SYNTHESIS, STRUCTURAL CHARACTERIZATION AND CHEMISTRY OF TRIBENZOHETEROTRIQUINANE BASED MOLECULAR STRUCTURES

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SYNTHESIS, STRUCTURAL CHARACTERIZATION AND CHEMISTRY OF TRIBENZOHETEROTRIQUINANE BASED MOLECULAR STRUCTURES

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ABSTRACT

SYNTHESIS, STRUCTURAL CHARACTERIZATION AND CHEMISTRY OF TRIBENZOHETEROTRIQUINANE BASED MOLECULAR STRUCTURES

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The synthesis of heteroatom containing derivatives of triquinane structure by the Mascal group represents an important development in the field of fundamental organic chemistry. Some derivatives of hererotriquinane structures showed unusual reactivity and structure properties. For example, oxonium ions are known as fleeting intermediates in certain reaction mechanisms. However, oxatriquinane, the oxygen containing analogue of heterotriquinane family, shows extreme stability. It can be chromatographed and survives in boiling water for a week. Additionally, a pure S_N2 on a tertiary center was showcased on a methylated derivative of oxatriquinane. Substituted oxatriquinanes were also shown to have extremely long C-O bond lengths, one derivate being the record holder in the literature. Moreover, azatriquinane which is nitrogen atom containing derivative of triquinane is known to be the most powerful simple trialkylamine base. Additionally, the tribenzotriquinane which is benzo derivative of triquinane has attracted much attention like the triquinane, and a variety studies have been performed on this scaffold in number of different fields, such as fundamental chemistry and material science. However,

heteroatom containing derivatives of this molecule have not been available in the literature and it was expected that tribenzoheterotriquinane structures will exhibit unusual reactivity and structural properties as in the case of heterotriquinane derivatives. In this study, in order to synthesize target molecule, a multi-step synthetic approach was utilized. First, an important core unit in this synthetic approach has been synthesized successfully and with the functionalizations of this core unit tribenzooxatriquinane, the oxo analogue of tribenzotriquinane, was synthesized successfully first time in the literature. Synthesis of this molecule represents an important development for the field of fundamental organic chemistry as it represents the first bis-benzylic oxonium ion derivative in the literature. Furthermore, due to having three benzene rings in the structure, tribenzooxatriquinane opens number of possibilities for functionalization of the structure so that new derivatives with interesting structural properties can be synthesized.

Keywords: Triquinane, Unusual Reactivity, Tribenzooxatriquinane

ÖZ

TRİBENZOHETEROTRİKUİNAN TABANLI MOLEKÜLER YAPILARIN SENTEZİ, YAPISAL KARAKTERİZASYONU VE KİMYALARININ İNCELENMESİ

Kepil, Dilay
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Ocak 2020, 80 sayfa

Trikuinan yapısının heteroatom içeren türevlerinin Mascal grubu tarafından sentezlenmesi temel organik kimya alanı için çok önemli bir gelişmeyi temsil etmektedir. Sentezlenen bazı türevler sıradışı reaktivite ve yapı özelliği göstermiştir. Örneğin, oksonyum iyonları reaksiyon mekanizmalarında geçici ara ürünler olarak bilinir. Ancak heterotrikuinan ailesinin analoğunu içeren oksotrikuinan sıradışı bir kararlılık gösterir. Yapı kromatografiye tabi tutulabilir ve bir hafta boyunca suda kaynatılabilir. Buna ek olarak, üçüncül bir merkezdeki S_N2 reaksiyonu, metillenmiş bir oksatrikuinan üzerinde sergilenmiştir. Oksatrikuinan türevlerinin ayrıca son derece uzun C-O bağ uzunluklarına sahip oldukları gösterilmiştir. Hatta bir türev rekoru elinde tutmaktadır. Ayrıca trikuinanın azot atom içeren türevlerinden azatrikuinan ise bilinen en güçlü basit amin bazıdır. Bunlara ilaveten, trikuinan yapısının benzo türevi olan tribenzotrikuinan yapısı da trikuinan yapısı gibi çok ilgi çekmiştir ve bu yapı iskeleti üzerinde temel kimya ve malzeme bilimi gibi farklı alanlarda çeşitli çalışmalar yapılmıştır. Ancak bu yapının hetero atom içeren türevleri literatürde henüz bulunmamaktadır ve heteroatom içeren trikuinan örneklerinde olduğu gibi tribenzoheterotrikuinan yapılarının da sıradışı reaktivite ve

yapısal özellikler göstermesi beklenilmektedir. Bu çalışmada hedef molekülü sentezlemek için çok aşamalı sentetik bir yaklaşım kullanılmıştır. İlk olarak bu sentetik yaklaşımda önemli bir çekirdek birim başarıyla sentezlenmiştir ve be çekirdek birimin fonksiyonlandırılmalarıyla tribenzoheterotrikuinanın oksijen türevi olan tribenzooksotrikuinan literatürde ilk kez başarılı bir şekilde sentezlenmiştir. Bu molekülün sentezi, literatürdeki ilk bis-benzilik oksonyum iyon türevini temsil ettiği için çok önemli bir gelişmeyi temsil etmektedir. Ayrıca tribenzooksotrikuinan yapısının üç tane benzen halkasına sahip olması yapının fonksiyonlandırılabilmesi için birçok pozisyon açmaktadır ve bu sayede ilginç yapısal özelliklere sahip yeni türevler sentezlenebilecektir.

Anahtar Kelimeler: Trikuinan, Olağandışı Yapı, Reaktivite, Tribenzooksatrikuinan

To all people that I love

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LIST OF ABBREVIATIONS

ABBREVIATIONS

AcOH	acetic acid
DCM	dichloromethane
AIBN	azobisisobutyronitrile
DMF	*N*, *N*-dimethyl formamide
DIBAL-H	diisobutyl aluminum hydride
DFT	Density Functional Theory
DMSO	dimethyl sulfoxide
EtOAc	ethyl acetate
HRMS	High Resolution Mass Spectrometry
NICS	Nucleus Independent Chemical Shifts
NBS	*N*-bromosuccinimide
NMR	Nuclear Magnetic Resonance
p-TsOH	para-toluenesulfonic acid
S_N1	unimolecular nucleophilic substitution
S_N2	bimolecular nucleophilic substitution
TfOH	triflic acid
THF	tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	tetramethylsilane

LIST OF SYMBOLS

SYMBOLS

Å	Angstrom
ºC	Celcius

CHAPTER 1

INTRODUCTION

1.1 Discovery of Fullerenes

Carbon is the one of the most common elements in the whole universe and it is the basis of life. However, studying pure carbon might not seem that exciting for many researchers, but with the discovery of fullerenes which is one of the allotropes of the carbon, Sir Harold Walter Kroto, Richard E. Smalley and Robert F. Curl, Jr. were awarded the 1996 Nobel Prize in Chemistry. Fullerene (C_{60}) consists of closed hexagonal and pentagonal network of 60 carbon atoms bonded by single and double bonds [1]. The structure of this molecule seems like a soccer ball and it has icosahedral symmetry. It was claimed to be the first example of a spherical aromatic molecule upon its discovery in 1985 [2].

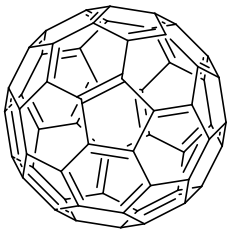


Figure 1.1. The structure of fullerene (**C_{60}**).

With the discovery of fullerene, new fields of research have been opened, especially in the field of basic science [3] and structures of fullerene fragments became attractive synthetic targets. A number of fullerene fragments were synthesized since then [4]. There are other fullerene structures with different number of carbons and the smallest possible fullerene is C_{20} which consists of twelve pentagons. C_{20} is the

most strained and least electronically stabilized form of fullerene. It has only been observed by mass spectrometry [5].

1.2 Triquinacene

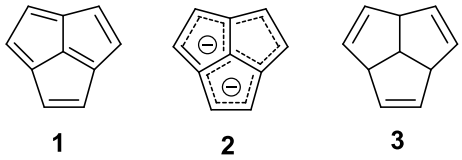


Figure 1.2 The structures of acepentalene **1**, dianion of acepentalene **2** and triquinacene **3**.

The smallest nonplanar fragment of C_{20} is acepentalene (**1**), $C_{10}H_6$ which is tricyclic compound [6]. Although acepentalene is an antiaromatic compound, the dianion of acepentalene (**2**) is a non-planar aromatic compound which was synthesized by dehydrogenation of triquinacene (**3**) [7]. Triquinacene was first synthesized by Woodward and his colleagues [8]. Since then, it holds an important position in structural and synthetic chemistry. Triquinacene chemistry has on the center of various areas such as possible presence of homoaromatic stabilization, rearrangement chemistry [9], metal complexation [10] and most importantly as a starting material for dodecahedrane synthesis [11]. Until now, a number of derivatives of triquinacene were synthesized (Figure 1.3.).

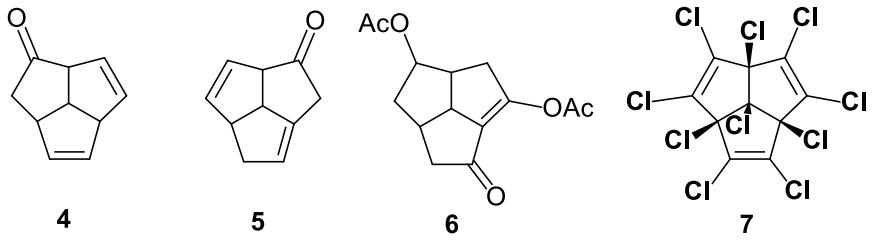


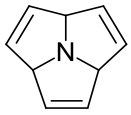
Figure 1.3. The structures of some derivatives of triquinacene (**4**-**7**).

1.3 Heterotriquinanes and Heterotriqunacenes

Although synthesis of triquinane, triquinacene and its derivatives have been the subject of many interesting studies, their derivatives which contain heteroatoms have not been studied for decades. In this section heteroatom containing triquinanes and triquinacenes will be discussed.

1.3.1 Synthesis of Azatriquinane and Azatriquinacene

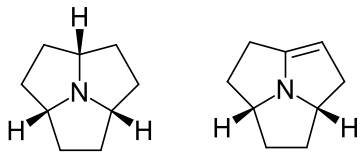
In literature, Mascal group made the first studies on heteroatom containing derivatives of triquinane [12]. When they synthesized **8**, it showed unique reactivity compared to triquinacene because it has reactive lone pair on nitrogen atom (Figure 1.4.) [13].



8

Figure 1.4. The structure of azatriquinacene (**8**).

Mascal group also became interested in the synthesis of the fully saturated derivatives of azatriquinacenes (Figure 1.5.), azatriquinane (**9**), a bowl-shaped heterocycle in terms of the concave/convex topology notion which was popularized by Cram [14]. Also, it was proved that **9** is the most basic trialkylamine in the literature since its pKa value is 0.5 units greater than quinuclidine [12].



9 **10**

Figure 1.5. The structures of azatriquinane (**9**) and azatriquinenamine (**10**).

In addition to this, it was observed that the molecules azatriquinane (**9**) and azatriquinacene (**8**) were stable under atmospheric conditions. However, when azatriquinenamine (**10**) (Figure 1.5.), an intermediate in the synthesis of **9**, was heated up over 100 °C with the proton source, trimerization was observed (Figure 1.6.). It was believed that this was a unique enamine trimerization because when N-methyl-Δ^2- pyrroline enamine was trimerized, the central enamine first acts as enamine nucleophile, then after it acts as imine electrophile [16,17]. However, when azatriquinenamine was trimerized, the central enamine first acts as a nucleophile, after tautomerization it acts again as a nucleophile [18]. In addition to this unique reactivity, **11** is an extraordinary type of chiral and neutral superbase [18].

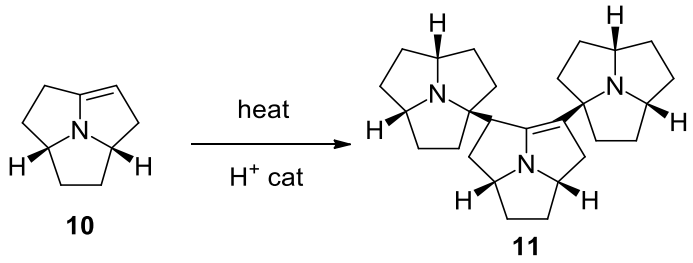


Figure 1.6. Trimerization of azatriquinenamine (**10**).

1.3.1.1 Aromaticity in Heteroacepentalenes

Although, **1**, acepentalene is antiaromatic, its dehydrogenated form (dianion, $\mathbf{2}^{2-}$) is non- planar aromatic and it can be persistent in THF at -40 ºC [7, 19]. Therefore, azaacepentalenide anion, **12** was of interest. NICS calculations revealed that **12** is more aromatic than compound **2** according to the aromaticity criterion [20].

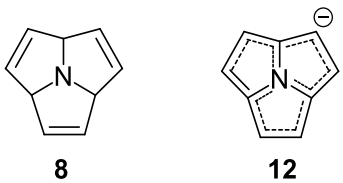


Figure 1.7. The structures of **8** and **12**.

When the aromatic anion **12** was synthesized, it was observed that electrons were highly delocalized within C_{3v} symmetry group according to NMR analysis. Computational studies showed that total CNC angles were to be 325.9° and 353.5° for **8** and **12** respectively [21]. In addition, the deviations of N atoms from the planes for **8** and **12** were found to be 1.31 Å and 0.41 Å respectively [21]. These results showed that curvature was reduced by aromatization, however aromatic **12** was still not planar. On the other hand, unlike aza substitution at the central atom, peripheral aza substituted derivatives of triquinacene (Figure 1.8.) tends to have reduced aromaticity due to increase in curvature [22].

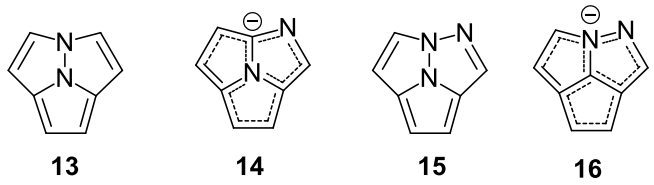


Figure 1.8. The structures of peripheral aza substitution derivatives of azatriquinacene (**13**-**16**).

1.3.1.2 The Chemistry of Perchloroazatriquinacene

Perchloroazatriquinacene (**17**) can be attained in one step with high yield by photochemical chlorination [23]. With the presence of bis-allylic functions in **17**, the potential to produce cationic intermediates which are capable of alkylating electron rich π-systems was demonstrated and **18** and **19** was produced from **17** in high yields with Lewis acid catalyst (Figure 1.9.) [24].

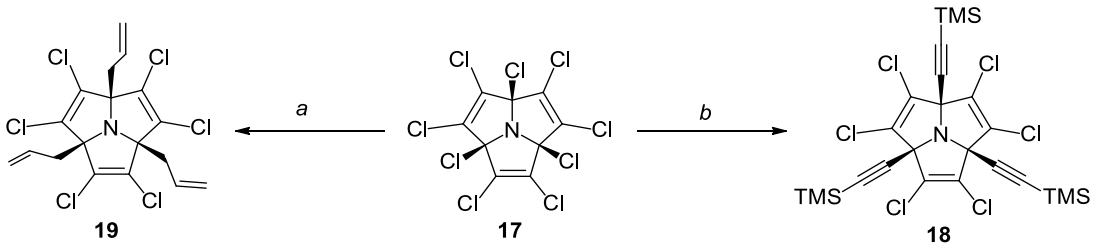


Figure 1.9. Reagents and conditions: a. $H_2CCHCH_2SiMe_3$, $AlCl_3$, CH_2Cl_2, 90%; b. $Me_3SiCCSiMe_3$, $AlCl_3$, CH_2Cl_2, 68%.

With the synthesis of **18** and **19**, a new field for utilization of azatriquinacene has emerged. It was envisioned that the new derivative of azatriquinane **17** may be applied as scaffold for tripodal ligands [24]. In other words, alpha substitutions of central atom have formed novel and conformationally stable polydentate ligands (**20** and **21**) (Figure 1.10.).

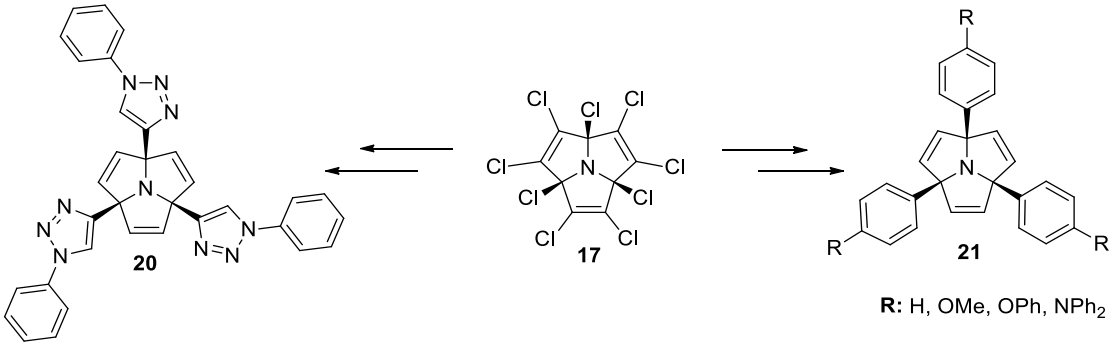


Figure 1.10. The structures of molecule **20** and molecule **21**.

1.3.2 Oxatriquinane and Its Derivatives

1.3.2.1 The Oxonium Ion

The term oxonium means a cationic oxygen atom with three bonds. The simplest oxonium ion is hydronium ion, H_3O^+. The oxonium ions which have trigonal pyramidal molecular shape are usually very reactive and unstable intermediates. Although most of the alkyl oxonium ions are highly reactive, they can be isolated. These are known as Meerwein salts ($R_3O^+X^-$) (Figure 1.11.) which can be stable when they contain an inert X^- (like BF_4^-, PF_6^-) and they can be used as strong alkylating agents [25].

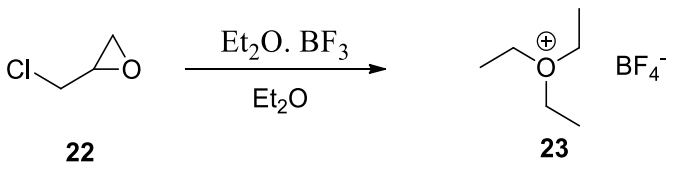


Figure 1.11. Synthesis of Meerwein salt (**23**).

1.3.2.2 Oxatriquinane

The oxygen analogue of triquinane, oxatriquinane (**26**) was first synthesized by Mascal group [26]. Until the synthesis of oxatriquinane, there were a few examples of bicyclic and tricyclic oxonium ions in literature (**24** [27] and **25** [28]). Although these derivatives are structurally interesting, their reactivity was similar to standard oxonium salts (Figure 1.12.).

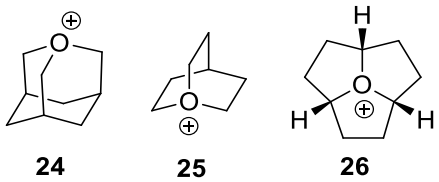


Figure 1.12. Structures of **24**, **25** and oxatriquinane (**26**).

When oxatriquinane was synthesized, it was called as extraordinary oxonium ion because it is stable in water (can be refluxed for 72 hours without decomposition) unlike a Meerwein salt. NMR spectrum could be obtained in D_2O. Moreover, it can be purified by column chromatography on silica gel without undergoing hydrolysis. In addition, it was figured out that oxatriquinane can also be persistent in other solvents like alcohols, acetone, DMSO and DMF. However, it decomposes in the presence of strong nucleophiles. To understand this unusual stability of **26**, X-ray structural analysis was performed. According to this, the bond length (1.54 Å) of **26** is longer than the bond length (1.47 Å) of known oxonium salt (Me_3O^+ AsF_6^-) and it has lower C-O-C bond angle (109.8°) than Me_3O^+ AsF_6^- (113.1°) [26]. However, this did not explain the unusual stability. This was explained in a detailed computational

study with rigid tricyclic structure, with favorable orbital interactions and angle strain [26].

1.3.2.3 Oxatriquinacene

Oxatriquinacene (**27**) was also first synthesized by Mascal group [26]. Although oxatriquinacene is not as stable as oxatriquinane (decomposes in water), it is still an unusual molecule according to its NMR spectrum. It was shown that protons which are in the alpha position of O atom appear in the aromatic region (6.80 ppm) even they are not olefinic hydrogens [26].

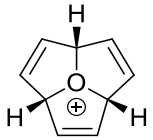


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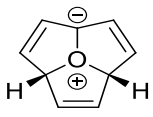
Figure 1.13. Structure of oxatriquinacene.

After the synthesisi of aromatic azaacepentalenide anion (**12**) by Mascal group, the possibility for the synthesis of the aromatic form of oxatriquinacene, **29** was investigated. NICS calculations of **29** showed that the aromaticity would be much higher than **12** [22]. Also, it was found that the new aromatic compound will be even more aromatic than benzene [22]. However no reported data was found in the literature for the synthesis of this highly interesting compound. In addition to this, Mascal group also studied on synthesis of oxonium ylide **28**. However, direct deprotonation of **27** could not be stabilized and it decomposed [22].



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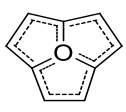

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Figure 1.14. Structures of ylide of oxatriquinacene (**28**) and aromatic form of oxatriquinacene (**29**).

1.3.2.4 1,4,7- Trimethyloxatriquinane

Mascal group was synthesized special derivative of oxatriquinane called 1,4,7-trimethyloxatriquinane, **31** [30]. It is special because at the tertiary carbon center of the molecule, can undergo S_N2 type reaction unlike written in the textbooks [30]. It is well-known that at the tertiary center, S_N1 reactions can occur. When 1,4,7-trimethyloxatriquinane was refluxed in ethanol for many hours, there were no reaction [30]. It means that there were no substitution or elimination reaction (no unimolecular mechanism). However, when there were basic nucleophiles (methoxide, cyanide) in the reaction medium, reaction occurred and **32** was obtained [30] (Figure 1.15.). In addition to this, when there was tetrabutylammonium azide in the reaction medium, **30** was obtained by S_N2 mechanism [30] (Figure 1.15.).

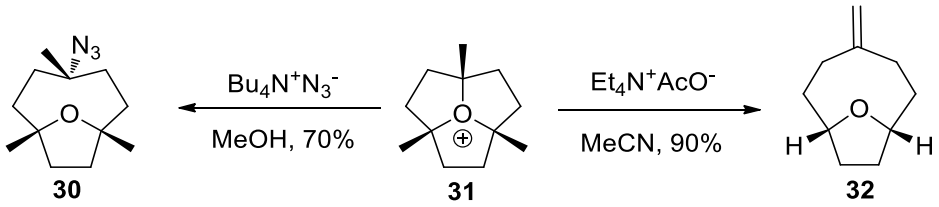


Figure 1.15. Reactions of 1,4,7-trimethyloxatriquinane.

1.3.2.5 C-O Bond Lengths

Mascal group also studied on crystal structure of oxatriquinane and they discovered that the C-O bond of the molecule was 1.537 Å which was higher than the reported average C-O bond length in the literature (1.43 Å) [26]. In order to understand limits of covalency, Mascal group studied on derivatives (Figure 1.16.) of oxatriquinane and they found much longer bond lengths for C-O bond such as 1.622 Å (**35**) [31]. In addition to this, they set a new record in 2013 by synthesizing **37** (1.658 Å) [32]. Studies showed that **35** has longer C-O bond length due to steric effect [31] and **37** has the longest C-O bond length because of electron donation of lone pairs of the oxygen atom on C-O antibonding orbital [32].

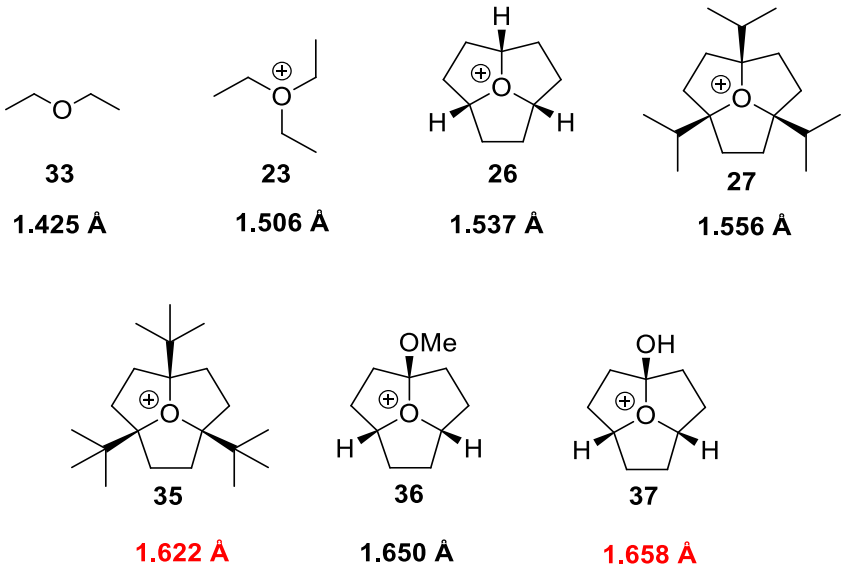


Figure 1.16. The bond lengths of C-O bonds.

1.4 Tribenzotriquinacene and Its Derivatives

Tribenzotriquinacene is one of the derivatives of triquinacene. It belongs to C_3v symmetry group and highly stable bowl-shaped structure. Until now, a lot of tribenzotriquinacene derivatives have been synthesized (Figure 1.17.) [33].

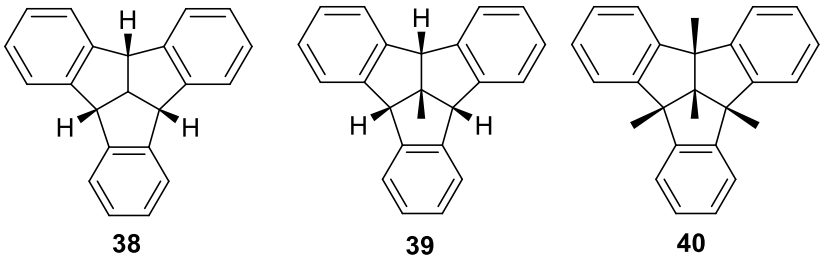


Figure 1.17. Some derivatives of tribenzotriquinacene (**38**-**40**).

