

**FACTORS INFLUENCING THE STEREOCHEMISTRY IN
BIS-BRIDGING REACTIONS OF CALIX[6]ARENES**

THESIS

Presented to the Graduate Council of
Southwest Texas State University
in Partial Fulfillment of
the Requirements

For the Degree

Master of SCIENCE

By

Kenneth Albert Pavlat, B. S.

San Marcos, Texas
August, 2003

ACKNOWLEDGEMENTS

I would like to thank my parents for their constant love and support. From you, I learned how to work hard, be persistent and always strive for better goals. I know that I can never say thank you enough for all that you have given me and all the self-less acts you did for me. I am thankful for the best little brother ever. I don't know if I could laugh as hard as I do without you around. You were the one to have a wise-crack at the appropriate time and it always seemed to make me laugh for days, thanks.

I really need to thank my thesis adviser, Dr. Michael T. Blanda. Your second semester organic lecture really got me enthused about chemistry and giving me a chance to work in your lab is something that I will always be indebted for. I learned so much from you that words cannot describe. I wish you and your family all the best in your future endeavors.

I would also like to thank my committee members for there time and insight into this project. Sitting down eating lunch with you, Dr. Beall, was always a blast, and I will cherish every conversation we had. Dr. Watkins, your metabolism class was very informative and I still think it was one of the best classes I ever took.

This manuscript was submitted on July 17, 2003.

Table of Contents

LIST OF TABLES.....	vi
LIST OF FIGURES.....	vii
ABSTRACT.....	ix
1. 0 INTRODUCTION.....	1
1. 1 Calixarenes.....	1
1. 2 Calix[6]arene.....	2
1. 2. 1 Lettering and Numbering Scheme for Calix[6]arenes.....	2
1. 2. 2 Conformational Mobility.....	3
1. 2. 3 Conformational Analysis.....	4
1. 2. 4 Selective Functionalization.....	5
1. 2. 5 Bridging.....	8
1. 3 Thesis Proposal.....	14
2. 0 SYNTHETIC STRATEGIEY.....	16
2. 1 Synthesis of 5, 11, 17, 23, 29, 35-hexa- <i>p-tert</i> -butyl- 37, 38, 39, 40, 41, 42-hexahydroxy calix[6]arene (1).....	16
2. 2 Synthesis of 37, 38, 39, 40, 41, 42-hexahydroxy calix[6]arene (2).....	17
2. 3 Synthesis of 37, 40-diallyloxy-38, 39, 41, 42-tetrahydroxy calix[6]arene (3).....	17
2. 4 Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-bis- <i>m</i> -xylenyloxy calix[6]arene (4 and 5).....	18
2. 5 Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-biscrown[4]ether calix[6]arene (6 and 7).....	19
3. 0 RESULTS AND DISCUSSION.....	20
3. 1 <i>m</i> -Xylenyl Bis-Bridged Calix[6]arenes.....	20

3. 2 Triethyleneglycol Bis-Bridged Calix[6]arenes.....	23
3. 3 General Observations of Both Bis-Bridging Reactions.....	26
4. 0 EXPERIMENTAL.....	27
4. 1 Synthesis of 5, 11, 17, 23, 29, 35-hexa- <i>p-tert</i> -butyl -37, 38, 39, 40, 41, 42-hexahydroxy calix[6]arene (1).....	27
4. 2 Synthesis of 37, 38, 39, 40, 41, 42-hexahydroxy calix[6]arene (2).....	27
4. 3 Synthesis of 37, 40-diallyloxy-38, 39, 41, 42-tetrahydroxy calix[6]arene (3).....	27
4. 4 Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-bis- <i>m</i> -xylenyloxy calix[6]arene (4 and 5).....	27
4. 5 Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-biscrown[4]ether calix[6]arene (6 and 7).....	29
5. 0 CONCLUSIONS.....	32
References.....	33

List of Tables

Table 3. 1 Stereoselective Synthesis of 37, 40-diallyloxy- (38, 41)-(39, 42)-bis- <i>m</i> -xylenyloxy calix[6]arene.....	21
Table 3. 2 Stereoselective Synthesis of 37, 40-diallyloxy- (38, 41)-(39, 42)-biscrown[4]ether calix[6]arene.....	25

List of Figures

Figure 1. 1 Synthesis of Calix[n]arene.....	1
Figure 1. 2 Defining Upper and Lower Rims of Para-tert-butyl Calix[6]arene.....	2
Figure 1. 3 The Lettering and Numbering Scheme for a Generic Calix[6]arene.....	3
Figure 1. 4 Representations of Cone, 1,4-Alternate and 1,2,3-Alternate Calix[6]arenes.....	4
Figure 1. 5 Orientations of Aryl Rings in the Macrocyclic Skeleton.....	5
Figure 1. 6 Tetra-pyridylmethyl Substituted Calix[6]arene.....	6
Figure 1. 7 Different Substitution Patterns for Tri-Methylated Calix[6]arenes.....	7
Figure 1. 8 Synthesis of 37, 40-diallyloxy-38, 39, 41, 42-tetrahydroxy calix[6]arene.....	7
Figure 1. 9 Regioselective Bridging of the A/B Rings.....	9
Figure 1. 10 First Known Regioselective A/C Bridged Calix[6]arene.....	9
Figure 1. 11 Varying Bridging Units for A/D Bridged Calix[6]arene.....	10
Figure 1. 12 A Triply-Bridged Calix[6]arene.....	11
Figure 1. 13 A = Three Leg Capped Calix[6]arene B = Four Leg Capped Calix[6]arene.....	11
Figure 1. 14 Upper Rim Bridging of Calix[6]arene.....	12
Figure 1. 15 Selective Functionalization Leading to Bis-Bridged Calix[6]arene.....	12
Figure 1. 16 All Possible Conformations of Bis-Bridged Calix[6]arenes.....	14
Figure 2. 1 Synthesis of Compound 1.....	16
Figure 2. 2 Synthesis of Compound 2.....	17

Figure 2. 3 Synthesis of Compound 3	18
Figure 2. 4 Synthesis of Compounds 4 and 5	18
Figure 2. 5 Synthesis of Compounds 6 and 7 using NaH as the Base.....	19

FACTORS INFLUENCING THE STEREOCHEMISTRY IN BIS-BRIDGING REACTIONS OF CALIX[6]ARENES

Abstract

Calix[6]arenes are larger than their calix[4]arene counterparts thus are subject to greater conformational mobility⁷. The flexibility must be restricted in order to create well-defined preorganized binding sites for supramolecular applications. Strategies that have been utilized involve mono-bridging across the macrocyclic annulus with difunctional electrophiles and capping with multi-functional electrophiles^{11,35}. Our methodology utilized a conformationally mobile A, D-difunctionalized calix[6]arene as the starting material in which the four remaining rings were predisposed for transannular bridging with difunctional electrophiles³⁹. In our studies we employed a rigid aromatic bridging unit (*m*-xylylenyl) containing five atoms in the tether and a flexible aliphatic bridging unit (triethyleneoxy) containing 8 atoms in the tether.

While there was the possibility of forming 18 stereoisomers, previous studies in our group have shown that only two distinct stereoisomeric bis-bridged calix[6]arenes were formed. The cone isomer is distinguished by a syn orientation of the bridging units with respect to the macrocyclic annulus while the 1,2,3-alternate conformer is characterized by anti-oriented bridging units. The two isomers are readily distinguished by both ¹H and ¹³C NMR spectroscopy.

The current study was undertaken to investigate reaction parameters which affect the stereochemical course of the bridging reactions. Towards that end, a systematic approach was taken wherein the base and solvent were changed to ascertain the effects on

the product distribution. Five solvents with different polarities were chosen (benzene, acetone, acetonitrile, N,N-dimethylformamide and tetrahydrofuran) while three types of bases were investigated (metal hydrides, carbonates and t-butoxides) with different metal ions.

The *m*-xylylenyl bis-bridged calix[6]arenes were affected more by the changing reaction conditions. The potassium cation from the carbonate base provided for 75% of the reaction being 1, 2, 3-alternate in THF, to a maximum of 91% in acetonitrile. By using cesium, the cation provided the cone conformation for at least 85% of the reaction in acetone, to a maximum of 96% in acetonitrile. Triethyleneoxy bis-bridged calix[6]arenes were less selective based on changing reaction conditions as evidenced by the best stereoselectivity for 1, 2, 3-alternate was 61% when cesium carbonate was used in THF. Some of the few exceptions to this are NaH synthesizing only cone in acetone, and potassium tert-butoxide in THF yielding 85% cone. Although characterization is incomplete, two new bridged isomers were synthesized in DMF.

1. 0 INTRODUCTION

1. 1 Calixarenes

The term calixarene (calix = chalice or vase) was coined by Dr. David Gutsche in 1966 to describe cyclooligomers formed via phenol-formaldehyde reactions¹. Each calixarene is a macrocycle containing a repeating phenolic moiety with methylene carbons at both ortho positions used as spacing units, where $n = \#$ of phenolic moieties. Calix[n]arenes have been known to have between 3 and 20 units, although the majority with analytical activity have been tetramers ($n = 4$) and to a lesser extent hexamers ($n = 6$) and octamers ($n = 8$)¹. The varying size of calix[n]arenes is due to the templating effect of the metal ion in the hydroxide base used during synthesis. Larger alkali metal hydroxides tend to produce larger calix[n]arenes; such that NaOH yields calix[4]arene, RbOH yields calix[6]arene and CsOH yields calix[8]arene.

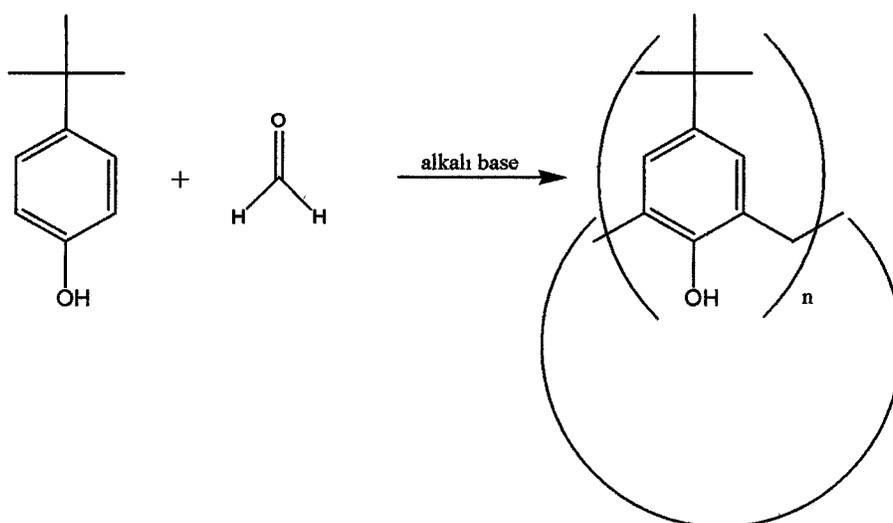


Figure 1. 1 *Synthesis of Calix[n]arene.*

Calix[n]arenes have two well-defined rims, an upper rim defined by the *para* substituents of the phenolic rings and a lower rim defined by the phenolic hydroxy groups². The methylene units function as points around which the phenolic groups rotate in space.

