I. The RCM Approach Towards 1,6-methano-bridged[12] & [14]Annulenes and their Bisdehydro-derivatives
II. 1,5-bisdehydro[10]Annulene Revisited

by

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Abstract

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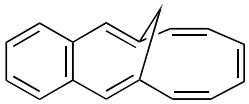
Part I of my dissertation presents a new efficient synthesis of 3,4-benzo-1,6-methano[12]annulene (3). This novel synthetic approach involves a grignard addition to 3,4-benzo-cycloheptatriene-1,6-dialdehyde followed by a ring closing olefin metathesis (RCM) reaction giving the bridged 12-menber ring of 3,4-benzo-1,6-methano[12]annulene (3) was obstained in six steps and an overall yield 44%. This allowed the complete structural and spectroscopic characterization as a paratropic ethano-bridged benzo[12]annulene with a 28% reduction of the paramagnetic ring current relative to the non-benzannulated molecule. A careful comparison of the 1H NMR of (3) with its 9,10-dihydro derivative (104) suggests an extended paratropic 16π system. The RCM approach is general and thus formally presents a 6 steps route to the parent 1,6-methano[12]annulene, previously reported by E. Vogel et al. Combination of cis-selective Wittig reaction of (36) with the ylide derived from 4-bromo-1-butene followed by RCM reaction yielded the 9,12-dihydro-3,4-benzo-1,6-methano[14]annulene (35).

Attempts to convert this molecular in to the expectedly diatropic 14π system did not succeed so far. In course of this investigation, an efficient synthesis for 3,4-benzo-1,6-ethynylcycloheptatriene was developed. Diketone (37) obtained through Jones oxidation of the diasteromeric alcohols (26) was converted into the 3,4-benzo-1,6-methano-7,12-bis(dibromomethylene)-8,11-dihydro[12]annulene (38). Treatment of this molecule with two moles of n-butyllithium did not yield the anticipated diacetylene (39). From diketone (37) a series of 7,12-disubstituted bridged [12]annulene can be synthesized, this illustrating the generality of this approach.

In part II of my dissertation, approaches toward 1,5-bisdehydro[10]annulenes were investigated with the goal to increase the activation energy for the known Bergmann rearrangement or even mark it impossible for the molecule to undergo it. This would enable us to investigate the expected 10π aromaticity of the 1,5-bisdehydro[10]annulene system. An initial approach utilizing the Ramberg Bakelund rearrangement failed due to the irreproducibility of the formation of the cyclic sulfide (70). Elimination was the major pathway even at pH8, most likely due to the very acidic propargylic hydrogens. The second approach started with the 10 menber ring diyneacetals (78), (85), (91). In course of this investigation a new reaction sequence was discovered as outline on scheme 3-9. This valuable fragmentation deprotection of stable cyclic benzylidene acetals leads directly to allylic alcohols such as compound (86). The introduction of the last double bond via the mesylate followed by treatment with potassium t-butoxide gave unexpectedly Benz(a)anthacene (89) and tetracene (88) in a ratio of 40:1. This result is being interpreted as an initial acetylene-allene isomerization followed by an allene-acetylene cyclization (Myers-Saito cyclization), hydrogen abstraction and aromatization

as shown on scheme 3-14. Treatment of the mesylate (93) derived from the allylic alcohol with potassium t-butoxide gave phenanthrene and anthracene in a ratio of 2:3. Treatment of the mesylate with triethylamine gave only anthracene, the expected product of the Bergmann rearrangement.



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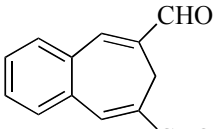

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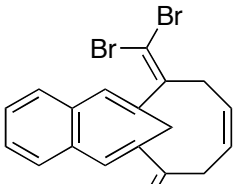

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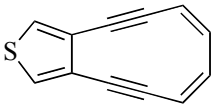

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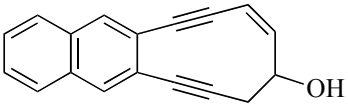

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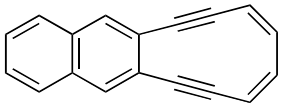