Tribenzotriquinacene and its derivatives are more stable than triquinacene because of three benzene rings. In addition to this, aromatic forms of tribenzotriquinacene were more stable than dianion of acepentalene (Figure 1.18.) [34].

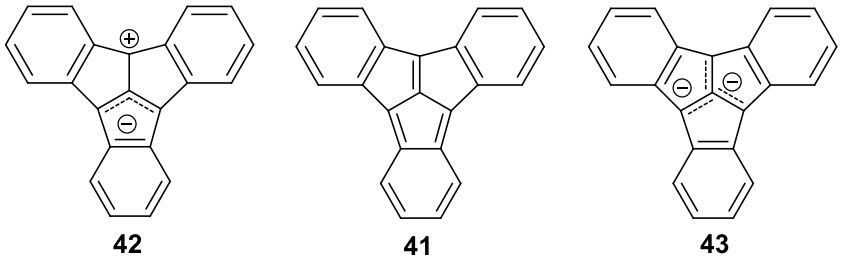


Figure 1.18. Some aromatic forms of tribenzotriquinacene (**41**-**43**).

In tribenzotriquinacene chemistry, there are a lot of studies in the literature. Some of those;

1.4.1 Regioselective Synthesis of Tribenzotriquinacene

In the literature, Schneebeli and his colleagues first introduced chiral-assisted, enantioselective electrophilic aromatic nitration [35]. They synthesized tri-nitrated tribenzotriquinacene which have C_{3V} symmetry group and 9:1 enantiomeric excess (figure 4) [35].

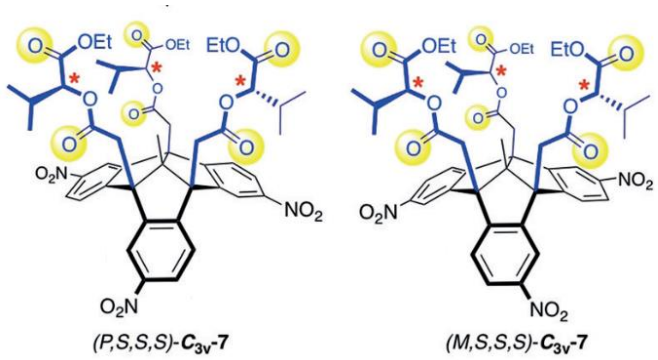
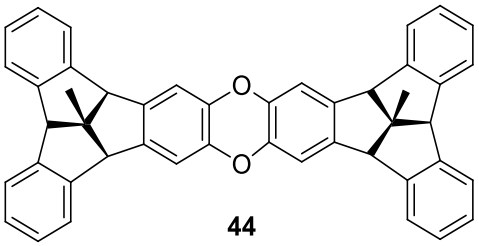


Figure 1.19. Structures of tri-nitrated tribenzotriquinacenes.

1.4.2 Tribenzotriquinacene- Dimer

There are many enantiomeric derivatives of tribenzotriquinacene which form nano-cube [36] and molecular squares [37] because synthesis of three dimensional, enantiomerically pure derivatives of tribenzotriquinacene has been attracted the

attention of chemists. One example of these derivatives was syn-bi-concave tribenzotriquinacene dimer which was synthesized [38] by Ullman-type condensation (Figure 1.20.).



44

Figure 1.20. Structure of syn-bi-concave tribenzotriquinacene dimer.

1.4.3 Nano-squares From Derivative of Tribenzotriquinacene

Tribenzotriquinacene and its derivatives can be used in supramolecular chemistry because of its orthogonal disposition [39]. Also, they are ideal organic ligands to form metallosquares (Figure 1.21.) [40].

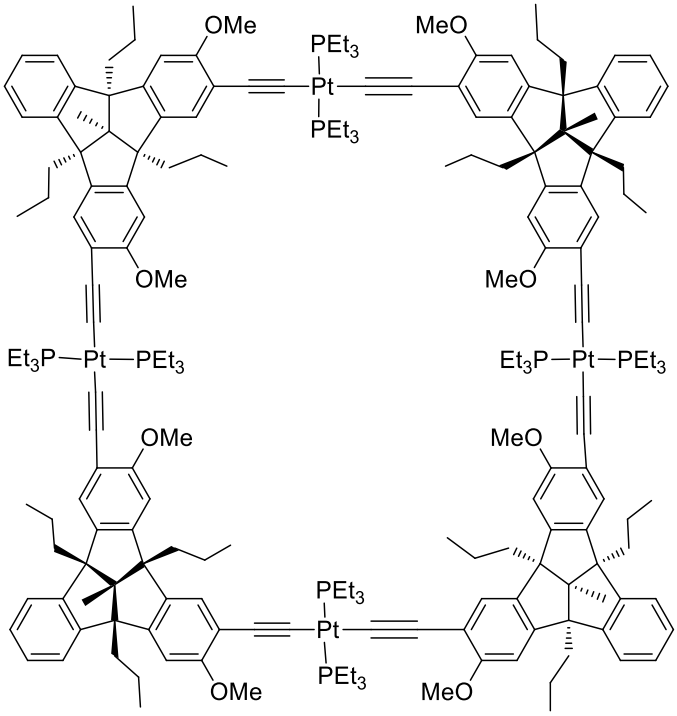


Figure 1.21. Structure of metallosquare.

1.4.4 Tribenzotriquinacene as Fluorescent Chemosensor

Synthesis of chemosensors which detects silver ion has been investigated for a long time [41] due to coordination ability of Ag^+ ion and difficulty to detect compared to other heavy metal ions [42]. Because tribenzotriquinacene and its derivatives are ideal to form concave shape, they can be used as chemosensors (Figure 1.22.) [42].

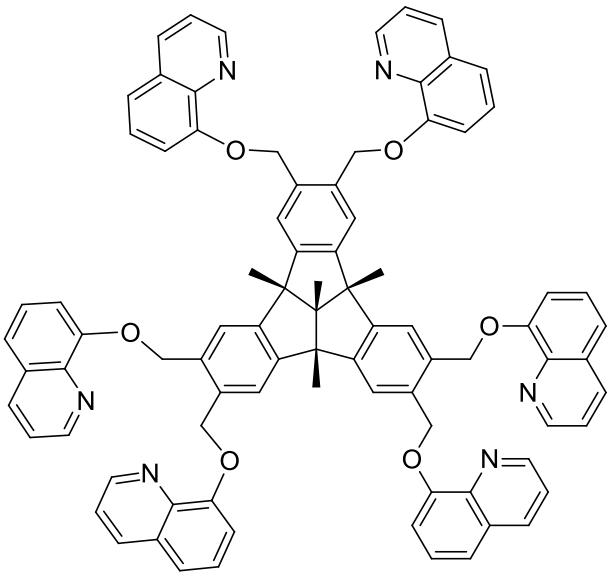


Figure 1.22. Structure of chemosensor.

1.5 Aim of the Study

In the literature, there are many derivatives of heterotriquinane and heterotriquinacene. Some of these derivatives showed many unusual reactivity and structural properties. For example, oxatriquinane known as extraordinary oxonium ion can be refluxed for 72 hours without decomposition. Also, one derivative of oxatriquinane shows S_N2 reaction at the tertiary carbon center of the molecule unlike written in the textbooks. In addition to these, the molecule having longest C-O bond in the literature is also an oxatriquinane derivative. As in the derivatives of heterotriquinane and heterotriquinacene, it is expected that hetero derivatives of tribenzotriquinane will also show unusual properties. The main aim in this study was

the synthesis of tribenzooxatriquinane which is one of the derivatives of tribenzoheterotriquinane and to investigate its potential unusual reactivity and properties. The target structure will also represent the first bis-benyzlic oxonium ion in the literature.

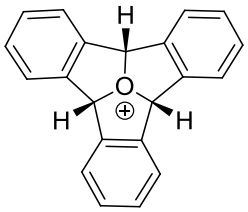


Figure 1.23. Structure of Tribenzooxatriquinane.

Since tribenzooxatriquinane has 3 benzene rings, it is also possible to add functional groups. Therefore, many derivatives of tribenzooxatriquinane could potentially be synthesized. Especially one derivative could be utilized to synthesize first isolable oxonium ylide (Figure 1.24.).

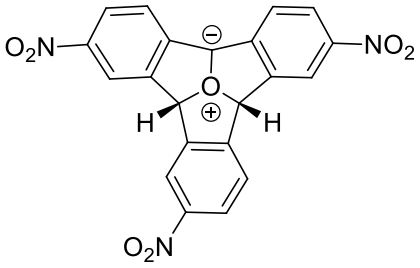


Figure 1.24. Structure of oxonium ylide.

CHAPTER 2

RESULTS AND DISCUSSION

2.1 Theoretical Studies

According to our calculations by Gaussian program, both tribenzooxatriquinane and tribenzooxoacepentalene which is the non-planar aromatic derivative of tribenzooxatriquinane are energetically favored ground state structures (Figure 2.1.). It was found that C-O bond length of tribenzooxatriquinane is 1.53 Å which is similar but shorter than oxatriquinane and its derivatives. Also, calculations of NICS (Nucleus-Independent Chemical Shifts) (RB3LYP 6-311+G(2d,p)) parameters showed that tribenzooxoacepentalene is highly aromatic (RB3LYP/6-31+G(d,p)) even more aromatic than benzene (NICS(1) = -10.22). Also, according to its NMR calculations, 2 different proton signals (8.00 ppm and 8.90 ppm) are expected in the spectrum.

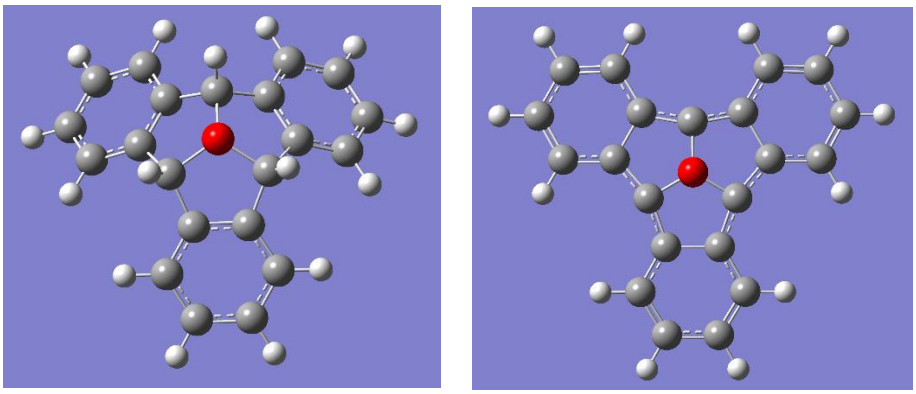


Figure 2.1. Structures of tribenzooxatriquinane (left) and tribenzooxoacepentalene (right).

In addition to this, calculations were made for the compound oxonium ylide (Figure 2.2.). DFT (Density Functional Theory) based calculations show that this target

molecule is energetically favorable. Optimizations proceeded smoothly and no virtual frequency was observed in frequency calculations.

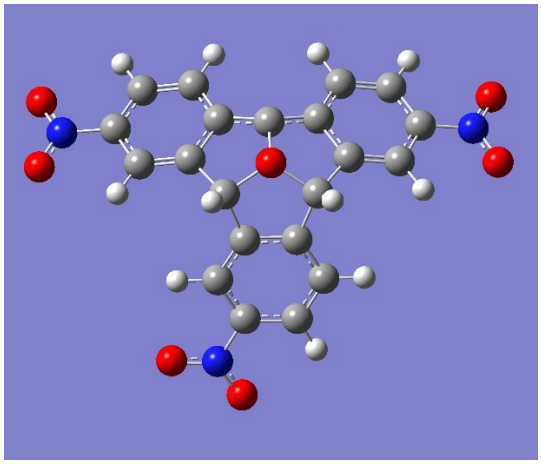


Figure 2.2. Structure of oxonium ylide.

2.2 Retrosynthetic Analysis of Tribenzooxatriquinane

In order to synthesize tribenzooxatriquinane, retrosynthetic analysis was performed (Figure 2.3.), and it was observed that there were two possible synthetic approaches. However, for both pathways it was crucial to synthesize 10,15-dihydro-5H-tribenzo[*a*,*d*,*g*][9]annulene.

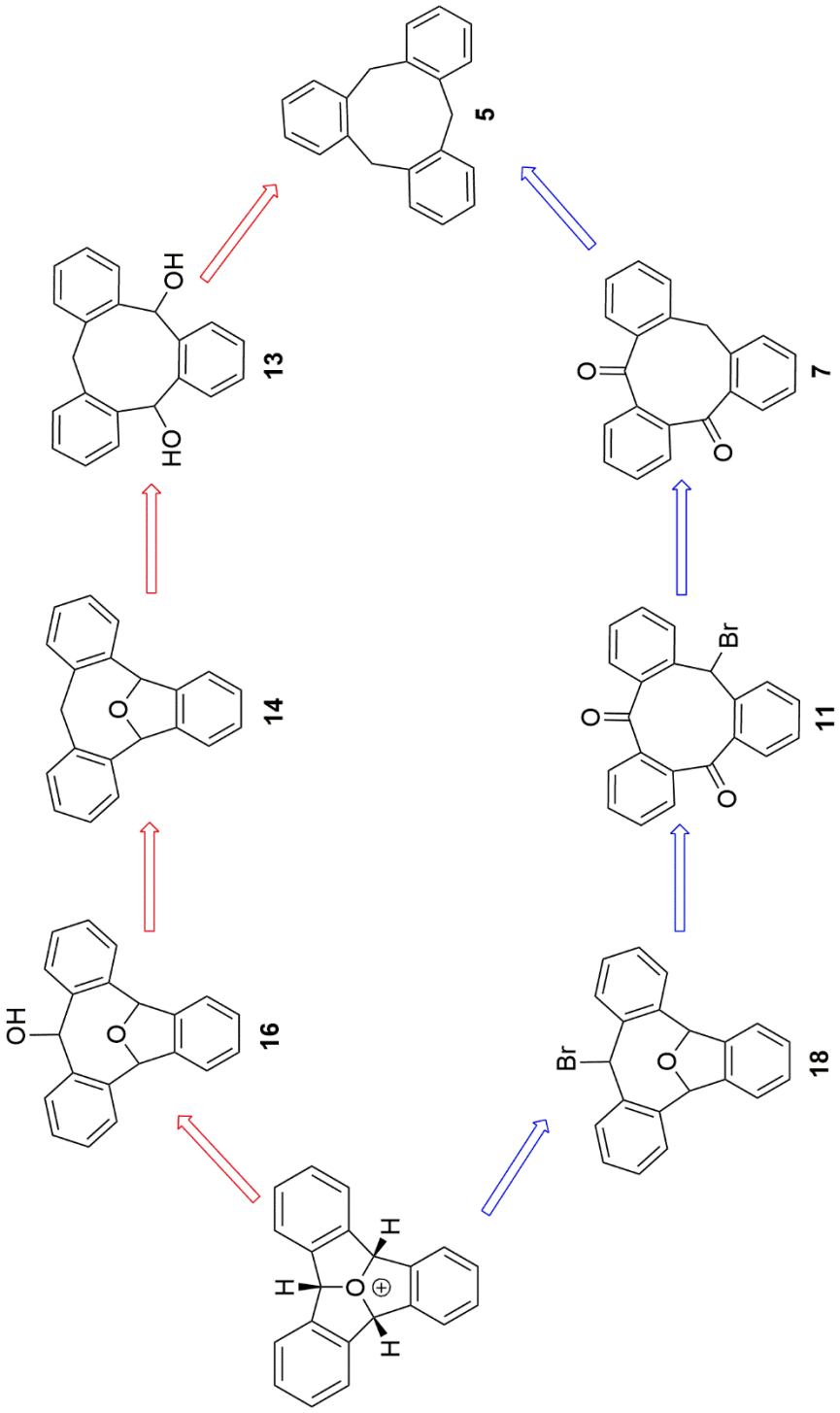
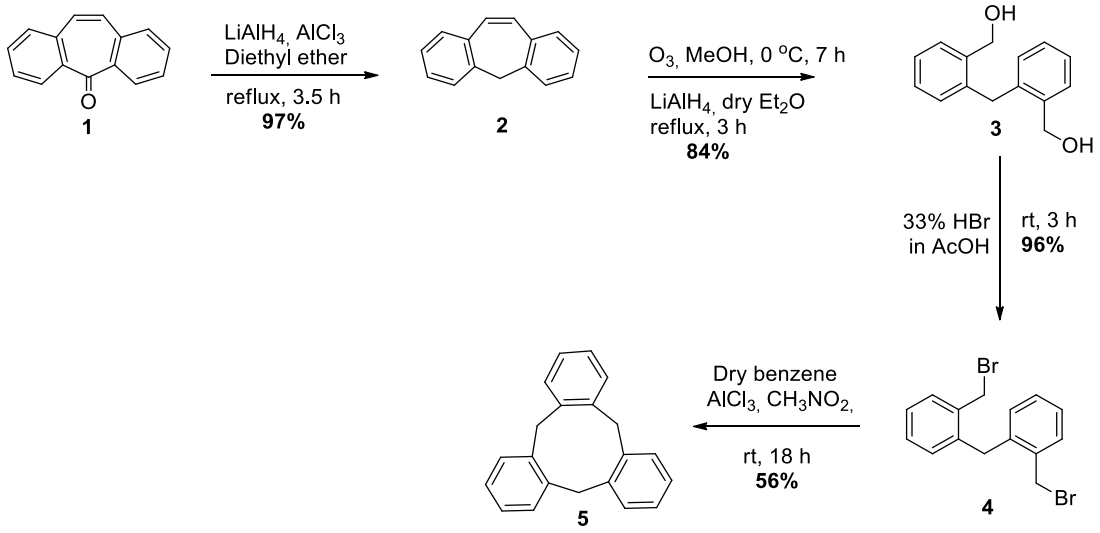


Figure 2.3. Retrosynthetic analysis of tribenzooxatriquinane.

2.3 Synthesis of 10,15-dihydro-5H-tribenzo[*a,d,g*][9]annulene

To synthesize central unit, Cansu İğci, a past member of Günbaş Research Group, tried to follow a synthetic pathway in the literature [43]. However, in the second step where a Grignard reaction is performed, there were serious issues as this reaction was very sensitive to conditions. Therefore, it was decided to synthesize the target molecule 10,15-dihydro-5H-tribenzo[*a,d,g*][9]annulene, **5** by another published method (Scheme 2.1.) [46].



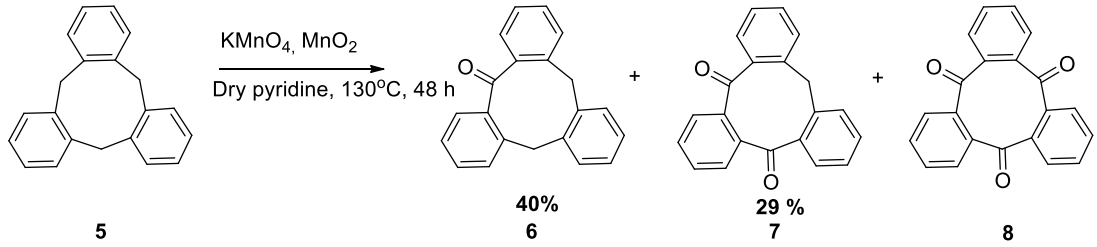
Scheme 2. 1. Synthetic pathway to the molecule **5**.

In the first step of synthesis, commercially available **1** was reduced to **2** in high yield by using the system of $AlCl_3$-$LiAlH_4$. Because the high reactivity of $LiAlH_4$, weighing and addition of it was done fast and to stop the reaction, excess $LiAlH_4$ quenched with distilled water which was added dropwise. In the second step, ozonolysis was performed. Because the reaction produces peroxide intermediates, solvent of the reaction was removed at low temperature and yellow oily product was obtained. Then, this product was reduced by using $LiAlH_4$. To purify the product, benzene was used as recrystallization solvent in literature. However, it is known that benzene have harmful effects on health [29]. Therefore, other solvents have been tried and toluene was used as recrystallization solvent and target product **3** was

obtained in high yield (84%). To synthesize dibromo **4** from diol **3**, HBr in AcOH was used. In the final step, although target molecule **5** is found in literature, there is no experimental part in the articles. Therefore, many optimizations were made and **5** was obtained in 48% yield. In order to increase the product yield, it was decided to double the amount of benzene used in the reaction and the starting material **4** was added slowly by using dropping funnel. Reaction yield increased from 48% to 56%.

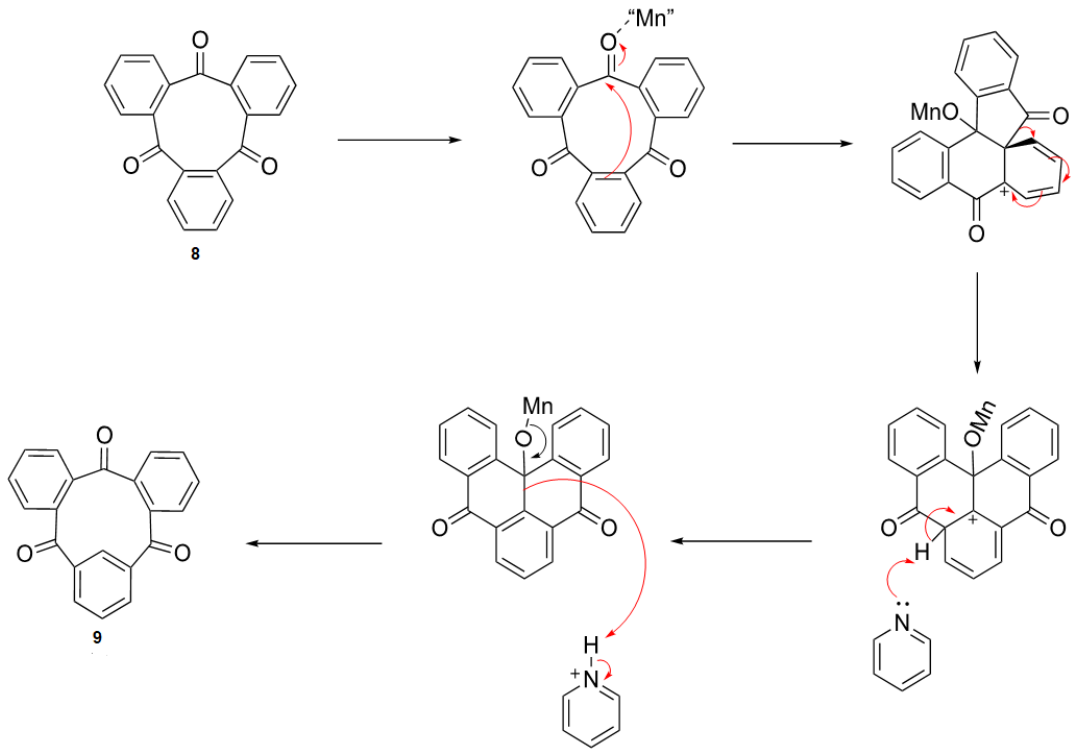
2.4 Oxidation of 10,15-dihydro-5H-tribenzo[*a,d,g*][9]annulene

In the literature, the oxidation products, monoketone and diketone were synthesized with the yields of 74% and 25% respectively [44] and diketone forms in 7 days. In order to increase reaction yield compared to literature, studies have been made and diketone was successfully obtained with a 29% yield in 3 days by a new method (Scheme 2.2.) [45].



Scheme 2. 2. Oxidation of molecule 5.

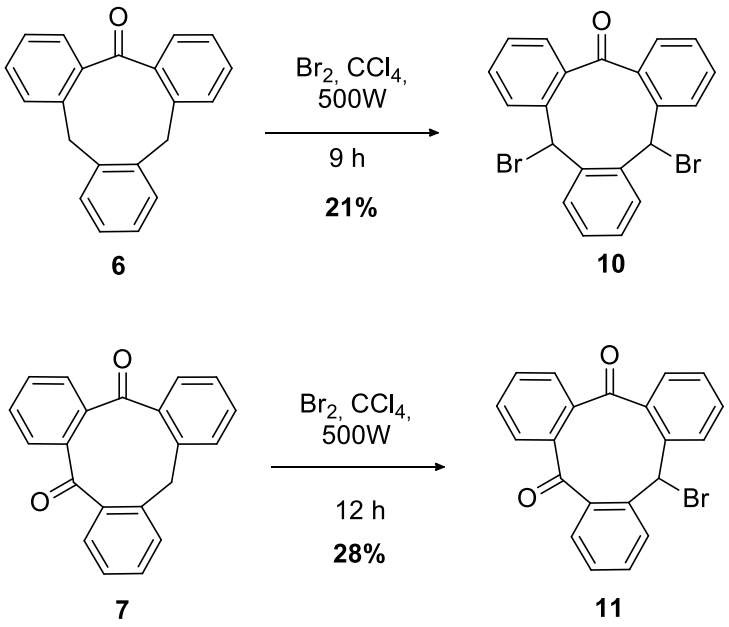
Oxidation of **5** was performed with $KMnO_4$ and MnO_2 and it was observed that when $KMnO_4$ was grounded, the reaction yield was better. In addition to this, apart from these monoketone **6** and diketone **7**, another product was obtained in very low yield and it was thought to be triketone **8**. However, after NMR analysis, it was clearly seen that the product obtained was not compound **8** (Scheme 2.3.). Nevertheless, although the exact clarity of this structure could not be achieved, it was predicted as **9** due to having only aromatic protons in proton NMR, observing two different peaks in carbon NMR and having appropriate peak in the mass spectrometer [51].



Scheme 2. 3. Possible reaction mechanism for compound **9**.

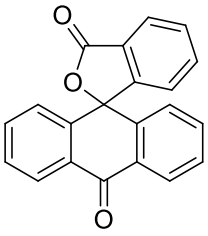
2.5 Bromination of 6 and 7

Brominations of both molecule **6** and molecule **7** were the most challenging part of the synthesis. Since radical bromination was aimed, NBS (N-Bromosuccinimide) was used as the source for bromine. To synthesize the target molecule, NBS and radical initiators (AIBN and benzoyl peroxide) were used. However, desired product could not be obtained. Additionally, although both reaction time and amount of NBS were increased, there were no product. Also, radical bromination was attempted by using 500W light and NBS in CCl_4 with no success. Finally, **10** and **11** were synthesized by using Br_2 and light (Scheme 2.4.). However, while **11** was obtained in pure form, **10** could not be purified.