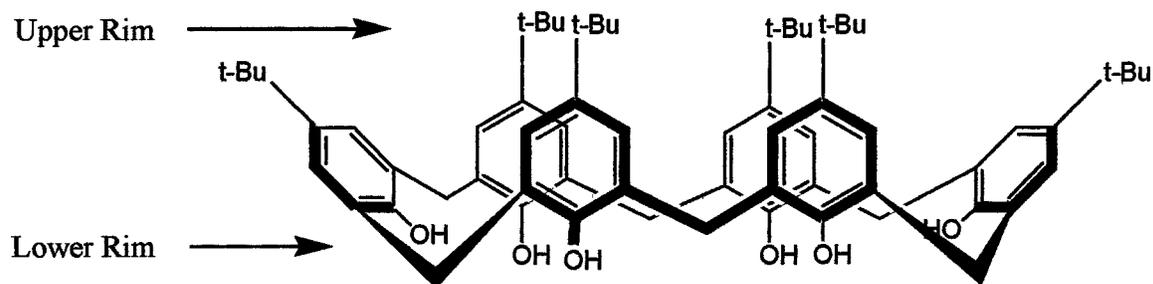


Figure 1. 2 *Defining Upper and Lower Rims of Para-tert-butyl Calix[6]arene.*

By bridging across the annulus of the calixarene, the resulting molecule would have less flexibility and would assume a more fixed or locked structural arrangement. Calix[n]arenes can have a cavity-shaped architecture which is useful as a building block for biomimetic binding, and catalysts through appropriate modification of the rims³. This host-guest model is similar to the “lock and key” model used to describe how an enzyme would be used to reversibly bind to a substrate to increase the rate of a reaction.

1. 2 Calix[6]arene

1. 2. 1 Lettering and Numbering Scheme for Calix[6]arenes

A lettering system is commonly used for identifying the location of the aryl rings in the calix[6]arene and a numbering scheme has been used to identify the carbon atoms of the calix[6]arene as shown in Figure 1. 3. This is extremely useful when trying to describe features that are characteristic to certain locations on the macrocycle.

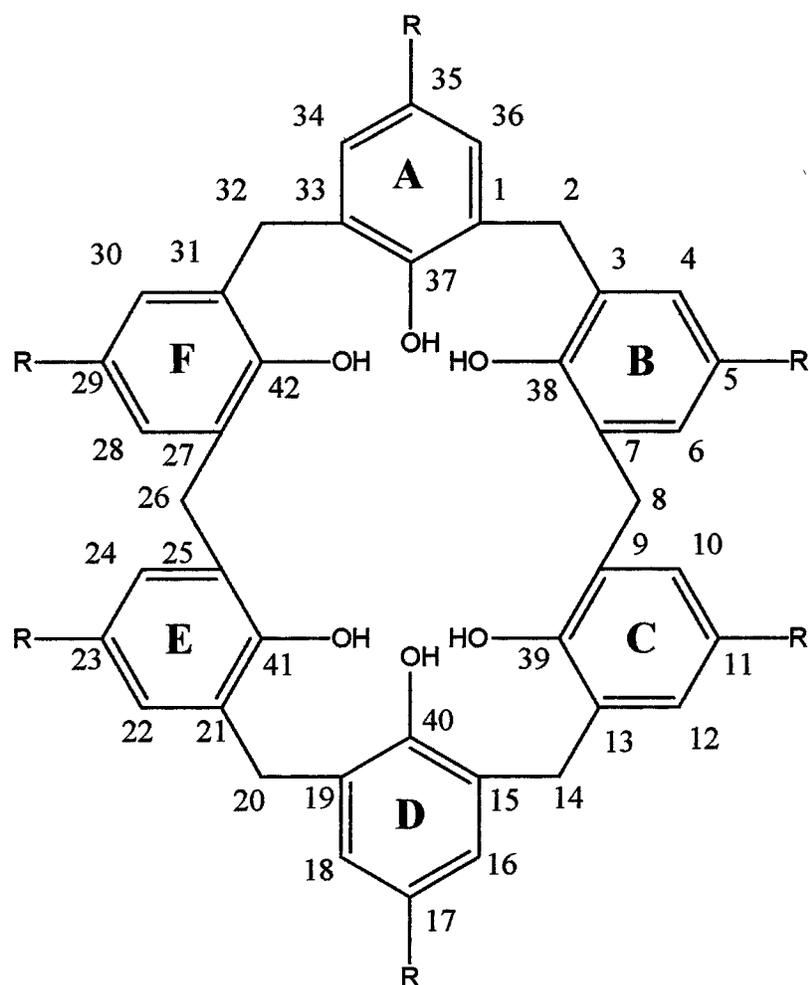


Figure 1. 3 *The Lettering and Numbering Scheme for a Generic Calix[6]arene.*

1. 2. 2 Conformational Mobility

The conformations of calix[6]arenes have hardly been studied due to their high degree of functionality and conformational mobility⁴. Even with bulky alkyl groups *para* to the hydroxyl group, the phenolic ring is able to rotate freely through the annulus of the macrocycle. Larger alkyl groups such as cholesteryl and *p*-phenylbenzyl placed on the lower rim will still exhibit conformational interconversion, albeit slow⁴⁻⁶. The rotation of the phenolic moieties can lead to 18 calix[6]arene conformations. A common way to describe the differences in conformation is to use a series of six abbreviations, one for

each of the aryl rings in the macrocycle. The abbreviations are as follows: u = up, d = down, i = in, o = out, di = down and in, uo = up and out, etc.

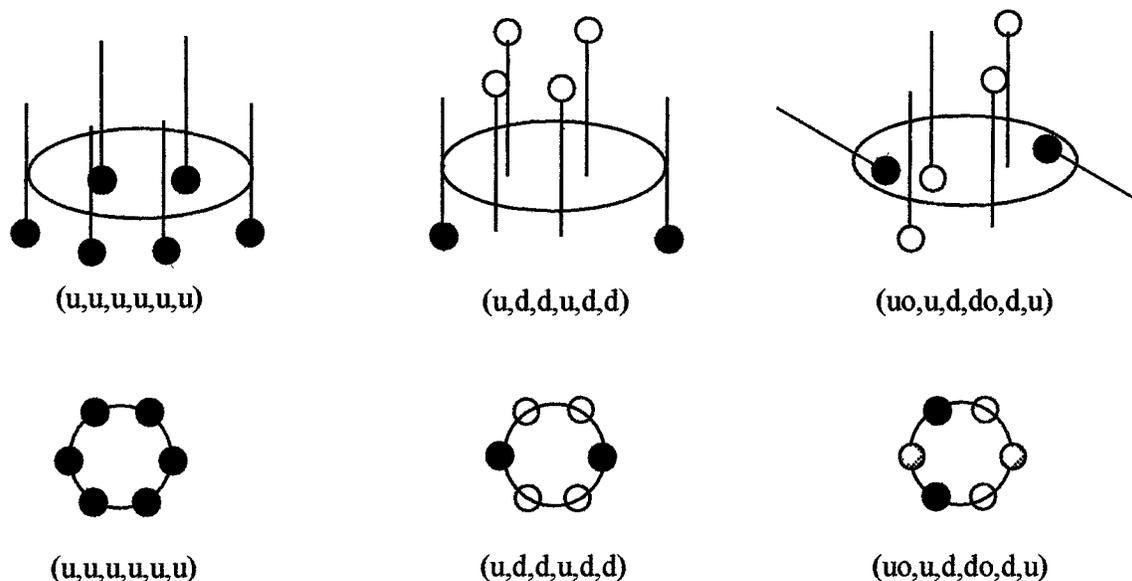
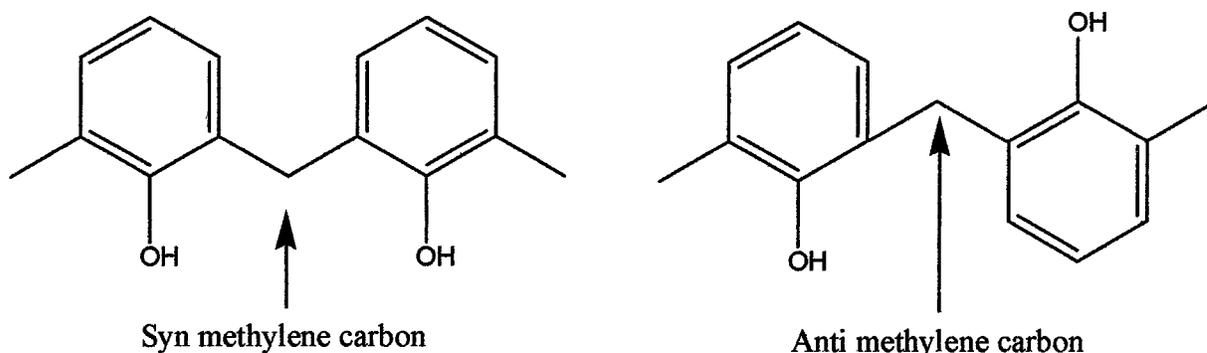


Figure 1. 4 Representations of Cone, 1,4-Alternate and 1,2,3-Alternate Calix[6]arenes.

Figure 1. 4 gives three conformations of calix[6]arenes and their corresponding letter abbreviations. In the 1,2,3-alternate calix[6]arene the reference ring is the first ring in the three ring sequence (u,uo,u,d,do,d) where the A, B and C rings are up and the D, E and F rings are down⁷.

1. 2. 3 Conformational Analysis

One of the ways to characterize different conformations is by the methylene carbon in the Ar-CH₂-Ar bonds of the macrocycle. As shown in Figure 1.5, there are two differing arrangements of that set of bonds, the syn orientation and the anti orientation.



Syn methylene carbon

Anti methylene carbon

Figure 1. 5 *Orientations of Aryl Rings in the Macrocyclic Skeleton.*

If both of the aryl rings are in the same orientation, either both up or both down, then the methylene carbon is said to be in the syn orientation. If one of the aryl rings is up and the other is down, then the methylene carbon is said to be in the anti orientation. A fortunate consequence of these differing orientations is that each has its own characteristic ^{13}C peaks around 30 ppm. The carbons in the anti position have peaks separated by < 1 ppm, and the carbons in the syn positions have peaks separated by $\sim 2\text{-}3$ ppm.

