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Reactions for the functionalization of the lower rim of calix[4]resorcinarenes and synthesis of η6-[1,3-bis-(2'4 '6'-trimethoxybenzyl)benzene]tricarbonylchromium

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REACTIONS FOR THE FUNCTIONALIZATION OF THE LOWER RIM OF CALIX[4]RESORCINARENES AND SYNTHESIS OF η^6-[1,3-BIS-(2'4'6'-TRIMETHOXYBENZYL) BENZENE]TRICARBONYLCHROMIUM

By

Jeannine Malakoti-Negad

A Thesis

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ABSTRACT

In this project, the intent was to design and synthesize a calixresorcinarene that has a cleft in the tail of the molecule and would serve in molecular recognition processes. Calix[4]resorcinarene (**79**) was prepared and treated with NBS and Me_2SiCl_2 to obtain a bridged resorcinarene (**82**) with a rigid cavity and to protect the phenol groups at the top rim of the molecule. Many reactions were tried on **82** in order to functionalize the pendant groups at the rear end of the molecule, but none of the conditions met with success. Compound **82** was soluble only in DMF, therefore all the reactions were performed in that solvent. This limitation may have influenced the outcome of the reactions.

The synthesis of basic cyclophane frameworks very similar to calixarene molecules was also studied in this project. Chromium complexes of *m*-xylene-α, α'-diol (**91**) and 5-amino-1,3-hydroxymethylbenzene (**96**) were synthesized and then reacted with trimethoxybenzene (**92**). No product was identified from the reaction of **91**, but the chromium complex of 1,3-bis-(2',4',6'-trimethoxybenzyl) benzene (**93**) was obtained and fully characterized.

DEDICATION

To my loving husband Masoud and my beautiful children

Nasim Gabriela and Nima Andre.

ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS

AB	AB quartet
br	broad (IR)
°C	degrees Celsius
cm	centimetres
cm^{-1}	wavenumbers
CPK	Corey-Pauling-Koltun
d	doublet (NMR)
dd	doublet of doublets
dec.	decomposes
DMF	dimethylformamide
Et_2O	diethyl ether
eq.	equivalents
g	grams
h	hours
HMQC	Heteronuclear Multiple Quantum Coherence
IR	infrared
LSIMS	Liquid Secondary Ion Mass Spectrometry
m	multiplet (NMR)
M	molarity
Me	methyl
min	minutes
mm Hg	millimeters of mercury
mL	milliliters
mmol	millimole
mNBA	*m*-nitrobenzyl-alcohol
m.p.	melting point
MS	mass spectrometry
NMR	Nuclear Magnetic Resonance
ORTEP	Oak Ridge Thermal Ellipsoid Plot
ppm	parts per million
q	quartet (NMR)
rt	room temperature
s	strong (IR), singlet (NMR)
t	triplet (NMR)
THF	tetrahydrofuran
TLC	Thin Layer Chromatography
TMB	1,3,5-trimethoxybenzene
TMS	trimethylsilyl
vs	very strong (IR)
w	weak (IR)

1. INTRODUCTION

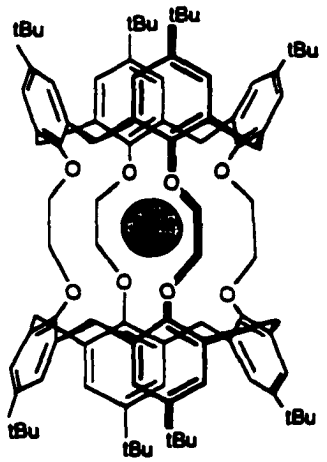
1.1 Background of Host-Guest Chemistry

The field of supramolecular chemistry is concerned with the study of two or more molecules held together by non-covalent forces. These forces can vary from hydrogen bonding, ion-pairing, π-acid and π-base interactions, electrostatic metal-ligand interaction, van der Waals attractive forces, or solvent reorganization to partially made and broken covalent bonds[1].

Host-guest chemistry is the part of supramolecular chemistry that refers specifically to molecular entities that form complexes with suitable guest molecules. Normally, the host is relatively large and has a cavity, cleft, or pocket, which accommodates the smaller guest (Figure1). A guest in a host-guest complex is the molecular entity that has divergent binding sites.

The inspiration for working with supramolecular structures and molecular recognition processes can certainly come from the chemistry of biological systems at the molecular level. The remarkable abilities of enzymes to catalyze organic reactions encourages researchers to design organic compounds that can complex with other molecules to simulate the substrate selectivity of enzymes. In host-guest chemistry, the host molecule must "recognize" the guest molecule binding sites and steric features[2] at some time during the complexation event.

In 1967 C.J. Pedersen[3] reported the discovery of crown ethers, cyclic polyether compounds containing repeating ethylene oxy units, ($-CH_2CH_2O-$), and their ability to selectively bind alkali metal cations. It was demonstrated that the metal cation was bound in the center of the crown ether by electrostatic forces between the positively charged metal ion and the electron-rich oxygen atoms. The study of these compounds showed that the size of the ring is an important factor influencing the selectivity of the host toward different cations.



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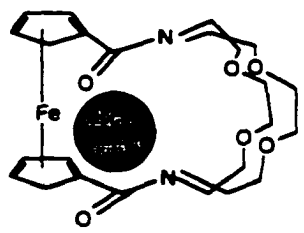
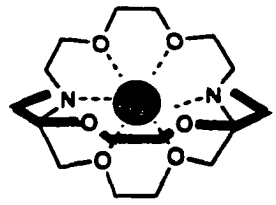


2

Figure 1: Examples of supramolecular complexes.[4,5]

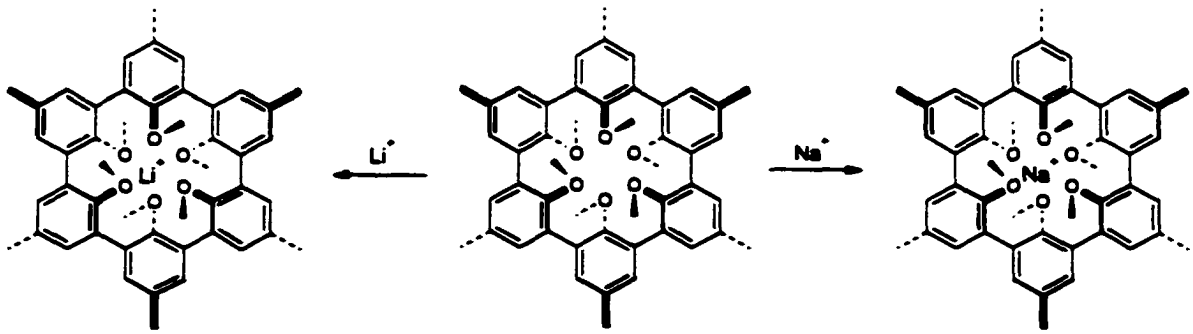
J. M. Lehn also contributed to the field of host-guest chemistry with the synthesis of the first cryptand compound,[6-8] a bicyclic macrocycle host structure. Cryptands are bicyclic or polycyclic compounds with nitrogen bridgeheads and repeating ethylene oxy units ($-CH_2CH_2O-$) as binding sites. These compounds were found to complex with alkali metals more effectively than the crown ethers due to their three dimentional shape that allows the spherical cation guest to form an inclusion complex with the host (Figure 2).



3

Figure 2: Sample of a cryptand molecule complexed with a cation.

The discovery of crown ether compounds and the design and synthesis of structures like cryptands caught the attention of Donald J. Cram who, using Corey-Pauling-Koltun (CPK) molecular models, designed a new family of compounds called spherands. These compounds are completely preorganized systems that contain an enforced cavity with binding sites directed to the interior of the cavity (Figure 3). Spherands exhibited stronger binding toward Li^+ and Na^+ ions than either crown ethers or cryptands.



5 4 6

Figure 3: A spherand binding Li^+ and Na^+ ions.[9]

Through the development of this new class of compounds, Cram formulated the principles of preorganization and complementarity. The principle of preorganization,

states that "the more highly hosts and guests are organized for binding and low solvation prior to their complexation, the more stable will be their complexes".[9]

Crystal structures of crown ethers and cryptands (Figure 4) show that in their uncomplexed states, the binding sites are not organized into a cavity. For the complexation to occur, the host and solvent must both reorganize.

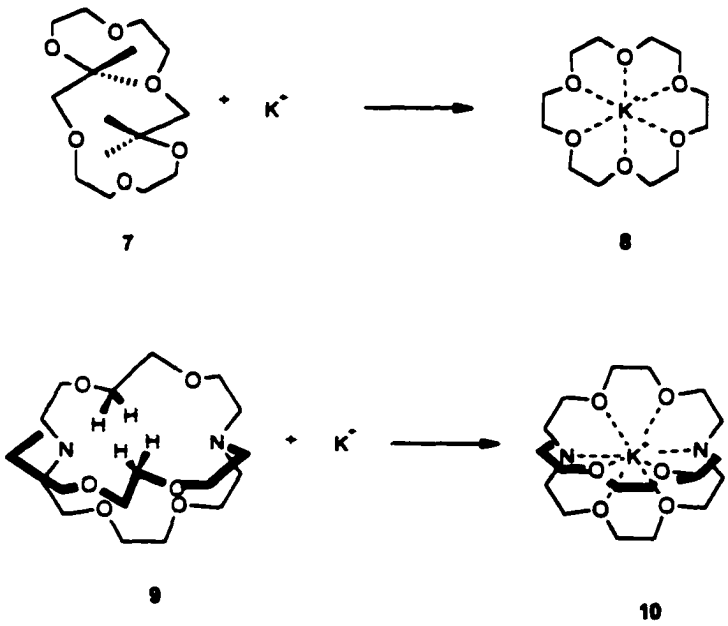


Figure 4: Uncomplexed and complexed states of crown ethers and cryptands.[9]

In the spherand compounds, the molecule is already organized to complex the guest. This accounts for the formation of more stable complexes with alkali metal cations.

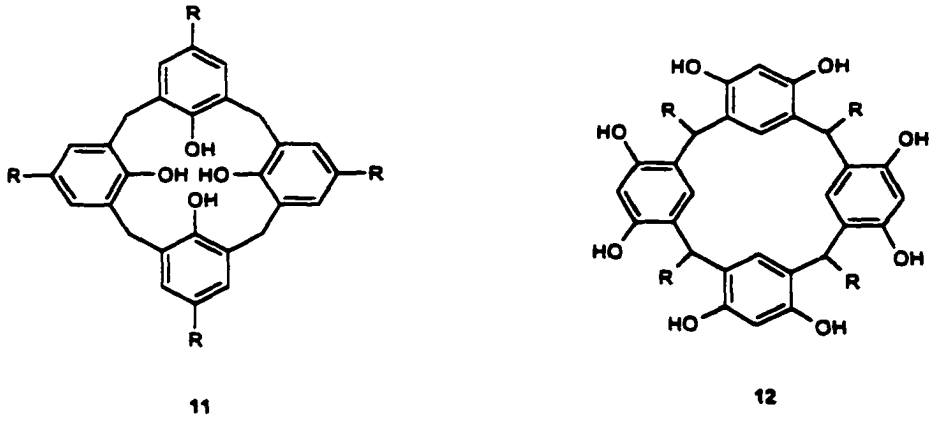
The principle of complementarity states that, in order "to complex, hosts must have binding sites that cooperatively contact and attract the binding sites of the guest without the generation of strong non-bonding repulsions".[9]

1.1.1 History of Calixarenes

The field of supramolecular chemistry has evolved rapidly since the publication of the first paper on crown ethers by Pedersen in 1967. The study of polymolecular entities (supramolecular complexes), their structure, and the non-covalent intermolecular forces that held them together is now recognized worldwide as an important technological frontier in the chemistry field.

Calixarene molecules, shown in Figure 5, are cup shaped macrocycles that play an important part in supramolecular chemistry; they act as receptors for the inclusion of small organic molecules and ions. Although, the synthesis of cyclic tetrameric structures was first mentioned in the 1940's by A. Zinke, it was not until the 1970's that researchers like Gutsche,[10] Patrick and Egan,[11,12] and others,[13-15] realized that calixarenes were potentially valuable macrocyclic receptor molecules for host-guest chemistry.

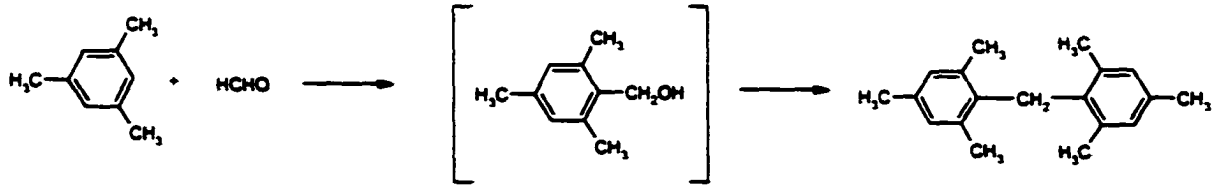
Through the study of Zinke's tetrameric structures, Gutsche soon realized that this attractive class of synthetic cavity-containing compounds needed a more descriptive name. Conforth,[16] Megson,[17] and Ott and Zinke[18] referred to the non-planar character of these compounds. Gutsche[10] designated the name calixarene in 1975, derived from the Greek *calix* meaning "vase" or "chalice" and *arene*, which indicates the presence of arene units in the molecule. Resorcinarene replaces arene in the name of **12** to distinguish the phenol and resorcinol derived macrocycles. A bracketed number is added after the calix prefix; to designate the number of arene rings in the macrocycle.



11 12

Figure 5. Basic structure of calix[4]arenes and calix[4]resorcinarenes.

In 1872, Baeyer published a series of papers on the reactions of aldehydes with phenols in the presence of strong acids.[19,20] Baeyer was interested in these reactions, but unfortunately, mixtures of products with resin like consistency were produced. Baeyer describes that what happened was a thickening of the reaction mixture with the formation of a "cement-like substance" which could not be purified. As a result of the inability to characterize these compounds through elemental analysis, a structure was not postulated.[20] In other experiments[21] however, Baeyer obtained a more tractable product using mesitylene rather than phenol and reacting it with formaldehyde under acid conditions. The product obtained was identified as dimesitylene and is shown in Scheme 1.



13 mesitylene

14 hydroxymethylmesitylene

15 dimesitylmethane

Scheme 1: Reaction to obtain dimesitylmethane.[21]

Baeyer also expected to identify hydroxymethylmesitylene as the logical precursor of the product but, instead, he obtained a complex product which was unable to characterize.

Although Baeyer could not identify the products in his phenol-formaldehyde reactions, his work was the first step in the development of phenol-formaldehyde chemistry and it attracted other researchers like L. Lederer[22] and O. Manase[23] who succeeded in isolating *o*-hydroxymethylphenol and *p*-hydroxymethylphenol from the base-catalyzed reaction of phenol and formaldehyde under mild conditions. Stronger conditions would produce a resinous tar just like the acid catalyzed reaction.

For several years, these resinous tars remained just that, unidentifiable materials that had interesting properties but no practical applications. The analytical tools in 1872 could not characterize these products, which later studies would show to be polymers.

It was not until 1902 that Leo Baekeland started studies in the phenol-formaldehyde reaction and after several years of careful work he was able to prove that by using a small amount of base, a product was obtained with interesting marketable qualities. Baekeland filed for a patent in this process in 1907 and called the material Bakelite. This constituted the first step in the production of synthetic plastic.

Following investigations of the Bakelite process eventually identified the basic structural units in the resins, which were a pair of aromatic rings linked by either CH_2 or CH_2OCH_2 groups. These compounds shown, in Figure 6, were given the trivial names of "resoles" and "novolaks".[24]

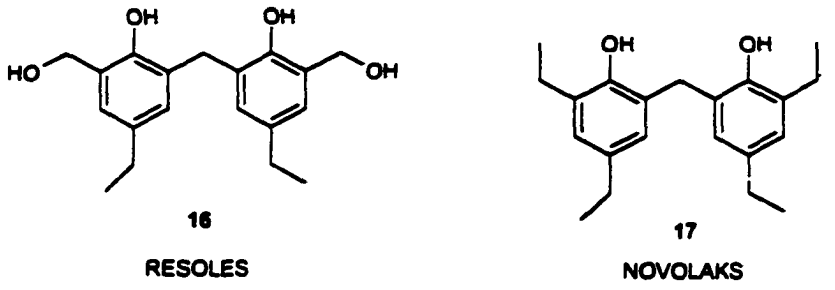


Figure 6: Basic units of "resoles" and "novolaks".[24]

The next episode in the field of phenol-formaldehyde chemistry is the work of Zinke and Ziegler[23] in 1942. *Para*-substituted phenols were used in the condensation reaction with formaldehyde so that the number of links between the arene units would be reduced and a linear polymer could be obtained, which would be easier to characterize.

Phenols can react at the *ortho* and *para* positions giving a highly cross-linked product **(18)**, but *para*-substituted phenols can only react at the two *ortho* positions **(19)** (Figure 7).[24]

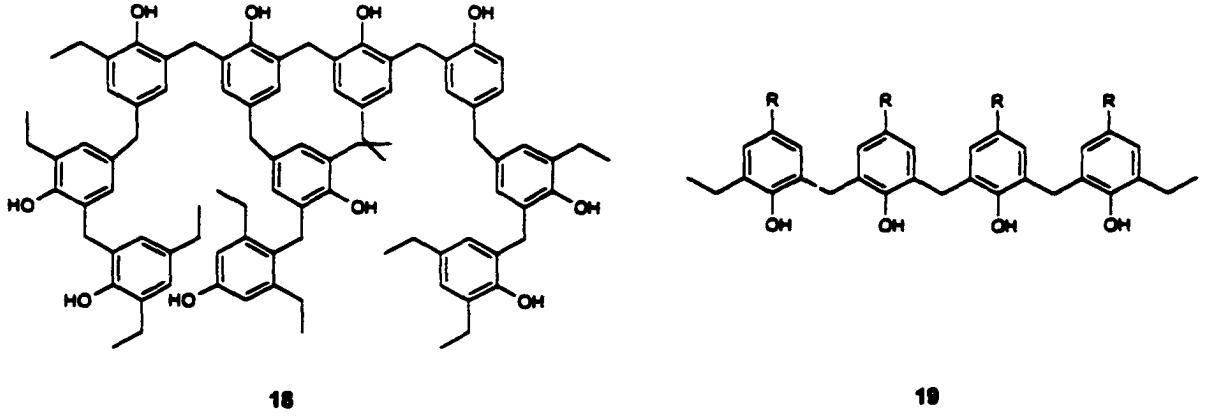


Figure 7: Product of phenols (18) and *para*-substituted phenols (19) after condensation reaction with formaldehyde.[24]

In 1944, Zinke postulated that the products of the reaction of *para*-substituted phenols with formaldehyde were cyclic tetrameric structures (Figure 8).[26]

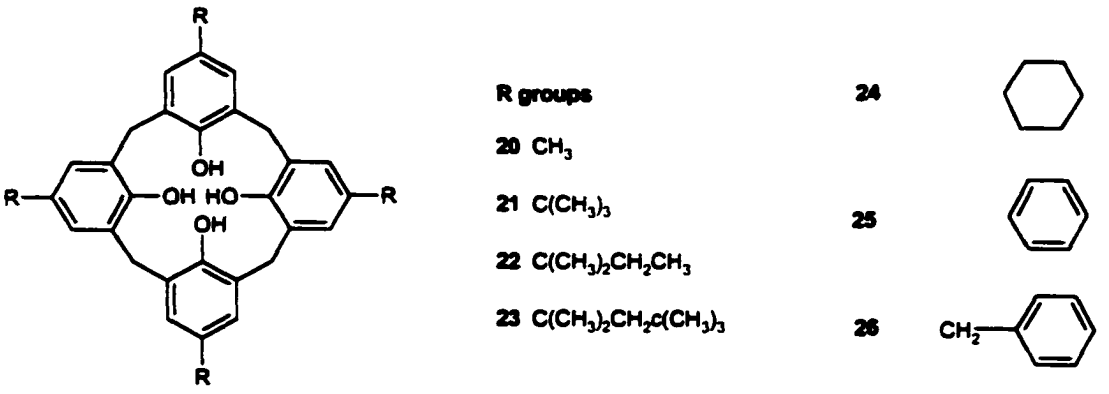
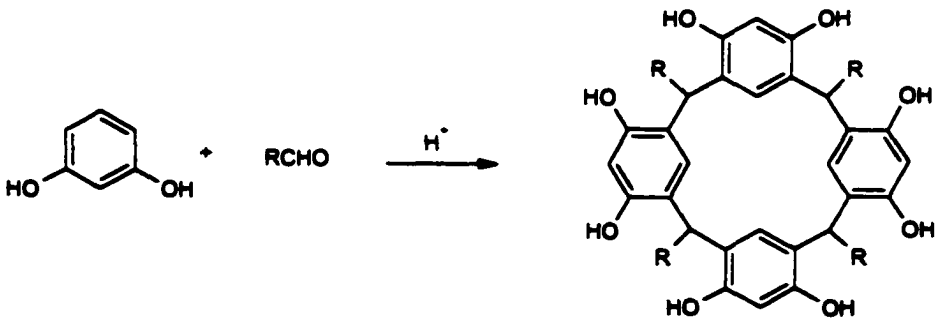


Figure 8: Compounds introduced by Zinke and his coworkers.[26]

Niederl and Vogel also proposed cyclic tetrameric structures and described the reaction between resorcinol and aldehydes under acid catalyzed conditions. The products were suggested to have the structure shown in Scheme 2.[27]



27 28

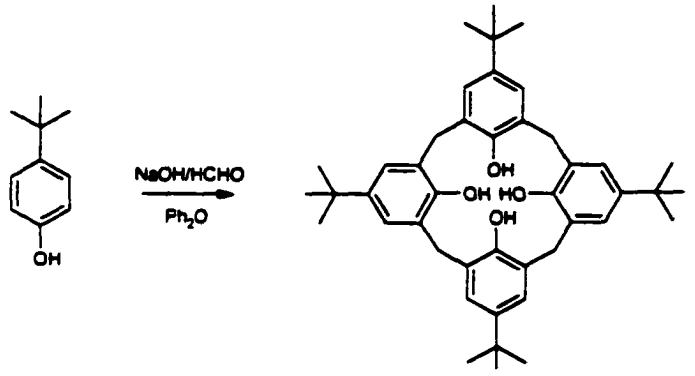
Scheme 2: Reaction between resorcinol and aldehydes under acid catalyzed conditions.[27]

These classes of compounds are now known as calixarenes (Figure 8) and resorcinarenes, (Scheme 2) respectively.

