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Functionalization of Resorcinarenes and Study of Antimicrobial Activity

Kirankirti Muppalla
University of South Florida

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Functionalization of Resorcinarenes and Study of Antimicrobial Activity

by

Kirankirti Muppalla

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science
Department of Chemistry
College of Arts and Sciences
University of South Florida

Major Professor: Kirpal S Bisht, Ph.D.
Roman Manetsch, Ph.D.
Abdul Malik, Ph.D.

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DEDICATION

I would like to dedicate my thesis as a token of appreciation to my beloved mother Mrs. Bhanumati Muppalla who motivated me to pursue this degree and to my father Mr. M.B.V. Subrahmanyam for his guidance. I wish to dedicate this thesis to my brother Mr. M.C. Dharmadeep for his inspiration and guidance. I would also like to dedicate this thesis to my husband Mr. Vinod Gudavalli for his support.

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LIST OF ABBREVIATIONS

RCM	Ring closing metathesis	4
BF ₃	Boron trifluoride	4
NBS	N-Bromosuccinimide	9
NMR	nuclear magnetic resonance	10
ORTEP	oak ridge thermal ellipsoid plot	10
MALDI MS	matrix assisted laser desorption ionization mass spectrometry	12
APCI MS	atmospheric pressure chemical ionization mass spectrometry	13
¹³ C NMR	carbon nuclear magnetic resonance	13
¹ H NMR	proton nuclear magnetic resonance	14
R _f	retention factor for chromatography	16
DEPT NMR	distortionless enhancement by polarization transfer nuclear magnetic resonance	19
DCM	dichloromethane	27
TLC	thin layer chromatography	27
THF	tetrahydrofuran	27
δ	chemical shifts for nuclear magnetic resonance	34
DMSO	dimethylsulfoxide	34
<i>J</i>	coupling constant for NMR	34

m/z

mass/charge for mass spectrometry

42

Functionalization of Resorcinarenes and Study of Antimicrobial Activity

KiranKirti Muppalla

ABSTRACT

Cavitands are very important class of compounds in supramolecular chemistry. These molecules contain rigid enforced cavity, and have attracted considerable attention in supramolecular chemistry as building blocks for the construction of carcerands, hemicarcerands, and other host guests complexes. Nearly 40 years ago, Niederl and Vogel laid foundation for the study of such type of condensation reactions. In our laboratory we are involved in synthesis of resorcinarenes with readily available substrates such as resorcinol and aldehydes to form a cyclic tetramer.

Herein, I present detailed studies about the functionalization of the synthesized tetramers and their antimicrobial activity. Octahydroxy resorcinarenes were synthesized and perallylated which served as acyclic diene precursors for ring closing metathesis reaction. Studies were carried out to see effect of C-2 substituent of resorcinol and effect of aryl substituents, and aliphatic substituents on ring closing metathesis. This thesis describes the synthesis of bridged resorcinarenes and study of antimicrobial activity of resorcinarenes.

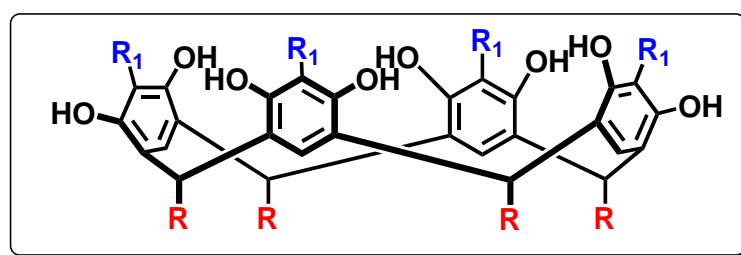
CHAPTER 1. INTRODUCTION

1.1. Introduction to Resorcinarenes

Cavitands namely bridged resorcinarenes can be defined as molecules that have constrained structure large enough to host other molecules^{1,2}. The original term cavitand was coined by noble laureate D.J.Cram, who defined cavitands as “synthetic organic compounds with enforced cavities large enough to complex complementary organic compounds or ions”¹. They have been established as fruitful platform for the attachment of different ligating sites giving rise to ionophores for anions, cations, neutral molecules.^{4,5,6} Resorcinarenes such as **1** (**Figure 1**) are cyclic tetramers readily formed by the acid-catalyzed condensation of resorcinol with aldehydes.^{1,3} Resorcinarenes have been widely exploited as a basis for making macrocyclic host molecules in a variety of supramolecular systems, These cavitands have the ability to encapsulate and stabilize guests molecules, and to catalyze chemical transformations within their “microreactor” cage like structure.⁷

In 1870, Adolf Von Baeyer observed a red-colored solution upon addition of concentrated sulfuric acid to an ethanolic solution of benzaldehyde and resorcinol.⁸ The red-colored solution yielded, in several days, a crystalline compound. In 1883, Michael determined that the crystalline compound formed was from an equal number of benzaldehyde and resorcinol molecules with loss of water molecules.⁹ In 1940, Vogel and Niederl¹⁰ prepared the crystalline compound described by Baeyer and its

peracetate derivative. Molecular weight determinations of the crystalline compound and the peracetate derivative led them to establish the ratio of the resorcinol and the aldehyde to be 4:4, i.e., each molecule of the resorcinarene contained four molecules of the resorcinol with four molecules of the aldehyde, with loss of 4 molecules of water.¹¹ The crystal structure of the resorcinarene was first solved by Erdtman and coworkers in 1968.¹²

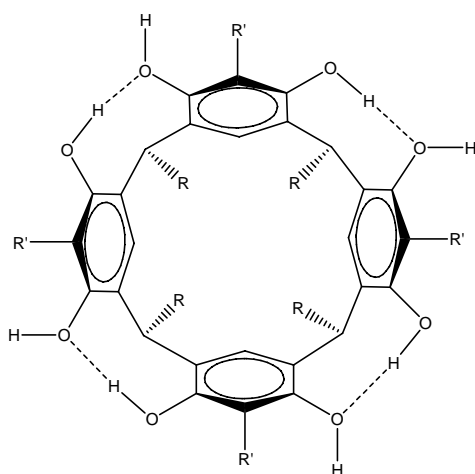


$R_1 = \text{H, CH}_3, \text{OH, Br, NO}_2$

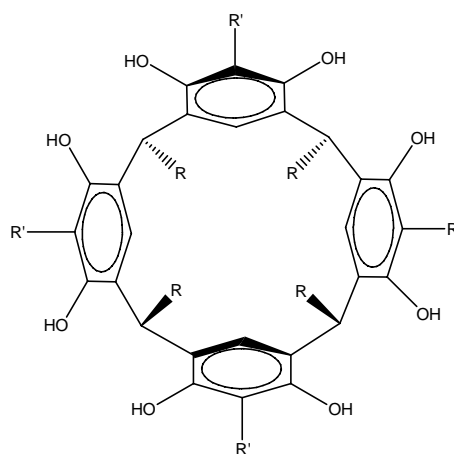
$R = \text{Aliphatic or Aromatic substituents}$

Figure 1. Structure of Resorcinarene

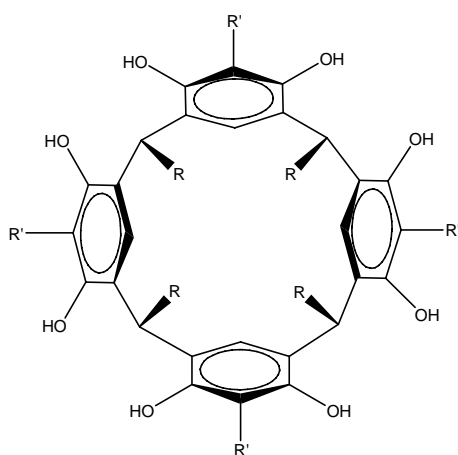
Macrocyclic ring of resorcinarenes can adopt five symmetrical arrangements, namely, crown, chair, boat, diamond and saddle (**Figure 2**).^{1a,b,12} However boat and chair are the two majorly preferred conformations depending on different R and R_1 substituents on the cavitands.¹³



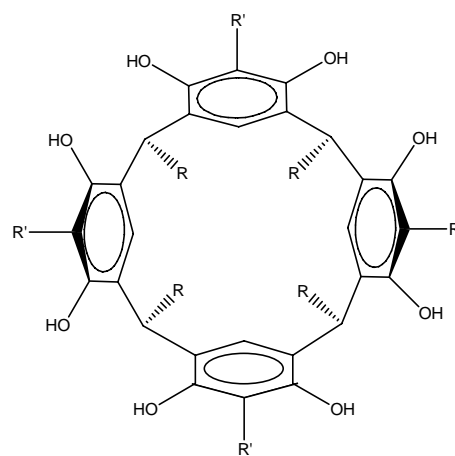
C_{4v} : Crown



C_{2h} : Chair



D_{2d} : saddle



C_{2v} : boat

Figure 2. Conformations of Resorcinarene (Top View)

Resorcinarene cavitands are of particular interest due to their robust cavity which can be modified at the upper or lower rims without compromising the structural integrity of the inner cavity.^{14,1c} Intramolecular cyclizations, linkage of the neighboring phenolic groups

on the adjacent phenyl rings, are the method of choice which can lead to conformationally locked "bowl shaped" resorcinarene cavitands.¹⁵ Owing to the ease of their synthesis, resorcinarenes often have been used as a starting material for a wide variety of compounds.¹⁶ Additionally, in these molecules the upper rim can be varied by different functionalities, i.e., substituents can be added between two electron releasing hydroxyl groups. Further modification have been reported with bridging groups, e. g., methylene bridged, ethylene bridged, and propylene bridged compounds have been prepared.¹⁷

Resorcinarenes can be prepared in high yields by condensation of resorcinol and aldehydes without using any template or high dilution techniques. In recent years, other methods of preparation of resorcinarenes have been developed. Notably, Lewis acid catalyzed tetramerization of cinnamates to a series of C-alkyl resorcinarenes has been developed by Bruno Botta *et al*¹⁸. Specifically, 2, 4-dimethoxycinnamic acid was used as starting material under carefully controlled reaction conditions employing BF₃ as a Lewis acid catalyst. This method allows preparation of the resorcinarenes with different functionalities at the lower rim, which require multi-step approach by original condensation reaction.

Ring closing metathesis (RCM) is increasingly becoming an efficient approach for the synthesis of medium to large ring systems. Advancement in the design of the catalyst leading to their remarkable functional group tolerance, operational simplicity, high stability and commercial availability has greatly contributed to the popularity of the RCM reaction. In a recent report McKervey¹⁹ and Chen²⁰ have reported use of RCM in bis- and tetracalix[4]arenes. The bridging reaction, tandem RCM ring closing, can be

used to manipulate the cavity size and hence can be used to modify the properties of the cavitand. However, there has been no report in literature of RCM reaction to manipulate the cavity size in resorcinarene cavitands.

In chapter 2 I will describe our effort on RCM reaction on resorcinarene and its effect on the cavity size. The ring closing metathesis reaction using Grubb's catalyst (Gen I) was investigated on perallylated resorcinarenes, where allyl groups on adjacent phenyl rings serve as acyclic diene precursors, led to the formation of bridged resorcinarene cavitands. The diameter of the upper rim was thus enlarged and the cavity size can be further manipulated by functionalization. This report discusses in detail the effect of C-2 substituents of resorcinol along with effect of small chain aliphatic, long chain aliphatic, and aryl substituents on ring closing metathesis reaction.

The pursuit of antimicrobially active compounds against a variety of microorganisms is an area of intense and important research. Antimicrobial activity of calixarenes was tested by Lamartine²¹ *et al* in 2002. They conducted preliminary screening of 57 calixarenes to assay their potential as antimicrobially active compounds against *Corynebacterium fusarium*. Of these compounds tested, calixarenes which containing sulfonate group and hydroxyl group were found to exhibit antimicrobial activity.²¹ Surprisingly, there has been no report on antimicrobial activity of resorcinarenes in the literature. In the chapter 3, I report the antimicrobial activity of resorcinarenes having different side chains, substitution groups against a diverse set of bacteria and yeasts.

CHAPTER 2

SYNTHESIS OF RESORCINARENES

2.1 Synthesis of Octahydroxy Resorcinarenes

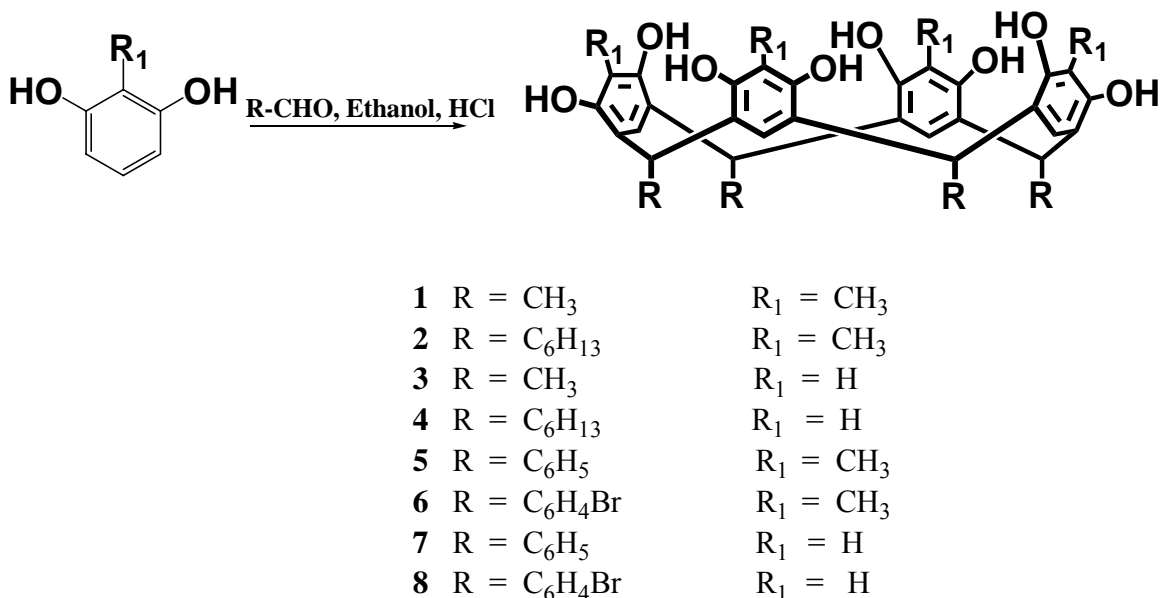
2.1a- Synthesis of Octahydroxy Resorcinarenes with aliphatic substituents (1-4)

Resorcinarenes **1** and **2** were prepared by condensation of methyl resorcinol and acetaldehyde/heptaldehyde catalyzed by hydrochloric acid in ethanol (**Scheme 1**). The reaction mixture was refluxed for 12hrs which led to precipitation of yellow-colored solids. Compounds **1** and **2** were isolated in 67% and 88% respectively. The ^1H NMR spectrum of compound **1** in DMSO d_6 recorded at 400MHz shows a single resonance for H_a at 4.4 ppm (benzylic proton), H_b at 8.6ppm (Hydroxy protons), H_c at 1.9ppm (ArCH_3), H_d at 1.6ppm (CHCH_3) (**Figure 3**) and H_a at 4.2 ppm for compound **2**. The resonances match with literature reported values.¹

Resorcinarenes **3** and **4** were synthesized following a similar procedure except for the reaction temperature which was maintained at 45°C. Products were precipitated in ice cold water as light yellow colored solids with 48% and 78% yields, respectively. The ^1H NMR spectra of compounds **3** and **4** was similar to compounds **1** and **2** except for resonance of methyl proton at 1.97 ppm. The ^{13}C spectrum of these compounds were interpreted and they match with literature reported values.¹

2.1b Synthesis of Octahydroxy Resorcinarenes with Aromatic substituents (5-8)

In a procedure similar to that described for compounds **1-4**, resorcinarenes **5** and **6** were prepared by condensation of methyl resorcinol and benzaldehyde/bromobenzaldehyde (**Scheme 1**). The reaction mixture was refluxed for 12hrs which led to precipitation of yellow-colored solids. Resorcinarenes **5** and **6** were isolated in 88% and 90% yield, respectively. The ^1H NMR spectra of compounds **5** and **6** in DMSO-d_6 , recorded at 400 MHz, showed two resonances for H_a at 5.3 ppm and 6.1 ppm (**Figure 4**) suggesting two different chemical environment around H_a , i.e., the compounds **5** and **6** exists in the chair conformation. Literature reports on compound **5** and **6** have confirmed their chair conformation.¹ Using a similar experimental procedure, the condensation of resorcinol with benzaldehyde /bromobenzaldehyde gave compounds **7** and **8** in 56% and 67% yield. The structure of the compound was confirmed from their ^1H and ^{13}C NMR spectral data and it was found to match with the data in literature.¹



Scheme 1. Condensation reaction between resorcinol and aldehyde

The conformational analysis of the compound **1-8**, revealed the existence of two distinct conformations. Compounds **1-4** with alkyl groups (from the aliphatic aldehydes) on the lower rim preferred the crown conformation in solution, while compounds **5-8**, with phenyl ring on the lower rim of the resorcinarene were observed in the chair conformation. **Figure 3** and **Figure 4** shown below are the ^1H NMR spectra for compounds **1** and **6**. The data is in agreement with the structures reported in literature ².

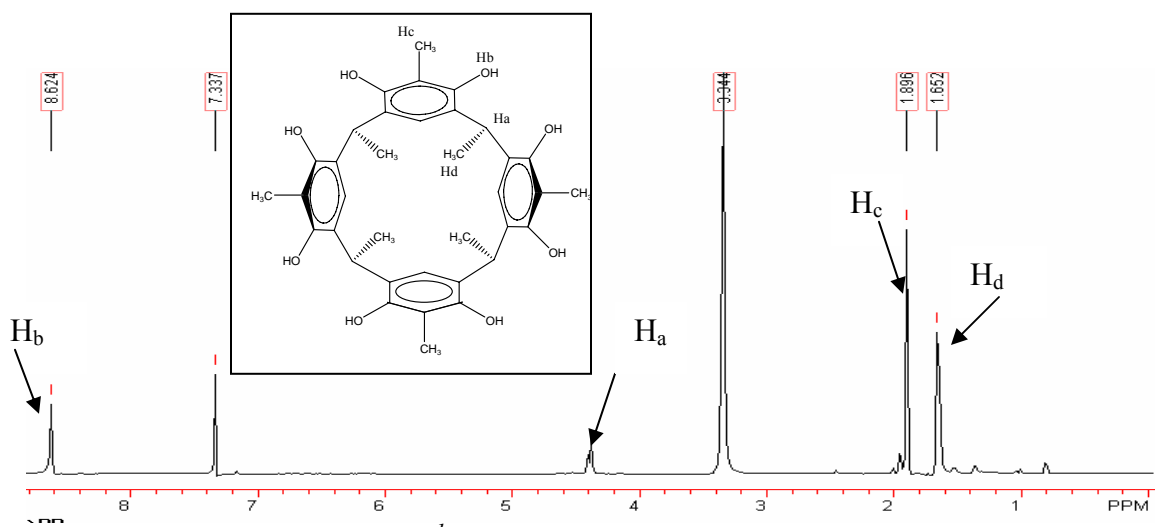


Figure 3. ^1H NMR Spectrum of Compound **1**

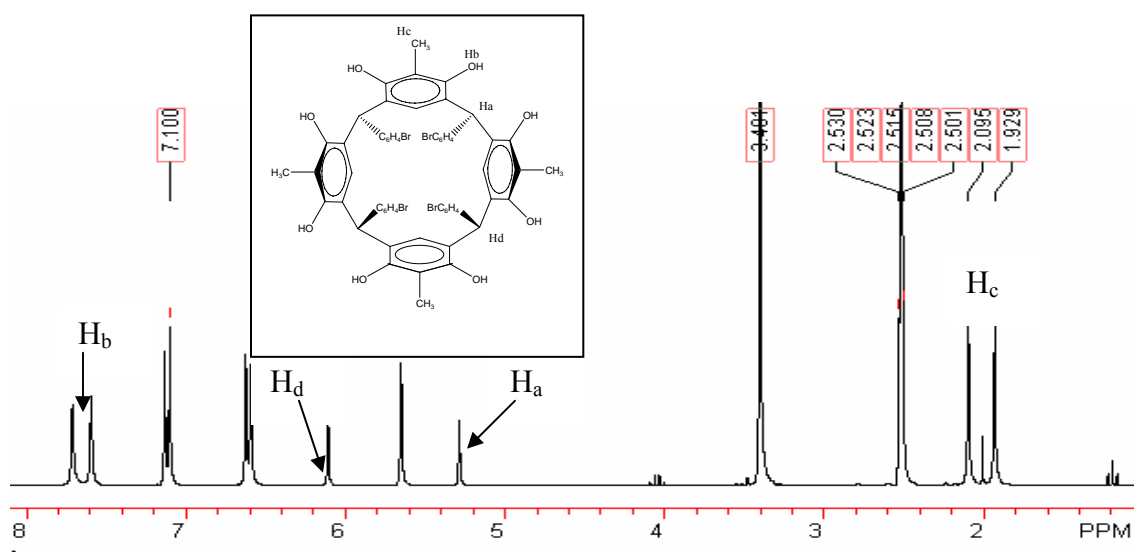
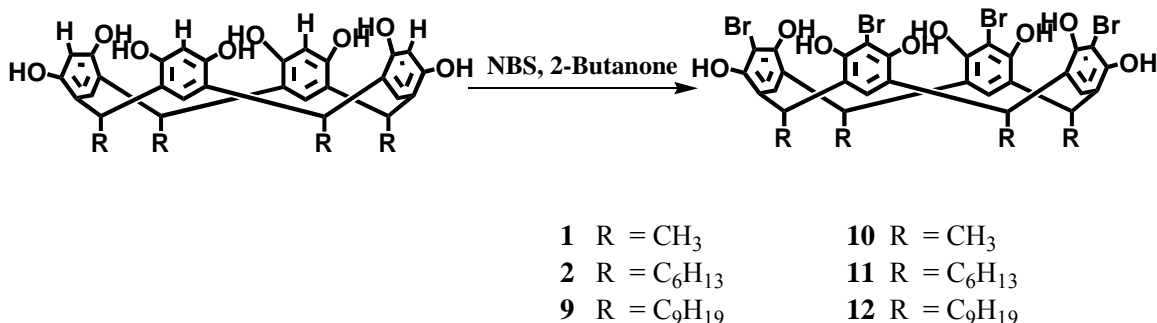


Figure 4. ^1H NMR Spectrum of Compound **6**

2.1c. Bromination of Octahydroxy Resorcinarenes

Bromination of resorcinarenes **1**, **2** and **9** was successfully achieved in ethyl methyl ketone (2-butanone) with NBS at room temperature (**Scheme 2**). The reaction mixture was concentrated *in vacuo*, dissolved in methanol and was precipitated in ice cold water.



Scheme 2. Bromination of Octahydroxy Resorcinarene

¹H NMR of brominated resorcinarenes **10-12** lacked the resonance for the C-2 aromatic proton at 6.3 ppm and in the ¹³C NMR the C-2 (brominated carbon) was shifted upfield from 130.0 ppm to 110.0 ppm.

2.2 Allylation of Octahydroxy resorcinarenes

2.2a Allylation of Octahydroxy resorcinarenes (**1**, **2**, **10**, **11**, **12**)

Resorcinarenes, **1**, **2**, **10**, **11**, **12** were perallylated by reaction with allyl bromide in presence of potassium carbonate in refluxing acetone (**Scheme 3**). The solid residue was filtered off and the reaction mixture was concentrated *in vacuo*. Compound **13-17** were purified by recrystallization from 7:3 mixture of acetone and methanol which yielded colorless crystals. Perallylation in compound **14** was confirmed from the signal's integral values in its ¹H NMR spectrum. Allylic proton (O-CH₂) appeared at 4.1 ppm, the

vinyl proton ($\text{CH}=\text{CH}_2$) appeared at 5.0-5.2 ppm and the non-terminal vinyl proton ($\text{CH}=\text{CH}_2$) appeared at 5.9 ppm. In the ^{13}C NMR spectrum, the allylic carbon appeared at 65.0 ppm, the terminal vinyl carbon appeared at 117.0 ppm and the non-terminal carbon appeared at 134.0 ppm. ^1H NMR of compound **13** had broad resonances, which made it difficult to assign individual resonances. Its ^{13}C NMR showed resonances for the allylic carbon at 74.0 ppm, the terminal vinyl carbon appeared at 116.3 ppm and the non-terminal carbon appeared at 134.7 ppm. Perallylated compounds **15-17** were in accordance with compound **14**. **Figure 5 and 6** shows the ORTEP plot of compound **13**, and **17** which confirmed the existence of molecule in the boat conformation, with all methyl groups in axial position. The crown conformation that existed in hydroxy resorcinarene no longer existed because of the absence of hydrogen bonding, a stabilizing force for the crown conformation.

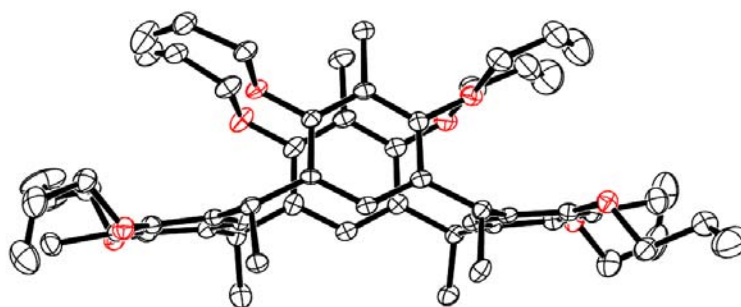
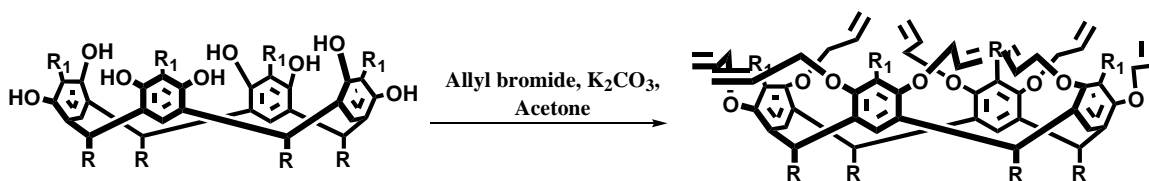


Figure 5. Crystal Structure of Compound 13



Compound No	R	R ₁	% yield
13	CH ₃	CH ₃	76%
14	C ₆ H ₁₃	CH ₃	55%
15	C ₆ H ₁₃	Br	68%
16	C ₉ H ₁₉	Br	35%
17	CH ₃	Br	48%

Scheme 3. Alkylation reaction of octahydroxy resorcinarene

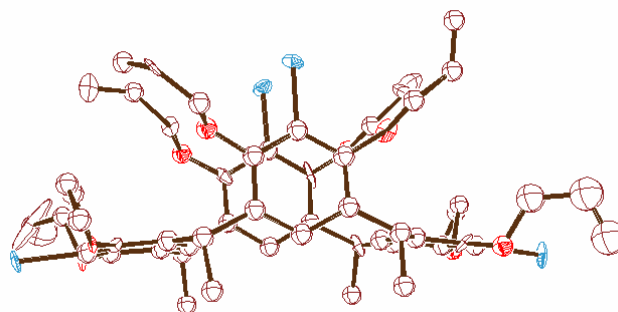


Figure 6: Ortep Plot Compound 17

Figure 7 shown below is the crystal structure of compound **16**, which was crystallized from mixture of acetone and methanol showing the nonyl group in axial position.

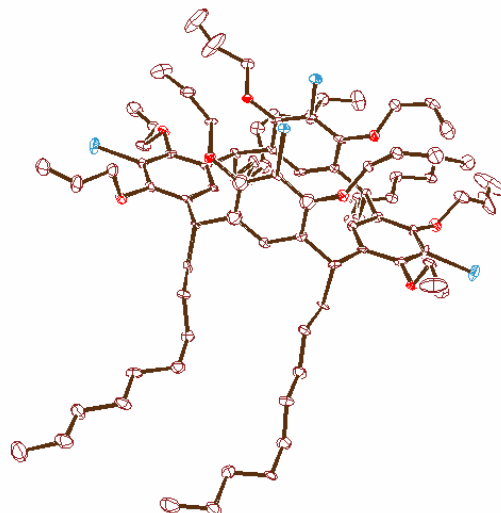
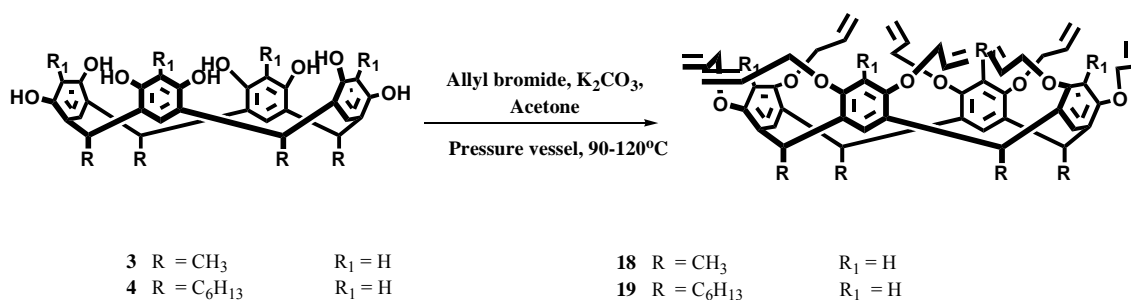


Figure 7: Ortep plot of compound 16

2.2b Allylation of Octahydroxy resorcinarenes (3, 4)

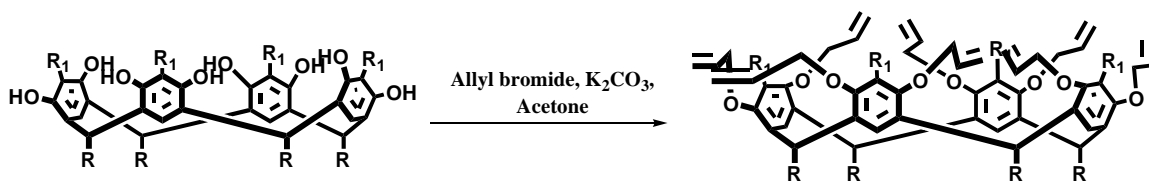
Allylation reaction was tried on compounds **3** and **4** following the established procedure, described earlier, but the desired product yield was low. So, reaction conditions were modified and optimized; Allylation was performed in a pressure vessel, which allowed reaction to be performed at higher temperature and pressure (**Scheme 4**). Reactions in pressure vessel were performed at 120⁰C, and pure products **18** and **19** were obtained upon column chromatography in 78% and 22% yield, respectively. Structures of compounds **18** and **19** were analyzed by ¹H NMR and ¹³C NMR. Mass spectral data (MALDI) on compound **19** [calculated m/z = 1144.77 (M⁺); observed m/z = 1167.985 (M+Na⁺)] was in agreement with the structure.