1. 2. 4 Selective Functionalization

With six equivalent phenolic moieties in an unsubstituted calix[6]arene, it is of the utmost importance to drive and direct synthesis at certain locations on the macrocycle to ensure the highest yield of tailored calix[6]arenes. Inducing certain rings for functionalization, by substitution, and leaving others unsubstituted is the basis by which selective functionalization works. Selective functionalization uses sterics and changes in reaction conditions to proceed in building calix[6]arenes that have certain substitution patterns.

Substitution at a targeted ring can be affected by small changes in reaction conditions such as changing the amount of base added⁸. Also, changing the base used in

the reaction can change the substitution locations as evidenced by A, B, D, E-tetrasubstitution was found when NaH was used as the base, whereas only A, D-disubstitution was found when Me_3SiOK was used as the base⁹⁻¹².

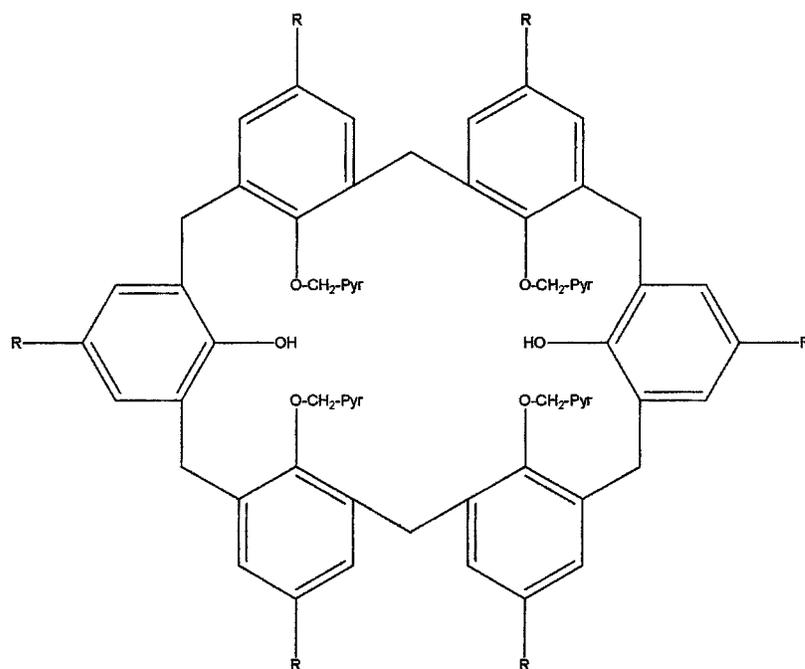


Figure 1. 6 *Tetra-pyridylmethyl Substituted Calix[6]arene.*

Various mono-substituted calix[6]arenes have been synthesized⁸. Mono-methylated calix[6]arene has been isolated in very small amounts with CH_3I and K_2CO_3 , while a mono-benzylated compound has been synthesized with good yields⁸. A penta-substituted calix[6]arene has been isolated using CH_3I and acetone. When hexa-substituted calix[6]arenes were synthesized, they were instrumental in elucidating the through the annulus rotation of conformationally mobile calix[6]arenes^{3, 8, 13, 14}.

Tri-substituted calix[6]arenes usually have their substitutions on the A, B, C rings or on the A, C, E rings. Examples of these substitution patterns are usually seen with methyl groups or pyridylmethyl groups as the substituents^{8, 15-18}. The formation of A, C,

E-trisubstituted calix[6]arenes with larger alkyl halides or with polyethylene glycol have also been synthesized^{19, 20}.

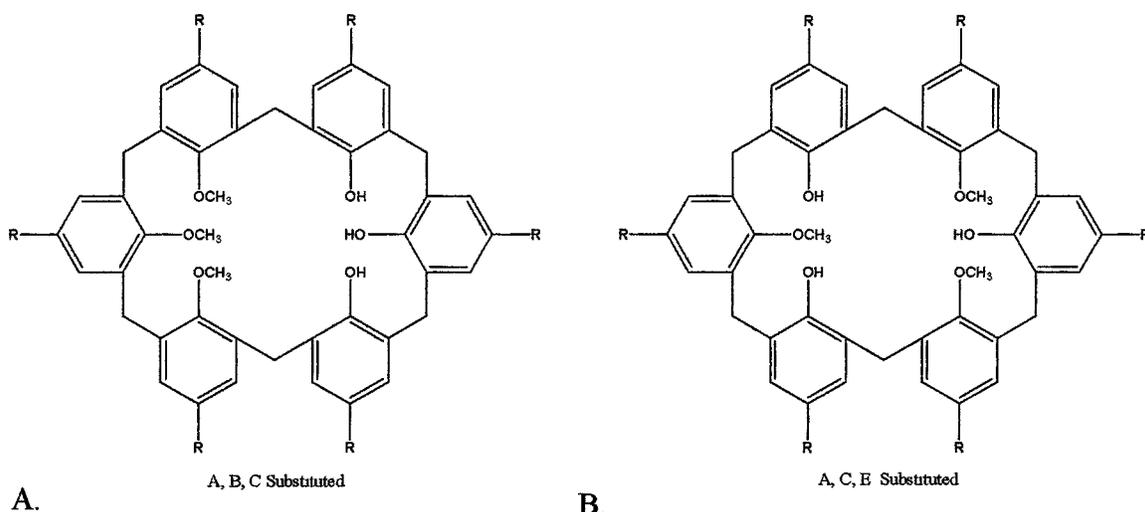


Figure 1. 7 *Different Substitution Patterns for Tri-Methylated Calix[6]arenes.*

An excellent example of selective functionalization would be the synthesis of 37, 40-diallyloxy-38, 39, 41, 42-tetrahydroxy calix[6]arene (**3**). When two molar equivalents of allyl bromide are used as the alkylating agent, the A and D rings are the rings substituted preferentially. All six of the hydroxyl groups are equivalent in the calix[6]arene used as the precursor for this reaction.

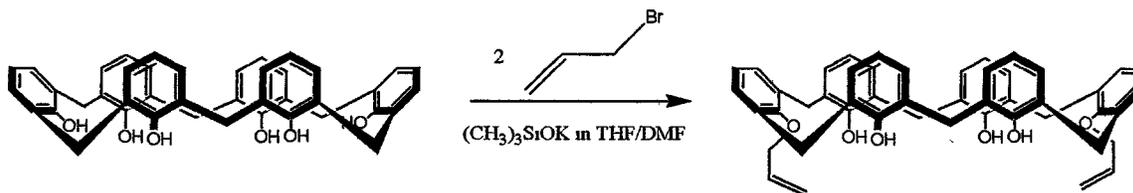


Figure 1. 8 *Synthesis of 37, 40-diallyloxy-38, 39, 41, 42-tetrahydroxy calix[6]arene.*

Once the first allyl group has been added to the ring (that ring would by definition become the A ring), the position on the calix[6]arene that would give the most stable intermediate would be the D ring. It would be the ring directly across the macrocycle from the A position and it would be the only one whose intermediate anion would be

stabilized by two flanking hydrogen bonds. That stabilization would lead the next allyl group to be added at that specific location.

1. 2. 5 Bridging

Bridging is an important synthetic step in the formation of well-defined calix[6]arene conformations because this is what enables the conformation to become locked and rigid due to restricted rotations. Bridging is a phenomenon that occurs via selective functionalization of unsubstituted phenolic rings in the macrocycle. To date, lower-rim-bridged calix[6]arenes are most common, although upper-rim-bridged and even some through-the-annulus-bridged calix[6]arenes have been synthesized.

Depending on the amount of substitution on the calix[6]arene and the molar amounts of bridging units added to the reaction; mono, bis and triply bridged calix[6]arenes can be produced.

Mono-bridged calix[6]arenes have been prepared where the A/B rings, the A/C rings or the A/D rings were tethered²¹⁻³⁰. A/D-bridged calix[6]arenes are the most prevalent of the mono-bridged calix[6]arenes³¹. Both rigid and flexible bridging units may be used. Typically aromatic units are used for rigid bridged calix[6]arenes, while polyethylene glycol units are used for more flexible bridges.

A/B-bridged calix[6]arenes have been synthesized by using K_2CO_3 as the base with KI as the catalyst in benzene, or when only K_2CO_3 was used without a catalyst in acetonitrile using a different bridging unit^{21, 22}. Longer bridging units tend to give better yields.

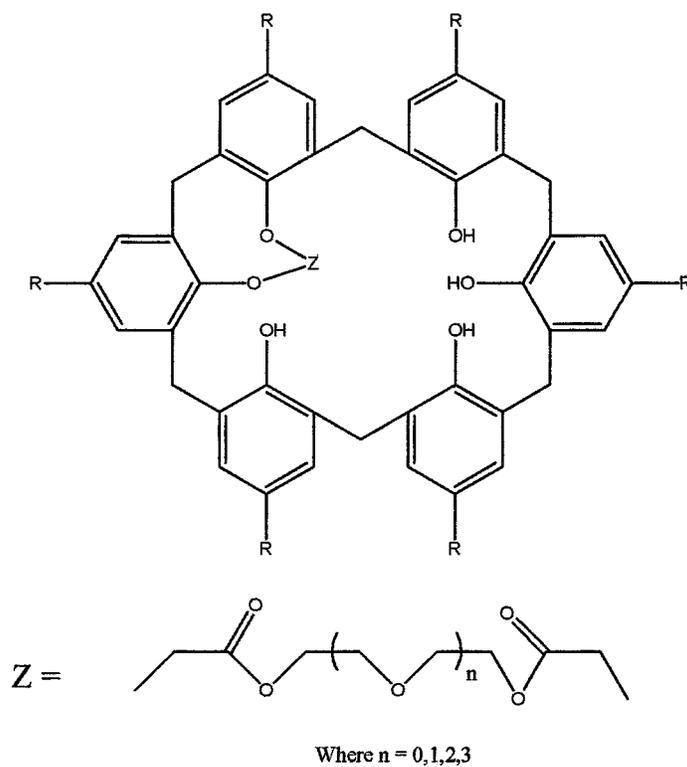


Figure 1. 9 *Regiospecific Bridging of the A/B Rings.*

The first A/C-bridged calix[6]arene synthesized used KOt-Bu as the base to give a 24% yield^{25, 26}. Better yields have been obtained as research progressed, and with partial methylation prior to the bridging, reactions have produced yields better than 90%²⁷

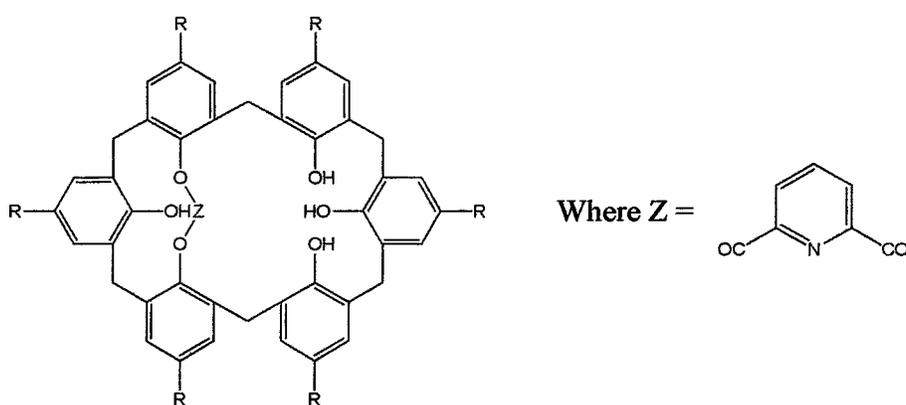


Figure 1. 10 *First Known Regiospecific A/C Bridged Calix[6]arene.*

A/D-bridged calix[6]arenes have been synthesized with bases such NaH and Me_3SiOK ^{11, 28-30}. There are many examples of A/D bridging using various base and solvent combinations, not to mention the types of bridging units used.