1.1.2 Synthesis of calix[n]arenes

Base Catalyzed Procedures:

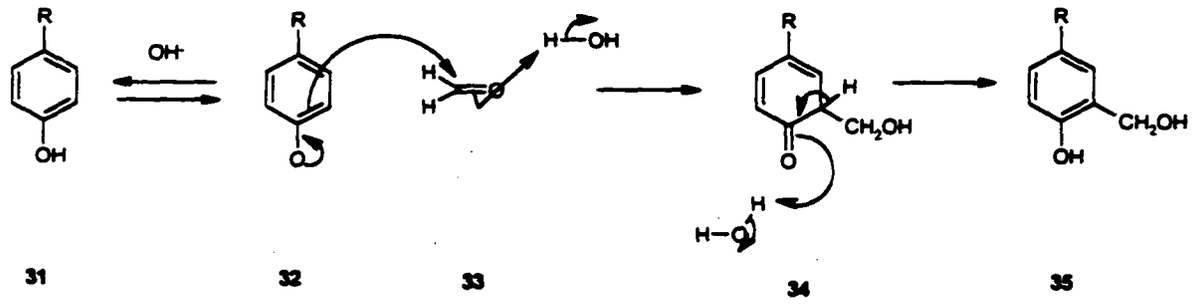
To prepare calixarenes, a base-catalyzed condensation of formaldehyde with *p*-substituted phenols can be used (Scheme 3). Different products are obtained depending on changes made to the reaction conditions.[28-31]



29 30

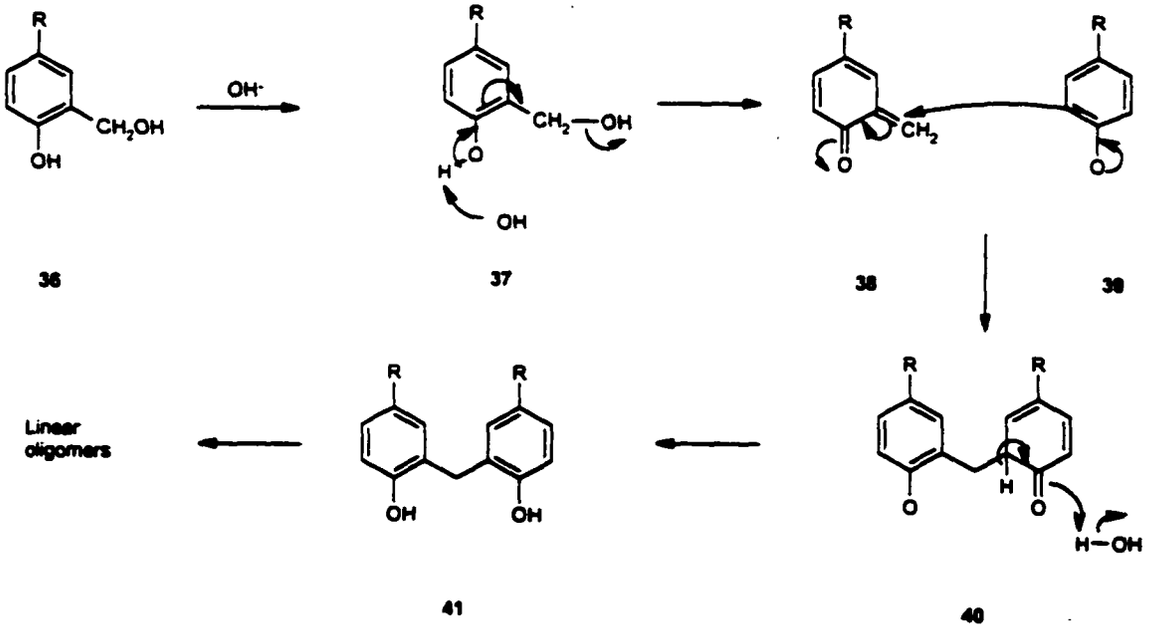
Scheme 3: Base catalyzed synthesis of calixarenes.[24]

The cyclic tetramer is the product of thermodynamic control, the cyclic hexamer is the product of template control by potassium and rubidium cations and, the cyclic octamer is the product of kinetic control. The pathways to the formation of some of the products have been postulated:[24] The first step is the oligomerization of phenols through the formation of a phenoxide ion which then reacts as a nucleophile with the carbonyl group of the formaldehyde (Scheme 4).



Scheme 4: Base catalyzed condensation of formaldehyde with *p*-substituted phenols.[24]

The reaction can continue further to form linear oligomers via a pathway that uses *o*-quinonemethide intermediates (Scheme 5).



Scheme 5: Formation of linear oligomers.[24]

These oligomers are transformed into calixarenes but the exact mechanism is not yet known.

Changes in the number of equivalents of base, time of heating and solvent used can give rise to macrocycles with an odd number of aryl rings, although at lower yields compared to the yields obtained for macrocycles with an even number of aryl rings.

The base induced reaction is very sensitive to the *p*-substituent effect. Phenols with electron withdrawing groups do not react with formaldehyde, whereas phenols with strong electron donating groups condense with formaldehyde, but form linear oligomers and not calixarenes.[32]

Acid Catalyzed Procedure:

Acid catalyzed reactions of phenols and aldehydes produce mixtures of linear oligomers.[33] Although calixarenes have not been isolated from acid catalyzed reactions, there is evidence that they are present in small amounts.[32] Resorcinol, however, has been found to react with aldehydes to produce cyclic tetramers as Niederl and Vogel showed in 1940.

Although the formation of calixarenes under basic conditions forms different products depending on factors such as temperature and alkali metal templates, the reaction between resorcinol and aldehydes, excluding formaldehyde and catalyzed by any mineral acid in water or alcohol, forms calix[4]resorcinarenes in respectable yields. According to Weinelt and Schneider,[34] this is due to the fact that the cyclic tetramers are the thermodynamic product of the reaction. Although the efficiency of the acid catalyzed procedures is very high, factors that influence the possibility of hydrogen bond formation between the hydroxy groups of adjacent resorcinol units and/or produce steric hindrance strongly decrease the macrocycle formation.[34]

1.1.3 Stereochemistry of calixarenes

Calixarenes made up of phenol and methylene units are known to have several conformational isomers; a calix[4]arene, for example, could have up to four different conformers. These different isomers are the direct result of the rotational freedom of the phenol unit, which can, depending on the ring size, invert its position in two ways: *para*-substituent through the annulus rotation and, oxygen through the annulus rotation (Figure 9).[35]

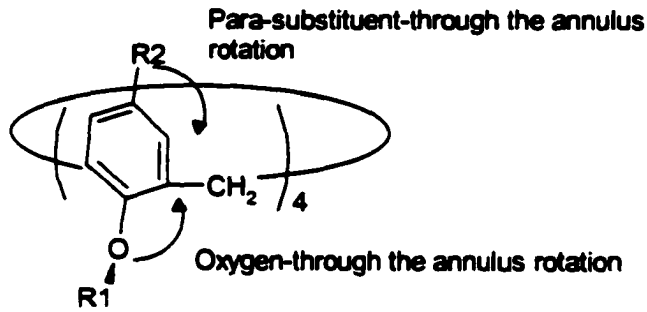


Figure 9. Rotational freedom of phenol units.[35]

Because of the diversity and the properties of the isomers available, calixarenes and calixresorcinarenes are good candidates for the design of molecules which can act as receptors for host-guest type chemistry. The design of such molecules requires: first, the study of the stereochemistry and properties of the different conformations of calixarenes; second, a study of the ways in which these conformations can be immobilized so that the compound contains, in the words of Cram, an "enforced cavity" large enough to engulf ions or molecules.

Great attention has been put on the different conformers of calixarenes. The tetramers have been specially studied to analyze the factors that influence their stereochemistry.

Stereochemistry of Calix[4]arene:

Four basic conformers can exist for phenol derived calixarenes. They are cone, partial cone, 1,2-alternate and 1,3-alternate (Figure 10).

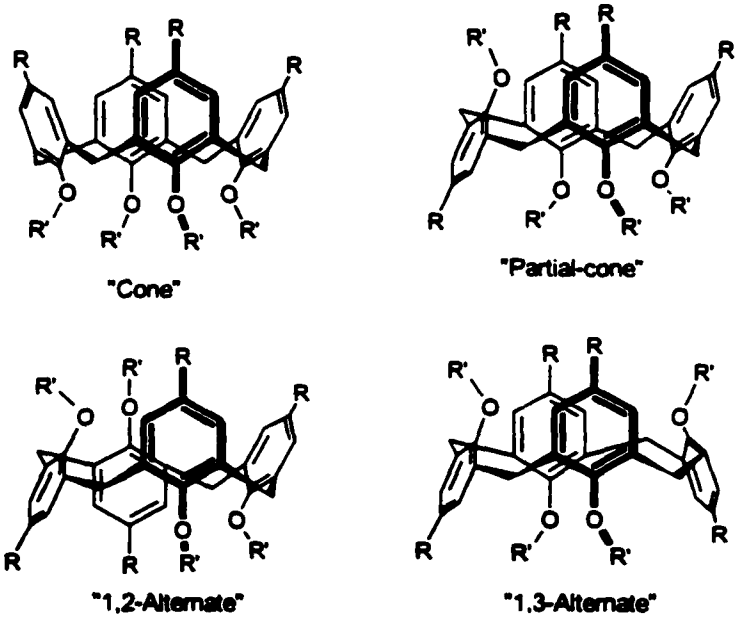


Figure 10: Different conformations of calix[4]arene.

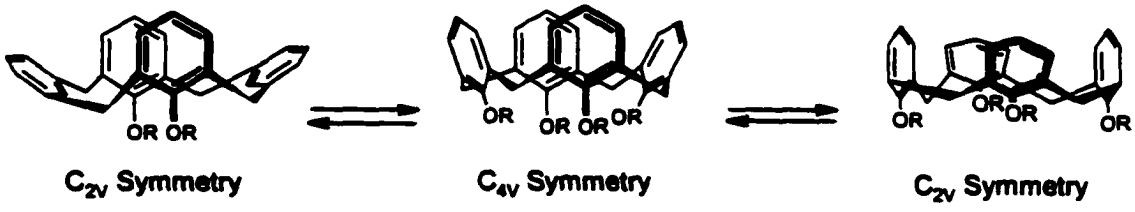
Calixarenes containing free intraannular OH groups, including calix[4]arenes, are conformationally mobile in solution at room temperature; however, they favorably adopt a cone conformation due to the stabilization by intramolecular hydrogen bonding interactions.[35]

O-Alkylation of calixarenes, on the other hand, may eliminate the possibility of the oxygen through the annulus rotation, preventing interconversions between conformers

and producing separable isomers. Shinkai and co-workers found that alkyl groups, the size of an *n*-propyl or larger, are sufficient to inhibit the rotation.[36]

The cone conformer has received the greatest attention as a framework for constructing molecular templates. In spite of ^{1}H NMR spectra of homo-tetrasubstituted calix[4]arenes consistent with the notion of the molecule having a C_{4v} symmetry when in cone conformation, studies have shown that the cone structure exists in a C_{2v} symmetry, which is more stable than the more highly symmetrical C_{4v} structure.[37, 38, 39]

This C_{2v} structure has been called the pinched-cone conformation. In solution the two C_{2v} symmetry conformers interconvert via a C_{4v} symmetrical cone conformation (Scheme 6). The fact that the pinched-cone conformation cannot be detected in the ^{1}H NMR spectra is explained in terms of a rapid interconversion of the two C_{2v} structures under normal operating conditions.



Scheme 6: Interconversion of the calixarene from one C_{2v} symmetry to the other.

Stereochemistry of calix[4]resorcinarenes:

The absence of intraanular OH groups in calix[4]resorcinarenes makes this type of molecule more flexible than calix[4]arenes; therefore, the different conformations, although similar to the ones of calixarenes, have more flexibility and can adopt "out"

alignments in addition to "up-down" alignments. These conformers are now termed the cone, the flattened cone, the 1,3-alternate, and the partial flattened cone (Figure 11).

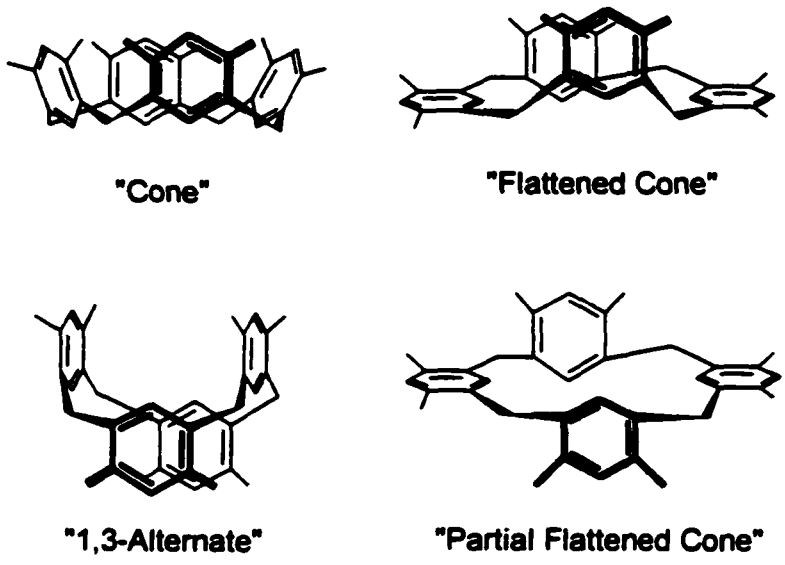


Figure 11: Calix[4]resorcinarene conformers.

The groups attached to the bridging methylenes bring configurational as well as conformational isomers into play. Theoretically, there are four different configurations of the cyclic tetramer. Figure 12 shows the different configurations depending on the orientation of the alkyl or aryl groups originating from the aldehyde used in the condensation.

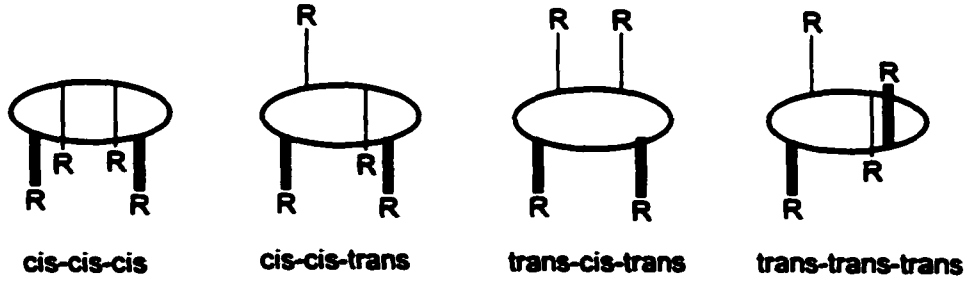


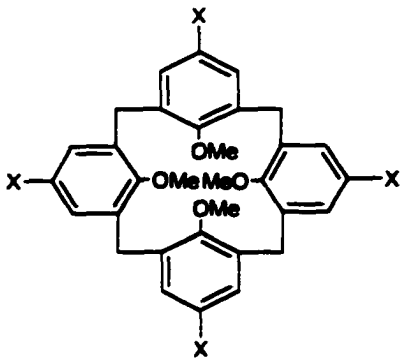
Figure 12: Calix[4]resorcinarene configurations.

The cone and flattened-cone conformers only exist in the *cis-cis-cis* configuration and the partial flattened cone only in the *trans-cis-trans* configuration. The *cis-cis-trans* has only been identified in situ by proton NMR experiments done by Weinelt and Schneider.[34]

Conditions that influence conformational isomerism:

Shinkai *et al.*[40] demonstrated that solvent effects influence the conformational isomerism of tetra-O-methyl calix[4]arenes. On the basis of the 400 MHz proton NMR measurements at -25°C in $CDCl_3$ 5,11,17,23-tetrabutyl-25,26,27,28-tetramethoxy calix[4]arene cone and partial cone, appear as the major conformers whereas, 1,3-alternate is not detected or is present only as a minor conformer. This is an unexpected result considering that computational studies predict that 1,3-alternate is the most stable conformer among the four possibilities. The only reasonable explanation is that probably these results are due to solvent effects. To test this hypothesis, water soluble anionic and cationic calix[4]arenes were synthesized (Figure 13). The conformer distribution in water was one in which the main species was 1,3-alternate and the other was partial cone. The distribution of conformers was easily affected by the solvent composition. The fraction of 1,3-alternate increases with more polar solvent and, the fraction of partial cone is increased in less polar solvents. This behavior can be explained by considering the basic skeleton of calix[4]arenes as a hydrophobic surface, which has minimum contact with water molecules when in 1,3-alternate conformer. For example, the equilibrium between the cone and partial cone of conformers of **44** is affected by solvent polarity; the percentage of cone increases with an increase in solvent polarity. This can be explained

by the more polar character of cone-44 being stabilized in polar solvents over partial cone-44 (Figure 14).



42. $X=SO_3^-$ Na^+
43. $X= CH_2NMe_3^+Cl^-$

Figure 13: Water soluble calixarene.[40]

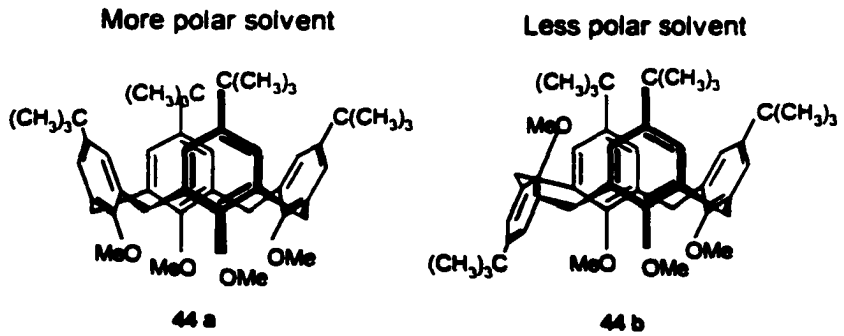


Figure 14: Effect of the polarity of the solvent on the different conformations of calixarenes.