Scheme 2. 4. Bromination of molecule **6** and molecule **7**.

After **11** was obtained in pure form, studies were carried out to increase the reaction yield. At the beginning, an alternative solvent was investigated instead of CCl_4 due to carcinogenic properties and unavailability on the market. For these reasons, bromination was performed in different solvents like chloroform, DCM and cyclohexane. However, product **11** could not be synthesized and starting material **7** was recovered. In addition to this, in the literature, a successful CCl_4 alternative, α,α,α-trifluorotoluene, was successfully utilized in various transformations. In our hands, although various optimization studies were performed only a small amount of product was obtained. There was always major spot in the TLC which did not belong to either starting material or product. This major spot was identified as **12** (Scheme 2.5.).



12

Scheme 2. 5. Structure of molecule **12**.

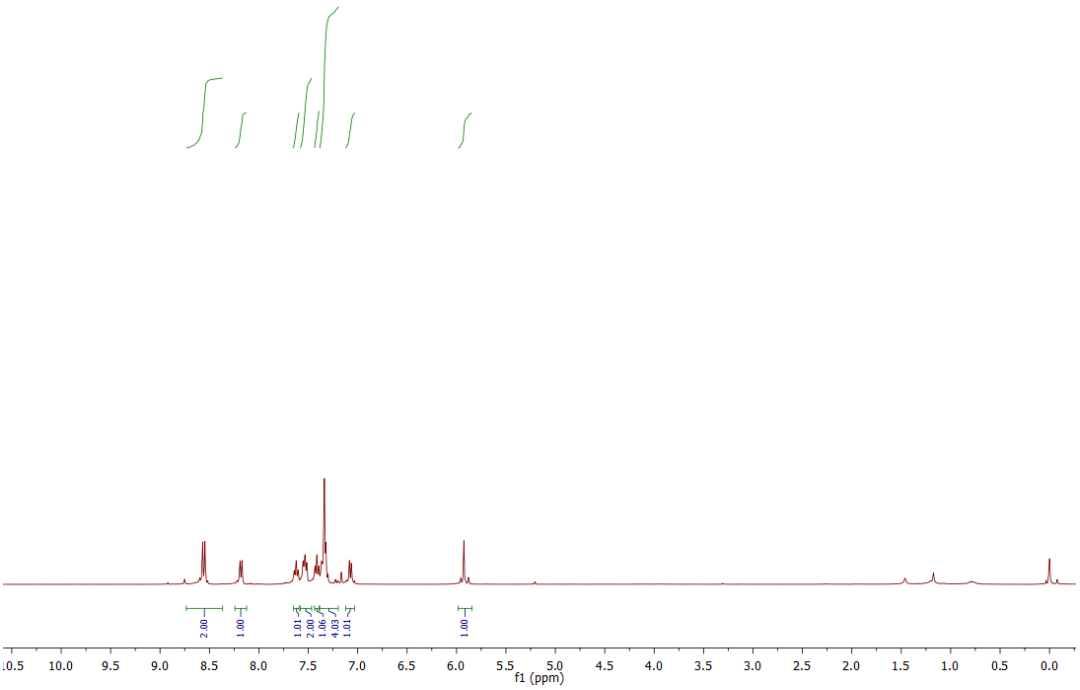


Figure 2.4. ^{1}H Spectrum of **12**.

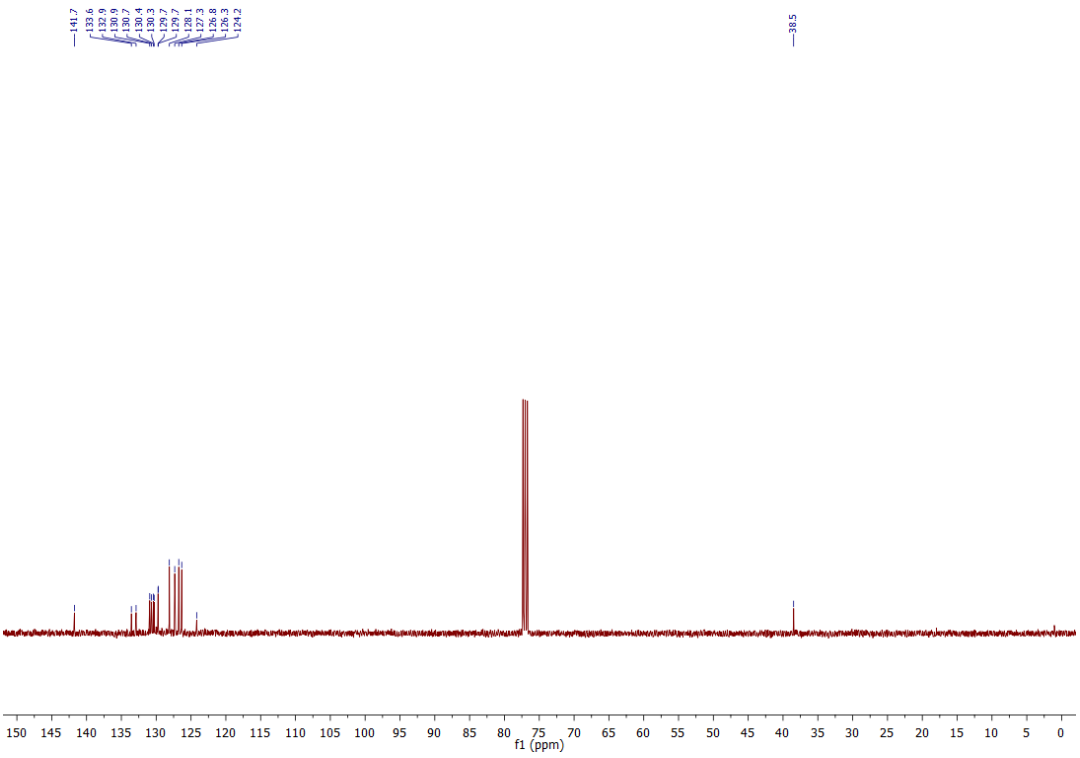
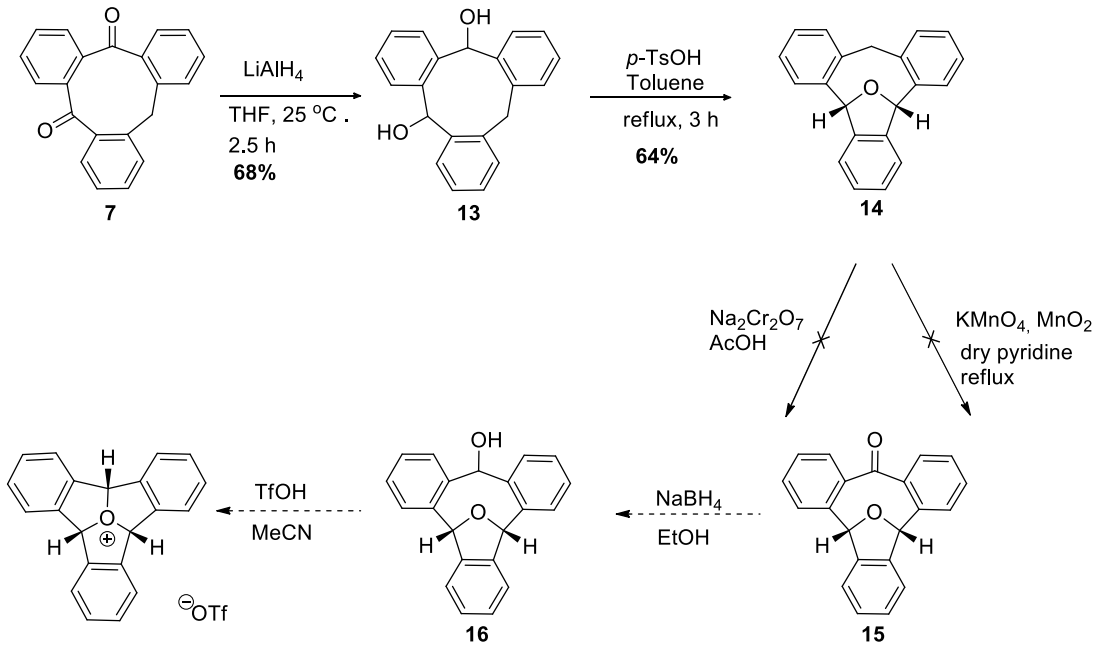


Figure 2.5. ^{13}C Spectrum of **12**.

Therefore, CCl_4 was used as bromination solvent. However, **12** was still major product. In order to increase yield of **11**, CCl_4 was distilled over CaH_2 and collected on 3 Å molecular sieves. Also, K_2CO_3 was used as weak base to neutralize HBr in the reaction medium. Finally, although starting material was not consumed completely in the reaction, target molecule **11** was obtained as major product.

2.6 Synthesis of Tribenzooxatriquinane

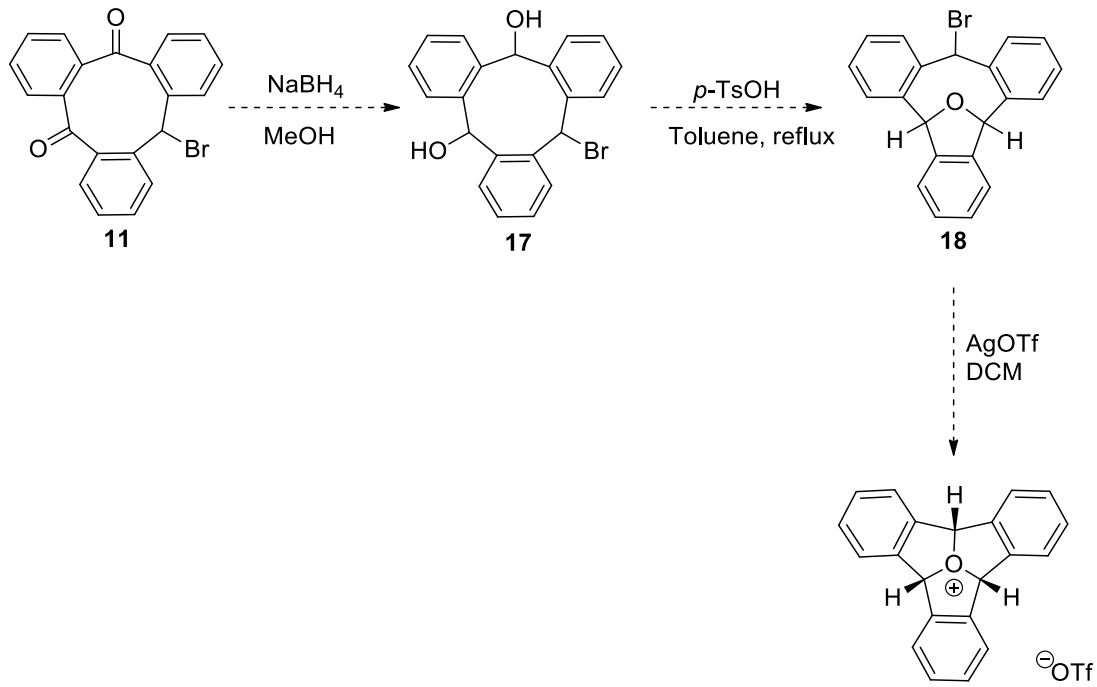
In order to synthesize target molecule, tribenzooxatriquinane various synthetic pathways were followed.



Scheme 2. 6. Synthetic pathway 1 for tribenzooxatriquinane.

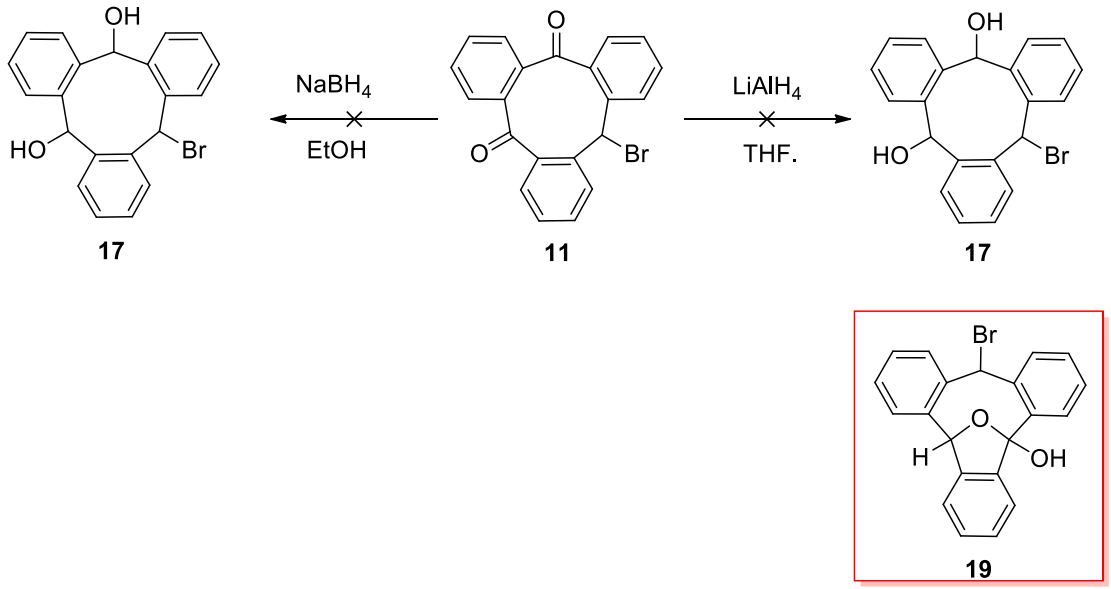
First approach started with the reduction of molecule **7**. **13** was successfully synthesized by using $LiAlH_4$ in THF. Then, in the acidic medium, target molecule **14** was obtained. In order to synthesize **15**, two different procedures were utilized. However, in both oxidations, instead of obtaining **15**, diketone **7** was obtained in high yields (Scheme 2.6.).

After this failed attempt (Scheme 2.6.), synthetic pathway 2 was designed (Scheme 2.7.).



Scheme 2. 7. Synthetic pathway 2 for tribenzooxatriquinane.

In order not to reduce bromide in **11**, $NaBH_4$ which is a mild reducing agent was chosen. However, according to NMR spectrum, bromide was reduced. It was thought that since the reaction was carried out in EtOH, bromide was reduced by S_N1 type reaction. Therefore, it was decided to replace the solvent with an aprotic one. However, $NaBH_4$ does not dissolve in aprotic solvents. Thus, $LiAlH_4$ was selected as reducing agent and THF as solvent. In order not to reduce bromide in the molecule, substoichiometric amounts of $LiAlH_4$ were used. However, different products were obtained based on the amount of $LiAlH_4$ used in the reaction and reaction times. Characterization of most of these products has not been fruitful. Nonetheless, one product was clearly characterized as the compound **19**.



Scheme 2. 8. Reduction of **11**.

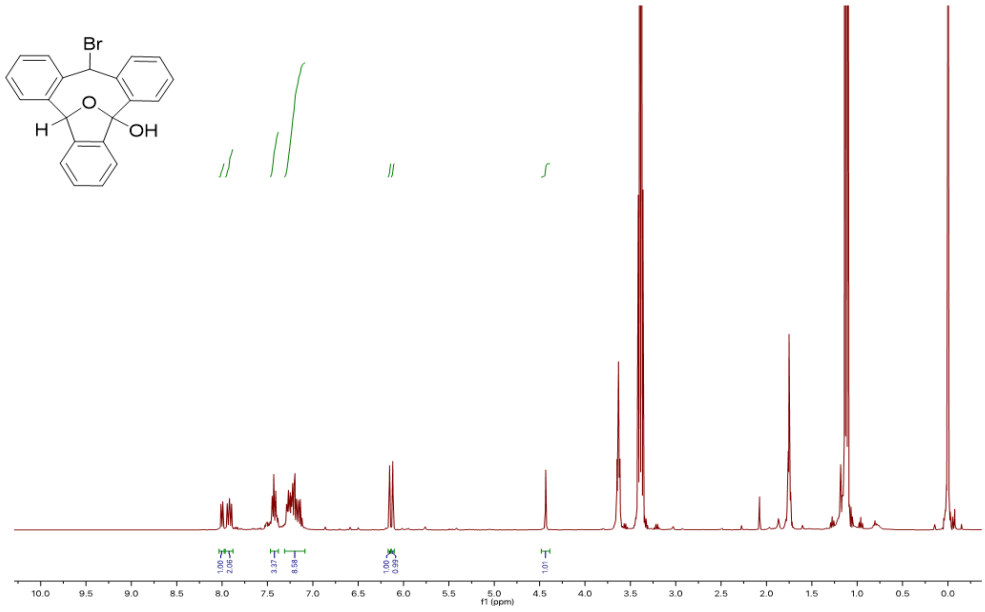


Figure 2.6. ^{1}H NMR Spectrum of **19**.

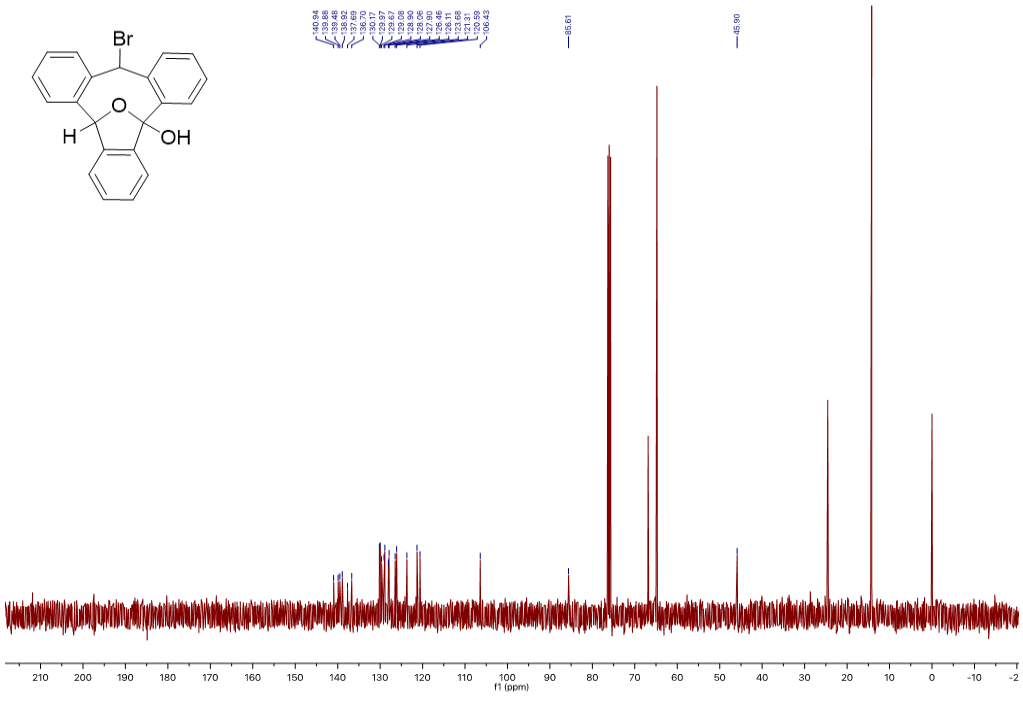
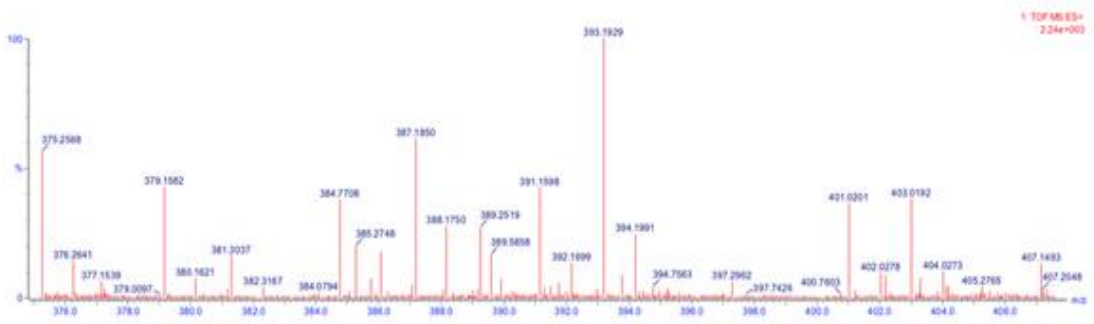


Figure 2.7. ^{13}C NMR Spectrum of **19**.

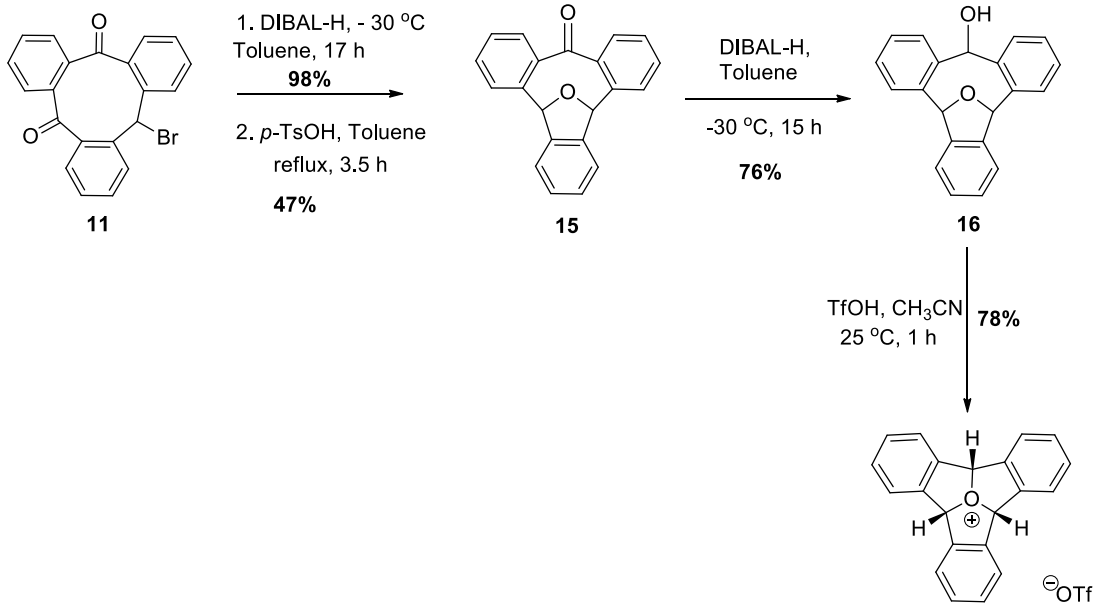


Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
403.0192	403.0133	5.9	14.6	13.5	282.9	0.0	$C_{21}H_{15}O_2Na^{81}Br$

Figure 2.8. HRMS Spectrum of **19**.

Although one can envision pathways for the synthesis of tribenzooxatriquinane using **19**, it was not used to synthesize tribenzooxatriquinane due to reproducibility issues related to synthesis of **19**.

In our final synthetic approach, tribenzooxatriquinane was synthesized successfully (Scheme 2.9.).



Scheme 2. 9. Synthetic pathway 3 for tribenzooxatriquinane.

In the first step, DIBAL-H (Diisobutyl Aluminum Hydride) which is a strong and bulky reducing agent was used in order to reduce **11**. The reduction mechanism of DIBAL-H differs from $NaBH_4$ because while $NaBH_4$ directly donates a hydride, DIBAL-H first coordinates to lone pairs of the carbonyl group, then delivers the hydride. Therefore, it was thought that bromine in the compound **11** would not be reduced and **17** (Figure 2.11) would be obtained. When the spot of starting material **11** was disappeared in the TLC, a number of spots were observed in the TLC and we attributed this to the possibility of generating numerous diastereomers due to different orientation that are possible after the reduction. Since the next step is formation of THF ring and all the diastereomers will collapse into two possible products. Hence, a standard work-up procedure was applied, and the residue was used in the next step without purification. In the next step, cyclization was attempted in the acidic medium and after purification of the compound with major spot in the TLC and NMR analyses, it was found that compound **15** was obtained in moderate yield. This was surprising since the expected product was compound **18** (Scheme 2.8.). There are two possible explanations for this observation. First, compound **15** was formed in the first step, second, compound **19** was formed which converted into compound **15** during acid treatment. To synthesize **16**, standard reduction conditions were utilized. However, no change was observed in TLC in both reduction reactions using $NaBH_4$ or $LiAlH_4$ ($+ZnCl_2$). DIBAL-H was used as reducing agent again and we were able to obtain alcohol **16**. Since diastereomers could not be separated from each other, crude product was used in the final step without purification. In the final step, triflic acid (TfOH), which is one of the super acids was used in acetonitrile and after purification by precipitation in ether, target molecule tribenzooxatriquinane was obtained in 78% yield.

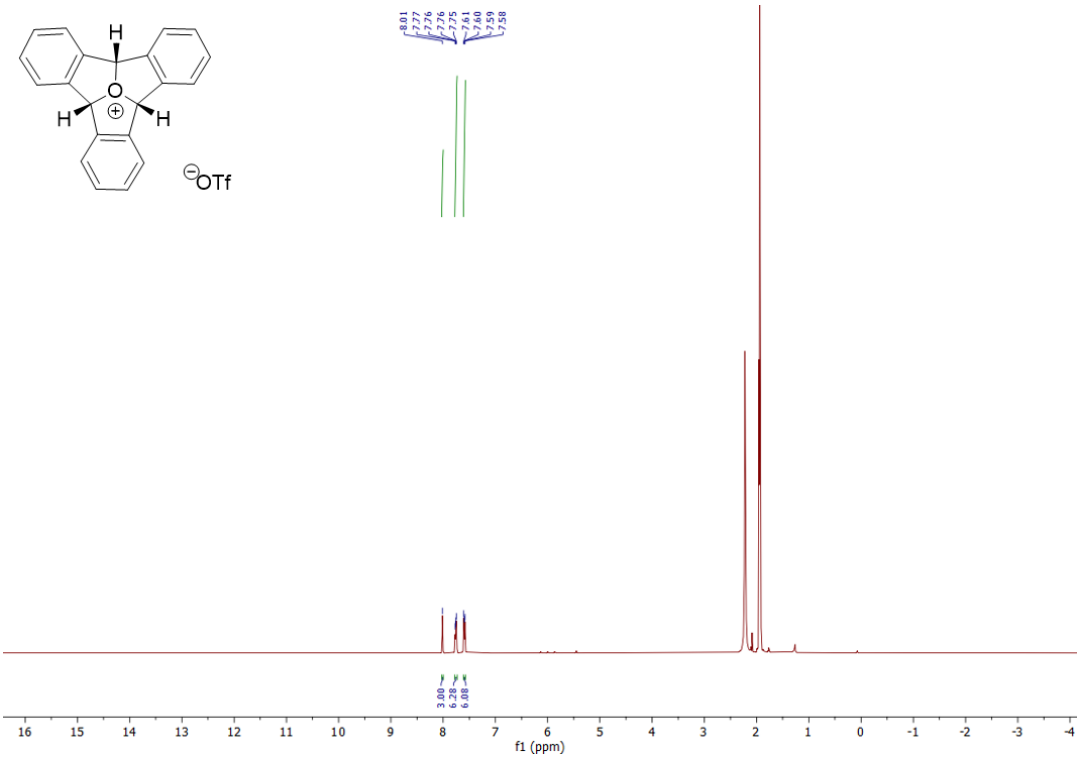


Figure 2.9. ^{1}H NMR Spectrum of **Tribenzooxatriquinane** in d_3-MeCN.