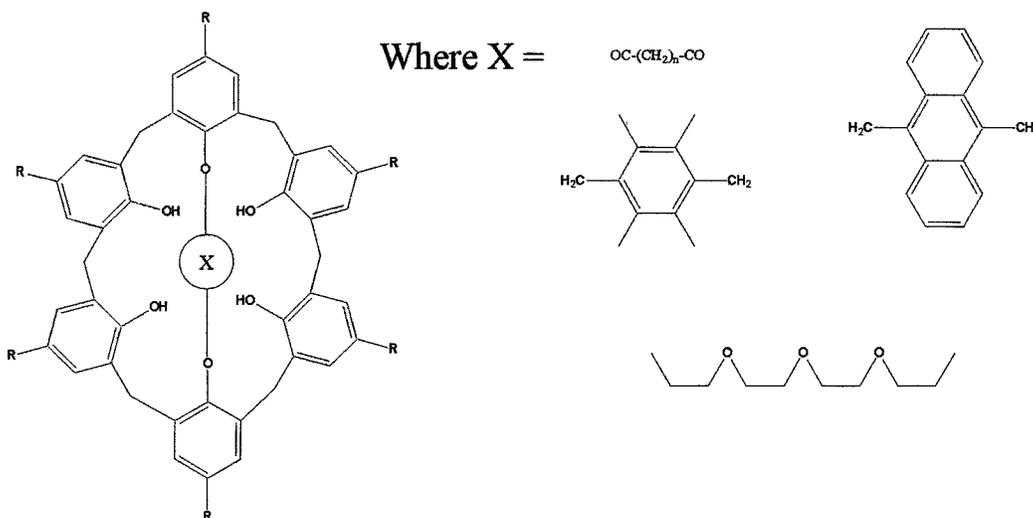


Figure 1. 11 *Varying Bridging Units for A/D Bridged Calix[6]arene.*

The triply-bridged calix[6]arene would have bridges joining the A/B rings, the C/D rings, and the E/F rings as shown in Figure 1. 12³². Another way to achieve a triply-bridged calix[6]arene would be to bridge the A/D, B/C, and E/F rings³³. One unique aspect of the compound shown in Figure 1. 12 is that it stays conformationally mobile even though it is a bridged calix[6]arene³². If larger bridging units were used then the calix[6]arene would become conformationally immobile³⁴.

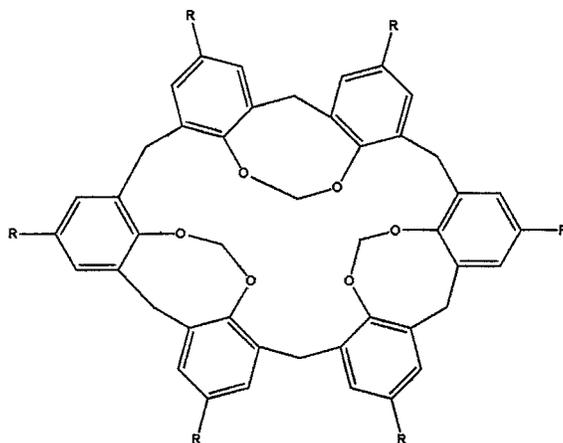


Figure 1. 12 *A Triply-Bridged Calix[6]arene.*

Another way to decrease the mobility of a calix[6]arene is to ‘cap’ the lower rim as shown in Figure 1. 13. Both of these compounds had their respective rings substituted before the capping reaction took place^{35,36}.

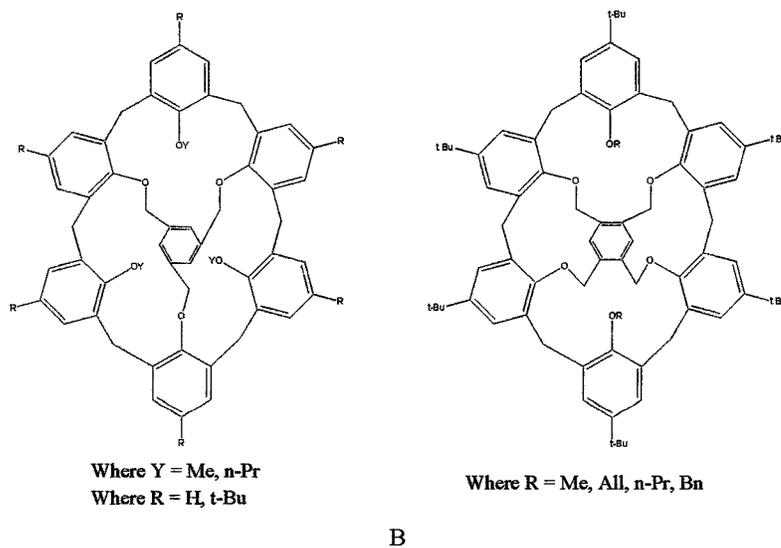


Figure 1. 13 *A = Three Leg Capped Calix[6]arene B = Four Leg Capped Calix[6]arene*

There are very few synthesized upper-rimmed-bridged calix[6]arenes, although they are analogous to their lower-rim-bridged counterparts. Both of the calix[6]arenes presented in Figure 1. 14 are conformationally immobile as evidenced by their variable-temperature NMR spectra^{37, 38}.

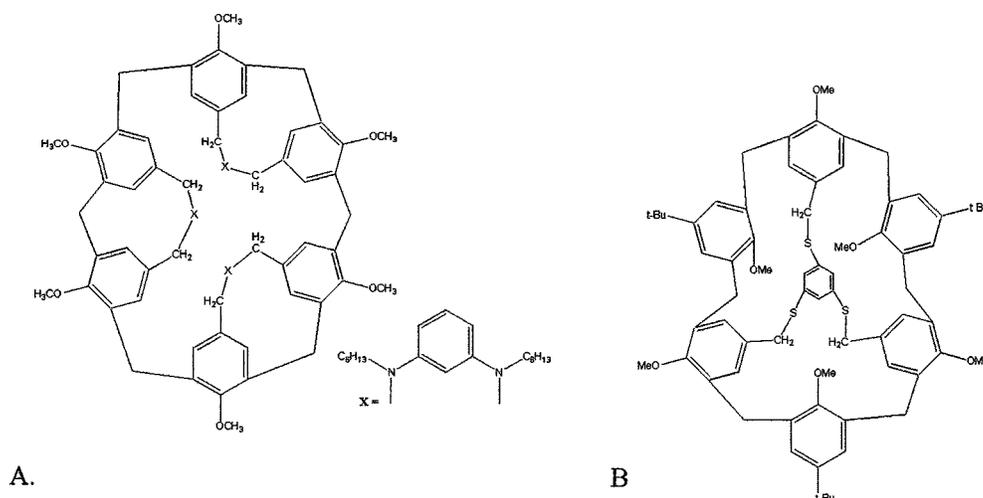


Figure 1.14 *Upper Rim Bridging of Calix[6]arene.*

As shown in Figure 1.15, A, D-disubstituted calix[6]arenes are extremely useful when a bis-bridged calix[6]arene is the desired product. With two of the rings already substituted, the remaining four are selectively targeted for deprotonation when reacted with the appropriate base and solvent combination. If the alkylating agent is di-substituted at the correct positions and is of the correct length, then it could bond at two positions on the calix[6]arene macrocycle resulting in a bis-bridged calix[6]arene.

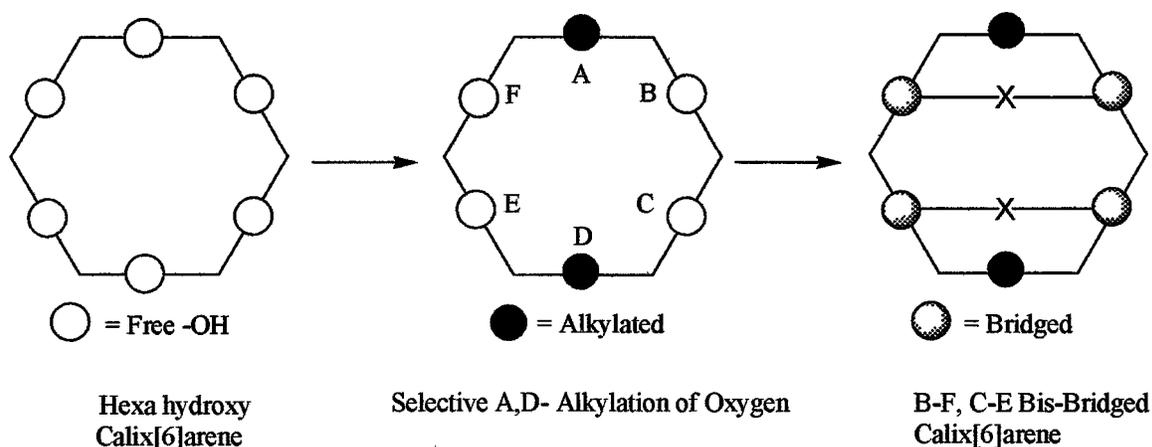


Figure 1.15 *Selective Functionalization Leading to Bis-Bridged Calix[6]arene.*

Bis-Bridging of calix[6]arene leads to two distinct families, the syn bis-bridged family and the anti bis-bridged family. Together, both families contain a total of 18

isomers. The syn bis-bridged family has their bis-bridging units on the same side of the macrocyclic annulus, while the substituted A and D rings could be on either side. There are nine isomeric possibilities that could arise from the syn bis-bridged calix[6]arenes, although three have a criss-cross shape to them and are usually negligible due to steric hindrance.

