7.3 Hz, 3H). ^{13}C NMR (300 MHz, $CDCl_3$) δ (ppm) 53.3, 63.6, 88.3, 119.0, 122.5, 136.8, 157.4, 159.7. IR (film) cm^{-1} 3356 (broad), 2927, 2857, 1606, 1581, 1462, 1227, 1093, 1008, 784. MS m/z 368 $[M+H]^+$. Anal. Calcd. for $C_{20}H_{21}N_3O_4$•$0.5H_2O$: C, 63.80; H, 5.98. Found: C, 63.79; H, 5.81.

Tris(2-(picolinic acid)methanol methyl ether 84

To a suspension of **97** (0.18 g, 0.49 mmol) and NaOH (0.060g, 1.5 mmol) in 20 mL H_2O was added solid $KMnO_4$ (0.70g, 4.4 mmol). The mixture was stirred at rt for 12 h. An excess of methanol was added to quench the reaction and the mixture was stirred for a further 10 min. The precipitates formed were filtered off and the filtrate was acidified with concentrated HCl. Removal of the solvent under reduced pressure gave the crude product as a white solid. The pure triacid **84** (68 mg, 0.17 mmol, 69%) was isolated by washing the crude product with THF and recrystalization from methanol. Mp. > 400ºC with decomposition. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 3.24 (s, 3H), 7.81 (dd, *J* = 7.6 Hz, 2.0 Hz, 3H), 7.96 (m, 6H), 13.2~12.8 (broad, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 53.2, 88.2, 123.8, 127.9, 137.9, 147.2, 161.1, 166.3. IR (film) cm^{-1} 3475 (broad), 2947, 2867, 1716, 1691, 1591, 1572, 1472, 1392, 1322, 1282, 1098, 1033, 1013,

799. MS m/z 410 $[M+H]^+$, 442 $[M+Na]^+$, 819 $[Dimer+H]^+$. Anal. Calcd. for $C_{20}H_{15}N_3O_7 \bullet H_2O$: C, 56.21; H, 4.00. Found: C, 56.47; H, 4.13.

Tetraphenylmethane (procedure A)

To a stirred solution of anhydrous $ZnCl_2$ (2.9 g, 0.021 mol) in 10 mL diethyl ether was added phenyllithium (27 mL, 1.51 M in cyclohexane / diethyl ether 70/30 solution, 0.040 mol) dropwise. The mixture was stirred at rt for 30 min. The solvent was then removed under reduced pressure, 114 mL CH_2Cl_2 was added to the remaining solid and the temperature was lowered to -42°C using an acetonitrile/dry ice bath. A solution of triphenylmethyl chloride (5.6 g, 0.020 mol) in 20 mL CH_2Cl_2 was then added and the mixture was kept at -42°C while stirring for 5 h. After this time, the flask was removed from the cold bath and warmed up to *ca*. 0°C over 20 min. 1M aqueous HCl was added to quench the reaction until acidic. The mixture was then partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure to give the crude product as a yellow solid. Small amount of diethyl ether was added and the resulting white precipitate was filtered off and washed with an additional small quantity of diethyl ether. The white solid was finally recrystalized from hot $CHCl_3$ to give tetraphenylmethane (2.7 g, 0.0085 mol, 42%) as colorless needles. Mp. 283°C (Lit.[140] 280 ~ 282°C). ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.15 ~ 7.28 (m, 20H).

Tetraphenylmethane (procedure B)

250 mL (flask A) and 35 mL (flask B) of condensed liquid ammonia were kept at -42°C using acetonitrile/dry ice cold baths. To both flasks were added *ca*. 0.1 g Fe_2O_3 catalyst, followed by the slow addition of *ca*. 1.0 g potassium metal in small pieces (**Extreme caution!**). The addition of the potassium metal resulted in deep blue colors in both solutions. Both mixtures were kept at -42ºC while stirring for an additional 30 min. After this time, triphenylmethane (3.0 g, 12 mmol) was added into flask A as a solid, which resulted in a deep red color mixture. After 30 min, chlorobenzene (4.5 mL, 43 mmol) was added to flask A dropwise. The mixture was then allowed to stir for another 30 min. Then the potassium amide solution in flask B was slowly cannulated into flask A over 45 min and the whole mixture was left to react for 1 h before carefully quenched with ammonium chloride salt and water (**Extreme caution!**). The flask was then removed from the cold bath and allowed to evaporate in a well-ventilated fume hood overnight to remove all ammonia solvent. To the remaining mixture was added water and benzene and the Fe_2O_3 catalyst was filtered off. The filtrated was then partitioned between benzene and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salt filtered off. Removal of the solvent under reduced pressure gave the crude product as a brown oil. The addition of small amount of diethyl ether resulted in the formation of white precipitates. The white precipitates were filtered off and washed with small amounts of diethyl ether twice. Recrystalization from hot $CHCl_3$ gave tetraphenylmethane (0.70 g, 2.2 mmol, 18%) as colorless needles.

Tetra(4-iodophenyl)methane 102

A mixture of tetraphenylmethane (1.50 g, 4.69 mmol), bis(trifluoro-acetoxy)-iodobenzene (11.8 g, 28.1 mmol) and I_2 (4.70 g, 18.3 mmol) in 50 mL CCl_4 was heated while stirring at 60°C for three days. After this time, the initial purple color had disappeared. The suspended solid was filtered off and washed continuously with acetone and ethanol. The remaining solid was recrystalized from hot THF to give tetra(4-iodophenyl)-methane **102**[145] (2.80 g, 3.40 mmol, 71%) as a white solid. M.p. > 400°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 6.88 (d, J = 8.4 Hz, 8H), 7.58 (d, J = 8.4 Hz, 8H).

Tetraaldehyde 103

A solution of **102** (1.00 g, 1.21 mmol) in 150 mL THF was cooled down to -78°C. *n*-BuLi (4.41 mL, 2.2 M in hexanes, 9.68 mmol) was added dropwise. After this addition, the flask was removed from the cold bath and slowly warmed up to *ca*. -30°C over 20 min. It was then put back to -78°C and a solution of 3 mL DMF in 20 mL THF was added. The mixture was stirred at -78°C for 3 h. After this time, the flask was taken out of the cold bath and warmed up to *ca*. 0°C. Aqueous 1M HCl was added to quench the reaction until the mixture became acidic. The mixture was then partitioned between water and $CHCl_3$ three times. The organic phases were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure to give the crude product as a yellow solid. Gradient column chromatography with a mobile

phase varying from 5 to 25% acetone in hexanes gave the tetraaldehyde **103** (0.377 g, 0.872 mmol, 72%) as a white solid. M.p. 215ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.43 (d, *J* = 8.4 Hz, 8H), 7.84 (d, *J* = 8.4 Hz, 8H), 10.01 (s, 4H). MS m/z 433 $[M+H]^+$. Anal. Calcd. For $C_{29}H_{20}O_4$: C: 79.76; H: 4.73. Found: C: 79.64; H: 4.75.

Tetrol 100

To a soution of tetraaldehyde **103** (0.38g, 0.87 mmol) in 10 mL THF and 10 mL methanol, was added solid $NaBH_4$ (0.14 g, 3.5 mmol). The mixture was stirred at rt for 16h. After this time, the solvent was removed under reduced pressure. The remaining solid was suspended in water and filtered off to give the tetrol **100** (0.38 g, 0.86 mmol, 99%) as a white solid. M.p. > 400°C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm) 4.45 (d, *J* = 5.6 Hz, 8H), 5.12 (t, *J* = 5.6 Hz, 4H), 7.10 (d, *J* = 8.4 Hz, 8H), 7.22 (d, *J* = 8.4 Hz, 8H). MS (ESI): 463 $[M + Na]^+$. Anal. Calcd. for $C_{29}H_{28}O_4 \bullet 1.5H_2O$: C, 74.50; H, 6.67. Found: C, 74.38; H, 6.27.

Bis-protected (TBDPS) 1,3-benzenedimethanol 104

To a solution of 1,3-benzendimethanol (0.500 g, 3.60 mmol) and imidazole (1.21 g, 17.8 mmol) in 10 mL DMF, was added *t*-butyldiphenylsilyl chloride (2.77 mL, 10.7 mmol). The mixture was stirred at 60°C for 16 h. The solvent was then removed under reduced pressure and the mixture partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under

reduced pressure. Column chromatography with a mobile phase of 10% acetone in hexanes gave the bis-protected benzenedimethanol **104** (1.75 g, 2.84 mmol, 80%) as a white solid. M.p. 45-47ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.09 (s, 18H), 4.76 (s, 4H), 7.30 ~ 7.45 (m, 16H), 7.69 ~ 7.71 (m, 8H). MS(ESI): 637 $[M + Na]^+$. Anal. Calcd. for $C_{40}H_{46}O_2Si_2$: C, 78.12; H, 7.54. Found: C, 78.32; H, 7.47.

Mono-protected(TBDPS) 1,3-benzenedimethanol 105

To a solution of 1,3-benzenedimethanol (0.400 g, 2.89 mmol) and imidazole (0.482 g, 7.23 mmol) in 10 mL DMF, was added *t*-butyldiphenylsilyl chloride (0.750 mL, 2.89 mmol). The mixture was stirred at 60°C for 16 h. The solvent was then removed under reduced pressure and the mixture partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with a mobile phase of 10% acetone in hexanes gave the mono-protected benzenedimethanol **105** (0.540 g, 1.44 mmol, 50%) as a colorless oil.[132] ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.10 (s, 9H), 4.68 (s, 2H), 4.78 (s, 2H), 7.30 ~ 7.45 (m, 10H), 7.68 ~ 7.72 (m, 4H).

Model reaction on 104 (Synthesis of *tert*-butyldiphenylsilanol 106)

To a stirred solution of **104** (100 mg, 1.63×10^{-4} mol) in 32 mL DMSO was added *t*-BuOK (96.0 mg, 8.13×10^{-4} mol). The mixture was stirred at rt for 5 h. After this time, the solvent was removed under reduced pressure and the mixture

partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with a mobile phase of 10% acetone in hexanes gave *t*-butyldiphenylsilanol **106** (68.0 mg, 2.67×10^{-4} mol, 82%) as a colorless oil which solidify upon standing. Mp. 61 ~ 63°C (Lit.[189] 62 ~ 64°C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.09 (s, 9H), 7.35 ~ 7.45 (m, 6H), 7.72 ~ 7.75 (m, 4H). MS(ESI): 279 $[M + Na]^+$, 535 $[2M + Na]^+$.

Model reraction on 105 (Synthesis of *tert*-butyldiphenylsilanol 106)

To a stirred solution of mono-protected benzenedimethanol **105** (50 mg, 1.3×10^{-4} mol) in 26 mL DMSO was added *t*-BuOK (37 mg, 3.3×10^{-4} mol), followed by the immediate addition of CH_2BrCl (17 μL, 2.7×10^{-4} mol). The mixture was stirred at rt for 5 h. After this time, the solvent was removed under reduced pressure and the mixture partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with a mobile phase of 10% acetone in hexanes gave *t*-butyldiphenylsilanol **106** (25 mg, 0.96×10^{-4} mol, 72%) as a colorless oil which solidify upon standing.

Model reaction on 4-bromobenzaldehyde (Synthesis of sulfoxides 107 and 108)

To a stirred solution of 4-bromobenzaldehyde (100 mg, 5.40×10^{-4} mol) in 54 mL DMSO was added *t*-BuOK (302 mg, 2.70×10^{-3} mol), followed by the

immediate addition of CH_2BrCl (140 μL, 2.16×10^{-3} mol). The mixture was stirred at rt for 5 h. After this time, the solvent was removed under reduced pressure and the mixture partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with a mobile phase of 25% acetone in hexanes gave: (1) *trans* adduct **107** (79.0 mg, 3.24×10^{-4} mol, 60%) as a white sold. M.p. 87-90ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.70 (s, 3H), 6.91 (d, J = 15.4 Hz, 1H), 7.19 (d, J = 15.4 Hz, 1H) 7.33 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H). MS(CI): 263 $[M + NH_4]^+$. (2) *cis* adduct **108** (13.0 mg, 5.40×10^{-5} mol, 10%) as a white sold. M.p. 85-87ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.72 (s, 3H), 6.52 (d, J = 11.2 Hz, 1H), 7.00 (d, J = 11.2 Hz, 1H) 7.26 (d, J = 6.4 Hz, 2H), 7.53 (d, J = 6.4 Hz, 2H). MS(CI): 263 $[M + NH_4]^+$.

Mono-protected (SEM) 1,3-benzenedimethanol 109

To a solution of 1,3-benzenedimethanol (1.0 g, 7.6 mmol) in 16 mL THF and 4 mL CH_2Cl_2, was added *N,N*-diisopropylethyl amine (4.0 mL, 23.0 mmol), followed by the addition of 2-(trimethylsilyl)ethoxymethyl chloride (0.66 mL, 3.7 mmol). The mixture was stirred at rt for 24 h. The mixture was then partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with a mobile phase of 30% acetone in hexanes gave the mono-protected benzenedimethanol **109** (0.98 g, 3.7 mmol,

99%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.03 (s, 9H), 0.93 ~ 0.98 (m, 2H), 3.64 ~ 3.69 (m, 2H), 4.61 (s, 2H), 4.70 (s, 2H), 4.76 (s, 2H), 7.26 ~ 7.37 (m, 4H). MS (ESI): 291 $[M + Na]^+$. Anal. Calcd. for $C_{14}H_{24}O_3Si$: C, 62.64; H, 9.01. Found: C, 62.60; H, 8.99.

Model reaction on 109 (Synthesis of 110c)

To a stirred solution of mono-protected benzenedimethanol **109** (50.0 mg, 1.88×10^{-4} mol) in 20 mL DMSO was added *t*-BuOK (110 mg, 9.33×10^{-4} mol), followed by the immediate addition of CH_2BrCl (48.0 μL, 7.44×10^{-4} mol). The mixture was stirred at rt for 5 h. After this time, the solvent was removed under reduced pressure and the mixture partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with a mobile phase of 5% acetone in hexanes gave the **110c** (66.0 mg, 1.65×10^{-4} mol, 88%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.24 (t, J = 7.0 Hz, 6H), 3.65 (q, J = 7.0 Hz, 4H), 4.61 (s, 4H), 4.66 (s, 4H), 4.77 (s, 4H), 4.85 (s, 2H), 7.26 ~ 7.36 (m, 8H). MS (ESI): 427 $[M + Na]^+$. Anal. Calcd. for $C_{23}H_{32}O_6$: C, 68.29; H, 7.97. Found: C, 68.28; H, 8.13.

Model reaction on 109 (Synthesis of 110a)

To a stirred solution of mono-protected benzenedimethanol **109** (50.0 mg, 1.87×10^{-4} mol) in 20 mL DMSO was added *t*-BuONa (45.0 mg, 4.68×10^{-4} mol), followed by the immediate addition of CH_2BrCl (24.0 μL, 3.74×10^{-4} mol). The

mixture was stirred at rt for 5 h. After this time, the solvent was removed under reduced pressure and the mixture partitioned between water and $CHCl_3$ three times. The organic phases were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with a mobile phase of 10% acetone in hexanes gave **110a** (95.0 mg, 1.74×10^{-4} mol, 93%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.03 (s, 18H), 0.94~0.99 (m, 4H), 3.64~3.70 (m, 4H), 4.61 (s, 4H), 4.66 (s, 4H), 4.76 (s, 4H), 4.85 (s, 2H), 7.29 ~ 7.35 (m, 8H). MS (ESI): 571 $[M + Na]^+$. Anal. Calcd. for $C_{29}H_{48}O_6Si_2$: C, 63.46; H, 8.82. Found: C, 63.28; H, 8.81.