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Chapter 1. Introduction

Historically, aromatic compounds were classified as organic compounds with aroma. Vanilla and oil of wintergreen are representatives of this class of flavoring agents isolated from plants and containing chemical substances called aromatic because of their characteristic fragrances. The commonly seen model of aromatic rings, named benzene, was formed by a six membered carbon ring with alternating single and double bonds (cyclohexatriene), and was developed by Kekulé. The model of benzene consists of two resonance forms. (Figure 1-1)

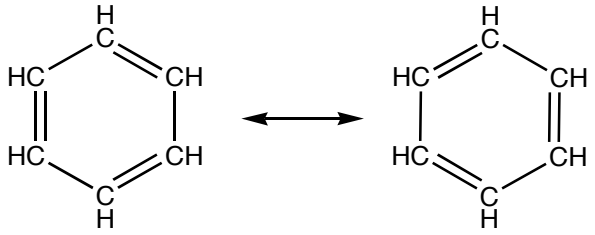


Figure 1-1. Kekulé benzene model

When the Kekulé theory was proposed, benzene and its derivatives were called aromatic compounds to distinguish them from saturated acyclic and cyclic hydrocarbons and simple unsaturated compounds. Still later, the term was refined to include compounds that do not have benzene ring but have chemical properties resembling those of benzene. Such compounds are said to have aromaticity.

In modern chemisty, aromatic molecules are a large class of organic compounds associated with a special chemical reactivity and increased chemical stability resulting from the delocalization of electrons in a ring system containing usually multiple conjugated double bonds, each bond within the ring being identical. Also, the meaning of the word aromaticity has evolved

as understanding of the special properties of benzene and other aromatic molecules has deepened[1].

1.1 History of "Aromaticity"

In the earlier stage of the history (before 1925), people identified aromatic compounds just by the smell. Later on, base on the experimental results, people knew that aromatic compounds have high carbon-hydrogen ratios and unexpected stability despite their considerable unsaturation.

In 1855, a German chemist, August Wilhelm von Hofmann, first used "aromatic" as a chemical term, namely to apply to compounds, isolated from coal tar and distinguished by odor much stronger than those of other classes of hydrocarbons.

The cyclohexatriene structure for benzene was first proposed by Friedrich August Kekulé von Stradonitz, as known as August Kekulé, in 1865, as one of the most prominent chemists in Europe in the 1850s. He suggested that the benzene structure contains a six member ring of carbon atoms with alternating single and double bonds. He was also the principal formulator of the theory of chemical structure. This theory developed from the idea of atomic valence, especially the tetravalence of carbon, the ability of carbon atoms to link to each other, and the determination of the bonding order of all of the atoms in a molecule.

In 1887 a British chemist, Henry Edward Armstrong became interested in classifying substituents of benzene in term of their *ortho*-, *meta*- and *para* directing influences in his study with aromatic compounds. Later, he had his first proposal of the centric formula for benzene (1890). This six affinities acting within a cycle predated both the discovery of the electron and modern theories of aromaticity. Here, Armstrong was describing at least four modern concepts.

First, his “affinity” is better known nowadays as the electron, which was only to be discovered seven years later by J. J. Thomson. Second, he was describing electrophilic aromatic substitution, proceeding (third) through a Wheland intermediate, in which (fourth) the conjugation of the ring was broken. He introduced the symbol “C” centered on the ring as shorthand for the inner cycle, thus anticipating Eric Clar’s notation. It is argued that he also anticipated the nature of wave mechanics, since he recognized that conjugation could be altered by introducing substituents onto the benzene ring (much as the distribution of the electric change in a body is altered by bringing it near to another body).

The quantum mechanical origins of this stability, or aromaticity, were first modeled by Erich Armand Arthur Joseph Hückel in 1931. He was also the first chemist to separate the bonding electrons into sigma and pi electrons. Hückel was a German physical chemist. He is known for two major contributions, first: the Debye-Hückel theory of electrolytic solutions. Second: the Hückel method of approximate molecular orbital (MO) calculations on π electron systems. Based on his analysis by formulating both valence bond (VB) and molecular orbital (MO) descriptions of benzene and other cycloconjugated hydrocarbons, he proposed the 4n+2 rule (known as *Hückel’s rule*) at 1931.