The anti bis-bridged calix[6]arene family has their bridging units on opposite sides of the macrocyclic annulus, while the substituted A and D rings could be on either side. Again, there are nine isomeric possibilities from the anti family of bis-bridged calix[6]arenes and all of them are formed.

Once the calix[6]arene is locked due to bis-bridging, the rotation through the annulus of the B, C, E and F rings is prevented. This is what keeps the families of bis-bridged calix[6]arenes from interconverting even at high temperatures. Two major isomers have been found by bis-bridging, the cone conformation and the 1, 2, 3–alternate conformation. The cone is a member of the syn family and the 1, 2, 3–alternate is a member of the anti family.

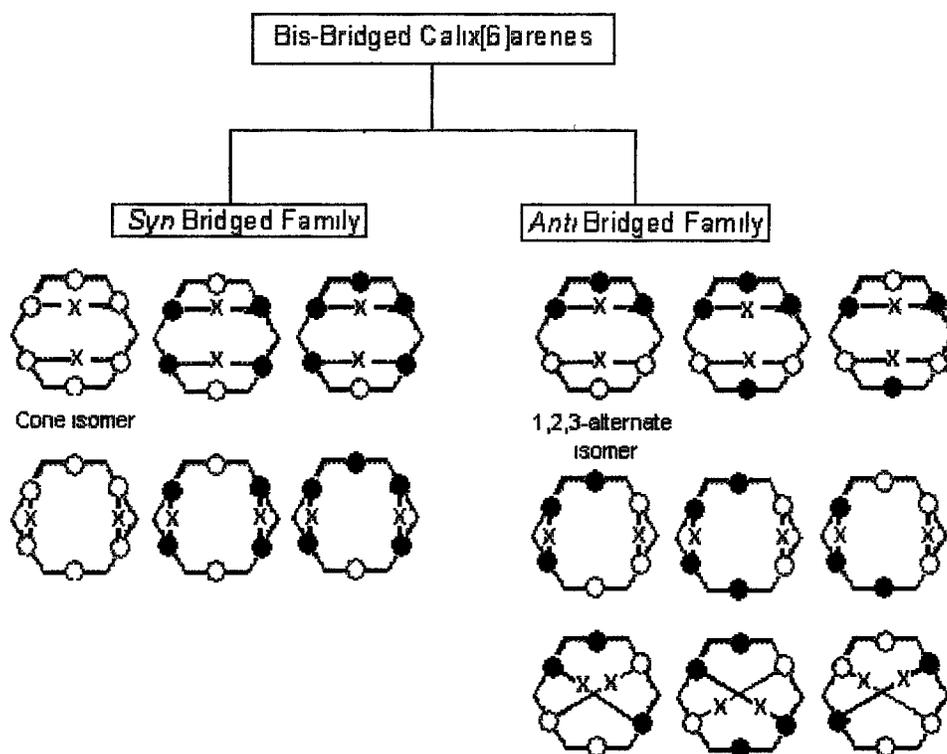


Figure 1. 16 All Possible Conformations of Bis-Bridged Calix[6]arenes.

1. 3 Thesis Proposal

There are more difficulties involved with working with calix[6]arenes than with the smaller calix[4]arenes due to the increase in ring size. This leads to the macrocycle having more flexibility. A more flexible calix[6]arene is much more troublesome synthetically and ultimately as a supramolecular entity as compared to a calix[6]arene that has been locked into its specific conformation. A way to lock the calix[6]arene is to bis-bridge an A, D di-substituted one. Previous work has been done to synthesize two bis-bridged calix[6]arenes with different bridging units³⁹.

The purpose of this research was to survey various reaction conditions to determine the effect on the stereochemical outcome of bis-bridged calix[6]arenes.

Reaction conditions that were changed include: base, solvent, temperature and type of bridging unit used. By varying different conditions, information could be obtained to selectively synthesize different conformations.

With the arrangement of the macrocycle already known, investigation was commenced to identify the relationship reaction conditions had with the conversion of a non-bridged calix[6]arene to a bis-bridged calix[6]arene by using ^1H NMR integrations. In addition, the different reaction conditions were analyzed to understand any selectivity and preference that one might have for the different conformations of bis-bridged calix[6]arene.

2.0 SYNTHETIC STRATEGY

2.1 Synthesis of 5, 11, 17, 23, 29, 35-hexa-*p-tert*-butyl-37, 38, 39, 40, 41, 42-hexahydroxy calix[6]arene (1)

Compounds 1 and 2 have been studied and well characterized which provides the scaffold for all work with calix[6]arenes. The basic starting materials for 1 are *p-tert*-butyl phenol and paraformaldehyde. Exact amounts of RbOH (0.45 molar equivalents) are used as the base in this condensation reaction performed in refluxing xylene as shown in Figure 2. 1⁴⁰. The base used is believed to have a templating effect in generating the size of the calix[*n*]arene.

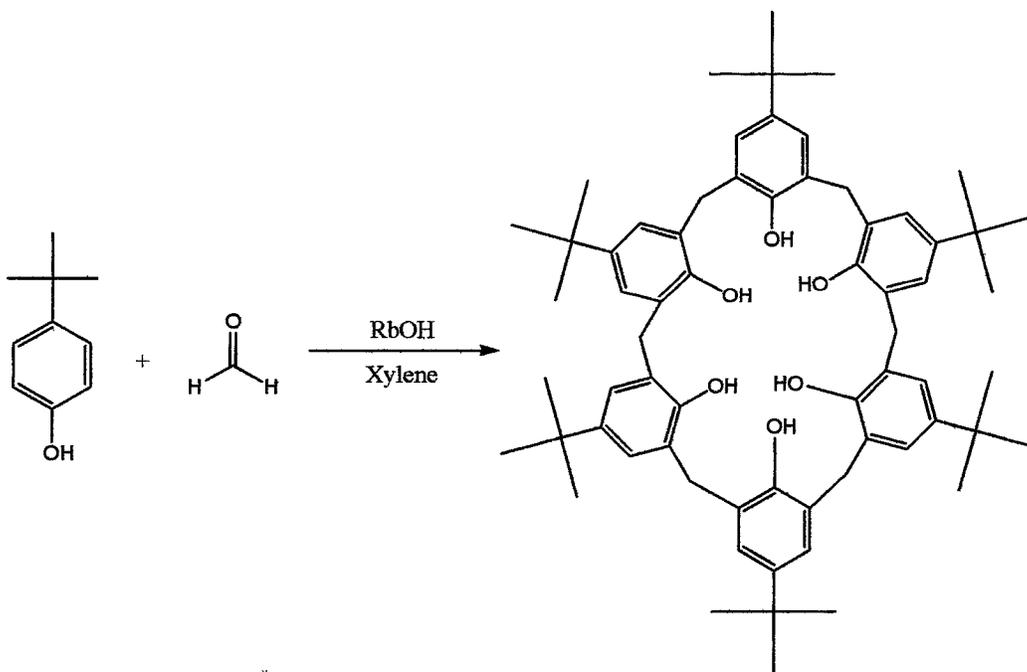


Figure 2. 1 *Synthesis of Compound 1.*

2. 2 Synthesis of 37, 38, 39, 40, 41, 42-hexahydroxy calix[6]arene (2)

As shown in Figure 2. 2, synthesis of **2** is a reverse Friedel-Crafts alkylation using AlCl_3 in toluene. This is the standard way to remove the *t*-butyl groups from the calix[6]arene⁷. This dealkylation step provides for more flexibility in the calix[6]arene and greater synthetic versatility.

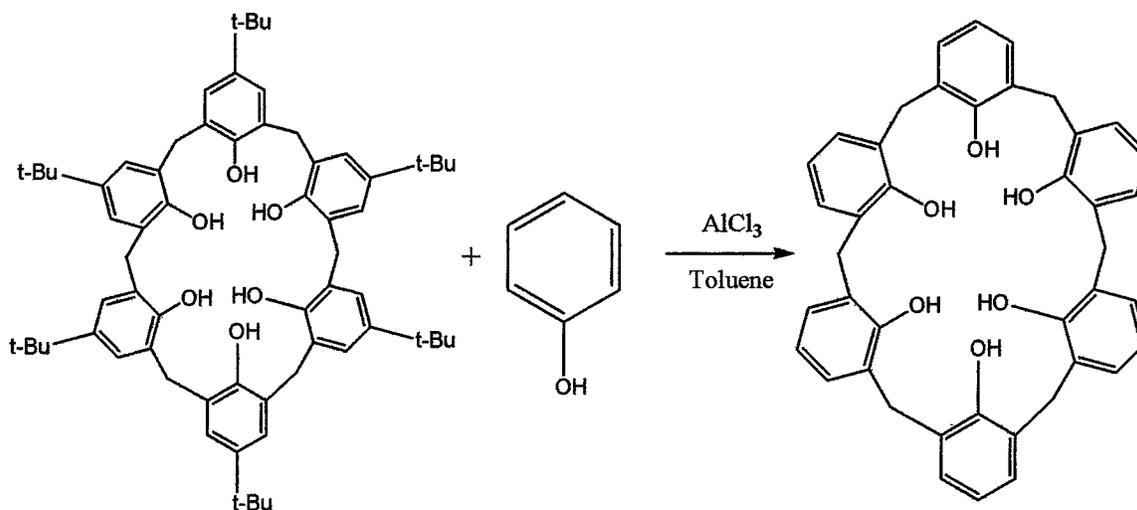


Figure 2. 2 *Synthesis of Compound 2.*

2. 3 Synthesis of 37, 40-diallyloxy-38, 39, 41, 42-tetrahydroxy calix[6]arene (3)

As previously stated, A, D-disubstituted calix[6]arenes are extremely well suited for bis-bridging. As shown in Figure 2. 3, synthesis of **3** is carried out via selective functionalization of the A and D rings of compound **2** using Me_3SiOK as the base and allyl bromide as the alkylating agent.

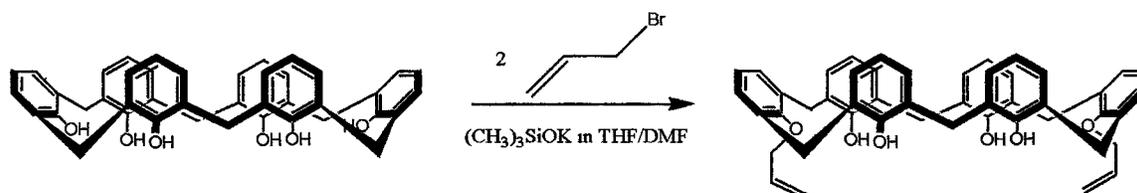


Figure 2. 3 *Synthesis of Compound 3.*

2. 4 Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-bis-*m*-xylenyloxy calix[6]arene (4 and 5)

With **3** having its A and D rings substituted, six molar equivalents of base was used with 2 molar equivalents of α, α' -dibromo-*m*-xylene used as the bridging unit. The bis-bridged calix[6]arenes **4** and **5** were produced. Calix[6]arene **4** is locked into the cone conformation, while **5** is locked into the 1, 2, 3-alternate conformation. Reactions were allowed to reflux for 24 hrs using various solvents and bases to better understand the synthetic possibilities available by stabilizing the transition states of the various bis-bridged calix[6]arene conformations.