Bis-protected subunit 112 and Mono-protected subunit 113

To a solution of tetrol **100** (0.36 g, 0.82 mmol) in 26 mL DMF was added *N,N*-diisopropylethylamine (1.43 mL, 8.2 mmol), followed by the addition of 2-(trimethylsilyl)ethoxymethyl chloride (0.58 mL, 3.3 mmol). The mixture was stirred at rt for 24 h. After this time, the solvent was removed under reduced pressure and the residue was partitioned between water and $CHCl_3$ three times. The organic phases were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Gradient column chromatography with a mobile phase varying from 10 to 40% acetone in hexanes gave: (1) Bis-protected species **112** (0.24 g, 3.4×10^{-4} mol, 41%) as a colorless oil which gradually solidify upon standing over hexanes to give a white solid. Mp. 82-84°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.02 (s, 18H), 0.93 ~ 0.99 (m, 4H), 3.64 ~ 3.70 (m, 4H), 4.56 (s, 4H), 4.66 (s, 4H), 4.76 (s, 4H), 7.20 ~

7.24 (m, 16H). MS (ESI): 723 $[M + Na]^+$. Anal. Calcd. for $C_{41}H_{56}O_6Si_2$: C, 70.24; H, 8.05. Found: C, 70.42; H, 7.93. (2) Mono-protected species **113** (0.12 g, 2.1×10^{-4} mol, 26%) as a white solid. Mp. 43-46°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.02 (s, 9H), 0.94 ~ 0.99 (m, 2H), 3.65 ~ 3.69 (m, 2H), 4.56 (s, 6H), 4.76 (s, 2H), 7.20 ~ 7.24 (m, 16H). MS (ESI) 593 $[M + Na]^+$. Anal. Calcd. for $C_{35}H_{42}O_5Si \bullet 0.5H_2O$: C, 72.50; H, 7.48. Found: C, 72.50; H, 7.48.

Self-assembly of subunit 112 (Synthesis of dimer 114 and trimer 115)

Representative procedure: To a solution of **112** (50 mg, 7.1×10^{-5} mol) in 28 mL DMSO was added *t*-BuONa (35 mg, 3.6×10^{-4} mol), followed by the immediate addition of CH_2BrCl (19 μL, 2.9×10^{-4} mol). The mixture was stirred at rt for 5 h. After this time, the solvent was removed under reduced pressure and the mixture partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure. Gradient column chromatography with a mobile phase varying from 5 to 20% acetone in hexanes gave: (1) Dimer **114** (17 mg, 1.2×10^{-5} mol, 33%) as white solid. Mp. 173°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.02 (s, 36H), 0.93 ~ 0.99 (m, 8H), 3.63 ~ 3.69 (m, 8H), 4.48 (s, 8H), 4.53 (s, 8H), 4.75 (s, 8H), 4.95 (s, 4H), 7.06 (d, J = 8.1 Hz, 8H), 7.14 (d, J = 8.1 Hz, 8H), 7.16 (br, 16H). MS (MALDI): 1533 $[M + Ag]^+$. Anal. Calcd. for $C_{84}H_{112}O_{12}Si_4$: C, 70.74; H, 7.92. Found: C, 70.62; H, 7.89. (2) Trimer **115** (7.6 mg, 3.6×10^{-6} mol, 15%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.02 (s, 54H), 0.94 ~ 0.99 (m, 12H), 3.64 ~ 3.70 (m, 12H), 4.55 (s, 12H), 4.60 (s,

12H), 4.76 (s, 12H), 4.83 (s, 6H), 7.18 ~ 7.23 (br, 48H). MS (MALDI): 2246 [M + Ag]$^+$. Anal. Calcd. for $C_{126}H_{168}O_{18}Si_6$: C, 70.74; H, 7.92. Found: C, 70.64; H, 7.79.

Tetrol 116

A stirred mixture of dimer **114** (36 mg, 2.5×10^{-5} mol), CsF (46 mg, 3.0×10^{-4} mol) in 4 mL DMF was heated at 130°C for 48 h. After this time, the solvent was removed under reduced pressure. The remaing solid was suspended in water and filtered off to give **116** (20 mg, 2.3×10^{-5} mol) as a white solid. Mp. > 250°C with decomposition. ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm) 4.43 (br, 16H), 4.85 (s, 4H), 5.10 (t, J = 6.0 Hz, 4H), 7.02 ~ 7.05 (m, 24H), 7.15 (d, J = 8.4 Hz, 8H). MS (MALDI): 1012 [M + Ag]$^+$. Anal. Calcd. for $C_{60}H_{56}O_8$: C, 79.62; H, 6.24. Found: C, 79.35; H, 6.27.

Redorcinarene (Octol) 117

A solution of resorcinol (44 g, 0.40 mol) in 320 mL 95% ethanol and 80 mL concentrated 37% aqueous HCl was cooled down to 0ºC. To this solution was added hydrocinnamaldehyde (53 mL, 0.40 mol) dropwise over 30 min. After the addition the solution was allowed to warm up to rt and the heated to reflux for 7 d. The yellow precipitates formed were then filtered to dryness and washed consequtively with water until the filtrate was no longer acidic. After drying under reduced pressure, the octol **117**[162] (76 g, 84 mmol, 85%) was obtained as a

yellow solid. ^{1}H NMR (Acetone-d_6, 400 MHz) δ (ppm) 2.50~2.70 (m, 16H), 4.38 (t, J = 5.5 HZ, 4H), 6.29 (s, 4H), 7.10 ~ 7.25 (m, 20H), 7.74 (s, 4H), 8.54 (s, 8H).

3,5-Dibromobenzaldehyde

A solution of 1,3,5-tribromobenzene (30.0 g, 95.3 mmol) in 500 mL diethyl ether was cooled down to -78ºC. To this solution was added *n*-BuLi (38.1 mL, 2.50 M solution in hexanes, 95.3 mmol) dropwise. This was followed by the slow addition of a solution of *ca*. 14 mL DMF in 20 mL ether. After stirring at -78ºC for 1 h, the mixture was allowed to warm up to *ca*. 0ºC and quenched with 10% aqueous HCl until acidic. The mixture was then partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and the salts filtered off. Romoval of the solvent under reduced pressure gave the crude product as a yellowish solid. Recrystalization of the solid from hot hexanes gave 3,5-dibromobenzaldehyde (22.6 g, 85.8 mmol, 90%) as colorless needles. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.91 (t, J = 2.0 Hz, 1H), 7.93 (d, J = 2.0 Hz, 2H), 9.90 (s, 1H).

3,5-Dibromobenzal bromide

To a solution of 3,5-dibromobenzaldehyde (22.6 g, 85.8 mmol) in 300 mL CH_2Cl_2 was added BBr_3 (72.6 mL, 1.3 M solution in CH_2Cl_2, 94.4 mmol) and the mixture was stirred at rt for 24 h. The solution was then run through a column with hexanes and the solvent removed under reduced pressure. Recrystalization from hexanes gave 3,5-dibromobenzal bromide[165] (27.2 g, 66.9 mmol, 78%) as

colorless crystals. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 6.49 (s, 1H), 7.62 (t, *J* = 2.0 HZ, 1H), 7.64 (d, *J* = 2.0 Hz, 2H).

Octabromide 118

To a stirred solution of 3,5-dibromobenzal bromide (18.0 g, 44.2 mmol), DBU (7.27 mL, 0.388 mol) in 200 mL degassed DMA was added a solution of octol **117** (5.0 g, 5.5 mmol) in 50 mL DMA over 64 h. The mixture was then heated at 60ºC for 4 d. After this time, the solvent was removed under reduced pressure and the mixture was partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and the salts filtered off. Romoval of the solvent under reduced pressure gave the crude product as brown oil. The crude product was then dissolved in 50 mL $CHCl_3$ and *ca*. 100 mL of silica gel was added. After removing the solvent and dried under reduced pressure, the dry silica was loaded onto a column and washed with a mobile phase of hexanes to collect the excess 3,5-dibromobenzal bromide. Then the eluent was switched to 50% $CHCl_3$ in hexanes. Removal of the solvent gave the crude product as a yellowish solid. The crude mixture was finally recrystalized from 50% $CHCl_3$ in hexanes to give octabromide **118**[165] (6.7 g, 3.6 mmol, 65%) as a white solid.[192] ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.55 ~ 2.80 (m, 16H), 4.99 (t, *J* = 8.0 Hz, 4H), 5.37 (s, 4H), 6.66 (s, 4H), 7.16~7.28 (m, 24H), 7.69 (t, *J* = 2.0 Hz, 4H), 7.72 (d, *J* = 2.0 Hz, 8H).

Basket 119

For 5 min N_2 was bubbled through a suspension of octabromide **118** (0.25 g, 0.13 mmol), resorcinol (88 mg, 0.78 mmol), and anhydrous K_2CO_3 (0.22 g, 1.6 mmol) in 30 mL pyridine. CuO (0.13 g, 1.6 mmol) was then added and the stirring mixture was vigorously refluxed for 7 d. After this time, the mixture was cooled and the solvent was removed under reduced pressure. The remaining solid was re-suspended in $CHCl_3$ and run through a short silica gel plug with a mobile phase of $CHCl_3$. Removal of the solvent gave the crude product as a white solid. Column chromatography with a mobile phase of 50% $CHCl_3$ in hexanes gave basket **119**[153] (0.19 g, 0.11 mmol, 88%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.40 ~ 2.60 (m, 16H), 4.55 (s, 4H), 4.85 (t, J = 8.0 Hz, 4H), 6.01 (s, 4H), 6.52 (d, J = 2.0 Hz, 8H), 6.64 (t, J = 2.0 Hz, 4H), 6.99 (t, J = 2.0 Hz, 4H), 7.05~7.22 (m, 20H), 7.58 (t, J = 8.0 Hz, 4H).

Basket 120

For 5 min N_2 was bubbled through a suspension of octabromide **118** (0.25 g, 0.13 mol), 2,7-dihydroxy naphthalene (0.22 g, 1.3 mmol), and anhydrous K_2CO_3 (0.37 g, 2.7 mmol) in 30 mL pyridine. CuO (0.21 g, 2.7 mmol) was then added and the stirring mixture was vigorously refluxed for 7 d. After this time, the reaction was cooled and the solvent was removed under reduced pressure. The remaining solid was re-suspended in $CHCl_3$ and run through a short silica gel plug with a mobile phase of $CHCl_3$. Removal of the solvent gave the crude product as a brown solid. Column chromatography with a mobile phase of 50%

$CHCl_3$ in hexanes gave basket **120** (0.17 g, 0.093 mmol, 70%) as a white solid. Mp. > 250°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.30 ~ 2.50 (m, 16H), 4.76 (t, *J* = 8.0 Hz, 4H), 5.23 (s, 4H), 5.94 (s, 4H), 6.81 (d, *J* = 2.4 Hz, 8H), 6.90 ~ 7.01 (m, 8H), 7.02 (s, 4H), 7.09 ~ 7.14 (m, 12H), 7.22 (t, *J* = 2.4 Hz, 4H), 7.36 (dd, *J* = 8.8 Hz, 2.4 Hz, 8H), 7.57 (d, *J* = 2.4 Hz, 8H), 8.00 (d, *J* = 8.8 Hz, 8H). MS (MALDI): 1989 $[M + Ag]^+$. Anal. Calcd. for $C_{128}H_{88}O_{16}$: C, 81.69; H, 4.71. Found: C, 81.97; H, 4.91.

Basket 121

For five min N_2 was bubbled through a suspension of octabromide **118** (0.25 g, 0.13 mmol), hydroquinone (0.15 g, 1.3 mmol), and anhydrous K_2CO_3 (0.37 g, 2.7 mmol) in 30 mL of pyridine. CuO (0.21 g, 2.7 mmol) was then added and the stirring mixture was vigorously refluxed for 7 d. After this time, the reaction was cooled and the solvent was removed under reduced pressure. The remaining solid was re-suspended in $CHCl_3$ and run through a short silica gel plug with a mobile phase of $CHCl_3$. Removal of the solvent gave the crude product as a brown solid. Column chromatography with a mobile phase of 50% $CHCl_3$ in hexanes gave basket **121** (0.10 g, 0.060 mol, 45%) as a white solid. Mp. > 250°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.50 ~ 2.70 (m, 16H), 4.74 (s, 4H), 4.91 (t, *J* = 8.0 Hz, 4H), 6.06 (s, 4H), 6.40 (s, 8H), 6.78 (s, 8H), 6.70 ~ 7.30 (m, 7H), 7.39 (s, 8H). MS (MALDI): 1798 $[M + Ag]^+$. Anal. Calcd. for $C_{112}H_{80}O_{16}$: C, 77.59; H, 4.66. Found: C, 77.40; H, 4.79.

3,5-dihydroxy benzyl alcohol

To a stirred solution of BH_3-Me_2S (19.5 mL, 2.0 M solution in THF, 0.0390 mol) and 10 mL $B(OMe)_3$ in 100 mL THF, was added a solution of 3,5-dihydroxy benzoic acid (3.0 g, 0.019 mol) in 25 mL THF in small portions over 30 min. After the addition, the mixture was heated to reflux for 24 h and then quenched with 50 mL methanol. The solvent was then removed under reduced pressure. Another 50 mL methanol was added to the residue and solvent removed under reduced pressure. Column chromatography with a mobile phase of 40% acetone in $CHCl_3$ gave 3,5-dihydroxybenzyl alcohol (2.4 g, 0.017 mol, 90%) as a white solid. Mp. 182-183°C (Lit.[190] 182-184 °C). ^{1}H NMR (Acetone-d_6, 400 MHz) δ (ppm) 4.02 (t, J = 6.0 Hz, 1H), 4.46 (d, J = 6.0 Hz, 2H), 6.21 (t, J = 2.0 Hz, 1H), 6.34 (dt, J = 2.0 Hz, 0.8 Hz, 2H), 8.07 (s, 2H).

Basket 124

For 5 min N_2 was bubbled through a suspension of octabromide **118** (0.20 g, 0.106 mmol), 3,5-dihydroxy benzyl alcohol (0.15 g, 1.1 mmol), and anhydrous K_2CO_3 (0.29 g, 2.1 mmol) in 15 mL pyridine. CuO (0.17 g, 2.1 mmol) was then added and the stirring mixture was vigorously refluxed for 7 d. After this time, the mixture was cooled and the solvent was removed under reduced pressure. The remaining solid was re-suspended in $CHCl_3$ and run through a short silica gel plug with a mobile phase of 50% acetone in $CHCl_3$. Removal of the solvent gave the crude product as a white solid. Column chromatography with a mobile phase of 10% acetone in $CHCl_3$ gave basket **124** (0.12 g, 0.064 mmol, 60%) as a white

solid. Mp. > 250°C. ^{1}H NMR (DMSO-d_6, 500 MHz, 55°C) δ (ppm) 2.50 ~ 2.70 (m, 16H), 4.47 (s, 4H), 4.61 ~ 4.64 (m, 12H), 5.35 (t, J = 5.5 Hz, 4H), 5.87 (s, 4H), 6.47 (d, J = 1.5 Hz, 4H), 6.49 (t, J = 2.0 Hz, 4H), 7.02 (br, 4H), 7.13 ~ 7.21 (m, 20H), 7.24 (d, J = 2.0 Hz, 8H), 7.69 (s, 4H). MS (MALDI): 1909 $[M + Ag]^+$. Anal. Calcd. for $C_{116}H_{80}O_{20}\bullet 2H_2O$: C, 75.85; H, 5.01. Found: C, 75.70; H, 5.03.

Basket 125

To a solution of basket **124** (0.20 g, 1.1×10^{-4} mol) in 20 mL THF was added a few pellets of solid KOH (*ca*. 0.4g), followed by the addition of solid *p*-toluenesulfonyl chloride (0.40 g, 2.1×10^{-3} mol). The mixture was stirred vigorously at rt for 16 h. The mixture was then partitioned between water and $CHCl_3$ three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. Removal of the solvent under reduced pressure gave the crude products as yellowish solid. Column chromatography with a mobile phase of $CHCl_3$ gave basket **125** (0.26 g, 1.1×10^{-4} mol, 97%) as a white powder. Mp. > 250°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.41 (s, 12H), 2.45 ~ 2.67 (m, 16H), 4.53 (s, 4H), 4.84 (t, J = 8.0 Hz, 4H), 5.11 (s, 8H), 5.98 (s, 4H), 6.46 (d, J = 2.0 Hz, 8H), 6.51 (t, J = 2.0 Hz, 4H), 6.93 (d, J = 2.0 Hz, 4H), 7.04 (d, J = 2.0 Hz, 8H), 7.11~7.14 (m, 8H), 7.19~7.25 (m, 16H), 7.33 (d, J = 8.0 Hz, 8H), 7.83 (d, J = 8.0 Hz, 8H). MS (MALDI): 2419 $[M + H]^+$, 2441 $[M + Na]^+$, 2482 $[M + Cu]^+$, 2526 $[M + Ag]^+$. Anal. Calcd. for $C_{144}H_{112}O_{28}S_4$: C, 71.51; H, 4.67. Found: C, 71.30; H, 4.66.