Scheme 4. Alkylation reaction of octahydroxy resorcinarene **3, 4**

2.2c Alkylation of Octahydroxy compounds 5-8

Resorcinarenes **5-8** were perallylated using acetone as a solvent and potassium carbonate as a base in 46-68% yield (**Scheme 5**). It is important to point out that we also investigated a number of bases (NaH, KO^tBu, etc.) in DMF but a complex mixture of products with low yield became a problem. Also, the removal of DMF by distillation was tedious and might have attributed to the decomposition or side reactions. Compounds **20-23** were analyzed by ¹H- and ¹³C NMR and ^{APCI} MS data. ¹H NMR spectrum clearly showed the changes occurred between 4.0 and 6.0 ppm after perallylation reaction. Allylic proton (O-CH₂) appeared between 4.0-4.4 ppm, the vinylic proton (CH=CH₂) appeared between 5.0-5.4 ppm and the non-terminal vinylic proton (CH=CH₂) appeared between 5.8-6.0 ppm (**Figure 8**). In the ¹³C NMR spectrum, the allylic carbon appeared between 65.0-75.0 ppm, the terminal vinylic carbon appeared between 115.0-120.0 ppm and the non-terminal carbon peak appeared between 125.0-130.0 ppm.



5 R = C ₆ H ₅	R ₁ = CH ₃	20 R = C ₆ H ₅	R ₁ = CH ₃
6 R = C ₆ H ₄ Br	R ₁ = CH ₃	21 R = C ₆ H ₄ Br	R ₁ = CH ₃
7 R = C ₆ H ₅	R ₁ = H	22 R = C ₆ H ₅	R ₁ = H
8 R = C ₆ H ₄ Br	R ₁ = H	23 R = C ₆ H ₄ Br	R ₁ = H

Compound No	DMF/KO ^t Bu	Acetone/K ₂ CO ₃
20	48%	54%
21	68%	68%
22	46%	57%
23	65%	70%

Scheme 5. Alkylation reaction of octahydroxy resorcinarene 5-8

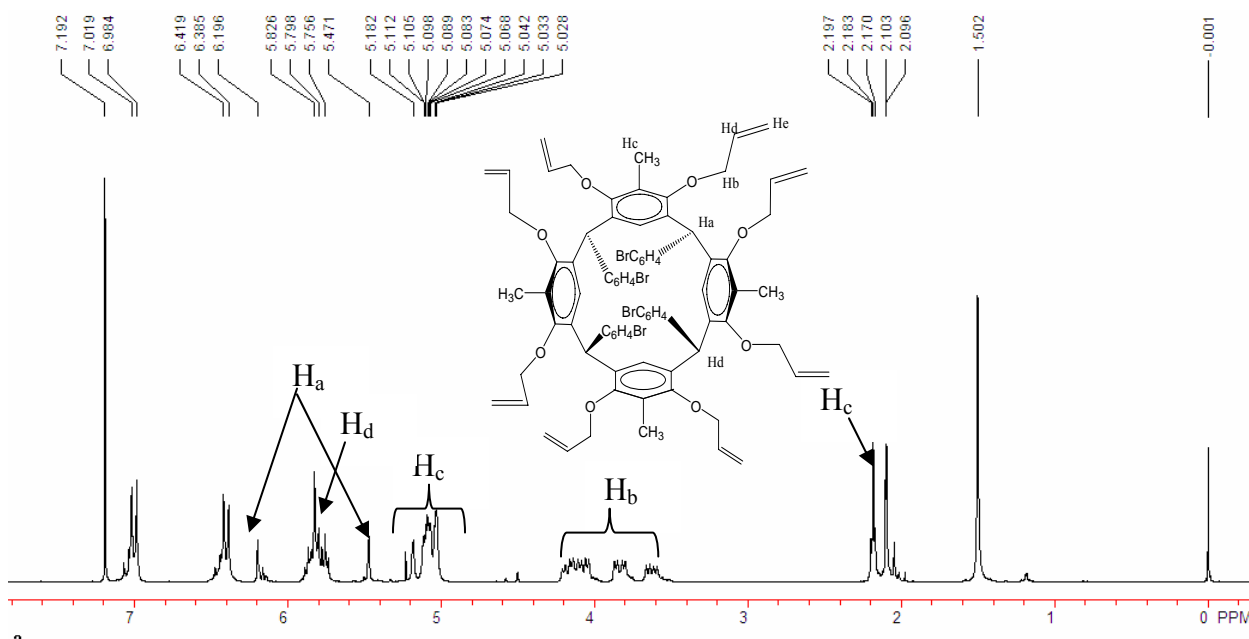


Figure 8: ¹H NMR spectrum of compound 21

Compound **21** was recrystallized as light yellow colored crystals from acetone and methanol solvent (7:3) system. The ORTEP plot of compound **21** (**Figure 9**), shows the resorcinarene ring in the preferred chair conformation with the allyloxy groups on upper rim and the two phenyl rings in axial position and other two in equatorial position .

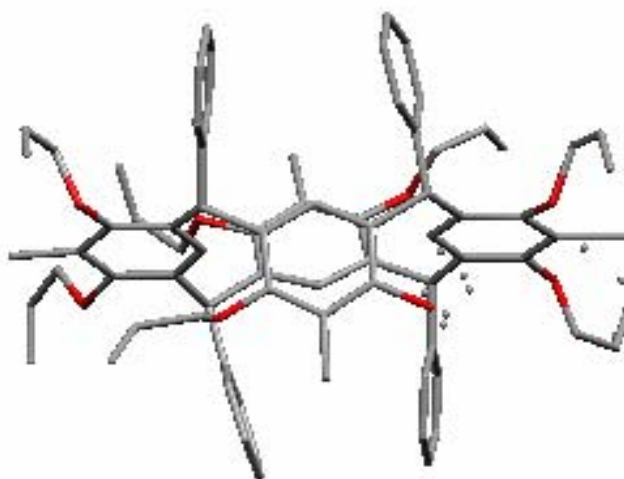


Figure 9. Crystal Structure of Compound 21

2.3. Study of Ring closing metathesis on Resorcinarenes

2.3a Introduction to Ring closing metathesis

Intramolecular cyclizations leading to a bridged structure have been a very important to the synthesis of many cavitands. Ring-closing metathesis (RCM) is becoming a preferred approach to synthesis of medium and large sized macrocyclic molecules. Resorcinarenes have two well-defined rims; a lower rim defined by alkyl or phenyl substituents from corresponding aldehyde and an upper rim defined by hydroxyl groups of resorcinol. The RCM reaction on perallylated resorcinarenes can be utilized to manipulate the cavity size.

In this chapter, I report the RCM reaction on resorcinarenes with small aliphatic chain, longer aliphatic chain, and aromatic rings. Also effect of the resorcinol's C-2 substituent on RCM was investigated. Grubbs' generation I catalyst, which has been widely used for ring closing metathesis due to its remarkable functional group tolerance, operational simplicity, high stability and commercial availability was utilized in this investigation. Interesting conformational dynamics in the octaallyloxy resorcinarene, due to its flexibility, (**Figure 10**) resulted in interesting observations summarized in the following sections.

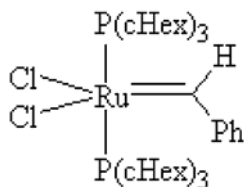
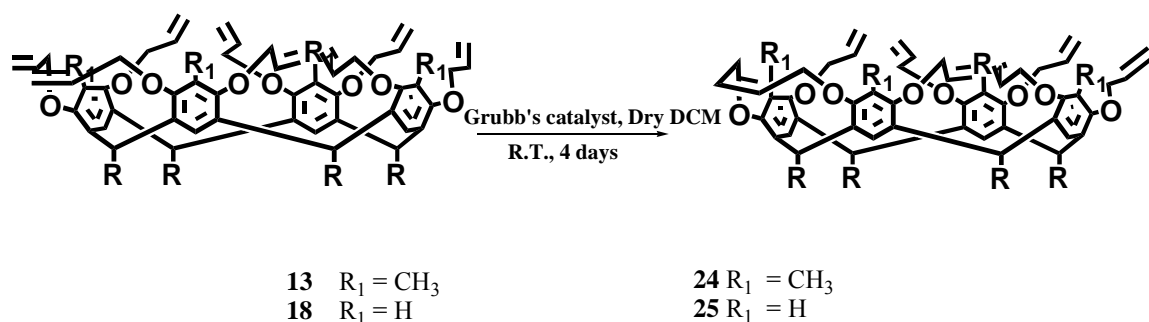


Figure 10. Grubbs' generation I catalyst.

2.3b Ring closing metathesis on compounds **13** and **18**

Resorcinarenes **13** and **18** were subjected to RCM to obtain compounds **24** and **25**, respectively (**Scheme 6**). The reactions were carried out under nitrogen atmosphere in dry dichloromethane using 8 mol % of Grubbs' catalyst (Gen I). The reaction was monitored for 4 days. The desired product was separated by column chromatography in 13-16% yield. Starting material was recovered by column chromatography and was reused in subsequent reaction. The characterization was done by mass spectral data and ^{13}C data. In the ^{13}C NMR spectrum of compound **24** [APCI MS $m/z = 893.5$ ($\text{M}+\text{H}^+$)], the terminal allylic carbon ($\text{C}=\text{CH}_2$) resulted in two resonances at 117.0, 117.8 ppm; the O- CH_2 carbon region had three peaks at 70.0, 73.0 74.0, ppm; the non terminal vinylic carbon was observed as three different resonances at 133.0, 133.7, 134.2 ppm. A careful

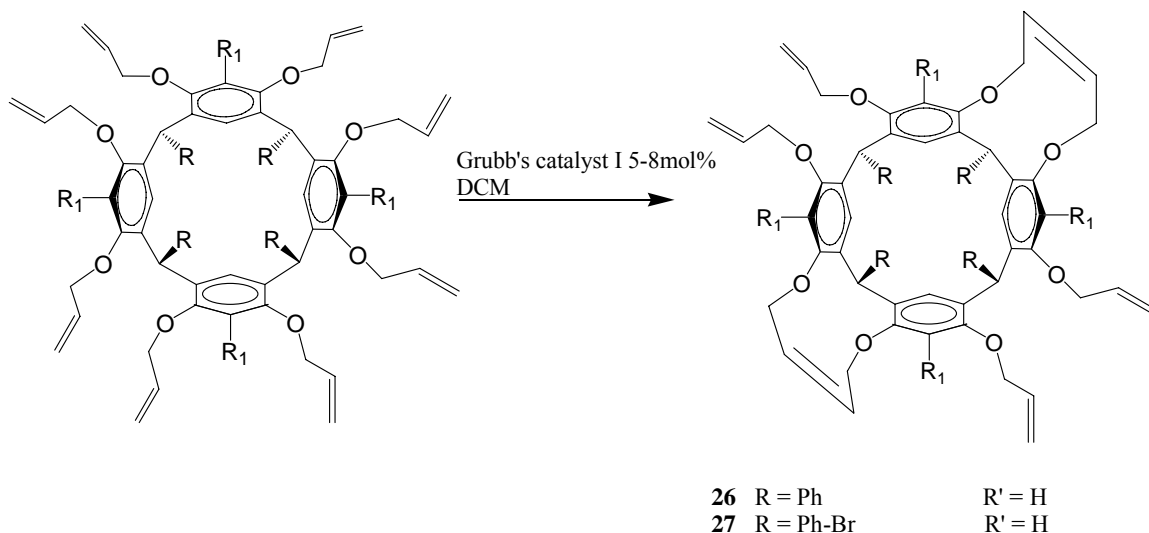
analysis of the NMR data and its molecular weight suggested formation of the one bridged cavitand. The multiplicities in the ^{13}C NMR spectrum can be explained considering that the structure **24** has a plane of symmetry. Mass spectral data (APCI MS) on compound **24** [calculated $m/z = 892.49$ (M^+); observed $m/z = 893.5$ ($\text{M}+\text{H}^+$)] , **25** [calculated $m/z = 836.43$ (M^+); observed $m/z = 837.4$ ($\text{M}+\text{H}^+$)] was in agreement with the structure.



*Scheme 6. Ring Closing Metathesis of Octaallyloxy Resorcinarene **24** and **25**.*

2.3c. Ring Closing on compounds **20-23**

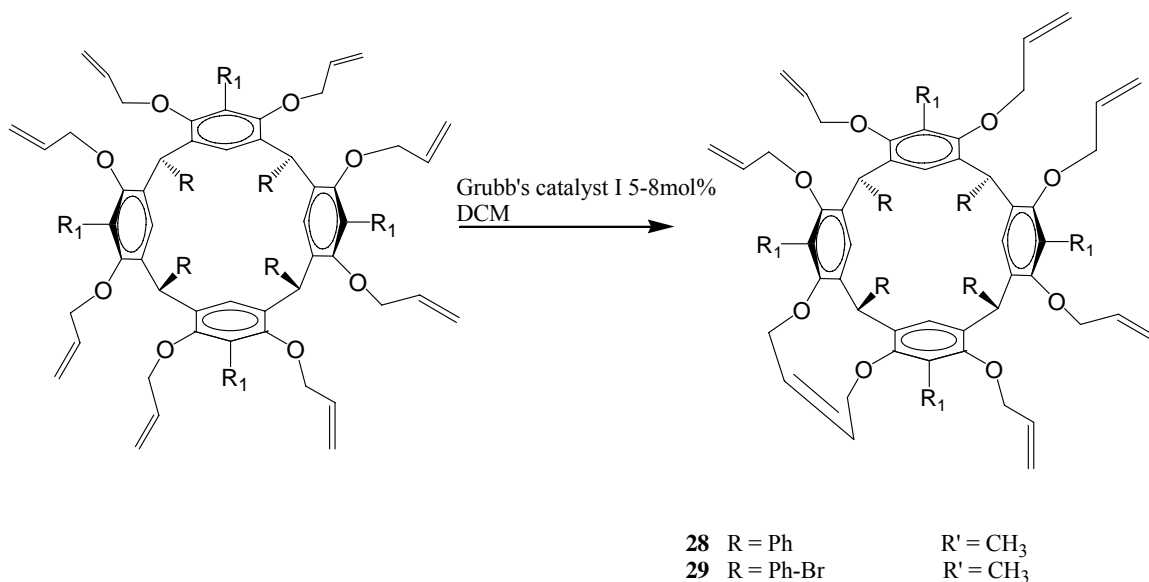
Compounds **20-23** were treated with Grubb's catalyst (Gen I) under conditions described earlier, leading to formation resorcinarene **26-29** in 17-22% yield. Several reactions were performed with increasing concentration of Grubbs catalyst (5-10 mole %), but without increased product yields. Products were isolated by column chromatography using 6% ethyl acetate and hexane mixture as an eluent. **Scheme 7** shown below is the top view representation of the synthetic scheme.



Scheme 7. Ring Closing Metathesis on Resorcinarenes with aryl substituents

^1H NMR data had overlapping, broad resonances and could not be used for confirmation of the structure. Therefore, ^{13}C NMR data was used because of its wider (0-200 ppm) and sharp carbon resonances. Careful analysis of the products suggested a two bridged cavitand. The two fold symmetry, indicated by the doubling of the carbon resonances upon bridge formation, suggested the two bridges were formed across from each other. MALDI Mass spectral measurements confirmed the structure as a two bridged structure; **26** Mass spectral data (APCI MS) on compound **26** [calculated $m/z = 1056.00 (M^+)$; observed $m/z = 1056.46 (M^+)$], **27**, [calculated $m/z = 1368.10 (M^+)$; observed $m/z = 1385.00 (M^+ + \text{H}_2\text{O})$] were in agreement with the structure of the respective compounds. Unfortunately, the compound could not be crystallized for x-ray diffraction data collection.

Following a similar reaction procedure, compound **28** and **29** were synthesized via ring closing metathesis of their respective allyloxy precursors **11** and **12** (Scheme 8). A detailed structural analysis of the products was undertaken. The ^1H and ^{13}C NMR data suggested formation of a single bridged compound.



Scheme 8. Ring Closing Metathesis in case of methyl C-aryl Octaallyloxy Resorcinarene

MALDI Mass spectral data on compound **28** [calculated $m/z = 1140.55 (M^+)$; observed $m/z = 1163.48 (M+Na^+)$], **29** [calculated $m/z = 1456.20 (M^+)$; observed $m/z = 1479.54 (M+Na^+)$] was in agreement with the structure. Yields in both cases were around 10%.

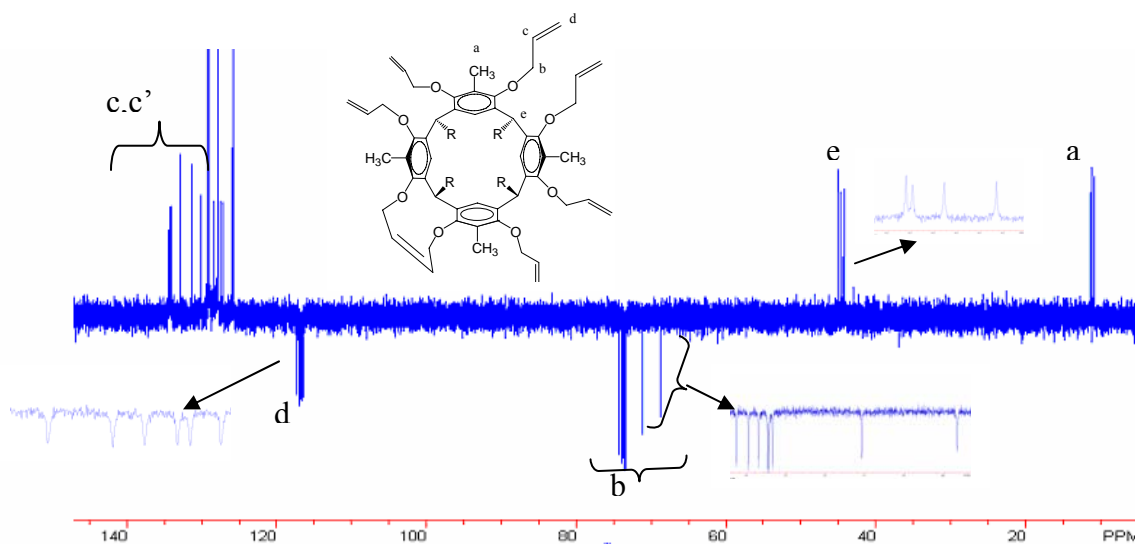
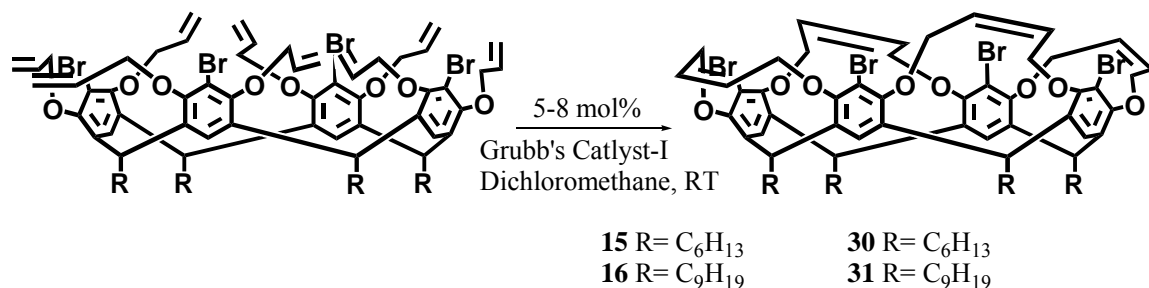


Figure 11. DEPT ¹³C-NMR of compound **29**

2.3d Ring Closing Metathesis on Resorcinarenes **15** and **16**

The perallylated resorcinarenes **15** and **16** served as acyclic diene precursors for ring closing metathesis reaction. Compounds **15**, **16** were treated with Grubb's catalyst (Generation I) in dichloromethane (**Scheme 9**). Reaction was carried out at room temperature for 96 hrs which led to the observation of two spots having lower R_f value than starting substrate on thin layer chromatography. The reaction mixture was subjected to column chromatography in 6% ethyl acetate and hexane. The compound **30** and **31** were isolated in 23% and 32%, respectively. The absence of the terminal vinylic proton (-C=CH₂) peak at 4.5 ppm in ¹H NMR and at 117.0 ppm in ¹³C NMR spectra suggested formation of a bridged cavitands. **Figure 12** shown below is the comparative proton spectrum of compound **31** with its precursor molecule compound **16**.



Scheme 9. Synthesis of Four bridged Resorcinarenes

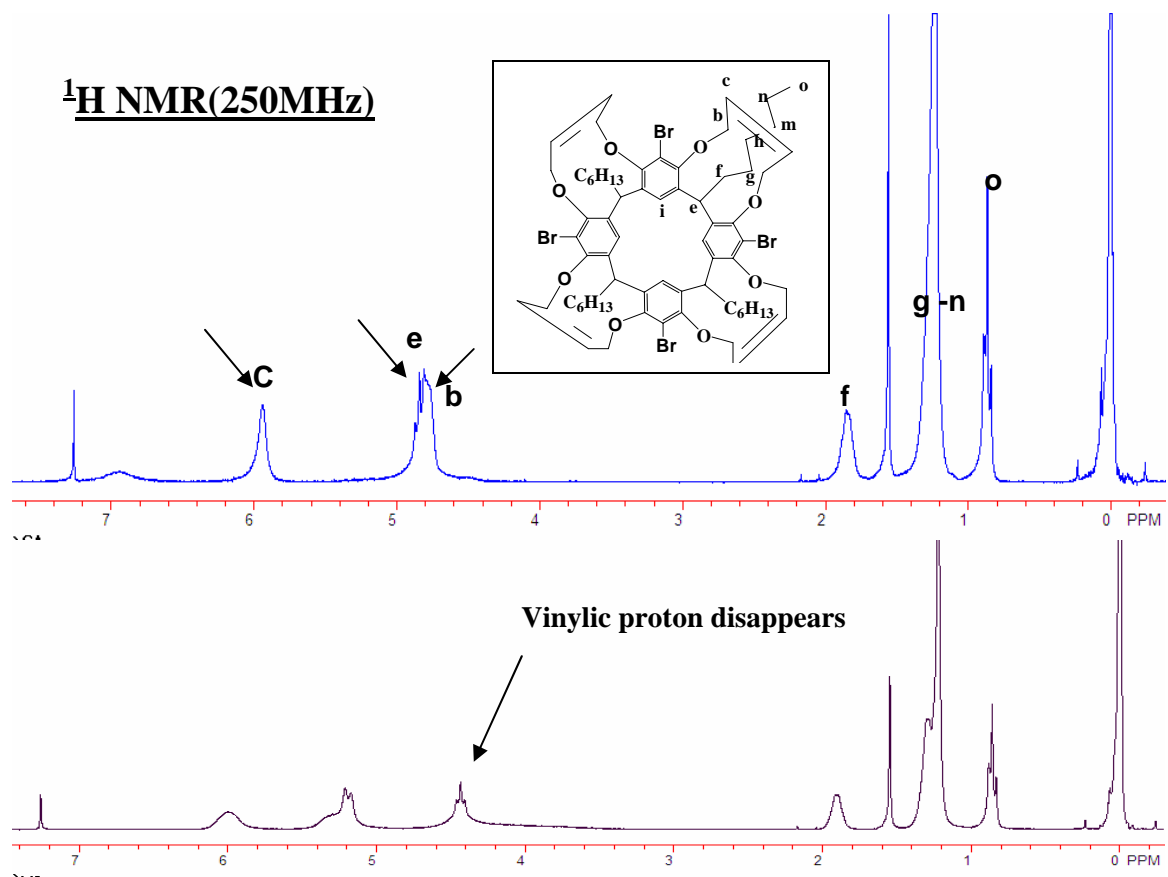
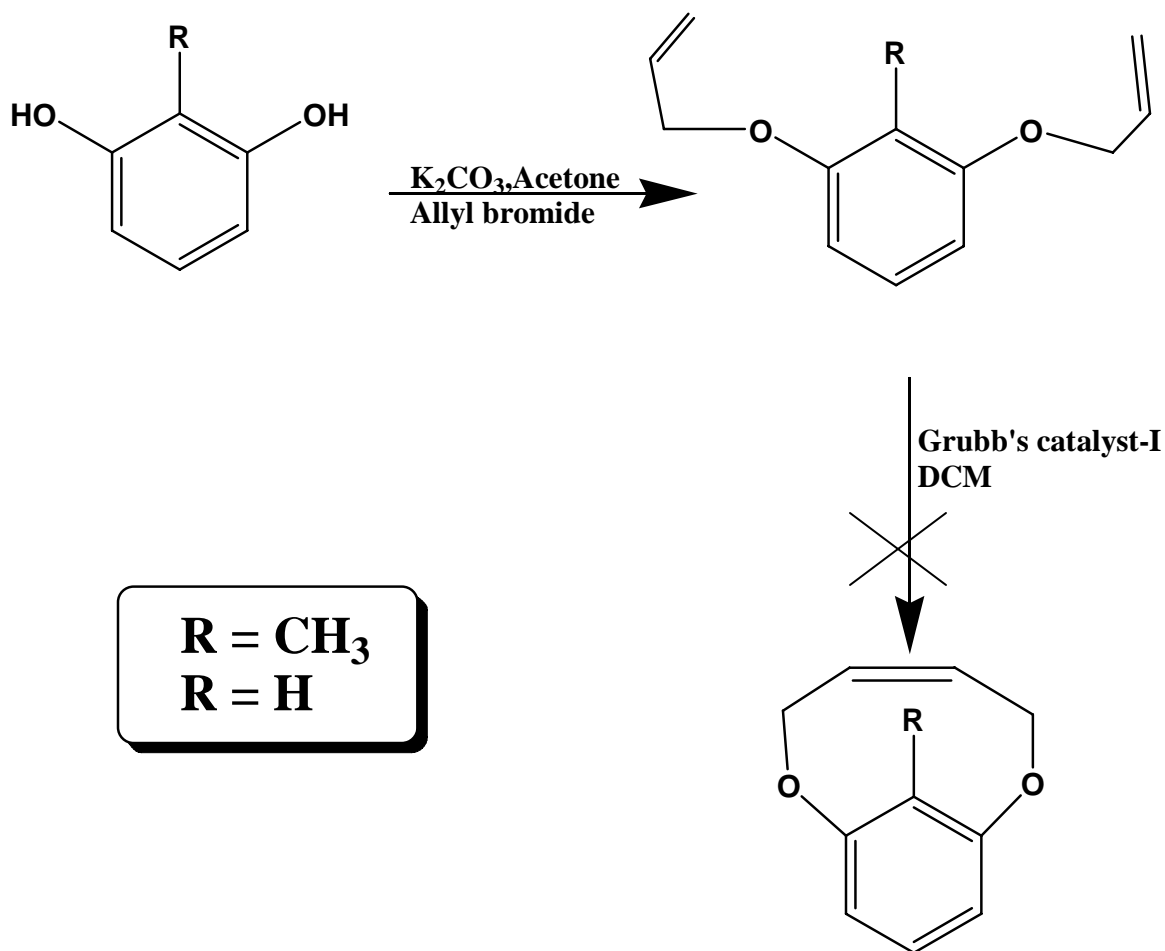


Figure 12. Comparative proton NMR spectrum of compound **31** and its precursor molecule compound **16**

2.4. Study of Inter/Intramolecular Ring Closing

To understand ring closing metathesis and investigate the intra- or inter- molecular ring formation we subjected perallylated resorcinol to RCM reaction using Grubb's catalyst. Reactions were tried with varying reaction concentration and mol % of catalyst. The intra-molecular ring closing was never observed.



Scheme 10. Study of Inter/Intra molecular ring closing

Energy minimization calculation using MM2 MODEL on the resorcinarene **13**, indicated that the intermolecular ring closed structure was about 6 Kcal less than the intermolecular ring closed structure.

Summary

Below given is the table which summarizes the data.(**Table 1**)

<i>Compound No:</i>	<i>R</i>	<i>R₁</i>	<i>Bridges formed</i>
24	CH ₃	CH ₃	one
25	CH ₃	H	one
30	C ₆ H ₁₃	Br	four
31	C ₉ H ₁₉	Br	four
28	C ₆ H ₅	CH ₃	one
29	C ₆ H ₄ Br	CH ₃	one
26	C ₆ H ₅	H	two
27	C ₆ H ₄ Br	H	two

Table 1: Results of Ring closing metathesis

Conclusion

In conclusion to this study, I have investigated the effect of alkyl and aryl substituent on ring closing metathesis. It was observed that longer hydrophobic aliphatic chains favor ring closing metathesis. It was also observed formation of four bridged compound is more favored in compounds with crown conformation over chair conformation. From the studies described in this chapter bulky groups at C-2 position of resorcinol favor ring formation. When smaller group such as hydrogen is present it does not favor ring formation due to steric effects.

CHAPTER 3

LEWIS ACID CATALYZED SYNTHESIS OF RESORCINARENES FROM 2, 4-DIMETHOXY CINNAMIC ACID AND STUDY OF RESORCINARENE'S ANTIMICROBIAL ACTIVITY

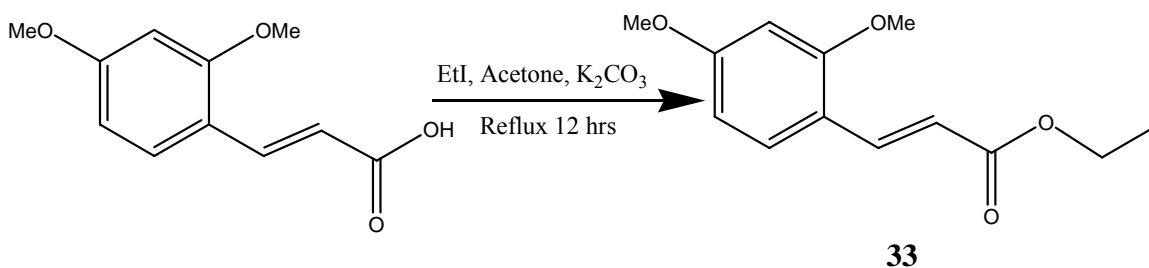
3.1 Synthesis of resorcinarenes from 2, 4 dimethoxy cinnamic acid

Bruno ²⁰ *et al* first described the Lewis acid catalyzed synthesis of resorcinarene starting from 2,4- dimethoxycinnamic acid. It involved esterification of 2, 4-dimethoxy cinnamic acid followed by treatment with BF₃ etherate under carefully controlled conditions leading to the formation of tetramerized resorcinarenes. Influence of Lewis acid, temperature, and reaction time and their effects on the resorcinarene conformation had also been described. Interestingly, it was noted that longer reaction times always led to chair conformation. Using the procedure described by Bruno *et al.*, compound 33 was isolated after a reaction time of 10hrs. This chapter discusses in detail the strategy I employed in preparation of resorcinarenes and their functionalization.