The inclusion of cations also influences the equilibrium between conformers. When $LiClO_4$ or $NaClO_4$ was added into $CDCl_3/CD_3OD$ (4:1 v/v) the ^1H NMR spectra showed peaks consistent with cone-44-M^+ and partial cone-44-M^+ structures. The spectra changed to indicate partial cone-44 and 1,3-alternate-44 when $KClO_4$ or $AgClO_4$

was added. The reason suggested for this is that Li^+ and Na^+ cations bind to the lower rim of the structure whereas, K^+ and Ag^+ bind to the upper rim through the interaction with one or two oxygens and two benzene rings.[41] Ammonium ions are bound in the cone cavity in between the four arene rings, which form a π-basic cavity owing to the cation-π interaction. The inclusion of the ammonium cation makes the cone conformation more stable than the partial cone isomer. Ungaro, *et al.*[42] also reported studies which indicate that conformer stability is affected by the size of the bound metal cation (Figure 15).

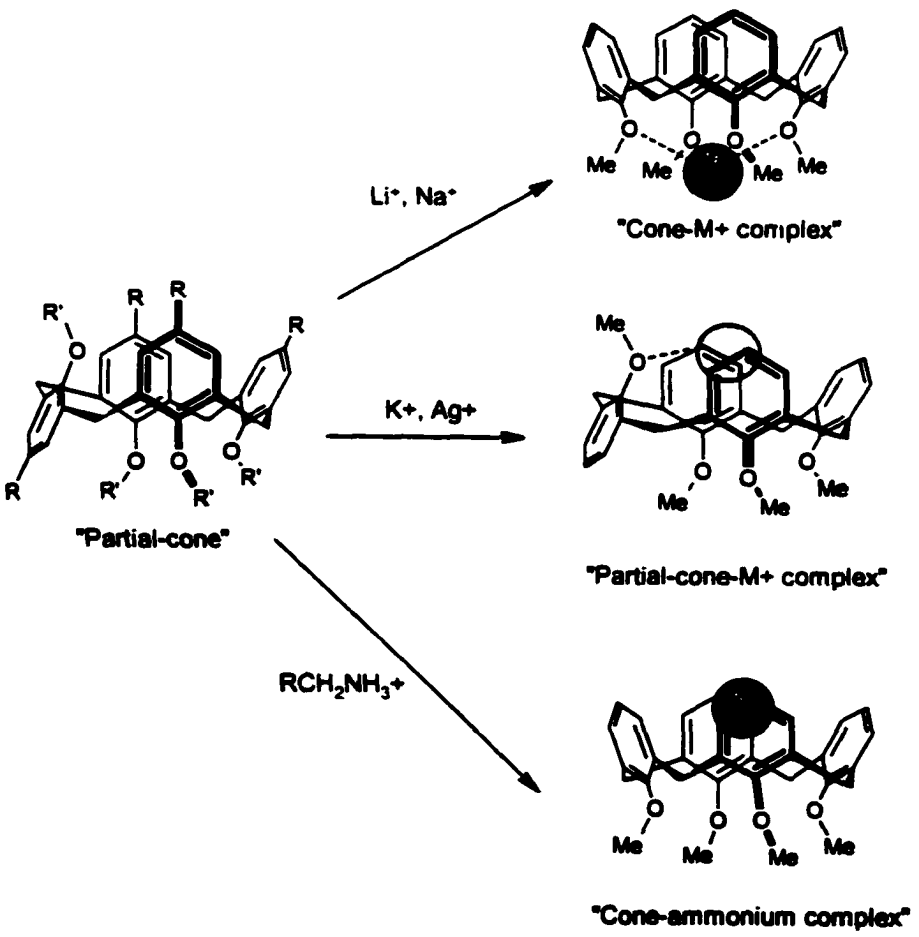


Figure 15: Inclusion of metal cations and the ammonium cation.[41]

1.1.4 Stereochemical control of calix [4]arenes

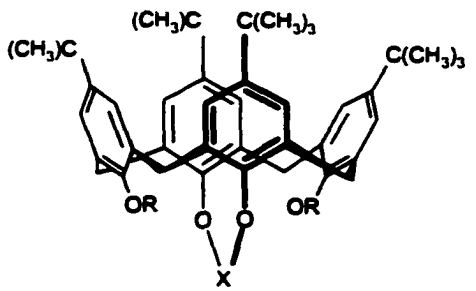
Tetra-O-Alkylation:

It has been shown that in calix[4]arenes the *p*-substituent through the annulus rotation is entirely inhibited (even when the para-substituent X=H) whereas the oxygen through the annulus rotation is allowed for OR=OH, OMe, and OEt, but is blocked when R = n-Pr or n-Bu.[43]

In the case of calix[4]arenes with OR = OH even though each phenol unit can potentially invert via oxygen through the annulus rotation mechanism, they preferentially adopt cone conformations because of the stabilization by intramolecular hydrogen bonding interactions among OH groups.[44]

Bridging calixarenes:

A different way of immobilizing the calixarene conformation is by crosslinking the upper rim. Crown ether bridges at the upper rim have been used to immobilize the conformations of calixarenes. Structures like the ones in Figure 16 have been prepared[42] in which single bridges were used to staple two of the phenol units in a 1,3-fashion. Structures bridged in this way but having an R=H or CH_3, like **45** and **46**, have aryl units that are still conformationally mobile and can invert to produce the cone, partial cone and 1,3-alternate conformers. In compound **47**, O-alkylation of the other two phenol units was used to reduce the conformational freedom of the molecule.



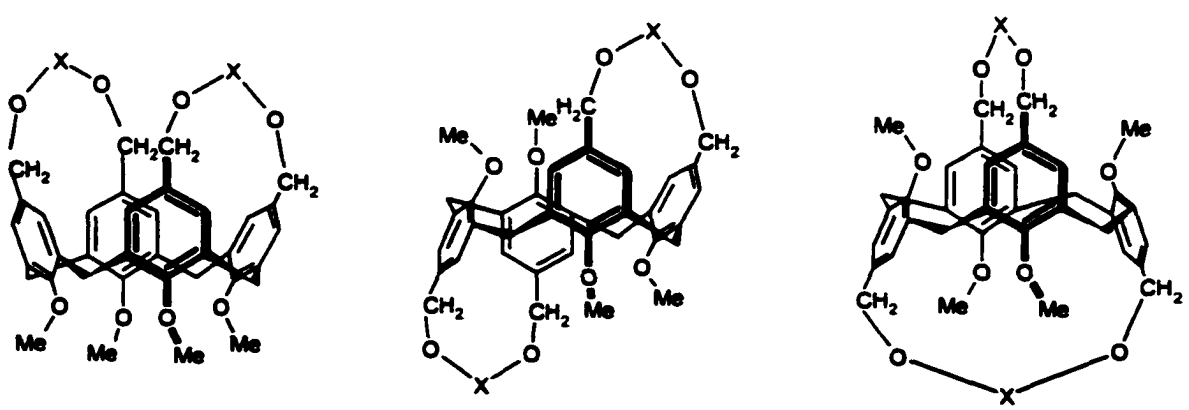
45. R=H, X= $-CH_2CH_2(OCH_2CH_2)_3$

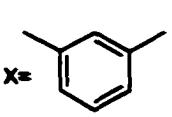
46. R=CH_3, X= $-CH_2CH_2(OCH_2CH_2)_3$

47. R=$CH_2C_6H_5$, X= $-CH_2CH_2(OCH_2CH_2)_3$

Figure 16: Crown ether bridges on calixarenes.[42]

Compounds **48** and **49** (Figure 17), have double bridges at the upper rim. **48** has been isolated as 1,2-alternate and 1,3-alternate and **49** as cone, 1,2-alternate and 1,3-alternate conformers. The isolated conformers were heated and shown not to isomerize, therefore are said to be conformationally immobile.[45]



48. X= 

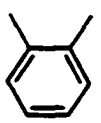
49. X= 

Figure 17: Doubly bridged calix[4]arenes.[45]

Reinhoudt *et al.* also reported almost completely rigid molecules bridged with a 2,6-dianisylpyridine or an *m*-teranisyl moiety (Figure 18).[42]

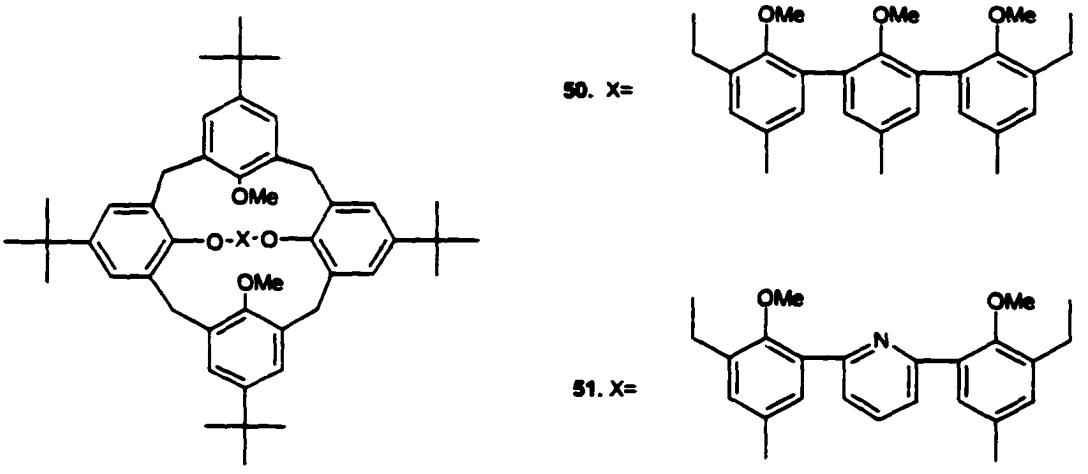


Figure 18: Bridged calix[4]arenes.[42]

1.1.5 Molecular recognition and metal binding

The interest of many scientists in the design of calixarenes as platforms for host-guest chemistry is in view of the development of devices such as optical sensors and molecular switches.[46-49] The ability to change the pendant groups on the molecule, makes calixarenes a framework which can be modify to potentially bind neutral molecules, metal ions, and organic anionic or cationic molecules.

Complexes of neutral molecules with calixarene molecules have been successfully identified. For example, *p-tert*-butylcalix[4]arene forms a solid complex with toluene (Figure 19)[50] and complexes with benzene, phenol, and pyridine have also been identified by Andreetti and coworkers.[51]

Although the complex with toluene has only been identified in the solid state, other examples of calixarene complexes show that calixarenes can not only serve as hosts for neutral organic molecules, but also be used in the separation and purification of compounds. Ungaro *et al.*[52] has used *p-tert*-butyl calix[8]arene as the stationary phase in the gas-solid chromatography for the separation of alcohols, chlorinated hydrocarbons and aromatic compounds. Calixarenes also have been used in the separation and purification of C_{60} [53] and scientists continue to investigate the extraction and separation properties of different calixarenes in the attempt to use them in the separation of compounds on an industrial scale.[54]

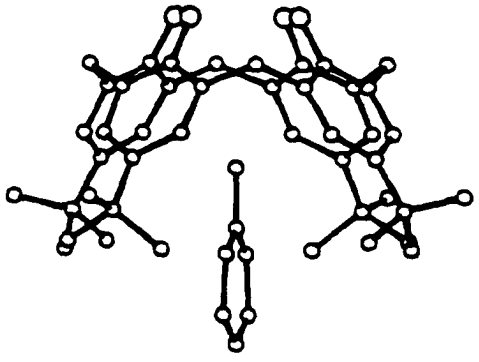
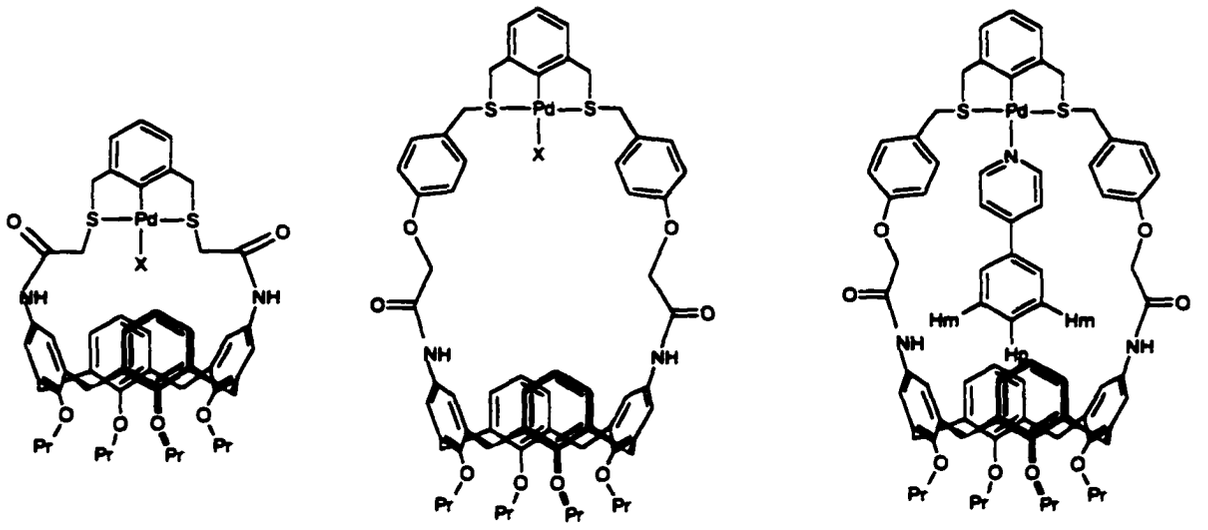


Figure 19: Calixarene - toluene complex.[50]

Calixarene metalloreceptors which contain an organopalladium binding site for molecular recognition have been synthesized[55] (Figure 20). Binding of a substrate to **52** and **53** occurs through σ bonding to the palladium center when the guest displaces the labile acetonitrile ligand. Interaction between the guest and the hydrophobic site provided by the calixarene also occurs.



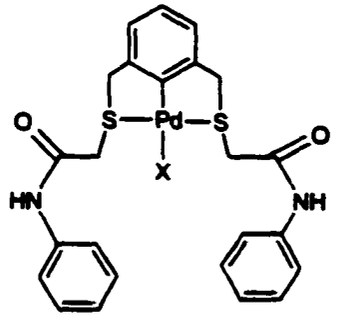
52. X=MeCN

53. X=MeCN

54

Figure 20: Calixarene based metalloreceptors.[55]

Compound **54** was compared with a model receptor containing no calixarene unit (See **55** in Figure 21). The results (Table 1) show a greater ability of **53** compared to **55**, to selectively bind 4-Phpy over 2-Phpy or 3-Phpy. These results support the notion that having a perfect fit of the guest in the host cavity is important in a molecular recognition event.



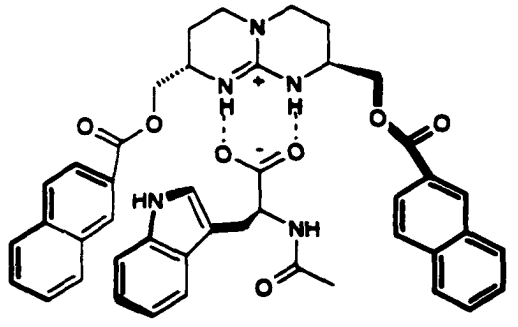
55. X= MeCN

Figure 21: Palladium metalloreceptor.[55]

Table 1. Competition reactions showing molecular recognition of 4-Phpy.[55]

Substrate pair	55	54	Selectivity
4-Phpy/2-Phpy	50/50	80/20	4
4-Phpy/3-Phpy	4/96	60/40	38

Recently, hosts have been designed, that can have a cleft or tweezers like systems that bind guests without completely encapsulating them. These systems bind organic molecules through hydrogen bonding and π-stacking interactions (Figure 22).



56

Figure 22: Sample of cleft shaped receptor.[86]

Calixarenes can also be made to have pendant groups attached to the upper or lower rims of the molecule which are shaped like cleft systems. This mode of host-guest binding does not need a perfect preorganization of the binding sites of the free host but it requires the host to be fitted for the guest at some point during the complexation process without an excessive demand of conformational energy.

Complexation of metal cations:

Since they were first isolated, calixarenes have been studied for the complexation of metal cations. The ability to functionalize the molecule and the electron-rich cavity of the compounds, makes calixarenes the perfect prospect for cation binding. The versatility of the molecule due to the different conformations can also change the shape and size of the cavity, making it more suitable for a specific cation. The first series of calixarenes with cation receptor properties was obtained by introducing ether chains [$(CH_2CH_2O)_m$-CH_3] on the phenolic oxygen atoms of calix[4]-, calix[6]- and calix[8]arenes.[56] These compounds showed to be less powerful than normal crown ethers but still efficient in complexing cations such as cesium and guanidinium.

Calixarene molecules with crown ether bridges attached in a 1,3-fashion also demonstrate the potential arising from the combination of structural and conformational factors. The crown ether provides the calixarene with size selectivity properties (Figure 23). While crown-4 derivative **(57a)** (cone or partial cone) has been demonstrated to be the ligand with higher selectivity for Na^+ over K^+ ions, the crown-5 derivative **57b** (partial cone) and **57c** (1,3-alternate) show higher selectivity for K^+ over Na^+ ions.[57]

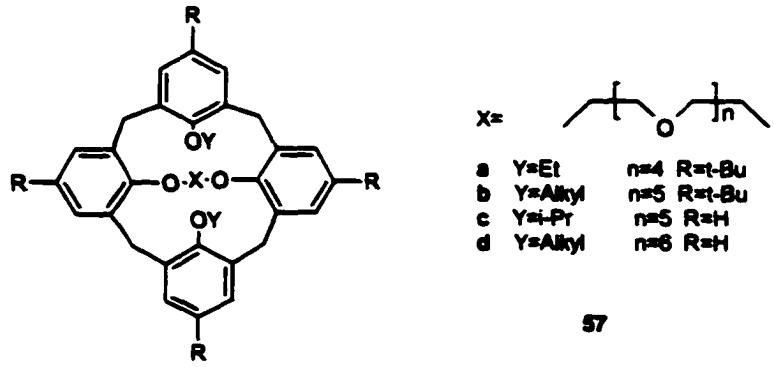


Figure 23: Crown ether calixarenes for cation binding.[57]

Anion binding:

Calixarene anion receptors, although relatively rare, are of great importance in view of their potential applications in the biochemical, medical and environmental field. Recently the calixarene anion receptors **58**, **59** and **60** were synthesized (Figure 24) and have been shown to exhibit remarkable selectivity for $H_2PO_4^-$ over Cl^-.[58]

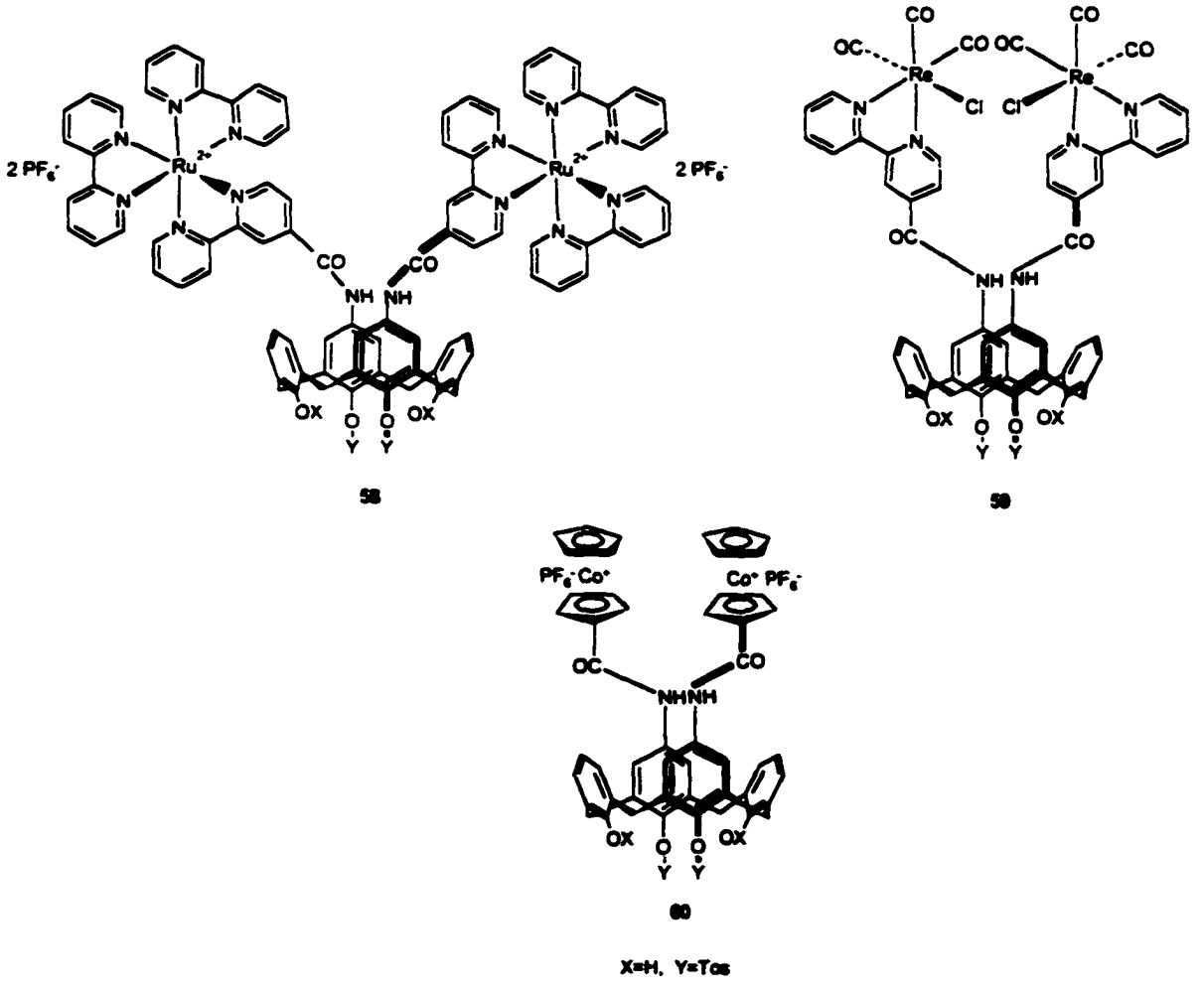


Figure 24: Calixarenes with anion recognition properties.[58]

Molecular modeling calculations and examination of CPK models support the idea that the bulky lower rim tosyl groups *para* to the upper rim amide substituents play

an important role in altering the receptor conformation so that the upper rim Lewis acidic units are rigidly held in close proximity to each other, therefore affecting the receptor's anion coordination properties. Figure 25 shows the crystal structure of bis-nitro derivative which illustrates this postulation.