Basket 126

To a solution of basket **125** (0.19 g, 7.7×10^{-5} mol) in THF (4 mL) was added "anhydrous" TBAF[39] (3.9 mL 0.4 M solution in THF, 1.6×10^{-3} mol). The solution was refluxed for 24 h. After this time, the solvent was removed under reduced pressure. Column chromatography with a mobile phase of 60% $CHCl_3$ in hexanes gave basket **126** (74 mg, 4.1×10^{-5} mol, 53%) as a white powder. Mp. > 250°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.50 ~ 2.63 (m, 16H), 4.57 (s, 4H), 4.85 (t, J = 8.0 Hz, 4H), 5.48 (d, $J_{(H,F)}$ = 46.8 Hz, 8H), 6.03 (s, 4H), 6.54 (br, 8H), 6.58 (br, 4H), 7.00 (br, 4H), 7.11~7.25 (m, 32H). MS (MALDI): 1810 $[M + H]^+$, 1832 $[M + Na]^+$, 1873 $[M + Cu]^+$, 1917 $[M + Ag]^+$. Anal. Calcd. for $C_{116}H_{84}O_{16}F_4\bullet0.5H_2O$: C, 76.22; H, 4.74. Found: C, 76.47; H, 4.69.

Deep-cavity Cavitands 129 and 130a

For 5 min N_2 was bubbled through a suspension of octabromide **118** (1.00 g, 0.529 mmol), resorcinol (0.350 g, 3.18 mmol), and anhydrous K_2CO_3 (0.877 g, 6.36 mmol) in 60 mL pyridine. CuO (0.505 g, 6.36 mmol) was then added and the stirring mixture was vigorously refluxed for 3 d. After this time, the mixture was cooled and the solvent was removed under reduced pressure. The remaining solid was re-suspended in $CHCl_3$ and run through a short silica gel plug with a mobile phase of $CHCl_3$. Removal of the solvent gave the crude product as a white solid. Gravity column chromatography with a mobile phase of 50% $CHCl_3$ in hexanes gave: (1) A/C *bis*-bridged species **130a** (0.173 g, 0.0950 mmol, 18%) as a white solid. Mp. > 250°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.50 ~ 2.70 (m, 16H),

4.92 (t, J = 8.0 Hz, 4H), 5.05 (s, 4H), 6.21 (s, 2H), 6.40 (broad, 4H), 6.61 (s, 2H), 6.88 (dd, J = 8.0 Hz, 2.0 Hz, 4H), 7.03 (t, J = 2.0 Hz, 2H), 7.10 ~ 7.30 (m, 24H), 7.35 (t, J = 8.0 Hz, 2H), 7.45 (t, J = 2.0 Hz, 4H), 7.71 (s, 4H). MS (MALDI): 1893 $[M + Ag]^+$. Anal. Calcd. for $C_{100}H_{72}O_{12}Br_4 \bullet H_2O$: C, 66.60; H, 4.14. Found: C, 66.20; H, 4.12. (2) *Tris*-bridged species **129**[171] (0.320 g, 0.185 mmol, 35%) as a white solid. Mp. > 250°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.50 ~ 2.70 (m, 16H), 4.74 (s, 2H), 4.85 (s, 2H), 4.88 (m, 4H), 6.01 (s, 2H), 6.11 (s, 1H), 6.45 (broad, 2H), 6.53 (s, 1H), 6.54 (m, 2H), 6.63 (m, 2H), 6.68 (t, J = 2.0 Hz, 1H), 6.75 (t, J = 2.0 Hz, 2H), 7.00~7.04 (m, 4H), 7.10~ 7.15 (m, 8H), 7.18~7.30 (m, 20H), 7.40 (t, J = 2.0 Hz, 2H), 7.54 (t, J = 8.0 Hz, 2H), 7.61 (t, J = 8.0 Hz, 1H), 7.64 (s, 2H). (3) Basket **119**[153] (0.220 g, 0.132 mmol, 25%) as a white solid.

Basket 127

For five min N_2 was bubbled through a suspension of the tris-bridged species **129** (100 mg, 5.77×10^{-5} mol), 2-methylresorcinol (36.0 mg, 2.88×10^{-4} mol), and anhydrous K_2CO_3 (80.0 mg, 5.77×10^{-4} mol) in 10 mL of pyridine. CuO (46.0 mg, 5.77×10^{-4} mol) was then added and the stirring mixture was vigorously refluxed for 2 d. After this time, the reaction was cooled and the solvent was removed under reduced pressure. The remaining solid was re-suspended in $CHCl_3$ and run through a short silica gel plug with a mobile phase of $CHCl_3$. Removal of the solvent gave the crude product as a white solid. Column chromatography with a mobile phase of 50% $CHCl_3$ in hexanes gave the monomethyl basket **130** (88.0 mg, 5.19×10^{-5} mol, 90%) as a white solid. Mp. >

250°C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 1.69 (s, 3H), 2.50 ~ 2.70 (m, 16H), 4.55 (s, 2H), 4.57 (s, 2H), 4.85 (t, *J* = 8.0 Hz, 4H), 5.96 (s, 1H), 6.01 (s, 1H), 6.02 (s, 2H), 6.50 (br, 4H), 6.55 (br, 4H), 6.60 (t, *J* = 2.0 Hz, 1H), 6.68 (t, *J* = 2.0 Hz, 2H), 6.99 (t, *J* = 2.0 Hz, 2H), 7.03 (t, *J* = 2.0 Hz, 2H), 7.10 ~ 7.30 (m, 32H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 2H). MS (MALDI): 1803 $[M + Ag]^+$. Anal. Calcd. for $C_{113}H_{82}O_{16}\bullet H_2O$: C, 79.19; H, 4.94. Found: C, 79.10; H, 4.87.

Protected Pyrogallol (X = $OCH_2OCH_2CH_3$)

To a solution of pyragallol (4.0 g, 0.032 mol) in 100 mL THF was added *N,N*-diisopropylethyl amine (6.1 mL, 0.035 mol), followed by the slow (over *ca*. 20 min) addition of chloromethyletheyl ether (3.2 mL, 0.035 mol). The mixture was then heated at 60 °C for 16 h. After cooling, the solvent was removed under reduced pressure and the mixture partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and the salts filtered off. The filtrate was concentrated under reduced pressure to give a pale yellow oil. Column chromatography with a mobile phase of $CHCl_3$ gave the desired 2-ethoxy-methoxy-resorcinol (1.6 g, 9.0 mmole, 28%) as a colorless oil. Bp. 140°C (0.03 mmHg). ^{1}H NMR (Acetone-d_6, 500 MHz) δ (ppm) 1.21 (t, *J* = 7.0 Hz, 3H), 3.85 (q, *J* = 7.0 Hz, 2H), 5.14 (s, 2H), 6.39 (d, *J* = 8.0 Hz, 2H), 6.78 (t, *J*= 8.0 Hz, 1H), 7.86 (s, 2H). MS (ESI-): 183 $[M - H]^-$. Anal. Calcd. for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.22; H, 6.65.

Basket 132

For 5 min N_2 was bubbled through a suspension of tris-bridged species **129** (318 mg, 0.184 mmol), mono-protected pyrogallol (X = $OCH_2OCH_2CH_3$), (338mg, 1.84 mmol), and anhydrous K_2CO_3 (507 mg, 3.67 mmol) in 3 mL of pyridine. CuO (292 mg, 3.67 mmol) was then added and the stirring mixture was vigorously refluxed for 4 d. After this time, the solvent was removed under reduced pressure. The remaining solid was re-suspended in $CHCl_3$ and run through a short silica gel plug with a mobile phase of $CHCl_3$. Removal of the solvent gave the crude product as a white solid. Column chromatography with a mobile phase of 50% $CHCl_3$ in hexanes gave basket **132** (102 mg, 0.0590 mmol, 32%) as a white solid. Mp. > 250°C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 1.14 (t, *J* = 7.0 Hz, 3H), 2.50 ~ 2.70 (m, 16H), 3.66 (q, *J* = 7.0 Hz, 2H), 4.56 (s, 2H), 4.59 (s, 2H), 4.85 (t, *J* = 8.0 Hz, 4H), 4.91 (s, 2H), 6.02 (s, 3H), 6.04 (s, 1H), 6.50 (br, 2H), 6.55 (br, 4H), 6.57 (br, 2H), 6.60 (t, *J* = 2.0 Hz, 1H), 6.65 (t, *J* = 2.0 Hz, 2H), 6.98 (t, *J* = 2.0 Hz, 2H), 6.99 (t, *J* = 2.0 Hz, 2H), 7.10 ~ 7.30 (m, 32H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 3H). MS (MALDI): 1709 [M – OCH_2CH_3]$^+$, 1818 [M – OCH_2CH_3 + Ag]$^+$. Anal. Calcd. for $C_{115}H_{86}O_{18}$•H_2O: C, 77.86; H, 5.00. Found: C, 77.91; H, 4.82.

Basket 128

To a solution of basket **132** (76.0 mg, 4.33×10^{-5} mol) in 5 mL of THF was added 1 mL *conc*. HCl. The mixture was heated at 60°C for 3 h. The solvent was then removed under reduced pressure and the mixture was partitioned

between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and salts filtered off. The filtrate was concentrated under reduced pressure to give the crude product as a white solid. Column chromatography with a mobile phase of 50% $CHCl_3$ in hexanes gave the monophenol basket **132** (74.0 mg, 4.29×10^{-5} mol, 99%) as a white solid. Mp. > 250 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 2.50 ~ 2.70 (m, 16H), 4.54 (s, 2H), 4.58 (s, 2H), 4.85 (m, 4H), 4.93 (s, 1H), 6.00 (s, 1H), 6.02 (s, 2H), 6.03 (s, 1H), 6.50 (br, 2H), 6.54 (br, 2H), 6.60 (br, 4H), 6.61 (t, *J* = 2.0 Hz, 1H), 6.68 (t, *J* = 2.0 Hz, 2H), 6.99 (t, *J* = 2.0 Hz, 2H), 7.07 ~ 7.30 (m, 34H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 3H). MS (MALDI): 1805 $[M + Ag]^+$. Anal. Calcd. for $C_{112}H_{80}O_{17}\bullet H_2O$: C, 78.18; H, 4.82. Found: C, 78.18; H, 4.70.

Unsuccessful synthesis of basket 132 (Synthesis of DCC 133)

For 5 min N_2 was bubbled through a suspension of tris-bridged species **127** (50.0 mg, 2.88×10^{-5} mol), pyragallol (18.0 mg, 1.44×10^{-4} mol) in 10 mL pyridine. CuO (23.0 mg, 2.88×10^{-4} mol) was then added and the stirring mixture was vigorously refluxed for 4 d. After this time, the reaction was cooled and the solvent was removed under reduced pressure. The remaining solid was re-suspended in $CHCl_3$ and run through a short silica gel plug with a mobil phase of $CHCl_3$. Removal of the solvent gave the crude product as a white solid. Column chromatography with a mobile phase of 50% $CHCl_3$ in hexanes gave the debrominated species **133** (43.0 mg, 2.74×10^{-5} mol, 95%) as a white solid. Mp. > 250°C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 2.50 ~ 2.70 (m, 16H), 4.78 (s,

2H), 4.88 ~ 4.94 (m, 4H), 4.90 (s, 2H), 6.07 (s, 2H), 6.13 (s, 1H), 6.53 (s, 1H), 6.55 (br, 2H), 6.58 (br, 2H), 6.64 (br, 2H), 6.70 (t, J = 2.0 Hz, 1H), 6.77 (t, J = 2.0 Hz, 2H), 7.02 (t, J = 2.0 Hz, 2H), 7.05 (dd, J = 8.0 Hz, 2.0 Hz, 2H), 7.10 ~ 7.30 (m, 30H), 7.43 (t, J = 8.0 Hz, 2H), 7.48 (br, 1H), 7.50 (br, 1H), 7.52 (t, J = 8.0 Hz, 2H), 7.61 (t, J = 8.0 Hz, 1H). MS (MALDI): 1576 $[M + H]^+$, 1638 $[M + Cu]^+$. Anal. Calcd. for $C_{106}H_{78}O_{14}\bullet H_2O$: C, 79.88; H, 5.06. Found: C, 79.98; H, 5.04.

Crown ether 136

To a solution of basket **119** (0.10 g, 0.059 mmol) in 10 mL CH_2Cl_2, was added BBr_3 (0.30 mL, 1.2 M solution in CH_2Cl_2, 0.36 mmol). The mixture was stirred at rt for 1 h. After this time, 5 mL methanol was added to the mixture to quench the reaction. The solvent was removed under reduced pressure. The remaining solid was run through a short silica gel plug with a mobile phase of $CHCl_3$. Combine all the eluent and the solvent was removed under reduce pressure. The remaining solid was dissolved in 5 mL CH_2Cl_2, to which 1 mL 10% aqueous HCl was added. The biphasic mixture was stirred at rt for 5 h. The mixture was the partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and the salt filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with a mobile phase of $CHCl_3$ gave crown ether **136** (0.044g, 0.051 mmol, 87%) as a white solid. Mp. > 250°C with decomposition. ^{1}H NMR (Acetone-d_6, 400 MHz) δ (ppm) 6.75 (t, J = 2.0 Hz, 4H), 6.93 (dd, J = 8.0 Hz, 2.0 Hz, 8H), 6.96 (d, J =

2.0 Hz, 4H), 7.27 (d, *J* = 2.0 Hz, 8H), 7.44 (t, *J* = 8.0 Hz, 4H), 9.92 (s, 4H). MS (MALDI): 955 $[M + Ag]^+$. Anal. Calcd. for $C_{52}H_{32}O_{12}\bullet 2H_2O$: C, 70.59; H, 4.10. Found: C, 70.46; H, 4.09.

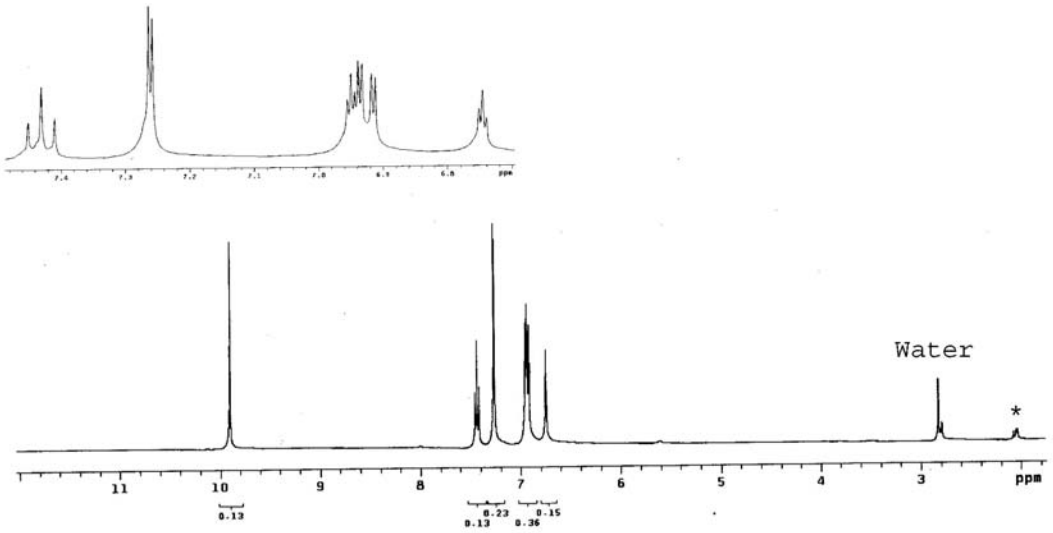


Figure 7.1 ^{1}H NMR spectrum of **136** (* solvent = Acetone-d_6)

Crown ether 137

Similar procedure as that for the synthesis of **136** was followed, starting from basket **120**. Crown ether **137** was obtained in 90% yield as an off-white solid. Mp. > 250°C with decomposition. ^{1}H NMR (Pyridine-d_5, 400 MHz) δ (ppm) 7.36 (t, *J* = 2.0 Hz, 4H), 7.39 (dd, J = 8.8 Hz, 2.0 Hz, 8H), 7.53 (t, J = 2.0 Hz, 8H), 7.55 (d, *J* = 2.0 Hz, 8H), 7.93 (d, J = 8.8 Hz, 8H), 10.02 (s, 4H). MS (MALDI): 1156 $[M + Ag]^+$. Anal. Calcd. for $C_{68}H_{40}O_{12}\bullet 4H_2O$: C, 72.85; H, 4.32. Found: C, 72.71; H, 4.43.