3.2 Synthesis of resorcinarenes

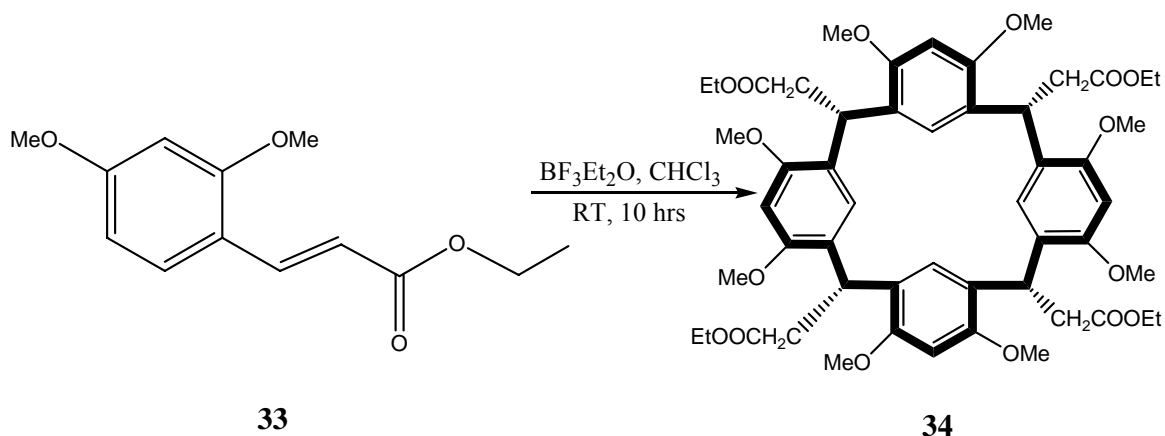
Another high yielding synthesis of resorcinarenes involves the lewis acid catalyzed tetramerization of 2, 4-dimethoxy cinnamates. The synthesis began with the base catalyzed esterification of our starting material 2, 4-dimethoxy cinnamic acid in acetone

with potassium carbonate and ethyl iodide. The reaction was refluxed for 12hrs and filtration of the solid provided us with quantitative yield of ethyl ester of dimethoxy cinnamic acid. **Scheme 12** shown below is the esterification reaction. The compound was characterized by ^1H NMR; the ethyl ester resonances were observed at 1.34 ppm (t, $J=7.25$) for (CH_2CH_3), 4.24 ppm (q, $J= 7.25$) for (CH_2CH_3).



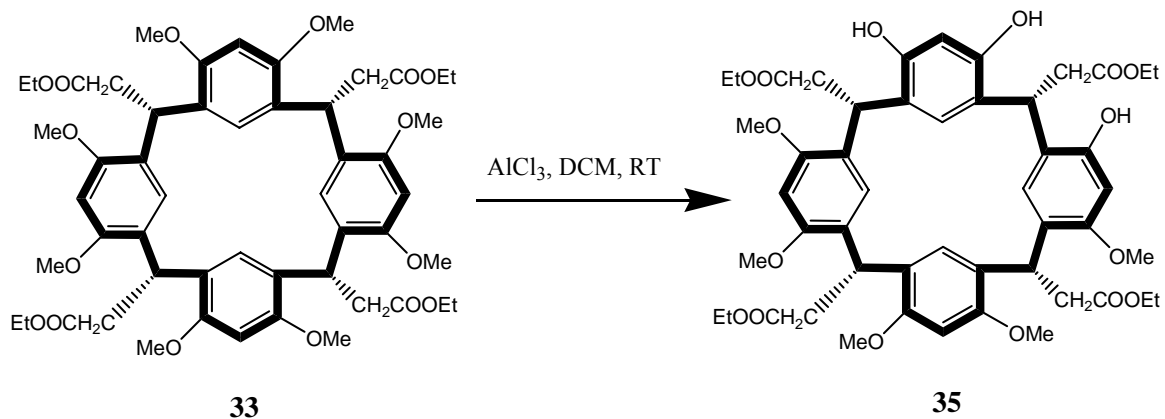
Scheme 11: Esterification of Dimethoxy cinnamic acid

The ester **33** was treated with BF_3 etherate in chloroform at room temperature for 10 hrs, after which the reaction was quenched with methanol and concentrated *in vacuo*. The product **34** was isolated by column chromatography in 6% methanol/dichloromethane mixture in 67% yield. The compound was analyzed by NMR. ^1H NMR- 1.03 (d, $J= 9\text{Hz}$) for methyl protons, 2.87 (d, $J= 7.75\text{Hz}$) for ArCHCH_2 , 3.5ppm (s) for OCH_3 protons, 3.72 (q, $J=4.75\text{Hz}$) for CH_2CH_3 , 4.86 (s) for benzylic proton, 6.19 (d, $J= 9.75\text{hz}$), 6.54 (s) for aromatic protons confirmed that compound exist in crown conformation with the ethyl groups all pointing in axial position. The NMR data was in agreement with the data reported in the literature.²⁰



Scheme 12: Formation of C-ethyl resorcinarene 34

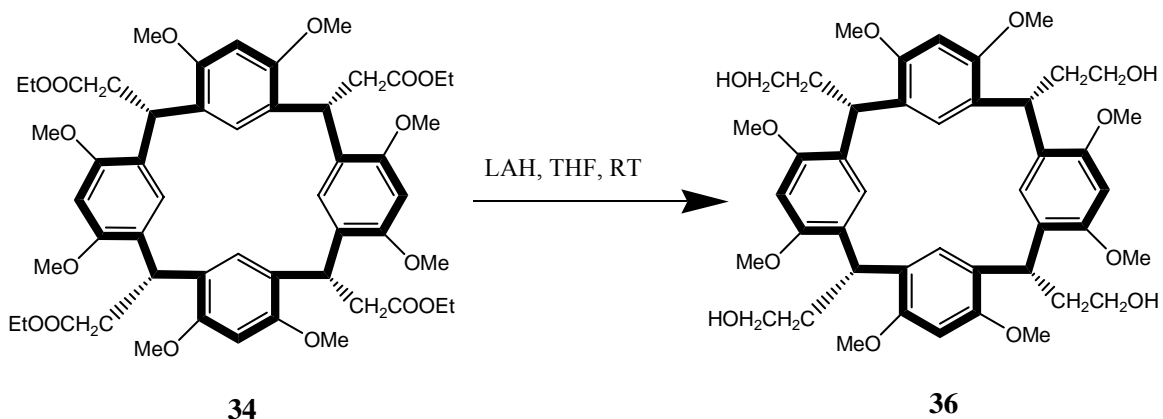
The compound **34** was subjected to demethylation using aluminum trichloride in dichloromethane (**Scheme 14**). The reaction was performed at room temperature for 12 hrs, diluted with dichloromethane and washed with 100ml of water, brine and was separated on a column with 44% yield. The compound was analyzed by NMR which showed resonance for methoxy as well as hydroxyl protons indicating that the compound was partially demethylated to compound **35**.



Scheme 13: Demethylation of compound 35

Compound **34** was subjected to reduction using lithium aluminium hydride in THF. The reaction was monitored by TLC. LAH was added to reaction mixture at 0^oc and reaction

mixture was allowed to warm up to room temperature. Reaction was carried out for 10 hrs after which it was quenched by 0.5ml of water, 0.5ml of saturated sodium chloride solution and extracted into DCM in a separatory funnel. It was concentrated in vacuum, dried and NMR of the product was taken, which indicated the conversion of ester to primary alcohol in 56% yield. New resonance was found for hydroxyl groups at 2.0 ppm with absence of resonances for ethyl peaks. Scheme 15 shown is the reduction reaction of ester to alcohol.



Scheme 15: Conversion of Ester to alcohol

To the conclusion of this chapter, I have employed the easier route in the synthesis of resorcinarenes that cannot be synthesized by normal condensation method.

3.3 Introduction to Study of Antimicrobial activity of Resorcinarenes

The pursuit of antimicrobially active compounds against a wide variety of microorganisms is an area of intense and important research. Antimicrobial activity of calixarenes was tested by Lamartine²¹ *et al* in 2002. In the present study, we examined the relative antimicrobial activity of resorcinarenes having different side chains, substitution groups against bacteria and yeasts. Antimicrobial activity against the various

species was evaluated by zone of inhibition to distinguish between the compounds for this desired property.²¹ Calixarenes can be modified for host molecules with defined structure and function. I have tested resorcinarenes against wide variety of bacteria includes (*P.aeruginosa*, *S. aureus*, *M.luteus*, *E.coli*, *B.subtilis*) and yeasts(*C.albicans*). Not much research was carried out in this field, so we have chosen this area of interest to test the compounds for desired property.

3.4. Testing of resorcinarenes for Antimicrobial activity

I employed Kirby Bauer's disk diffusion method which a standard method that has been used for years to test the compounds for antimicrobial activity and is initial stage to test the activity of compounds. The disk-diffusion method (Kirby-Bauer) is more suitable for routine testing in a clinical laboratory where a large number of isolates are tested for susceptibility to numerous antibiotics. An agar plate is uniformly inoculated with the test organism and a paper disk impregnated with a fixed concentration of an antibiotic is placed on the agar surface. Growth of the organism and diffusion of the antibiotic commence simultaneously resulting in a circular zone of inhibition in which the amount of antibiotic exceeds inhibitory concentrations. The diameter of the inhibition zone is a function of the amount of drug in the disk and susceptibility of the microorganism.

3.4a Preparation of Agar plates

Below shown are the organisms that are employed for testing and nutrient media used for their growth.

a) <i>Bacillus subtilis</i>	}	Nutrient medium
b) <i>Micrococcus luteus</i>		
c) <i>Pseudomonas aeruginosa</i>		
d) <i>Candida albicans</i>		Saboraud Medium
e) <i>Escherichia coli</i>	}	Liquid broth
f) <i>Staphylococcus aureus</i>		

Preparation of Nutrient /Liquid /Saboraud medium

11.5 g of nutrient agar/20g of LB/ 32.5g of Saboraud media that is available commercially were taken into clean 500mL deionized water, heated till the mixture was homogenous. It was autoclaved for 17 min at temperature of 121⁰C to sterilize the media .It was carefully removed from autoclave and cooled down to 50⁰C and 20ml of this media was poured into Petri plates under aseptic conditions. The Petri plates were allowed to cool to room temperature and can be used as and when needed.

Preparation of Broth for growth of Organisms

The broth was prepared similarly to the above described procedure, broth media was used instead. 20ml aliquot of this solution was taken into test tubes and used when needed.

Preparation of Single colony of organism

In order to test the activity of compound it was always advisable that single colony of the organism to be tested. The single colony of the organism was prepared by taking the organism culture and streaking the organism onto Petri plate containing the appropriate medium for growth. It was incubated for 2 days at 37⁰C in incubator, when the growth was seen, a single colony from this Petri plate was transferred into broth medium under aseptic conditions and allowed to incubate for 2 days on a rotary shaker. This culture is good for 2 weeks if stored in the refrigerator. Below shown (**Figure 13**) is the schematic representation of above described procedure.

Preparation of Discs

Paper discs are available commercially. The compound to be tested (25mg) is taken into clean vial and diluted with miscible solvent to 1ml. 40 μ L of this solution contains 1mg of compound , 4 μ l contains 0.1mg and 0.4 μ l contains 0.01mg. The appropriate solution of this was transferred onto paper discs using microlitre pipettes and was dried carefully.

Transfer of Discs onto Agar media

The agar filled plates are warmed to 37⁰C in incubator for 2 hrs before the transfer of discs. The organism was streaked onto agar plates and compound filled disc was carefully transferred onto Petri plate under aseptic conditions. It was incubated at ambient temperature for 1 day and zone of inhibition if seen was noted.

Schematic representation

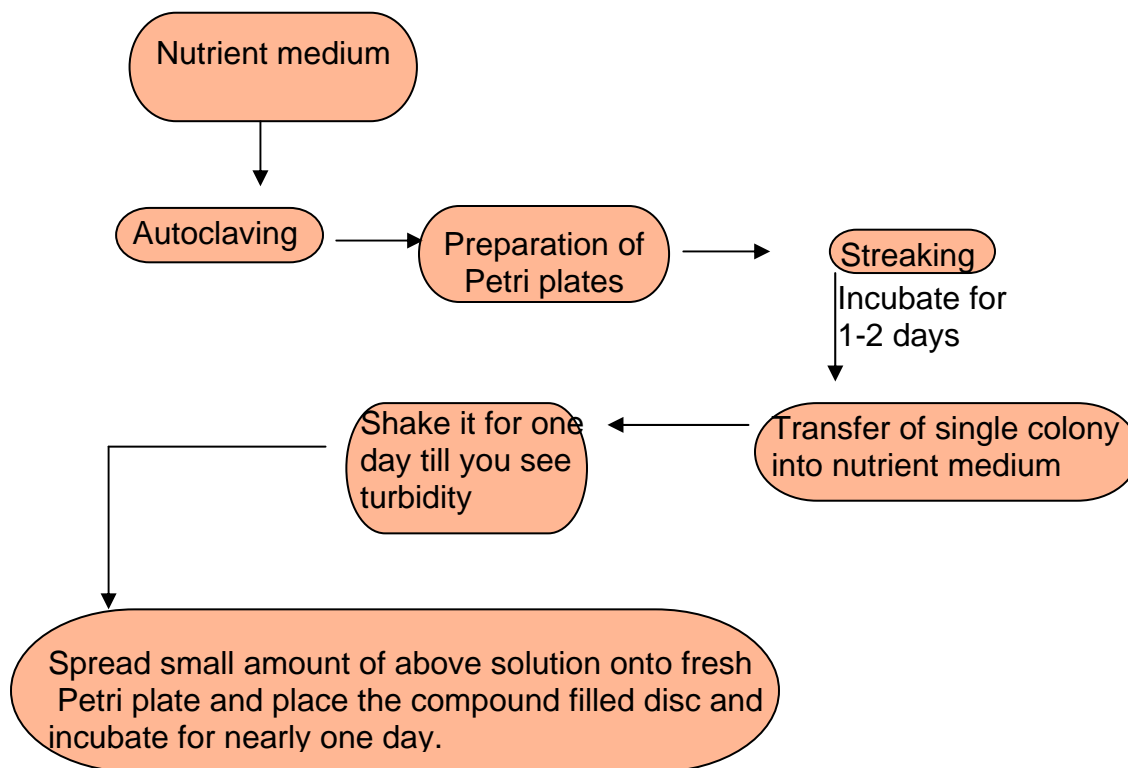


Figure 13 : Schematic representation for preparation of Petri plates

Results and Discussion

I have tested 30 resorcinarenes for antimicrobial activity. The results are summarized in following tables. It was observed that- (1) resorcinarenes prepared from resorcinol had higher activity than those from methyl resorcinol, (2) the allylation of the phenolic hydroxyl resulted in decreased potency, (3) Presence of polar groups on the upper rim led to higher potency.

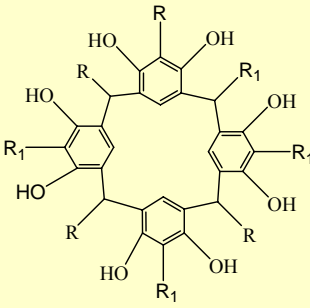
Structure of compound	R	R ₁	Zone of Inhibition	Organism
	CH ₃	C ₆ H ₁₃	12mm	M.luteus
	CH ₃	CH(CH ₂ CH ₃) ₂		
	CH ₃	CH ₃		
	H	CH ₃		
	H	C ₆ H ₁₃		
	H	C ₉ H ₁₉		
	H	CH(CH ₂ CH ₃) ₂		
	H	C ₆ H ₅		
	H	C ₆ H ₄ Br		
H	C ₆ H ₄ Cl			

Table 2: Antimicrobial activity of Hydroxy Resorcinarenes

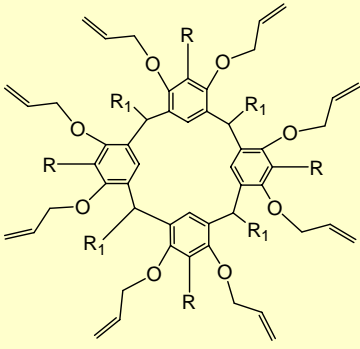
Structure of compound	R	R ₁	Zone of Inhibition	Organism	
	CH ₃	C ₉ H ₁₉	8mm	P. aeruginosa M. luteus	
	CH ₃	CH(CH ₂ CH ₃) ₂			
	CH ₃	CH ₃			
	H	C ₆ H ₁₃			
	H	C ₉ H ₁₉			
	H	CH(CH ₂ CH ₃) ₂			
	H	C ₆ H ₅		8mm	S. aureus
	H	C ₆ H ₄ Br		8mm	P. aeruginosa M. luteus E.coli S.aureus
	H	C ₆ H ₄ Cl			

Table 3: Antimicrobial activity of Perallylated Resorcinarenes

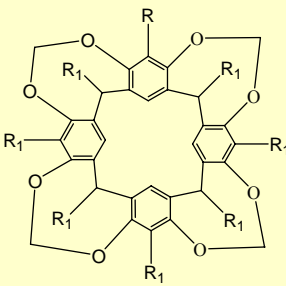
Structure of compound	R	R ₁	Zone of Inhibition	Organism
	CH ₂ Br	C ₆ H ₁₃		
	CH ₂ CH ₂ COOH	C ₆ H ₁₃	12mm 10mm 8mm	M.luteus S.aureus E.coli
	CH ₂ (CHCOOEt) ₂	C ₆ H ₁₃		
	CHCH ₂ COOCH ₃	C ₆ H ₁₃		
	CH ₂ (CHCH ₂ -OGlu) ₂	C ₆ H ₁₃		
	CH ₂ (CHCH ₂ OH) ₂	C ₆ H ₁₃		
	CH ₃ CH ₃	C ₆ H ₅ C ₆ H ₄ Br		

Table 4: Antimicrobial activity of Methylene Bridged Resorcinarenes

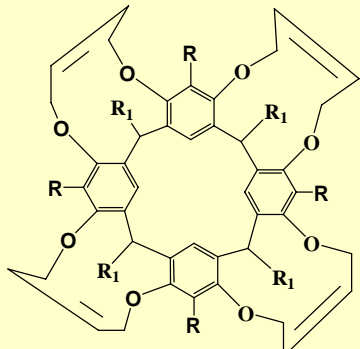
Structure of compound	R	R ₁	Zone of Inhibition	Organism
	CH ₃	C ₆ H ₁₃		
	CH ₃	CH(CH ₂ CH ₃) ₂		

Table 5: Antimicrobial activity of bridged Resorcinarenes

In conclusion to this study, we have observed antimicrobial activity on certain resorcinarenes which had hydrogen in C-2 position of resorcinol. Further extensive studies have to be carried out to figure the antimicrobial activity of resorcinarenes on wide variety of bacteria and fungi.

CHAPTER 4

EXPERIMENTAL SECTION

4.1 General experimental procedure

All solvents and reagents were commercially available. Heptanal was purified by distillation. NMR spectra were recorded on 250 MHz, 400 MHz and 500 MHz spectrometers. Mass spectra were recorded in APCI mode and using MALDI.

Synthesis of octahydroxy resorcinarene (1): -Methyl resorcinol (10g, 0.081mol) was dissolved in (62.7mL, 775mL/mol) ethanol and (14.9mL, 185mL/mol) 37% aqueous HCl. The solution was cooled in ice bath and (3.56mL, 0.081mol) acetaldehyde (which was maintained at 0⁰C) was added to above solution slowly over a period of 30 min. Then the mixture was allowed to warm to room temperature. The reaction was refluxed for nearly 12 hrs. Then the reaction mixture was poured onto 500mL of ice cold water. So obtained yellow colored precipitate was filtered through buchner funnel and the precipitate is washed several times until it turns neutral to pH paper. It is dried and NMR was taken in DMSO d₆. It was synthesized in **67%** yield (8.4g). ¹H NMR (DMSO) δ 1.75(d, 12H J= 7.5Hz), 1.93(s, 12H), 4.4 (q, 4H J= 7.5Hz), 7.4 (s, 4H), 8.7(s, 8H).

Synthesis of octahydroxy resorcinarene (2): - Methyl resorcinol (10g, 0.081mol) was dissolved in (62.7mL, 775mL/mol) ethanol and (15.1mL, 185mL/mol) 37% aqueous HCl. The solution was cooled in ice bath and (11.3mL, 0.081mol) heptaldehyde was

added to above solution slowly over a period of 30 min. Then the mixture was allowed to warm to room temperature. The reaction refluxed for nearly 12 hrs after which I observed yellow colored precipitate. So obtained precipitate was filtered through buchner funnel and the precipitate is washed several times until it turns neutral to pH paper. It is dried and NMR was taken in DMSO d_6 (250MHz). It was synthesized in **88 %** (10.7g) yield.

^1H NMR (DMSO) δ 0.84 (t, 12H, $J = 6.25\text{Hz}$), 1.23(m, 32H), 1.93(s, 12H), 2.21(s, 8H), 4.18 (t, 4H $J = 7.75\text{Hz}$), 7.21 (s, 4H), 8.69(bs, 8H).

Synthesis of octahydroxy resorcinarene (3): - Resorcinol (10g, 0.091mol) was dissolved in mixture of 35mL ethanol, 35mL of water and (16.8mL, 775mL/mol) 37% aqueous HCl. The solution was cooled in ice bath and acetaldehyde (4mL, 0.091mol) was added to above solution slowly over a period of 30 min. Then the mixture was allowed to warm to room temperature and allowed to stir at room temperature for nearly one day. Then the reaction mixture was poured into 500mL of ice cold water .So obtained light yellowed colored precipitate was filtered through buchner funnel and the precipitate is washed several times until it turns neutral to pH paper. It is dried and NMR was taken in DMSO d_6 . It was synthesized in 48% (4.23g) yield.

^1H NMR (DMSO) δ 1.29 (d, 12H, $J = 7.0\text{Hz}$), 1.93(s, 3H), 4.4(q, 4H, $J = 7.5\text{Hz}$), 7.4(s, 4H), 8.7(s, 8H).

Synthesis of octahydroxy resorcinarene (4): -Resorcinol (10g, 0.091mol) was dissolved in (71mL, 775mL/mol) ethanol and (16.8mL, 185mL/mol) 37% aqueous HCl. The solution was cooled in ice bath and (12.7mL, 0.091mol) heptaldehyde was added to above solution slowly over a period of 30 min. Then the mixture was allowed to warm to room temperature. The reaction was then maintained at temperature of 60°C for nearly 36

hrs. Then the reaction mixture was poured onto 500mL of ice cold water .So obtained precipitate was filtered through buchner funnel and the precipitate is washed several times until it turns neutral to pH paper. It is dried and NMR was taken in DMSO d₆. It was synthesized in 78% (8.4g) yield.

¹H NMR (DMSO) δ 0.82 (t, 12H), 1.21 (m, 32H) 2.07 (m, 8H), 4.23 (t, 4H), 6.13 (s, 4H), 7.12 (s, 4H), 8.55 (s, 8H).

Synthesis of octahydroxy resorcinarene (5): - Methyl resorcinol (10g, 0.081mol) was dissolved in (62.7ml, 775mL/mol) anhydrous ethanol and (15.1mL, 185mL/mol) 37% aqueous HCl. The solution was cooled in ice bath and (7.6mL, 0.081mol) benzaldehyde was added to above solution slowly over a period of 30 min. Then the mixture was allowed to warm to room temperature. The reaction was then maintained at temperature of 80⁰C for nearly 12 hrs, forms yellow colored precipitate .So obtained precipitate was filtered through buchner funnel and the precipitate is washed several times until it turns neutral to pH paper. It is dried and NMR was taken in DMSO d₆ (250Hz). It was obtained in **88%** (8.4g) yield.

¹H NMR (DMSO) δ 1.9 (d, 12H), 5.25 (s, 2H), 5.6(s, 4H), 6.1 (s, 2H), 6.6 (d, 8H), 7.1 (d, 12H), 7.6 (d, 8H).

Synthesis of octahydroxy resorcinarene (6): - Methyl resorcinol (10g, 0.081mol) was dissolved in (62.7mL, 775mL/mol) ethanol and (15.1mL, 185mL/mol) 37% aqueous HCl. The solution was cooled in ice bath and (14.4g, 0.081mol) bromobenzaldehyde was added to above solution slowly over a period of 30 min. Then the mixture was allowed to warm to room temperature. The reaction was then maintained at temperature of 80⁰C for nearly 12 hrs after which I observe formation of yellow colored precipitate .So obtained

precipitate was filtered through buchner funnel and the precipitate is washed several times until it turns neutral to pH paper. It is dried and NMR was taken in DMSO d_6 (250Hz).Compound 6 was synthesized in **90 %** (8.8g) yield.

^1H NMR (DMSO) δ 1.9 (d, 12H), 5.25 (s, 2H), 5.6 (s, 4H), 6.1 (s, 2H), 6.6 (d, 8H), 7.1 (d, 8H), 7.6 (d, 8H).

Synthesis of octahydroxy resorcinarene (7): - Resorcinol (10g, 0.091mol) was dissolved in (71mL, 775mL/mol) ethanol and (16.8mL, 185ml/mol) 37% aqueous HCl. The solution was cooled in ice bath and (8.8mL, 0.091mL/mol) benzaldehyde was added to above solution slowly over a period of 30 min using syringe. Then the mixture was allowed to warm to room temperature. The reaction was then maintained at temperature of 80⁰C for nearly 12 hrs after which we can see yellow colored precipitate. So obtained precipitate was filtered through Buchner funnel and the precipitate is washed several times until it turns neutral to pH paper. It was synthesized in 56% (5.34g) yield. NMR was taken in DMSO.

^1H NMR (DMSO) δ 5.65 (s, 4H), 6.17 (s, 4H), 6.32 (bs, 4H), 6.72-6.8 (m, 8H), 6.92-7.02 (m, 12H), 8.88 (d, 8H).

Synthesis of octahydroxy resorcinarene (8): - Resorcinol (10g, 0.091mol) was dissolved in (71mL, 775mL/mol) ethanol and (16.8mL, 185mL/mol) 37% aqueous HCl. The solution was cooled in ice bath and (16g, 0.091mol) bromobenzaldehyde was added to above solution slowly over a period of 30 min using syringe. Then the mixture was allowed to warm to room temperature. The reaction was then maintained at temperature of 80⁰C for nearly 12 hrs after which we can see yellow colored precipitate. So obtained precipitate was filtered through buchner funnel and the precipitate is washed several

times until it turns neutral to pH paper. It is dried and NMR was taken in DMSO. It was synthesized in 67% (6.3g) yield.

¹H NMR (DMSO) δ 5.32 (s, 2H), 5.48 (d, 2H), 6.14 (s, 2H), 6.2 (d, 2H), 6.58 (d, 8H), 6.62 (d, 0.5H), 6.94 (d, 8H), 7.02 (d, 2H), 8.7 (d, 8H).

Synthesis of Octahydroxy Resorcinarene (10):- 1g of Octahydroxy resorcinarene **1** was taken in 2- butanone (10mL/mmol) into round bottomed flask, stirred for 10 min. 6 eq of N-bromo succinimide was added to the above stirred solution in small amounts and reaction was stirred at room temperature for 12 hours. Reaction was monitored by thin layer chromatography. 2- Butanone was evaporated on Rota vapor which resulted in yellow color precipitate which was filtered and washed with cold 2- butanone.

NMR was taken in DMSO. 1.42 (d,12H), 4.62 (d,4H), 6.82 (s,4H), 8.38 (s,8H).

Synthesis of Octahydroxy Resorcinarene (11):- 1g of Octahydroxy resorcinarene **2** was taken in 2- butanone (10mL/mmol) into round bottomed flask, stirred for 10 min. 6 eq of N-bromo succinimide was added to the above stirred solution in small amounts and reaction was stirred at room temperature for 12 hours. Reaction was monitored by thin layer chromatography. 2- Butanone was evaporated on Rota vapor which resulted in yellow color precipitate which was filtered and washed with cold 2- butanone.

NMR was taken in DMSO. 0.84 (s, 12H), 1.24 (s, 32H) , 2.2 (s,8H), 4.35 (t,4H), 7.35 (s,4H), 9.1 (s,8H).

Synthesis of Octahydroxy Resorcinarene (12):- 1g of Octahydroxy resorcinarene in 2- butanone (10mL/mmol) was taken into round bottomed flask, stirred for 10 min. 6 eq of N-bromo succinimide was added to the above stirred solution in small amounts and reaction was stirred at room temperature for 12 hours. Reaction was monitored by thin

layer chromatography. 2- Butanone was evaporated on Rota vapor which resulted in yellow color precipitate which was filtered and washed with cold 2- butanone.

NMR was taken in DMSO. 0.84 (s, 12H), 1.24 (s, 54H), 2.2 (s,8H), 4.35 (t,4H), 7.35 (s,4H), 9.1 (s,8H).

Synthesis of octaallyloxy resorcinarene (13): -1g of Octahydroxy compound **1** was taken into round-bottomed flask and (20mL/mol) acetone was added to RBF. The reaction mixture was stirred till homogenous mixture was formed. Then (30eq) potassium carbonate was slowly added over a period of half an hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (30eq) allyl bromide was added. The reaction mixture was heated to temperature of 60⁰C for nearly 24-48 hrs. The reaction mixture was filtered and then concentrated and was recrystallized using 70% acetone methanol mixture. It was synthesized in 76% (1.2g) yield. Dept 135 was taken on this compound since the proton NMR of this compound gave broad peaks. Peaks at following ppm values were observed. δ (in ppm) 10.54, 20.96, 32.79, 73.25, 116.12, 123.67, 134.49.

Synthesis of octaallyloxy resorcinarene (14): -1g of Octahydroxy compound **2** was taken into round-bottomed flask and (20mL/mol) acetone was added to RBF. The reaction mixture was stirred till homogenous mixture was formed. Then (30eq) potassium carbonate was slowly added over a period of half an hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (30eq) allyl bromide was added. The

reaction mixture was heated to temperature of 60⁰C for nearly 24-48 hrs. It was synthesized in 55% yield (0.7g).

¹H NMR (CDCl₃) δ 0.8 (t, 12H), 1.2 (m, 56H), 1.85 (m, 8H), 2.15 (s, 12H), 4.25 (dd, 16H), 4.55 (t, 4H), 5.2 (dd, 16H) 6.1 (m, 8H), 6.55 (s, 4H);

¹³C NMR δ 10.6, 14.2, 22.8, 28.6, 29.5, 30.2, 32.1, 34.1, 35.4, 36.5, 40.0, 73.3, 116.2, 124.0, 133.9, 153.6.

Synthesis of octaallyloxy resorcinarene (15): -1g of Octahydroxy bromo compound **11** was taken into round-bottomed flask and (20mL/mol) acetone was added to RBF. The reaction mixture was stirred till homogenous mixture was formed. Then (30eq) potassium carbonate was slowly added over a period of half an hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (30eq) allyl bromide was added. The reaction mixture was heated to temperature of 60⁰C for nearly 24-48 hrs. The reaction mixture was filtered and then concentrated and was recrystallized using 70% acetone methanol mixture. NMR was taken in CDCl₃. 0.77 (t, 12H), 1.16 (d, 32H), 1.48 (t,8H), 1.82 (s,4H), 4.36 (t,16H), 5.14 (d,16H), 5.92 (s,8H).

¹³C : 14.3, 22.8, 22.9, 28.8, 29.8, 32, 32.1, 35.0, 39.4, 74.1, 110.0, 117.4, 126, 133.9, 154.