2.7 Reactivity of Tribenzooxatriquinane

Tribenzooxatriquinane is the first isolated and characterized bis-benzylic oxonium ion in the literature. Therefore, it represents an important development in the field of fundamental organic chemistry. NMR spectrum was recorded in non-nucleophilic solvent *d*$_3$-MeCN. NMR analyses in *d*$_4$-MeOH showed significant decomposition. In order to understand how long the tribenzooxatriquinane structure persists in MeCN with weak nucleophiles, tribenzooxatriquinane: MeOH (1:10) by mass was prepared in *d*$_3$-MeCN and NMR spectrum was recorded after 10 minutes, 1 hour, 2 hours, 4 hours and 1 day and it was observed that tribenzooxatriquinane, was not completely decomposed at the end of 24 hours (Figure 2.9.) One other interesting feature observed in tribenzooxatriquinane was the extreme chemical environment of the

bridgehead protons. These aliphatic protons appear at 8.01 ppm in the NMR spectrum. To best of our knowledge this is one of the lowest field shifted, if not the highest, shift recorded for an aliphatic proton in NMR spectroscopy.

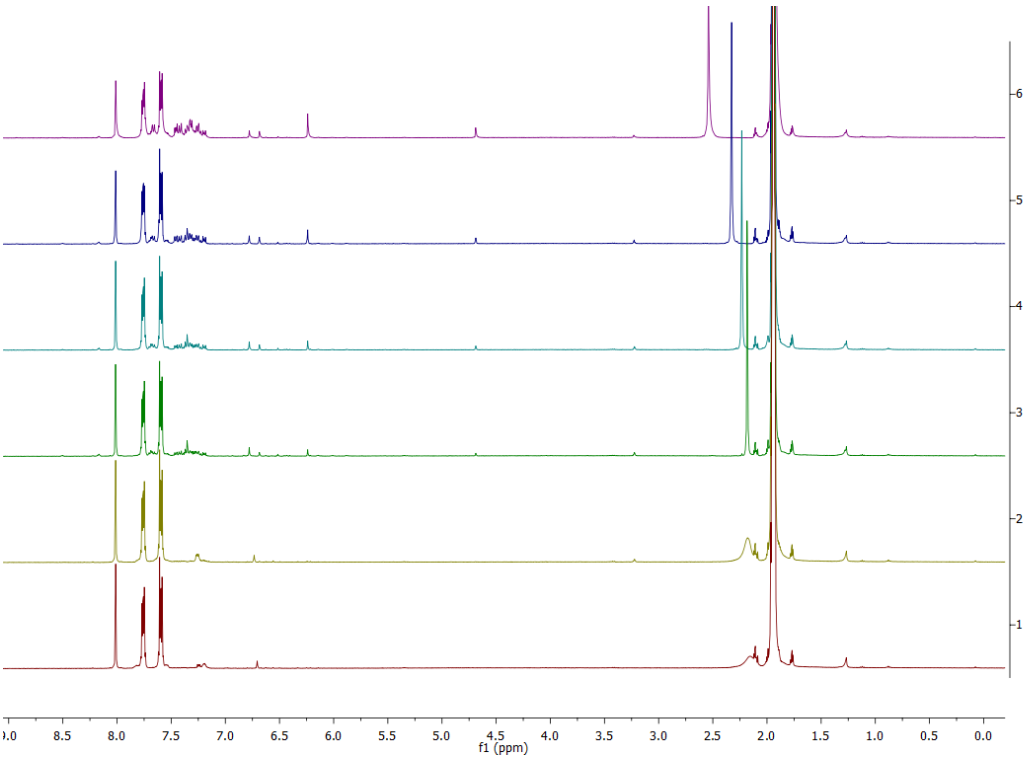
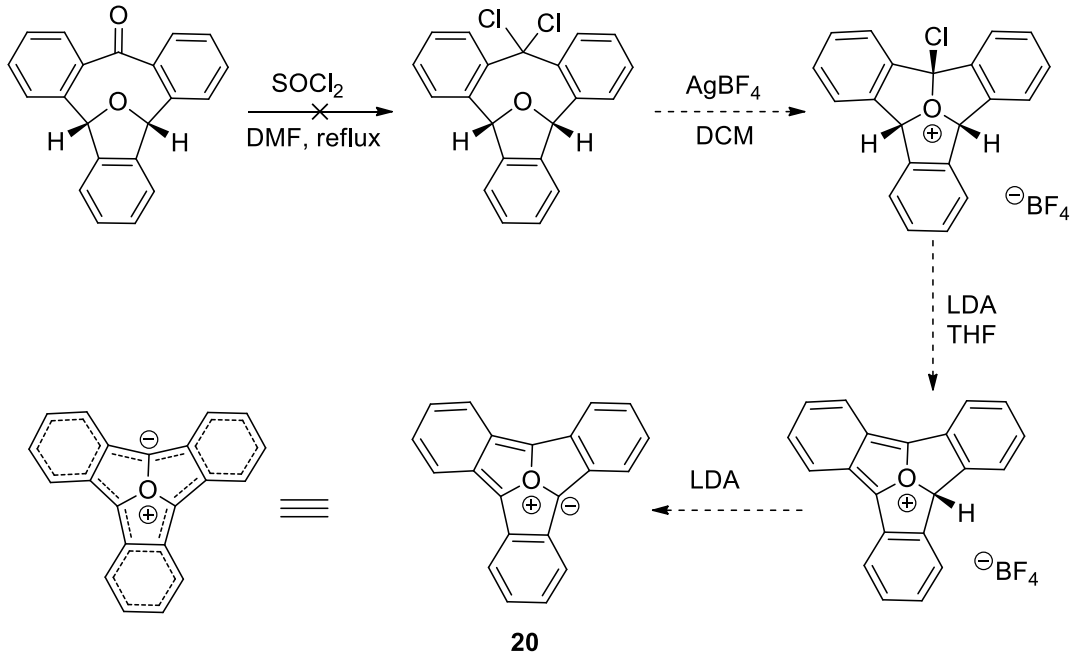


Figure 2.10. ^{1}H NMR Spectrums of Tribenzooxatriquinane: MeOH (1:10) by mass.

2.8 Studies on Synthesis of Aromatic Derivative of Tribenzooxatriquinane

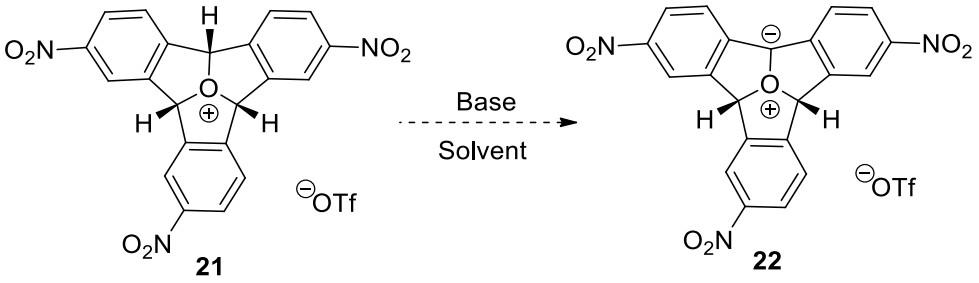


Scheme 2. 10. Synthetic pathway for molecule **20**.

In order to synthesize aromatic derivative of tribenzooxatriquinane, synthetic pathway in Scheme 2.10. was designed. However, chlorination in the first step could not be achieved and the starting material was completely recovered. We believe electron density donation from the perfectly situated oxygen atom in the structure diminished the reactivity of the ketone significantly. Hence stronger electrophilic reagent will be utilized in the future.

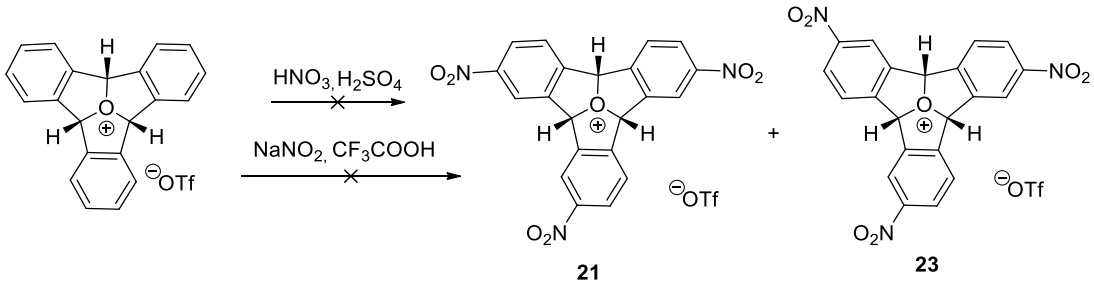
2.9 Studies on Synthesis of Oxonium Ylide

Since tribenzooxatriquinane has 3 benzene rings, it is possible to add functional groups and it is thought that these modifications to benzene rings are expected to influence structure and reactivity in a significant manner. Firstly, studies were carried out on nitration because the product of nitrification is planned to be used for the synthesis of first isolable oxonium ylide (**22**).



Scheme 2. 11. Studies on synthesis of oxonium ylide **22**.

In order to synthesize compound **21**, two standard nitration conditions have been utilized (Scheme 2.11.). However, desired product could not be observed in NMR analysis. The decomposition of the tricyclic oxonium core was observed in both cases. We are going to concentrate our efforts on the nitration of intermediates before the tricyclic oxonium ring formation.



Scheme 2. 12. Nitration reactions.

CHAPTER 3

CONCLUSION

In order to achieve the synthesis of tribenzooxatriquinane, various synthetic pathways were envisioned. For all these pathways it was crucial to synthesize 10,15-dihydro-5H-tribenzo[*a,d,g*][9]annulene (**5**). This compound was successfully synthesized in five steps and in relatively high yields. Then, oxidation products of compound **5** (**6** and **7**) were obtained. Bromination of the diketo core **7** became the most important step in the synthesis since other methods towards functionalization of the bisbenzylic carbon did not give fruitful results. Although many attempts have been realized and failed, pure compound **11** has been successfully synthesized using Br_2 and light with CCl_4 as the solvent. Reduction of **11** towards realization of diol **17** without reducing the bromo substituent was not fruitful under standard conditions. However, strong and bulky reducing agent DIBAL-H was able to reduce a ketone in compound **11** DIBAL-H without interfering with the bromo substituent. Treatment of the crude with acid resulted in formation of bicyclic ketone **15**. Finally, reduction followed by super acid treatment gave the desire product in good yield. Tribenzooxatriquinane is the first isolated and characterized bis-benzylic oxonium ion in the literature. NMR spectrum was recorded in non-nucleophilic solvent d_3-MeCN. One interesting feature observed in tribenzooxatriquinane was the extreme chemical environment of the bridgehead protons. These aliphatic protons appear at 8.01 ppm in the NMR spectrum. To best of our knowledge this is one of the highest, if not the highest downfield shift recorded for an aliphatic proton in NMR spectroscopy.

To sum up, in this study tribenzooxatriquinane which is one derivative of tribenzoheterotriquinane was successfully synthesized and its reactivity was investigated. Tribenzooxatriquinane is the first characterized bis-benzylic oxonium

ion in the literature and therefore we believe its synthesis represents an important development in the field of fundamental organic chemistry.

CHAPTER 4

EXPERIMENTAL

4.1 Materials and Methods

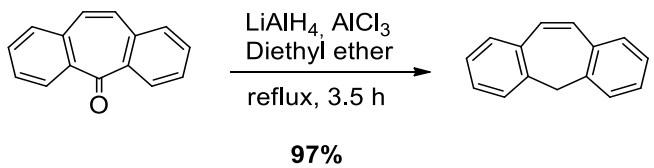
Most of the reactions were carried out under inert atmosphere (argon) and reaction solvents which are DCM, THF, Et_2O and toluene were used directly solvent drying system (Mbraun MBSPS5). CCl_4 was dried over $CaCl_2$ and freshly distilled before use. For all chromatographic purifications on silica gel, Merck Silica Gel 60 (230-400 mesh) was used and for Thin Layer Chromatography (TLC), Merck Silica 60 F254 was used.

4.2 Equipments

NMR analysis (^1H and ^{13}C) was carried on Bruker Spectrospin Avance DPX-400 Spectrometer (tetramethylsilane as internal reference) and as solvents $CDCl_3$, d_6-DMSO and d_3-CD_3CN were used. High Resolution Mass Spectroscopy (HRMS) was performed using Waters Synapt MS System at METU Central Laboratory.

4.3 Synthesis of Tribenzooxatriquinane

4.3.1 Synthesis of Molecule 2

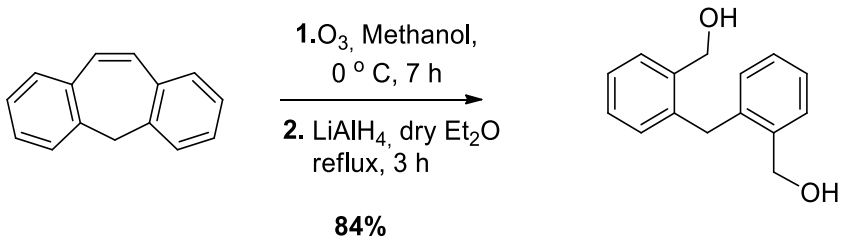


Scheme 4. 1. Synthesis of molecule **2**.

Synthesized with small modifications to published procedure [46].

To a solution of $LiAlH_4$ (2.00 g, 52 mmol) in dry Et_2O (38 mL) in two-neck balloon, a solution of $AlCl_3$ (7.10 g, 54 mmol) in dry diethyl ether (25 mL) was added slowly. The mixture was stirred 15 minutes at room temperature. Then, a solution of 5-dibenzosuberenone, **1** (10.00 g, 48 mmol) in dry THF (56 mL) was added into the mixture slowly at 0 °C. After heating the mixture for 3 hours at reflux temperature (75 °C), the reaction was stirred overnight at room temperature. The reaction was diluted with Et_2O (120 mL) and distilled water (2 mL) was added at 0 °C followed by addition of 15% aq NaOH solution (2 mL) and distilled water (6 mL). After addition of anhydrous $MgSO_4$, the mixture was filtered through Celite and washed thoroughly with Et_2O. Solvent was removed under reduced pressure to obtain pure white crystals (9.0 g, **97%**). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.24 (m, 6H), 7.22 – 7.15 (m, 2H), 7.01 (s, 2H), 3.72 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 135.3, 131.7, 128.5, 128.2, 128.0, 126.2, 41.8.

4.3.2 Synthesis of Molecule 3



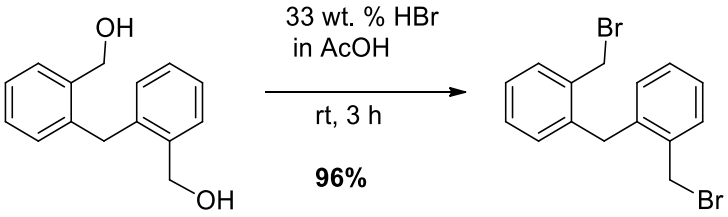
Scheme 4. 2. Synthesis of molecule **3**.

Synthesized with small modifications to published procedure [46].

To produce molecule **3**, starting material (2.5 g, 13 mmol) was suspended with methanol (100 mL) at 0 °C and ozone gas was bubbled through it for 7 hours. The ozonolysis was finished by checking TLC (1 EtOAc: 3 Hexane). After purging argon gas for 40 minutes at room temperature, methanol was removed from reaction medium under reduced pressure and yellow oily substance was obtained. Then, this

substance was dissolved in dry Et_2O (40 mL) and added to the solution of $LiAlH_4$ (2.484, 65 mmol) in dry Et_2O (46 mL) by dropwise. After addition was complete, the mixture was heated to reflux (55 °C) for 3 hours and then reaction was stirred overnight at room temperature. To work up, the reaction was diluted with Et_2O (90 mL). Then, distilled water (2.5 mL) was added at 0 °C and then added 15% aq NaOH solution (2.5 mL) and distilled water (7.5 mL) into reaction respectively. After addition of anhydrous $MgSO_4$, the mixture was filtered through celite and washed with Et_2O (500 mL) and EtOH (500 mL). Solvent was removed under reduced pressure and obtained yellow substance. To purify crude product, recrystallization was performed with toluene (50 mL) and pure white product was obtained (2.5 g, **84%**).^{1}H NMR (400 MHz, DMSO) δ 7.44 (d, *J* = 7.5 Hz, 2H), 7.18 (dt, 4H), 6.85 (d, *J* = 7.4 Hz, 2H), 5.18 (s, 2H), 4.48 (s, 4H), 3.98 (s, 2H). ^{13}C NMR (100 MHz, DMSO) δ 140.3, 137.3, 128.9, 126.9, 126.8, 125.9, 60.1, 33.5.

4.3.3 Synthesis of Molecule 4



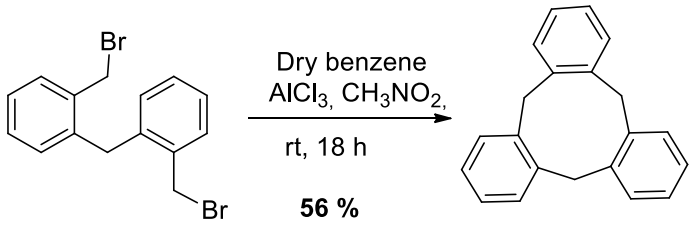
Scheme 4. 3. Synthesis of molecule **4**.

Synthesized with small modifications to published procedure [47].

To synthesize **4**, starting material, **3** (1.44 g, 6.32 mmol) was stirred with 33 wt. % HBr in acetic acid (29 mL) for 3 hours. The reaction was finished by adding DCM (60 mL) and extracted with saturated $NaHCO_3$ solution. The organic phase was dried over anhydrous Na_2SO_4 and filtered. Then, by evaporating solvent under reduced pressure, yellow product was obtained (2.16 g, **96%**).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.16 – 7.07 (m, 4H), 6.87 – 6.80 (m, 2H), 4.38 (s, 4H), 4.17 (s,

2H).[13]C NMR (100 MHz, $CDCl_3$) δ 138.8, 136.1, 130.8, 130.4, 129.3, 127.3, 34.7, 31.9.

4.3.4 Synthesis of Molecule 5

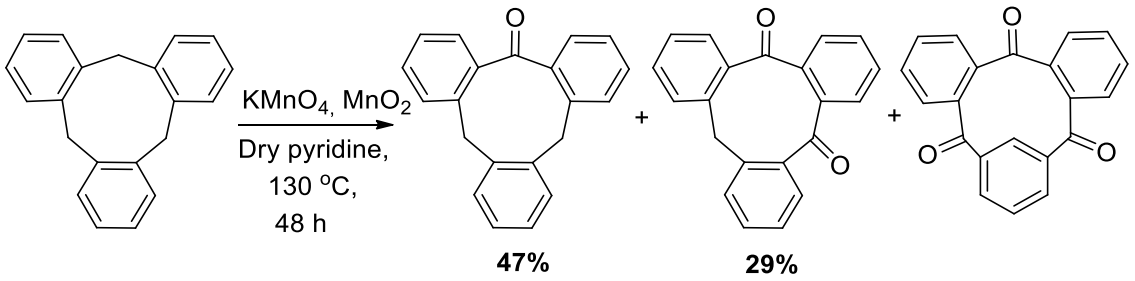


Scheme 4. 4. Synthesis of molecule **5**.

Synthesized with small modifications to published procedure [48].

After preparation of $AlCl_3$ (1.37 g, 10.2 mmol) solution with dry benzene (71.2 mL) and CH_3NO_2 (3.6 mL), the solution of starting material, **4** (1.78 g, 5.0 mmol) in dry benzene (260 mL) was added into this solution by using dropping funnel at room temperature and the reaction was stirred overnight. 1% HCl solution (309 mL) was added into the reaction and extracted with Et_2O. Organic layer was dried over anhydrous $MgSO_4$ and solvent was removed under reduced pressure. To purify crude product, column chromatography (silica gel, DCM: Petroleum Ether- 1: 6) was performed and white product was obtained. (726 mg, **56%**).[1]H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 9.1 Hz, 6H), 7.11 (dd, *J* = 9.1 Hz, 6H), 4.93 (d, *J* = 13.3 Hz, 3H), 3.78 (d, *J* = 13.4 Hz, 3H).[13]C NMR (100 MHz, $CDCl_3$) δ 139.6, 130.2, 127.1, 37.9.

4.3.5 Synthesis of Molecule 6, Molecule 7 and Molecule 9



Scheme 4. 5. Synthesis of molecule **6**, molecule **7** and molecule **9**.

Synthesized with small modifications to published procedure [45].

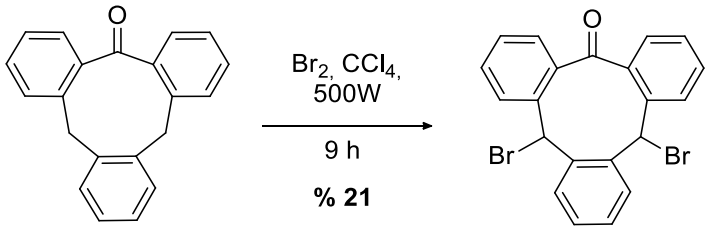
Starting material, **5** (0.800 g, 2.96 mmol), finely ground $KMnO_4$ (19 g, 120 mmol) and MnO_2 (21 g, 242 mmol) was dissolved in dry pyridine (40 mL) and heated to reflux (130 °C) for 48 hours. Then, the mixture was filtered through Celite while it was still hot and washed with EtOAc (500 mL) and DCM (500 mL). Solvent was removed under reduced pressure. Column chromatography (silica gel, DCM: Hexane - 5: 1) was performed and white products (**6**, **7**, **9**) was obtained.

Molecule **6** (400 mg, **47%**)^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (m, *J* = 9.4 Hz, 2H), 7.48 – 7.35 (s, 4H), 7.26 (s, 4H), 7.16 (d, *J* = 9.1 Hz, 2H), 3.89 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 140.7, 139.9, 138.0, 132.7, 131.5, 130.5, 129.5, 127.3, 127.1, 37.8.

Molecule **7** (255 mg, **29%**) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 6.1 Hz, 2H), 7.48 (ddd, *J* = 27.4, 5.8, 3.4 Hz, 4H), 7.33 – 7.16 (m, 4H), 7.02 (d, *J* = 7.5 Hz, 2H), 3.87 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 140.4, 139.9, 139.4, 132.4, 130.9, 130.4, 129.2, 128.1, 127.4, 37.8.

Molecule **9** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.2 Hz, 2H), 7.60 – 7.33 (m, 6H), 7.29 (t, *J* = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 194.8, 139.9, 137.8, 135.9, 131.9, 130.0, 129.6, 128.9, 128.7, 127.9, 127.3.

4.3.6 Synthesis of Molecule 10

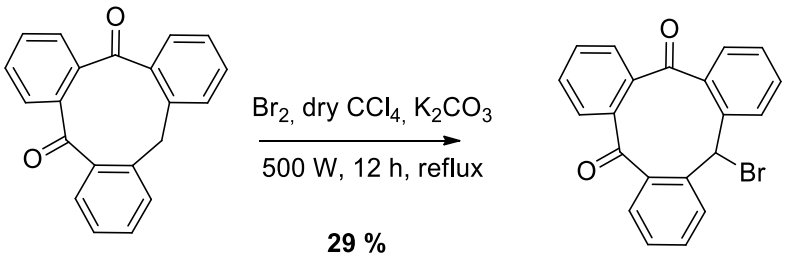


Scheme 4. 6. Synthesis of molecule **10**.

Synthesized with small modifications to published procedure [49].

Starting material, **6** (100 mg, 0.35 mmol) was suspended in freshly distilled CCl_4 (18 mL). Br_2 solution (1 M, 0.7 mL) was prepared in dry CCl_4 and added dropwise into reaction balloon at 50 ºC. The solution was exposed to 500 W lights for 9 hours. The reaction was finished by checking TLC (3 DCM: 1 Hexane) and the solvent of reaction was removed under reduced pressure. Column chromatography (silica gel, DCM: Hexane - 3: 1) was performed and white product was obtained. (33 mg, **21 %**).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 9.1 Hz, 2H), 7.75 (d, *J* = 7.5 Hz, 2H), 7.48 – 7.42 (m, 4H), 7.36 – 7.32 (m, 4H), 6.47 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 139.3, 137.9, 136.9, 133.0, 131.6, 129.5, 129.1, 129.0, 128.8, 48.6.

4.3.7 Synthesis of Molecule 11

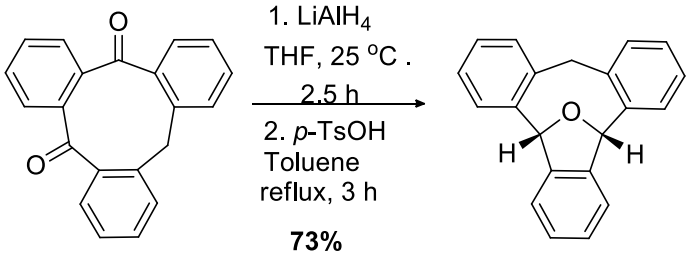


Scheme 4. 7. Synthesis of molecule **11**.