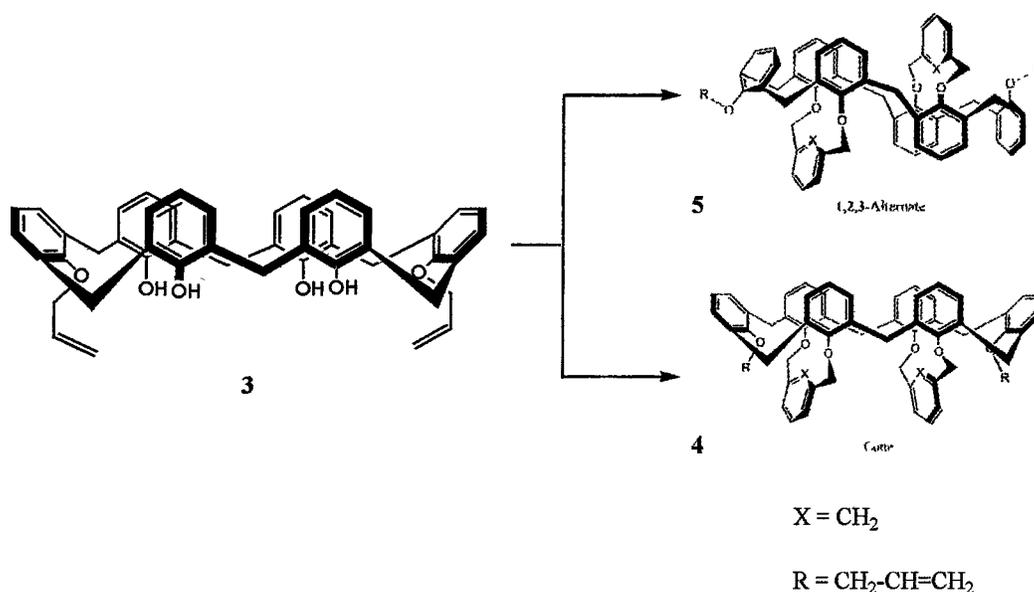


Figure 2. 4 *Synthesis of Compounds 4 and 5.*

2. 5 Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-biscrown[4]ether calix[6]arene (6 and 7)

The same principles that were applied to **3** to produce **4** and **5** were used in the synthesis of **6** and **7**, but a different bridging unit was used. Triethylene glycol di-*p*-tosylate was used as the bridging unit instead of using α, α' -dibromo-*m*-xylene. As shown in Figure 2. 5, both the cone (**6**) and 1, 2, 3-alternate (**7**) conformations of the crown[4]ether bis-bridged calix[6]arenes were synthesized. Again, various bases and solvents were used in their synthesis to better understand the synthetic possibilities available by stabilizing the transition states of the various bis-bridged calix[6]arene conformations.

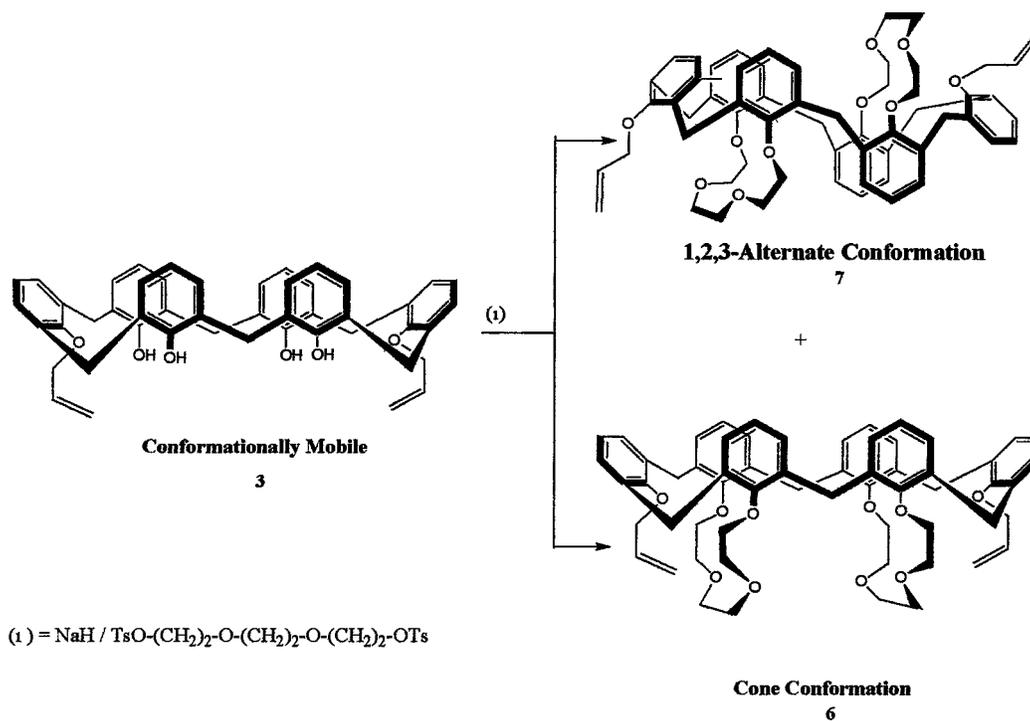


Figure 2. 5 *Synthesis of Compounds 6 and 7 using NaH as the Base.*

3. 0 RESULTS AND DISCUSSION

3. 1 *m*-Xylenyl Bis-Bridged Calix[6]arenes

There are known to be two major stereoisomers of bis-bridged calix[6]arenes that use *m*-xylene as the bridging unit⁴⁴. One is the cone conformation (**4**), which has an identifying ¹H NMR signal, a doublet at 6. 4 ppm. It also has a pair of identifying ¹³C NMR signals separated by ~2-3 ppm at around 30 ppm. The other conformation is the 1, 2, 3-alternate conformation (**5**); which has an identifying ¹H NMR signal, again a doublet, at 6. 2 ppm and a pair of identifying ¹³C NMR signals separated by <1 ppm around 30 ppm. The two isomers are not interconvertible Compound **3** is the precursor used in the bis-bridging reactions, and has a pair of identifying ¹H NMR signals, doublets at 5. 1 ppm and 5. 4 ppm. By using integrations of the unique ¹H NMR signals, percentages of reactant and the two known stereoisomers were determined. Percent by mass was used to determine the amount of new calix[6]arenes synthesized. The results of all the various base and solvent combinations used in the bis-bridging reactions of **3** with α , α' -dibromo-*m*-xylene are shown in Table 3. 1.

Although no one single factor was determined to be a major cause for determining the stereochemistry of the bis-bridging reactions, several general trends could be established. Trends were observed based solvent polarity and boiling point, base solubility and strength, and size of the cation. For example, lower boiling point solvents like acetone tended to yield the intermediary B/F mono-bridged calix[6]arene indicating

Table 3. 1 Stereoselective Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-bis-*m*-xylenyloxy calix[6]arene.

	Benzene	THF	Acetone	DMF	Acetonitrile
Sodium Carbonate	No Rxn	No Rxn	Mono-Bridged	Mono-Bridged	Mono-Bridged
Potassium Carbonate	* Mono-Bridged with 10 molar excess	* 10 molar excess 25 % Cone 75% 1,2,3-alternate	14% Cone 86% 1,2,3-Alternate	* 10 molar excess Mostly unreacted and little cone or 1,2,3-Alternate	9% Cone 91% 1,2,3-Alternate
Cesium Carbonate	91% Cone 9% 1,2,3-Alternate	91% Cone 9% 1,2,3-Alternate	85% Cone 15% 1,2,3-Alternate	88% Cone 12% 1,2,3-Alternate	96% Cone 4% 1,2,3-Alternate
Sodium Tert-Butoxide	No Rxn	8% Cone 92% 1,2,3-Alternate	Mono-Bridged	70% Mono-Bridged 30% 1,2,3-Alternate	9% Cone 91% 1,2,3-Alternate
Potassium Tert-Butoxide	17 % Cone 83% 1,2,3-Alternate	25% Cone 75% 1,2,3-Alternate	Mono-Bridged	No Rxn	No Rxn
Sodium Hydride	No Rxn	21% Mono-Bridged 79% 1,2,3-Alternate	Mono-Bridged	Mono-Bridged	6% Cone 94% 1,2,3-Alternate

* denotes changes in reaction conditions

there was not enough energy to drive the reaction to completion. The importance of the mono-bridged intermediate is that while it has been bridged, it is not locked into a specific conformation. Once the second bridge has been added, only then does a bis-bridged calix[6]arene become locked into a specific conformation, i. e. cone or 1, 2, 3-alternate.

Bases in which sodium was the cation typically gave unreacted or mono-bridged compounds, but when the reaction went to completion the 1, 2, 3-alternate conformation was the major product. This would indicate that the sodium ion is poor at stabilizing the transition states of bis-bridged calix[6]arenes, but it best stabilizes the 1, 2, 3-alternate conformation. The stronger bases, *t*-butoxides and sodium hydride, tended to yield 1, 2, 3-alternate as their bis-bridged product if the reaction went to completion; while the carbonate bases seemed to be more dependent on the size of the cation in the base. Likewise, the solubility of the bases in those solvents was a concern.

Generally solvent polarity seems to have no real significant effect on the stereoselectivity. One exception to this was with the bases that used potassium as the cation. K_2CO_3 in increasing polar solvents tended to yield the 1, 2, 3-alternate conformation; while the opposite was true with potassium *tert*-butoxide. The 1, 2, 3-alternate conformation was synthesized in more non-polar solvents.

A very noticeable trend was that when Cs_2CO_3 was used, the cone conformation was the major product, 85% or better, no matter what solvent was used. Of all the thermodynamically feasible possibilities, this result suggests that the cesium cation is very effective at stabilizing the transition state of the cone conformation and not as

effective as stabilizing the transition states to other bis-bridged calix[6]arenes. No other base consistently gave such high results with the various solvents.

One nice overall trend was that all of the reactions tended to be selective for one of the conformations. The highest percentage of cone as the major product (96%) was found when Cs_2CO_3 was used in acetonitrile, and the lowest percentage of cone as the major product (85%) was found when Cs_2CO_3 was used in acetone. Again, it would seem that reactions were incomplete in the lower boiling acetone. The highest percentage of 1, 2, 3-alternate as the major product (94%) was found when NaH was used in acetonitrile, while the lowest percentage of 1, 2, 3-alternate as the major product (75%) was found when potassium tert-butoxide was used in THF.