1.2 HMO Theory and Hückel’s Rule

Before computers enabled elaborate MO calculations to be performed routinely, it was essential that greatly simplifying approximations be applied to molecules of interest to organic chemists. Hückel molecular orbital (HMO) theory for treatment of conjugated systems was one of the most useful approximations. HMO theory is based on the assumption that the π system can be treated independently of the σ framework in conjugated planar molecules and that it is the π

system that is of paramount importance in determining the chemical and spectroscopic properties of conjugated polyenes and aromatic compounds. The basis for treating the σ and π systems as independent of each other is their orthogonality. The σ skeleton of a planar conjugated system lies in the nodal plane of the π system and does not interact with it.

In the HMO approximation, the π-electron wave function is expressed as a linear combination of the P_z atomic orbitals. Minimizing the total π-electron energy with respect to the coefficients leads to a series of equations from which the atomic coefficients can be extracted. The success of simple HMO theory in dealing with the relative stabilities of cyclic conjugated polyenes is impressive. Simple resonance arguments do not explain the unique stability of benzene as compared with elusive and unstable nature of cyclobutadiene. This contrast in stability is readily explained by Hückel's rule.

Hückel's rule estimates whether a planar ring molecule will have aromatic properties. Hückel first worked out the quantum mechanical basis for its formulation in 1931. The succinct expression as the 4n+2 rule as been attributed to von Doering (1951), although several authors were using this formulation at around the same time.

A cyclic ring molecule follows Hückel's rule when the number of its π-electrons equals 4n+2 where n is zero or any positive integer, although clearcut examples are really only established for values of n=0 up to about n=6. By this criterion, benzene, with six π electrons, is aromatic, whereas cyclobutadiene, with four, is not.

Hückel's rule was originally based on calculations by using Hückel's Molecular Orbital (HMO) theory; it can also be justified by considering a particle in a ring system, by the LCAO method and by the Pariser-Parr-Pople method.

For cyclic polyenes, the general solution for the energy level is

$E = \alpha + m_j\beta$

Where

$m_j = 2\cos(2j\pi/n)$ for $j = 0, \pm1, \pm2, \ldots, (\pm(n-1)/2$ for n odd; $\pm n/2$ for n even)

And n is the number of carbon atoms in the ring. Aromatic compounds are more stable than theoretically predicted by alkene hydrogenation data; the "extra" stability is due to the delocalized cloud of electrons, called delocalization energy (DE).

A useful mnemonic device for quickly setting down the HMOs for cyclic systems is *Frost's circle*[2]. If a regular polygon of n sides is inscribed in a circle of diameter 4β with one corner at the lowest point, the point at which the corners of the polygon touch the circle define the energy levels. The energy levels obtained for benzene and cyclobutadiene with Frost's circle are shown in Fig. 1-2.

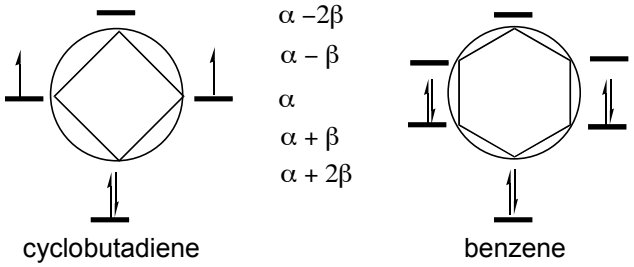


Figure 1-2. Energy level diagrams for cyclobutadiene and benzene, illustrating the application of Frost's circle.

The total π-electron energy of benzene is 6α + 8β, corresponding to a DE of 2β. Cyclobutadiene is predicted to have a triplet ground state (for a square geometry) and zero DE, since the total π-electron energy is 4α + 4β, the same as that for two independent double bonds. Thus, at this level of approximation, HMO theory predicts no stabilization for cyclobutadiene from delocalization and furthermore predicts that the molecule will have unpaired electrons,

which would lead to very high reactivity. In addition, cyclobutadiene would suffer angle stain, which is not present in benzene. The extreme instability of cyclobutadiene is then understandable. The dramatic difference in properties of cyclobutadiene and benzene is explicable. The pattern of two half-filled degenerate levels persists for larger rings containing 4n π electrons. In contrast, all 4n+2 π electrons' systems are predicted to have all electrons paired in bonding MOs with net stabilization relative to isolated double bonds. This pattern provides the theoretical basis of Hückel's rule.