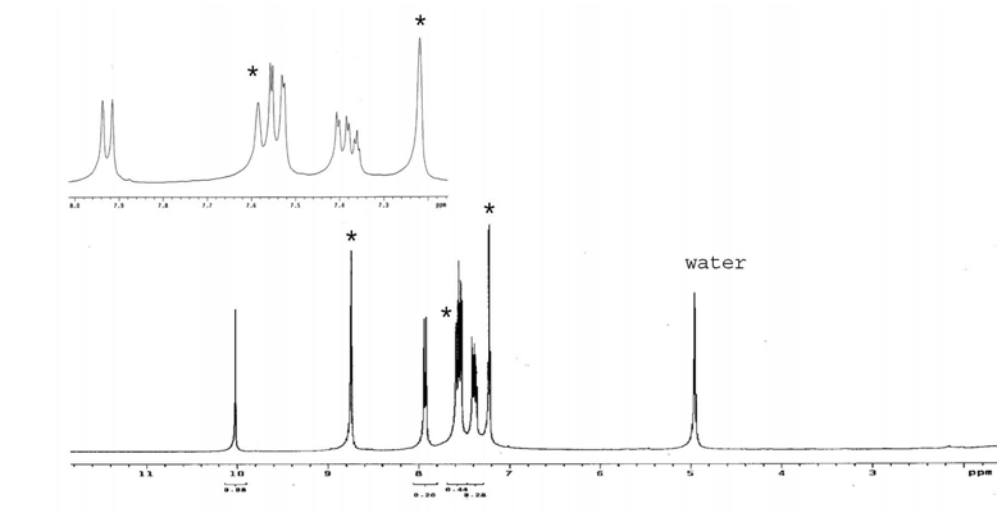


Figure 7.2 ^{1}H NMR spectrum of **137** (∗ solvent = Pyridine-d_5)

Crown ether 138

Similar procedure as for the synthesis of **136** was followed, starting from basket **121**. Crown ether **138** was obtained in 95% yield as a white solid. Mp. >250°C with decomposition. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 6.69 (t, J = 2.0 Hz, 4H), 7.04 (s, 16H), 7.23 (t, J = 2.0 Hz, 8H), 9.91 (s, 4H). MS (MALDI): 955 $[M + Ag]^+$. Anal. Calcd. for $C_{52}H_{32}O_{12}\bullet 2H_2O$: C, 70.59; H, 4.10. Found: C, 70.63; H, 4.08.

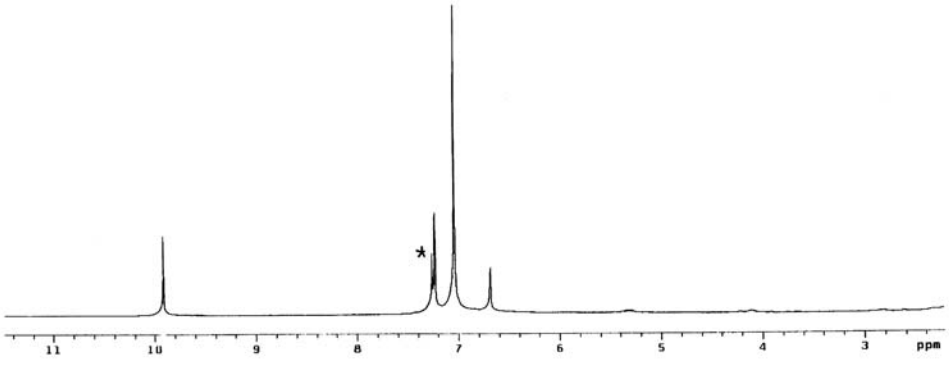


Figure 7.3 ^{1}H NMR spectrum of **138** (∗ solvent = $CDCl_3$)

Crown ether 139

Similar procedure as for the synthesis of **136** was followed, starting from basket **122**. Crown ether **139** was obtained in 85% yield as a white solid. Mp. > 250°C with decomposition. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.05 (s, 12H), 6.55 (t, J = 2.0 Hz, 4H), 6.78 (d, J = 8.0 Hz, 8H), 7.16 (t, J = 8.0 Hz, 4H), 7.21 (d, J = 2.0 Hz, 8H), 9.92 (s, 4H). MS (MALDI): 1011 $[M + Ag]^+$. Anal. Calcd. for $C_{56}H_{40}O_{12}$: C, 74.33; H, 4.46. Found: C, 74.47; H, 4.78.

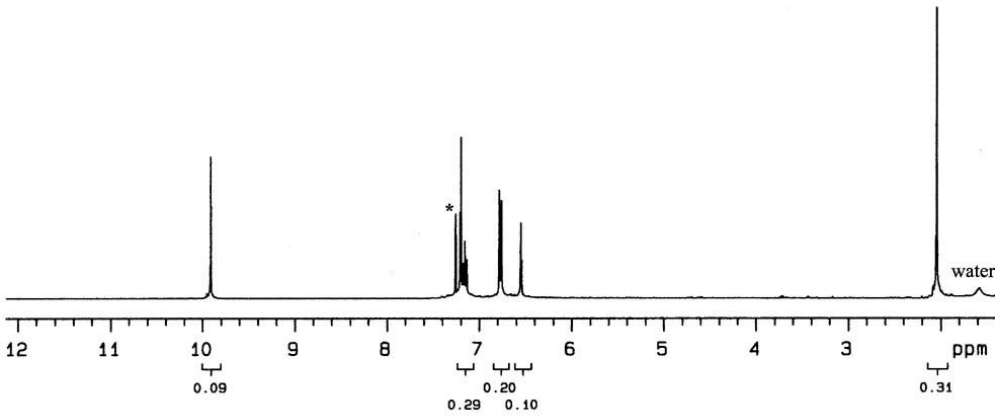


Figure 7.4 ^{1}H NMR spectrum of **139** (* solvent = $CDCl_3$)

Crown ether 140

Similar procedure as fir the synthesis of **136** was followed, starting from basket **123**. Crown ether **140** was obtained in 85% yield as a white solid. Mp. > 250°C with decomposition. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.34 (s, 12H), 6.41 (t, J = 2.0 Hz, 4H), 6.71 (d, J = 2.0 Hz, 8H), 6.89 (t, J = 2.0 Hz, 4H), 7.14 (d,

J = 2.0 Hz, 8H), 9.84 (s, 4H). MS (MALDI): 1011 $[M + Ag]^+$. Anal. Calcd. for $C_{56}H_{40}O_{12}$: C, 74.33; H, 4.46. Found: C, 74.37; H, 4.81.

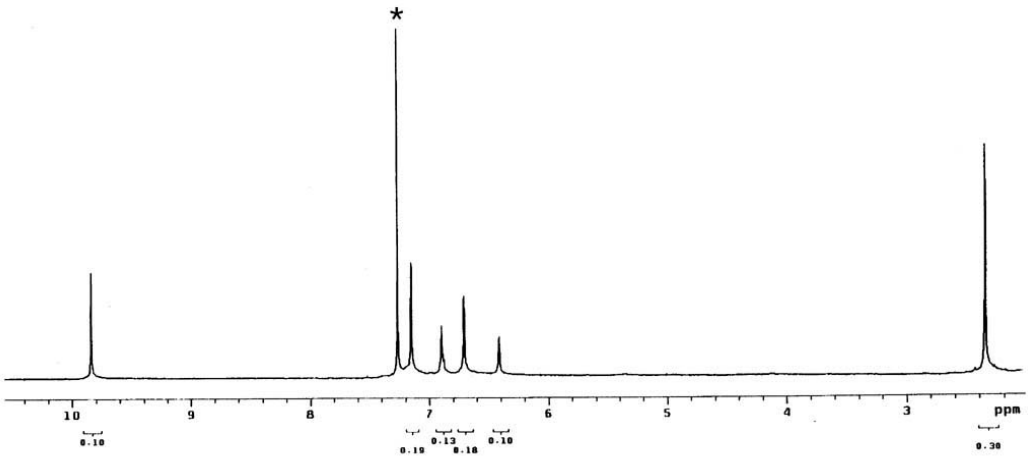


Figure 7.5 ^{1}H NMR spectrum of **140** (* solvent = $CDCl_3$)

Crown ether 141

To a solution of basket **124** (30 mg, 0.017 mmol) in 2 mL $SOCl_2$, was added BCl_3 (0.14 mL, 1.0 M solution in hexanes, 0.14 mmol). The mixture was stirred at rt for 1 h. After this time, solvent was removed under reduced pressure. 5 mL methanol was then added to the remaining solid and the solvent was removed under reduced pressure. The remaining solid was run through a short silica gel plug with a mobile phase of $CHCl_3$. Combine all the eluents and the solvent was removed under reduce pressure. The remaining solid was dissolved in 5 mL CH_2Cl_2 and 1 mL 37% aqueous HCl was added. The biphasic mixture was stirred at rt for 3 h. The mixture was partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and the salt filtered off. The filtrate was concentrated under reduced pressure.

Column chromatography with a mobile phase of $CHCl_3$ gave crown ether **141** (12 mg, 0.012 mmol, 71%) as an off-white solid. Mp. > 250°C. ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm) 4.71 (s, 8H), 6.73 (t, J = 2.0 Hz, 4H), 7.02 (d, J = 2.0 Hz, 8H), 7.06 (t, J = 2.0 Hz, 4H), 7.30 (d, J = 2.0 Hz, 8H), 9.89 (s, 4H). MS (MALDI): 1149 $[M + Ag]^+$. Anal. Calcd. for $C_{56}H_{36}O_{12}Cl_4 \bullet 2H_2O$: C, 62.35; H, 3.74. Found: C, 62.52; H, 3.50.

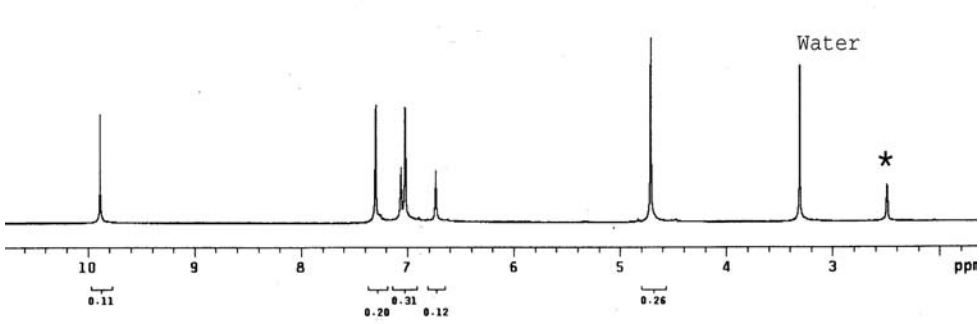


Figure 7.6 ^{1}H NMR spectrum of **141** (* solvent = DMSO-d_6)

Crown ether 142

Similar procedure as for the synthesis of **136** was followed, starting from basket **130**. Crown ether **142** was obtained in 83% yield as a white solid. Mp. > 250°C with decomposition. ^{1}H NMR (CD_2Cl_2, 400 MHz) δ (ppm) 1.97 (s, 3H), 6.64 (t, J = 2.0 Hz, 2H), 6.69 (t, J = 2.0 Hz, 1H), 6.76 (t, J = 2.0 Hz, 2H), 6.81 ~ 6.90 (m, 10H), 7.10 ~ 7.30 (m, 9H), 7.34 (t, J = 8.0 Hz, 1H), 7.37 (t, J = 8.0 Hz, 2H), 9.86 (s, 4H). MS (MALDI): 969 $[M + Ag]^+$. Anal. Calcd. for $C_{68}H_{40}O_{12} \bullet H_2O$: C, 72.27; H, 4.12. Found: C, 72.52; H, 4.22.

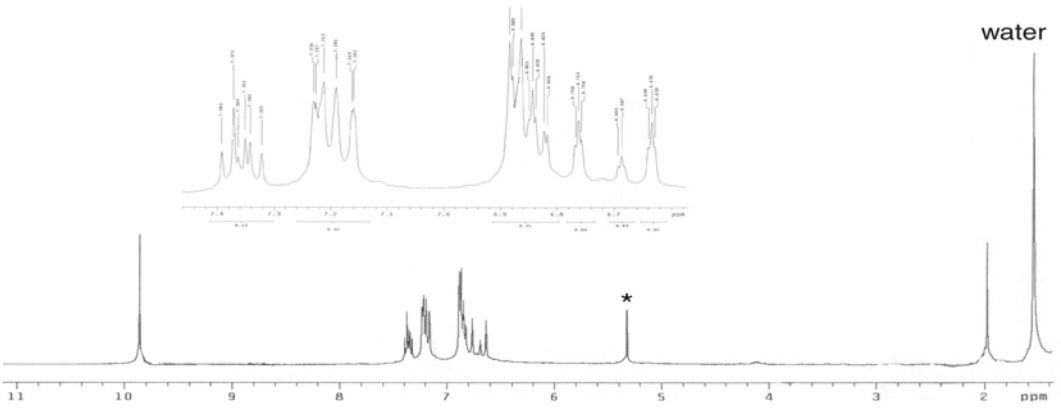


Figure 7.7 ^{1}H NMR spectrum of **142** (* solvent = CD_2Cl_2)

Synthesis of 143

To a solution of **127** (0.10 g, 0.058 mmol) in 10 mL CH_2Cl_2, was added BBr_3 (0.22 mL, 1.2 M solution in CH_2Cl_2, 0.26 mmol). The mixture was stirred at rt for 1 h. After this time, 5 mL methanol was added to the mixture to quench the reaction. The solvent was removed under reduced pressure. The remaining solid was run through a short silica gel plug with a mobile phase of $CHCl_3$. Combine all the eluent and the solvent was removed under reduce pressure. The remaining solid was dissolved in 5 mL CH_2Cl_2, to which 1 mL 10% aqueous HCl was added. The biphasic mixture was stirred at rt for 1 d. The mixture was partitioned between $CHCl_3$ and water three times. The organic layers were combined, dried with anhydrous Na_2SO_4 and the salt filtered off. The filtrate was concentrated under reduced pressure. Column chromatography with $CHCl_3$ gave **143** (0.042g, 0.047 mmol, 80%) as a white solid. Mp. 60~65°C. ^{1}H NMR (Acetone-d_6, 400 MHz) δ (ppm) 6.86 (t, J = 2.0Hz, 1H), 6.90 (t, J = 2.0 Hz, 2H), 6.93~7.00 (m, 7H), 7.06 (t, J = 2.0 Hz, 2H), 7.31 (t, J = 2.0 Hz, 4H), 7.46 (t, J =

8.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.50~7.54 (m, 4H), 7.80 (t, J = 2.0 Hz, 1H), 9.95 (s, 2H), 9.96 (s, 2H). MS (MALDI): 1007 $[M + Ag]^+$.