Synthesis of octaallyloxy resorcinarene (16): -1g of Octahydroxy bromo compound **12** was taken into round-bottomed flask and (20mL/mol) acetone was added to RBF. The reaction mixture was stirred till homogenous mixture was formed. Then (30eq) potassium carbonate was slowly added over a period of half an hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (30eq) allyl bromide was added. The

reaction mixture was heated to temperature of 60⁰C for nearly 24-48 hrs. The reaction mixture was filtered and then concentrated and was recrystallized using 70% acetone methanol mixture. NMR was taken in CDCl₃. 0.86 (t, 12H), 1.22 (d, 56H), 1.9 (s, 8H), 4.45 (t, 20H), 5.23 (d, 16H), 6.01 (s, 8H), 6.96 (s, 4H).

¹³C (in ppm) 14.3, 22.9, 28.8, 29.6, 29.9, 30.1, 32.2, 35.0, 39.4, 74.08, 110.0, 113.9, 117.3, 126.1, 133.9, 138.6, 157.1.

Synthesis of octaallyloxy resorcinarene (17): -1g of Octahydroxy bromo compound **10** was taken into round-bottomed flask and (20mL/mol) acetone was added to RBF. The reaction mixture was stirred till homogenous mixture was formed. Then (30eq) potassium carbonate was slowly added over a period of half an hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (30eq) allyl bromide was added. The reaction mixture was heated to temperature of 60⁰C for nearly 24-48 hrs. The reaction mixture was filtered and then concentrated and was recrystallized using 70% acetone methanol mixture. NMR was taken in CDCl₃. 1.45 (t, 12H), 3.5 (s, 4H), 4.2 (s, 14H), 4.57 (m, 16H), 5.04 (dd, 8H), 5.7 (s, 4H).

¹³C (in ppm) 20.9, 33.9, 74.2, 117.1, 117.6, 125.2, 133.9, 134.1, 138.7, 152.8, 153.9.

Synthesis of octaallyloxy resorcinarene (18): -1g of Octahydroxy compound **3** was taken into round-bottomed flask and (20mL/mol) acetone was added to RBF. The reaction mixture was stirred till homogenous mixture was formed. Then (30eq) potassium carbonate was slowly added over a period of half an hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (30eq) allyl bromide was added. The

reaction mixture was heated to temperature of 60⁰C for nearly 24-48 hrs. ¹³C NMR was taken in CDCl₃. δ (in ppm) 20.96, 32.79, 73.25, 116.12, 123.67, 134.49.

Synthesis of octaallyloxy resorcinarene (19): -1g of Octahydroxy compound **4** was taken into round-bottomed flask and (20mL/mol) acetone was added to RBF. The reaction mixture was stirred till homogenous mixture was formed. Then (30eq) potassium carbonate was slowly added over a period of half an hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (30eq) allyl bromide was added. The reaction mixture was heated to temperature of 60⁰C for nearly 24-48 hrs. ¹H NMR (CDCl₃) δ (in ppm) 0.65 (t, 24H), 1.2 (m, 16H), 1.4 (m, 4H), 4.2 (d, 16H), 4.3 (t, 4H), 5.2 (dd, 16H), 5.9 (m, 8H), 6.2 (s, 4H), 6.9 (s, 4H).

Synthesis of octaallyloxy resorcinarene (20): - 1g of Octahydroxy compound **5** was taken into round bottomed flask and (20mL/mol) DMF was added to RBF. The reaction mixture was stirred till homogenous mixture was formed .Then (16eq) potassium tertiary butoxide was slowly added over a period of one hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (16eq) allyl bromide was added. The reaction mixture is heated to temperature of 70⁰C for nearly 12 hrs. After the reaction is complete the reaction mixture is filtered from potassium tertiary butoxide and DMF was distilled over reduced pressure. Dichloromethane was added and reaction was washed with water, then with brine and then concentrated and compound was recrystallized in 70% mixture of ethyl acetate and hexane. NMR of compound was taken in CDCl₃ .

δ (in ppm) 2.12 (d, J=9.2Hz, 6H), 2.25 (d, J=9.2Hz, 6H), 3.64 (m, 16H), 5.05-5.20(m, 16H), 5.60 (d, 2H, J=9.6Hz), 6.31 (d, 2H, J=9.6Hz), 5.85 (m, 8H), 5.93 (d, 4H), 6.60 (d, 8H, J= 7.6Hz), 6.84 (d, 8H, J= 7.6Hz), 6.86 (s, 4H).

Synthesis of octaallyloxy resorcinarene (21): - 1g of Octahydroxy compound **6** was taken into round bottomed flask and (20mL/mol) DMF was added to RBF. The reaction mixture was stirred till homogenous mixture was formed .Then (16eq) potassium tertiary butoxide was slowly added over a period of one hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (16eq) allyl bromide was added. The reaction mixture is heated to temperature of 70⁰C for nearly 12 hrs. After the reaction is complete the reaction mixture is filtered from potassium tertiary butoxide and DMF was distilled over reduced pressure. Dichloromethane was added and reaction was washed with water, then with brine and then concentrated and compound was recrystallized in 70% mixture of ethyl acetate and hexane. NMR of compound was taken in CDCl₃. δ 2.12 (d, J=9.2Hz, 6H), 2.25 (d, J=9.2Hz, 6H), 3.64-4.42 (m, 16H), 5.05-5.20 (m, 16H), 5.60 (d, 2H, J=9.6Hz), 6.31 (d, 2H, J=9.6Hz), 5.85 (m, 8H), 5.93 (d, 4H), 6.60 (d, 8H, J= 7.6Hz), 6.84 (d, 4H, J= 7.6Hz), 6.86 (s, 4H).

Synthesis of octaallyloxy resorcinarene (22): - 1g of Octahydroxy compound **7** was taken into round bottomed flask and (20mL/mol) DMF was added to RBF. The reaction mixture was stirred till homogenous mixture was formed .Then (16eq) potassium tertiary butoxide was slowly added over a period of one hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (16eq) allyl bromide was added. The

reaction mixture is heated to temperature of 70⁰C for nearly 12 hrs. After the reaction is complete the reaction mixture is filtered from potassium tertiary butoxide and DMF was distilled over reduced pressure. Dichloromethane was added and reaction was washed with water, then with brine and then concentrated and compound was recrystallized in 70% mixture of ethyl acetate and hexane. NMR of compound was taken in CDCl₃.

Synthesis of octaallyloxy resorcinarene (23): - 1g of Octahydroxy compound **8** was taken into round bottomed flask and (20mL/mol) DMF was added to RBF. The reaction mixture was stirred till homogenous mixture was formed .Then (16eq) potassium tertiary butoxide was slowly added over a period of one hour where the reaction mixture is ice cooled. Here we observe the change in color from brown to purple. Then the reaction mixture was brought to room temperature and (16eq) allyl bromide was added. The reaction mixture is heated to temperature of 70⁰C for nearly 12 hrs. After the reaction is complete the reaction mixture is filtered from potassium tertiary butoxide and DMF was distilled over reduced pressure. Dichloromethane was added and reaction was washed with water, then with brine and then concentrated and compound was recrystallized in 70% mixture of ethyl acetate and hexane. NMR of compound was taken in CDCl₃.

Synthesis of bridged resorcinarene (24): - To a stirred solution of octa-allyloxy methyl resorcinarene (**13**) (1gm, .877 mmole) in dry methylene chloride (90mL) was added Grubb's catalyst (5 mole%, 0.034gm, 0.042 mmole) in dry methylene chloride (25mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated using a rotary evaporator and compound was obtained by column chromatography.

Synthesis of bridged resorcinarene (25): - To a stirred solution of octa-allyloxy methyl resorcinarene (**18**) (1gm, .877 mmole) in dry methylene chloride (90mL) was added Grubb's catalyst (5 mole%, 0.034gm, 0.042 mmole) in dry methylene chloride (25mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated over rotary evaporator and was separated by column.

Synthesis of bridged-resorcinarene (26): - To a stirred solution of octa-allyloxy-phenyl-resorcinarene (**22**) (1gm, 0.89 mmole) in dry methylene chloride (93mL) was added grubb's catalyst (8 mole%, 0.058gm, 0.071 mmole) in dry methylene chloride (20mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated over rotavapor and column chromatography was run using 10% ethyl acetate and 90% hexane solvent system to separate two spots. Second spot (fraction) showed that four allyl groups are closed forming two bridges. It was confirmed by ^{13}C , DEPT, Mass spectroscopy. DEPT (CDCl_3) δ in ppm 41.8, 63.8, 68.6, 96.2, 98.99, 115.3, 124.3, 126.6, 126.8, 127.3, 127.9, 128.1, 132.1, 132.7; MALDI m/z 1057.785 ($\text{M}^+ + \text{H}$), 1079.814 ($\text{M}^+ + \text{Na}$).

Synthesis of bridged-resorcinarene (27): - To a stirred solution of octa-allyloxy-bromophenyl-resorcinarene (**23**) (1gm, 0.89 mmole) in dry methylene chloride (93mL) was added grubb's catalyst (8 mole%, 0.058gm, 0.071 mmole) in dry methylene chloride (20mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated over rotavapor and column chromatography was run using 10% ethyl acetate and 90% hexane solvent system to separate two spots. Second spot (fraction) showed that four allyl groups are closed forming two bridges. It was confirmed by ^{13}C , DEPT, Mass spectroscopy. DEPT (CDCl_3) δ in ppm 41.8, 63.8, 68.6, 96.2, 98.99, 115.3,

124.3, 126.6, 126.8, 127.3, 127.9, 128.1, 132.1, 132.7; MALDI m/z 1057.785 ($M^+ + H$), 1079.814 ($M^+ + Na$).

Synthesis of bridged-resorcinarene (28): - To a stirred solution of octa-allyloxy-phenyl-methylresorcinarene (**20**) (1gm, 0.82 mmole) in dry methylene chloride (86mL) was added grubb's catalyst (8 mole%, 0.054gm, 0.066 mmole) in dry methylene chloride (19mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated over rotavapor and column chromatography was run using 10% ethyl acetate and 90% hexane solvent system to separate two spots. Second spot (fraction) showed that two allyl groups are closed forming one bridge. It was confirmed by ^{13}C , DEPT, Mass spectroscopy. ^{13}C NMR ($CDCl_3$) δ in ppm (10.8, 10.9, 11.1, 11.3), 24.9, 36.8, (44.2, 44.7, 44.9, 45.0), (68.6, 71.0, 73.9, 74.2), (116.4, 116.6, 116.6, 116.8, 117.0, 117.3), (123.8, 124.1, 125.3, 125.8, 125.9, 126.3, 127.4, 127.4, 127.8, 127.8, 128.3, 129.0, 129.2, 130.1, 131.2, 132.2, 132.4, 132.5, 132.7, 132.82, 132.8, 133.1, 133.2), (134.1, 134.1, 134.2, 134.2, 134.3, 134.3, 134.4), (141.4, 143.4, 143.6, 144.0), (154.1, 154.3, 154.8, 154.9, 155.0, 155.0, 155.1, 155.6).

Synthesis of bridged-resorcinarene (29): - To a stirred solution of octa-allyloxy-bromophenyl-methylresorcinarene (**21**) (1gm, 0.67 mmole) in dry methylene chloride (70mL) was added grubb's catalyst (8 mole%, 0.044gm, 0.054 mmole) in dry methylene chloride (15mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated over rotavapor and column chromatography was run using 10% ethyl acetate and 90% hexane solvent system to separate two spots. Second spot (fraction) showed that two allyl groups are closed forming one bridge. It was confirmed by ^{13}C , DEPT, Mass spectroscopy. ^{13}C NMR ($CDCl_3$) δ in ppm 10.9, 11.0, 11.2, 11.3,

14.4, 29.9, 43.7, 44.1, 44.3, 44.5, 69.2, 73.8, 74.2, 74.5, 110.0, 116.6, 116.8, 116.9, 117.3, 117.5, 117.8, 120.0, 120.1, 120.1, 124.3, 124.7, 125.8, 126.4, 126.8, 128.2, 129.7, 130.6, 130.7, 130.8, 130.9, 130.9, 131.0, 132.3, 132.4, 132.5, 132.6, 133.8, 134.0, 134.1, 134.2, 140.5, 142.6, 142.9, 143.6, 154.3, 154.8, 155.0, 155.2, 155.3, 155.4, 155.9.

Synthesis of bridged resorcinarene (30): - To a stirred solution of octa-allyloxy bromo heptyl resorcinarene (**15**) (1gm, .684 mmole) in dry methylene chloride (72mL) was added Grubb's catalyst (5 mole%, 0.028gm, 0.034 mmole) in dry methylene chloride (25mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated over Rota vapor and was precipitated from mixture of acetone and dichloromethane. .

^1H NMR 0.86 (t, 12H), 1.23 (d, 56H), 1.9 (s, 8H), 4.82 (t, 20H), 5.95 (s, 8H), 6.96 (s, 4H).

^{13}C NMR 14.3, 22.9, 27.8, 29.6, 29.8, 29.9, 32.2, 36.6, 37.7, 77.5, 109.9, 113.6, 125.3, 130.1, 135.3, 154.2.

Synthesis of bridged resorcinarene (31): - To a stirred solution of octa-allyloxy bromo decyl resorcinarene (**16**) (1gm, .614 mmole) in dry methylene chloride (65mL) was added Grubb's catalyst [8 mole%, 0.025gm, 0.031 mmole] in dry methylene chloride (25mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated over Rota vapor and was recrystallised from mixture of ethyl acetate and hexane. ^1H NMR (CDCl_3) 0.86 (t, 12H), 1.22 (d, 56H), 1.9 (s, 8H), 4.8 (d, 12H), 6.01 (s, 8H), 6.96 (s, 4H).

^{13}C NMR 14.3, 22.9, 28.8, 29.6, 29.9, 30.1, 32.2, 35.0, 39.4, 74.08, 110.0, 113.9, 126.1, 133.9, 138.6, 157.1.

Synthesis of bridged resorcinarene (32): - To a stirred solution of octa-allyloxy bromo methyl resorcinarene (**17**) (1gm, .877 mmole) in dry methylene chloride (90mL) was added Grubb's catalyst (5 mole%, 0.034gm, 0.042 mmole) in dry methylene chloride (25mL) at room temperature. Reaction was continued for 4days. Reaction mixture was then concentrated over Rota vapor and was precipitated from mixture of acetone and dichloromethane. NMR was taken in CDCl₃.(ppm) 20.9, 33.9, 74.3, 117.1, 117.3, 125.0, 134.1, 139.5, 153.9.

Synthesis of Ethyl ester of 2,4 dimethoxy Cinnamic acid (33):- 0.3g of 2,4 dimethoxy cinnamic acid was taken into RBF and 14ml of acetone(10mL/mmol) was added and stirred still homogenous solution was obtained. To this solution 1g (5eg) of potassium carbonate was added in portion wise and 0.3mL (2eq) of ethyl iodide was added and the reaction was refluxed for 12 hrs. It was allowed to cool and base was filtered off, concentrated in vacuum, and so obtained product was taken for NMR.

¹H NMR revealed the existence of compound. Following peaks were found in CDCl₃

1.30 (t, J=7.25) 3.83 (d, J=7.5) 4.23 (q, J= 7) 6.40 (s), 6.45 (m), 6.48 (m), 7.42 (d ,J= 8.75) 7.94 (d, J= 16.25).

Synthesis of C-Ethyl Dimethoxy resorcinarene (34):-1g of compound **33** was taken into RBF and 6.5mL of chloroform (5mL/mmol) was added to the compound and allowed to stir for 5 min. 0.26mL of BF₃ etherate (0.2mL/mmol) was added to the reaction mixture and the continued for 10hrs.The reaction was monitored by TLC and after 10hrs the reaction was quenched with methanol and so obtained precipitate was filtered off and it was concentrated in vacuum. The reaction mixture was purified by column chromatography (5% methanol and dichloromethane) and NMR was taken in CDCl₃

1.01 (d, J= 9Hz), 1.13 (m), 2.87 (d, J= 7.75Hz), 3.72 (q, J=4.75Hz), 4.86(s), 6.19 (d, J= 9.75Hz), 6.54(s).

Synthesis of demethylated Resorcinarene (35):- 1g of compound **34** was taken into RBF and 40mL of dichloromethane was added to the reaction mixture. The reaction mixture was cooled in ice bath for 15 min and 2.8g of aluminium trichloride (20eq) was added in portion wise and reaction was allowed to continue for 12 hrs. The reaction was monitored by TLC. The reaction mixture was quenched with water and extracted into Dichloromethane and concentrated in vacuum. The major lower Rf spot was separated by column chromatography and NMR was taken in DMSO d_6 . 1.01 (d, J= 9Hz), 1.13 (m), 2.87 (d, J= 7.75Hz), 3.72 (q, J=4.75Hz), 4.86 (s), 6.19 (d, J= 9.75hz), 6.54 (s) 8.8 (m).

Synthesis of Hydroxy ethyl Resorcinarene (36):- 0.5g of compound **34** was taken into RBF and 16mL of tetrahydrofuran was added to the reaction mixture. The reaction mixture was cooled in ice bath for 15 min and 80mg of Lithium aluminium hydride (4 eq) was added in portion wise and reaction was allowed to continue for 12 hrs. The reaction was monitored by TLC and quenched with 0.5mL of water followed by 0.5 mL of saturated sodium chloride solution and extracted into ethyl acetate. It was concentrated in vacuum. The major lower Rf spot was separated by column chromatography and NMR was taken in $CDCl_3$. 1.13 (m), 2.01 (s) 2.87 (d, J= 7.75Hz), 4.86 (s), 6.19 (d, J= 9.75hz), 6.54 (s).

4.2 Crystal data of Resorcinarenes

(1) Crystal data of allyloxy-resorcinarene (13): -

Colorless parallelepiped, $C_{60}H_{72}O_8$, F.W= 921.18, triclinic, space group P1, $a= 12.066(10)$, $b= 15.927(12)$, $c= 20.122(15)$ Å, $\beta= 84.594(16)^\circ$, $V= 3368(5)$ Å³, $Z= 2$, $D_\alpha = 1.129$ Mg m⁻³, $T= 115$ K. Data were collected on Kappa CCD diffractometer ($2.5^\circ < \theta < 29.5^\circ$) using Mo K α radiation, ($\lambda= 0.71073$ Å). From the 80902 reflections measured, 11348 ($I > 2\sigma(I)$) were used in the refinements.

(2) Crystal data of allyloxy-resorcinarene (15): -

Colorless fragment, $C_{56}H_{56}O_8Br_4$, F.W.= 1176.65, orthorhombic, space group P2, $a= 8.826(17)$, $b= 19.85(4)$, $c= 29.78(4)$ Å, $\beta= 90^\circ$, $V= 5217.6(17)$ Å³, $Z= 4$, $D_\alpha = 1.185$ Mg m⁻³, $T= 110$ K. Data were collected on Kappa CCD diffractometer ($2.5^\circ < \theta < 29.5^\circ$) using Mo K α radiation, ($\lambda= 0.71073$ Å). From the 9131 reflections measured, 6563 ($I > 2\sigma(I)$) were used in the refinements.

(3) Crystal data of allyloxy-resorcinarene (16): -

Colorless fragment, $C_{88}H_{124}O_8Br_4$, F.W.= 1629.51, monoclinic, space group P2(1), $a= 27.061(3)$, $b= 18.98(18)$, $c= 16.289(13)$ Å, $\beta= 90.746(2)^\circ$, $V= 8366.2(13)$ Å³, $Z= 4$, $D_\alpha = 1.294$ Mg m⁻³, $T= 100$ K. Data were collected on Kappa CCD diffractometer ($2.5^\circ < \theta < 29.5^\circ$) using Mo K α radiation, ($\lambda= 0.71073$ Å). From the 40537 reflections measured, ($I > 2\sigma(I)$) were used in the refinements.

(4) Crystal data of allyloxy-resorcinarene (21): -

Colorless fragment, $C_{80}H_{80}O_8Br_4$, F.W= 1529.44, triclinic, space group P1, $a= 12.36(2)$, $b= 13.691(3)$, $c= 19.796(4)$ Å, $\beta= 92.301(11)^\circ$, $V= 3189(11)$ Å³, $Z= 2$, $D_\alpha = 1.218$ Mg m⁻³, $T= 110$ K. Data were collected on Kappa CCD diffractometer ($2.5^\circ < \theta < 29.5^\circ$) using

Mo K α radiation, ($\lambda= 0.71073\text{\AA}$). From the 9131 reflections measured, 6984 ($I > 2\sigma(I)$) were used in the refinements.

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APPENDICES
(Spectra of Compounds)

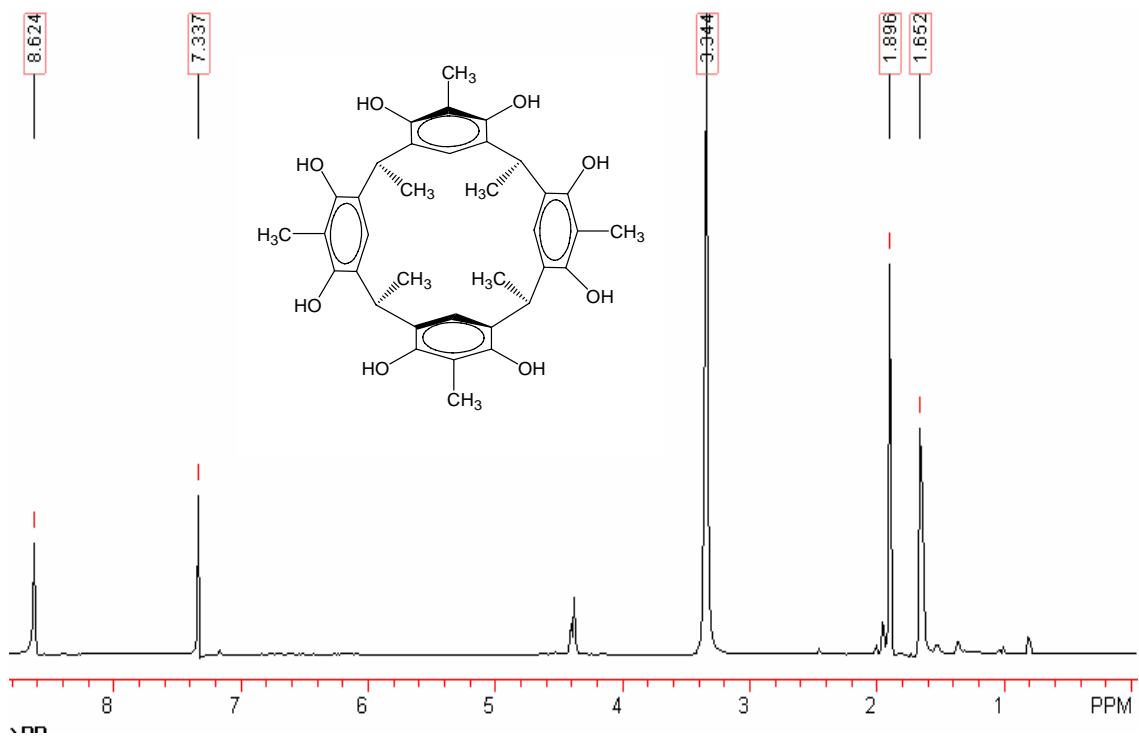


Figure 14. $^1\text{H NMR}$ of compound 1

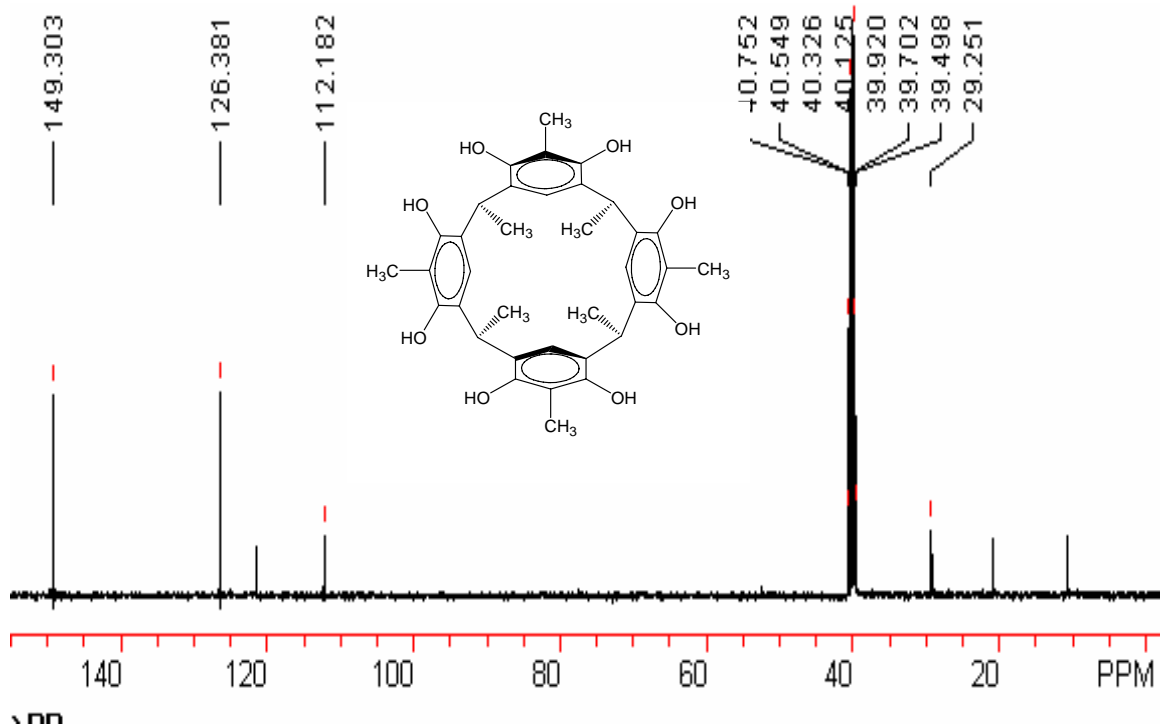


Figure 15. $^{13}\text{C NMR}$ of compound 1.