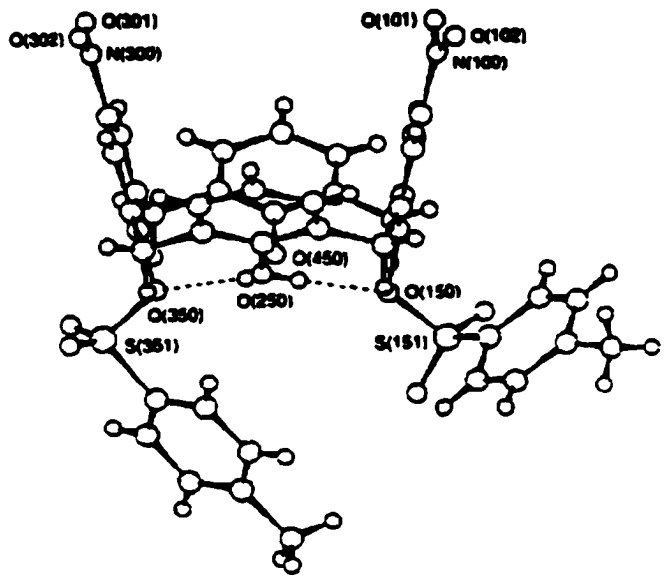
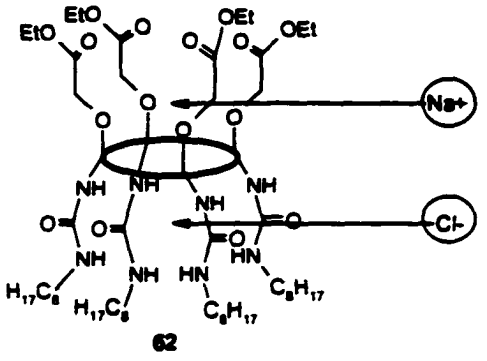


Figure 25: Crystal structure of **61**.

Ditopic receptors:

Because of the ability to functionalize both the upper and lower rim of the calixarene moiety, receptors can be developed which can bind simultaneously to cations and anions. An example of ditopic calixarene receptor is **62** that can solubilize NaCl in $CHCl_3$ up to a concentration of 0.1 M.[59]



62

Figure 26: Ditopic receptor.[59]

1.1.6 Background on chromium tricarbonyl complexes

Calixarenes are one kind of cyclophane structures therefore, cyclophane macrocycles in general are also suitable for host-guest chemistry.

Chromium chemistry can potentially be used to synthesize cyclophanes.[83] In this project it has been explored for the synthesis of macrocycle frameworks similar to calixarenes.

The use of arene chromium tricarbonyl complexes in organic synthesis has been an expanding area since η^6-benzene tricarbonylchromium was synthesized for the first time in 1958.[60] (Figure 27).

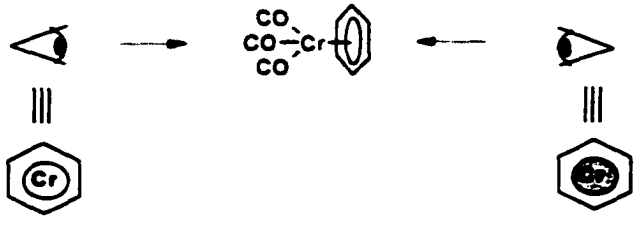
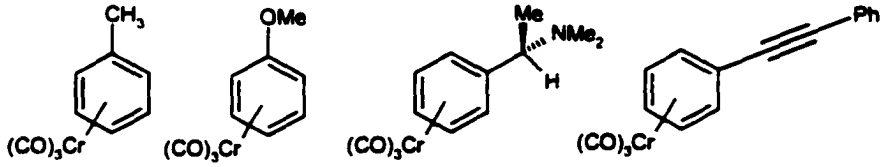


Figure 27: Symbolism for chromium complexes used in this paper. The non shaded Cr on the left symbolizes view of the arene unit from the tricarbonyl chromium side. The shaded Cr on the right symbolizes view of the arene unit from the side with no tricarbonyl chromium group.

Figure 28 shows phenyl rings of various compounds, some bearing alkyne moieties, that have been complexed in order to study the change in the chemical properties of the molecules.[61-64]



63 64 65 66

Figure 28: Examples of chromium tricarbonyl complexes.[61-64]

The effects of the complexation on the reactivity of the arene include.[65]

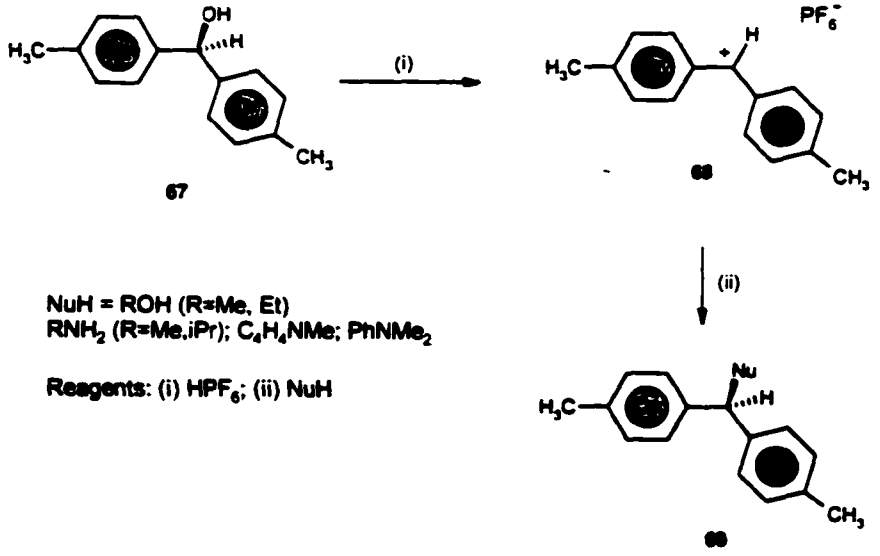
1. Enhanced acidity of ring protons.
2. Enhanced acidity of α- and β- protons.
3. Stabilization of α- and β- cations.
4. Increased reactivity of the ring with nucleophiles to yield products of nucleophilic aromatic substitution.
5. Decreased reactivity of the ring with electrophiles affecting also the regioselectivity of attack in substituted arenes.
6. Stereoselectivity due to steric effect of the chromium tricarbonyl group and the destruction of the plane of symmetry of the benzene ring.

While many of these modifications in the reactivity of the arene are due to the strong withdrawal of electron density from the ring, the stabilization of the benzylic cation is due to the delocalization of the positive charge from the benzylic carbon to the

transition metal. Direct electron donation from a filled d orbital of the chromium to the benzylic carbon can be represented by the resonance structures below. (Figure 29)[66]

Figure 29: Resonance structures showing the stabilization of the cation.[66]

Some cationic compounds have also been isolated and analyzed spectroscopically. Seyferth *et al* obtained the cation **68** (Scheme 7) as dark blue crystals and was able to show that the cation can be captured by different nucleophiles.[67]



Scheme 7: Synthesis of cation **68**.[67]

Preparation of arene chromium tricarbonyl complexes:

A practical and efficient method for the formation of arene chromium complexes is direct thermal replacement of other ligands on the metal. Good yields of compounds

can be obtained when an arene and hexacarbonyl chromium are refluxed together in a high boiling point solvent mixture like *n*-butyl ether/THF (10:1) or a mixture of diglyme/octane. These solvent mixtures allow temperature control in the 130° – 140°C range, which causes the opening of a coordination site on the metal and allows the arene to complex.

Hexacarbonyl chromium can also be treated thermally to replace three of the carbon monoxide ligands by molecules such as pyridine, picoline, acetonitrile or ammonia which in turn can be replaced by an arene at much lower temperatures (60° – 70°C)[65].

A second method of preparing arene chromium complexes is by taking advantage of the equilibrium between an arene and an arene chromium tricarbonyl, in which, the most stable complex would form when both compounds are heated at approximately 200°C. The best of these is naphthalene tricarbonylchromium, which transfers the $Cr(CO)_3$ unit nearly quantitatively to the vast majority of all other arenes. [85]

1.1.7 Goals of Study:

The use of calix[4]resorcinarenes in the complexation of metal cations and in molecular recognition processes is the basis of this thesis. More specifically, the goal of this project has been to design and devise ways of synthesizing calix[4]resorcinarene frameworks that could be used as molecular sensors. This synthesis may be achieved by functionalization of the upper and lower rims of existing calixarene structures. The use of chromium chemistry has also been explored in this project, for the synthesis of basic calixarene frameworks.

2. RESULTS AND DISCUSSION

2.1 Design of a cleft at the lower rim of the calixresorcinarene

Calixarenes have a potential use in industry[68] for the separation of different substances[69] or as molecular sensors.[70-73] Their ability to serve as hosts for a variety of organic compounds or ions, metals or metal ions prompted the decision to work on the synthesis of cavitands that could be used in molecular recognition processes.

The luminescence properties of lanthanide ions has generated interest in a variety of areas of chemistry and biology. It has been shown that certain calix[4]arenes[74-77] and calix[4]resorcinarenes[20] derivatives (Figure 30), are useful as ligands for energy transfer luminescence of Tb^{3+} ions.

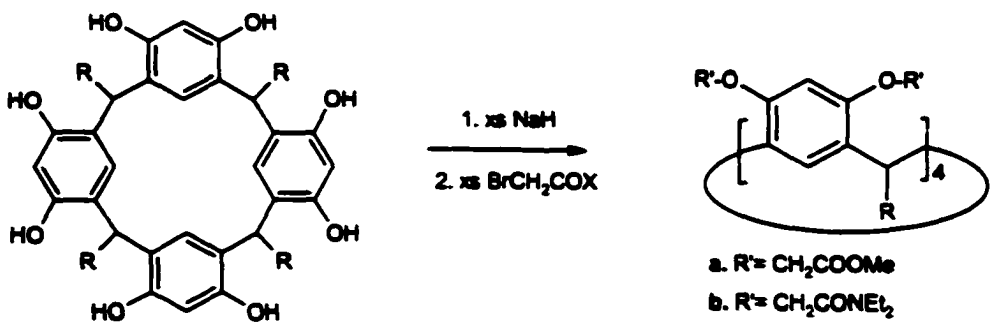


Figure 30: Octafunctionalized derivatives of calixarenes which were found to exhibit energy transfer luminescence when complexed with terbium (III) ion.

Our goal in this project was to design and synthesize a calixresorcinarene that can serve as sensor for molecular recognition events. The complexation of different guests by the resorcinarene might be detected by changes in the luminescence properties of lanthanide ions.

It was proposed to synthesize a calix[4]resorcinarene such as **77** (Figure 31). The ionophoric amide groups at the to rim of the molecule allow the efficient encapsulation of Tb^{3+} ions and the arene units on the pendant groups of the molecule form a cleft in the tail of the macrocycle that could "clip" to a guest molecule, such as aromatic amino acids, using π-stacking interactions. UV spectroscopy can be used to study the effect of the complexation of different guests at the lower rim of the molecule.

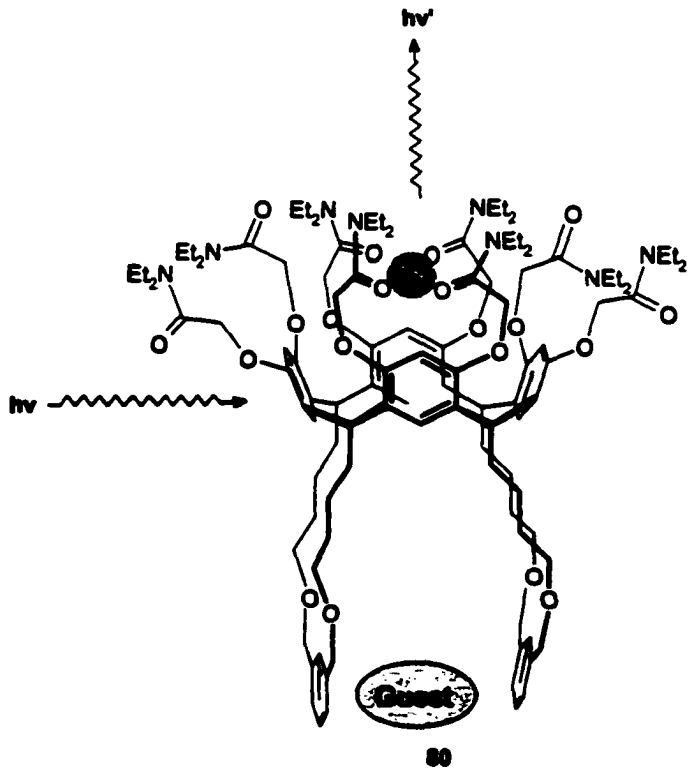
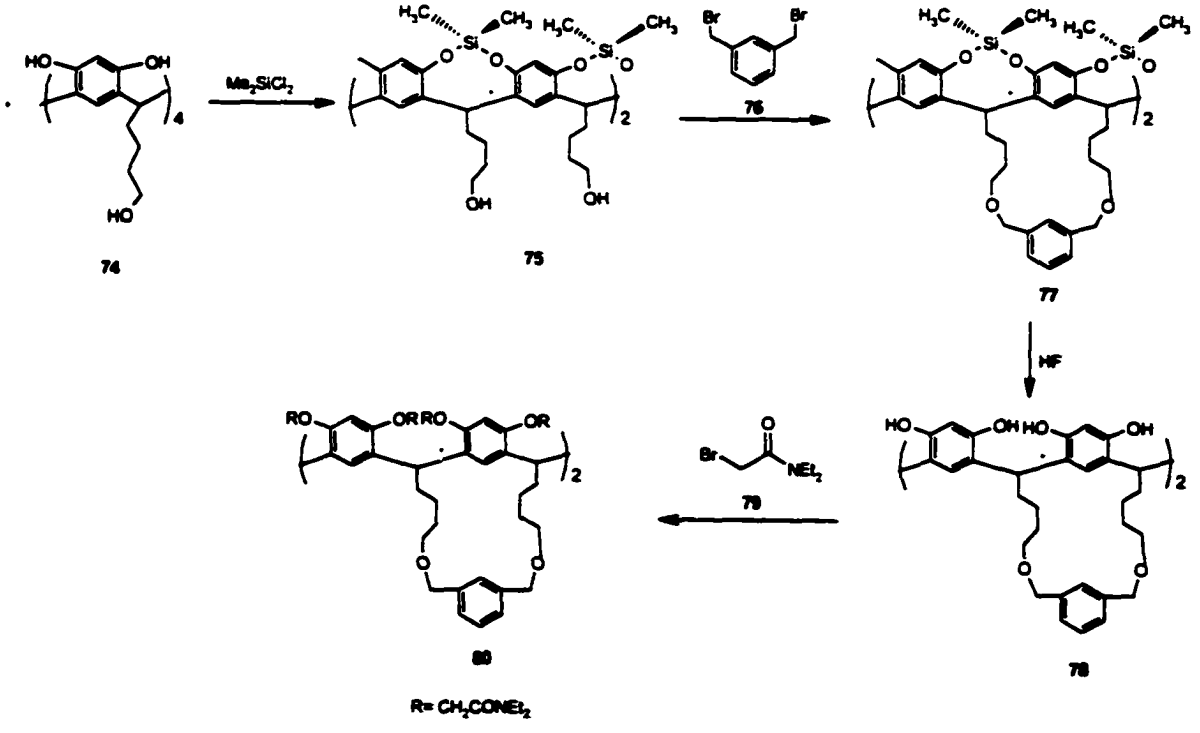


Figure 31: Example of a possible target molecule in this project (80) showing the excitation of the calixarene and the energy transfer luminescence of the Tb ion in the presence of different guests.

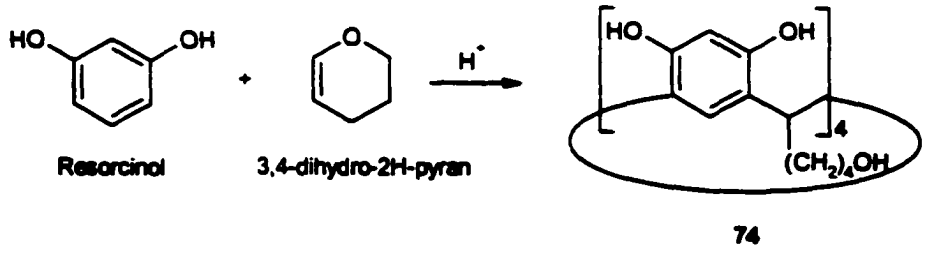
The proposed synthesis is outlined in scheme 8. The first step is to prepare a basic resorcinarene framework (74) in which the phenol functionalities can be protected via formation of silicone bridges at the top rim of the molecule (75). Subsequent functionalization of the pendant alcohol groups would produce a cleft in the tail of the macrocycle. The next step would then be the deprotection of the phenol groups and the incorporation of amides at the top rim of the molecule. More robust molecules could be prepared by incorporating groups such as naphthalene on the pendant alcohols. Clefts formed from naphthalene units would presumably form stronger π-stacking interactions with the guest. Cleft systems don't demand perfect preorganization of the bonding sites of the free host, but require that the host's binding sites fit the guest without an excessive demand of conformational energy.[88]



Scheme 8: Proposed synthesis of functionalised resorcinarenes.

2.1.1 Synthesis of butanol footed dodecol

The synthesis begins with a calixarene prepared by Cram and Sherman.[78] Butanol footed dodecol **74** was prepared from the reaction of resorcinol with 3,4-dihydro-2H-pyran under acidic conditions in 55% yield and following a procedure similar to Sherman's (Scheme 9)[79] which required the reaction to be heated at 50°C for 7 days. These conditions produced only a hard red solid which, would not dissolve in any solvent. The impression was that polymerization had occurred, possibly due to excessive heating of the reaction. Higher temperatures than 50°C can readily lead to polymer products. The procedure was modified. The reaction was heated at 40°C for 4 days and the product was precipitated with water as an oily solid. The oily solid obtained was then purified by triturating with acetone. Butanol footed dodecol was obtained as a very pure off-white solid at a 55% yield. (**74**)



Scheme 9: Synthesis of butanol footed dodecol.