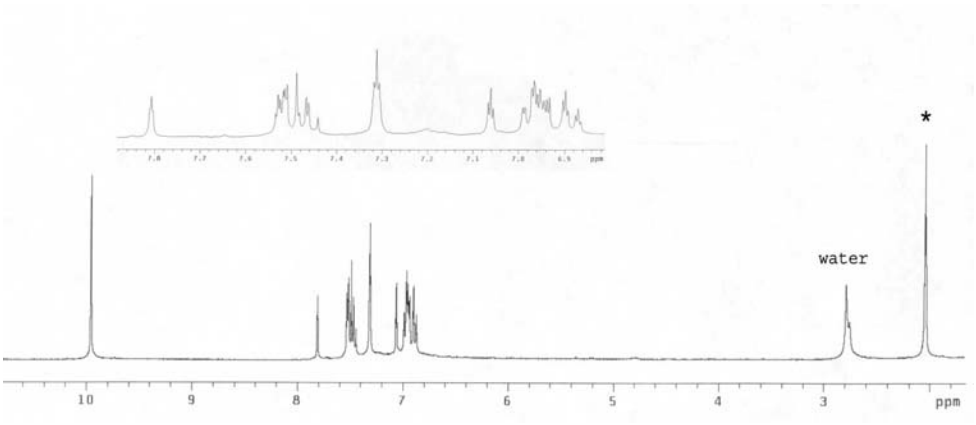


Figure 7.8 ^{1}H NMR spectrum of **143** (* solvent = Acetone-d_6)

7.3 X-ray Structure Analysis of Basket 124

The crystal was grown *via* a slow evaporation of a solution of basket **124** in THF/$CHCl_3$ in a closed vial. The crystal structure of **124** was determined by X-ray diffraction by Dr. Edwin D. Stevens at the University of New Orleans (Figure 4.1). Data were collected at 113K on Bruker SMART 1K CCD and a graphite monochronator utilizing MoK_α radiation (λ = 0.71073 Å). Cell parameters were refined using up to 8773 reflection. The structure was solved by the direct methods in SHELXTL, and refined using full-matrix least squares.

Table 7.1 Crystal data and structure refinement for basket **124**.

Empirical formula	$C_{120.93}\ H_{92.53}\ Cl_{14.77}\ O_{20}$
Formula weight	2389.35
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 16.2663(7)Å α = 86.1780(10) deg.
	b = 16.9619(8)Å β = 82.8550(10) deg.
	c = 21.0161(10)Å γ = 80.3040(10) deg.
Volume	5665.1(5) $Å^3$
Z, Calculated density	2, 1.401 Mg/m^3
Absorption coefficient	0.428 mm^{-1}
F(000)	2459
Crystal size	0.35 x 0.40 x 0.60 mm
Theta range for data collection	1.53 to 30.57 deg.
Limiting indices	$-23 \le h \le 23, -24 \le k \le 24, -29 \le l \le 29$
Reflections collected / unique	145984 / 32627 [R(int) = 0.0413]
Completeness to theta = 30.57	93.7 %
Absorption correction	Empirical
Max. and min. transmission	1.000000 and 0.853945
Refinement method	Full-matrix-block least-squares on F^2
Data / restraints / parameters	32627 / 2650 / 1934
Goodness-of-fit on F^2	2.123
Final R indices [I>2sigma(I)]	R1 = 0.1007, wR2 = 0.2922
R indices (all data)	R1 = 0.1332, wR2 = 0.3102
Largest diff. peak and hole	1.699 and -1.697 $e.Å^{-3}$

Table 7.2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for basket **124**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	13197(2)	390(2)	1459(2)	24(1)
C(138)	6103(4)	4918(4)	-1090(4)	87(2)
Cl(1)	5301(2)	4474(1)	-1326(1)	108(1)
Cl(2)	6779(2)	5159(2)	-1744(2)	120(1)
Cl(3)	5711(2)	5735(2)	-634(2)	106(1)
C(142)	10535(5)	5847(4)	2863(3)	80(2)
C(146)	10814(13)	990(9)	3431(8)	173(5)
Cl(7)	11037(8)	1256(7)	2641(6)	201(4)
Cl(8)	11291(6)	1566(4)	3849(3)	185(3)
Cl(9)	11482(8)	149(5)	3642(5)	246(5)
C(150)	8106(7)	-2031(6)	1371(6)	97(3)
Cl(12)	8012(7)	-1926(7)	597(5)	206(4)
Cl(10)	9112(2)	-2464(3)	1527(2)	97(1)
Cl(11)	7905(2)	-1050(2)	1560(1)	83(1)
C(154)	10543(11)	1140(8)	3305(7)	134(6)
Cl(19)	10999(2)	1294(2)	2534(2)	58(1)
Cl(20)	9829(6)	486(4)	3404(3)	169(3)
Cl(21)	9884(4)	1950(3)	3636(3)	125(2)
C(156)	14970(10)	3525(8)	2477(7)	191(4)
Cl(25)	15112(7)	2960(5)	1794(4)	213(3)
Cl(26)	15092(3)	2721(3)	2972(2)	118(2)
Cl(27)	15885(4)	3889(4)	2437(3)	162(2)
C(155)	15030(11)	3591(11)	2321(7)	206(5)
Cl(28)	15990(7)	3341(6)	1923(3)	169(3)
Cl(29)	14999(10)	2612(8)	2220(7)	237(4)
Cl(30)	15437(4)	3463(4)	3038(3)	108(2)
C(160)	8880(10)	-2305(9)	883(8)	141(4)
Cl(13)	8360(8)	-2719(7)	1537(6)	187(3)
Cl(14)	7984(3)	-2119(5)	527(3)	78(2)
Cl(15)	8533(6)	-1312(5)	1047(5)	157(3)
C(168)	11049(10)	-510(15)	4883(10)	78(6)
Cl(34)	11699(5)	150(6)	4619(5)	89(3)
Cl(35)	10017(6)	-298(6)	4840(5)	89(3)
Cl(36)	11189(5)	-970(6)	5615(4)	79(3)
C(161)	8948(16)	-2116(17)	797(12)	141(5)
Cl(41)	8242(15)	-1442(12)	427(10)	110(4)

Cl(40)	8678(13)	-1860(11)	1576(9)	105(4)
Cl(39)	8232(14)	-2754(12)	985(10)	115(4)
C(2)	12610(2)	248(2)	1070(2)	24(1)
C(3)	12111(2)	-348(2)	1215(2)	24(1)
C(4)	11459(2)	-489(2)	783(2)	26(1)
Cl(4)	9500(2)	6253(2)	3042(1)	99(1)
C(5)	10622(2)	12(2)	1006(2)	25(1)
Cl(5)	11081(1)	5825(1)	3537(1)	75(1)
C(6)	10375(2)	799(2)	766(2)	24(1)
Cl(6)	11003(3)	6259(2)	2172(2)	171(2)
C(7)	9630(2)	1273(2)	1006(2)	23(1)
C(8)	9370(2)	2141(2)	773(2)	23(1)
C(9)	9663(2)	2699(2)	1207(2)	23(1)
C(10)	10445(2)	2953(2)	1076(2)	23(1)
C(11)	10744(2)	3424(2)	1489(2)	22(1)
C(12)	11618(2)	3658(2)	1363(2)	23(1)
C(13)	12242(2)	3040(2)	1685(2)	22(1)
C(14)	12697(2)	2379(2)	1368(2)	22(1)
C(15)	13260(2)	1798(2)	1657(2)	23(1)
C(16)	13720(2)	1062(2)	1318(2)	23(1)
C(17)	13274(2)	-92(2)	2022(2)	24(1)
C(18)	12785(2)	-680(2)	2187(2)	27(1)
C(19)	12205(2)	-802(2)	1786(2)	26(1)
O(20)	11704(2)	-1381(1)	1993(1)	28(1)
C(21)	10878(2)	-1039(2)	2250(2)	27(1)
O(22)	10305(2)	-1044(1)	1799(1)	28(1)
C(23)	10085(2)	-285(2)	1501(2)	26(1)
C(24)	9338(2)	163(2)	1739(2)	26(1)
C(25)	9121(2)	941(2)	1497(2)	25(1)
O(26)	8373(1)	1373(1)	1768(1)	27(1)
C(27)	8466(2)	1916(2)	2227(2)	26(1)
O(28)	8396(1)	2702(1)	1955(1)	26(1)
C(29)	9177(2)	2942(2)	1770(2)	25(1)
C(30)	9445(2)	3412(2)	2191(2)	26(1)
C(31)	10229(2)	3637(2)	2053(2)	24(1)
O(32)	10497(1)	4063(1)	2516(1)	25(1)
C(33)	11071(2)	3583(2)	2895(2)	24(1)
O(34)	11902(1)	3718(1)	2688(1)	26(1)
C(35)	12367(2)	3100(2)	2325(2)	24(1)
C(36)	12928(2)	2546(2)	2627(2)	25(1)
C(37)	13366(2)	1899(2)	2292(2)	23(1)
O(38)	13908(1)	1339(1)	2628(1)	26(1)
C(39)	13560(2)	648(2)	2855(2)	25(1)
O(40)	13845(1)	9(1)	2438(1)	26(1)
C(41)	13875(2)	-416(2)	3716(2)	32(1)
C(42)	13996(2)	-633(2)	4345(2)	34(1)

O(43)	14095(2)	-1430(2)	4563(1)	44(1)
C(44)	13667(3)	-1935(2)	4284(2)	40(1)
C(45)	12791(3)	-1832(3)	4398(2)	44(1)
C(46)	12401(3)	-2386(3)	4149(2)	45(1)
O(47)	11541(2)	-2346(2)	4326(2)	58(1)
C(48)	10982(3)	-2065(3)	3881(2)	40(1)
C(49)	11225(3)	-1784(2)	3265(2)	37(1)
C(50)	10620(2)	-1483(2)	2869(2)	31(1)
C(51)	9766(3)	-1467(2)	3079(2)	37(1)
C(52)	9547(2)	-1745(3)	3705(2)	40(1)
O(53)	8735(2)	-1757(2)	3968(2)	62(1)
C(54)	8051(3)	-1395(3)	3645(2)	44(1)
C(55)	7722(3)	-604(3)	3753(2)	41(1)
C(56)	6960(2)	-300(2)	3525(2)	34(1)
O(57)	6538(2)	460(2)	3668(2)	43(1)
C(58)	6933(2)	1117(2)	3504(2)	33(1)
C(59)	7482(2)	1165(2)	2945(2)	32(1)
C(60)	7808(2)	1870(2)	2793(2)	27(1)
C(61)	7592(2)	2513(2)	3193(2)	29(1)
C(62)	7041(2)	2445(2)	3744(2)	30(1)
O(63)	6764(2)	3057(2)	4160(1)	40(1)
C(64)	7213(2)	3694(2)	4116(2)	31(1)
C(65)	7937(2)	3603(2)	4420(2)	34(1)
C(66)	8326(2)	4271(2)	4423(2)	34(1)
O(67)	8995(2)	4220(2)	4787(1)	45(1)
C(68)	9803(2)	4018(2)	4500(2)	31(1)
C(69)	10004(2)	3973(2)	3834(2)	30(1)
C(70)	10848(2)	3755(2)	3597(2)	25(1)
C(71)	11467(2)	3586(2)	4007(2)	28(1)
C(72)	11233(2)	3632(2)	4660(2)	28(1)
O(73)	11792(2)	3450(2)	5117(1)	39(1)
C(74)	12635(2)	3154(2)	4933(2)	30(1)
C(75)	12897(2)	2342(2)	4994(2)	34(1)
C(76)	13753(2)	2065(2)	4908(2)	33(1)
O(77)	14049(2)	1247(2)	5026(1)	45(1)
C(78)	13973(2)	723(2)	4576(2)	34(1)
C(79)	13851(2)	969(2)	3939(2)	32(1)
C(80)	13799(2)	392(2)	3514(2)	29(1)
C(81)	14050(2)	-77(2)	4781(2)	34(1)
C(82)	14129(3)	-2559(3)	3933(2)	44(1)
C(83)	13717(3)	-3097(3)	3680(2)	50(1)
C(84)	12847(3)	-3013(3)	3791(2)	49(1)
C(85)	10148(3)	-2046(3)	4110(2)	42(1)
C(86)	7671(3)	-1873(3)	3311(2)	43(1)
C(87)	6911(3)	-1553(2)	3088(2)	43(1)
C(88)	6552(3)	-768(2)	3200(2)	38(1)

C(89)	6705(2)	1746(2)	3905(2)	33(1)
C(90)	6887(2)	4404(2)	3829(2)	33(1)
C(91)	7299(3)	5065(2)	3830(2)	37(1)
C(92)	8024(2)	4989(2)	4130(2)	35(1)
C(93)	10410(2)	3849(2)	4913(2)	30(1)
C(94)	13190(2)	3693(2)	4778(2)	33(1)
C(95)	14210(5)	-3757(4)	3268(4)	72(2)
O(98)	14907(2)	-4164(2)	3553(3)	80(1)
C(99)	6441(4)	-2057(3)	2739(3)	66(1)
O(100)	6956(3)	-2727(2)	2465(2)	71(1)
C(101)	6940(4)	5885(3)	3563(3)	63(1)
O(102)	6508(2)	5871(2)	3031(2)	46(1)
C(103)	14627(7)	4014(6)	4561(7)	52(3)
O(104)	14580(3)	4407(3)	3953(3)	60(2)
C(105)	14742(10)	3897(8)	4539(14)	44(4)
O(105)	14496(7)	4716(7)	4639(7)	74(4)
C(106)	11756(2)	-366(2)	65(2)	29(1)
C(107)	12522(2)	-995(2)	-154(2)	32(1)
C(108)	13104(2)	-719(2)	-708(2)	32(1)
C(109)	13282(3)	-1096(3)	-1277(2)	48(1)
C(110)	13835(3)	-815(4)	-1785(2)	63(2)
C(111)	14204(3)	-167(4)	-1715(2)	59(1)
C(112)	14044(3)	212(3)	-1143(3)	59(1)
C(113)	13501(3)	-62(3)	-646(2)	48(1)
C(114)	9638(2)	2290(2)	56(2)	28(1)
C(115)	9199(2)	3101(2)	-206(2)	31(1)
C(116)	8293(2)	3106(2)	-271(2)	31(1)
C(117)	7661(3)	3352(2)	219(2)	43(1)
C(118)	6827(3)	3321(3)	151(3)	58(1)
C(119)	6611(3)	3043(3)	398(3)	59(1)
C(120)	7230(3)	2797(3)	-884(3)	52(1)
C(121)	8060(3)	2831(2)	-822(2)	37(1)
C(122)	11920(2)	3808(2)	649(2)	25(1)
C(123)	11418(3)	4563(2)	348(2)	37(1)
C(124)	11640(3)	4644(2)	-365(2)	37(1)
C(125)	11047(4)	4624(3)	-780(3)	63(1)
C(126)	11239(5)	4700(4)	-1446(3)	87(2)
C(127)	12046(5)	4792(4)	-1699(3)	88(2)
C(128)	12645(5)	4820(3)	-1294(3)	72(2)
C(129)	12447(3)	4735(3)	-631(2)	51(1)
C(130)	13968(2)	1221(2)	599(2)	26(1)
C(131)	14559(2)	1844(2)	466(2)	33(1)
C(132)	14680(2)	2070(2)	-243(2)	30(1)
C(133)	15324(3)	1652(3)	-651(2)	46(1)
C(134)	15407(3)	1854(3)	-1304(3)	59(1)
C(135)	14847(4)	2461(3)	-1560(2)	55(1)

C(136)	14209(4)	2870(3)	-1165(2)	51(1)
C(137)	14144(3)	2677(2)	-510(2)	39(1)

Table 7.3 Bond lengths [Å] and angles [deg] for basket **124**.