Synthesized with small modifications to published procedure [49].

Starting material, **7** (421 mg, 1.41 mmol) was suspended in freshly distilled CCl_4 (56 mL) and K_2CO_3 (0.99 g, 7.16 mmol). Br_2 solution (1 M, 1.8 mL) was added dropwise into reaction balloon. The solution was exposed to 500 W lights for 12 hours. The reaction was finished by checking TLC (3 DCM: 1 Hexane) and the solvent of reaction was removed under reduced pressure. The residue was dissolved in DCM and extracted with $NAHSO_3$. Column chromatography (silica gel, DCM: Hexane - 3: 1) was performed and light pink product was obtained. (153 mg, **29 %**).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.66 (m, 2H), 7.61 – 7.54 (m, 6H), 7.49 (td, *J* = 7.7, 1.5 Hz, 2H), 7.38 (td, *J* = 6.8 Hz, 2H), 6.78 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 140.5, 139.7, 138.3, 132.7, 131.6, 129.9, 128.8, 128.5, 47.9.

Synthesis of Molecule 14

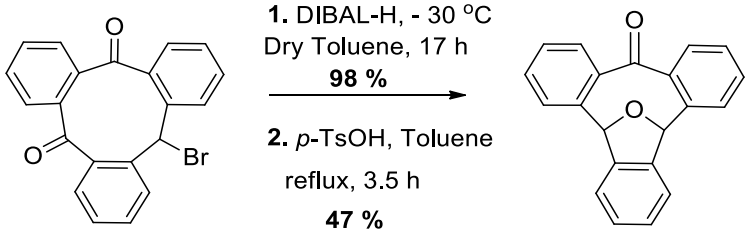


Scheme 4. 8. Synthesis of molecule **14**.

In the first step of the reaction, starting material (100 mg, 0.34 mmol) dissolved in dry THF (17 mL). $LiAlH_4$ (38 mg, 1.01 mmol) was put into reaction medium at 0 ºC and reaction stirred 2.5 h at room temperature. The reaction was diluted with THF (17 mL). Then, distilled water (0.1 mL) and 15% aq NaOH solution (0.1 mL) were added into reaction respectively. After addition of anhydrous $MgSO_4$, the mixture was filtered through Celite and washed with THF (100 mL). Solvent was removed under reduced pressure and obtained yellow substance. The crude product was used in second step without purification. It (80 mg) was dissolved in dry toluene (112 mL) and p- toluenesulfonic acid (p- TsOH) (24 mg, 0.15 mmol) was added into reaction. Then, the mixture was heated to 135 °C for 3 hours. For this reaction Dean- Stark Apparatus was used. When starting material was finished by checking TLC, the reaction was finished by adding distilled water at room temperature and extracted

with toluene, $NaHCO_3$ and brine respectively. The solvent was evaporated under reduced pressure and red crude product was obtained. Column chromatography (silica gel, DCM: Hexane - 2: 1) was performed and white product (55 mg, **73%**) was obtained. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.38 (m, 2H), 7.34 (dd, *J* = 8.5 Hz, 2H), 7.27 – 7.19 (m, 8H), 6.27 (s, 2H), 3.37 – 3.29 (m, 1H), 3.20 (s, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 141.0, 132.7, 128.8, 128.6, 126.8, 121.3, 88.9, 39.3. HRMS $C_{21}H_{17}O$, calculated: 285.1279, found: 285.1279.

4.3.8 Synthesis of Molecule 15

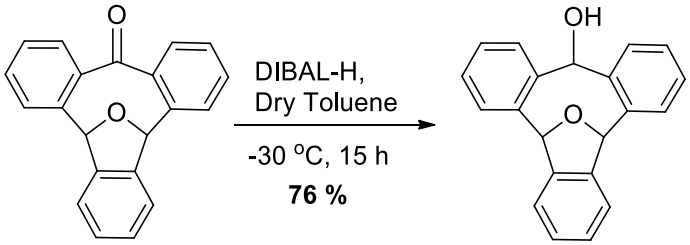


Scheme 4. 9. Synthetic of molecule **15**.

For the reaction 1, starting material (120 mg, 0.318 mmol) was put into 50 mL- two-neck balloon and dry toluene (12 mL) was added into it in Argon atmosphere. Diisobutylaluminium hydride (DIBAL-H) (0.6 mL) was added into reaction very slowly at – 30 °C and it was stirred overnight in room temperature. The reaction was finished by applying TLC (DCM: Hexane- 3:1). To work up the reaction, distilled water (10 mL) was added at 0 °C and extracted with toluene. The solvent was evaporated under reduced pressure and yellow crude product (118 mg, **98%**) was obtained and it was used without purification for next step. Second step was synthesized small changes with literature [50]. It (118 mg, 0.31 mmol) was dissolved in dry toluene (67 mL) in 250 mL- two- neck balloon in Argon atmosphere and p-toluenesulfonic acid (p- TsOH) (28 mg, 0.16 mmol) was added into reaction. Then, the mixture was heated to 135 °C for 3.5 hours. For this reaction Dean- Stark Apparatus was used. When starting material was finished by checking TLC, the

reaction was finished by adding distilled water at room temperature and extracted with toluene, $NaHCO_3$ and brine respectively. The solvent was evaporated under reduced pressure and red crude product was obtained. Column chromatography (silica gel, DCM: Hexane - 2: 1) was performed and white product (43 mg, **47 %**) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.97 (m, 2H), 7.49 – 7.45 (m, 2H), 7.39 – 7.31 (m, 6H), 7.28 – 7.20 (m, 4H), 6.34 (s, 1H), 6.23 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 208.0, 140.9, 140.5, 140.0, 129.8, 128.9, 128.0, 127.3, 124.0, 121.9, 84.3. HRMS $C_{21}H_{15}O_2$, calculated: 299.1072, found: 299.1074.

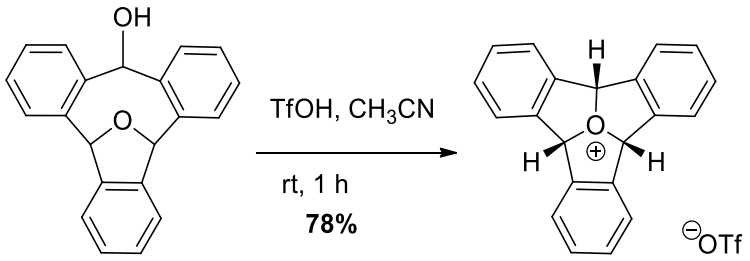
4.3.9 Synthesis of Molecule 16



Scheme 4. 10. Synthesis of molecule **16**.

To produce molecule **16**, starting material (18 mg, 0.06 mmol) was put into 10 mL Schlenk tube and dry toluene (2 mL) was added into it in argon atmosphere. Diisobutylaluminium hydride (DIBAL-H) (0.1 mL) was added into reaction very slowly at – 30 °C and it was stirred overnight in room temperature. The reaction was finished by applying TLC (DCM: Hexane- 3:1). Distilled water (2 mL) was added at 0°C and extracted with toluene. The solvent was evaporated under reduced pressure and yellow crude product (18 mg, **76%**) was obtained. The crude product was used without purification.

4.3.10 End Game: Synthesis of Tribenzooxatriquinane



Scheme 4. 11. Synthetic route of **Tribenzooxatriquinane**.

Starting material (23 mg, 0.08mmol) was dissolved in CH_3CN (1 mL) and Trifluoromethanesulfonic acid (CF_3SO_3H) (0.05 mL) was put into this solution at room temperature. After 1 h stirring, white crystals were formed. The solution was poured into dry diethyl ether (3.5 mL) in argon atmosphere at 0 °C. After the solution was stirred 30 minutes at room temperature, it was put in the freezer. Then, pure, white product (17 mg, **78%**) were collected. ^{1}H NMR (400 MHz, CD_3CN) δ 8.01 (s, 3H), 7.76 (dd, *J* = 8.9 Hz, 6H), 7.59 (dd, *J* = 8.9 Hz, 6H). ^{13}C NMR (100 MHz, Acetonitrile-d_3) δ 133.9, 131.6, 122.0, 107.9. HRMS $C_{21}H_{15}O^+$, calculated: 283.1123, found: 283.1115.

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APPENDICES

A. NMR Spectra

NMR analysis both ^{1}H and ^{13}C was carried on Bruker Spectrospin Avance DPX-400 Spectrometer and tetramethylsilane was used as internal reference. $CDCl_3$, d_6-DMSO and CD_3CN were used as NMR solvents Add appendix here.

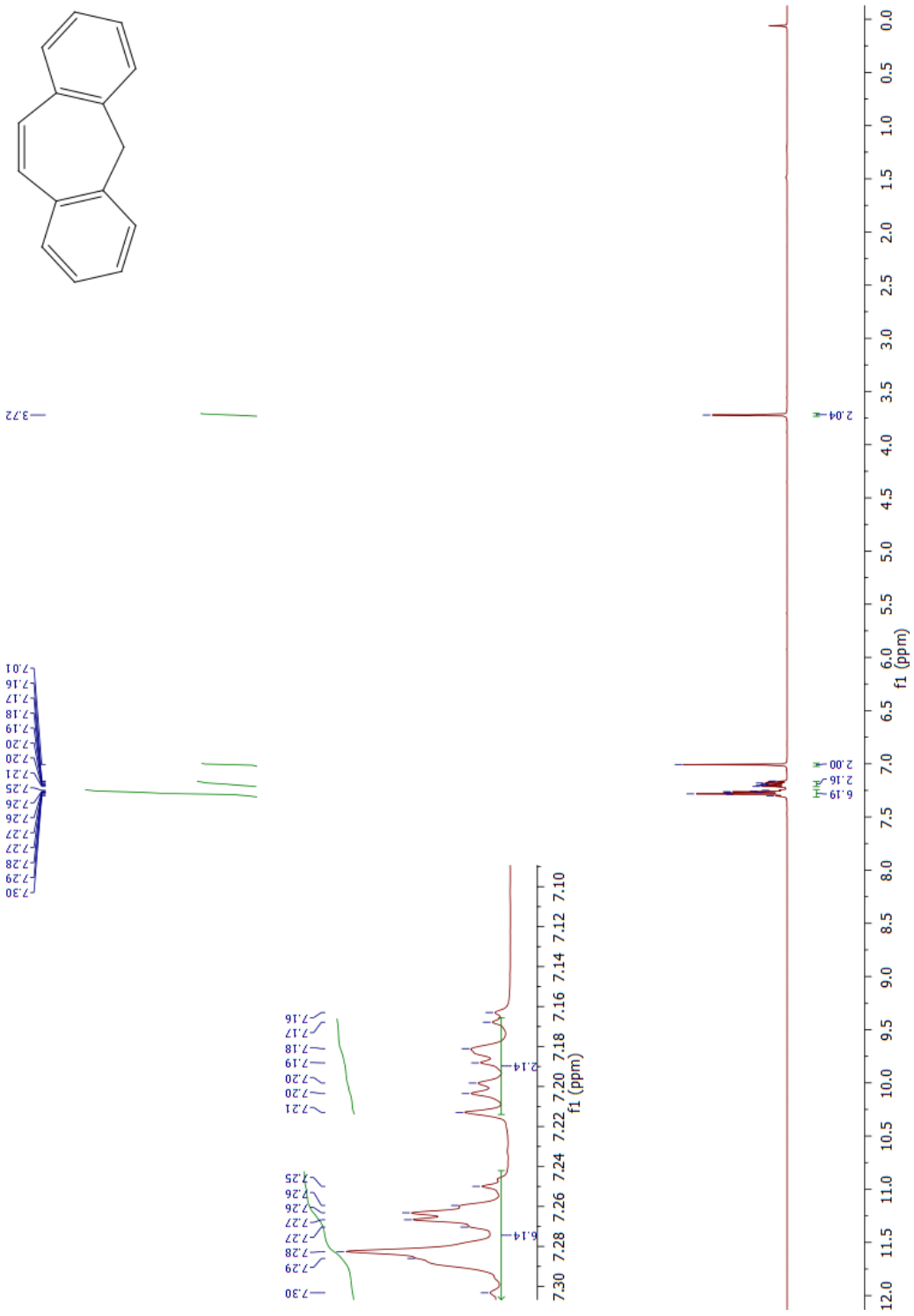


Figure A. 1. ^{1}H NMR Spectrum of molecule **2**.

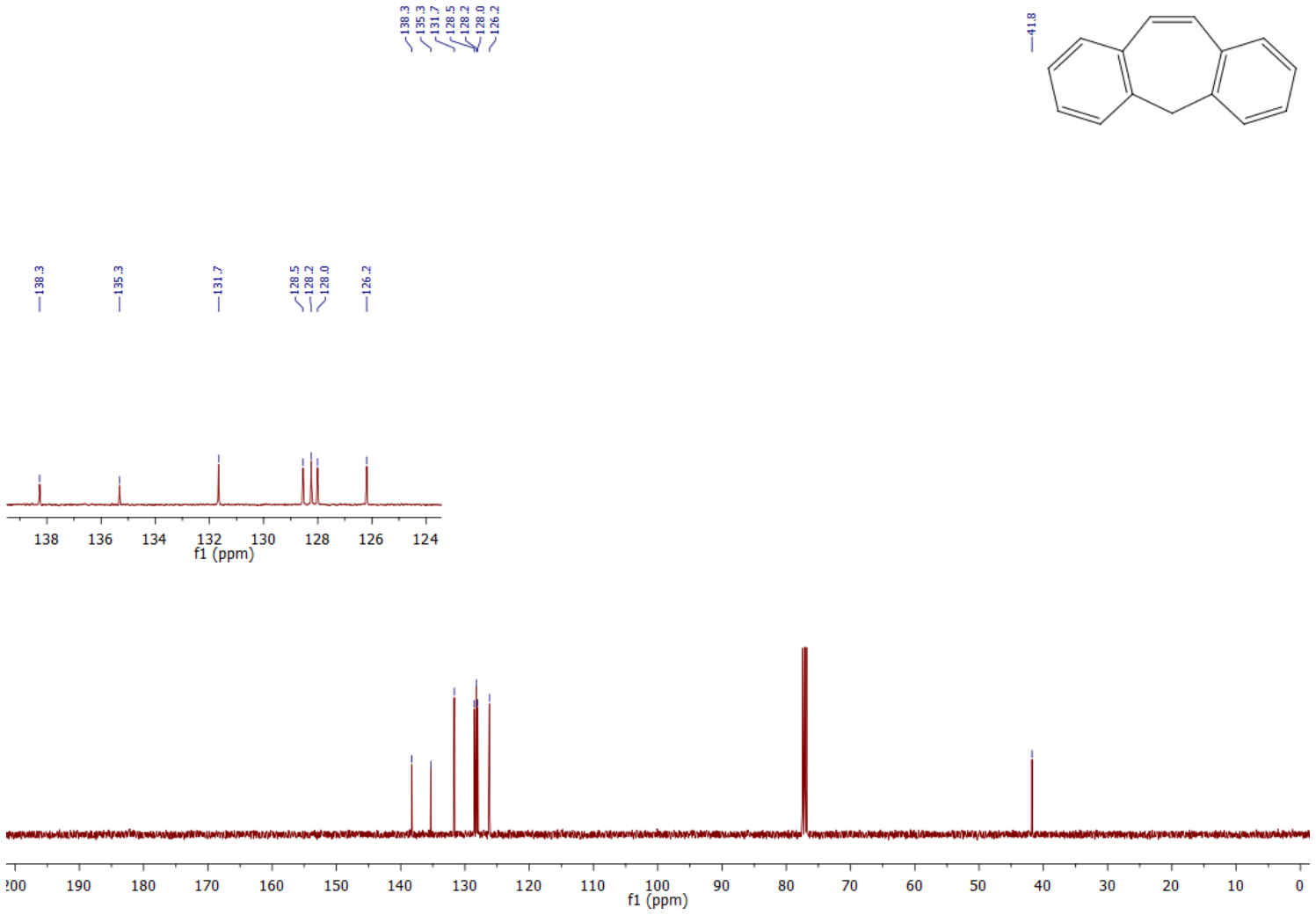


Figure A. 2. ^{13}C NMR Spectrum of molecule **2**.

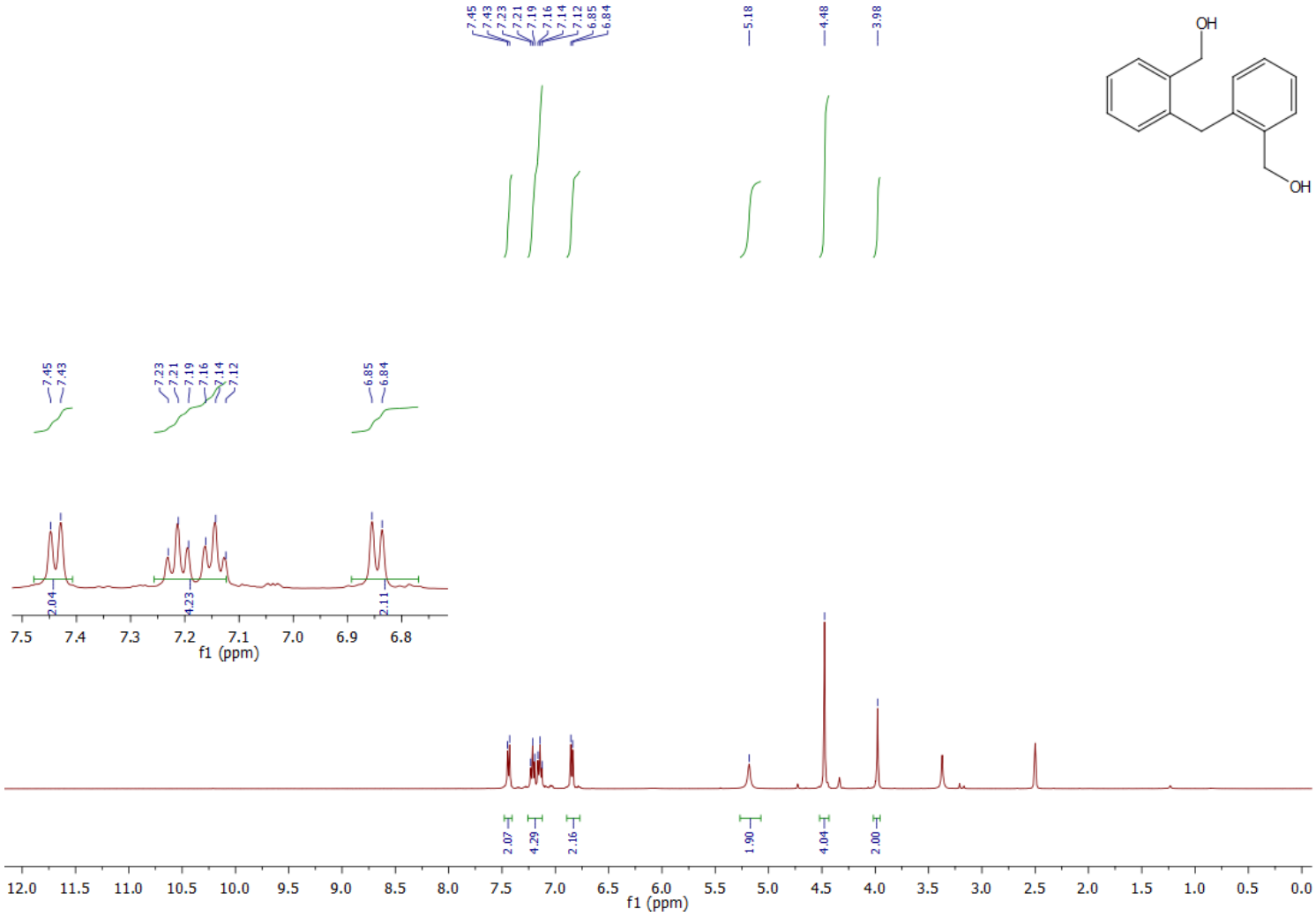


Figure A. 3.[1]H NMR Spectrum of molecule **3**.

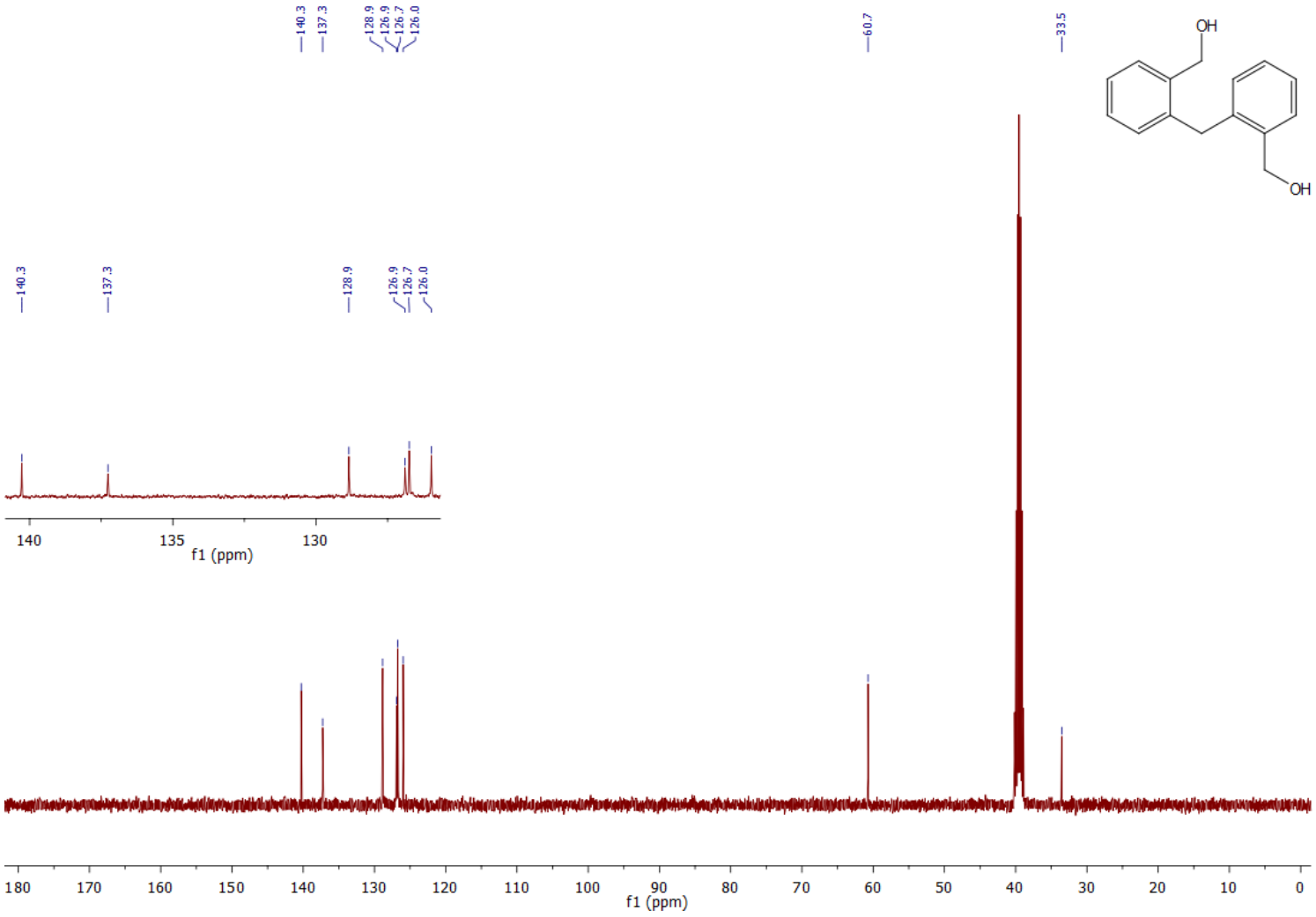


Figure A. 4.^{13}C NMR Spectrum of molecule **3**.

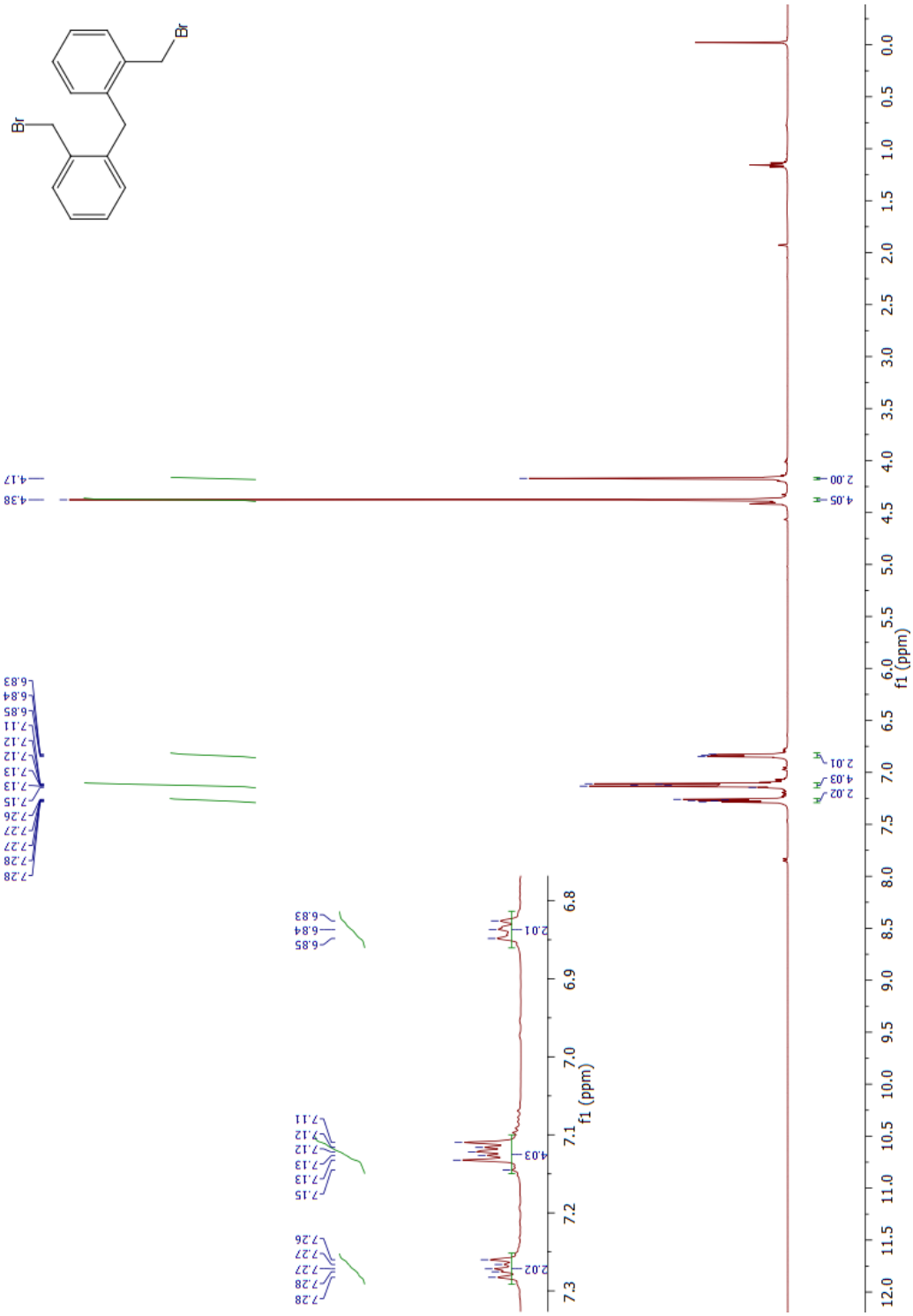


Figure A. 5. ^{1}H NMR Spectrum of molecule **4**.