Criteria for simple aromatics based on Hückel's rule are:

1. follow Hückel's rule, having 4n+2 electrons in the delocalized cloud;
2. be able to be planar and are cyclic;
3. every atom in the circle is able to participate in delocalizing the electrons by having a p-orbital or an unshared pair of electrons.

1.3 Types of aromatic compounds

Aromatic compounds need not only be hydrocarbons , but also can include heteroatoms. It can further be divided into 5 major types, they are annulenes; substituted aromatic compounds; heteocyclic rings; polycyclic aromatic hydrocarbons and charged ring systems with aromaticity.

1. Annulenes

   The term annulene was coined to refer to the completely conjugated monocyclic polyenes. The synthesis of annulenes has been extended well beyond the first two members of the series [4]annulene (cyclobutadiene) and [6]anulene (benzene). The next higher annulene, cyclooctatetraene, is nonaromatic. The bond lengths around the ring alternate as expected for a polyene. The C=C bonds are 1.33 Å while the C-C bonds are 1.462 Å in length[3].

Cyclooctatetraene is readily isolable, and its chemical reactivity is normal for a polyene. Structure determination shows that the molecule is tub-shaped[4] (Figure 1-3) and therefore is not a planar system to which the Hückel's rule applies.

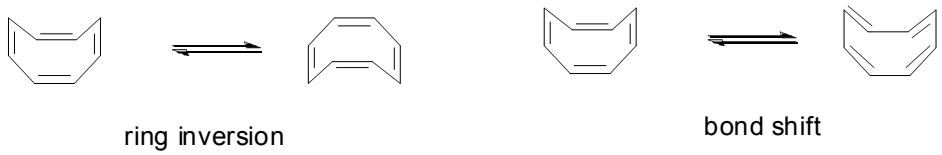
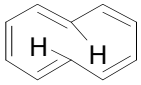


Figure 1-3. Tub-shaped structure of cyclooctatetraene.

Larger annulenes permit the incorporation of *trans* double bonds into to the rings. Beginning with [10]annulene, stereoisomeric structures are possible. According to Hückel's rule, [10]annulene should possess aromatic stabilization if it were planar. However, all the isomeric cyclodeca-1,3,5,7,9-pentaenes suffer serious steric and or angle strain that prevents the planar geometry. The Z,E,Z,Z,E-isomer, which has minimal bond-angle strain, suffers a severe nonbonded repulsion between the internal hydrogens (Figure 1-4).



Z,E,Z,Z,E-isomer

Figure 1-4. Z,E,Z,Z,E-isomer of [10]annulene.

The first three structures are shown in figure 1-5 are the other three different geometrical isomers. They are only stable below -40 ^{o}C. The Z,Z,Z,Z,Z-isomers (the second on the left) is required by geometry to have bond angles of 144°C to maintain planarity and would therefore be enormously destabilized by distortion of the normal trigonal bond angle. The most stable structure is a twisted form of the E,Z,Z,Z,Z-isomer (the third on the left).

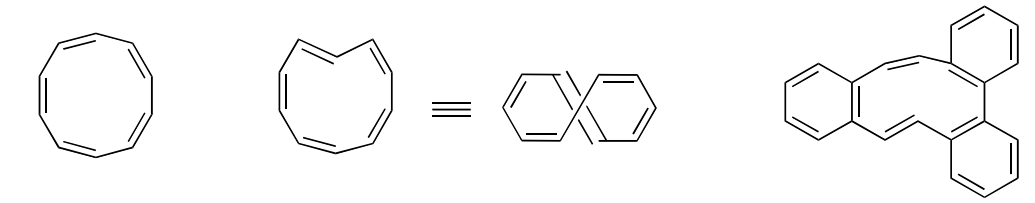


Figure 1-5. [10]annulenes

A number of structures have been prepared that do not have the steric problems associated with [10]annulene. For instance, if we add three benzenes on the [10]annulene (the first on the right), to give tribenz[10]annulene. This compound has a melting point at 121-122^{o}C[5]. Another way to avoid a steric problem is to add a bridge between C1 and C6. The compound showed in figure 1-6 avoids the H1 and H6 repulsion with only a slight loss of planarity in the π sytem[6]. More details will be discussed in chapter 2.