C(1)-C(2)	1.390(5)
C(1)-C(17)	1.400(5)
C(1)-C(16)	1.527(5)
C(138)-Cl(2)	1.723(8)
C(138)-Cl(3)	1.724(8)
C(138)-Cl(1)	1.747(6)
C(142)-Cl(4)	1.713(8)
C(142)-Cl(6)	1.717(7)
C(142)-Cl(5)	1.757(8)
C(146)-Cl(8)	1.693(14)
C(146)-Cl(7)	1.702(14)
C(146)-Cl(9)	1.710(15)
Cl(8)-Cl(9)	2.433(13)
C(150)-Cl(12)	1.648(12)
C(150)-Cl(11)	1.706(11)
C(150)-Cl(10)	1.739(11)
C(154)-Cl(19)	1.718(13)
C(154)-Cl(20)	1.722(14)
C(154)-Cl(21)	1.722(14)
C(156)-Cl(26)	1.659(13)
C(156)-Cl(27)	1.696(14)
C(156)-Cl(25)	1.750(13)
Cl(25)-Cl(26)	2.479(10)
C(155)-Cl(28)	1.677(15)
C(155)-Cl(29)	1.698(15)
C(155)-Cl(30)	1.706(15)
Cl(28)-Cl(29)	2.198(17)
Cl(28)-Cl(30)	2.412(9)
C(160)-Cl(14)	1.694(14)
C(160)-Cl(13)	1.697(15)
C(160)-Cl(15)	1.728(14)
Cl(13)-Cl(14)	1.396(14)
Cl(14)-Cl(15)	2.174(9)
C(168)-Cl(35)	1.670(14)
C(168)-Cl(34)	1.688(14)
C(168)-Cl(36)	1.701(14)
C(168)-Cl(35)#1	2.07(3)
Cl(35)-Cl(35)#1	1.24(2)
Cl(35)-C(168)#1	2.07(3)
C(161)-Cl(41)	1.701(16)
C(161)-Cl(40)	1.708(16)
C(161)-Cl(39)	1.714(16)

Cl(41)-Cl(39)	2.45(2)
Cl(40)-Cl(39)	2.28(2)
C(2)-C(3)	1.396(5)
C(3)-C(19)	1.392(5)
C(3)-C(4)	1.537(5)
C(4)-C(5)	1.516(5)
C(4)-C(106)	1.537(4)
C(5)-C(23)	1.397(5)
C(5)-C(6)	1.407(5)
C(6)-C(7)	1.394(5)
C(7)-C(25)	1.390(5)
C(7)-C(8)	1.527(5)
C(8)-C(9)	1.526(5)
C(8)-C(114)	1.531(4)
C(9)-C(29)	1.386(5)
C(9)-C(10)	1.400(5)
C(10)-C(11)	1.400(5)
C(11)-C(31)	1.394(5)
C(11)-C(12)	1.527(5)
C(12)-C(13)	1.518(5)
C(12)-C(122)	1.537(4)
C(13)-C(14)	1.395(5)
C(13)-C(35)	1.398(5)
C(14)-C(15)	1.391(5)
C(15)-C(37)	1.392(5)
C(15)-C(16)	1.515(5)
C(16)-C(130)	1.533(4)
C(17)-C(18)	1.379(5)
C(17)-O(40)	1.388(4)
C(18)-C(19)	1.390(5)
C(19)-O(20)	1.393(4)
O(20)-C(21)	1.425(4)
C(21)-O(22)	1.411(4)
C(21)-C(50)	1.509(5)
O(22)-C(23)	1.403(4)
C(23)-C(24)	1.376(5)
C(24)-C(25)	1.387(5)
C(25)-O(26)	1.387(4)
O(26)-C(27)	1.415(4)
C(27)-O(28)	1.408(4)
C(27)-C(60)	1.503(5)
O(28)-C(29)	1.399(4)
C(29)-C(30)	1.384(5)
C(30)-C(31)	1.383(5)
C(31)-O(32)	1.402(4)
O(32)-C(33)	1.416(4)

C(33)-O(34)	1.419(4)
C(33)-C(70)	1.510(5)
O(34)-C(35)	1.396(4)
C(35)-C(36)	1.376(5)
C(36)-C(37)	1.386(5)
C(37)-O(38)	1.401(4)
O(38)-C(39)	1.416(4)
C(39)-O(40)	1.420(4)
C(39)-C(80)	1.503(5)
C(41)-C(42)	1.377(6)
C(41)-C(80)	1.396(5)
C(42)-C(81)	1.378(6)
C(42)-O(43)	1.389(5)
O(43)-C(44)	1.389(5)
C(44)-C(82)	1.387(7)
C(44)-C(45)	1.398(6)
C(45)-C(46)	1.382(7)
C(46)-C(84)	1.391(8)
C(46)-O(47)	1.393(5)
O(47)-C(48)	1.391(5)
C(48)-C(85)	1.377(6)
C(48)-C(49)	1.384(6)
C(49)-C(50)	1.377(6)
C(50)-C(51)	1.401(6)
C(51)-C(52)	1.393(6)
C(52)-O(53)	1.370(5)
C(52)-C(85)	1.387(6)
O(53)-C(54)	1.406(5)
C(54)-C(86)	1.373(7)
C(54)-C(55)	1.380(7)
C(55)-C(56)	1.389(6)
C(56)-C(88)	1.378(6)
C(56)-O(57)	1.389(5)
O(57)-C(58)	1.381(4)
C(58)-C(89)	1.376(6)
C(58)-C(59)	1.392(5)
C(59)-C(60)	1.390(5)
C(60)-C(61)	1.394(5)
C(61)-C(62)	1.385(5)
C(62)-O(63)	1.382(5)
C(62)-C(89)	1.393(5)
O(63)-C(64)	1.395(5)
C(64)-C(90)	1.366(6)
C(64)-C(65)	1.390(6)
C(65)-C(66)	1.387(6)
C(66)-C(92)	1.370(6)

C(66)-O(67)	1.394(5)
O(67)-C(68)	1.374(4)
C(68)-C(93)	1.377(5)
C(68)-C(69)	1.401(5)
C(69)-C(70)	1.397(5)
C(70)-C(71)	1.387(5)
C(71)-C(72)	1.382(5)
C(72)-C(93)	1.377(5)
C(72)-O(73)	1.388(4)
O(73)-C(74)	1.395(4)
C(74)-C(75)	1.374(6)
C(74)-C(94)	1.386(6)
C(75)-C(76)	1.385(6)
C(76)-C(96)	1.378(6)
C(76)-O(77)	1.405(5)
O(77)-C(78)	1.370(5)
C(78)-C(81)	1.385(6)
C(78)-C(79)	1.404(5)
C(79)-C(80)	1.387(5)
C(82)-C(83)	1.388(7)
C(83)-C(84)	1.389(7)
C(83)-C(97)	1.517(7)
C(86)-C(87)	1.389(7)
C(87)-C(88)	1.384(6)
C(87)-C(99)	1.514(6)
C(90)-C(91)	1.400(6)
C(91)-C(92)	1.388(6)
C(91)-C(101)	1.514(6)
C(94)-C(95)	1.396(5)
C(95)-C(96)	1.396(6)
C(95)-C(103)	1.505(8)
C(95)-C(105)	1.508(10)
C(97)-O(98)	1.404(8)
C(99)-O(100)	1.404(6)
C(101)-O(102)	1.397(5)
C(103)-O(104)	1.407(11)
C(105)-O(105)	1.400(12)
C(106)-C(107)	1.543(5)
C(107)-C(108)	1.507(6)
C(108)-C(109)	1.370(6)
C(108)-C(113)	1.398(6)
C(109)-C(110)	1.420(8)
C(110)-C(111)	1.362(9)
C(111)-C(112)	1.378(9)
C(112)-C(113)	1.390(7)
C(114)-C(115)	1.540(5)

C(115)-C(116)	1.496(6)
C(116)-C(117)	1.393(6)
C(116)-C(121)	1.393(6)
C(117)-C(118)	1.392(8)
C(118)-C(119)	1.379(9)
C(119)-C(120)	1.376(9)
C(120)-C(121)	1.383(6)
C(122)-C(123)	1.541(5)
C(123)-C(124)	1.499(6)
C(124)-C(129)	1.389(7)
C(124)-C(125)	1.383(7)
C(125)-C(126)	1.399(8)
C(126)-C(127)	1.383(12)
C(127)-C(128)	1.380(11)
C(128)-C(129)	1.395(8)
C(130)-C(131)	1.535(5)
C(131)-C(132)	1.509(6)
C(132)-C(137)	1.370(6)
C(132)-C(133)	1.395(6)
C(133)-C(134)	1.387(8)
C(134)-C(135)	1.383(9)
C(135)-C(136)	1.367(8)
C(136)-C(137)	1.389(7)
C(2)-C(1)-C(17)	117.3(3)
C(2)-C(1)-C(16)	123.5(3)
C(17)-C(1)-C(16)	119.2(3)
Cl(2)-C(138)-Cl(3)	111.7(4)
Cl(2)-C(138)-Cl(1)	111.0(5)
Cl(3)-C(138)-Cl(1)	111.8(4)
Cl(4)-C(142)-Cl(6)	113.4(5)
Cl(4)-C(142)-Cl(5)	110.8(4)
Cl(6)-C(142)-Cl(5)	114.8(5)
Cl(8)-C(146)-Cl(7)	106.5(12)
Cl(8)-C(146)-Cl(9)	91.3(9)
Cl(7)-C(146)-Cl(9)	110.5(13)
C(146)-Cl(8)-Cl(9)	44.6(6)
C(146)-Cl(9)-Cl(8)	44.1(5)
Cl(12)-C(150)-Cl(11)	99.6(7)
Cl(12)-C(150)-Cl(10)	112.6(8)
Cl(11)-C(150)-Cl(10)	110.5(7)
Cl(19)-C(154)-Cl(20)	116.1(10)
Cl(19)-C(154)-Cl(21)	115.9(10)
Cl(20)-C(154)-Cl(21)	97.0(9)
Cl(26)-C(156)-Cl(27)	104.6(9)
Cl(26)-C(156)-Cl(25)	93.3(8)
Cl(27)-C(156)-Cl(25)	103.0(10)

C(156)-Cl(25)-Cl(26)	41.9(5)
C(156)-Cl(26)-Cl(25)	44.8(5)
Cl(28)-C(155)-Cl(29)	81.3(10)
Cl(28)-C(155)-Cl(30)	90.9(9)
Cl(29)-C(155)-Cl(30)	97.3(11)
C(155)-Cl(28)-Cl(29)	49.8(7)
C(155)-Cl(28)-Cl(30)	45.0(6)
Cl(29)-Cl(28)-Cl(30)	67.2(5)
C(155)-Cl(29)-Cl(28)	49.0(7)
C(155)-Cl(30)-Cl(28)	44.0(6)
Cl(14)-C(160)-Cl(13)	89.9(10)
Cl(14)-C(160)-Cl(15)	78.9(7)
Cl(13)-C(160)-Cl(15)	97.9(10)
C(160)-Cl(13)-Cl(14)	45.0(6)
C(160)-Cl(14)-Cl(15)	51.3(5)
C(160)-Cl(14)-Cl(13)	45.1(6)
Cl(15)-Cl(14)-Cl(13)	68.6(4)
C(160)-Cl(15)-Cl(14)	49.9(5)
Cl(35)-C(168)-Cl(34)	122.0(13)
Cl(35)-C(168)-Cl(36)	107.4(10)
Cl(34)-C(168)-Cl(36)	115.9(12)
Cl(35)-C(168)-Cl(35)#1	36.9(9)
Cl(34)-C(168)-Cl(35)#1	98.5(13)
Cl(36)-C(168)-Cl(35)#1	98.1(13)
Cl(35)#1-Cl(35)-C(168)	89.3(16)
Cl(35)#1-Cl(35)-C(168)#1	53.8(9)
C(168)-Cl(35)-C(168)#1	143.1(9)
Cl(41)-C(161)-Cl(40)	100.5(16)
Cl(41)-C(161)-Cl(39)	91.5(14)
Cl(40)-C(161)-Cl(39)	83.7(12)
C(161)-Cl(41)-Cl(39)	44.4(8)
C(161)-Cl(40)-Cl(39)	48.2(7)
C(161)-Cl(39)-Cl(40)	48.0(7)
C(161)-Cl(39)-Cl(41)	44.0(8)
Cl(40)-Cl(39)-Cl(41)	67.2(8)
C(1)-C(2)-C(3)	123.2(3)
C(19)-C(3)-C(2)	117.1(3)
C(19)-C(3)-C(4)	120.5(3)
C(2)-C(3)-C(4)	122.4(3)
C(5)-C(4)-C(106)	114.4(3)
C(5)-C(4)-C(3)	108.8(3)
C(106)-C(4)-C(3)	112.6(3)
C(23)-C(5)-C(6)	117.1(3)
C(23)-C(5)-C(4)	119.8(3)
C(6)-C(5)-C(4)	122.9(3)
C(7)-C(6)-C(5)	122.3(3)

C(25)-C(7)-C(6)	117.8(3)
C(25)-C(7)-C(8)	119.1(3)
C(6)-C(7)-C(8)	123.0(3)
C(7)-C(8)-C(9)	109.5(3)
C(7)-C(8)-C(114)	113.0(3)
C(9)-C(8)-C(114)	114.1(2)
C(29)-C(9)-C(10)	117.1(3)
C(29)-C(9)-C(8)	120.7(3)
C(10)-C(9)-C(8)	122.1(3)
C(9)-C(10)-C(11)	122.8(3)
C(31)-C(11)-C(10)	117.2(3)
C(31)-C(11)-C(12)	120.2(3)
C(10)-C(11)-C(12)	122.5(3)
C(13)-C(12)-C(11)	109.8(3)
C(13)-C(12)-C(122)	111.6(2)
C(11)-C(12)-C(122)	114.3(2)
C(14)-C(13)-C(35)	116.9(3)
C(14)-C(13)-C(12)	122.2(3)
C(35)-C(13)-C(12)	120.9(3)
C(15)-C(14)-C(13)	123.2(3)
C(14)-C(15)-C(37)	117.0(3)
C(14)-C(15)-C(16)	122.7(3)
C(37)-C(15)-C(16)	120.2(3)
C(15)-C(16)-C(1)	108.7(3)
C(15)-C(16)-C(130)	113.6(3)
C(1)-C(16)-C(130)	113.1(2)
C(18)-C(17)-O(40)	117.6(3)
C(18)-C(17)-C(1)	121.4(3)
O(40)-C(17)-C(1)	121.1(3)
C(17)-C(18)-C(19)	119.5(3)
C(18)-C(19)-O(20)	116.8(3)
C(18)-C(19)-C(3)	121.5(3)
O(20)-C(19)-C(3)	121.7(3)
C(19)-O(20)-C(21)	112.5(3)
O(22)-C(21)-O(20)	110.6(3)
O(22)-C(21)-C(50)	111.3(3)
O(20)-C(21)-C(50)	110.1(3)
C(23)-O(22)-C(21)	112.2(3)
C(24)-C(23)-C(5)	121.8(3)
C(24)-C(23)-O(22)	116.9(3)
C(5)-C(23)-O(22)	121.2(3)
C(23)-C(24)-C(25)	119.4(3)
C(24)-C(25)-O(26)	116.9(3)
C(24)-C(25)-C(7)	121.5(3)
O(26)-C(25)-C(7)	121.6(3)
C(25)-O(26)-C(27)	114.6(3)