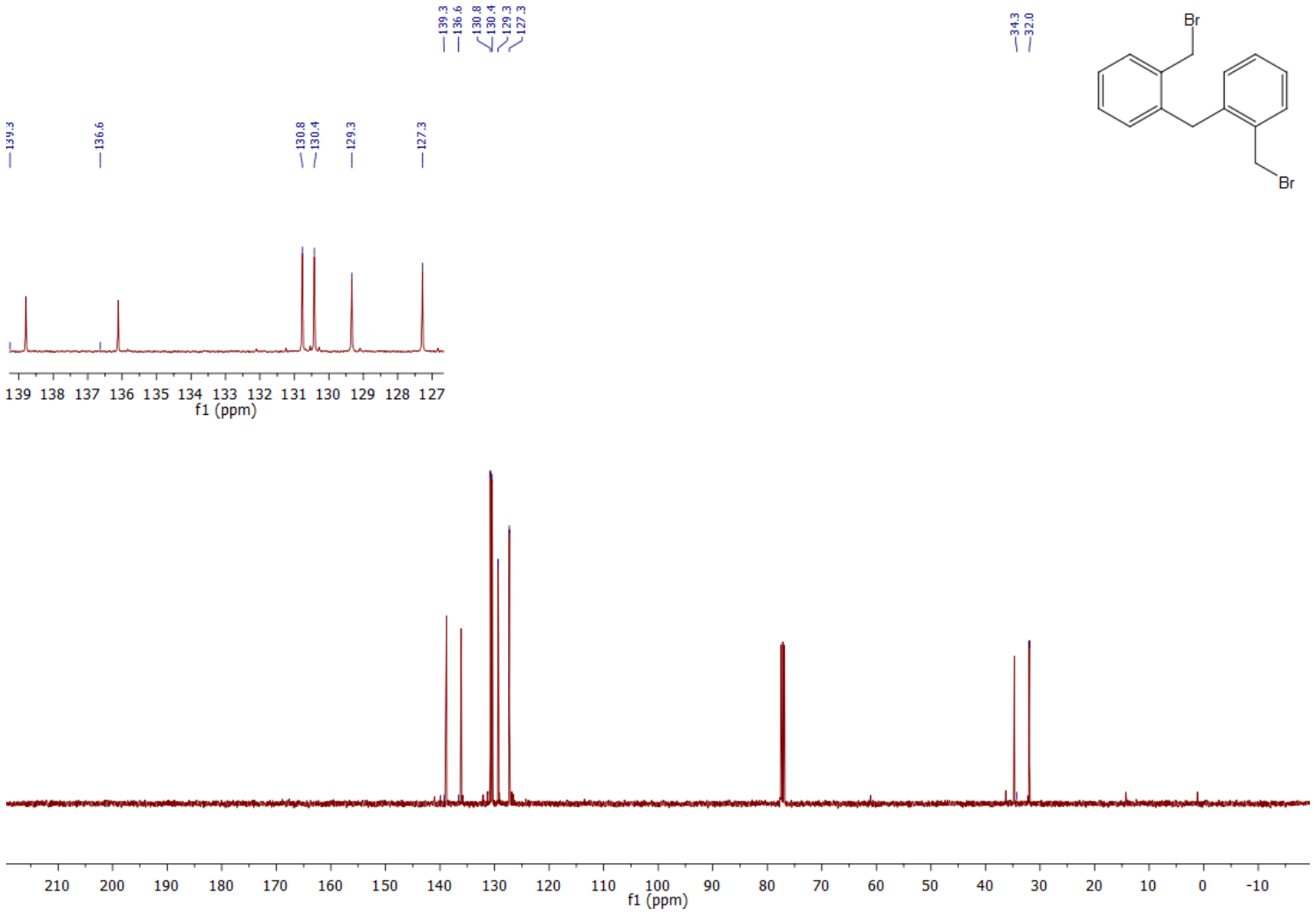


Figure A. 6. ^{13}C NMR Spectrum of molecule **4**.

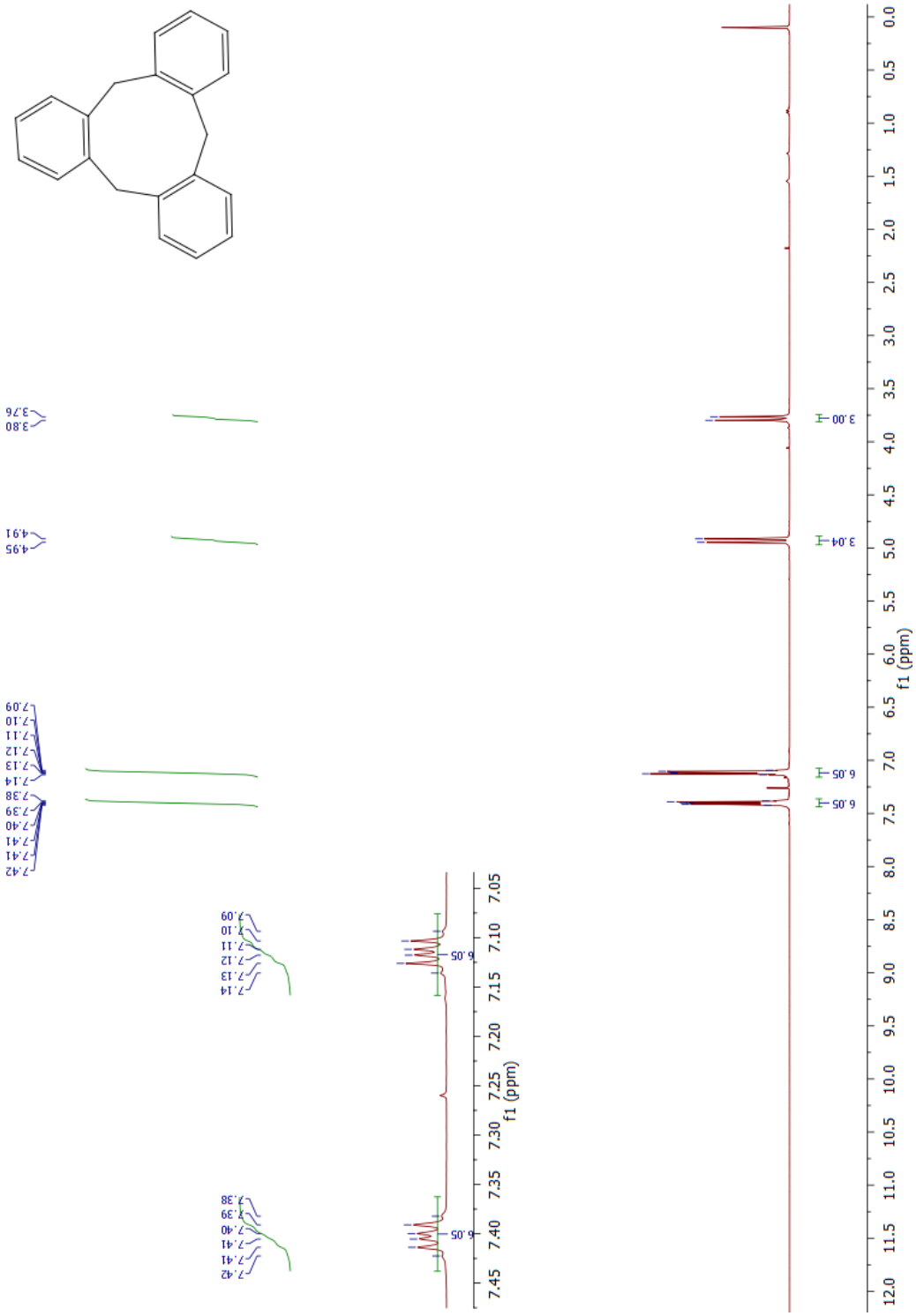


Figure A. 7.^{1}H NMR Spectrum of molecule **5**.

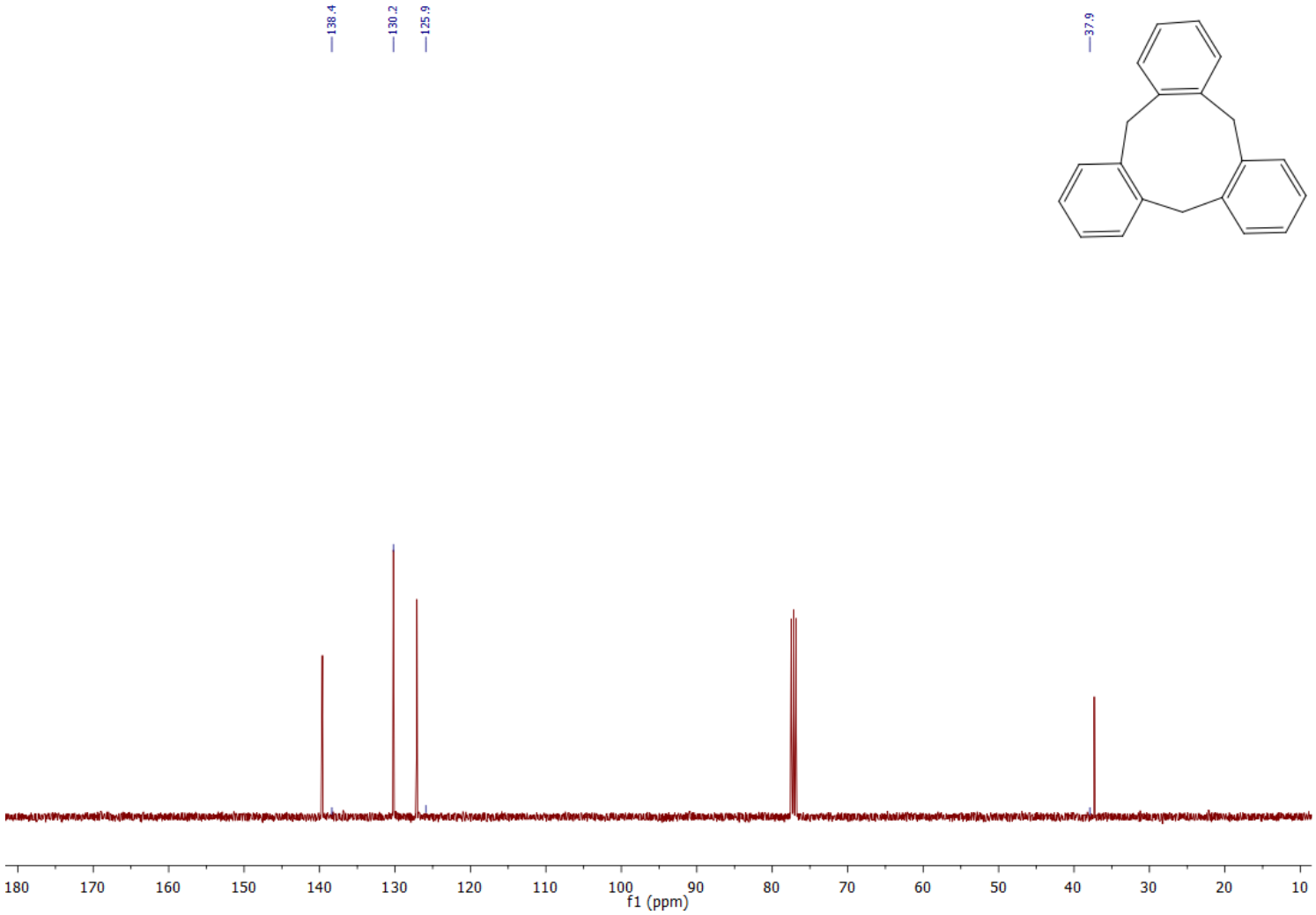


Figure A. 8.^{13}C NMR Spectrum of molecule **5**.

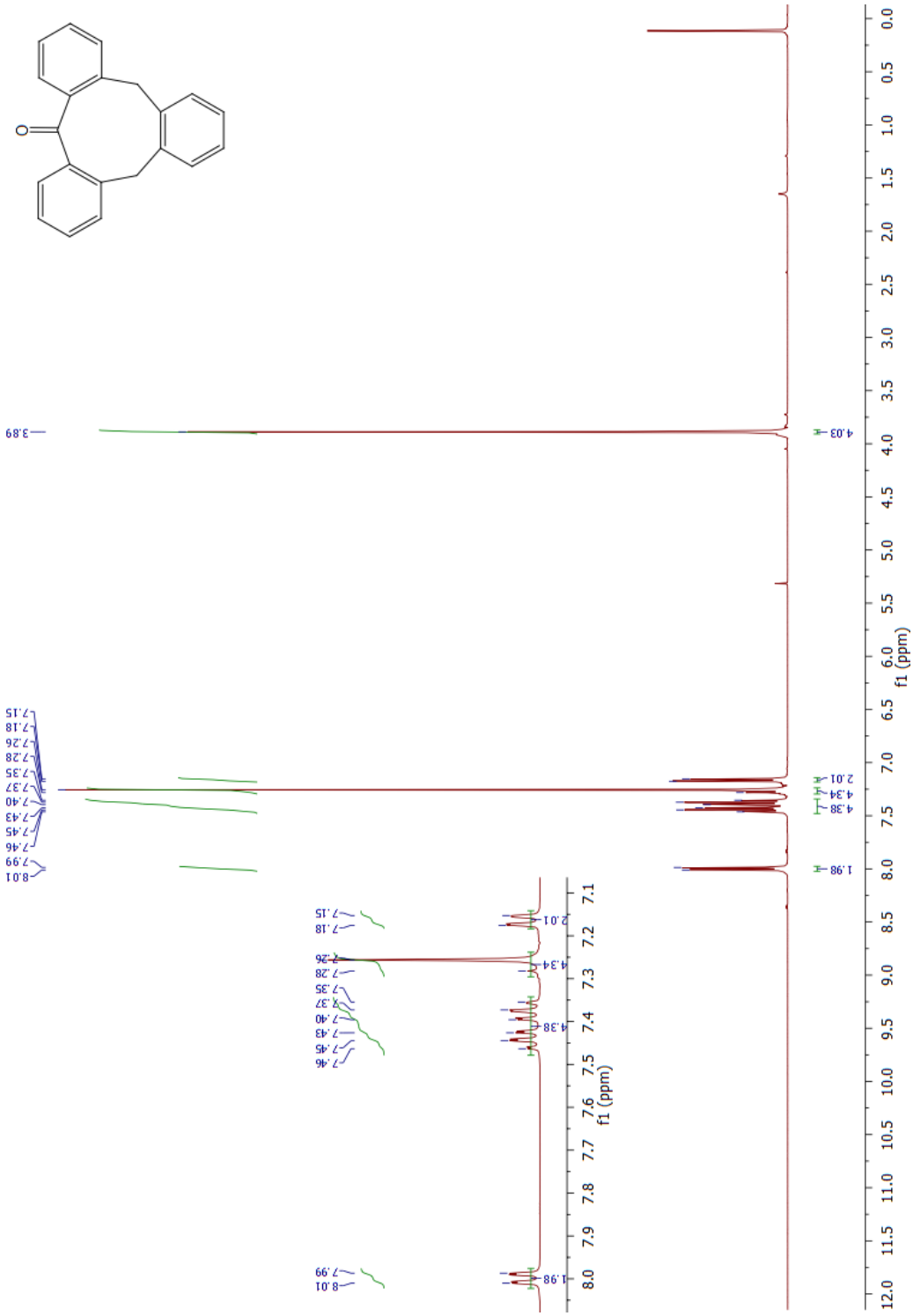


Figure A. 9. ^{1}H NMR Spectrum of molecule **6**.

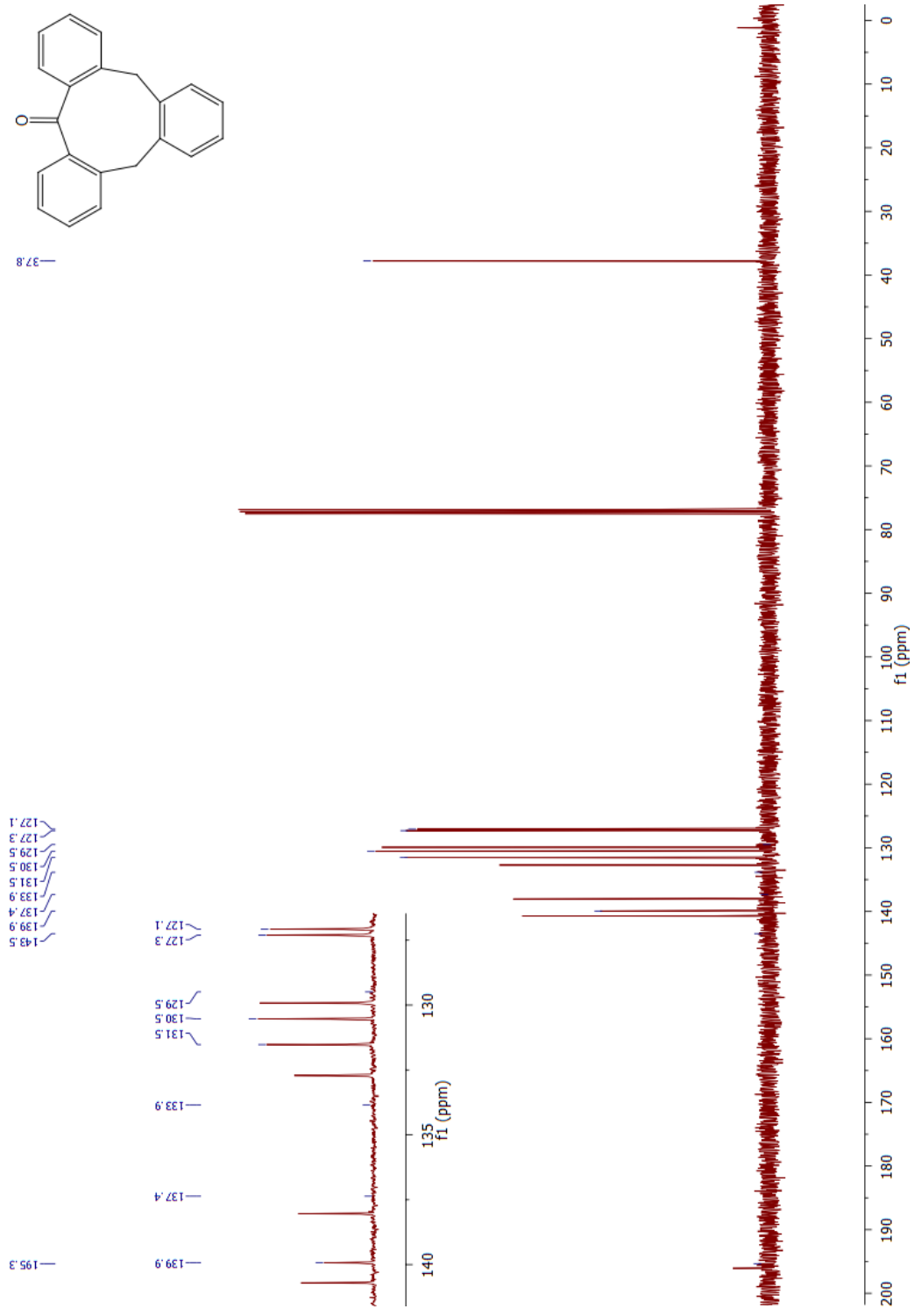


Figure A. 10. ^{13}C NMR Spectrum of molecule **6**.

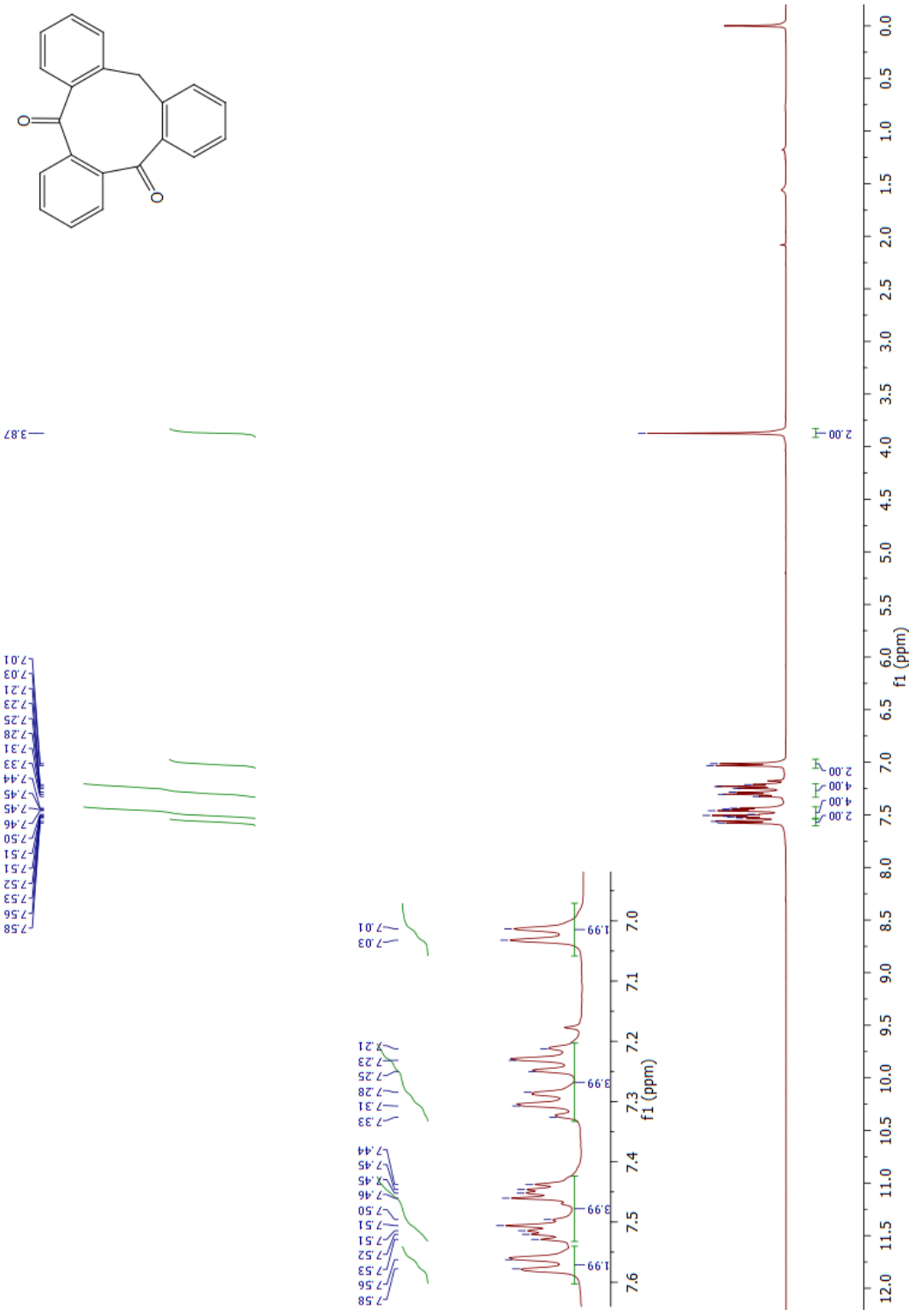


Figure A. 11. ^{1}H NMR Spectrum of molecule **7**.