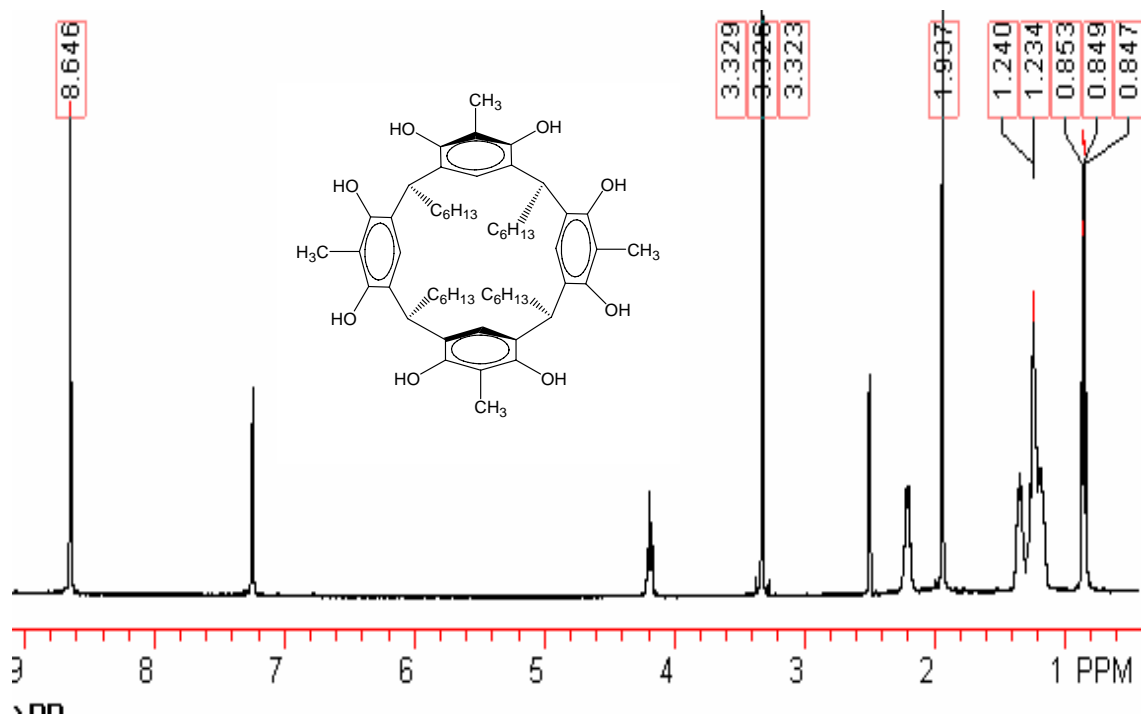


Figure 16. ^1H NMR of compound 2

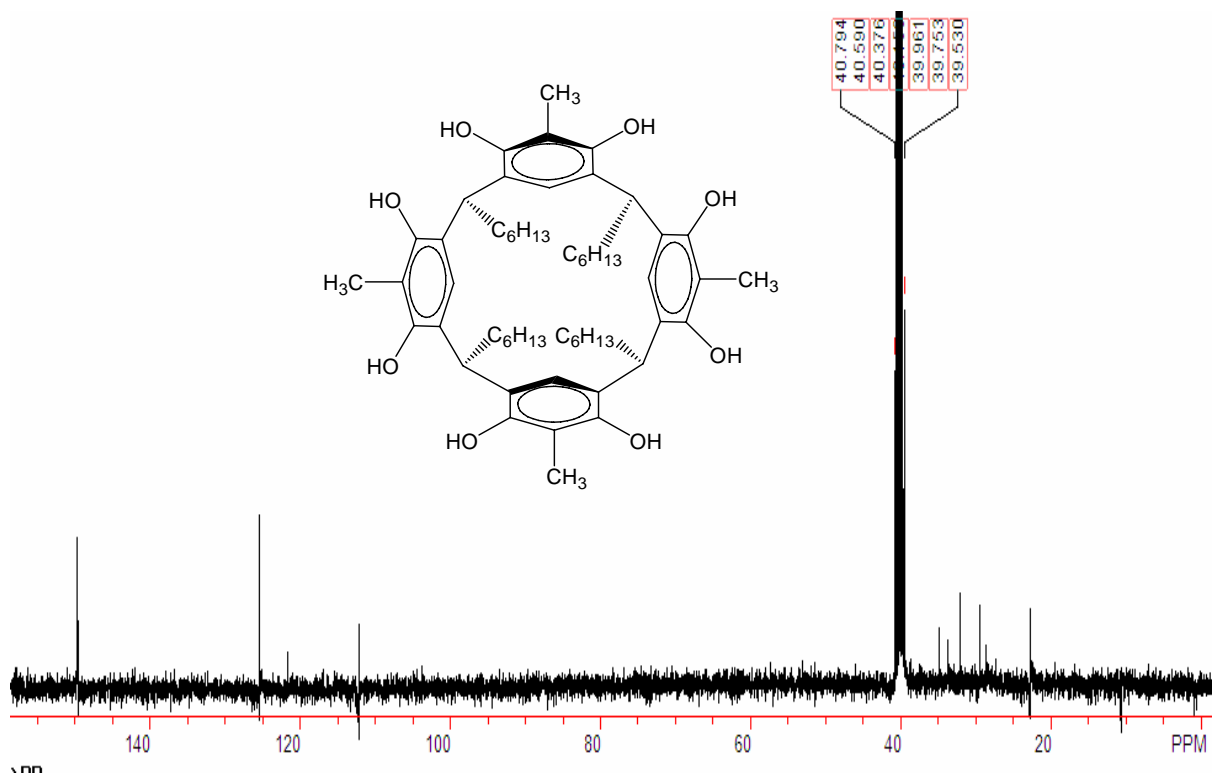


Figure 17. ^{13}C NMR of compound 2

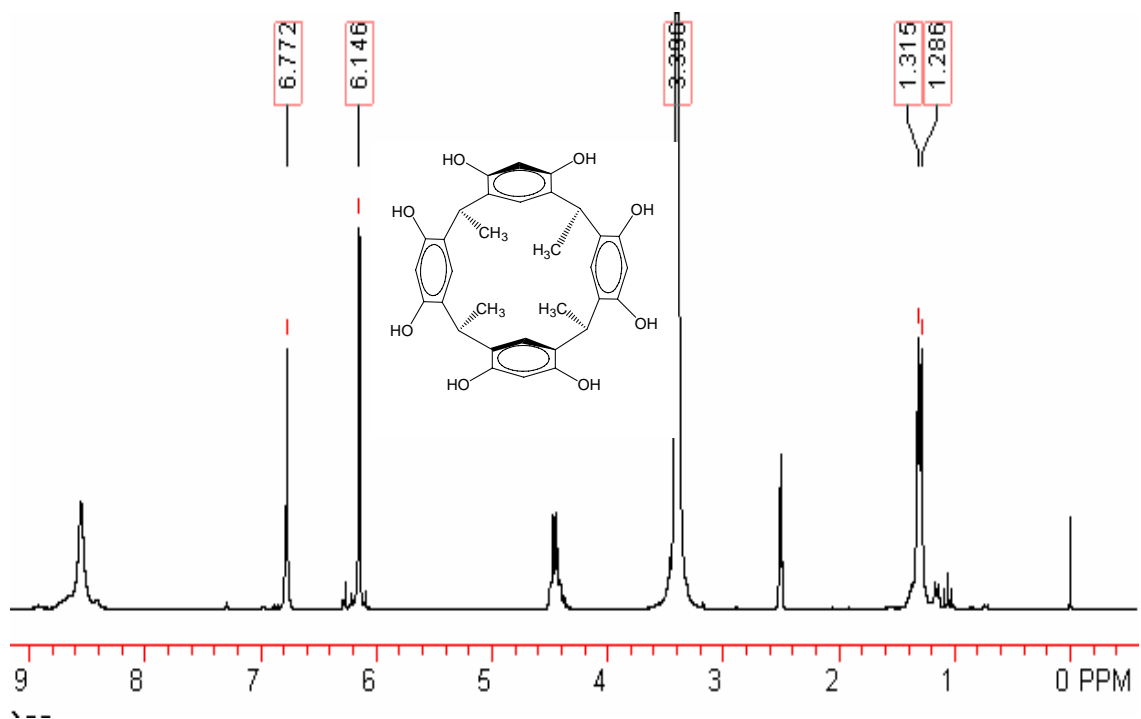


Figure 18. ^1H NMR of compound 3

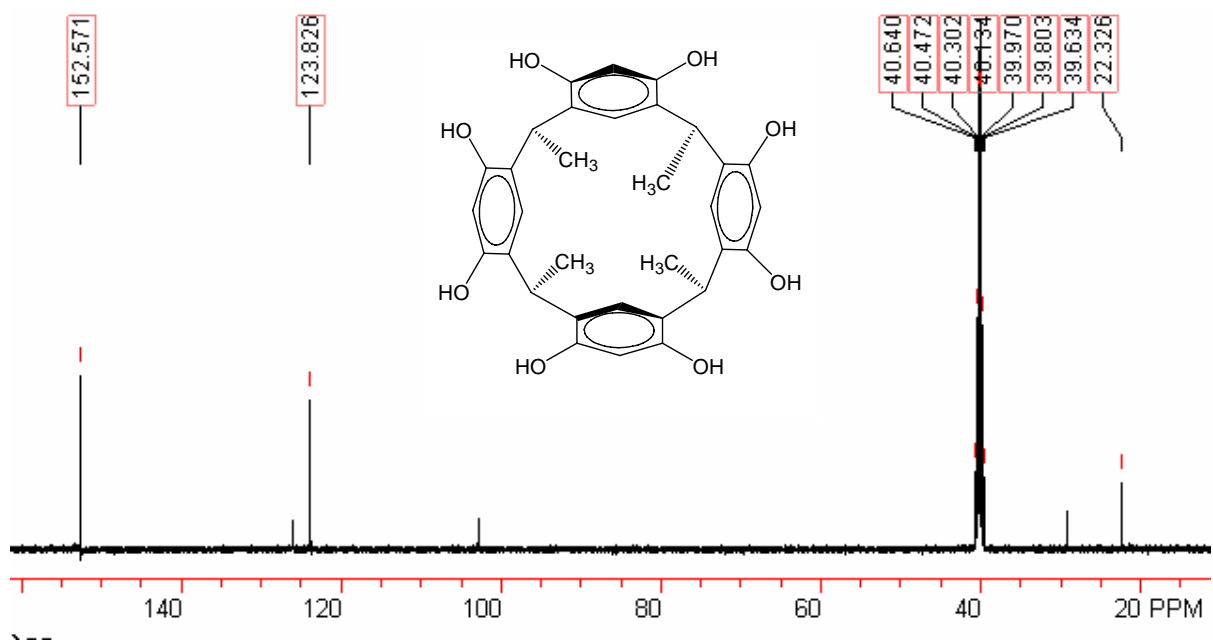


Figure 19. ^{13}C NMR of compound 3

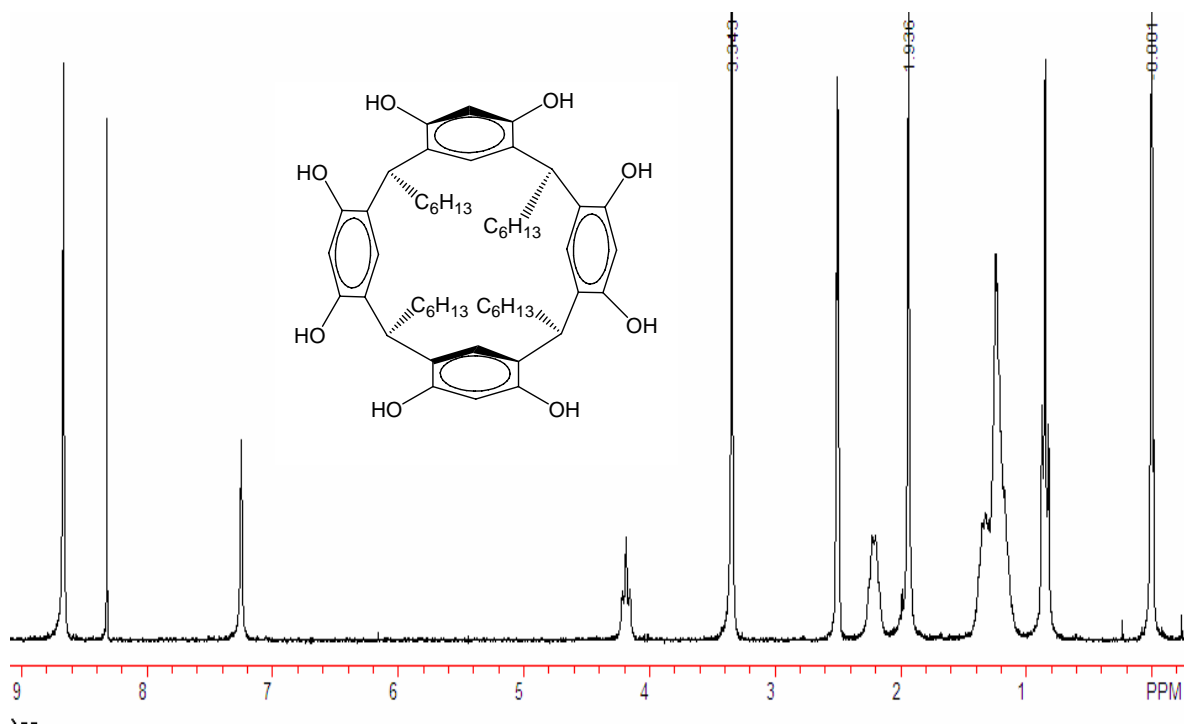


Figure 20. ^1H NMR of compound 4

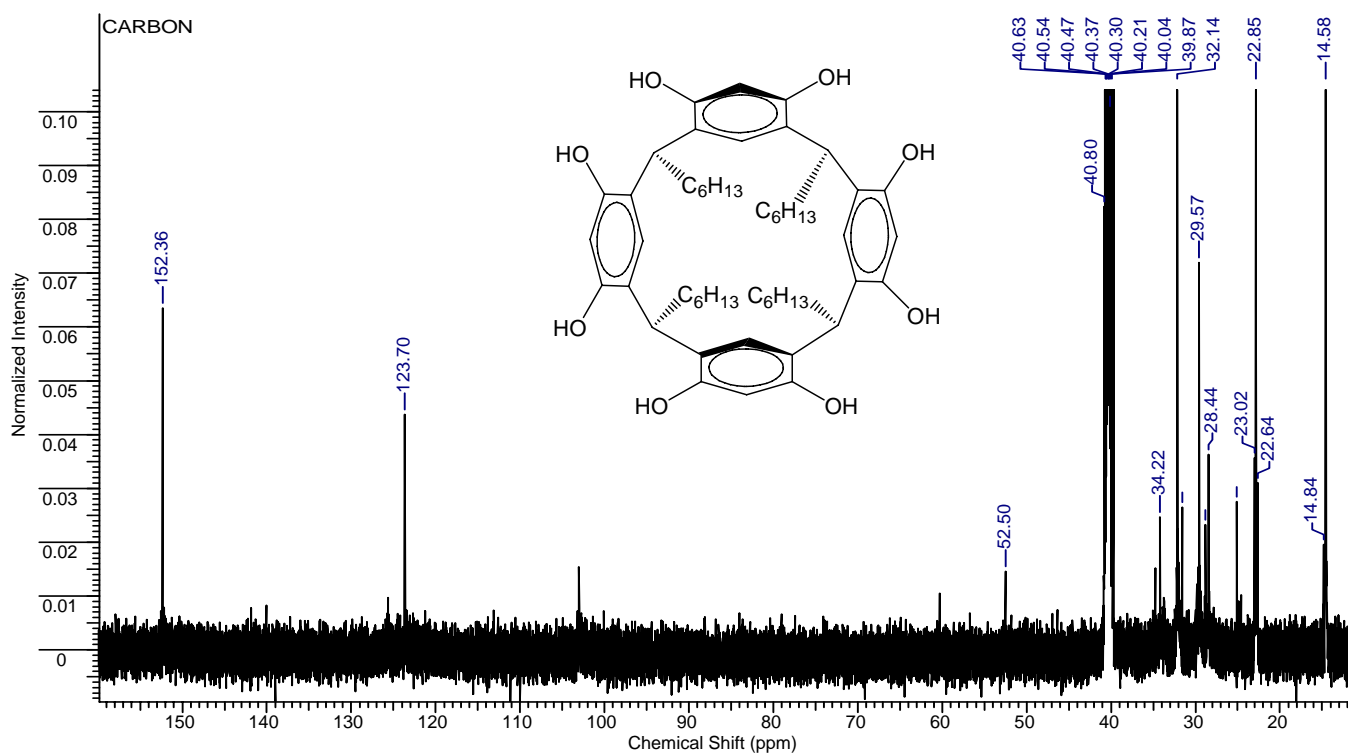


Figure 21. ^{13}C NMR of compound 4

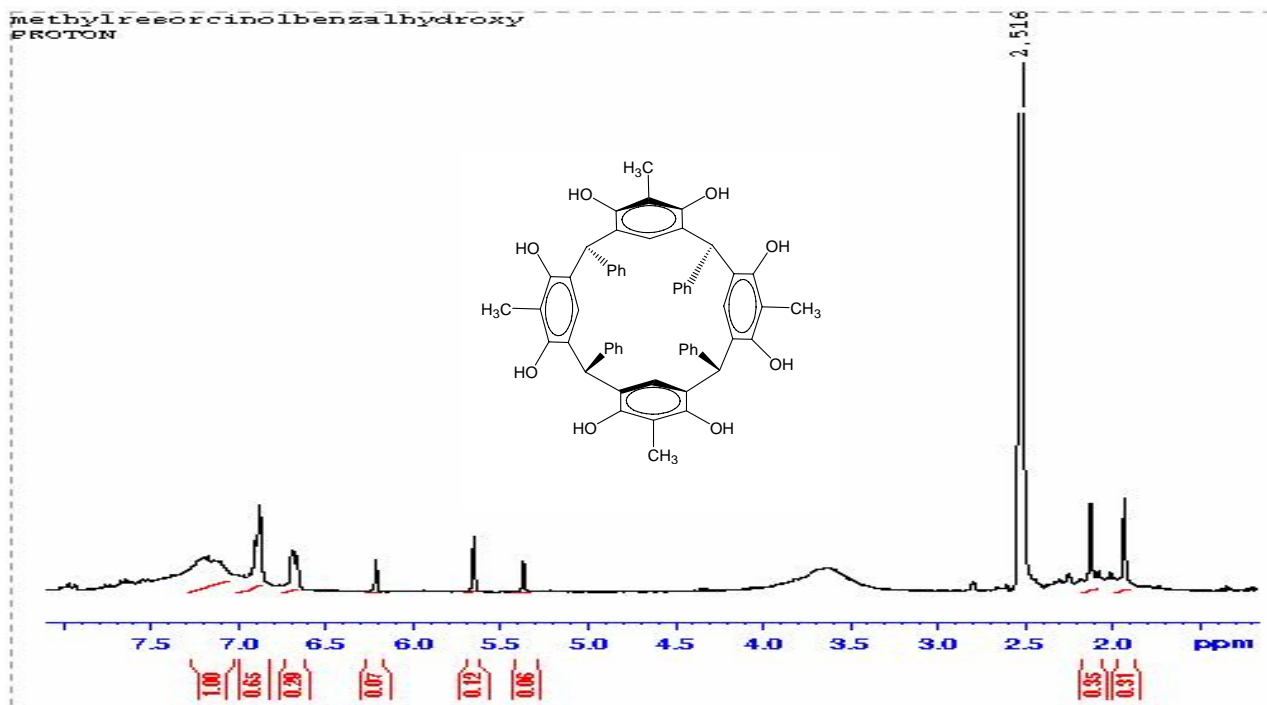


Figure 22. ^1H NMR of compound 5

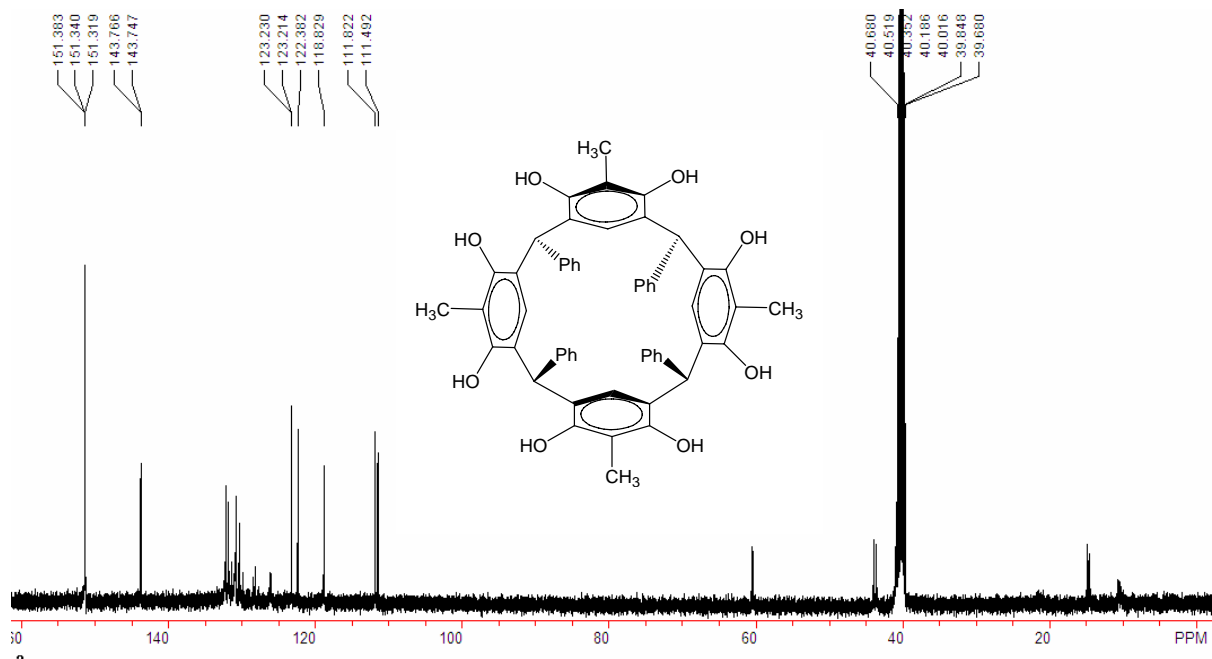


Figure 23. ^{13}C NMR of compound 5

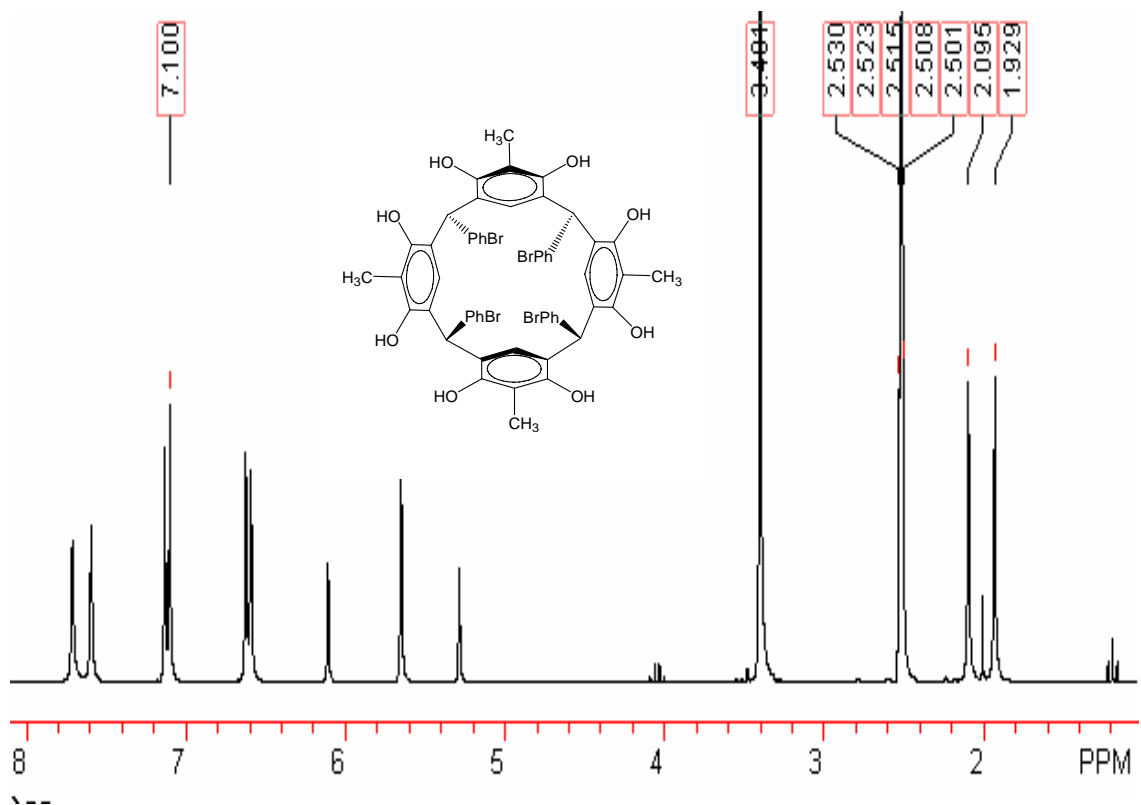


Figure 24. ¹H NMR of compound 6

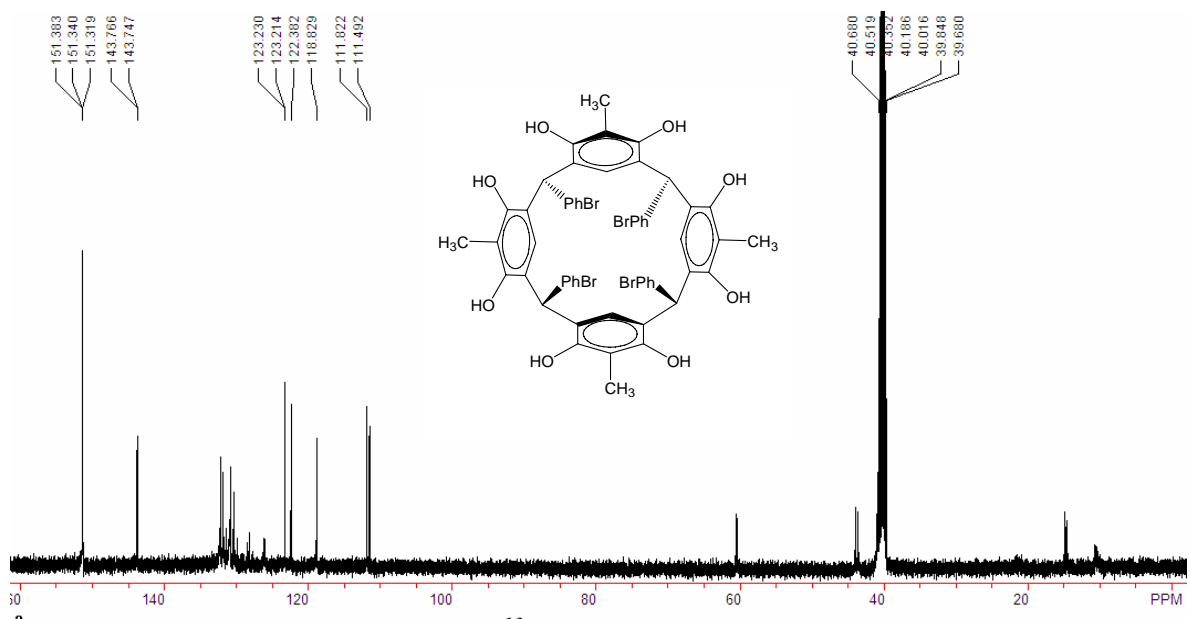


Figure 25. ¹³C NMR of compound 6

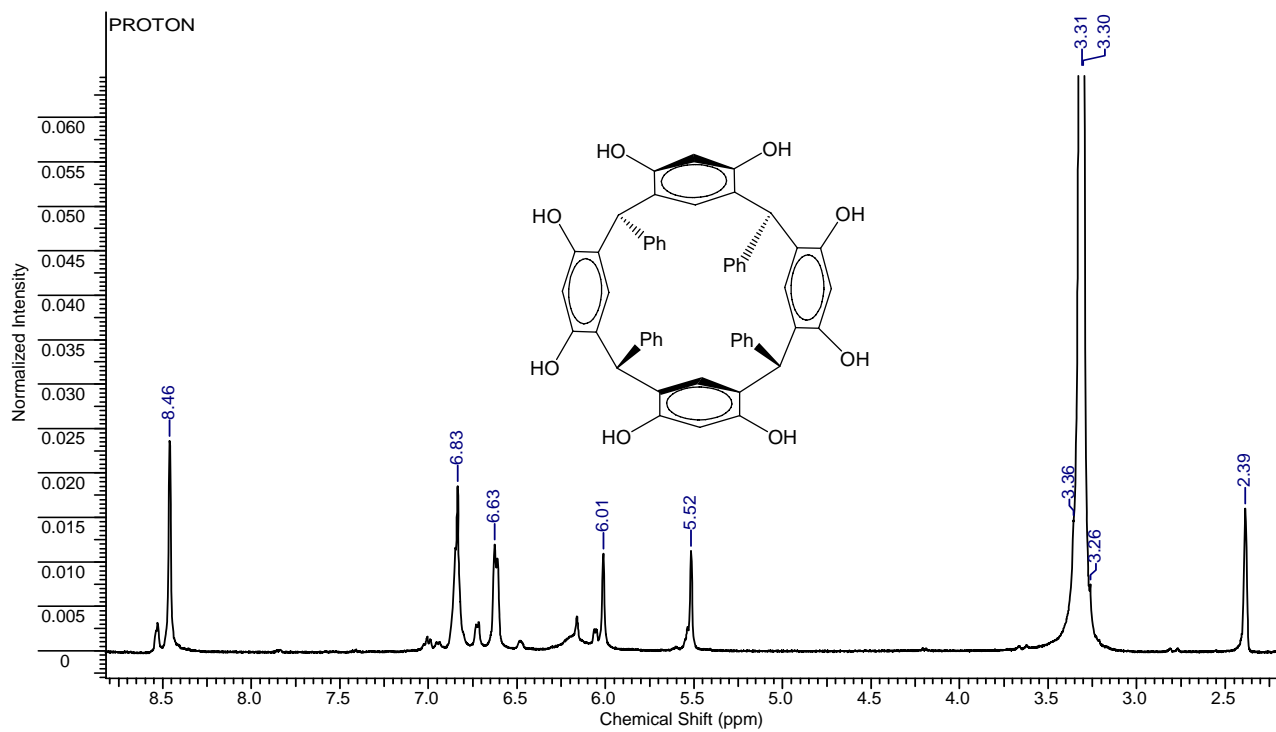


Figure 26. ^1H NMR of compound 7

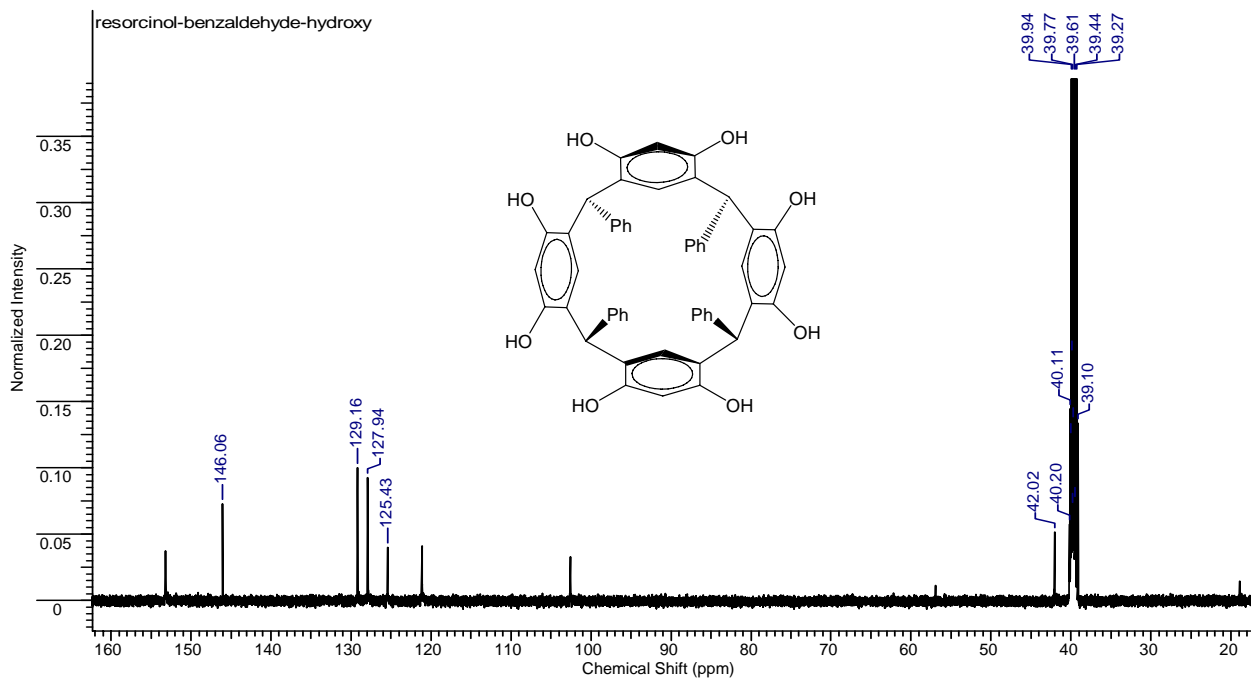


Figure 27. ^{13}C NMR of compound 7

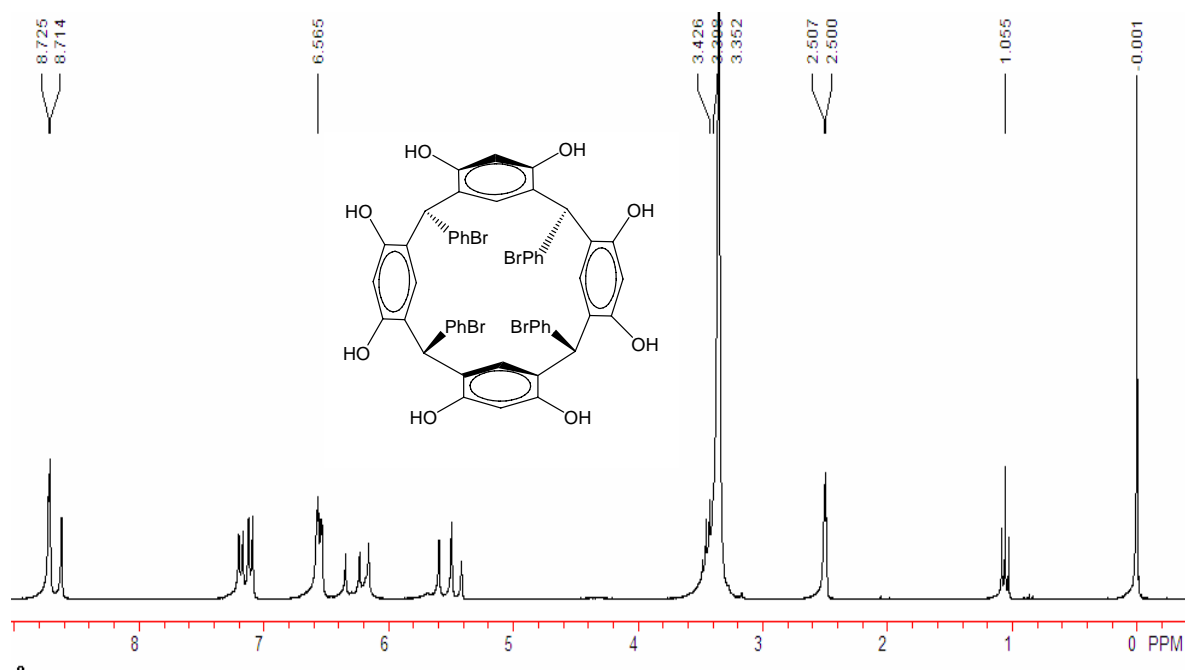


Figure 28. ^1H NMR of compound 8

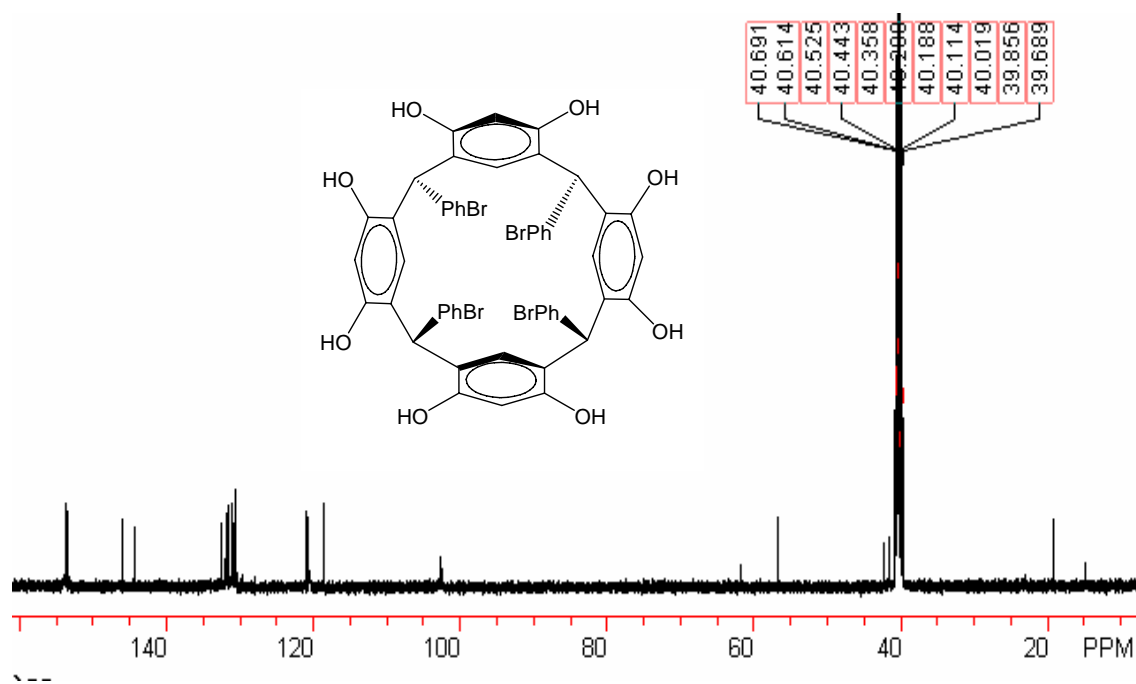