Compound **74** was fully characterized by Sherman,[79] using standard spectroscopic methods. In this thesis, the characterization (^{1}H and ^{13}C NMR, IR and melting point) of **74** matched those reported in the literature. In addition, we were able to recrystallize **74** from methanol / hexane and obtained x-ray quality crystals.

It is believed that the added step in the procedure to triturate in acetone purifies the product from unwanted polymer contamination and makes possible its recrystallization from methanol/hexane.

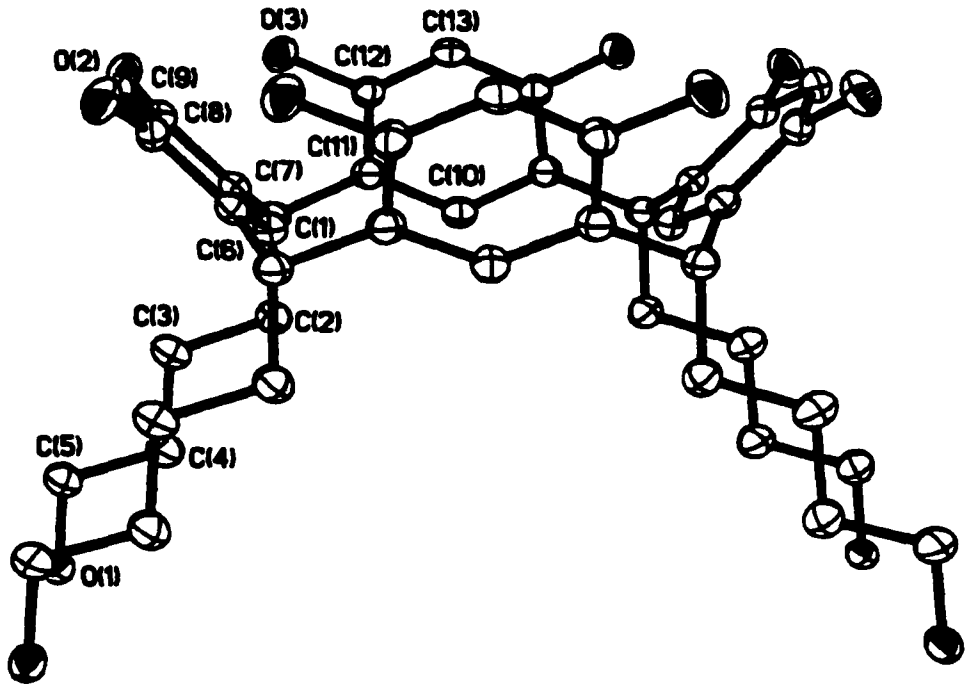


Figure 32: Crystal structure of 74.

As the ORTEP representation in Figure 32 indicates, the molecule adopts a cone conformation. The crystal packing of the calixarene, (Figure 33) shows hydrogen bonding between the molecules which stabilizes the crystal structure. A single diastereomer is observed, in which all alkyl chains are axial. The X-ray picture confirms the previous NMR spectra results. The molecules are arranged in rows that resemble ribbons. Each row interacts with other rows that are oriented on a 180° angle. This packing demonstrates the self-complementarity of the molecule. The axial alkyl chains are displayed at the bottom so that H bonds with other molecules can be formed.

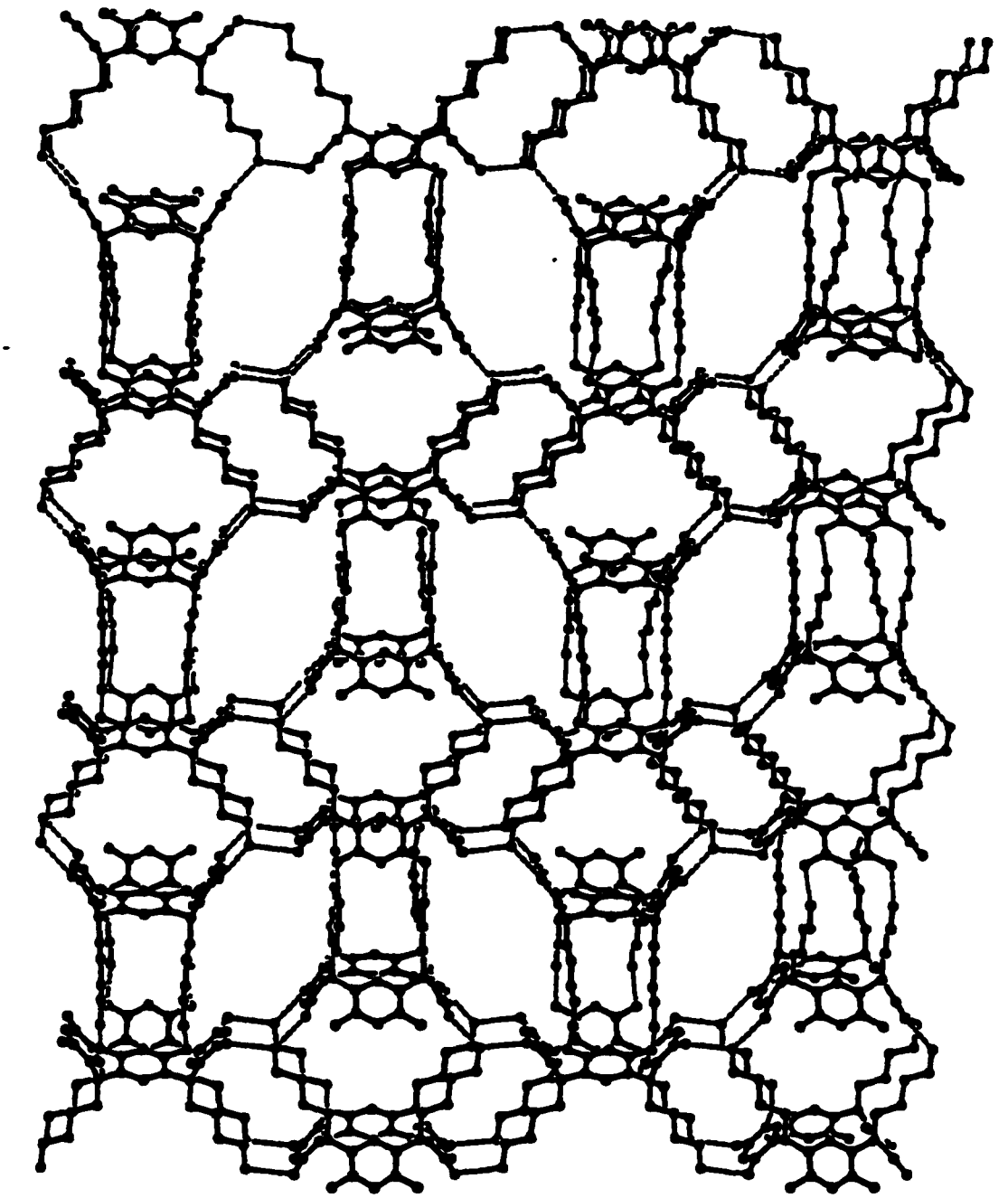


Figure 33: Self complementarity of butanol footed dodecol crystals (74).

2.1.2 Protection of the phenol functionalities

Having prepared the starting material for the project, the next step was to protect the phenol functionalities in the upper rim of the molecule, so that the alcohol groups in the lower rim could be functionalized without interference of the phenol groups.

The protection of the phenol groups can be done in many ways, including their transformation into ether groups.[80] However, having in mind that resorcinarene molecules are conformationally mobile,[20] it was decided to protect the phenol groups by bridging the upper rim of the molecule to form the rigid cavitand. The formation of bridges would constrain its conformational mobility by bridging phenol groups on adjacent aromatic rings (Figure 34).

The preorganization of the molecule on bridging substantially diminishes the competitive reactions caused by the pendant hydroxyl groups because it affects the relative nucleophilicities of phenyl and alcohol groups during the bridging process. Sherman's work[79] compares the reaction of calixresorcinarenes with Me_2SiCl_2 versus trimethylsilyl chloride (TMSCl). When using Me_2SiCl_2, respectable yields of the bridge products were obtained whereas, the reaction with TMSCl produced mixtures with TMS groups on both the phenols and the pendant alcohols. The explanation for these results is that the base deprotonates one set of four of the eight phenols, and intermediates of ArO-$SiMe_2Cl$ are formed. These intermediates can easily react with the adjacent phenol groups. Therefore, the remaining phenols are still more nucleophilic than the alcohols. The reaction with TMSCl, however, leaves the distal phenols unable to compete with the nucleophilic alcohol groups.

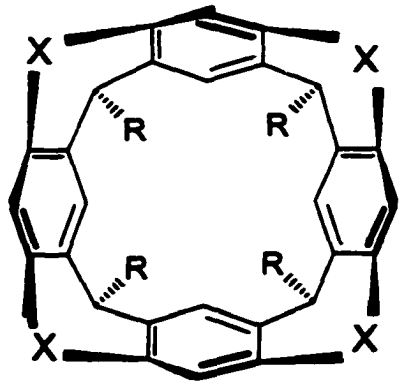
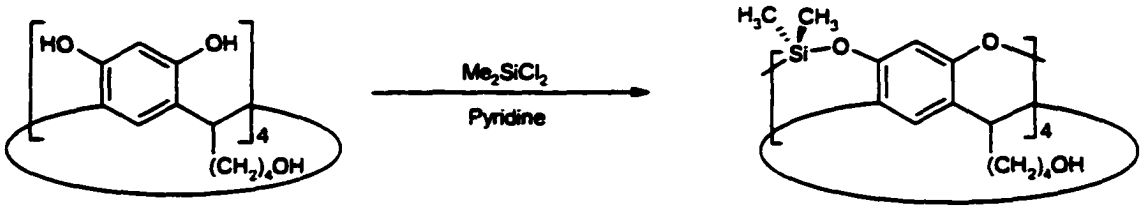


Figure 34: Bridged calixresorcinarene exhibiting a bowl-shaped cavity.

Sherman has described the preparation of silicon-bridge calix[4]resorcinarenes.[79] These cavitands have the advantage over methylene-bridged cavitands in that milder conditions are used for preparation and removal. This would be particularly useful if the pendant groups contained sensitive functionalities. The silicon-bridging reactions can be carried out at room temperature using pyridine as the base, whereas methylene bridge cavitands need higher temperatures (up to 65°C) and a stronger base such as K_2CO_3.[81] In addition, the silicon bridges can be removed under mild acidic conditions. The stability of the bridge is important since it limits the subsequent reactions to only basic conditions.

Butanol footed dodecol **74** was reacted with dimethyl dichlorosilane (Me_2SiCl_2) in the presence of pyridine to produce a molecule with silicon bridges at the upper rim (Scheme 10).



74 75

Scheme 10: Synthesis of **75**.

The product **75** obtained from this reaction showed an NMR spectrum very similar to the starting material with the exception of a new peak at 0.08 ppm that integrates to 24 H's. Although the chemical shift corresponds to the methyl groups attached to silicon, the result is not what was expected. The methyl groups attached to silicon in this molecule are not magnetically equivalent because one is expected to be oriented toward the inside of the molecule's cavity while the other in the opposite direction, to the outside of the molecule.

2.1.3 Functionalization at the lower rim of the calixresorcinarene

Even though the NMR spectrum was different from that expected, there was a slight possibility of having the right product and that it was difficult to identify from the NMR data. Therefore, several reactions were tried on the product attempting to change the pendant groups of the molecule (Table 2).

Table 2: Reactions tried on the resorcinarene to functionalize the rear end of the molecule.

Reactant	Base	Solvent	Temp.[a]	Concentration[a]	Result
PhCHO	None	DMF	rt	0.001M, 0.05M	No Reaction
Compound 76	NaH	DMF	50°C, 60°C	0.0005M; 0.001M	Decomposition
PhCHO	$ZnCl_2$	DMF	28°C	0.05M; 0.001M	No Reaction
$BnCl_2$	NaH	DMF	70°C	0.0005M	No Reaction
Compound 76	Cs_2CO_3	DMF	40°C	0.05M	No Reaction
TsCl	Pyridine	Pyridine	0°C	0.002M; 0.05M	No Reaction
TsCl	Et_3N	CH_2Cl_2	0°C	0.006M	Decomposition
Me_2SO_4	NaH	DMF	rt	0.001M	Decomposition
TsCl	$(^iPr)_2EtN$	DMF	0° -25°C; 0°C	0.001M; 0.05M; 0.0004M	Decomposition
BnBr	NaH	DMF	rt	0.02M	Decomposition
PhCHO	None	None	rt		No reaction
Compound 76	$(^iPr)_2EtN$	DMF	rt	0.0005M; 0.002M	No product was identified
Triethyleneglycol ditosylate[b]	NaH	DMF	60°C	0.001M	Decomposition
BnBr	$(^iPr)_2EtN$	DMF	rt	0.05M	Decomposition
MsCl	$(^iPr)_2EtN$	DMF	0°C-25°C	0.004M	Decomposition
MeI	NaH	DMF	60°C	0.01M	No product was identified

[a]Where two temperatures or concentrations are listed the reaction the reaction was attempted under both sets of conditions. [b] $(TsOCH_2CH_2OCH_2)_2$

From these results several things were obvious. Some reactions didn't proceed at all and in others a reaction occurred but it was not the addition of the reactant to the pendant groups of the calixarene. Instead, decomposition of the calixarene molecule occurred since the characteristic peaks were no longer present in the proton NMR. In the experiments where no reaction occurred, the peaks that distinguish the calixarene were present but the Si groups were clearly lost.

Silicon group instability was suspected. In addition, it was observed that the integral of the methyl groups on the Si was not consistent in the NMR spectra. This information reinforced our suspicions that the calixarene molecule was not stable. The silicon groups may not have been attached to the molecule as previously thought possibly because the phenol groups were not reactive enough. The isolated material was most likely not the target molecule.

To solve this problem Sherman's approach was taken, which was to brominate the calixarene using *N*-bromosuccinimide to give bromododecol **81**.[79] Compound **81** was obtained in 80% yield and when characterized, the results matched those reported in the literature.

The addition of bromine to the arene units results in more reactive phenol groups due to the de-stabilization of the phenolate by halogen resonance donation effect, which increases the nucleophilicity of the molecule (Figure 35). The ground state of the nucleophile is destabilized by the repulsion of the adjacent negative charges which, is decreased as bond formation occurs in the transition state.

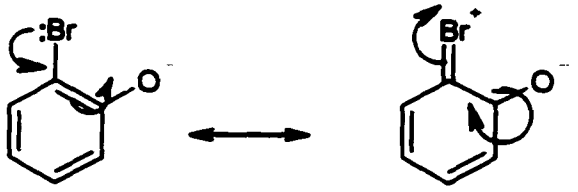
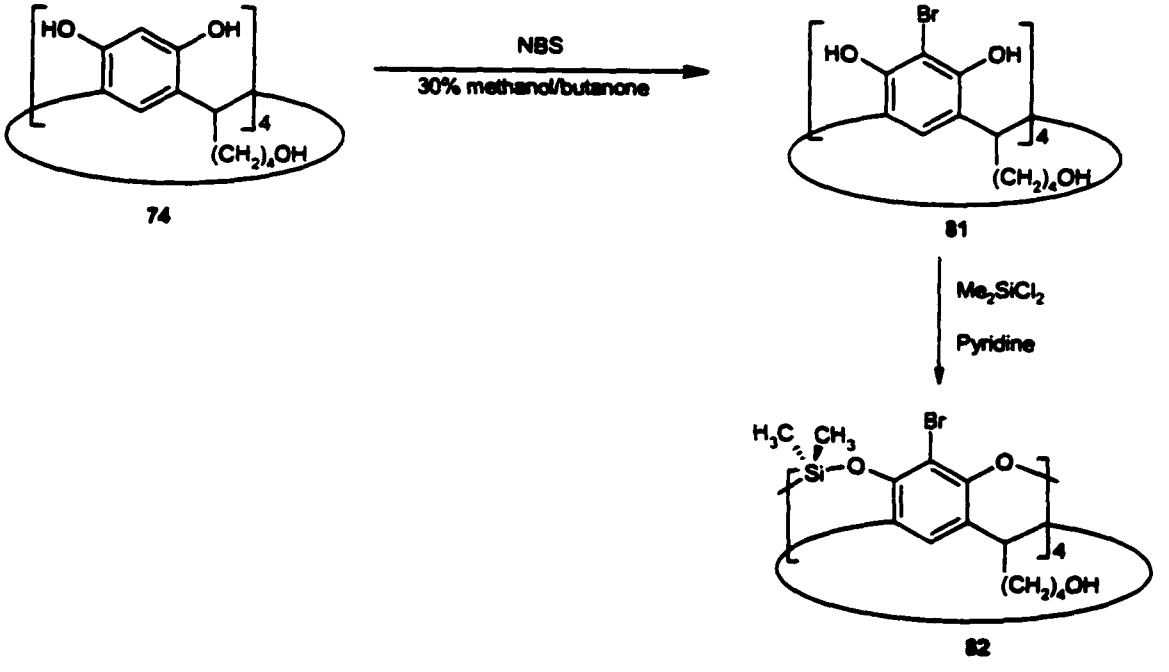


Figure 35: Halogen resonance donation.

The phenol group can then be protected using Me_2SiCl_2 to yield the silicon bridged cavitand **82** (Scheme 11).



Scheme 11: Synthesis of **82**.

In compound **82** the methyl groups attached to silicon were identified by two singlets at –0.63 and 0.54 ppm in the NMR spectrum each one integrating to exactly 12 H's, as expected.

Although **82** was isolable and more stable, it was found to be less soluble in organic solvents. This limits the number of solvents that can be used to perform subsequent reactions. Only a single solvent, DMF, was found to dissolve **82**.

Some considerations have to be made when planning the reactions to functionalize the pendant groups in the molecule: 1) Two equivalents of the nucleophile to one equivalent of calixarene should be used. 2) High dilution conditions increase the possibility of the nucleophile reacting with pendant groups of the same resorcinarene (Figure 36) and not with different molecules. Cross linking leads to unwanted polymerization.

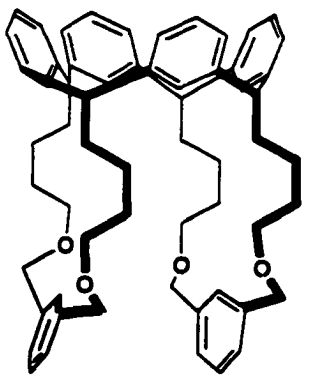


Figure 36: Functionalized alcohols in resorcinarene. (Phenol groups omitted for clarity.)

With these considerations in mind, compound **82** was reacted with α,α'-dibromo *m*-xylene. Several experiments were performed, each one slightly different with the intention of finding the set of conditions that would yield the right product.

The first experiments were tried using the same nucleophiles as in Table 1 with sodium hydride as the base. Decomposition of the resorcinarene was apparent in all cases. Trials with triethylamine were also done using high dilution conditions but no

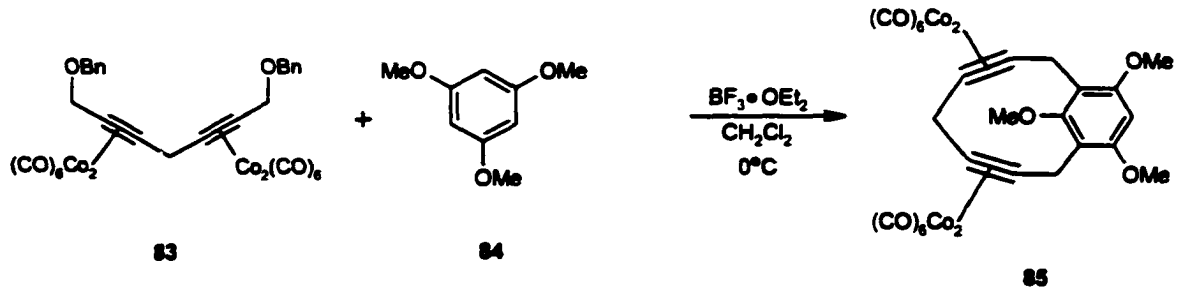
product could be identified. With diisopropylethylamine as the base (15 equivalents) and two equivalents of α,α'-dibromo *m*-xylene at rt for 48h more promising results were obtained. After extraction in ethyl acetate, NMR of the crude product showed sets of peaks in the right areas, but it was obvious that more than one product was present. Column chromatography was performed but the NMR spectra showed that one of the fractions was unreacted calixarene, and another fraction seemed to contain the product, although, we were never able to purify it even after several attempts of column chromatography and preparatory TLC. Therefore, the product was not identified.