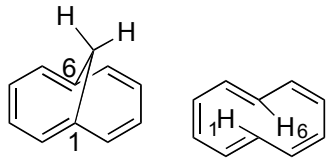


Figure 1-6. Bridged [10]annulene and ZEZZE [10]annulene

2. Substituted aromatic compounds (figure 1-7)

   Substituted aromatic compounds, such as trinitrotoluene (TNT), anisole, and acetaminophen (figure 1-7), refer to a vast series of functional group-substituted derivatives of their parent aromatic ring systems. They have wide applications in the world, some can be a material to make bombs (TNT); and some can be a medicine (acetaminophen).

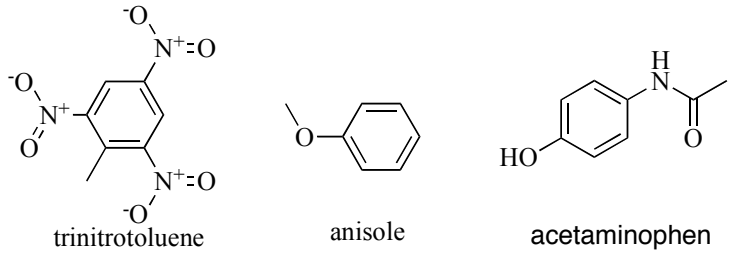


Figure 1-7. Examples of substituted aromatic compounds.

3. Heterocyclic rings (figure 1-8)

Certain structural units containing heteroatoms can be substituted into conjugated systems in such a way that the system remains conjugated and isoelectronic with the original hydrocarbon. It forms a heterocyclic ring. The most common examples are –CH=N- and –N=N- double bonds and divalent sp^2 –O-, -S- and –NR- units (Figure. 1-3). Each of these structural fragments can replace a –CH=CH- unit in a conjugated system and contribute two π electrons[7]. These compounds are also called heteroaromatic to recognize both the heterocyclic structure and the relationship to benzene and other aromatic structures. The heteroatom can increase the reactivity of heterocyclic aromatic compound.

Additional heteroaromatic structures can be built up by fusing benzene rings to the aromatic heterocyclic rings or by fusing together heterocyclic rings.

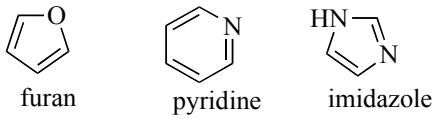


Figure 1-8. Heterocyclic compounds with aromaticity.

4. Polycyclic aromatic hydrocarbons (figure 1-9)

Many completely conjugated hydrocarbons can be built up from the annulenes and related structural fragments. Polycyclic aromatic hydrocarbons (PAHs) (like: naphthalene, and anthracene, etc...) are chemical compounds that consist of fused aromatic rings and do not contain heteroatoms or carry substituents. PAHs occur in oil, coal, and tar deposits, and are produced as byproducts of fuel burning (whether fossil fuel or biomass). As a pollutant, they are of concern because some compounds have been identified as carcinogenic, mutagenic, and teratogenic. PAHs are also found in foods. Studies have shown that most food intake of PAHs comes from cereals, oils and fats. Smaller intakes come from vegetables and cooked meats.

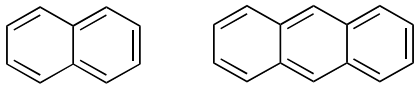


Figure 1-9. Structures of some polycyclic aromatic hydrocarbons.

5. Charged ring systems with aromaticity

There are also striking stability relationships due to aromaticity in charged ring systems. Two examples of cations and anions that have completely conjugated planar structures are shown in figure 1-10. Cation and anion aromatic compounds (like: cyclopentadienyl anion, and tropylium ion, etc…) are used to coordinate to metal atoms as a ligand to form an organometallic complex.

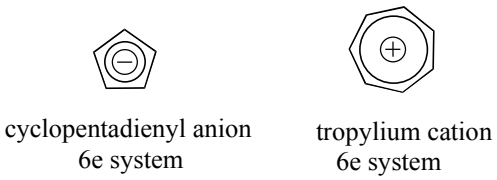


Figure 1-10. Examples of the charged ring systems with aromaticity.