Figure 29. ^{13}C NMR of compound 8

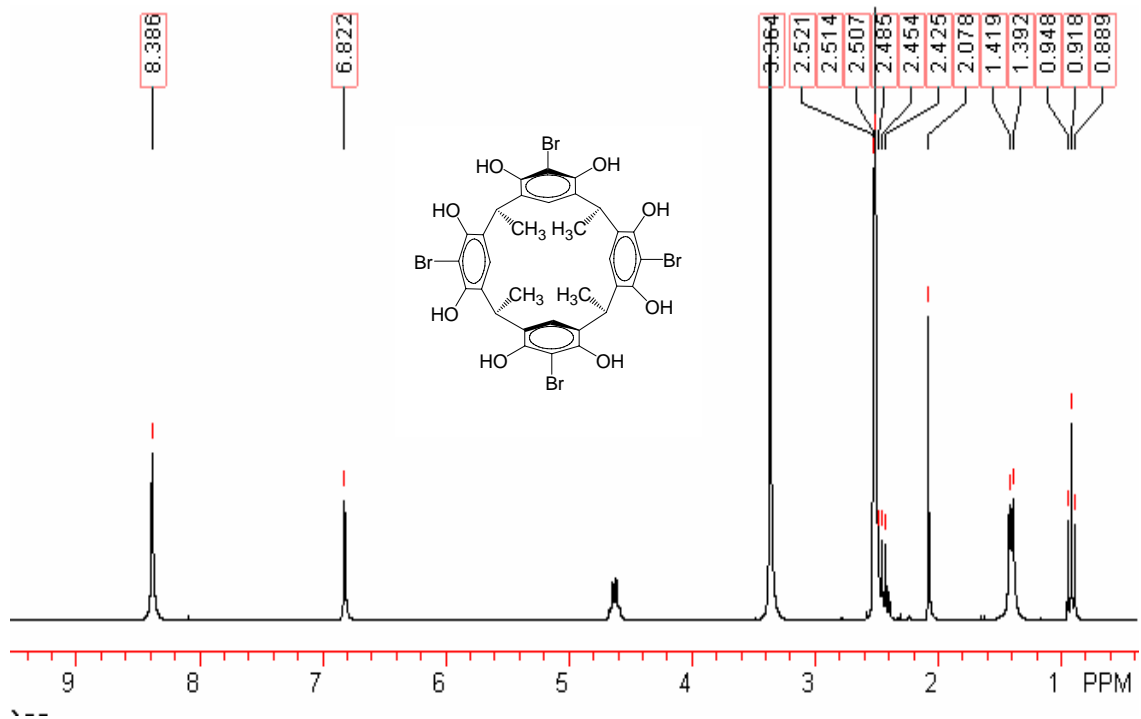


Figure 30. ^1H NMR of compound 10

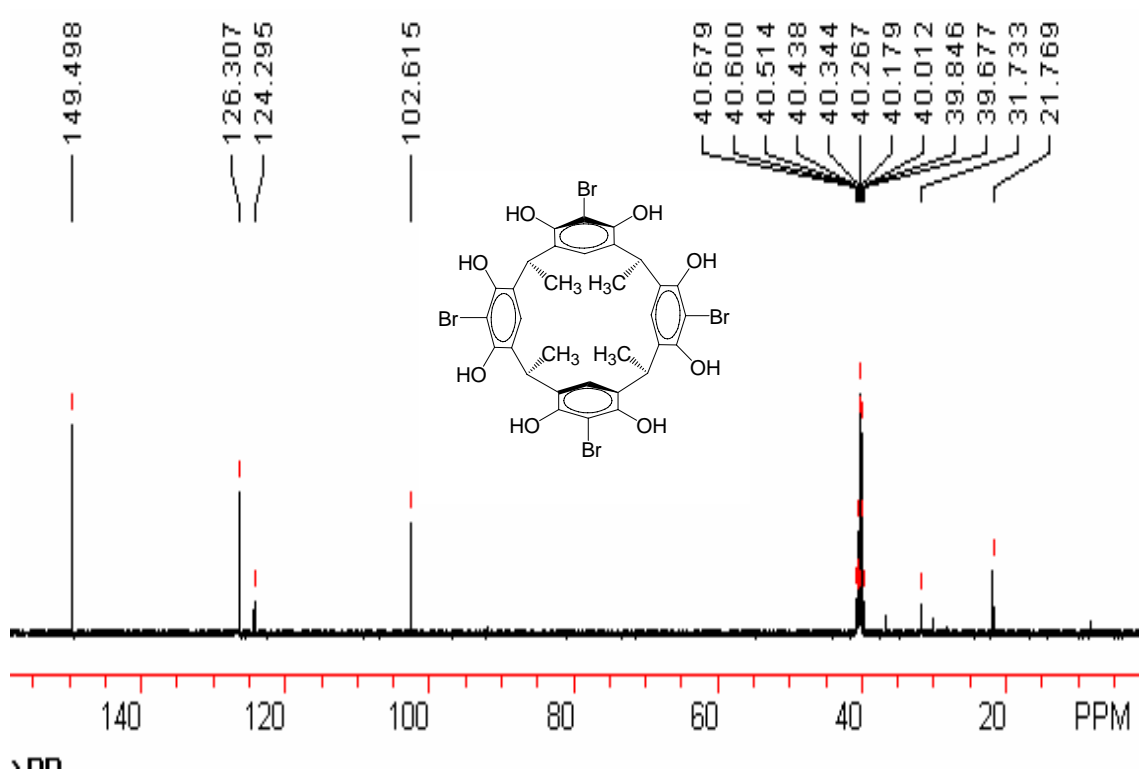


Figure 31. ^{13}C NMR of compound 10

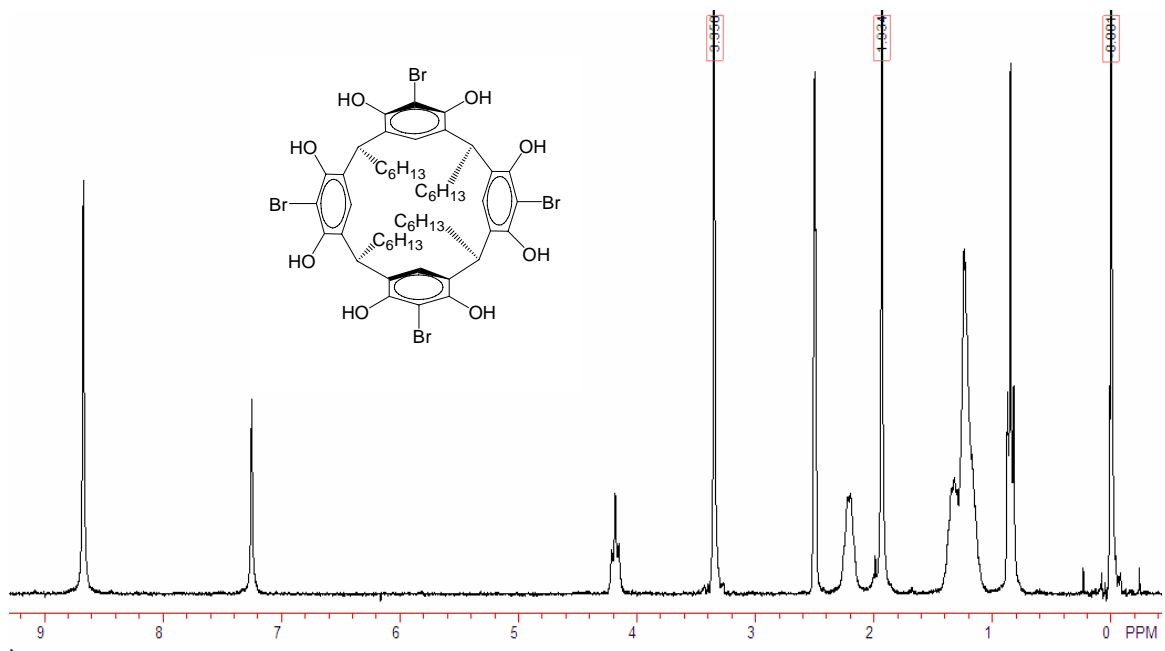


Figure 32. ^1H NMR of compound 11

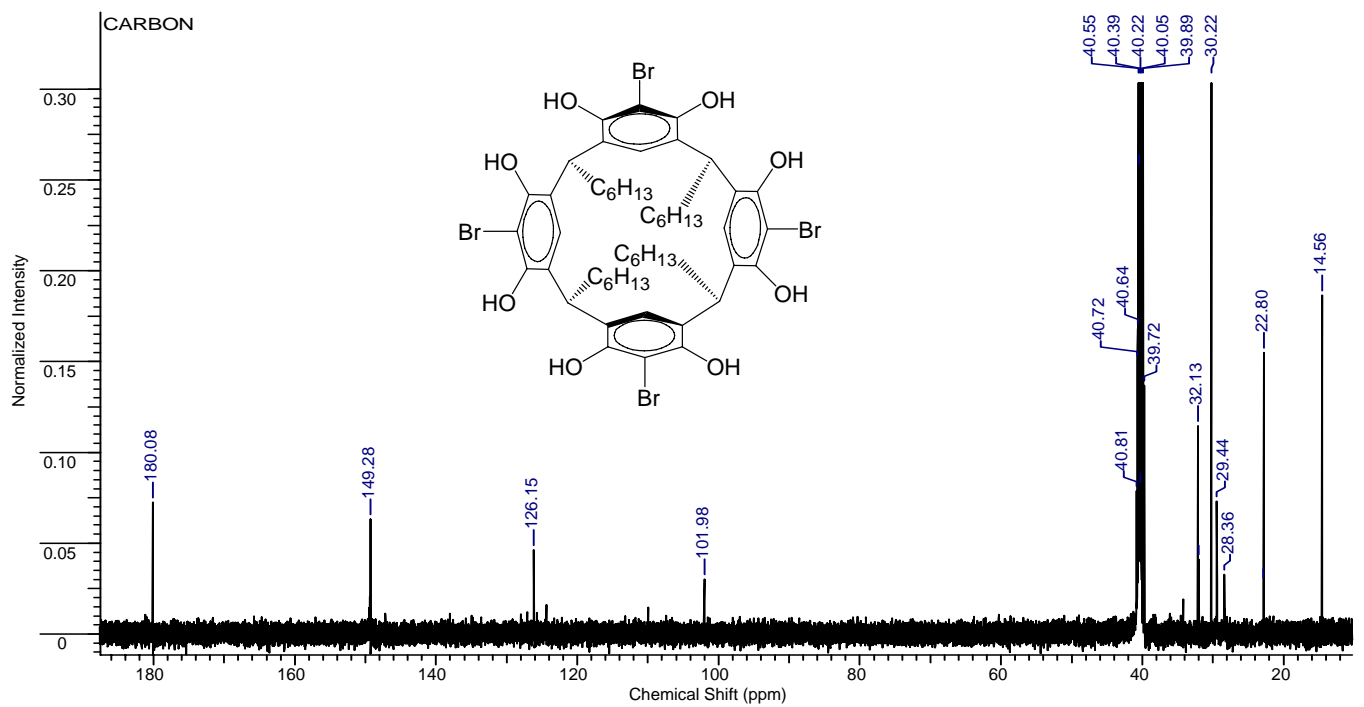


Figure 33. ^{13}C NMR of compound 11

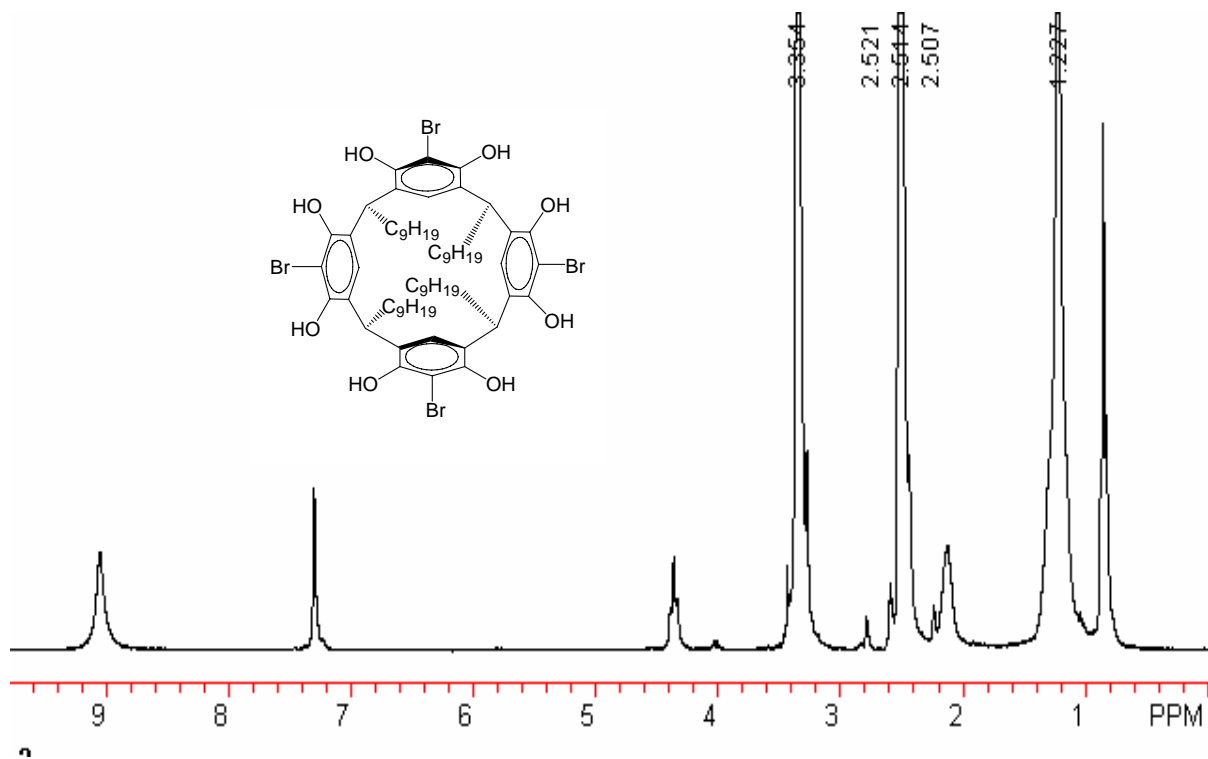


Figure 34. ^1H NMR of compound 12

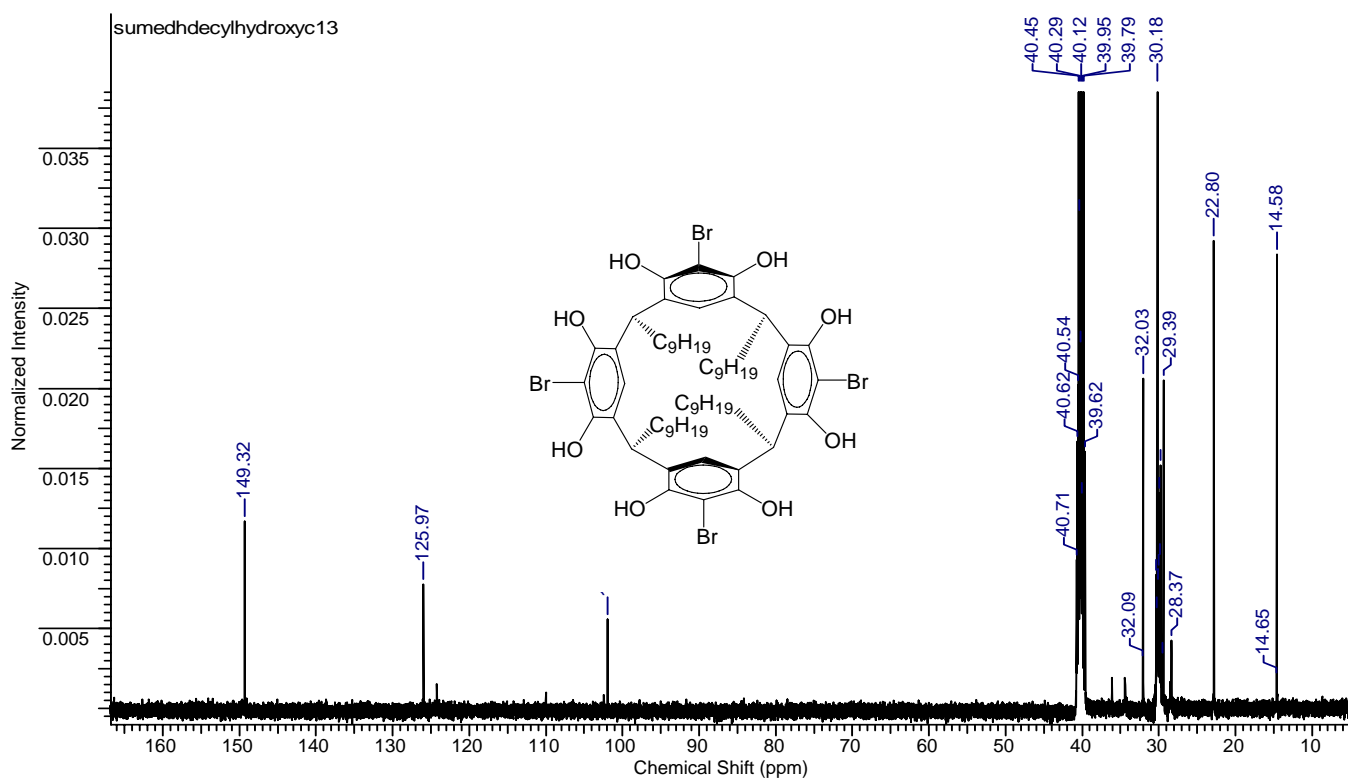


Figure 35. ^{13}C NMR of compound 12

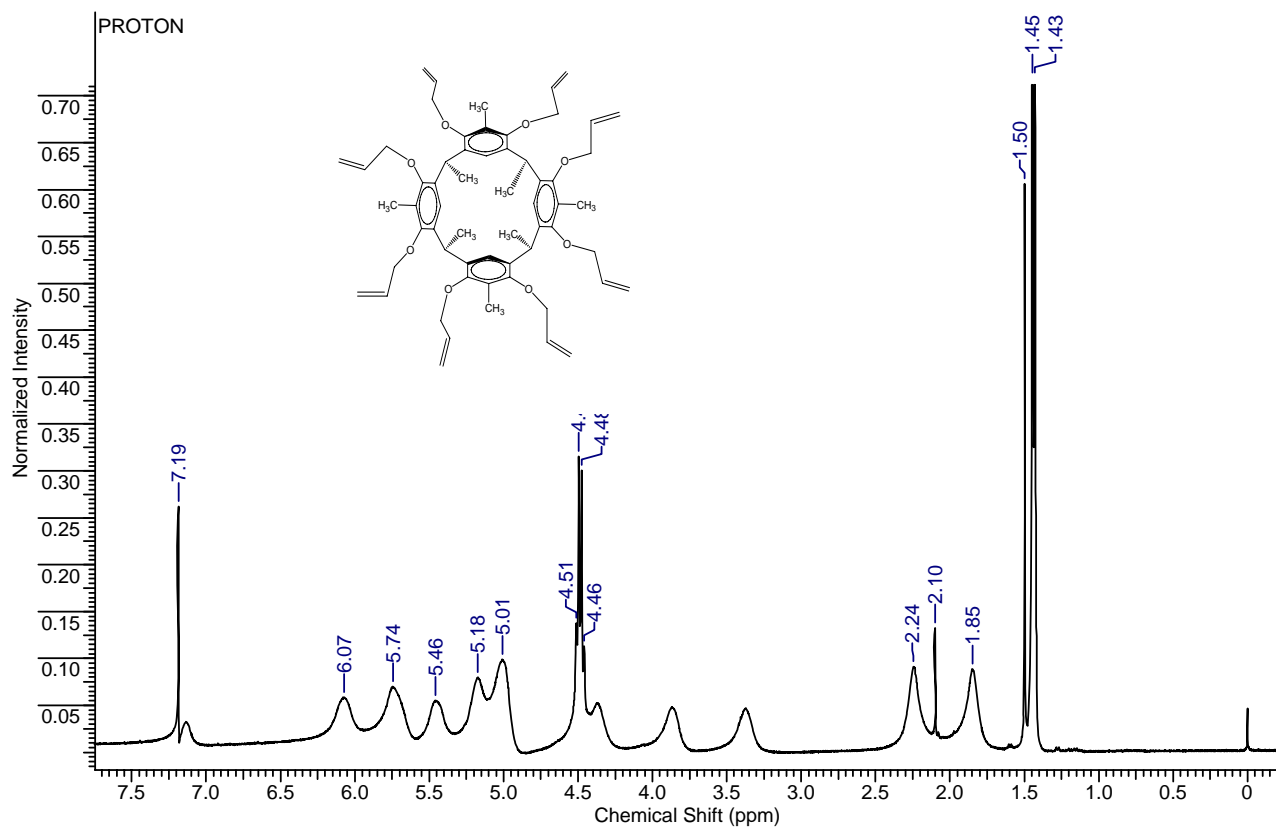


Figure 36. ^1H NMR of compound 13

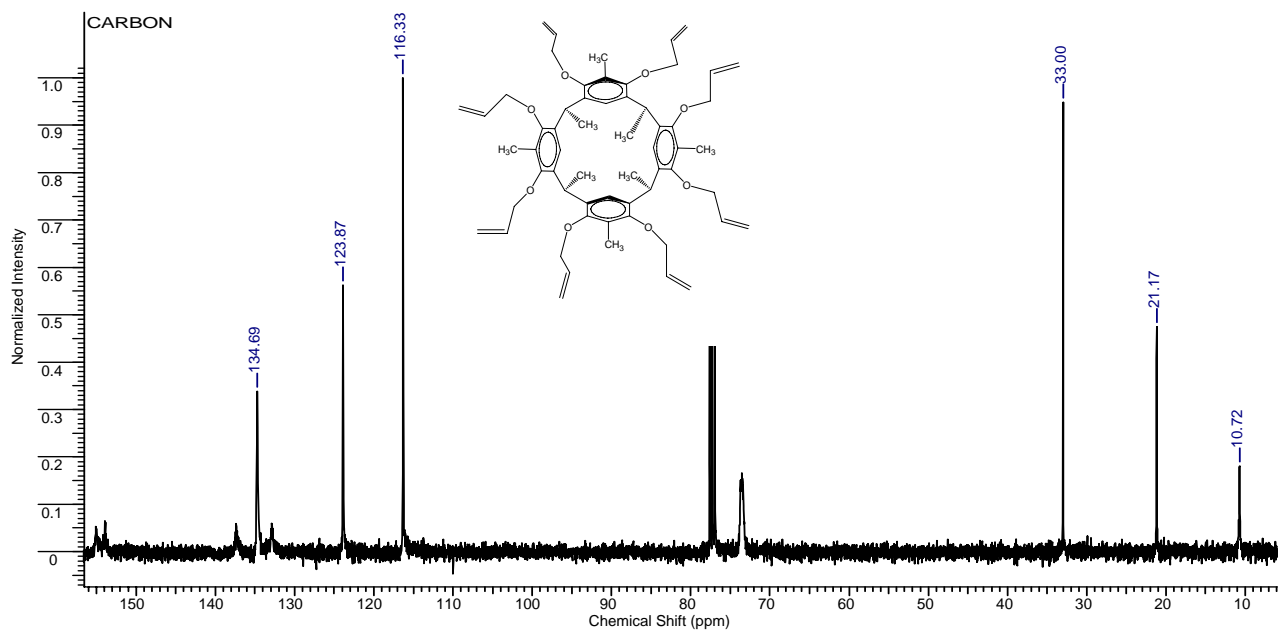


Figure 37. ^{13}C NMR of compound 13

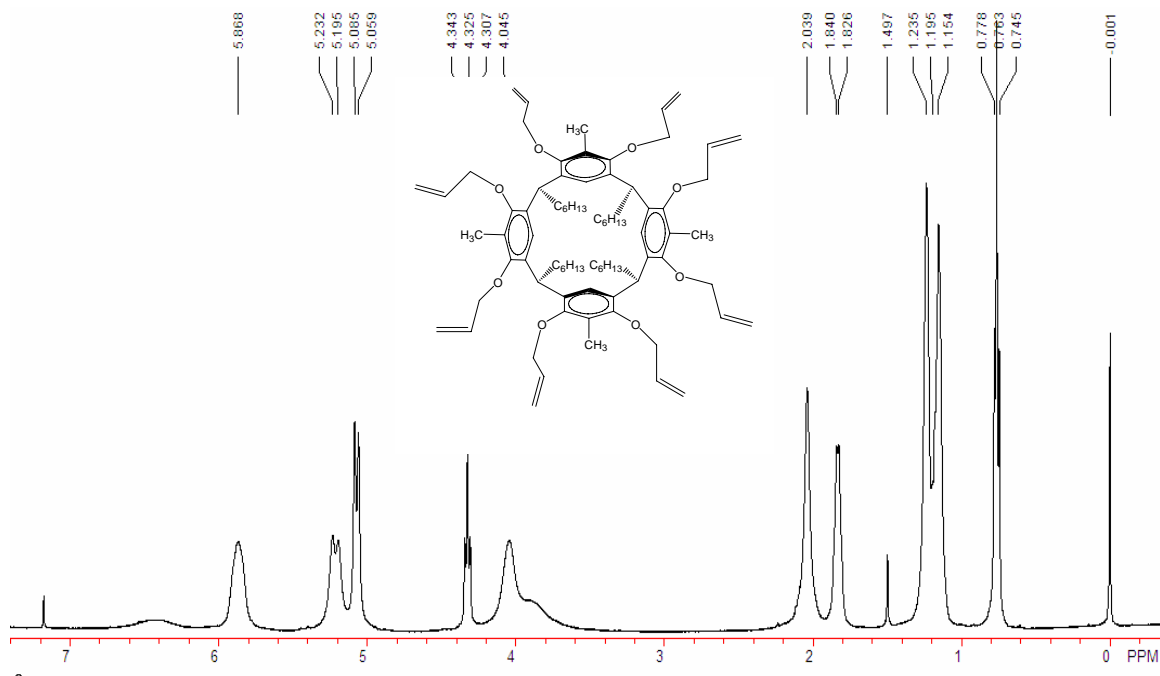


Figure 38. $^1\text{H NMR}$ of compound 14

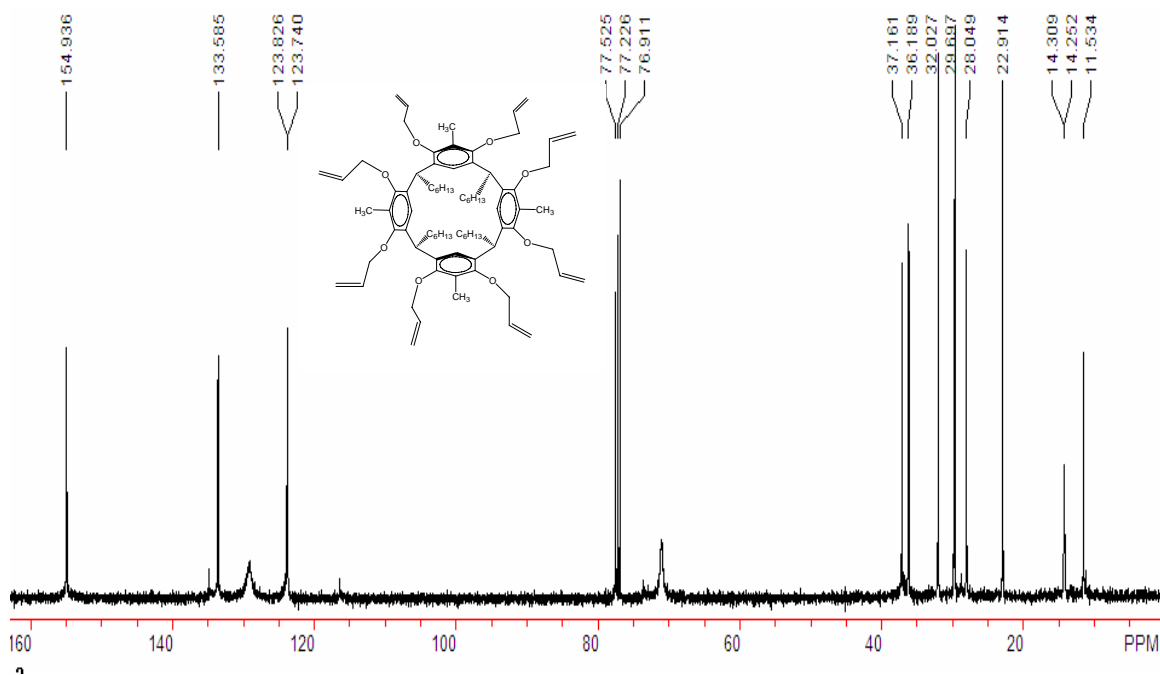


Figure 39. $^{13}\text{C NMR}$ of compound 14

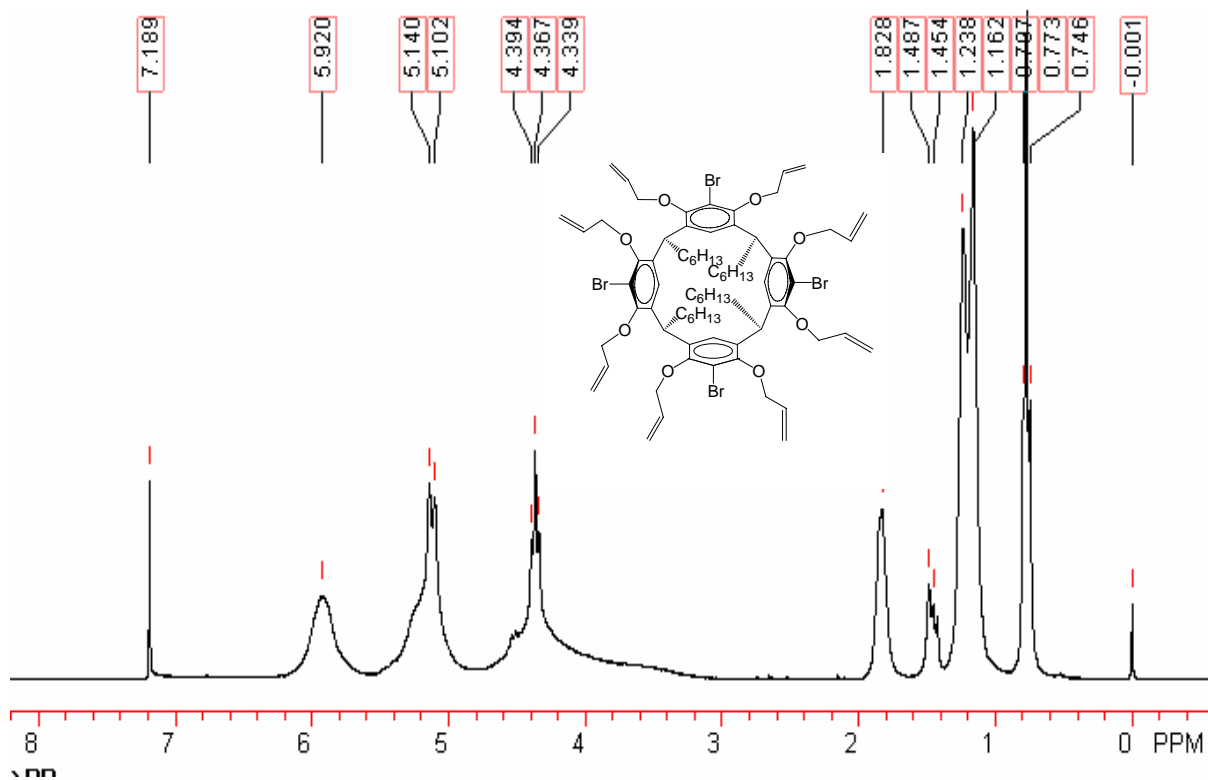


Figure 40. ^1H NMR of compound 15

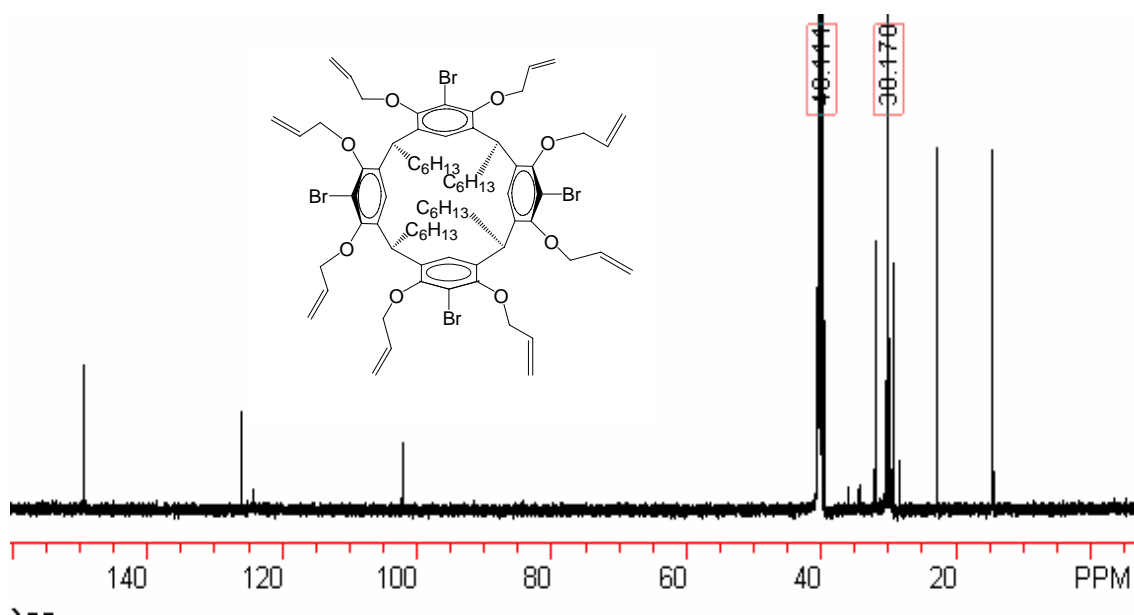


Figure 41. ^{13}C NMR of compound 15

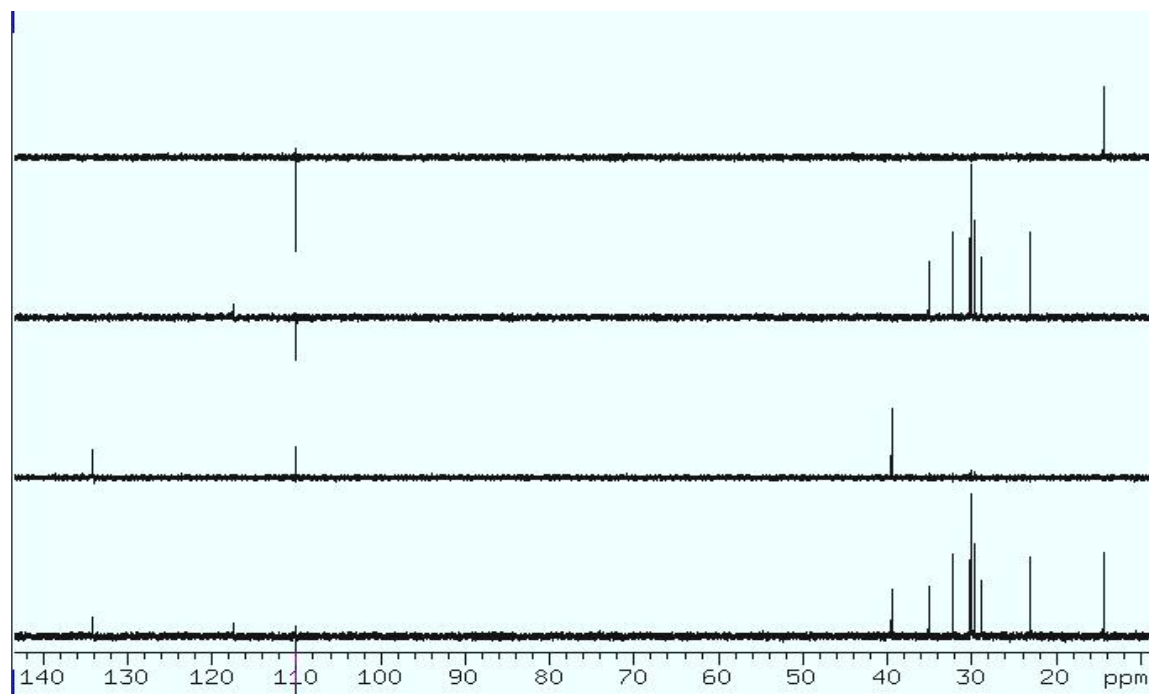
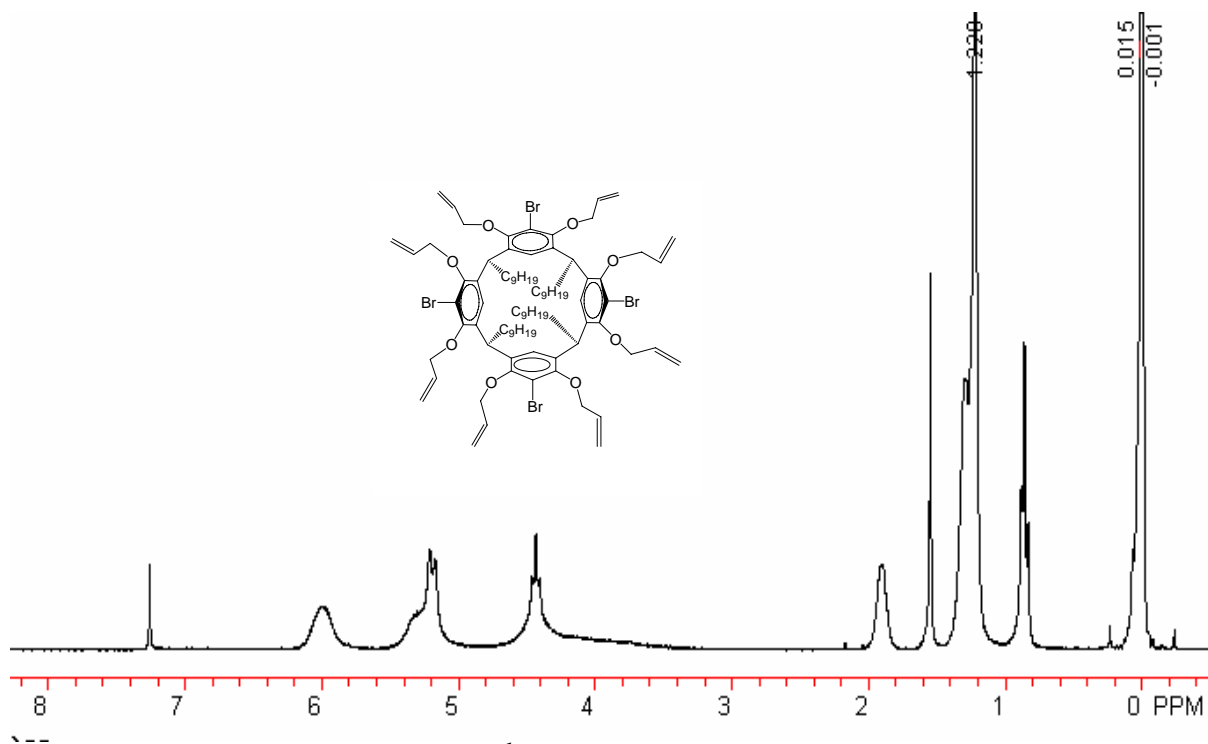