It was noticed that the common denominator in the experiments to functionalised the tail of the calixresorcinarene (Table 2) was the use of DMF as the solvent. Although the calixresorcinarene reagent (82) was found to dissolve only in DMF, acetonitrile was not tried. It is the recommendation that another experiment should be set up with acetonitrile to find out if it is a suitable solvent for the reaction and to see if good results are obtained.

2.2 Synthesis of basic cyclophane frameworks

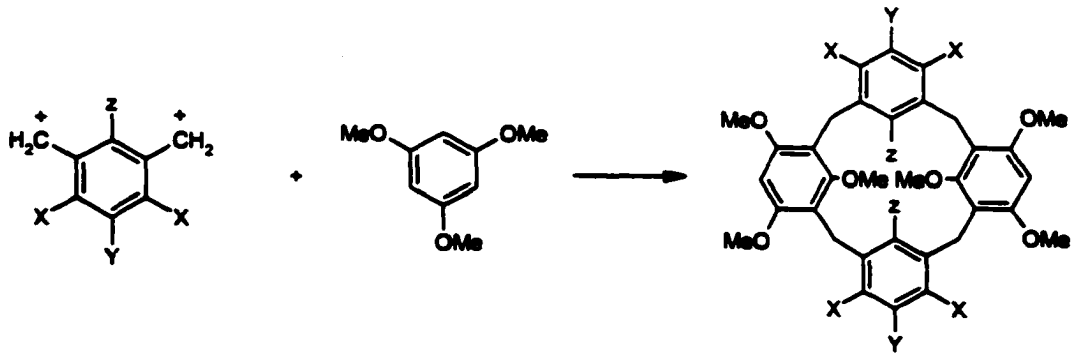
In view of the difficulty trying to change the lower rim of the calixarene and lack of progress in the project, a completely different approach was taken to create a slightly different kind of a macrocycle that was not a calixarene molecule but could in theory be used as a host in molecular recognition processes.

Cyclophane macrocycles are known for their use in supramolecular chemistry.[82] As with calixarenes, their importance is due to their structural properties and their ability to include either metal ions or neutral or charged organic molecules within them.[83]



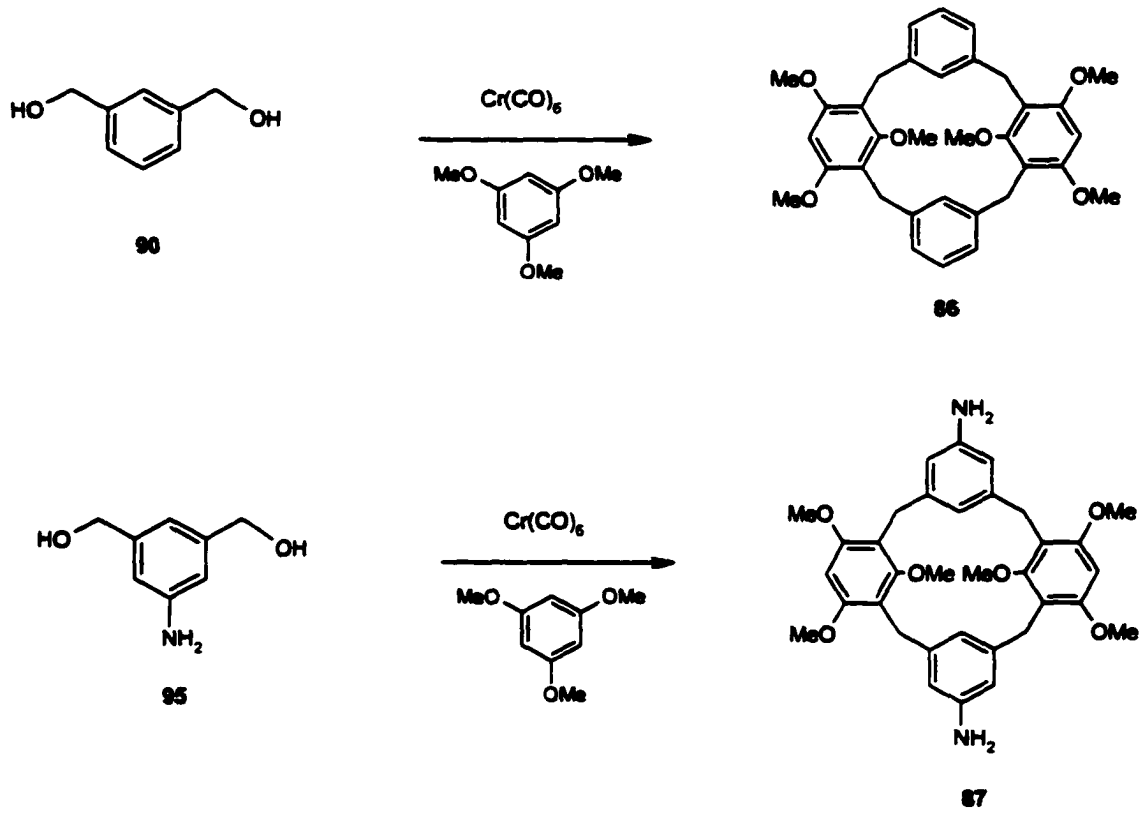
Scheme 12: Synthesis of [7]metacyclophanediyne complexes from bis(propargyldicobalt) by Guo and Green[84]

The recent one step synthesis of [7]metacyclophanediyne complexes from bis(propargyldicobalt) dication equivalents by Guo and Green[84] (Scheme 12), prompted the idea of synthesizing a cycle of aromatic units attached to each other by a methylene group. Macrocycles like the one shown in Scheme 13 are very similar to a calixarene. These may be synthesised by reacting 1,3,5-trimethoxybenzene (84) with an arene that can form carbocations on the benzylic positions.



Scheme 13: Proposed synthesis of a macrocycle with four arene units.

This synthesis can be versatile and result in a variety of interesting compounds depending on the substituents on the arene unit (x, y and z). The compounds used in this project and the results expected are outlined in Scheme 14.



Scheme 14: Proposed synthesis of different cyclophanes.

Substituents in positions x and z open the possibilities for other interesting compounds that could be prepared.

Such molecules like **86** or **87** could provide cavities with the ability to include cations or cationic species due to the electron rich environment of the aromatic rings forming the cavity. These macrocycles can also potentially host molecules using hydrogen bond interactions depending on the groups attached to the arene units.

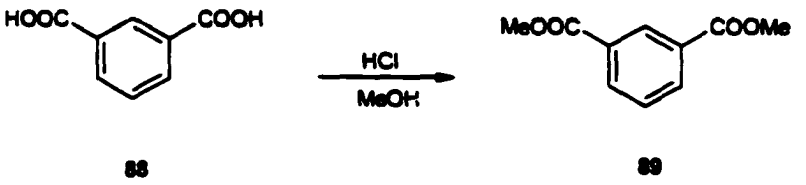
2.2.1 Synthesis of tricarbonylchromium complexes

Tricarbonyl chromium complexes have the ability to stabilize benzilic cations.[67] Therefore, in this project, the strategy was to prepare chromium complexes of compounds

90 and 95. These compounds may then be able to react with electron-rich arenes to form macrocycles suitable for molecular recognition processes

Synthesis of η^6-(m-xylene-α, α'-diol)tricarbonylchromium (91)

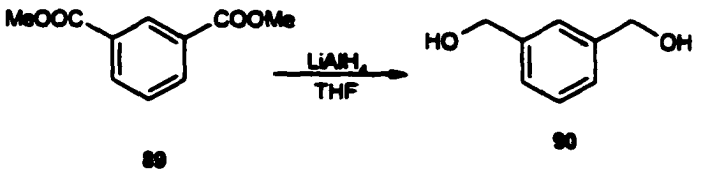
Isophthalic acid was esterified using HCl and methanol to dimethyl isophthalate, which was obtained in 83% yield (Scheme 15).



88 89

Scheme 15: Synthesis of dimethyl isophthalate (89).

Dimethyl isophthalate was reduced to *m*-xylene α,α'-diol using lithium aluminum hydride in THF. The reaction was quenched with methanol and the product was obtained as an off white solid in 98% yield (Scheme 16).

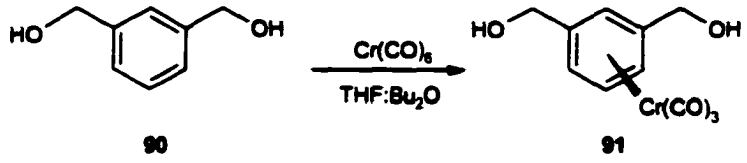


89 90

Scheme 16: Synthesis of *m*-xylene-α,α'-diol (90).

The diol along with hexacarbonyl chromium was refluxed in dibutylether/THF (10:1) for 72 h until sublimation of $Cr(CO)_6$ ceased (this was periodically returned into the reaction mixture). The reaction solution was clear yellow at the beginning of the experiment, and had a green tinge toward the end of the 72 hours. The change in colour is

due to the change in the oxidation state of the chromium. The product **91** was obtained after workup and recrystallization from toluene/heptane (Scheme 17).



90 **91**

Scheme 17: Synthesis of the chromium complex of *m*-xylene-α,α'-diol **(91)**.

The procedure used to complex **90**, was adapted from the experiments done by Siwek,[85] in which a mixture of dibutyl ether : THF (10:1) was used as the solvent. This solvent mixture refluxes at approximately 140°C and is enough to eject carbon monoxide from hexacarbonyl chromium to form the complex. A crystalline yellow solid of **91** was obtained in 54% yield. A previous synthesis[86] of **91** however, used a mixture of diglime and octane (bp = 162°C) as solvent and obtained 76% yield. It is recommended that in future experiments the latter solvent mixture should be used in order to improve the yield.

The NMR spectrum matched the data in the literature and the complexation can be identified by the aromatic peaks that shifted from 6.5 - 7.5 ppm to 5.4 - 5.7 ppm (Figure 37) due to withdrawal of electron density from the aromatic ring caused by the coordination to the metal. The presence of a peak at 235 ppm in the carbon-13 NMR spectrum is characteristic of carbonyl groups on chromium.

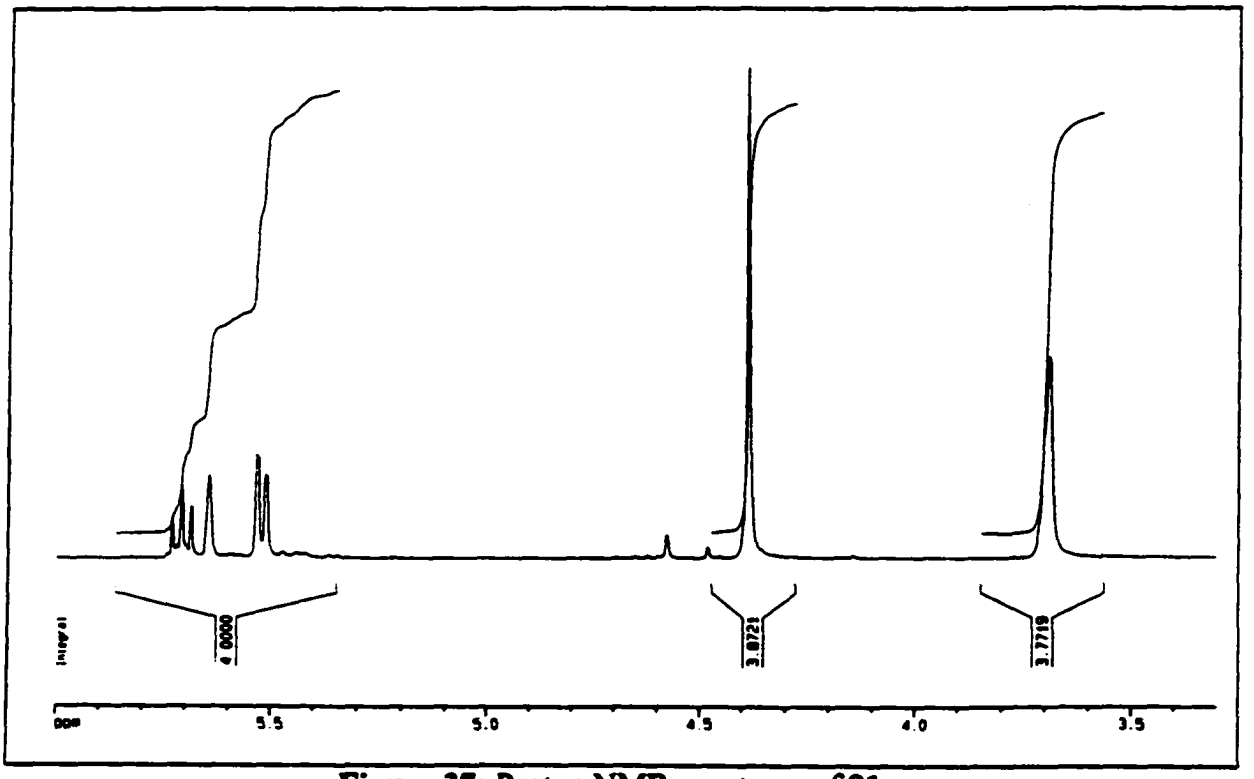
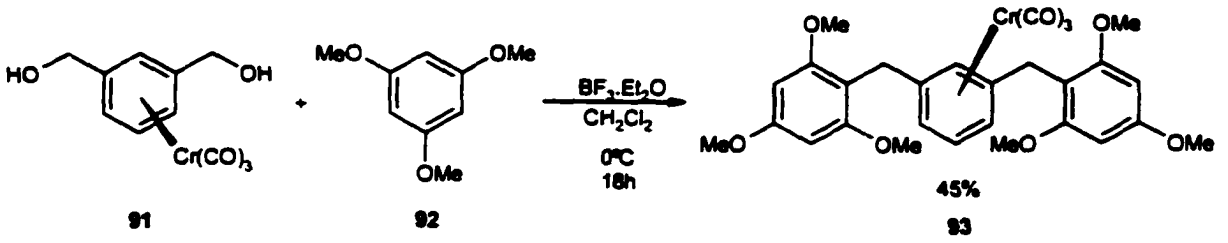


Figure 37: Proton NMR spectrum of **91**.

These compounds decomplex when exposed to sunlight and air, therefore care was taken when handling them and only small amounts were prepared each time.

Once the complex was recrystallized from toluene/heptane, the next step was to carry a reaction using 1 equivalent of the chromium complex and 1 equivalent of **92** to form a macrocycle with four arene units

By accident, 2 equivalents of TMB (**92**) instead of 1 equivalent were used. This reaction produced a compound in which the NMR results showed peaks in the right positions, except, the integral for the methoxy groups were higher than expected suggesting that the chromium–arene complex was attached to two units of TMB (Scheme 18). The product was recrystallized from a mixture of 1:2 petroleum ether : diethyl ether and the NMR spectra is shown in Figure 38.



Scheme 18: Synthesis of 93.

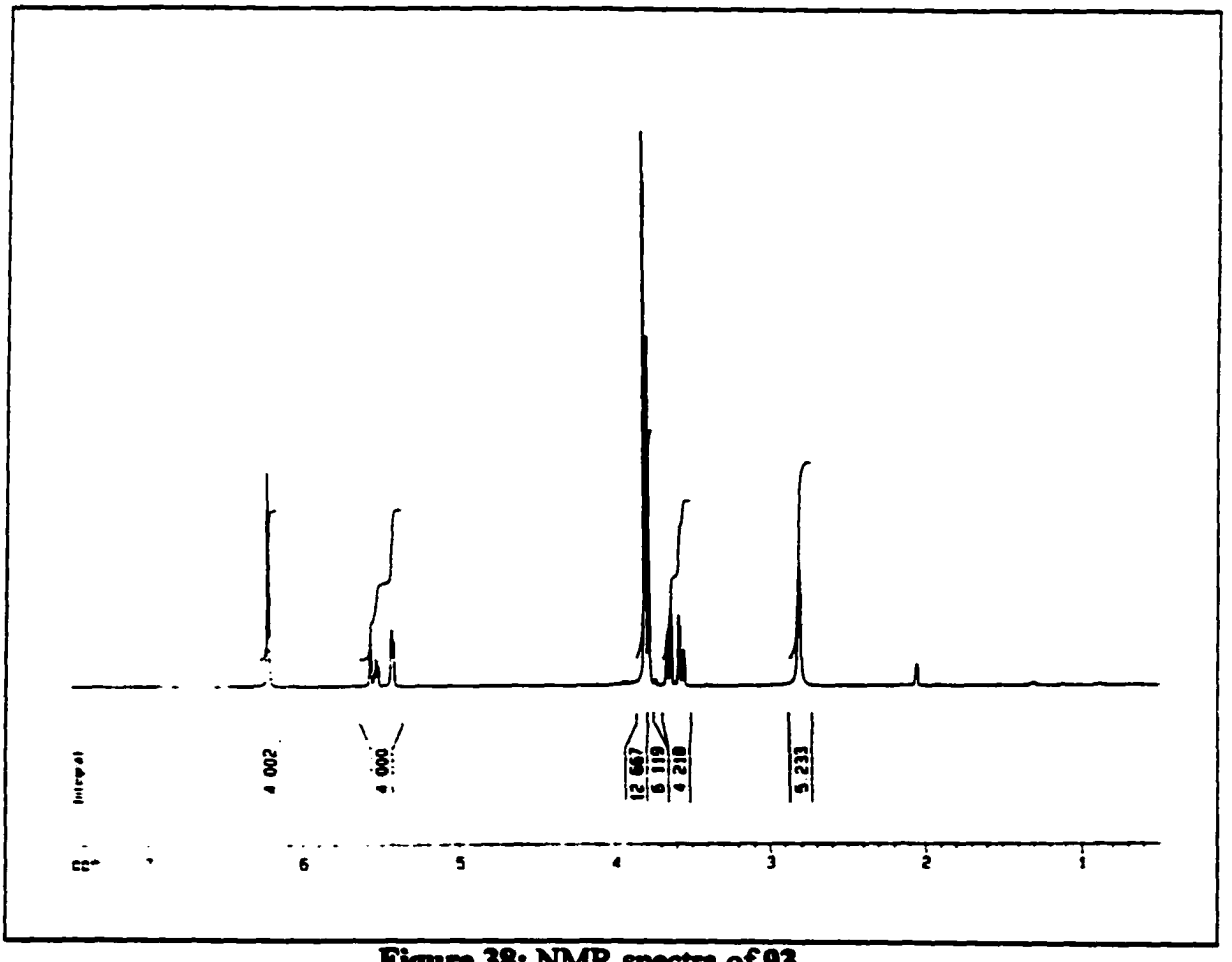


Figure 38: NMR spectra of 93.

In the NMR spectrum the characteristic singlet, triplet and doublet of doublets peaks for the complexed aromatic unit appear at 5.44 ppm, 5.55 ppm and 5.57 ppm,

respectively. The protons of the TMB units are represented as one singlet at 6.22 ppm that integrates to four protons suggesting that all four of them are magnetically equivalent. The methyl groups are represented by two different peaks one, at 3.81 ppm that integrates to twelve protons and another at 3.78 ppm that integrates to six protons. These two peaks differentiate the magnetically inequivalent methoxy groups on each TMB unit.

The methylene protons are represented by an AB pattern which suggests structural asymmetry of the methylene hydrogen atoms. The hydrogen atoms on each methylene unit must always be in different chemical environments from each other due to the chiral nature of the facially chromium substituted aromatic ring.