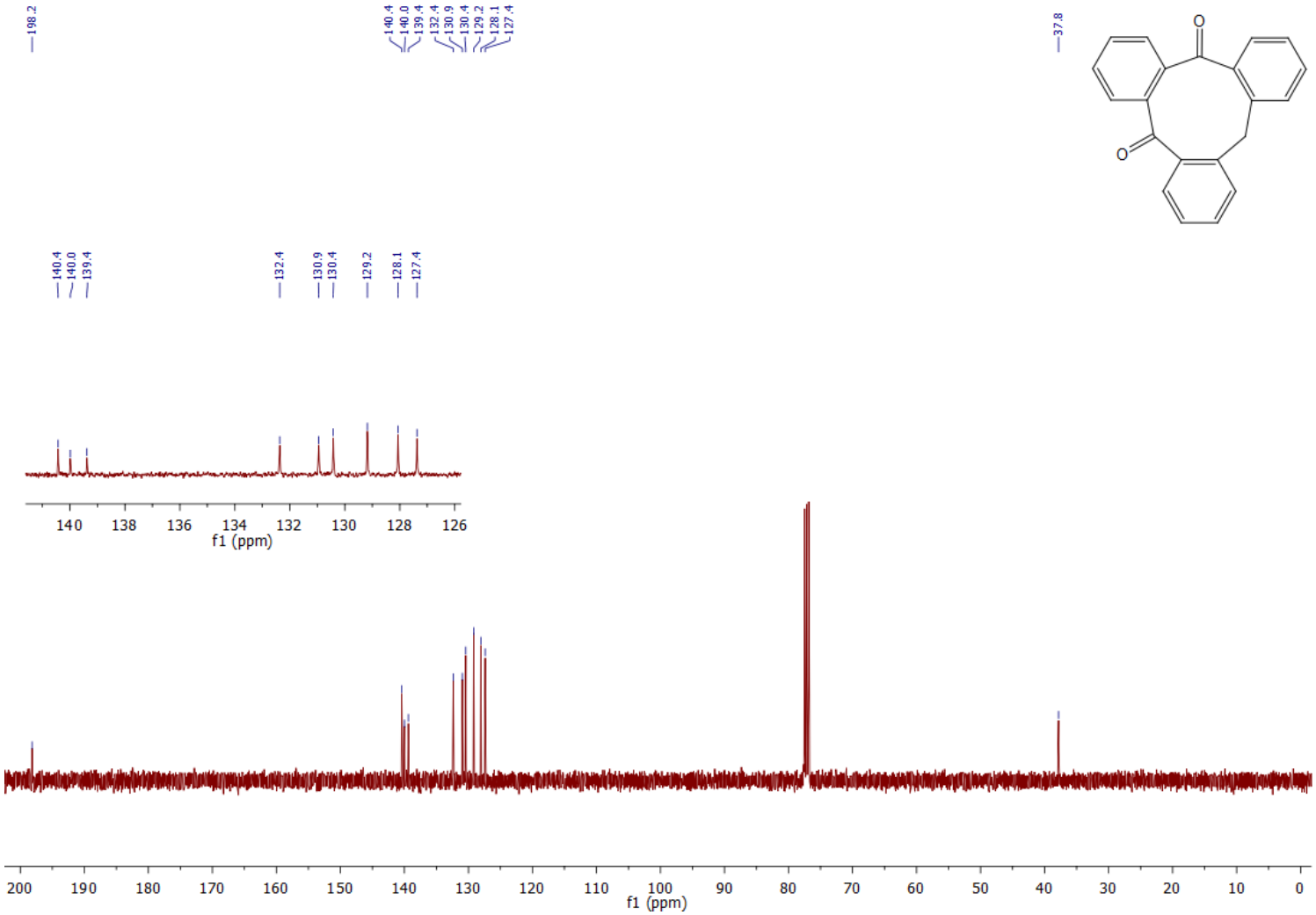


Figure A. 12. ^{13}C NMR Spectrum of molecule **7**.

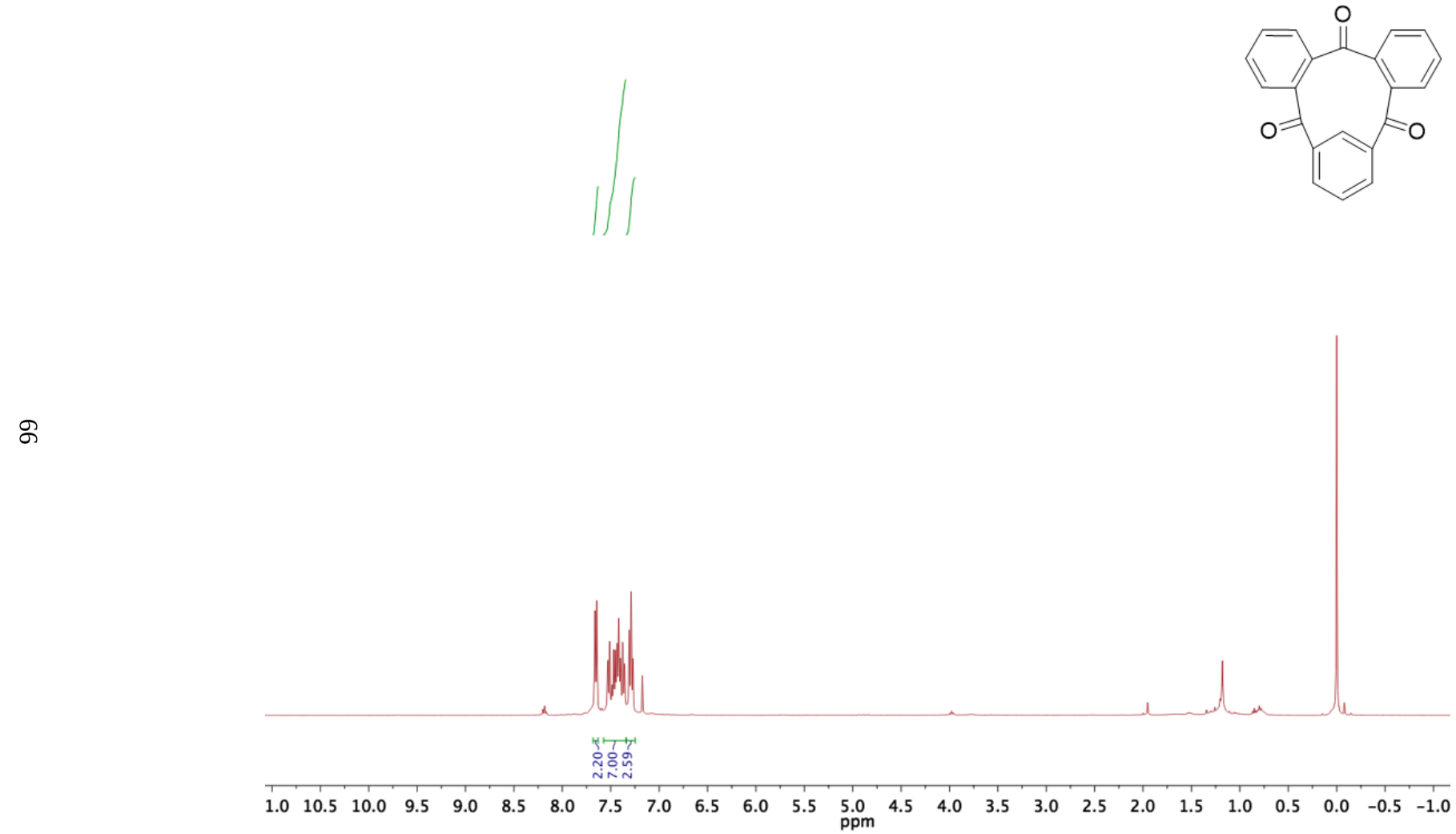


Figure A. 13. ^{1}H NMR Spectrum of molecule **9**.

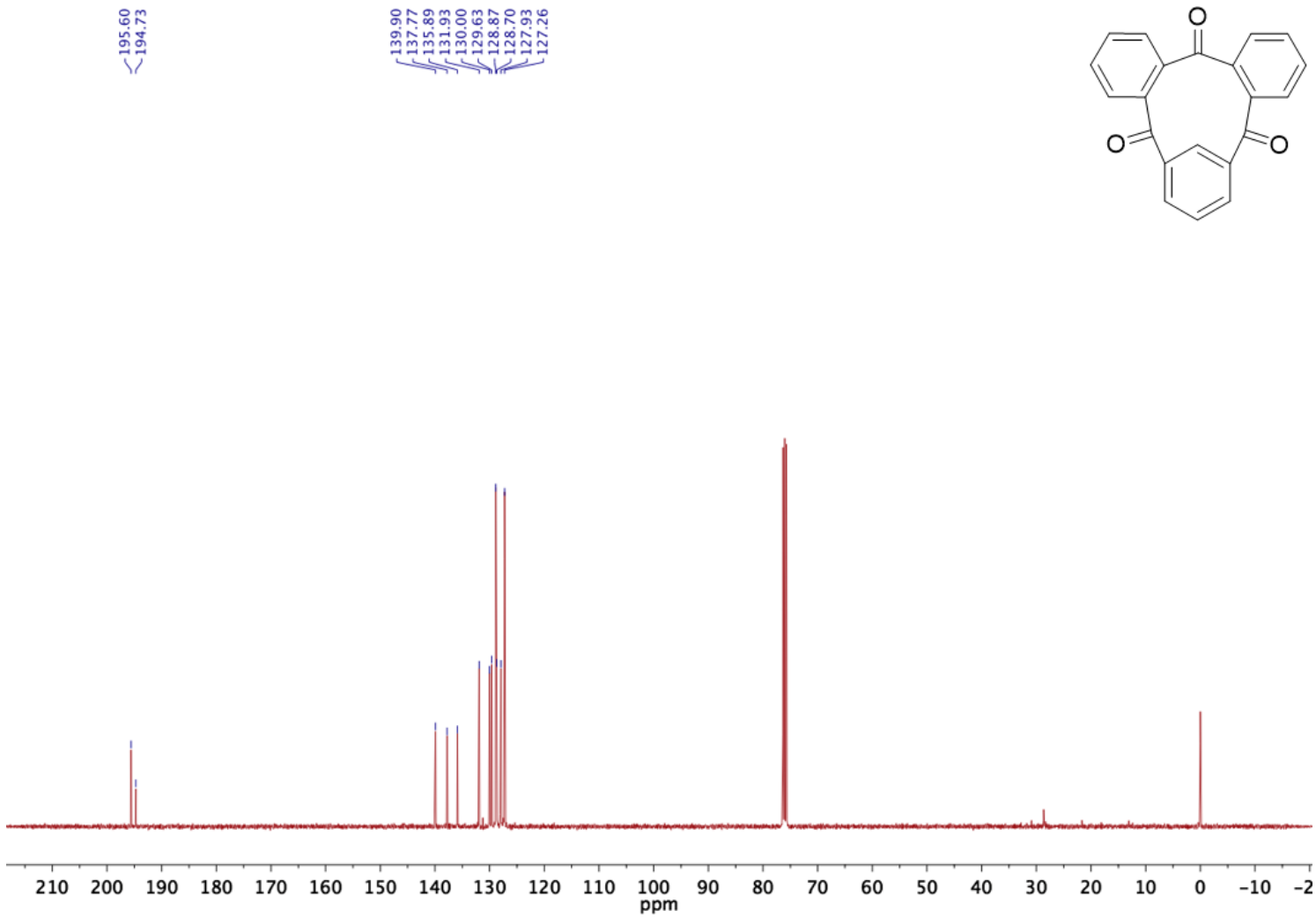


Figure A. 14. ^{13}C NMR Spectrum of molecule **9**.

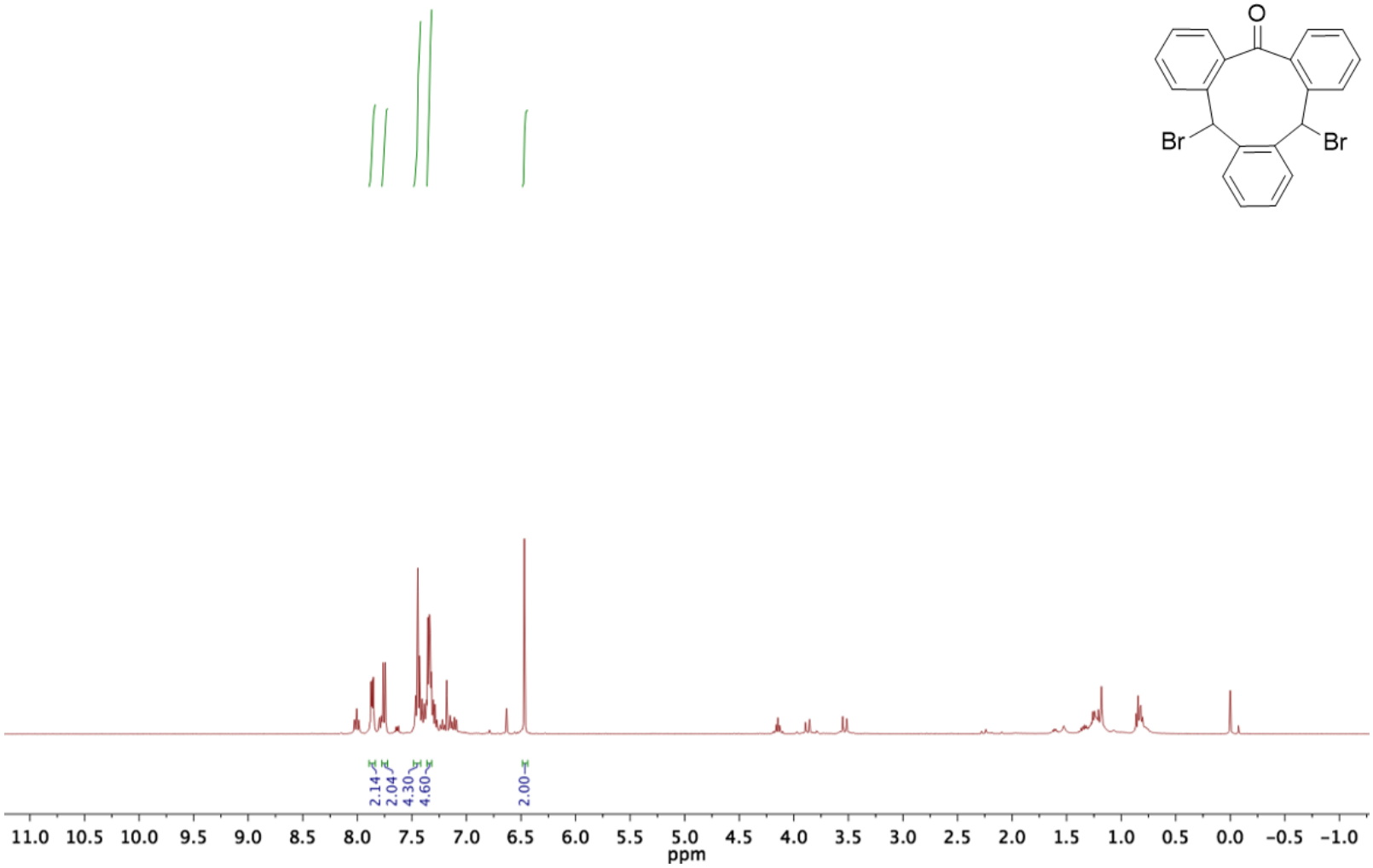


Figure A. 15. ^{1}H NMR Spectrum of molecule **10**.

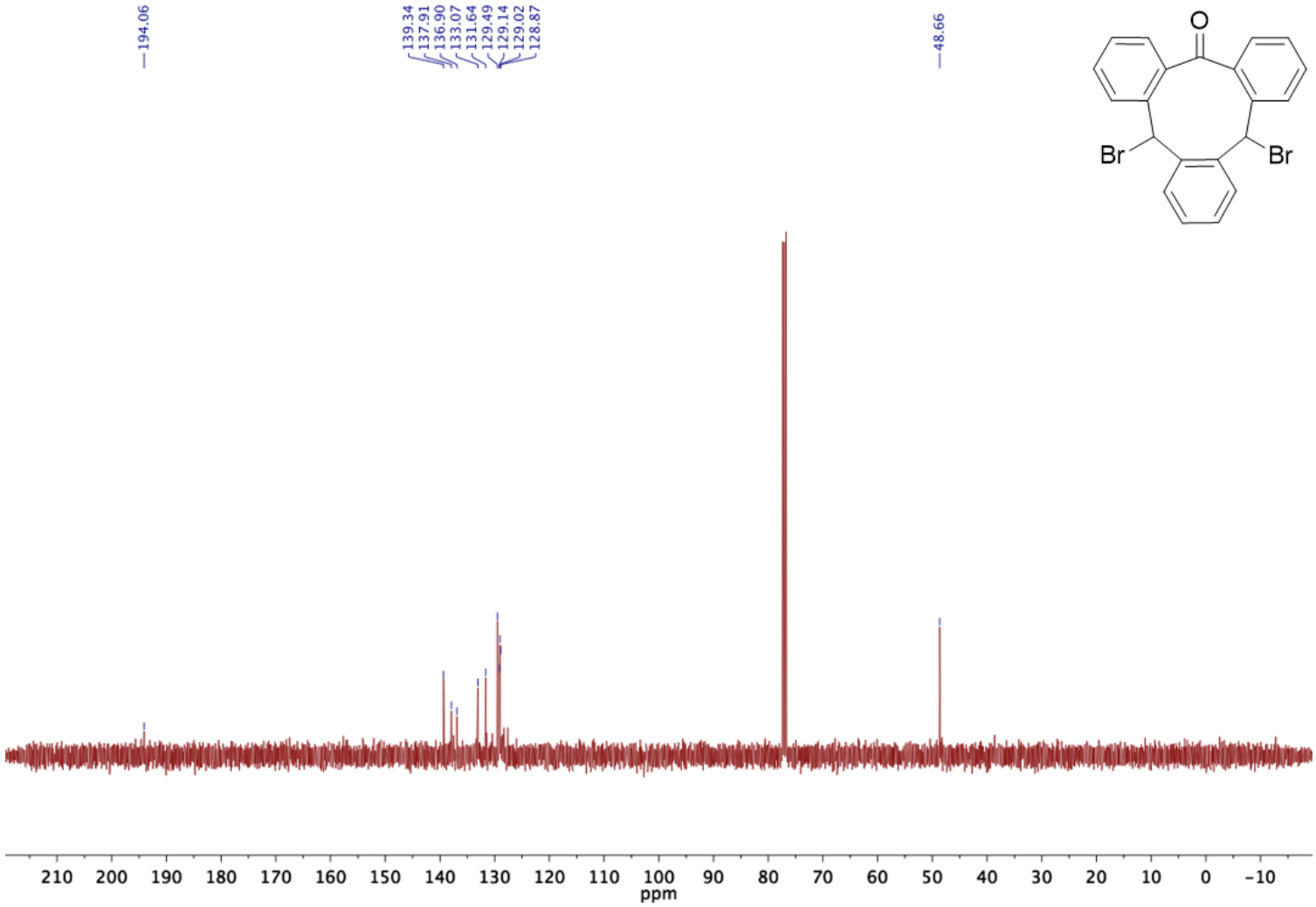


Figure A. 16. ^{13}C NMR Spectrum of molecule **10**.

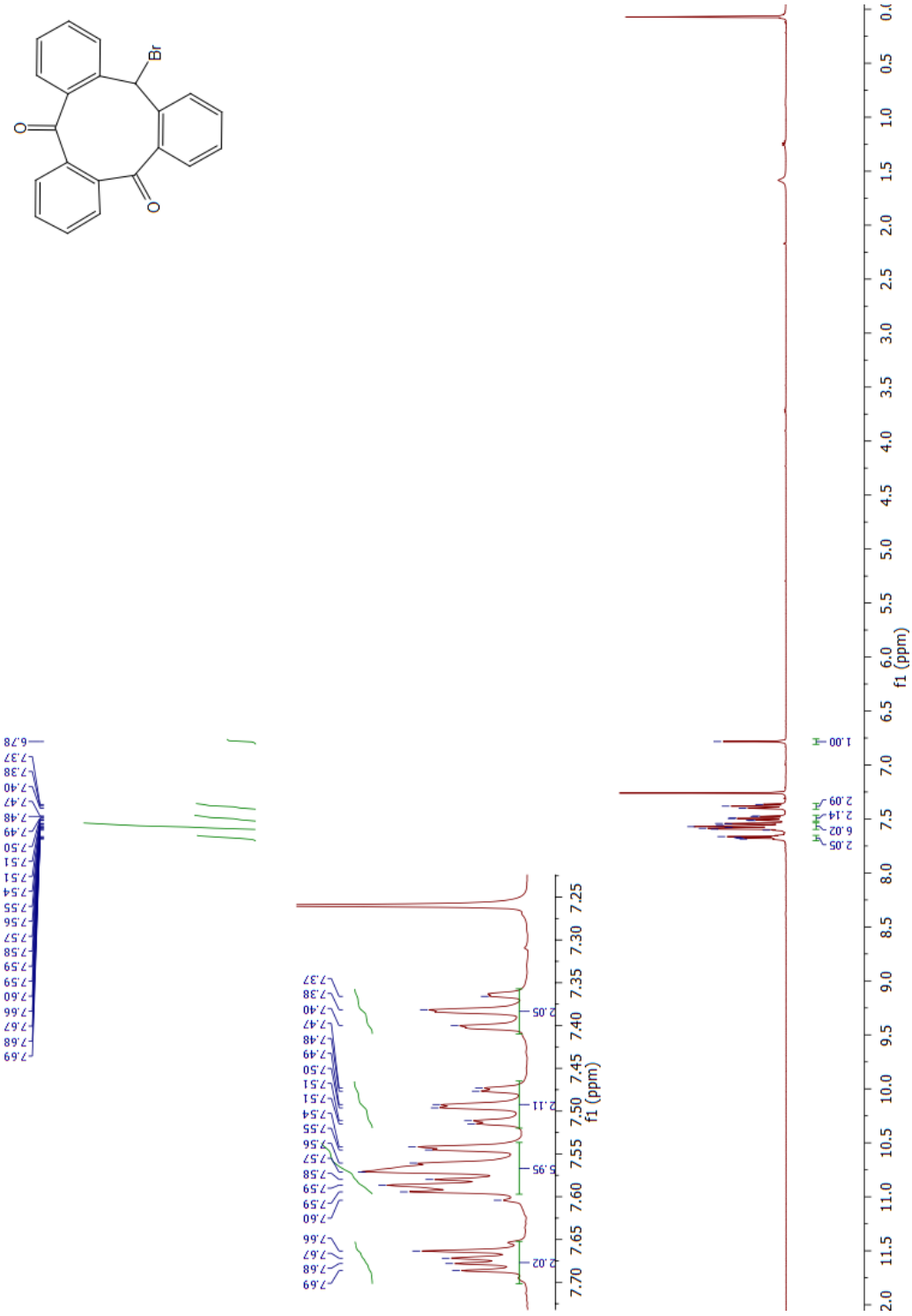


Figure A. 17. ^{1}H NMR Spectrum of molecule **11**.

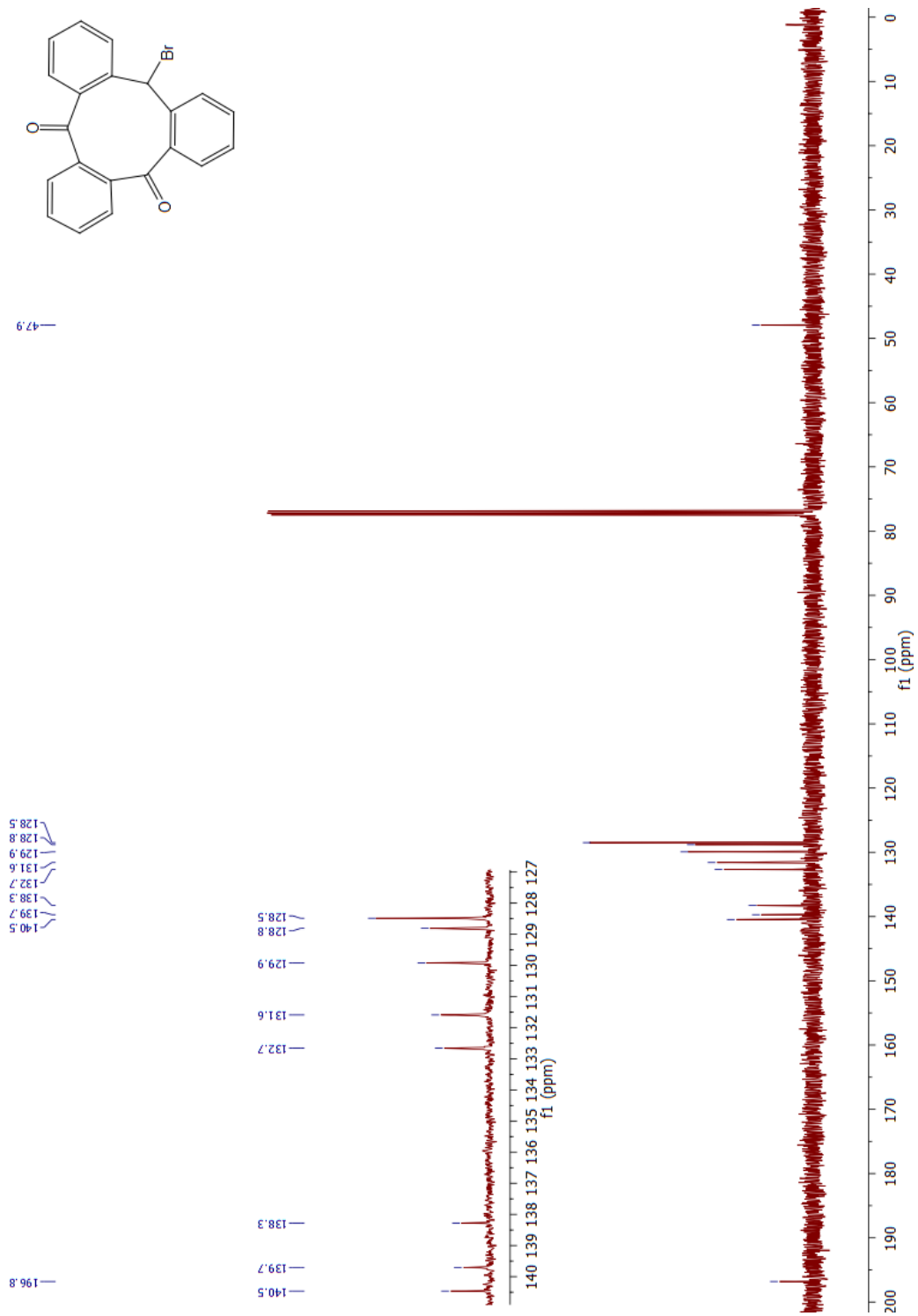


Figure A. 18. ^{13}C NMR Spectrum of molecule **11**.