3. 2 Triethyleneglycol Bis-Bridged Calix[6]arenes

Compound 3 was again used as the precursor for the bis-bridging reactions. Just as in the bis-bridged calix[6]arenes in Section 3. 1, there are known to be two major isomers of bis-bridged calix[6]arenes that use triethylene glycol as the bridging unit⁴⁴. And again, these are the cone calix[6]arene and the 1, 2, 3-alternate calix[6]arene. The cone calix[6]arene has two identifying signals in its ^1H NMR spectrum. One is a doublet at 6. 0 ppm and the other is a triplet at 6. 28 ppm. These peaks flank a multiplet that is at 6. 15 ppm. The two identifying ^1H NMR signals for the 1, 2, 3-alternate calix[6]arene are deshielded a little bit farther than the cone calix[6]arene. The doublet is at 6. 5 ppm and the triplet is at 6. 67 ppm. These two signals are to the left of the multiplet at 6. 15 ppm. Again, the integrations of the unique signals of the reactant and the known products were used to calculate the percentages of known products synthesized. Percent by mass was

used to determine the amount of new calix[6]arenes synthesized. The results of all the various base and solvent combinations used in the bis-bridging reactions of **3** with triethylene glycol di-*p*-tosylate are shown in Table 3. 2.

General trends were hard to establish for the factors contributing to the stereochemistry of bis-bridging **3** to **6** and **7**, and no one single factor could be pinpointed. There was good selectivity of the cone isomer when Cs₂CO₃ was used in benzene, potassium tert-butoxide in THF, and NaH in THF, acetone and DMF. Acetone was the only solvent that would synthesize mostly the cone conformation through all various bases, if the reaction proceeded. These results would suggest that for these reaction combinations various conditions can better stabilize the transition state of the cone conformation versus other bis-bridged crown calix[6]arenes.

The 1, 2, 3-alternate conformation was produced as the major product when Cs₂CO₃ was used in THF and when potassium tert-butoxide was used in benzene. There was one reaction, NaH in benzene that tended to give mostly 1, 2, 3-alternate as its product, but 41% of the starting material did not react so only a minimal amount of product was obtained. This would suggest that for these reaction combinations only a few reaction conditions are good at stabilizing the transition state of the 1, 2, 3-alternate conformation.

The solubility of the various bases in such a range of solvent polarity was a concern, although most reactions seemed to yield some sort of product. It seems that the stronger bases tended to have a good selectivity for the cone conformation when moderately polar solvents were used. The only base that would not synthesize any bis-bridged crown calix[6]arenes was K₂CO₃.

Table 3. 2 Stereoselective Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-biscrown[4]ether calix[6]arene.

	Benzene	THF	Acetone	DMF	Acetonitrile
Sodium Carbonate	No Rxn	No Rxn	No Rxn	Some unreacted plus Unknown Product #1	No Rxn
Potassium Carbonate	No Rxn	No Rxn	No Rxn	* 10 molar excess Mostly unreacted with little cone or 1,2,3-Alternate	* 30 molar excess No Rxn
Cesium Carbonate	83% Cone 17% 1,2,3-Alternate	39% Cone 61% 1,2,3-Alternate	94% Unreacted 6% Cone	Some unreacted plus Unknown Product #2	95% Unreacted 5% Cone
Sodium Tert-Butoxide	49% Unreacted 24% Cone 27% 1,2,3-Alternate	21% Unreacted 48% Cone 31% 1,2,3-Alternate	61% Cone 39% 1,2,3-Alternate	78% Cone 22% 1,2,3-Alternate	58% Unreacted 23% Cone 19% 1,2,3-Alternate
Potassium Tert-Butoxide	42% Cone 58% 1,2,3-Alternate	85% Cone 15% 1,2,3-Alternate	No Rxn	No Rxn	78% Unreacted 22% Cone
Sodium Hydride	41% Unreacted 19% Cone 40% 1,2,3-Alternate	61% Cone 39% 1,2,3-Alternate	Cone	66% Cone 34% 1,2,3-Alternate	52% Unreacted 27% Cone 21% 1,2,3-Alternate

* denotes changes in reaction conditions

Two unknown calix[6]arenes were synthesized when DMF was the solvent. The first unknown product was synthesized with Na_2CO_3 , and the second was synthesized with Cs_2CO_3 . Although some unreacted material was found, each reaction produced mostly their new product. These are the only two cases where a product was formed and it was neither the cone nor the 1, 2, 3-alternate conformation. Only general information about the new calix[6]arenes has been obtained. By using variable temperature $^1\text{H NMR}$, the product synthesized from the Na_2CO_3 in DMF reaction seemed to be a locked calix[6]arene and the product synthesized from the Cs_2CO_3 seemed to not be locked.

3. 3 General Observations of Both Bis-Bridging Reactions

The bis-bridging reactions involving the *m*-xylylenyl bridging unit seemed to be more selective and gave a better conversion of starting material to product than the bis-bridging reactions involving triethylene glycol as the bridging unit. This is more than likely due to the *m*-xylene bridging unit having a better fit to bridge across the annulus of the macrocycle. This seems to suggest that the more rigid bridging unit would be the better choice for a locked calix[6]arene that did not have any binding site. The crown ether bis-bridged calix[6]arenes have binding sites but their synthetic selectivity is limited and producing them are less effective.

4. 0 EXPERIMENTAL

^1H and ^{13}C NMR spectra were obtained on a Varian NMR 400 MHz in CDCl_3 and were referenced to the residual proton signal in CDCl_3 .

4. 1 Synthesis of 5, 11, 17, 23, 29, 35-hexa-*p-tert*-butyl-37, 38, 39, 40, 41, 42-hexahydroxy calix[6]arene (1)

Because 1 is a known compound, the synthesis of 1 was performed according to well-known and established procedures⁴¹⁻⁴³.

4. 2 Synthesis of 37, 38, 39, 40, 41, 42-hexahydroxy calix[6]arene (2)

Likewise, the synthesis of 2 was performed according to well-known and established procedures^{44, 45}.

4. 3 Synthesis of 37, 40-diallyloxy-38, 39, 41, 42-tetrahydroxy calix[6]arene (3)

The synthesis of 3 was performed according to a well-known and established procedure as well⁴⁶.

4. 4 Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-bis-*m*-xylenyloxy calix[6]arene (4 and 5)

In a 250 mL single neck round bottom flask 0.5 g (0.7 mmol) of 3 was placed, followed by 6 molar equivalents of the various bases and 100 mL of the different solvents. Acetone, acetonitrile, benzene, DMF and THF were the solvents used and

Na_2CO_3 , K_2CO_3 , Cs_2CO_3 , Sodium tert-butoxide, Potassium tert-butoxide and NaH were the bases used. For the reactions involving DMF, 2.0 g (2.8 mmol) of **3** was used in a 500 mL single neck round bottom flask was used, as well as 300 mL of solvent. The mixture was stirred 15 min in an inert argon atmosphere after which two molar equivalents of α, α' -dibromo-*m*-xylene dissolved in 10 mL of the same solvent was added slowly via a syringe. All of the solutions were heated to reflux except for the reactions using DMF as the solvent. Those reactions were heated to 73° C in a paraffin oil bath.

The reactions were heated for 24 h, at which time the solvent was removed under reduced pressure. The residue was re-dissolved in 200 mL of CHCl_3 and washed three times with equal volumes (150 mL) of 2M HCl. A back extraction was performed on the aqueous layer. Both the washed organic layer and back extraction were combined, dried over MgSO_4 and filtered. The CHCl_3 was removed using reduced pressure, leaving a crude reaction mixture. This reaction mixture was analyzed by tlc to reveal the various products.

If only previously known calix[6]arenes were found, then a crude ^1H NMR was obtained and the area under the curves of the known material' s peaks were used to calculate the percentage of **4** and **5** produced by this reaction. If a new calix[6]arene was found, then it was isolated by chromatography. The percent of new calix[6]arene produced was obtained by the percent mass of the new calix[6]arene relative to the total mass of calix[6]arenes recovered from the column.

Analytical data for **4**: ^1H NMR (400 MHz, CDCl_3 , 25 °C) δ = 7.401 (d of d, 2H, J = 8.8 Hz), 7.396 (d of d, 2H, J = 8.8 Hz), 7.184 (M, 8H), 7.050 (t, 2H, J = 14.8 Hz), 6.948

(d, 4H, J= 7.2 Hz), 6.555 (t, 2H, J= 15.6 Hz), 6.226 (d, 4H, J= 8.0 Hz), 5.853 (M, 2H), 5.465 (s, 2H), 5.139 (d of d, 2 H, J= 14 Hz), 4.215 (d, 8H, J=16 Hz), 4.063 (d of d, 4H, J= 1.2 Hz), 3.566 (d, 2H, J=14.4Hz), 3.443 (d, 4H, J=14.2 Hz). ^{13}C NMR (100MHz, CDCl_3 , 25 °C) δ = 156.4, 155.2, 137.0, 134.6, 134.0, 133.2, 130.2, 130.9, 129.9, 127.4, 125.7, 123.8, 115.5, 75.5, 71.3, 31.4, 28.8. Anal. Calcd. for $\text{C}_{64}\text{H}_{56}\text{O}_6$: C, 83.5 % H, 6.1%. Found C:80%, H:6%.

Analytical data for **5**: mp. 248-250 °C ^1H NMR (400MHz, $\text{C}_2\text{D}_2\text{Cl}_4$, + 140 °C) δ = 7.48 (t, 2H, J= 7.6 Hz), 7.23 (d, 4H, J= 8 Hz), 7.15 (d, 4H, J= 7.6 Hz), 7.04 (t, 4H, J= 7.2 Hz), 6.86 (d, 4H, J= 7.2 Hz), 6.03 (d, 4H, J= 8 Hz), 5.72 (m, 2H), 5.57 (d, 2H, J=7.2 Hz), 5.04 (s, 2H), 5.01 (d, 2H, J= 7.6 Hz), 4.56 (d, 4H, J= 12.4 Hz), 4.24 (s, 4H), 4.16 (d, 6H, J= 12.4 Hz), 4.11 (d, 4H, J= 15.2 Hz), 3.87 (d, 4H, J= 5.6 Hz), 3.16 (d, 4H, J= 14.8 Hz), 2.85 (s, 4H). ^{13}C NMR (100 MHz, $\text{C}_2\text{D}_2\text{Cl}_4$, +140 °C) δ = 157.36, 156.67, 124.00, 136.11, 135.83, 134.92, 134.74, 133.41, 130.00, 129.65, 125.48, 123.06, 122.54, 118.74, 116.10, 76.68, 74.84, 73.55, 31.032, 30.782. Anal. Calcd. for $\text{C}_{62}\text{H}_{54}\text{O}_6\text{N}_2$: C, 79.8%; H, 5.8%; O, 10.3%; N, 4.1%. Found C, 79.6% H, 5.9%.