1.4 Characteristics of aromatic compounds and evidence of aromaticity

Even though chemists are still arguing about what aromaticity means, the most commonly agreed-upon definition for an aromatic compound is that it contains a set of covalently bound atoms with specific characteristics:

1. A delocalized conjugated π system, most commonly an arrangement of alternating single and double bonds.
2. Coplanar structure, with all the contributing atoms in the same plane.
3. Contributing atoms arranged in one or more rings.
4. A number of π delocalized electrons that are even, but not a multiple of 4. That is, 4n+2 number of π electrons, where n=0, 1, 2, 3, and so on. This is known as Hückel's Rule.

As stated earlier, many of the earliest known examples of aromatic compounds, such as toluene, have distinctive pleasant smells. This property led to the term "aromatic" for this class of compounds, and hence the term "aromaticity" for the eventually discovered electronic properties.

Aromatic molecules typically display enhanced chemical stability, compared to similar non-aromatic molecules. A molecule that can be aromatic will tend to alter its electronic or conformational structure to be in this situation. This extra stability changes the chemistry of the molecule. Aromatic compounds undergo electrophilic aromatic substitution and nuleophilic aromatic substitution reactions.

As we mentioned in section 1.2, aromaticity is usually described in MO terminology, which is simplified as Hückel's rule. There is also other criteria that can give evidence of aromaticity.

One of them is a relatively large HOMO-LUMO gap, which can be expressed in terms of hardness, η[8].

$$\eta = (\varepsilon_{LUMO} - \varepsilon_{HOMO})/2$$

The numerical value of hardness obtained by MNDO-level calculations correlates with the stability of aromatic compounds[9]. The correlation can be extended to a wider range of compounds, including heterocyclic compounds, when hardness is determined experimentally on the basis of molar refractivity[10]. The relatively large HOMO-LUMO gap also indicates the absence of relatively high-energy, reactive electrons, in agreement with the reduced activity of aromatic compounds toward electrophilic reagents.

Besides MO characteristics, there are some physical measurements that can give evidence of aromaticity. The determination of the bond lengths in benzene by electron diffraction is a classic example of use of the bond length criterion of aromaticity. Spectroscopic methods of X-ray diffraction can also provide bond-length data.

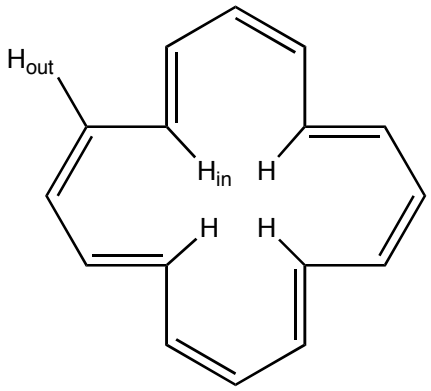
NMR spectroscopy also provides an experimental tool capable of assessing aromaticity. Aromatic compounds exhibit a diamagnetic ring current. Qualitatively, this ring current can be viewed as the migration of the delocalized electrons in the π system under the influence of the applied magnetic field in NMR spectrometer. The NMR signals of a proton in the plane of an aromatic ring are shifted substantially further down field than those on non-aromatic sp^2 carbons. This is an important way to detect aromaticity. By the same mechanism, the signals of protons located near the ring axis are shifted up field.

Another property associated with aromaticity is magnetic susceptibility. Magnetic susceptibility is determined by measuring the force exerted on the sample by a magnetic field[11]. It is noted that aromatic compounds have enhanced magnetic susceptibility, relative to values

predicted on the basis of the localized structural components[12]. Magnetic susceptibility can also be determined by using an NMR spectrometer. Because of the easy accessibility of NMR spectrometers, NMR data is one of the most important tools to determine aromaticity of large annulene systems (π electrons > 6). We will discuss this approach in more detail in chapter 2.

The most valuable characterization of Hückel (4n+2) π as aromatic and (4n) π as antiaromatic are based on the ring current model. The ring current model was first proposed by Pauling[13] et al. and later accurately calculated by Pople[14] et al. Without any exception, the chemical shift of the criteria as well as their hydrocarbon and heterocyclic systems are stay in their aromatic or antiaromatic range. More recent calculation methods by Kutzelnigg[15] and subsequently by Schleyer[16] indicated the significance of so call "local effects" on the chemical shift in smaller Huckel (4n+2) and (4n) systems by use of an individual gauge for the localized orbitals (IGLO) to calculate the π system, including C-H (σ) C-C (σ) and C-C (π) contributions. The calculation result led to the conclusion[16] that the ring current didn't affect the proton shielding or deshielding in smaller ring systems (like: Butadiene, Benzene, Naphthalene and Anthracene). However, the ring current model more satisfactorily explained the observed chemical shift in large ring systems as well as cation and anion ring systems. There are some examples shown in figure 1-11 to figure 1-14.