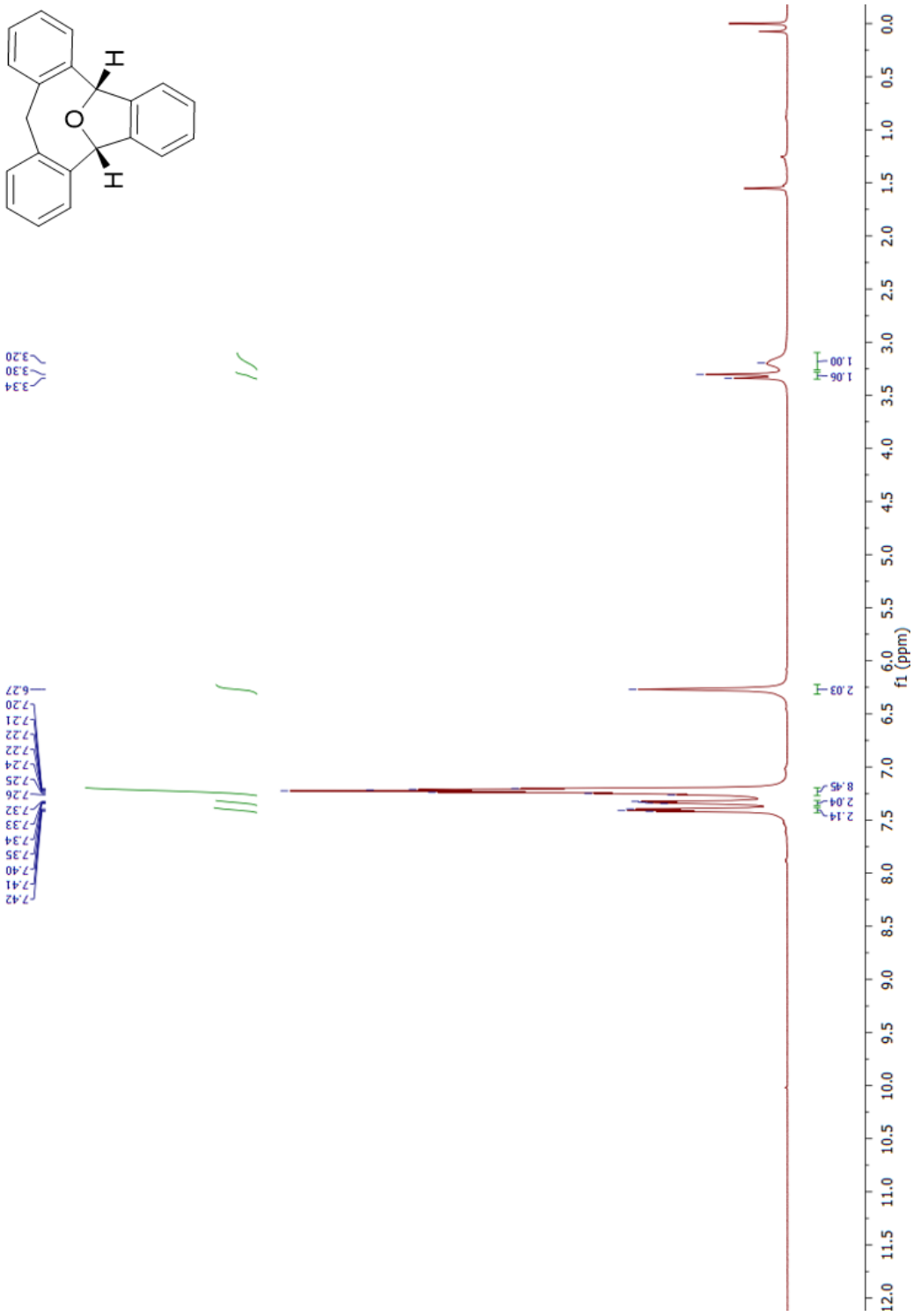


Figure A. 19. ^{1}H NMR Spectrum of molecule **14**.

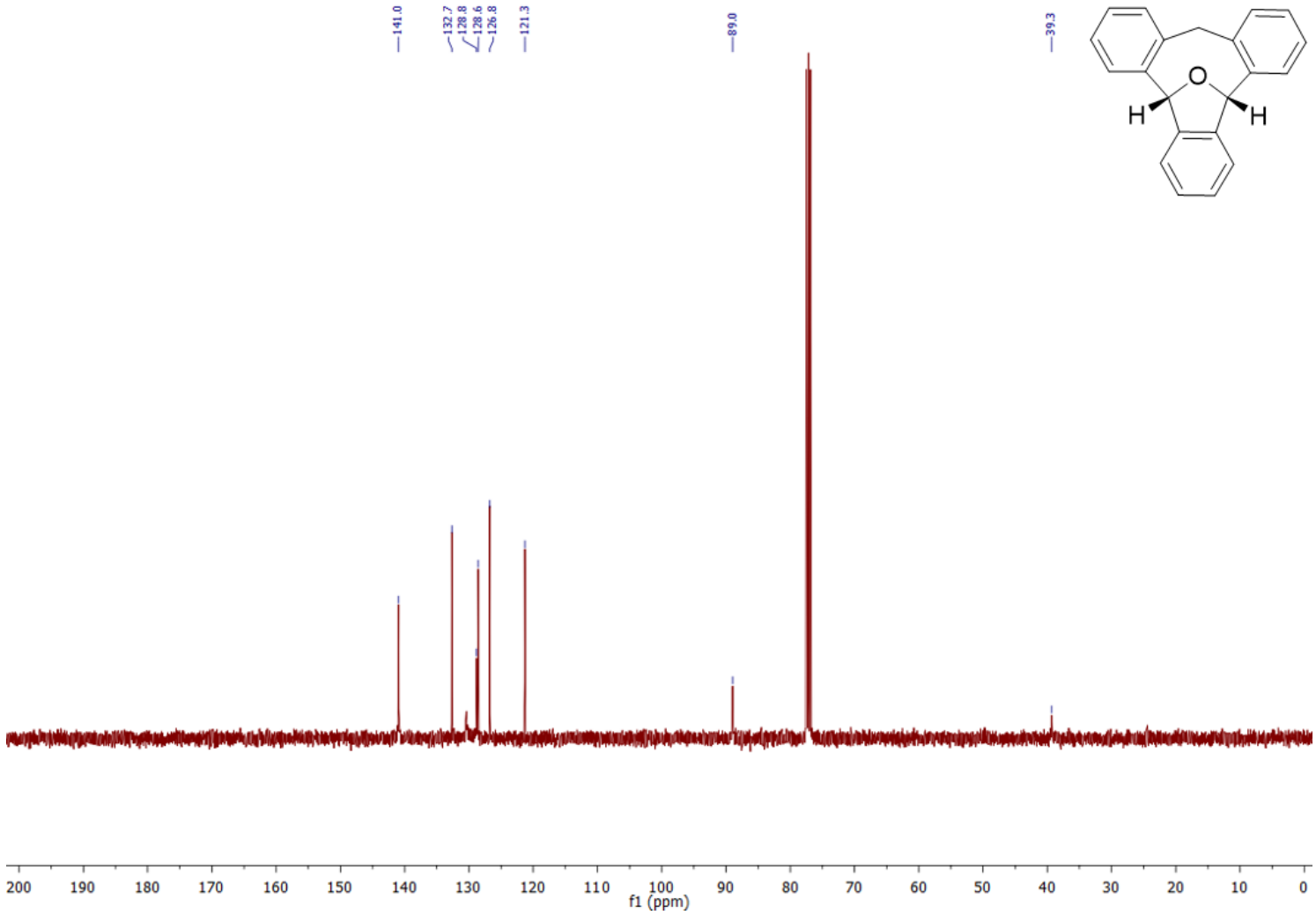


Figure A. 20. ^{13}C NMR Spectrum of molecule **14**.

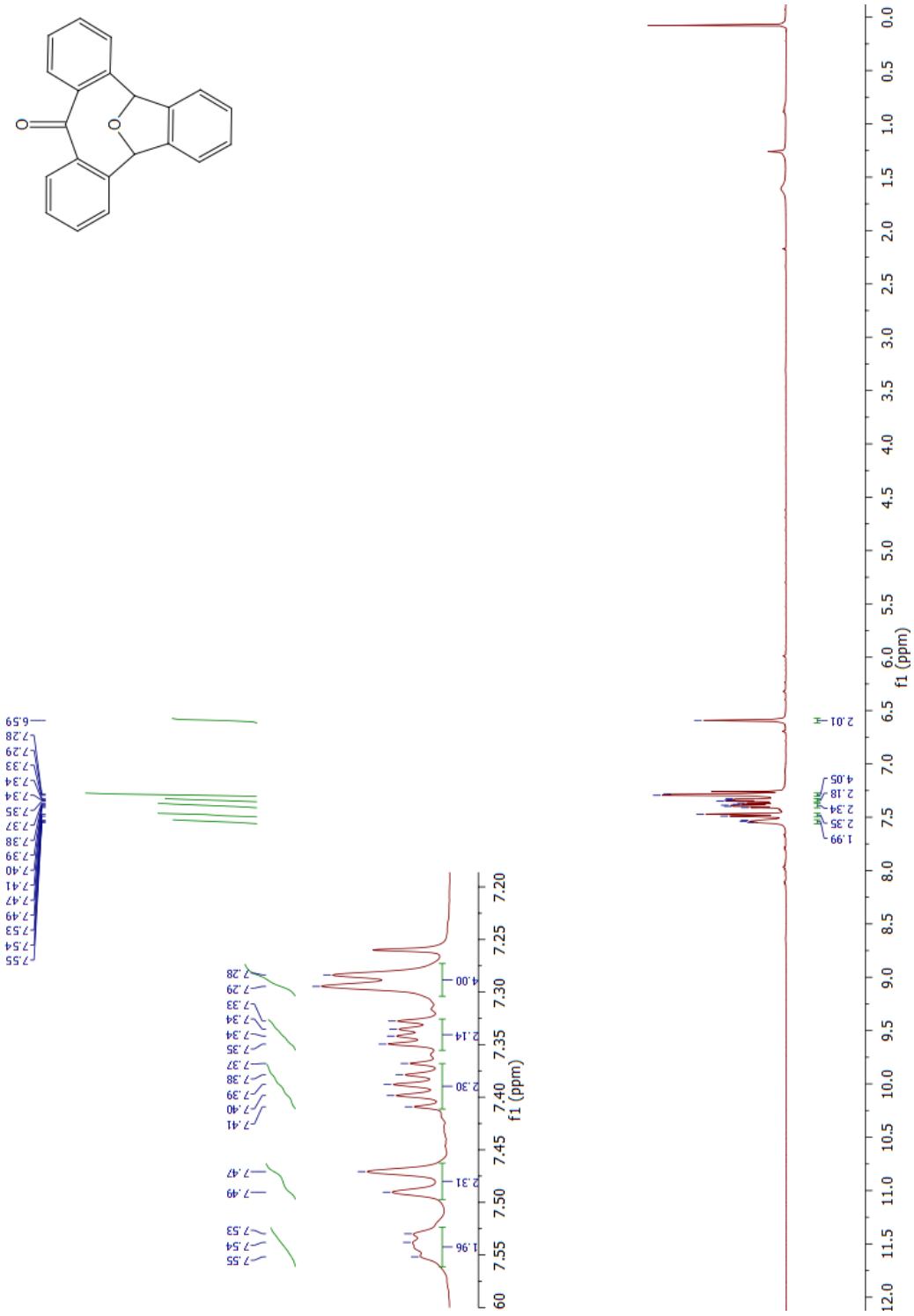


Figure A. 21. ^{1}H NMR Spectrum of molecule **15**.

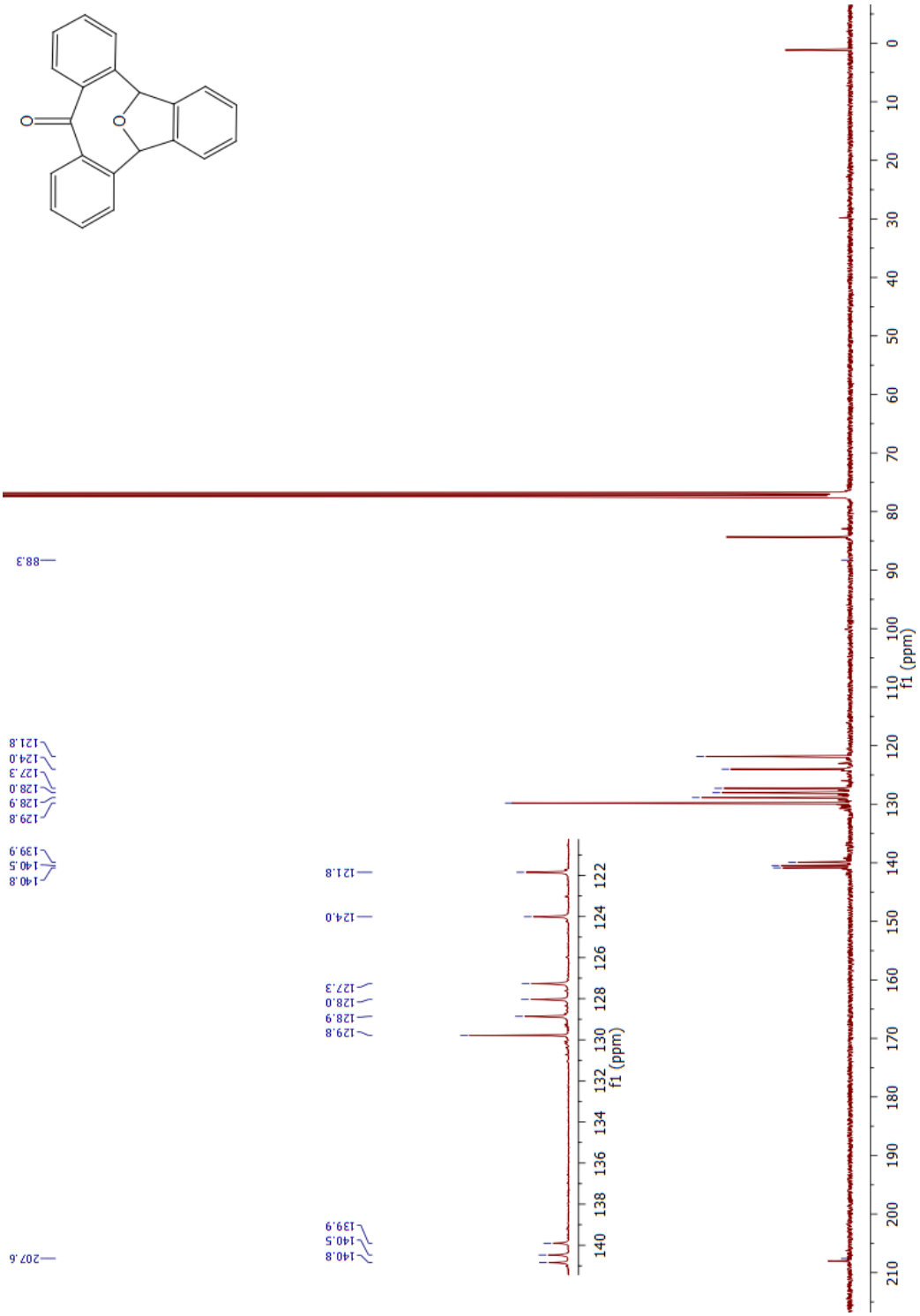


Figure A. 22. ^{13}C NMR Spectrum of of molecule **15**.

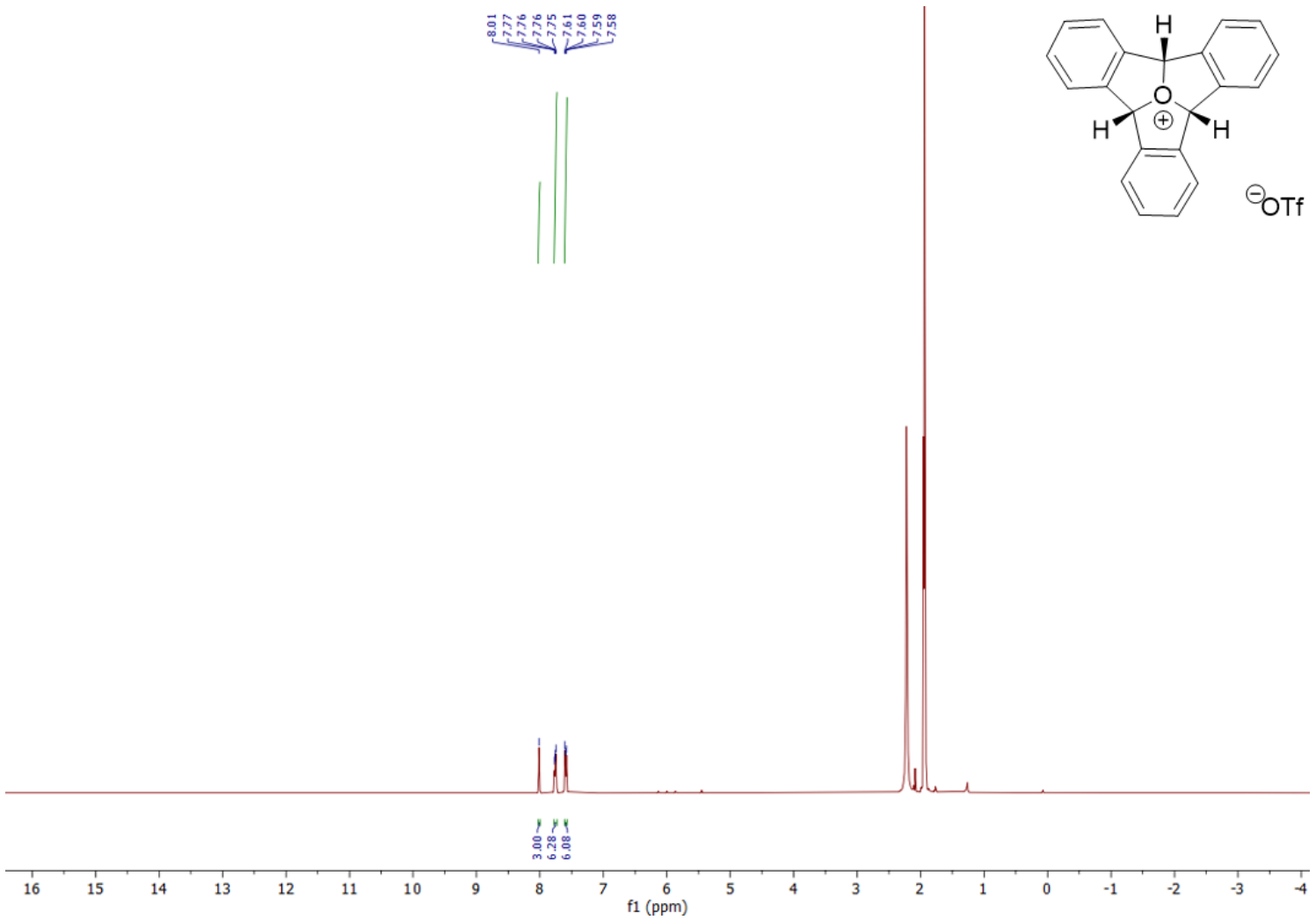


Figure A. 23. ^{1}H NMR Spectrum of **Tribenzooxatriquinane**.

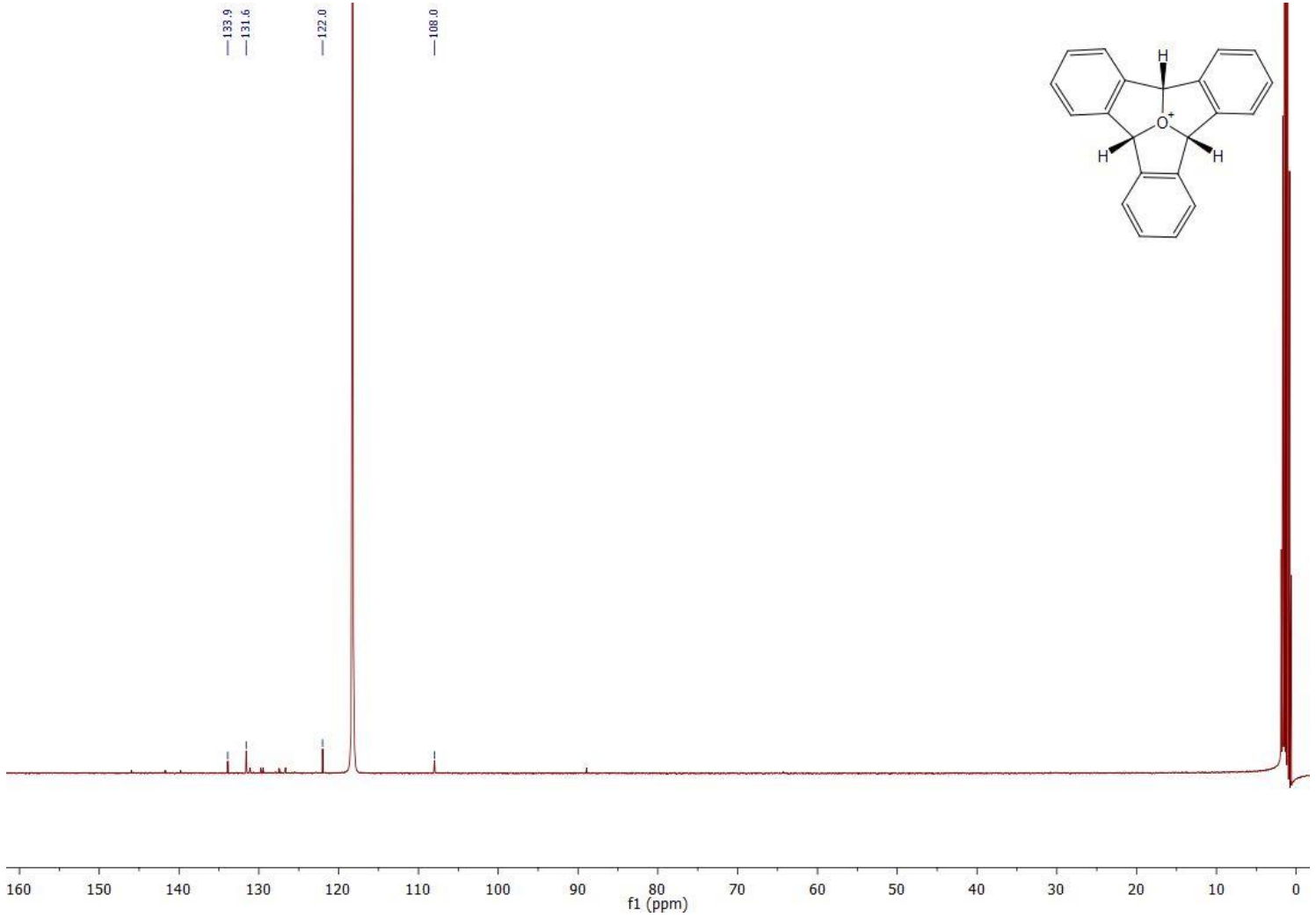
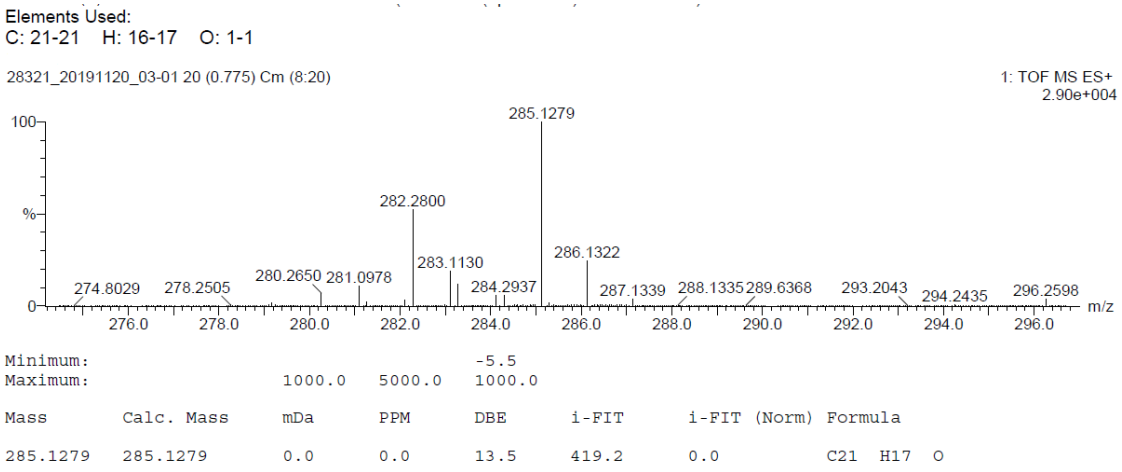


Figure A. 24. ^{13}C NMR Spectrum of **Tribenzooxatriquinane**.

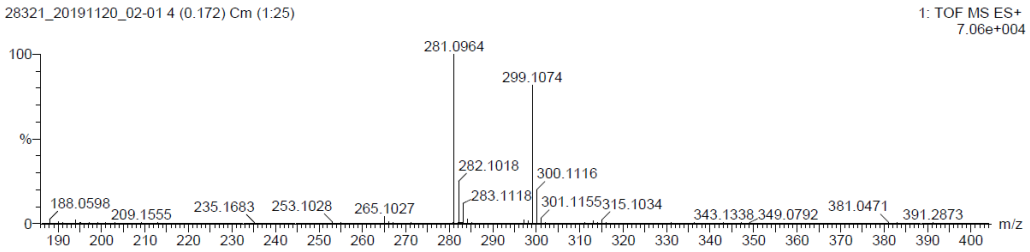
B. HRMS Result

High Resolution Mass Spectroscopy (HRMS) was performed using Waters Synapt MS System at METU Central Laboratory.



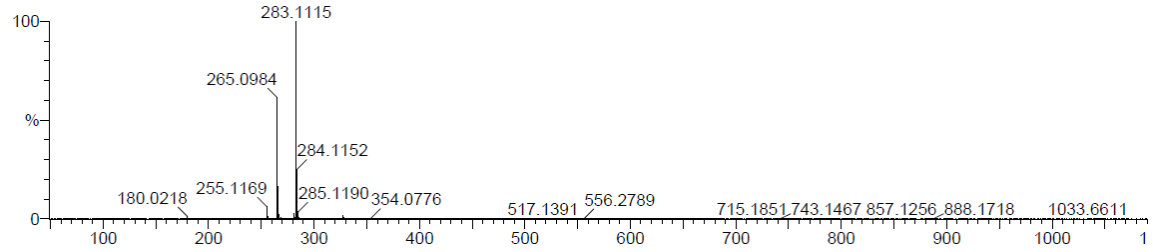
Minimum:				-5.5			
Maximum:		1000.0	5000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
285.1279	285.1279	0.0	0.0	13.5	419.2	0.0	C21 H17 O

Figure B. 1. HRMS Spectrum of Molecule **14**.



Minimum:				-5.5			
Maximum:		1000.0	5000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
299.1074	299.1072	0.2	0.7	14.5	489.0	0.0	C21 H15 O2

Figure B. 2.HRMS Spectrum of Molecule **15**.



Minimum:				-5.5			
Maximum:		1000.0	5000.0	1000.0			
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
283.1115	283.1123	-0.8	-2.8	14.5	481.2	0.0	C21 H15 O

Figure B. 3. HRMS Spectrum of **Tribenzooxatriquinane**.