O(28)-C(27)-O(26)	110.6(3)
O(28)-C(27)-C(60)	110.3(3)
O(26)-C(27)-C(60)	109.4(3)
C(29)-O(28)-C(27)	112.8(3)
C(30)-C(29)-C(9)	122.1(3)
C(30)-C(29)-O(28)	116.3(3)
C(9)-C(29)-O(28)	121.6(3)
C(29)-C(30)-C(31)	119.2(3)
C(30)-C(31)-C(11)	121.6(3)
C(30)-C(31)-O(32)	117.0(3)
C(11)-C(31)-O(32)	121.4(3)
C(31)-O(32)-C(33)	113.4(2)
O(32)-C(33)-O(34)	110.3(3)
O(32)-C(33)-C(70)	111.0(3)
O(34)-C(33)-C(70)	110.0(3)
C(35)-O(34)-C(33)	112.5(2)
C(36)-C(35)-O(34)	117.5(3)
C(36)-C(35)-C(13)	121.9(3)
O(34)-C(35)-C(13)	120.6(3)
C(35)-C(36)-C(37)	119.1(3)
C(36)-C(37)-C(15)	121.9(3)
C(36)-C(37)-O(38)	116.7(3)
C(15)-C(37)-O(38)	121.4(3)
C(37)-O(38)-C(39)	113.3(3)
O(38)-C(39)-O(40)	111.2(3)
O(38)-C(39)-C(80)	109.7(3)
O(40)-C(39)-C(80)	109.3(3)
C(17)-O(40)-C(39)	114.0(3)
C(42)-C(41)-C(80)	119.1(4)
C(41)-C(42)-C(81)	122.0(3)
C(41)-C(42)-O(43)	121.1(4)
C(81)-C(42)-O(43)	116.9(3)
C(44)-O(43)-C(42)	117.4(3)
O(43)-C(44)-C(82)	118.7(4)
O(43)-C(44)-C(45)	119.2(4)
C(82)-C(44)-C(45)	122.0(4)
C(46)-C(45)-C(44)	117.0(5)
C(45)-C(46)-C(84)	122.3(4)
C(45)-C(46)-O(47)	117.2(5)
C(84)-C(46)-O(47)	120.2(4)
C(48)-O(47)-C(46)	119.8(3)
C(85)-C(48)-C(49)	121.5(4)
C(85)-C(48)-O(47)	114.7(4)
C(49)-C(48)-O(47)	123.7(4)
C(50)-C(49)-C(48)	119.4(4)
C(49)-C(50)-C(51)	121.0(4)

C(49)-C(50)-C(21)	118.6(3)
C(51)-C(50)-C(21)	119.6(3)
C(52)-C(51)-C(50)	117.9(4)
O(53)-C(52)-C(85)	114.8(4)
O(53)-C(52)-C(51)	123.5(4)
C(85)-C(52)-C(51)	121.7(4)
C(52)-O(53)-C(54)	121.6(3)
C(86)-C(54)-C(55)	122.8(4)
C(86)-C(54)-O(53)	118.1(4)
C(55)-C(54)-O(53)	118.4(5)
C(54)-C(55)-C(56)	117.4(4)
C(88)-C(56)-C(55)	121.3(4)
C(88)-C(56)-O(57)	116.9(4)
C(55)-C(56)-O(57)	121.5(4)
C(58)-O(57)-C(56)	119.6(3)
C(89)-C(58)-O(57)	115.8(3)
C(89)-C(58)-C(59)	121.8(4)
O(57)-C(58)-C(59)	122.3(4)
C(60)-C(59)-C(58)	118.6(4)
C(59)-C(60)-C(61)	120.7(3)
C(59)-C(60)-C(27)	120.1(3)
C(61)-C(60)-C(27)	119.0(3)
C(62)-C(61)-C(60)	119.1(3)
O(63)-C(62)-C(61)	123.6(3)
O(63)-C(62)-C(89)	115.2(3)
C(61)-C(62)-C(89)	121.1(4)
C(62)-O(63)-C(64)	117.8(3)
C(90)-C(64)-C(65)	122.3(4)
C(90)-C(64)-O(63)	119.0(4)
C(65)-C(64)-O(63)	118.4(4)
C(66)-C(65)-C(64)	117.2(4)
C(92)-C(66)-C(65)	121.9(4)
C(92)-C(66)-O(67)	119.6(4)
C(65)-C(66)-O(67)	118.2(4)
C(68)-O(67)-C(66)	119.5(3)
O(67)-C(68)-C(93)	115.4(3)
O(67)-C(68)-C(69)	123.0(3)
C(93)-C(68)-C(69)	121.6(3)
C(70)-C(69)-C(68)	117.9(3)
C(71)-C(70)-C(69)	121.1(3)
C(71)-C(70)-C(33)	119.2(3)
C(69)-C(70)-C(33)	119.0(3)
C(72)-C(71)-C(70)	118.6(3)
C(93)-C(72)-C(71)	122.0(3)
C(93)-C(72)-O(73)	114.2(3)
C(71)-C(72)-O(73)	123.8(3)

C(72)-O(73)-C(74)	120.4(3)
C(75)-C(74)-C(94)	122.6(4)
C(75)-C(74)-O(73)	118.2(4)
C(94)-C(74)-O(73)	118.7(4)
C(74)-C(75)-C(76)	117.8(4)
C(96)-C(76)-C(75)	121.8(4)
C(96)-C(76)-O(77)	118.6(4)
C(75)-C(76)-O(77)	119.4(4)
C(78)-O(77)-C(76)	118.2(3)
O(77)-C(78)-C(81)	116.0(3)
O(77)-C(78)-C(79)	122.6(4)
C(81)-C(78)-C(79)	121.3(4)
C(80)-C(79)-C(78)	118.5(4)
C(79)-C(80)-C(41)	120.6(4)
C(79)-C(80)-C(39)	119.4(3)
C(41)-C(80)-C(39)	119.6(3)
C(42)-C(81)-C(78)	118.5(4)
C(83)-C(82)-C(44)	119.6(4)
C(82)-C(83)-C(84)	119.6(5)
C(82)-C(83)-C(97)	120.2(5)
C(84)-C(83)-C(97)	120.2(5)
C(83)-C(84)-C(46)	119.5(5)
C(48)-C(85)-C(52)	118.5(4)
C(54)-C(86)-C(87)	118.5(4)
C(88)-C(87)-C(86)	120.2(4)
C(88)-C(87)-C(99)	118.5(4)
C(86)-C(87)-C(99)	121.2(4)
C(56)-C(88)-C(87)	119.7(4)
C(58)-C(89)-C(62)	118.6(3)
C(64)-C(90)-C(91)	119.3(4)
C(92)-C(91)-C(90)	119.4(4)
C(92)-C(91)-C(101)	118.4(4)
C(90)-C(91)-C(101)	122.0(4)
C(66)-C(92)-C(91)	119.8(4)
C(68)-C(93)-C(72)	118.7(3)
C(74)-C(94)-C(95)	118.7(4)
C(94)-C(95)-C(96)	119.6(4)
C(94)-C(95)-C(103)	116.6(6)
C(96)-C(95)-C(103)	123.8(6)
C(94)-C(95)-C(105)	126.0(8)
C(96)-C(95)-C(105)	114.4(8)
C(103)-C(95)-C(105)	9.5(11)
C(76)-C(96)-C(95)	119.5(4)
O(98)-C(97)-C(83)	111.8(6)
O(100)-C(99)-C(87)	113.4(5)
O(102)-C(101)-C(91)	114.2(4)

O(104)-C(103)-C(95)	113.4(9)
O(105)-C(105)-C(95)	114.7(12)
C(4)-C(106)-C(107)	111.6(3)
C(108)-C(107)-C(106)	114.9(3)
C(109)-C(108)-C(113)	117.4(4)
C(109)-C(108)-C(107)	122.7(4)
C(113)-C(108)-C(107)	119.9(4)
C(108)-C(109)-C(110)	120.7(5)
C(111)-C(110)-C(109)	120.7(5)
C(110)-C(111)-C(112)	119.5(5)
C(111)-C(112)-C(113)	119.8(5)
C(112)-C(113)-C(108)	121.9(5)
C(8)-C(114)-C(115)	112.3(3)
C(116)-C(115)-C(114)	112.9(3)
C(117)-C(116)-C(121)	117.9(4)
C(117)-C(116)-C(115)	121.7(4)
C(121)-C(116)-C(115)	120.3(4)
C(118)-C(117)-C(116)	120.1(5)
C(119)-C(118)-C(117)	121.0(5)
C(120)-C(119)-C(118)	119.3(5)
C(119)-C(120)-C(121)	120.1(5)
C(120)-C(121)-C(116)	121.6(5)
C(12)-C(122)-C(123)	112.9(3)
C(124)-C(123)-C(122)	112.3(3)
C(129)-C(124)-C(125)	117.9(5)
C(129)-C(124)-C(123)	121.3(4)
C(125)-C(124)-C(123)	120.8(4)
C(124)-C(125)-C(126)	121.9(6)
C(127)-C(126)-C(125)	119.1(7)
C(128)-C(127)-C(126)	120.0(6)
C(127)-C(128)-C(129)	120.2(6)
C(124)-C(129)-C(128)	120.9(6)
C(16)-C(130)-C(131)	112.5(3)
C(132)-C(131)-C(130)	110.5(3)
C(137)-C(132)-C(133)	117.7(4)
C(137)-C(132)-C(131)	121.1(4)
C(133)-C(132)-C(131)	121.2(4)
C(134)-C(133)-C(132)	120.2(5)
C(135)-C(134)-C(133)	120.7(5)
C(136)-C(135)-C(134)	119.6(5)
C(135)-C(136)-C(137)	119.2(5)
C(132)-C(137)-C(136)	122.6(4)

Symmetry transformations used to generate equivalent atoms:
#1 -x+2,-y,-z+1

Table 7.4 Anisotropic displacement parameters ($Å^2$ x 10^3) for basket **124**. The anisotropic displacement factor exponent takes the form: $-2\ pi^2\ [\ h^2\ a^{*2}\ U11 + ... + 2\ h\ k\ a^*\ b^*\ U12\ ]$

	U11	U22	U33	U23	U13	U12
C(1)	22(2)	18(1)	30(2)	-3(1)	-2(1)	-1(1)
C(138)	84(5)	51(4)	141(7)	38(4)	-65(5)	-36(4)
Cl(1)	99(2)	95(2)	157(2)	33(2)	-73(2)	-65(1)
Cl(2)	95(2)	92(2)	183(3)	-12(2)	-13(2)	-47(1)
Cl(3)	85(2)	96(2)	153(2)	-6(2)	-43(2)	-33(1)
C(142)	121(6)	56(4)	62(4)	-13(3)	22(4)	-30(4)
C(146)	219(14)	153(11)	169(10)	-28(10)	-31(11)	-84(9)
Cl(7)	245(10)	145(7)	216(8)	-20(6)	-40(8)	-26(7)
Cl(8)	262(8)	185(6)	146(5)	10(4)	-56(5)	-126(6)
Cl(9)	329(12)	172(6)	212(8)	40(6)	46(8)	-43(7)
C(150)	112(7)	72(5)	111(6)	9(6)	-20(6)	-22(6)
Cl(12)	226(8)	223(9)	159(6)	-26(6)	-74(6)	34(7)
Cl(10)	85(2)	116(3)	85(2)	-11(2)	-16(2)	7(2)
Cl(11)	111(2)	62(2)	79(2)	-5(1)	-28(2)	-11(1)
C(154)	195(15)	100(10)	101(10)	-12(10)	8(11)	-27(9)
Cl(19)	49(2)	42(2)	88(2)	-18(2)	-10(2)	-10(1)
Cl(20)	228(8)	145(6)	142(5)	-15(4)	28(5)	-88(6)
Cl(21)	152(5)	90(3)	115(4)	-3(3)	27(3)	5(3)
C(156)	203(9)	200(9)	179(9)	23(7)	-46(9)	-59(8)
Cl(25)	252(7)	185(6)	217(6)	7(5)	-13(7)	-92(6)
Cl(26)	107(3)	124(3)	138(3)	-16(2)	-36(2)	-40(2)
Cl(27)	213(5)	175(5)	136(4)	44(3)	-80(4)	-113(4)
C(155)	234(9)	234(9)	157(9)	-2(10)	-37(8)	-51(10)
Cl(28)	238(8)	171(7)	103(4)	-25(4)	-2(5)	-52(6)
Cl(29)	256(8)	242(8)	214(8)	2(7)	-25(8)	-52(7)
Cl(30)	116(4)	118(4)	92(3)	-9(3)	-6(3)	-24(3)
C(160)	135(7)	145(7)	149(8)	-7(7)	-41(6)	-17(7)
Cl(13)	197(8)	174(7)	194(7)	15(6)	-40(6)	-36(6)
Cl(14)	51(2)	114(4)	79(3)	-56(3)	3(2)	-32(2)
Cl(15)	180(6)	137(5)	165(6)	-36(5)	-36(5)	-29(5)
C(168)	86(11)	78(14)	74(12)	-2(11)	-17(12)	-21(10)
Cl(34)	59(5)	104(7)	106(7)	31(6)	-32(5)	-19(5)
Cl(35)	75(5)	91(7)	90(7)	-7(5)	-1(5)	19(5)
Cl(36)	54(4)	89(6)	84(6)	23(5)	-5(4)	7(4)
C(161)	147(11)	135(11)	149(10)	-9(10)	-18(10)	-45(8)
Cl(41)	123(9)	103(8)	119(9)	-20(7)	-8(7)	-62(7)
Cl(40)	113(8)	85(7)	130(7)	15(6)	-52(7)	-36(7)

Cl(39)	134(9)	117(8)	107(8)	-3(7)	-27(8)	-45(7)
C(2)	24(2)	21(2)	26(2)	-3(1)	-1(1)	-1(1)
C(3)	22(2)	20(2)	30(2)	-5(1)	-2(1)	-1(1)
C(4)	27(2)	19(2)	32(2)	-4(1)	-4(1)	-6(1)
Cl(4)	81(2)	103(2)	108(2)	-8(1)	-6(1)	-2(1)
C(5)	26(2)	22(2)	28(2)	-2(1)	-7(1)	-6(1)
Cl(5)	71(1)	52(1)	106(2)	-10(1)	5(1)	-27(1)
C(6)	24(2)	22(2)	26(2)	-2(1)	-4(1)	-7(1)
Cl(6)	200(4)	138(3)	119(2)	65(2)	92(2)	26(2)
C(7)	24(2)	22(2)	25(2)	-2(1)	-7(1)	-6(1)
C(8)	20(2)	22(2)	28(2)	2(1)	-5(1)	-5(1)
C(9)	25(2)	17(1)	28(2)	3(1)	-6(1)	-3(1)
C(10)	23(2)	20(2)	26(2)	1(1)	-2(1)	-2(1)
C(11)	21(1)	18(1)	28(2)	1(1)	-4(1)	-2(1)
C(12)	23(2)	18(1)	27(2)	-2(1)	-1(1)	-4(1)
C(13)	19(1)	20(1)	26(2)	1(1)	-3(1)	-5(1)
C(14)	22(2)	22(2)	25(2)	-2(1)	-3(1)	-6(1)
C(15)	21(1)	19(1)	28(2)	0(1)	-2(1)	-6(1)
C(16)	20(2)	22(2)	27(2)	-1(1)	-5(1)	-3(1)
C(17)	21(2)	22(2)	28(2)	-3(1)	-4(1)	-1(1)
C(18)	27(2)	21(2)	33(2)	1(1)	-5(1)	-1(1)
C(19)	26(2)	19(2)	34(2)	-2(1)	-3(1)	-4(1)
O(20)	28(1)	18(1)	39(1)	3(1)	-3(1)	-6(1)
C(21)	27(2)	22(2)	32(2)	1(1)	-3(1)	-6(1)
O(22)	29(1)	21(1)	37(1)	4(1)	-8(1)	-8(1)
C(23)	30(2)	19(2)	32(2)	0(1)	-8(1)	-9(1)
C(24)	26(2)	26(2)	29(2)	2(1)	-4(1)	-10(1)
C(25)	21(2)	25(2)	31(2)	-3(1)	-6(1)	-6(1)
O(26)	22(1)	29(1)	31(1)	-3(1)	-2(1)	-6(1)
C(27)	20(2)	26(2)	31(2)	-1(1)	-4(1)	-5(1)
O(28)	19(1)	25(1)	33(1)	1(1)	-1(1)	-5(1)
C(29)	21(2)	22(2)	32(2)	3(1)	-3(1)	-5(1)
C(30)	25(2)	23(2)	29(2)	-1(1)	-1(1)	-1(1)
C(31)	25(2)	20(2)	27(2)	0(1)	-4(1)	-4(1)
O(32)	26(1)	21(1)	29(1)	-5(1)	-3(1)	-3(1)
C(33)	22(2)	21(2)	29(2)	-4(1)	-3(1)	-3(1)
O(34)	23(1)	24(1)	30(1)	-8(1)	2(1)	-6(1)
C(35)	22(2)	22(2)	29(2)	-6(1)	1(1)	-6(1)
C(36)	24(2)	27(2)	24(2)	-3(1)	-4(1)	-6(1)
C(37)	22(2)	22(2)	27(2)	1(1)	-5(1)	-5(1)
O(38)	24(1)	23(1)	30(1)	3(1)	-8(1)	-4(1)
C(39)	25(2)	23(2)	29(2)	0(1)	-5(1)	-5(1)
O(40)	24(1)	25(1)	30(1)	-2(1)	-7(1)	-1(1)
C(41)	35(2)	27(2)	36(2)	3(2)	-10(2)	-5(2)
C(42)	31(2)	31(2)	40(2)	8(2)	-11(2)	-4(1)
O(43)	57(2)	33(1)	47(2)	14(1)	-25(1)	-11(1)