Figure 43. DEPT NMR of compound 16

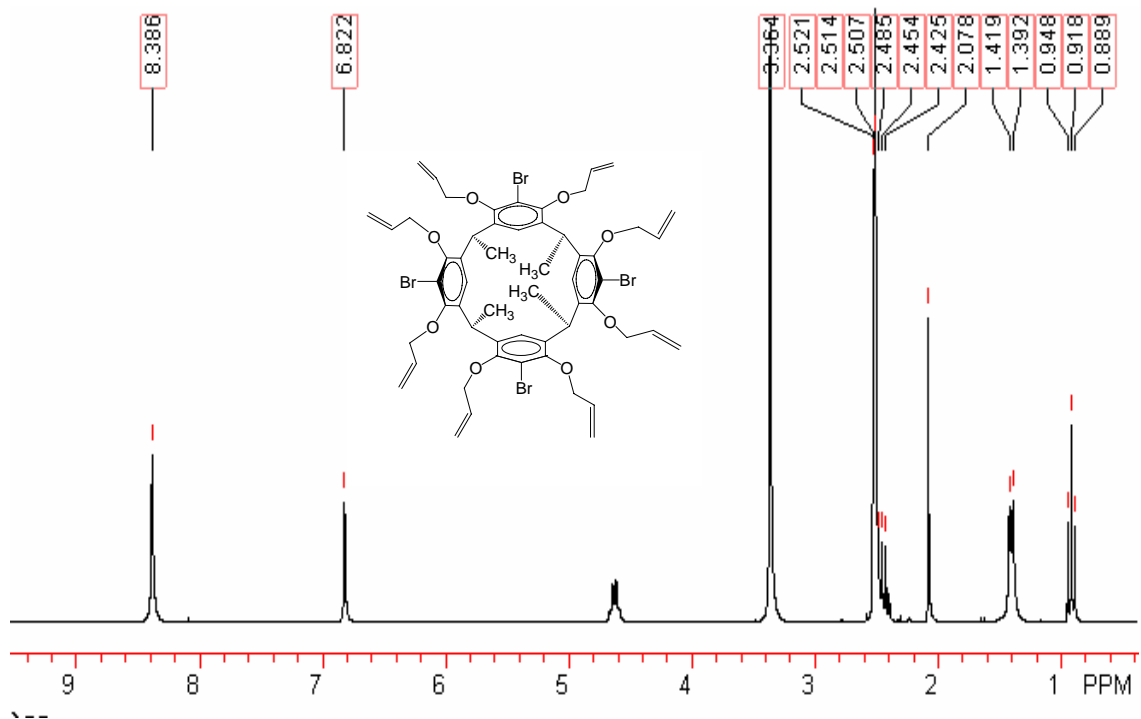


Figure 44. ^1H NMR of compound 17

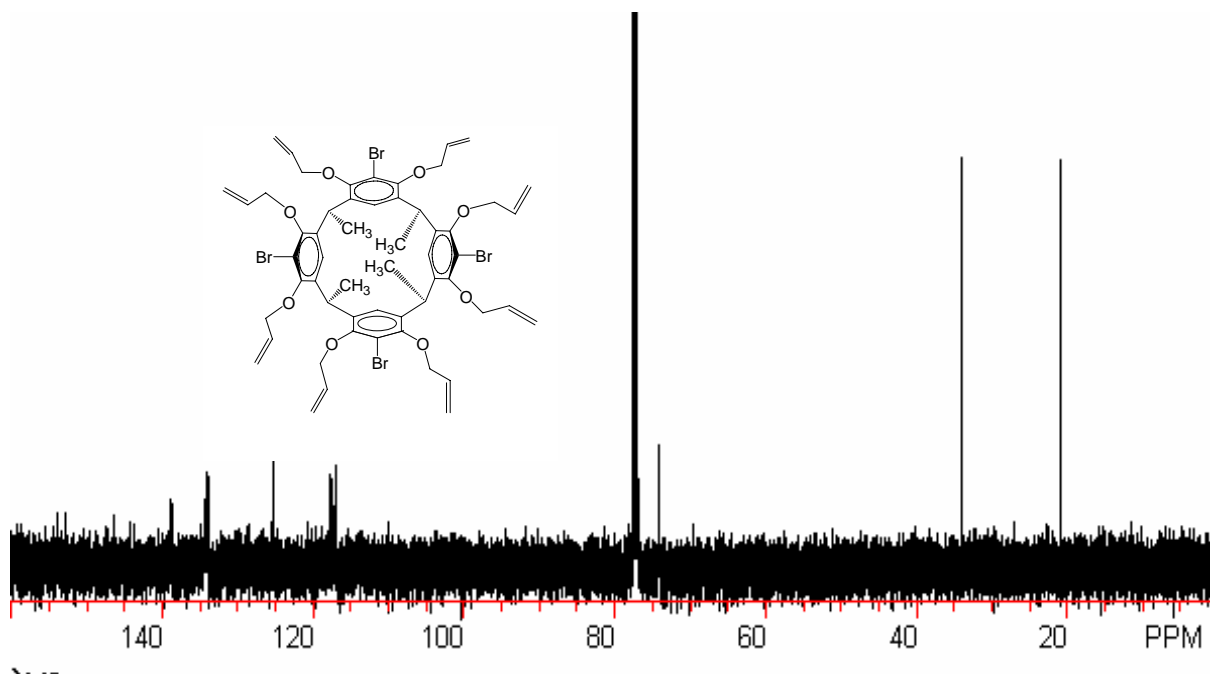


Figure 45. ^{13}C NMR of compound 17

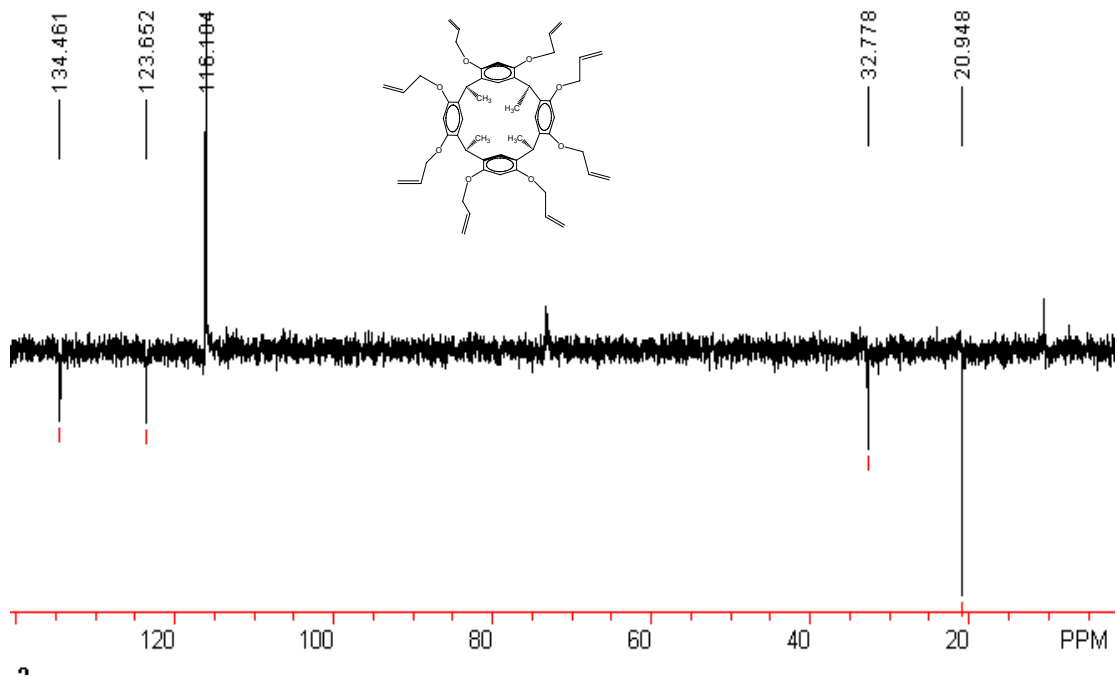


Figure 46. DEPT NMR of compound 18

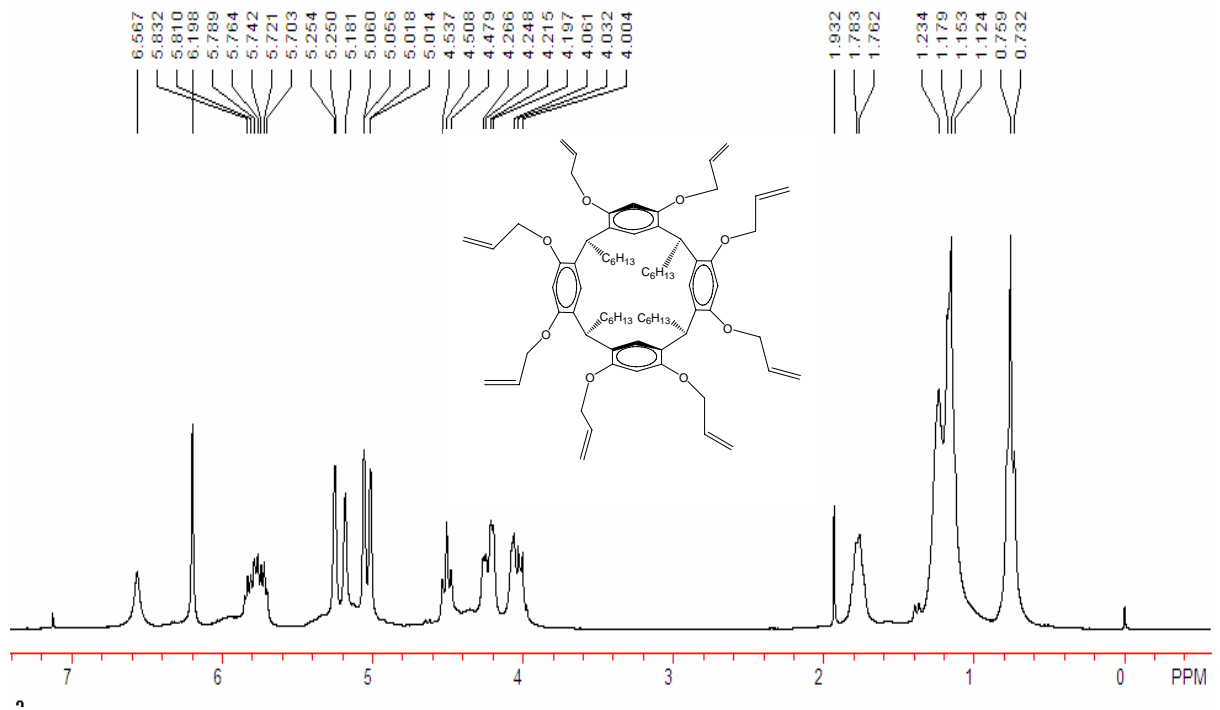


Figure 47. ¹H NMR of compound 19

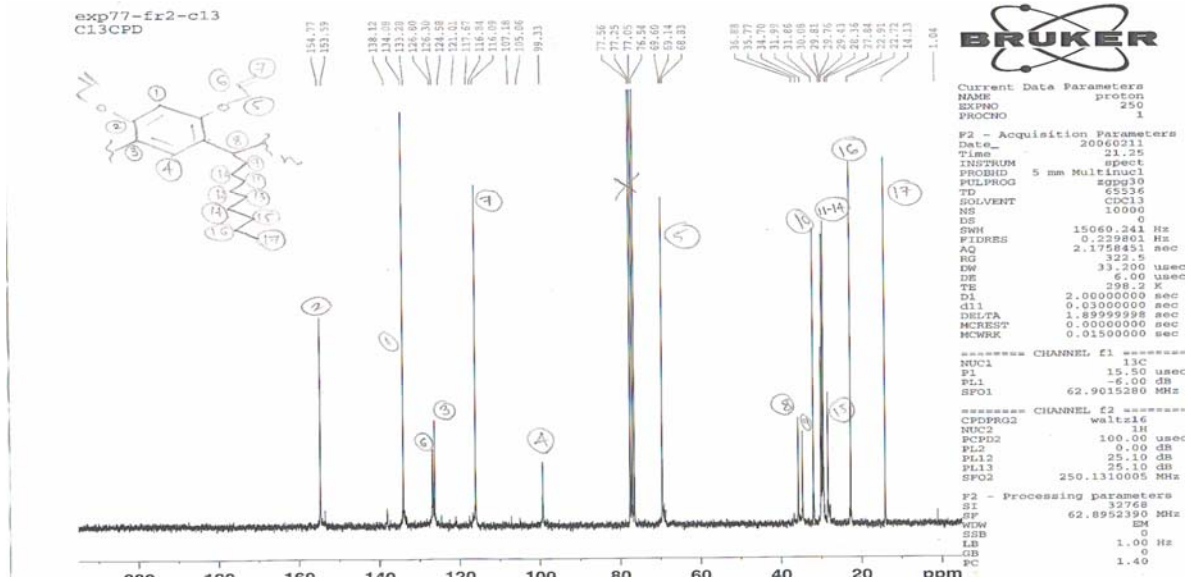


Figure 48. ^{13}C NMR of compound 19

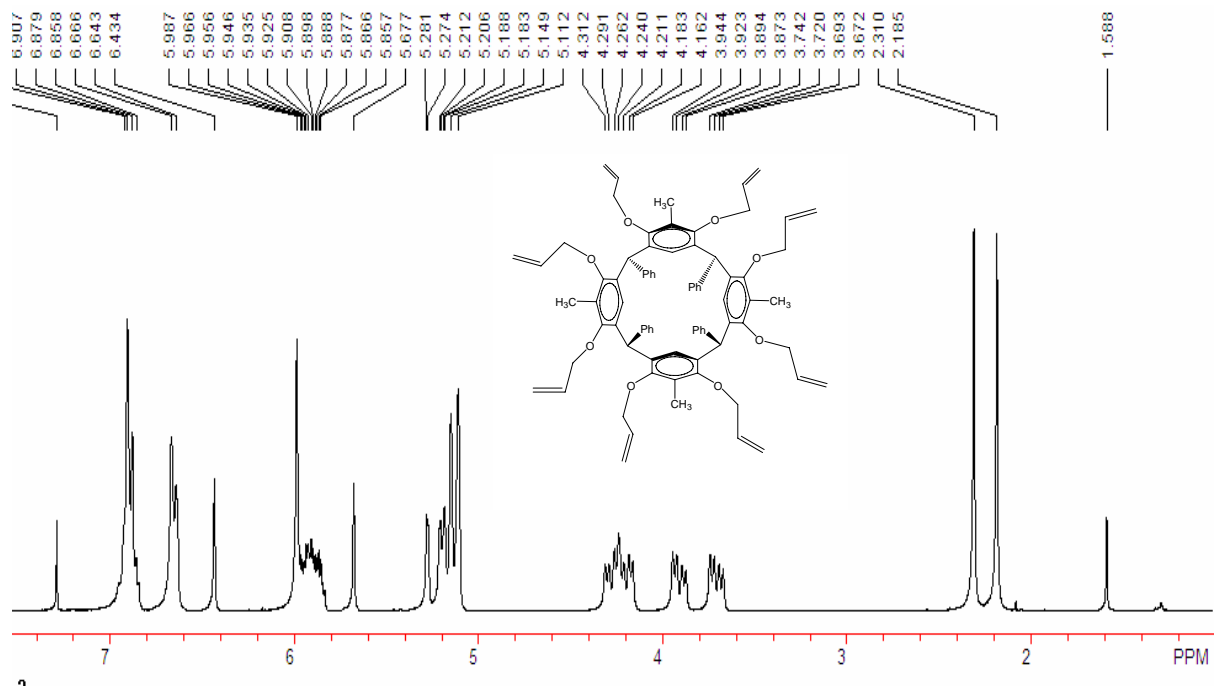


Figure 49. ^1H NMR of compound 20

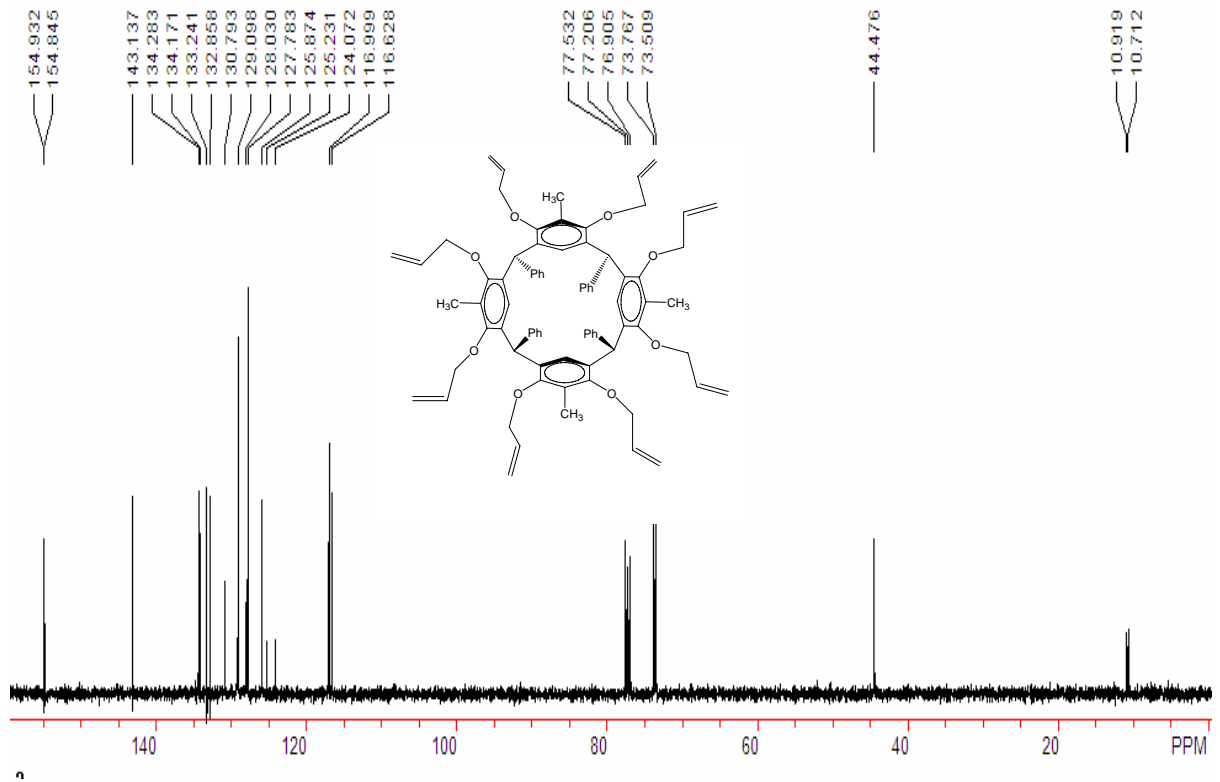


Figure 50. ^{13}C NMR of compound 20

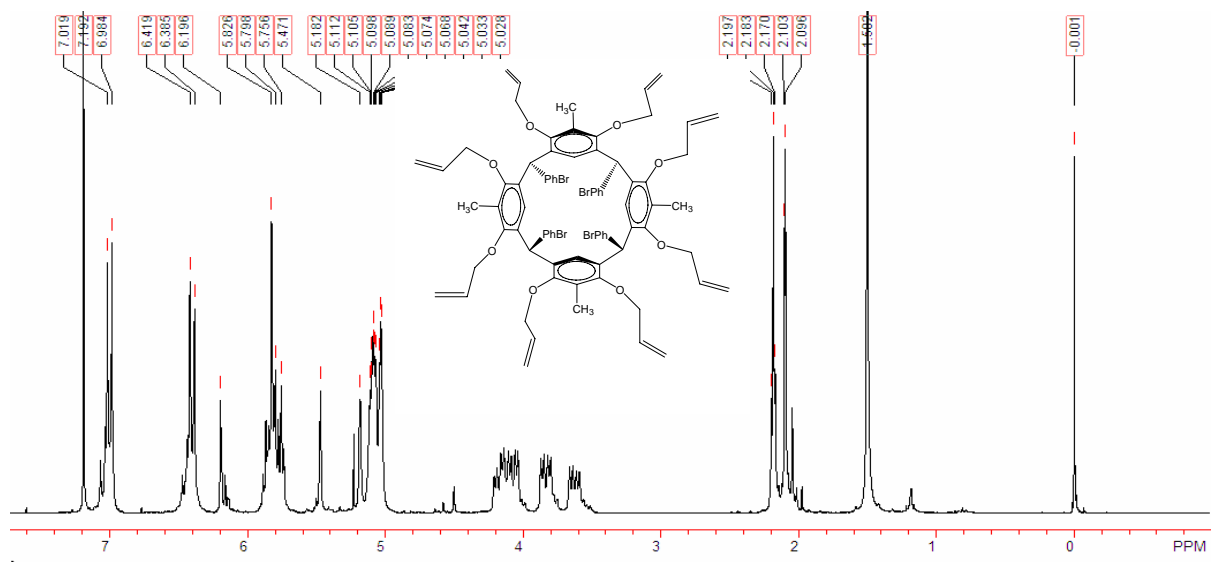


Figure 51. ^1H NMR of compound 21

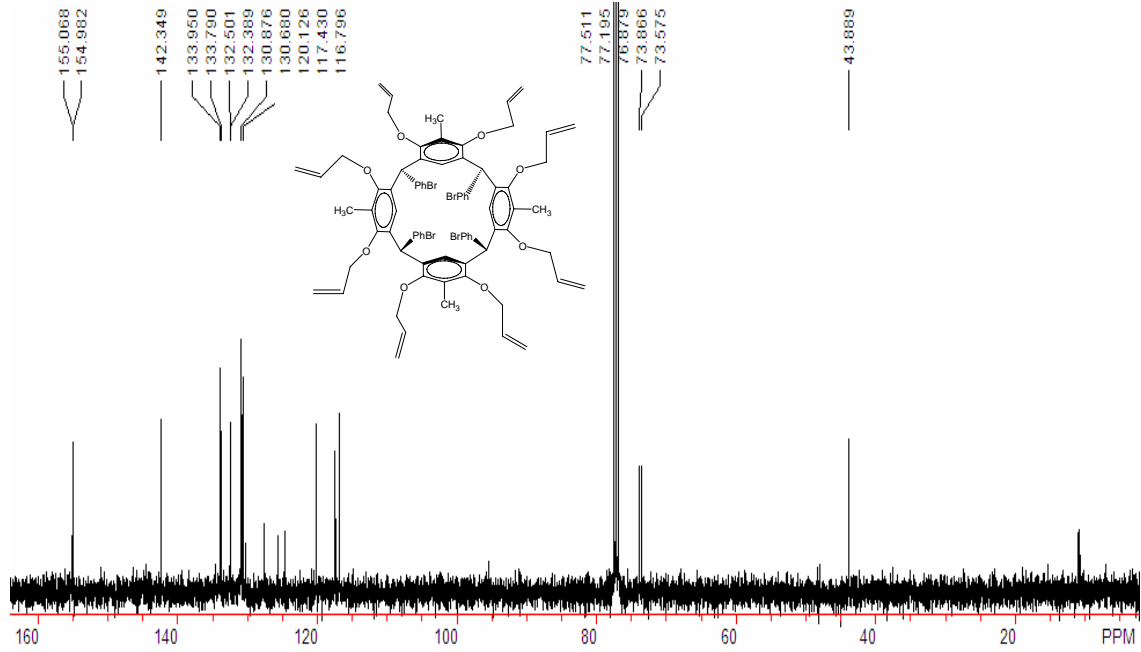


Figure 52. ¹³C NMR of compound 21