A ^{13}C NMR spectrum was also taken which, reinforced the structure suggested by the ^{1}H NMR spectrum. It can be seen that there exist twelve magnetically distinct carbon atoms in the structure which, on a two dimensional spectrum (HMQC) correspond to the protons in the ^{1}H NMR spectrum. Unfortunately, recrystallization attempts failed to yield a crystal suitable for x-ray crystallography. The solid compound **93** is stable if stored in the dark.

The next step was to carry out the original reaction intended which was 1 eq. of the complexed diol **91** with 1 equivalent of TMB **92**.

Several attempts were made in which different temperatures and equivalents of the reactants were used. The amount of Lewis acid used was changed from 2 equivalents in some experimentes to 4 and 10 equivalents in other reactions. In the same way, the temperatures were varied from –30°C, at which no reaction occurs, up to room temperature. The best conditions were found to be four equivalents of BF_3 and 0°C for

difficult to purify. The TLC showed several spots very close to each other and, when performing column chromatography, the product tends to decomplex and what was obtained could not be identified.

From the results, it is possible that many conformers of the molecule or macrocycles of different sizes are present.

Purification was attempted using column chromatography and preparatory TLC. The TLC plate in 100% ether showed eight different bands. An NMR of the fourth band was taken but the spectrum was still difficult to understand. NMR spectra was attempted at different temperatures (30°C, 100°C and 150°C) but the compound decomposes at high temperatures and the spectra are useless (Figure 39).

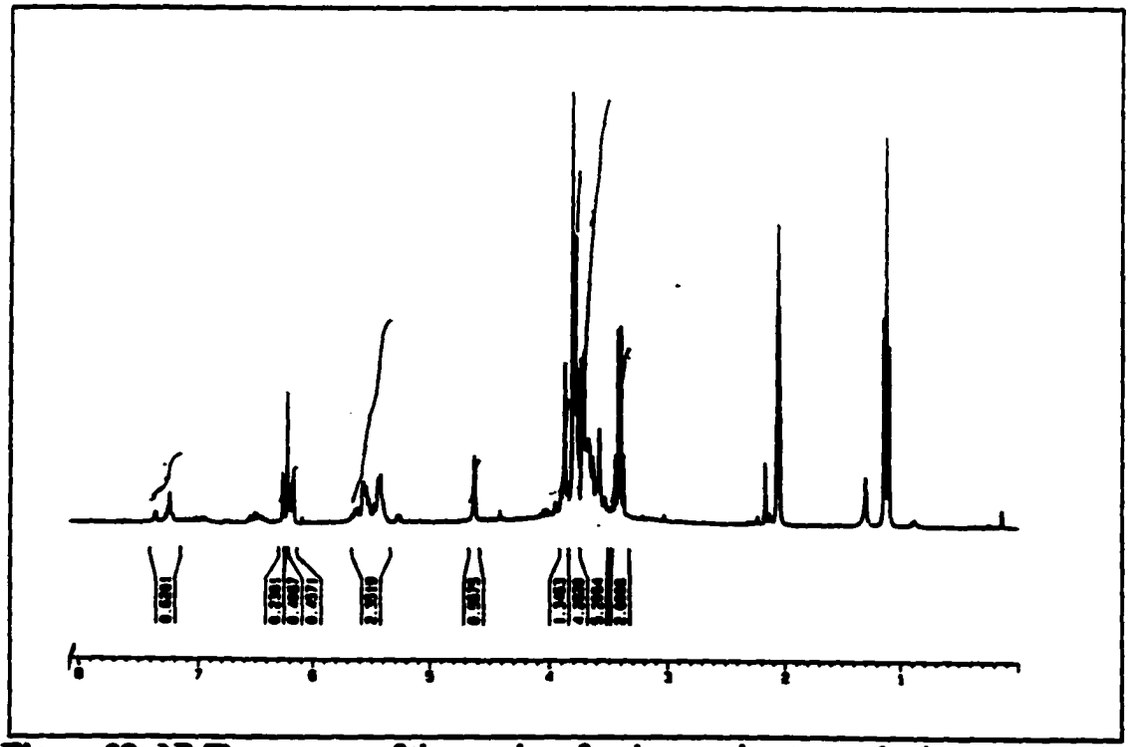
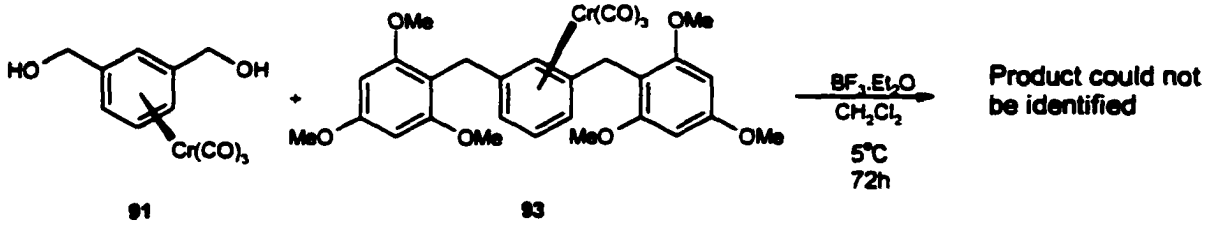


Figure 39: NMR spectrum of the product for the reaction to synthesize macrocycle.

The product was also subjected to light and air in an attempt to decomplex the arene fragments, the intention being to possibly diminish the number of conformers due

to free rotation of the arene units that would be created and therefore simplify the NMR spectrum. This decomplexation, however, met with no success because the solid recovered could not be identified. The reaction was also tried using compound **93** to react with **91** but the results were similar to the previous reactions (Scheme 19).



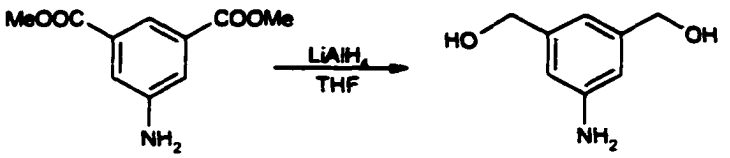
Scheme 19: Reaction of Chromium diol **(91)** with **93**.

Thin Layer Chromatography of the product showed at least six products. Attempts to separate by column chromatography met with no success and the products were not identified.

Synthesis of η^6-(m-xylene-5-amino-α,α'-diol)tricarbonyl chromium (96)

A different approach was taken which was to use a molecule like m-xylene-5-amino-α,α'-diol **(95)** to react with 1,3,5-trimethoxybenzene **(92)**. The change in electrophile may be important in this reaction. As in calixarene synthesis, reagents with electron donating groups or electron withdrawing groups can influence the success or failure of the reaction. The intention was to see if the number of conformers was reduced. We expected a simpler NMR spectrum and hoped the products would be easily separated.

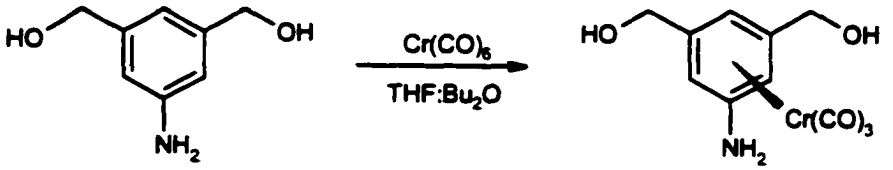
Dimethyl-5-aminoisophthalate was reduced with $LiAlH_4$ to the diol using THF as the solvent. The reaction afforded the product in 79% yield (Scheme 20).



94 95

Scheme 20: Synthesis of *m*-xylene-5-amino-α,α'-diol (**95**).

Compound **95** was then refluxed with hexacarbonylchromium using a mixture of 1:10 THF:Bu_2O as the solvent. The tricarbonyl chromium complex was obtained in a moderate 62.5% yield (Scheme 21).



95 96

Scheme 21: Synthesis of η^6-(*m*-xylene-5-amino-α,α'-diol)tricarbonylchromium.

The NMR data corresponded to the structure expected (Figure 40).

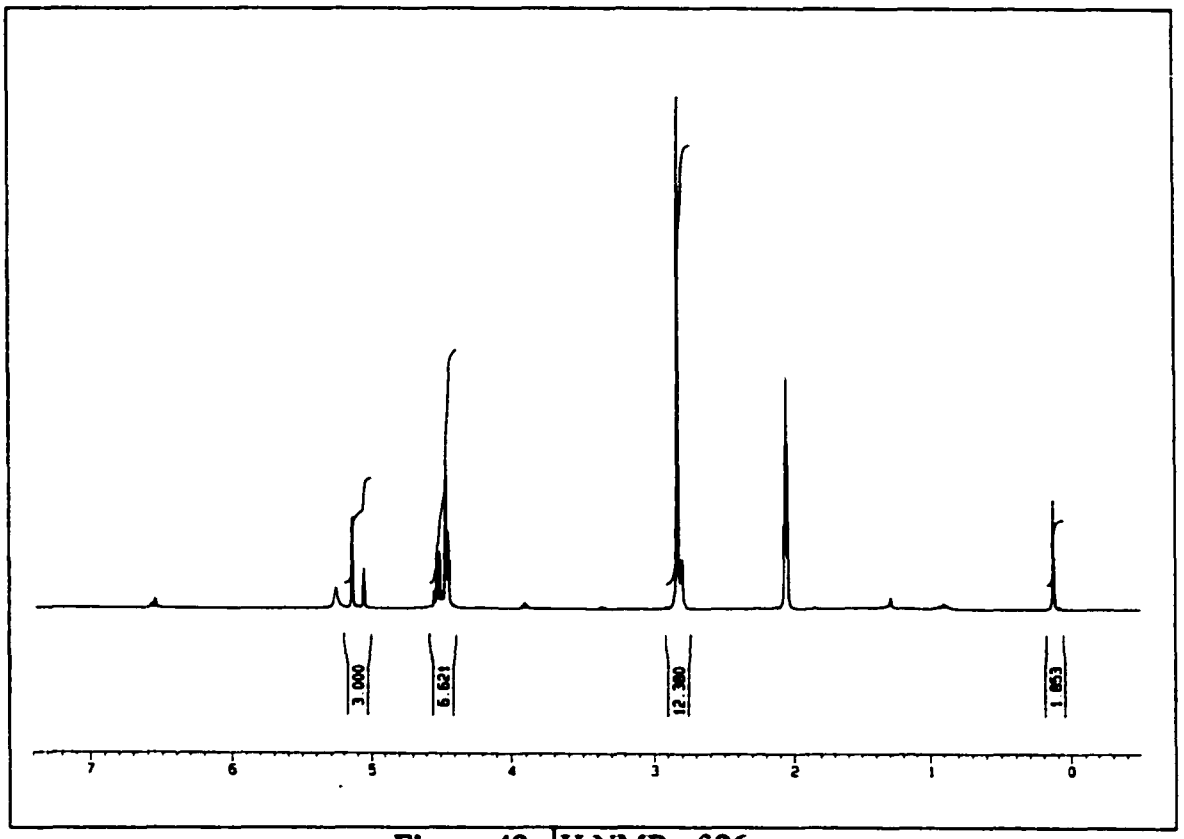


Figure 40: ^{1}H NMR of **96**.

While preparing the reactants for the following reaction, it was found that **96** does not dissolve in dichloromethane, even after heating the solvent. Therefore, no reaction occurs. Toluene was also tried as a solvent but the results were the same as with dichloromethane. In fact, the only solvent that was found that could solubilize the chromium complex was acetone. With hesitation, knowing that acetone can interfere with the reaction due to the available lone pair of electrons, another reaction was tried using acetone as the solvent. As expected, and judging by the NMR results, a combination of products were produced, but no traces of a macrocycle were found. Unsuccesful attempts were made to find a suitable solvent for the reaction. Compound **96** does not dissolve in

solvents like THF, CH_2Cl_2, toluene, DMF or DMSO. Therefore, reactions with this compound were no longer tried.

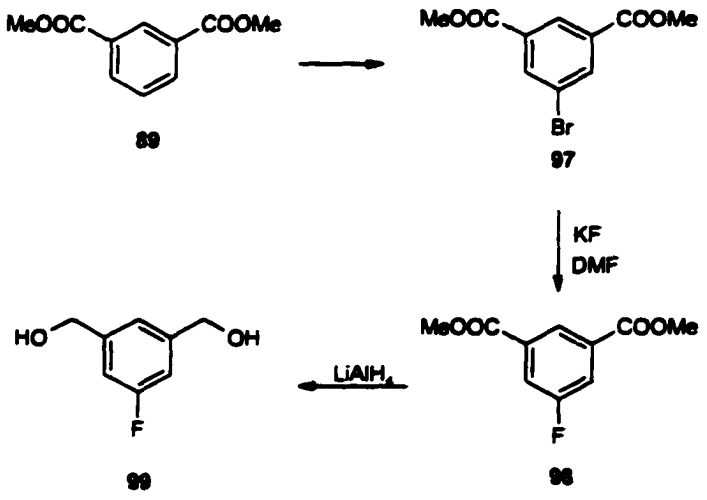
2.3 Conclusion:

Although this project did not achieve the goal of synthesizing the target molecule, a few conclusions can be made. X-ray of the crystal of butanol footed dodecol (**74**) confirmed that the resorcinarene has a cone conformation. Also, the Br group on bromododecol molecule (**81**) is essential for the synthesis of the silicone bridged cavitand. Finally we can conclude that the reactions for the functionalization of the pendant groups of molecule **82**, when using DMF as a solvent, result in decomposition of the resorcinarene.

2.4 Future work:

To continue this project, the reaction for the formation of the cyclophane can be tried using reactants that have substituents different from the amino group in the fifth position of the *m*-xylene α,α'-diol. This could solve the solubility problems of the compound and allow the reaction to proceed.

One of the possibilities considered is to incorporate a halogen group on compound **90**. This can be done by first, bromination of the diester, followed by a flourination with potassium fluoride; after which, the ester groups can be reduced to alcohols (Scheme 22).



Scheme 22: Synthesis of **99**.

The fluoride in the final product can be used to form hydrogen bonds with specific guests in the cyclophane. Compound **97** can also be used to convert the Br group to other functionalities for the synthesis of different macrocycles.

In the case of the reaction to functionalize the alcohols of the resorcinarene, it is recommended to try the reaction using acetonitrile as the solvent.

3. EXPERIMENTAL

3.1. General Procedures

Nuclear magnetic resonance spectra were run on a Bruker Avance 500 Spectrometer at 500 MHz for ^{1}H and 125 MHz for ^{13}C or a Bruker Avance 300 Spectrometer at 300 MHz for ^{1}H and 75 MHz for ^{13}C. IR spectra were done on a Bruker vector 22. The samples were dissolved in dichloromethane and spread onto NaCl plates. KBr pellets were prepared from solid samples not soluble in dichloromethane. Mass spectra were recorded using Kratos Concept IH spectrometer in positive LSIMS mode and using mNBA as matrix. Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected.

Diethyl ether and tetrahydrofuran (THF) were distilled from potassium benzophenone-ketyl immediately prior to use. Butyl ether was distilled from calcium hydride and acetone was refluxed with $KMnO_4$ and then distilled from $CaCl_2$ before use.

Column chromatography was performed using Silicycle 230-400 mesh silica gel and thick layer chromatography was done using Analtech silica gel GF* 1000 micron plates. Analytical thin layer chromatography was performed using Merck precoated silica gel 60 F_{254} aluminium sheets.

Procedures in which "reduced pressure" was used, refer to distillation at 14 mmHg.

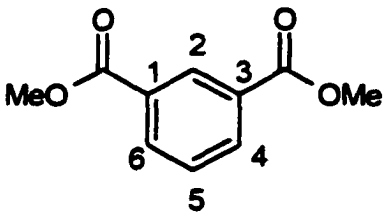
All reactions were performed under nitrogen atmosphere, unless otherwise noted. "Conventional work up" refers to extraction of the organic product from the aqueous phase with diethyl ether or dichloromethane; washing the organic phase with saturated solution of sodium bicarbonate, a solution of 2N hydrochloric acid and distilled water; and then drying the organic extract over anhydrous magnesium sulfate followed by filtration and evaporation of the solvent under reduced pressure to afford the crude products.

3.1.1. General procedure for the functionalization of the resorcinarene

Resorcinarene was dissolved in DMF under nitrogen atmosphere and tha base was added to the solution. When using NaH as the base, it was washed 3 times with dry pentane or dry pet ether and the calixarene solution was added to it. The reaction was stirred at the selected temperature for 1h. The electrophile was then predissolved and added to the reaction over 30min. using a pressure equalizing dropping funnel.

After stirring for 18h, the solvent was evaporated under reduced pressure and conventional work up was performed.

3.1.2. Dimethyl isophthalate (89)



Isophthalic acid (19.17 g, 0.115 mol), HCl (18 mL), and methanol (266.0 mL) were heated to reflux in a 500 mL round bottom flask under nitrogen atmosphere for 18 h. Methanol was evaporated under reduced pressure and the white solid obtained was dissolved in dichloromethane to perform a conventional work up which yielded a white solid product (18.65 g, 0.096 mol, 83%).

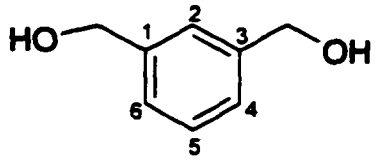
m.p.: 68-71°C

IR (cm^{-1}): (NaCl) 3007 (m); 2961 (m), 1719 (vs), 1285(s), 1309(s).

^1H NMR ($CDCl_3$): 3.94 (s, 6H, $ArCO_2C\underline{H}_3$); 7.52 (t, 1H, 7.74 Hz, $Ar\underline{H}^5$);

8.23 (dd, 2H, 3.57 Hz, 1.71 Hz, $Ar\underline{H}^4$ and $\underline{H}^6$); 8.68 (s, 1H, $Ar\underline{H}^2$)

3.1.3. m-Xylene-α,α'-diol (90)



Lithium aluminium hydride (5.6 g, 0.147 mol) was placed in a 1.0 L 3-neck round bottom flask under nitrogen atmosphere and tetrahydrofuran (150 mL) was added via syringe.

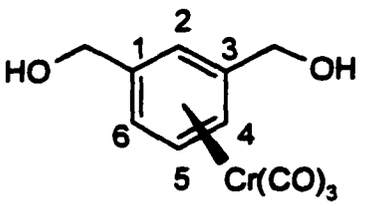
Compound **90** was dissolved in additional tetrahydrofuran (170 mL) under nitrogen and added to lithium aluminium hydride suspension over one hour using an pressure equalizing dropping funnel. The reaction mixture was heated to reflux for 18 h and quenched with methanol to obtain a precipitate, which was vacuum filtered. The supernatant was evaporated under reduced pressure, leaving a yellowish white solid (7.69 g, 0.056 mol, 98%)

m.p.: 56-60°C

IR cm^{-1}: 3260(br), 2855(m), 1430(s), 1165(m), 1010(m).

^1H NMR (D_2O): 4.50(s, 4H, $ArC\underline{H}_2OH$); 4.70 (s, 2H, $ArCH_2O\underline{H}$); 7.21 (t, 1H, J= 6.0 Hz, $Ar\underline{H}^5$); 7.28 (dd, 2H, J= 1.5 Hz, J= 6.0 Hz, $Ar\underline{H}^4$ and $Ar\underline{H}^6$); 7.32 (s, 1H, $Ar\underline{H}^2$).

3.1.4. η^6-(m-xylene-α,α'-diol)tricarbonylchromium (91)



A mixture of **90** (4.8 g, 0.025 mol) and hexacarbonyl chromium (13 g, 0.025 mol) in dibutyl ether / THF (66 mL, 10 : 1) was stirred at reflux under nitrogen for 72 hours. After filtration through Celite® the solvent was evaporated under reduced pressure, yielding a yellow solid, which was recrystallized from toluene/heptane (3.64 g, 0.013 mol, 54%).

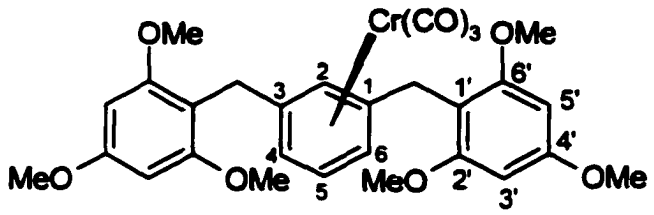
m.p.: 112-114°C

IR(cm^{-1}) (NaCl) : 3283 (br), 2924 (m), 1945(vs), 1869(vs).