Shown below (Figure 1-11 & 1-12), for the [18]annulene[17] (4n+2)π and [16]annulene[18] (4n)π system, where both rings are very similar in size. The 4nπ system ([16]annulene) proton inside the ring is deshielded and outside the ring is shielded. The 4n+2π system ([18]annulene) has its protons inside the ring shielded and outside the ring deshielded as predicteded by ring current model.



^{1}H NMR at 35^{o}C
(S) δ 6.73ppm 16H

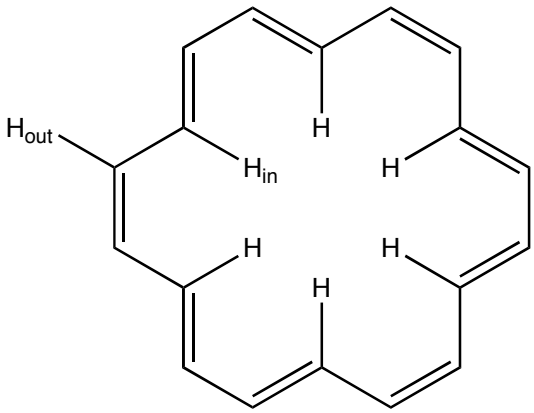
^{1}H NMR at -120^{o}C
(m) δ 10.43 4H
(m) δ 5.40 12H

[16]Annulene

Figure 1-11. The [16]Annulene

^{1}H NMR at 120^{o}C
(S) δ 5.45ppm 18H

^{1}H NMR at -60^{o}C
(m) δ 9.25ppm 12H
(m) δ -2.9ppm 6H



[18]Annulene

Figure 1-12. The [18]annulene

Compare the bridged [10]annulene and [12]annulene in the figure 1-13. The protons on the bridge are shielded (δ = -0.5ppm) in [10]annulene, and deshielded (δ = 6.06ppm) in [12]annulene. The peripheral protons are deshielded (δ = 6.9 – 7.5ppm) in [10]annulene, and shielded (δ = 5.1 – 5.5ppm) in [12]annulene.

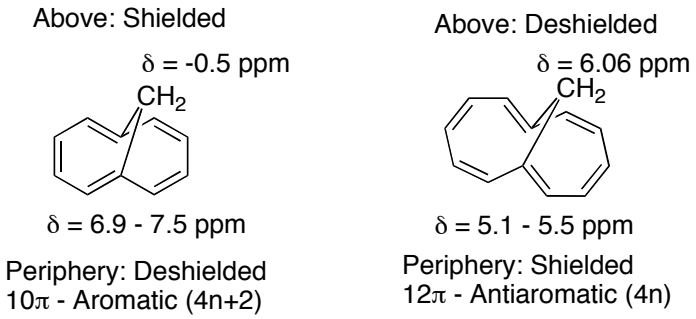


Figure 1-13. Bridge [10] and [12]annulene

Not only the neutral bridged annulenes, but also the bridged cation and anion annulenes show the ring current. The figure 1-14 shows that the bridged benzo-10π-cation and 12π-anion have the same behavior as the bridged 10π and 12π system.