4. 5 Synthesis of 37, 40-diallyloxy-(38, 41)-(39, 42)-biscrown[4]ether calix[6]arene (6 and 7)

In a 250 mL single neck round bottom flask 0.5 g (0.7 mmol) of **3** was placed, followed by 6 molar equivalents of various bases and 100 mL of various solvents. Acetone, acetonitrile, benzene, DMF and THF were the solvents used and Na_2CO_3 , K_2CO_3 , Cs_2CO_3 , Sodium tert-butoxide, Potassium tert-butoxide and NaH were the bases used. For the reactions involving DMF, 2.0 g (2.8 mmol) of **3** was used in a 500 mL single neck round bottom flask was used, as well as 300 mL of solvent. The mixture was

stirred 15 min in an inert argon atmosphere after which two molar equivalents of triethylene glycol di-*p*-tosylate dissolved in 10 mL of the same solvent was added via a syringe. All of the solutions were heated to reflux except for the reactions using DMF as the solvent. Those reactions were heated to 73° C in a paraffin oil bath.

The reactions were heated for 24 h, at which time the solvent was removed under reduced pressure. The residue was re-dissolved in 200 mL of CHCl₃ and washed three times with equal volumes (150 mL) of 2M HCl. A back extraction was performed on the aqueous layer. Both the washed organic layer and back extraction were combined, dried over MgSO₄ and filtered. The CHCl₃ was removed using reduced pressure, leaving a crude reaction mixture. This reaction mixture was analyzed by tlc to reveal the various products. If only previously known calix[6]arenes were found, then a crude ¹H NMR was obtained and the area under the curves of the known material' s peaks were used to calculate the percentage of 6 and 7 produced by this reaction. Calix[6]arenes 6 and 7 have previously been synthesized in certain reaction conditions³⁹. If a new calix[6]arene was found, then it was isolated by chromatography. The percent of new calix[6]arene produced was obtained by the percent mass of the new calix[6]arene relative to the total mass of calix[6]arenes recovered from the column.

With the t-butoxides in benzene, the ¹H NMR was unclear, so the crude reaction mixture was stirred with 350 mL of hot methanol. A sticky material formed, which was filtered off. Then the methanol was removed under reduced pressure leaving a residue. A ¹H NMR of the residue was then taken. If the ¹H NMR was still unclear, then the calix[6]arenes were isolated by chromatography. The percentage of each isomer of

calix[6]arene produced was obtained by the percent mass of that specific isomer of calix[6]arene relative to the total mass of calix[6]arenes recovered from the column.

5.0 CONCLUSIONS

With the more rigid design of the *m*-xylenyl bridge having less ionophoric capabilities and a less reactive leaving group as compared to its counterpart, this leads to better stereochemical control of the bis-bridging reactions. The only cation interaction involved the phenolates in the stabilization of the transition states. The bridging unit itself has better geometric complementarity as a result of it only being a five atom tether, to span the intraannular distances between the B/F and C/E rings. This enables more conversion of the starting material to various products.

Due to the less rigid design of the triethyleneoxy bridge having more ionophoric capabilities and a more reactive leaving group, less selectivity of crown[4]ether bis-bridged calix[6]arenes was produced. Eight atoms in the tether also helped to decrease the synthesis of products. While the crown[4]ether bis-bridged calix[6]arenes have a better ability to bind to various sized atoms in their binding site, this leads to less stereochemical control of the reaction. Because the reaction is less stereoselective, two new bridged calix[6]arenes were able to be synthesized.

REFERENCES

1. Diamond, D.; Nolan, K. *Analytical Chemistry* **2001**, *73*, 22A.
2. Pitarch, M.; McKee, V.; Nieuwenhuyzen, M.; McKervey, M. A. *J. Org. Chem.* **1998**, *63*, 946.
3. Otsuka, H.; Shinkai, S. *Supramolecular Science* **1996**, *3*, 189.
4. van Duynhoven, J. P. M.; Janssen, R. G.; Verboom, W.; Franken, S. M.; Casnati, A.; Pochini, A.; Ungaro, R.; de Mendoza, J.; Nieto, P. M.; Prados, P.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, 5814.
5. Otsuka, H.; Araki, K.; Shinkai, S. *Chem. Express* **1993**, *8*, 479.
6. Otsuka, H.; Araki, K.; Sakaki, T.; Nakashima, K.; Shinkai, S. *Tetrahedron Lett.* **1993**, *34*, 7275.
7. Gutsche, C. D. *Calixarenes Revisited* Monographs in Supramolecular Chemistry ed; Stoddart, J. F. The Royal Society of Chemistry: Cambridge, England, **1998**.
8. Janssen, R. G.; Verboom, W.; Reinhoudt, D. N.; Casnati, A.; Freriks, M.; Pochini, A.; Ugozzoli, F.; Ungaro, R.; Nieto, P. M.; Carramolino, M.; Cuevas, F.; Prados, P.; de Mendoza, J. *Synthesis* **1993**, 380.
9. Conner, M. D.; Janout, V.; Regen, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 1178.
10. Conner, M. D.; Janout, V.; Kudelka, I.; Dedek, P. Zhu, J.; Regen, S. L. *Langmuir* **1993**, *9*, 2389.
11. Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1992**, *57*, 3160.
12. Neri, P.; Foti, M.; Ferguson, G.; Gallagher, J. F.; Kaitner, B.; Pons, M.; Molins, M. A.; Giunta, L.; Pappalardo, S. *J. Am. Chem. Soc.* **1992**, *114*, 7814.
13. Groenen, L. C.; van Loon, J.-D.; Verboom, W.; Harkema, S.; Casnati, A.; Ungaro, R.; Pochini, A.; Ugozzoli, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1991**, *113*, 1285.
14. Han, S.-Y.; Kang, M.-H.; Jung, Y. E.; Chang, S.-K. *J. Chem. Soc., Perkin Trans.* **1994**, *2*, 835.
15. Otsuka, H.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1994**, *59*, 1542.
16. Otsuka, H.; Araki, K.; Shinkai, S. *Tetrahedron* **1995**, *51*, 8757.

17. Casnati, A.; Minari, P.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1991**, 1413.
18. Neri, P.; Pappalardo, S. *J. Org. Chem.* **1993**, *58*, 1048.
19. Neri, P.; Consoli, G. M. L.; Cunsolo, C.; Piattelli, M. *Tetrahedron Lett.* **1994**, *35*, 2795.
20. Herve, G.; Hahn, D. U.; Herve, A.-C.; Goodworth, K. J.; Hill, A. M.; Hailes, H. C. *Org. Biomol. Chem.* **2003**, *1*, 427.
21. Yang, F.; Chen, Y. *Eur. J. Org. Chem.* **2001**, 365.
22. Li, J.; Chen, Y.; Lu, X. *Tetrahedron* **1999**, *55*, 10365.
23. Kraft, D.; Bohmer, V.; Vogt, W.; Ferguson, G.; Gallagher, J. F. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1221.
24. Arnecke, R.; Bohmer, V.; Ferguson, G.; Pappalardo, S. *Tetrahedron Lett.* **1996**, *37*, 1497.
25. Ross, H.; Luning, U. *Angew. Chem.* **1995**, *107*, 2723.
26. Ross, H.; Luning, U. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2555.
27. Otsuka, H.; Araki, K.; Matsumoto, H.; Harada, T.; Shinkai, S. *J. Org. Chem.* **1995**, *60*, 4862.
28. Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1996**, *61*, 2511.
29. Casnati, A.; Jacopozi, P.; Pochini, A.; Ugozzoli, F.; Cacciapaglia, R.; Mondolini, L.; Ungaro, R. *Tetrahedron* **1995**, *51*, 591.
30. Kanamathareddy, S.; Gutsche, C. D. *J. Am. Chem. Soc.* **1993**, *115*, 6572.
31. Asfari, Z.; Bohmer, V.; Harrowfield, J.; Vicens, J. *Calixarenes 2001* ed. Saadioui, M. Kluwer Academic Publishers: Dordrecht, The Netherlands, **2001**.
32. Neri, P.; Ferguson, G.; Gallagher, J. F.; Pappalardo, S. *Tetrahedron Lett.* **1992**, *33*, 7403.
33. Ross, H.; Luning, U. *Liebigs Ann.* **1996**, 1367.
34. Ko, S. W.; Lee, S. H.; Park, K.-M.; Lee, S. S.; Nam, K. C. *Supramolecular Chemistry* **2003**, *2*, 117.

35. Otsuka, H.; Suzuki, Y.; Ikeda, A.; Araki, K.; Shinkai, S. *Tetrahedron* **1998**, *54*, 423.
36. Chen, Y.; Chen, Y. *Tetrahedron Lett.* **2000**, *41*, 9079.
37. Araki, K.; Akao, K.; Ikeda, A.; Suzuki, T.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 73.
38. Takeshita, M.; Nishio, S.; Shinkai, S. **1994**, *59*, 4032.
39. Blanda, M. T.; Farmer, D. B.; Brodbelt, J. S.; Goolsby, B. J. *J. Am. Chem. Soc.* **2000**, *122*, 1486.
40. Gutsche, C. D. *Calixarenes* Monographs in Supramolecular Chemistry ed, Vol. 1; Stoddart, J. F. The Royal Society of Chemistry: Cambridge, England, **1998**.
41. Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1990**, *68*, 234.
42. Gutsche, C. D.; Dhawan, B.; Leonis, M.; Stewart, D. *Org. Synth.* **1990**, *68*, 238.
43. Munch, J. H.; Gutsche, C. D. *Org. Synth.* **1990**, *68*, 243.
44. Kammerer, H.; Happel, G.; Bohmer V.; Rathay, D. *Monatsh. Chem.* **1978**, *109*, 767.
45. Gutsche, C. D.; Levine, J. A. *J. Am. Chem. Soc.* **1982**, *104*, 2652.
46. Nam, K. C.; Park, K. S. *Bull. Korean Chem. Soc.* **1995**, *16*, 153.

Vita

Kenneth Albert Pavlat is the son of Dr. William Albert Pavlat and Mrs. Mary Evelyn Pavlat and was born in San Antonio, Texas, on August 1, 1978. He grew up in Granger, Texas, and graduated from Granger High School in 1996. Following high school, he entered Southwest Texas State University and received the degree of Bachelor of Science in May, 2000. He went to work at The University of Texas Health Science Center at San Antonio for the summer until he entered the Graduate School of Southwest Texas State University in January 2001. In August, 2003, he received the degree of Master of Science.