^1H NMR (Acetone-d_6): 3.68 (s, 2H, D_2O exchange O<u>H</u>); 4.38 (s,4H, ArC<u>H_2</u>OH); 5.51 (dd, 2H, J= 3.0 Hz, J= 6.0 Hz, Ar<u>H</u>^{4} and <u>H</u>^{6}); 5.64 (s, 1H, Ar<u>H</u>^{2}); 5.70 (t, 1H, J= 6.0 Hz, Ar<u>H</u>^{5}).

^{13}C NMR (Acetone-d_6): 62.70(Ar<u>C</u>H_2OH); 91.13(Ar<u>C</u>^{4}); 94.96(Ar<u>C</u>^{5}); 114.34(Ar<u>C</u>^{3}); 124.99(Ar<u>C</u>^{2}); 234.11(Cr(<u>C</u>O)$_3$).

3.1.5. η^6-[1,3-bis-(2'4'6'-trimethoxybenzyl) benzene]tricarbonyl chromium (93)



A mixture of **91** (1.0 g, 3.65 mmol) and trimethoxybenzene (2.4 g, 14.27 mmol) was dissolved in dichloromethane (50 mL) in a 250 mL round bottom flask under nitrogen atmosphere at 0°C. Freshly distilled $BF_3 \cdot Et_2O$ (2.2g, 15.8 mmol) dissolved in dichloromethane (5 mL) was added over 2 h. The reaction was kept at 0°C for 24 h, and then was quenched with saturated aqueous sodium bicarbonate. A conventional work up and flash chromatography (1:2 petroleum ether / diethyl ether,) afforded **93** (0.93 g 45%) which can be recrystallized from 1 : 2 petroleum ether / diethyl ether).

m. p.: 147-148°C

IR (cm^{-1}) (NaCl): 3002 (m), 2941 (m), 1953 (vs), 1865 (vs).

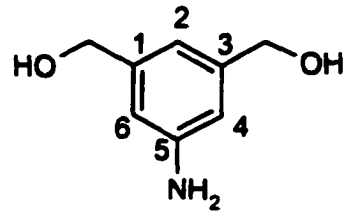
^1H NMR (Acetone-d_6):3.60 (AB, 4H, JAB= 10 Hz, Ar'C$\underline{H}_2$Ar); 3.78 (s, 6H,Ar'OC$\underline{H}_3$); 3.81 (s, 12H, Ar'OC$\underline{H}_3$); 5.44 (dd, 2H, 5.12 Hz, 1.15 Hz, Ar$\underline{H}^4$ and Ar$\underline{H}^6$); 5.55 (t, 1H, 6.46 Hz, Ar$\underline{H}^5$); 5.57 (s, 1H, Ar$\underline{H}^2$); 6.22 (s,4H, Ar'$\underline{H}^3$ and Ar'$\underline{H}^5$)

^{13}C NMR (Acetone-d_6): 58.71($C^{6'}O\underline{C}H_3$ and $C^{2'}O\underline{C}H_3$); 59.17($C^{4'}O\underline{C}H_3$); 94.63(Ar'C3 and Ar'C^5); 96.82(ArC^4 and C^6); 98.93(ArC^5); 100,05(ArC^2);

112.12(ArC^1 and ArC^3); 118.66(Ar'C^1); 162.67(Ar'C^2 and Ar'C^6); 164.62(Ar'C^4); 168.50(-$\underline{C}H_2$-).

M.S. (NBA): *m/z* Found: 574.1300 (M^+), calculated: 574.543 for 7.19 ppm error. 490.1 (M^+-3CO), 438.2 (M^+ -$Cr(CO)_3$), 407.0 (M^+ - $Cr(CO)_3$ – OMe) 375.1 (M^+ - $Cr(CO)_3$ – 2(OMe))

3.1.6. 5-amino-1,3-hydroxymethylbenzene (95)



Lithium aluminium hydride (1.75 g, 46 mmol, 4 equiv.) was placed in a 250 mL 3-neck round bottom flask under nitrogen atmosphere and diethyl ether (75 mL) was added via syringe. Dimethyl-5-aminoisophthalate (2.5 g, 12 mmol, 1equiv.) was dissolved in 125 mL of diethyl ether and added over 1 h by dropping funnel. The reaction was heated up to reflux for 18 h. Methanol was added to quench the reaction, the solid formed was filtered, the aqueous phase was separated and the solvent evaporated under reduced pressure to afford yellowish white solid (1.46 g, 9.5 mmol, 79%).

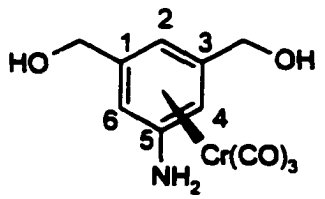
m.p.: 148°C dec.

IR (cm^{-1}): 3359(br), 1059(s), 1609(m), 1559(m)

^{1}H NMR (Acetone-d_6): 3.86 (t, 2H, 5.86 Hz $ArCH_2O\underline{H}$, D_2O exchange); 4.47 (s, br, D_2O exchange 2H, $ArN\underline{H}_2$); 4.47 (d, 4H, J= 5.94 Hz, $ArC\underline{H}_2OH$); 6.54 (s, 2H, $Ar\underline{H}^3$); 6.57(s, 1H, $Ar\underline{H}^1$)

^{13}C NMR (Acetone-d_6): 64 ($ArC\underline{H}_2OH$); 112 (ArC^4); 114 (ArC^2); 143 (ArC^3); 149 (ArC^5)

3.1.7. η^6- (5-amino-1,3-hydroxymethylbenzene) tricarbonylchromium (96)



A mixture of **95** (1.0 g, 6.53 mmol, 1 equiv.), and hexacarbonyl chromium (2.85 g, 12.95 mmol, 2 equiv.) in 77 mL of tetrahydrofuran : *n*-butyl ether (1 : 10) was stirred and heated to reflux under a nitrogen atmosphere for 72h. Diethyl ether (50 mL), was added and the reaction mixture was filtered through Celite®, evaporated under reduced pressure to yield a yellow solid (1.18 g, 4.08 mmol, 62.5%).

m.p.: 148°C dec.

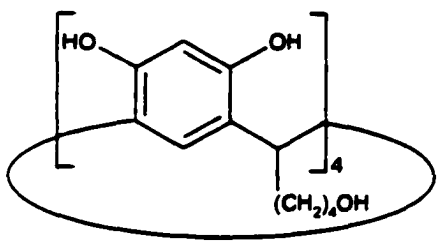
IR (cm^{-1}): 3453(br), 1066(s), 1555(m), 1647(m)

^{1}H NMR (Acetone-d_6): 4.46 (~d, 4H, 4.9 Hz, $ArC\underline{H}_2OH$); 4.54 (~t, 2H, 6.0 Hz, $ArCH_2O\underline{H}$, D_2O exchange); 5.06 (s, 1H, $Ar\underline{H}^4$); 5.14 (d, 2H, 0.9 Hz, $Ar\underline{H}^2$); 5.26 (br, s, 2H, $ArN\underline{H}_2$, D_2O exchange).

^{13}C NMR (Acetone-d_6): 64 ($ArCH_2OH$); 77 (ArC^2); 83 (ArC^4); 117 (ArC^3); 136 (ArC^5); 235 ($Cr(CO)_3$).

M.S. (NBA): Found: 289.0053(M^+), calculated: 289.2059 for 6.9 ppm error. 260.0 (M^+ - CO), 232.9 (M^+ - 2CO), 204.9 (M^+ -3CO)

3.1.8. 2,8,14,20-Tetrakis (4-hydroxybutyl) pentacyclo [19.3.1.1^{3,7}.1^{15,19}]octacosa-1(25),3,5,7,(28),9,11,13-(27),15,17,19(26),21,23-dodecaene-4,6-10,12,16,18,22,24-octol. (Butanol footed dodecol) (74)



Resorcinol (8.0 g, 72.6 mmol, 1 equiv.) was dissolved in 4 :1 methanol / 37% HCl (60 mL) under nitrogen atmosphere, and dihydropyran (6.01 mL, 67 mmol 0.9 equiv.) was added over 4.5 h. The reaction mixture was heated at 40°C for 4 days and was then precipitated with water. The solvent evaporated under reduced pressure. The solid left was triturated with acetone and a white yellowish powder was obtained as the product (7.21g, 0.037 mol, 55%).[79] Crystals were obtained from methanol/hexane. The product was recrystalized from methanol by allowing hexane to diffuse into the solution. The crystals obtained were washed with hexane.

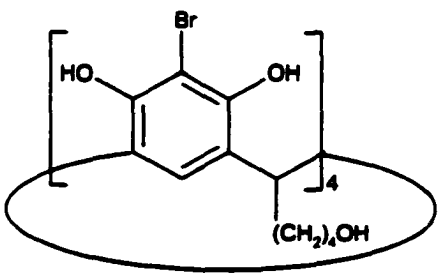
m.p.:250°C dec.

IR.(cm^{-1}) (NaCl): 3386 (br), 2928(s), 2861(s), 1616(s), 1503(s)

^1H NMR (Methanol-d_4): 1.3-1.4 (quartet, 8H, J= 7.14 Hz, ArCHC$\underline{H}_2$CH$_2$CH$_2$CH$_2$OH); 1.5-1.7 (quintet, 8H, J= 7.47 Hz, ArCHCH$_2$C$\underline{H}_2$CH$_2$CH$_2$OH); 2.1-2.3 (quintet, 8H, 7.24 Hz, ArCHCH$_2$CH$_2$C$\underline{H}_2$CH$_2$OH); 3.56 (t, 8H, 6.58 Hz, (m, 8H, ArCHCH$_2$CH$_2$CH$_2$C$\underline{H}_2$OH); 4.30 (t, 4H, J= 7.68 Hz, ArC$\underline{H}$CH$_2$CH$_2$CH$_2$CH$_2$OH); 4.87 (s, 12H, ~CH$_2$CH$_2$CH2O$\underline{H}$ and ArO$\underline{H}$, D_2O exchange); 6.21 (s, 4H, Ar$\underline{H}^1$); 7.25 (s, 4H, Ar$\underline{H}^4$).

M.S. (NBA): 777(M^+)

3.1.9. Bromododecol (81)



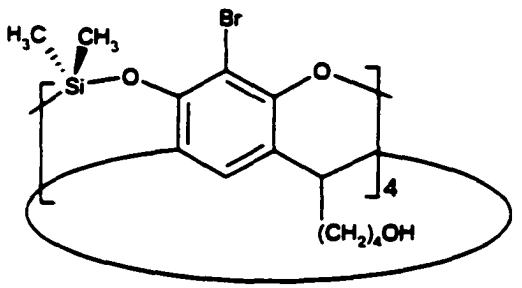
Butanol footed dodecol (2.78 g, 3.58 mmol) was added to 53 mL of 30% methanol in butanone under nitrogen atmosphere. N-Bromosuccinimide (NBS) (2.86 g, 40 mmol) was added and the reaction mixture was stirred at r.t. in the dark for 5 h. Additional NBS (1.28 g, 17.85 mmol) was added and let stir for 18h. The solid was filtered and washed with cold butanone to afford 2.97 g (2.72 mmol, 76%) of the product.[79]

m.p.:243°C dec.

IR (cm^{-1}): 3386(br), 2932(s), 2860(s), 1614(s), 1472(s).

^1H NMR (DMSO): 1.20 (m, 8H, $ArCHC\underline{H}_2$); 1.47 (m, 8H, $CHCH_2C\underline{H}_2$); 2.20 (m, 8H, $CH_2C\underline{H}_2CH_2OH$); 3.29 (s, 8H, $ArO\underline{H}$ D_2O exchange); 3.35 (t, 8H, 6.61 Hz, $CH_2C\underline{H}_2OH$); 4.32 (t, 4H, $ArC\underline{H}CH_2$); 7.41 (s, 4H, $Ar\underline{H}^4$); 9.14(s,4H, $-CH_2CH_2CH_2O\underline{H}$ D_2O exchange).

3.1.10. Silicon bridged cavitand (82)



Compound 81 (2.97 g, 2.71 mmol) was dissolved in pyridine (50 mL) under nitrogen atmosphere followed by dimethyldichlorosilane (2.75 mL, 22.6 mmol). The reaction mixture was allowed to stir for 2 h at r.t. after which the solvent was removed under reduced pressure. The solid was susoended in methanol, and the solvent was evaporated to help remove pyridine. The solid was triturated with MeOH, filtered and dried in vacuo. (2.85 g, 2.16 mmol, 80%)[79]

m.p.:280°C dec.

IR (cm^{-1}):342(br), 3060(m), 2934(s)

^1H NMR (DMSO): -0.63(s, 12H, $OSiC\underline{H}_3$); 0.54(s, 12H, $OSiC\underline{H}_3$); 1.20 m, 8H, $ArCHC\underline{H}_2CH_2CH_2CH_2OH$); 1.48 (m, 8H, $ArCHCH_2C\underline{H}_2CH_2CH_2OH$); 2.34 (m, 8H, $ArCHCH_2CH_2C\underline{H}_2CH_2OH$); 3.34 (t, 8H, 6.53 Hz, $ArCHCH_2CH_2CH_2C\underline{H}_2OH$); 3.5-3.9 (br,4H, $\sim CH_2CH_2CH_2O\underline{H}$ D_2O exchange); 4.48 (t, 4H, 7.98 Hz, $ArC\underline{H}CH_2CH_2CH_2CH_2OH$); 7.74 (s, 4H, $Ar\underline{H}^4$).

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APPENDIX

Table 1. Crystal data and structure refinement for pjd-1.

Identification code	pjd-1
Empirical formula	C42 H56 O12
Formula weight	752.98
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	tetragonal, P42/ncm
Unit cell dimensions	a = 18.3628(2) A alpha = 90 deg. b = 18.3628(2) A beta = 90 deg. c = 19.3845(3) A gamma = 90 deg.
Volume	6536.31(14) A^3
Z, Calculated density	6, 1.256 Mg/m^3
Absorption coefficient	0.168 mm^-1
F(000)	2632
Crystal size	0.24 x 0.22 x 0.34 mm
Theta range for data collection	2.10 to 20.00 deg.
Limiting indices	-12<=h<=17, -17<=k<=17, -17<=l<=18
Reflections collected / unique	19341 / 1615 [R(int) = 0.0301]
Completeness to theta = 20.00	99.6 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1615 / 0 / 145
Goodness-of-fit on F^2	1.724
Final R indices [I>2sigma(I)]	R1 = 0.1168, wR2 = 0.3455
R indices (all data)	R1 = 0.1211, wR2 = 0.3525
Largest diff. peak and hole	1.221 and -0.400 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for pjd-1.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	5583(2)	3825(2)	-1863(2)	65(1)
O(2)	5153(2)	3348(2)	2038(2)	57(1)
O(3)	4964(2)	1887(2)	2123(2)	59(1)
C(1)	4464(2)	2513(2)	912(2)	42(2)
C(2)	4462(2)	2543(2)	113(3)	47(2)
C(3)	4961(2)	3150(3)	-146(2)	60(2)
C(4)	4997(2)	3217(3)	-921(2)	57(2)
C(5)	5519(3)	3795(3)	-1140(2)	65(2)
C(6)	3499(2)	3499(2)	999(3)	41(2)
C(7)	4148(2)	3211(2)	1234(2)	39(1)
C(8)	4501(2)	3586(2)	1756(2)	43(1)
C(9)	4226(2)	4226(2)	2000(3)	51(2)
C(10)	3498(2)	1502(2)	925(3)	39(2)
C(11)	4106(2)	1843(2)	1218(2)	40(1)
C(12)	4362(2)	1549(2)	1830(2)	42(1)
C(13)	4051(2)	949(2)	2124(3)	48(2)

Table 3. Bond lengths [A] and angles [deg] for pjd-1.

O(1)-C(5)	1.407(6)
O(2)-C(8)	1.386(5)
O(3)-C(12)	1.390(5)
C(1)-C(11)	1.515(6)
C(1)-C(7)	1.540(6)
C(1)-C(2)	1.551(7)
C(2)-C(3)	1.527(6)
C(3)-C(4)	1.509(7)
C(4)-C(5)	1.493(7)
C(6)-C(7)#1	1.380(5)
C(6)-C(7)	1.380(5)
C(7)-C(8)	1.385(6)
C(8)-C(9)	1.365(5)
C(9)-C(8)#1	1.365(5)
C(10)-C(11)	1.401(5)
C(10)-C(11)#2	1.401(5)
C(11)-C(12)	1.385(6)
C(12)-C(13)	1.365(5)
C(13)-C(12)#2	1.365(5)
C(11)-C(1)-C(7)	110.8(4)
C(11)-C(1)-C(2)	114.8(3)
C(7)-C(1)-C(2)	111.9(3)
C(3)-C(2)-C(1)	110.7(4)
C(4)-C(3)-C(2)	114.3(4)
C(5)-C(4)-C(3)	111.7(4)
O(1)-C(5)-C(4)	111.4(4)
C(7)#1-C(6)-C(7)	123.6(5)
C(6)-C(7)-C(8)	117.0(4)
C(6)-C(7)-C(1)	120.8(4)
C(8)-C(7)-C(1)	122.2(4)
C(9)-C(8)-C(7)	120.6(4)
C(9)-C(8)-O(2)	117.0(4)
C(7)-C(8)-O(2)	122.4(4)
C(8)-C(9)-C(8)#1	121.1(6)
C(11)-C(10)-C(11)#2	123.2(5)
C(12)-C(11)-C(10)	116.3(4)
C(12)-C(11)-C(1)	120.3(4)
C(10)-C(11)-C(1)	123.3(4)
C(13)-C(12)-C(11)	122.1(4)
C(13)-C(12)-O(3)	121.5(4)
C(11)-C(12)-O(3)	116.4(3)
C(12)-C(13)-C(12)#2	120.0(6)

Symmetry transformations used to generate equivalent atoms:
#1 y,x,z #2 -y+1/2,-x+1/2,z #3 -x+1/2,-y+1/2,z
#4 y+1/2,-x+1,-z+1/2 #5 -y+1,x-1/2,-z+1/2
#6 -x+3/2,-y+1/2,z

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for pjd-1.
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
O(1)	79(3)	76(3)	39(2)	4(2)	-7(2)	-39(2)
O(2)	53(2)	55(2)	65(2)	1(2)	-22(2)	-9(2)
O(3)	61(2)	57(2)	60(2)	14(2)	-28(2)	-15(2)
C(1)	39(3)	50(3)	36(3)	1(2)	-1(2)	-3(2)
C(2)	48(3)	49(3)	46(3)	3(2)	2(2)	-2(2)
C(3)	67(3)	67(3)	45(3)	7(2)	10(2)	-8(2)
C(4)	56(3)	65(3)	48(3)	6(2)	2(2)	-8(2)
C(5)	80(4)	70(3)	44(3)	1(2)	8(2)	-22(3)
C(6)	41(2)	41(2)	41(4)	1(2)	1(2)	-8(3)
C(7)	45(3)	39(3)	34(3)	7(2)	1(2)	-7(2)
C(8)	43(3)	44(3)	42(3)	4(2)	-3(2)	-11(2)
C(9)	55(3)	55(3)	44(4)	-3(2)	-3(2)	-25(4)
C(10)	38(2)	38(2)	41(4)	5(2)	-5(2)	2(3)
C(11)	45(3)	37(3)	39(3)	0(2)	0(2)	1(2)
C(12)	42(3)	40(3)	43(3)	3(2)	-6(2)	-2(2)
C(13)	54(3)	54(3)	37(4)	8(2)	-8(2)	-2(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for pjd-1.

	x	y	z	U(eq)
H(1A)	5870	4148	-1970	97
H(2A)	5274	2964	1854	86
H(3A)	5078	1674	2479	88
H(1B)	4977	2494	1052	50
H(2B)	4626	2080	-71	57
H(2C)	3970	2628	-50	57
H(3B)	4793	3610	44	72
H(3C)	5448	3065	29	72
H(4A)	5146	2754	-1116	68
H(4B)	4516	3331	-1098	68
H(5A)	5354	4263	-969	78
H(5B)	5993	3697	-940	78
H(6A)	3242	3242	666	49
H(9A)	4480	4480	2339	62
H(10A)	3311	1689	516	47
H(13A)	4247	753	2525	58

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