C(44)	43(2)	33(2)	46(2)	17(2)	-18(2)	-10(2)
C(45)	39(2)	43(2)	46(2)	15(2)	-11(2)	0(2)
C(46)	34(2)	51(2)	52(2)	26(2)	-15(2)	-12(2)
O(47)	34(2)	85(2)	53(2)	34(2)	-13(1)	-14(2)
C(48)	34(2)	41(2)	46(2)	14(2)	-12(2)	-9(2)
C(49)	32(2)	36(2)	44(2)	12(2)	-7(2)	-9(2)
C(50)	31(2)	24(2)	39(2)	5(1)	-4(1)	-9(1)
C(51)	33(2)	34(2)	44(2)	14(2)	-5(2)	-10(2)
C(52)	31(2)	41(2)	48(2)	16(2)	-3(2)	-11(2)
O(53)	30(2)	88(3)	59(2)	42(2)	-2(1)	-8(2)
C(54)	31(2)	53(2)	43(2)	20(2)	1(2)	-9(2)
C(55)	39(2)	45(2)	41(2)	7(2)	-2(2)	-22(2)
C(56)	34(2)	31(2)	37(2)	4(2)	5(2)	-13(2)
O(57)	41(2)	32(1)	53(2)	-4(1)	15(1)	-15(1)
C(58)	32(2)	31(2)	37(2)	3(1)	1(2)	-14(1)
C(59)	30(2)	30(2)	36(2)	-4(2)	0(2)	-9(1)
C(60)	23(2)	27(2)	31(2)	2(1)	-3(1)	-6(1)
C(61)	25(2)	26(2)	36(2)	-1(1)	1(1)	-6(1)
C(62)	26(2)	29(2)	35(2)	-2(1)	0(1)	-4(1)
O(63)	36(1)	33(1)	48(2)	-9(1)	12(1)	-11(1)
C(64)	28(2)	31(2)	35(2)	-6(1)	5(1)	-7(1)
C(65)	27(2)	36(2)	35(2)	0(2)	1(1)	6(1)
C(66)	21(2)	50(2)	27(2)	-12(2)	1(1)	1(2)
O(67)	21(1)	81(2)	32(1)	-17(1)	-2(1)	0(1)
C(68)	25(2)	37(2)	31(2)	-8(1)	0(1)	-1(1)
C(69)	25(2)	32(2)	31(2)	-6(1)	-5(1)	-2(1)
C(70)	25(2)	22(2)	28(2)	-4(1)	0(1)	-4(1)
C(71)	23(2)	30(2)	32(2)	-8(1)	-1(1)	-3(1)
C(72)	24(2)	33(2)	29(2)	-8(1)	-4(1)	-5(1)
O(73)	23(1)	65(2)	28(1)	-12(1)	-4(1)	2(1)
C(74)	24(2)	45(2)	23(2)	-8(1)	-3(1)	-3(1)
C(75)	37(2)	42(2)	26(2)	-5(2)	-5(2)	-9(2)
C(76)	41(2)	35(2)	23(2)	-3(1)	-9(1)	1(2)
O(77)	67(2)	36(2)	30(1)	-2(1)	-17(1)	4(1)
C(78)	37(2)	36(2)	28(2)	-2(1)	-6(2)	-2(2)
C(79)	34(2)	30(2)	31(2)	3(1)	-7(1)	-2(1)
C(80)	24(2)	30(2)	30(2)	3(1)	-5(1)	-2(1)
C(81)	31(2)	40(2)	28(2)	8(2)	-7(1)	-3(2)
C(82)	36(2)	37(2)	59(3)	12(2)	-11(2)	-6(2)
C(83)	50(2)	38(2)	61(3)	7(2)	-11(2)	-5(2)
C(84)	50(2)	40(2)	62(3)	16(2)	-18(2)	-16(2)
C(85)	38(2)	45(2)	44(2)	15(2)	-7(2)	-13(2)
C(86)	40(2)	36(2)	47(2)	10(2)	5(2)	-7(2)
C(87)	52(2)	36(2)	42(2)	4(2)	-4(2)	-13(2)
C(88)	39(2)	34(2)	40(2)	4(2)	-2(2)	-10(2)
C(89)	26(2)	34(2)	36(2)	0(2)	2(1)	-5(1)

C(90)	29(2)	33(2)	37(2)	-6(2)	-6(2)	-1(1)
C(91)	42(2)	29(2)	39(2)	-5(2)	-8(2)	-4(2)
C(92)	35(2)	37(2)	33(2)	-10(2)	-1(2)	-8(2)
C(93)	26(2)	37(2)	27(2)	-9(1)	0(1)	-6(1)
C(94)	33(2)	37(2)	28(2)	-8(2)	-2(1)	-1(2)
C(95)	28(2)	46(2)	30(2)	-6(2)	-2(1)	-7(2)
C(96)	27(2)	46(2)	26(2)	-5(2)	-6(1)	2(2)
C(97)	72(4)	47(3)	95(5)	-10(3)	-12(4)	-2(3)
O(98)	52(2)	54(2)	125(4)	-3(2)	5(2)	1(2)
C(99)	78(4)	48(3)	78(4)	-15(3)	-17(3)	-15(3)
O(100)	111(3)	44(2)	58(2)	-7(2)	8(2)	-27(2)
C(101)	87(4)	37(2)	72(3)	7(2)	-39(3)	-10(2)
O(102)	53(2)	44(2)	43(2)	7(1)	-10(1)	-11(1)
C(103)	43(4)	53(5)	61(5)	-7(5)	0(4)	-17(4)
O(104)	57(3)	50(3)	73(4)	10(3)	-1(3)	-20(2)
C(105)	33(7)	50(7)	53(8)	-13(7)	-5(7)	-12(6)
O(105)	59(7)	68(7)	99(9)	-32(6)	2(6)	-23(5)
C(106)	28(2)	27(2)	32(2)	-5(1)	-2(1)	-6(1)
C(107)	32(2)	28(2)	36(2)	-6(2)	-1(2)	-5(1)
C(108)	27(2)	36(2)	32(2)	-5(1)	-5(1)	-1(1)
C(109)	27(2)	73(3)	45(2)	-26(2)	-5(2)	-2(2)
C(110)	37(2)	113(4)	33(2)	-18(3)	-4(2)	7(3)
C(111)	28(2)	93(4)	46(3)	20(3)	0(2)	3(2)
C(112)	50(3)	57(3)	66(3)	9(2)	11(2)	-13(2)
C(113)	52(3)	46(2)	46(2)	-8(2)	8(2)	-19(2)
C(114)	29(2)	29(2)	27(2)	0(1)	-5(1)	-8(1)
C(115)	41(2)	26(2)	29(2)	4(1)	-6(2)	-12(2)
C(116)	41(2)	18(2)	33(2)	5(1)	-7(2)	-3(1)
C(117)	47(2)	28(2)	48(2)	1(2)	-2(2)	7(2)
C(118)	46(3)	36(2)	78(3)	11(2)	12(2)	11(2)
C(119)	40(2)	37(2)	99(4)	16(2)	-17(3)	-3(2)
C(120)	51(3)	32(2)	78(3)	5(2)	-30(2)	-6(2)
C(121)	42(2)	27(2)	44(2)	5(2)	-17(2)	-7(2)
C(122)	25(2)	21(2)	29(2)	1(1)	1(1)	-3(1)
C(123)	40(2)	24(2)	39(2)	5(2)	6(2)	6(2)
C(124)	42(2)	23(2)	39(2)	7(1)	2(2)	5(2)
C(125)	59(3)	69(3)	52(3)	13(2)	-12(2)	15(3)
C(126)	111(5)	93(5)	47(3)	7(3)	-30(3)	26(4)
C(127)	123(5)	74(4)	43(3)	17(3)	13(3)	33(4)
C(128)	83(4)	51(3)	61(3)	15(3)	34(3)	6(3)
C(129)	59(3)	33(2)	53(3)	3(2)	15(2)	-6(2)
C(130)	24(2)	26(2)	27(2)	-2(1)	-1(1)	-5(1)
C(131)	29(2)	39(2)	33(2)	0(2)	-4(2)	-15(2)
C(132)	26(2)	30(2)	35(2)	-5(1)	3(1)	-10(1)
C(133)	32(2)	44(2)	59(3)	-12(2)	10(2)	-1(2)
C(134)	55(3)	65(3)	57(3)	-30(2)	23(2)	-22(2)

C(135)	77(3)	61(3)	35(2)	-6(2)	6(2)	-39(3)
C(136)	67(3)	45(2)	42(2)	5(2)	-9(2)	-14(2)
C(137)	42(2)	34(2)	38(2)	-2(2)	4(2)	-5(2)

Table 7.5 Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for basket **124**.

	x	y	z	U(eq)
H(138)	6433	4512	-814	104
H(142)	10537	5275	2776	96
H(146)	10206	985	3579	207
H(150)	7675	-2335	1604	117
H(154)	10994	951	3588	160
H(156)	14436	3914	2551	229
H(155)	14600	4050	2197	247
H(168)	11236	-956	4583	93
H(161)	9540	-2291	606	169
H(2)	12510(20)	610(20)	646(18)	20(9)
H(4)	11350(20)	-990(20)	871(16)	16(8)
H(6)	10730(20)	1020(20)	432(18)	22(9)
H(8)	8830(30)	2200(20)	851(19)	27(10)
H(10)	10800(20)	2800(20)	732(18)	23(9)
H(12)	11590(20)	4120(20)	1576(18)	23(9)
H(14)	12680(20)	2300(20)	900(20)	28(10)
H(16)	14140(30)	920(20)	1512(19)	27(10)
H(18)	12820(20)	-960(20)	2642(19)	32(10)
H(21)	10860(20)	-490(20)	2356(17)	19(9)
H(24)	8970(20)	-81(19)	2067(15)	9(7)
H(27)	8980(30)	1760(20)	2362(19)	29(10)
H(30)	9050(20)	3560(20)	2582(17)	19(9)
H(33)	11040(20)	3070(20)	2861(16)	14(8)
H(36)	13010(30)	2580(30)	3030(20)	40(12)
H(39)	12960(20)	780(20)	2850(16)	13(8)
H(41)	13880(30)	-760(30)	3510(20)	44(14)
H(45)	12500(30)	-1380(30)	4680(20)	32(10)
H(49)	11810(40)	-1690(40)	3210(30)	83(19)
H(51)	9310(30)	-1360(30)	2790(30)	61(15)
H(55)	8100(30)	-310(20)	4010(19)	30(10)
H(59)	7620(20)	750(20)	2687(19)	23(9)
H(61)	7820(20)	2980(20)	3118(15)	11(8)
H(65)	8100(30)	3130(30)	4620(20)	44(12)
H(69)	9560(30)	4040(20)	3563(19)	28(10)
H(71)	12030(30)	3500(30)	3900(20)	41(12)
H(75)	12470(20)	1930(20)	5133(17)	21(9)
H(79)	13840(20)	1500(30)	3784(19)	29(10)

H(81)	14110(30)	-220(30)	5200(20)	43(12)
H(82)	14720(40)	-2610(30)	3830(30)	64(16)
H(84)	12580(30)	-3410(30)	3670(20)	48(13)
H(85)	9940(30)	-2140(30)	4560(20)	40(11)
H(86)	7900(30)	-2460(30)	3320(20)	43(12)
H(88)	5980(30)	-490(30)	3070(20)	39(11)
H(89)	6270(20)	1690(20)	4322(17)	22(9)
H(90)	6350(30)	4450(30)	3600(20)	37(11)
H(92)	8250(30)	5520(30)	4180(20)	45(12)
H(93)	10200(40)	3890(40)	5360(30)	72(18)
H(94)	13000(20)	4260(20)	4753(17)	19(9)
H(96)	14930(30)	2370(20)	4755(18)	27(10)
H(97A)	13960(50)	-3930(50)	3150(40)	90(30)
H(97B)	14620(40)	-3680(40)	2850(30)	79(19)
H(98)	15200(130)	-4500(300)	3180(40)	1100(400)
H(99A)	5991	-2242	3045	79
H(99B)	6171	-1720	2396	79
H(100)	6570(50)	-3110(50)	2510(60)	230(60)
H(10A)	6554	6170	3906	76
H(10B)	7405	6195	3441	76
H(102)	5940(50)	5870(50)	3230(40)	130(30)
H(10C)	14485	4418	4894	62
H(10D)	15211	3746	4590	62
H(104)	14100(800)	4900(300)	4070(50)	2000(2000)
H(10E)	15202	3687	4803	53
H(10F)	14968	3831	4083	53
H(105)	14200(90)	4910(60)	4190(80)	89
H(10A)	11670(40)	-560(40)	-680(30)	80(18)
H(10B)	11850(30)	270(30)	45(19)	32(10)
H(10C)	12890(30)	-1150(20)	200(20)	30(10)
H(10D)	12410(20)	-1540(20)	-287(19)	28(10)
H(109)	13040(30)	-1560(30)	-1340(20)	56(14)
H(110)	13970(30)	-1240(30)	-2180(30)	69(17)
H(111)	14570(30)	-20(30)	-2080(20)	52(13)
H(112)	14460(40)	610(40)	-900(30)	100(20)
H(113)	13360(20)	190(20)	-250(20)	26(10)
H(11B)	9500(20)	1840(20)	-178(19)	30(10)
H(11A)	10300(20)	2240(20)	-38(17)	21(9)
H(11C)	9170(30)	3510(30)	40(20)	47(13)
H(11D)	9430(30)	3260(30)	-610(20)	42(12)
H(117)	7930(30)	3520(30)	590(20)	48(13)
H(118)	6510(30)	3510(30)	500(20)	49(14)
H(119)	5980(30)	3010(30)	-500(20)	58(14)
H(120)	7070(40)	2560(40)	-1360(30)	78(18)
H(121)	8480(30)	2720(30)	-1250(20)	54(14)
H(12A)	12500(20)	3840(20)	583(16)	12(8)

H(12B)	11860(20)	3340(20)	434(16)	17(8)
H(12C)	11560(20)	4970(20)	556(18)	23(9)
H(12D)	10780(30)	4510(30)	380(20)	36(11)
H(125)	10494	4557	-607	76
H(126)	10821	4688	-1721	104
H(127)	12190(50)	4710(50)	-2290(40)	120(30)
H(128)	13190(30)	4840(30)	-1490(30)	53(14)
H(129)	12940(40)	4950(40)	-440(30)	90(20)
H(13A)	14190(20)	660(20)	376(17)	17(8)
H(13B)	13430(20)	1380(20)	386(16)	14(8)
H(13C)	14280(30)	2310(30)	750(20)	43(12)
H(13D)	15040(30)	1650(30)	610(20)	34(11)
H(13E)	15720(30)	1250(30)	-490(20)	33(11)
H(13F)	15920(40)	1500(40)	-1710(30)	84(19)
H(13G)	15070(30)	2570(30)	-1970(30)	64(16)
H(13H)	13760(40)	3180(40)	-1320(30)	90(20)
H(13I)	13780(40)	3020(40)	-220(30)	82(19)

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DOCTORAL DISSERTATION REPORT

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MAJOR FIELD: Chemistry

TITLE OF DISSERTATION: Self-Assembly, Templation and Biomimetics

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