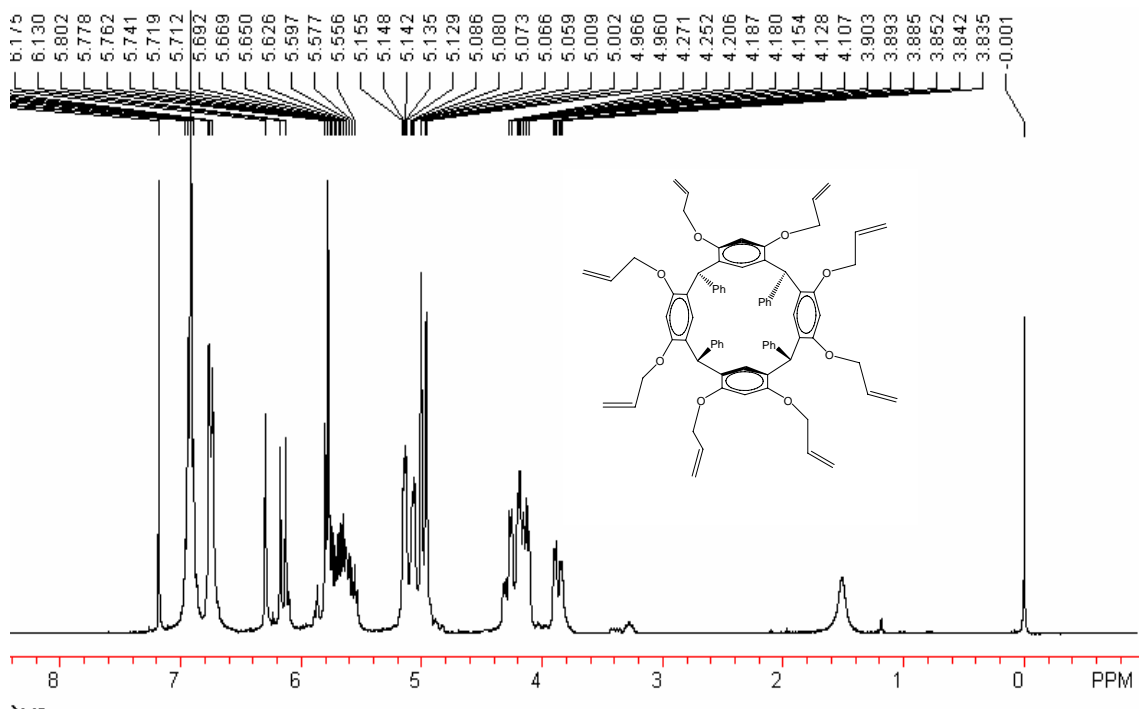


Figure 53. ¹H NMR of compound 22

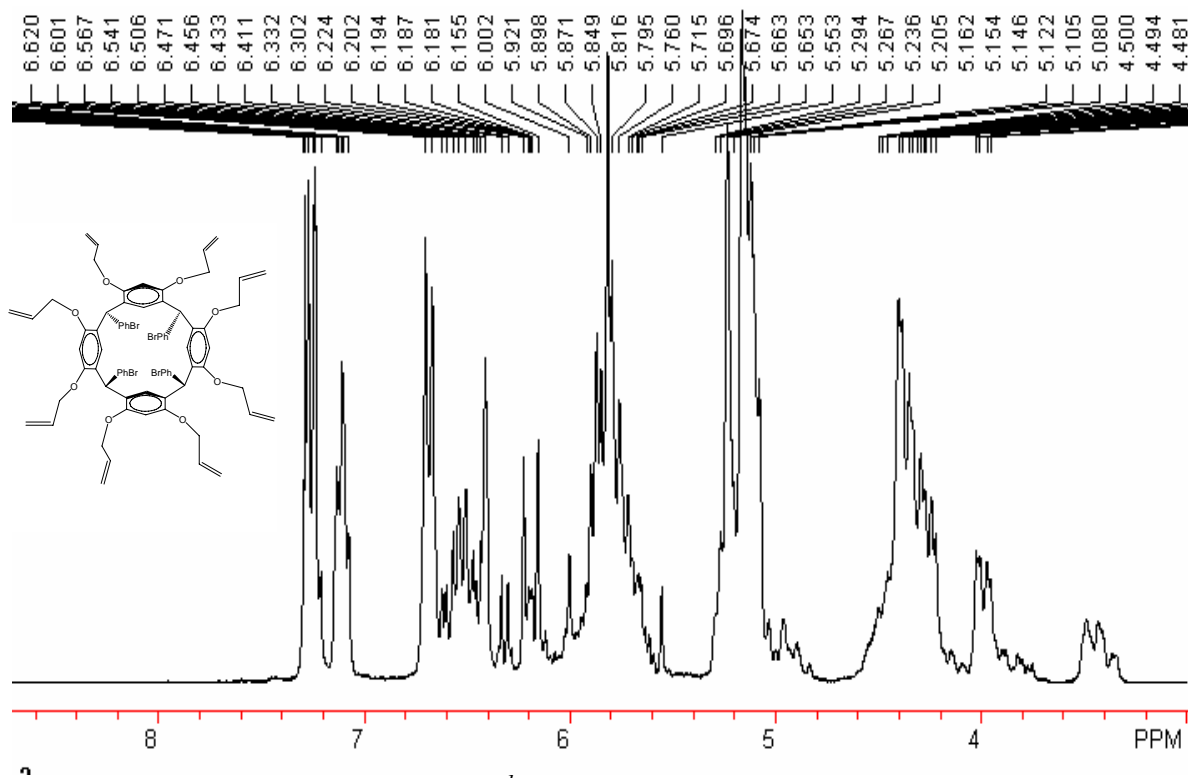


Figure 54. ^1H NMR of compound 23

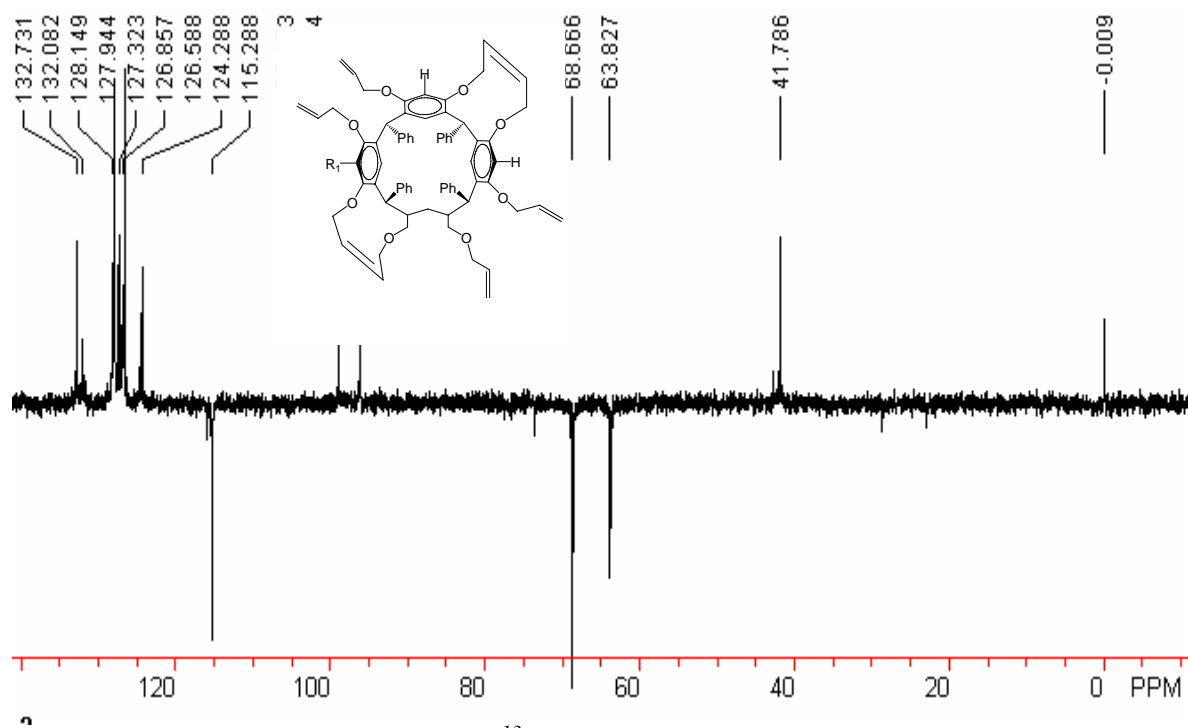


Figure 55. ^{13}C NMR of compound 26

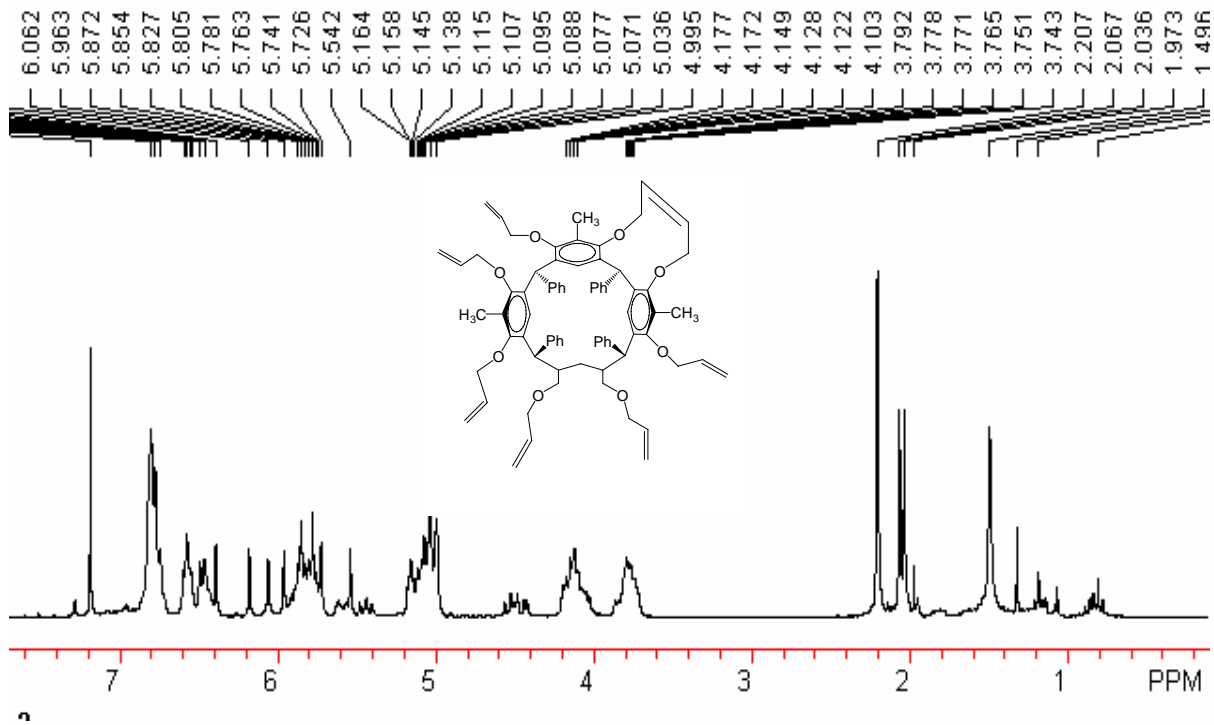


Figure 56. ^1H NMR of compound 28

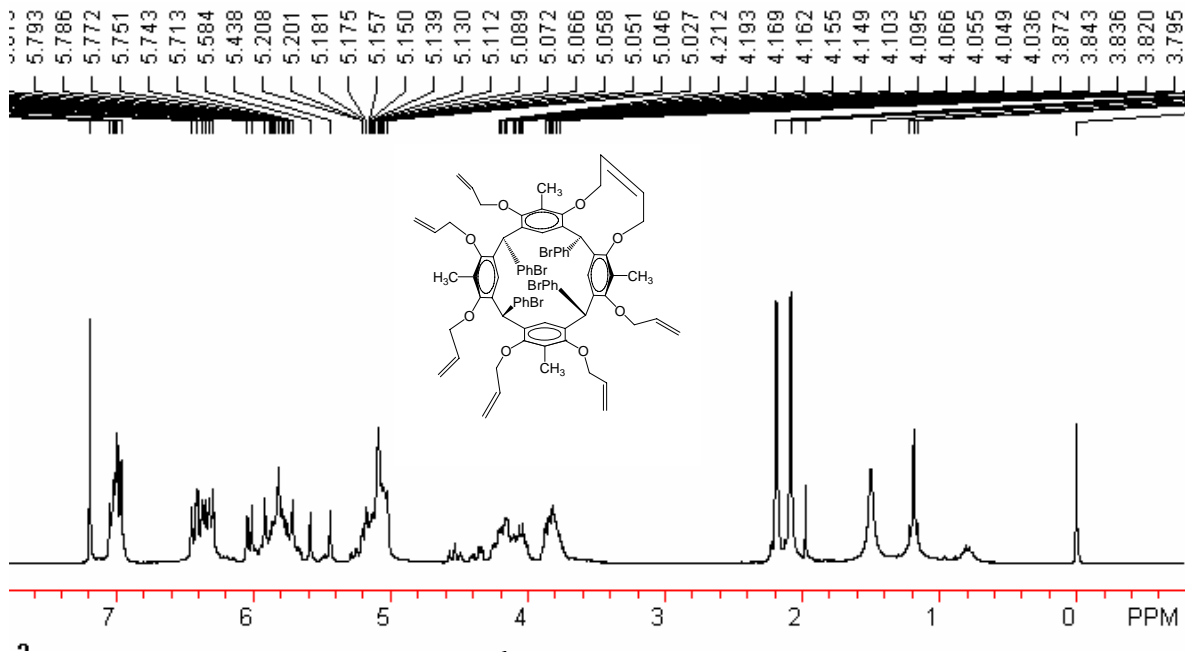


Figure 57. ^1H NMR of compound 29

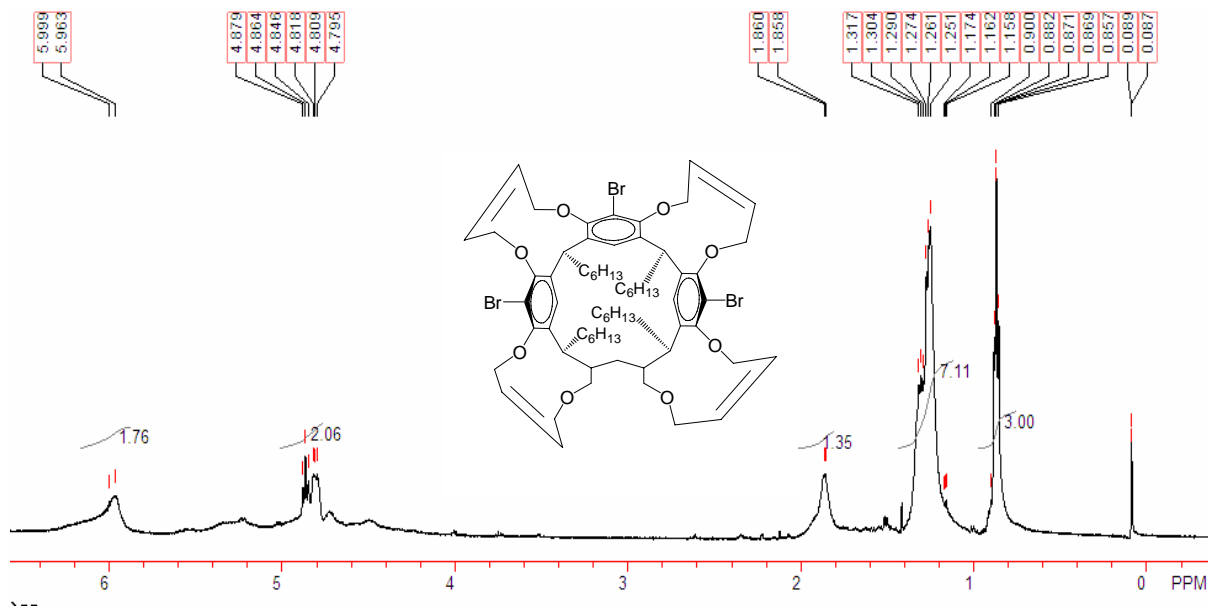


Figure 58. ^1H NMR of compound 30

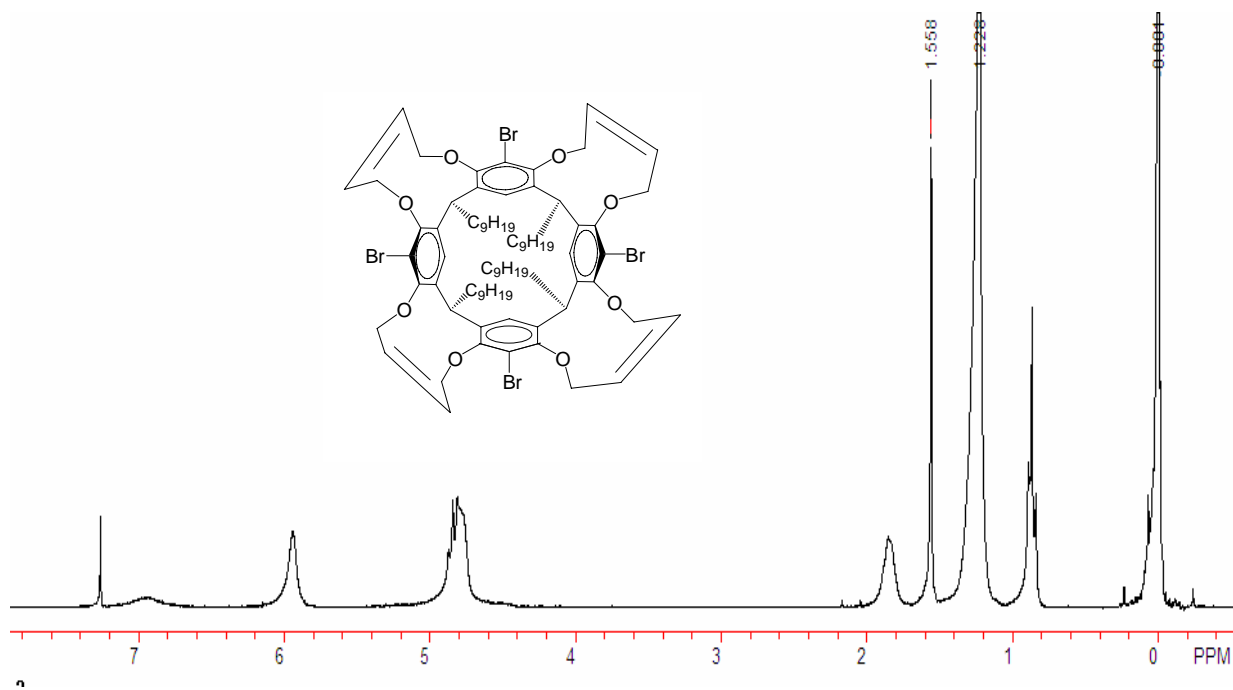


Figure 59. ^1H NMR of compound 31

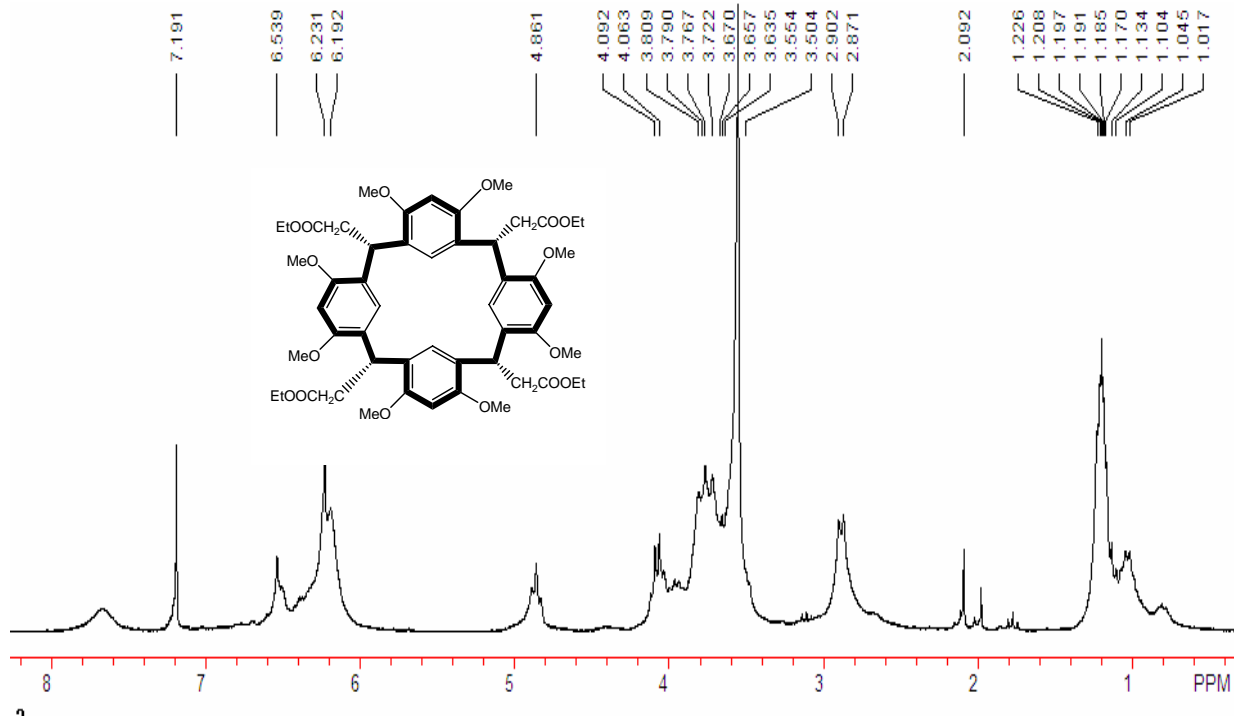


Figure 62. ¹H NMR of compound 34

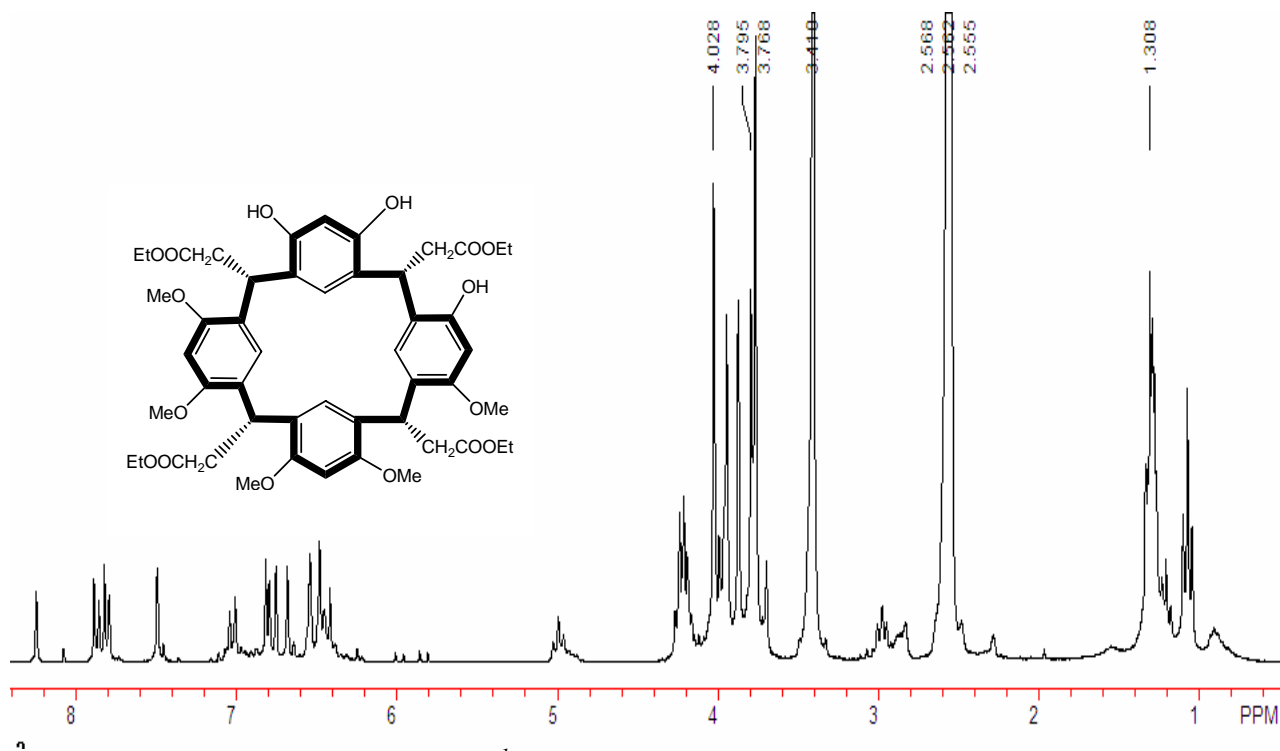


Figure 63. ¹H NMR of compound 35

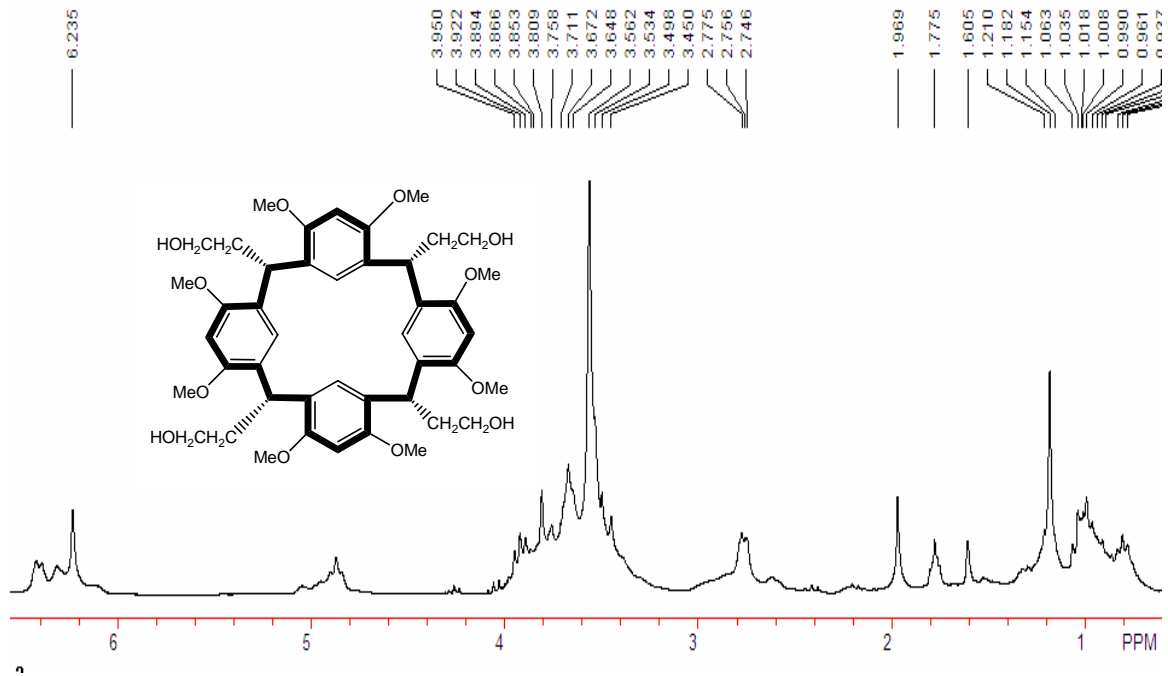


Figure 64. ¹H NMR of compound 36