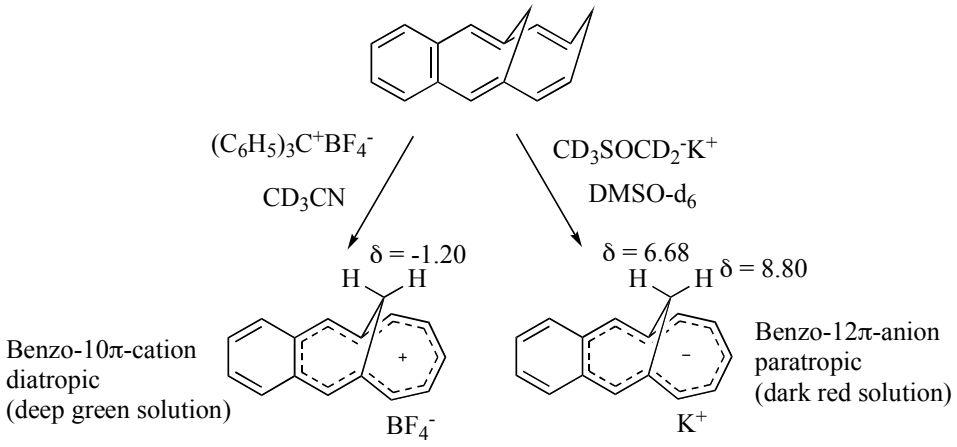


Figure 1-14. The bridge benzo-10π-cation and benzo-12π-anion

1.5 Toxicity of Aromatic Compounds

Polycyclic aromatic hydrocarbons' (PAHs) toxicity is very structurally dependent, with isomers (PAHs having the same formula and number of rings) varying from being nontoxic to being extremely toxic. Thus, highly carcinogenic PAHs may be small or large. One PAH compound, benzo[a]pyrene, is notable for being the first chemical carcinogen to be discovered (and is one of many carcinogens found in cigarette smoke). The Environmental Protection

Agency (EPA) has classified several PAH compounds as potent human carcinogens: benz[a]anthracene, benzo[b]fluroanthene, and indeno[1,2,3-cd]pyrene.

1.6 Reactions of aromatic compounds

Electrophilic Aromatic Substitution

With an understanding of the properties that make a compound aromatic, we now consider the reaction of aromatic compounds. Like an alkene, benzene has pi electron density above and below its sigma bond framework. Although benzene's pi electrons are in a stable aromatic system, they are available to attack a strong electrophile to give a carbocation, this ability devoted to the 1st type of reaction of aromatic compounds, electrophilic aromatic substitution. Figure 1-11 shows that sigma complex loses a proton to a base to regenerate the aromatic ring. The overall reaction is the substitution of an electrophile (E^+) for a proton (H^+) on the aromatic ring. The typical EAS include halogenation of figure 1-15 benzene and nitration of benzene. An aromatic system's pi electrons attack a strong electrophile to give a carbocation. This resonance stabilized carbocation is called a sigma complex because the electrophile is joined to the aromatic system by a new sigma bound.

The sigma complex (also called an arenium ion) is not aromatic because the sp^3 hybrid carbon atom interrupts the requisite closed loop of p orbitals. This loss of aromaticity contributes to the highly endothermic nature of this first step. The sigma complex regains aromaticity either by a reversal of the first step returning to the reactants or by loss of the proton on the tetrahedral carbon atom, leading to the substitution product.

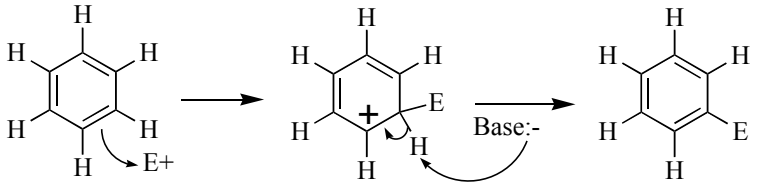


Figure 1-15. Mechanism for electrophilic aromatic substitution.

Many other substitution reactions of benzene have been observed; the five most useful are listing below. Since the reagents and conditions employed in these reactions are electrophilic, these reactions are commonly referred to as Electrophilic Aromatic Substitution.

Reaction Type	Typical Equation	Electrophile $E^{(+)}$
Halogenation	$C_6H_6 + Cl_2$ & Heat → $C_6H_5Cl + HCl$ $FeCl_3$ Catalyst Chlorobenzene	$Cl^{(+)}$
Nitration	$C_6H_6 + HNO_3$ & Heat → $C_6H_5NO_2 + H_2O$ H_2SO_4 catalyst Nitrobenzene	$NO_2^{(+)}$
Sulfonation	$C_6H_6 + H_2SO_4 + SO_3$ → $C_6H_5SO_3H + H_2O$ & Heat Benzenesulfonic acid	$SO_3H^{(+)}$
Alkylation: Friedel-Crafts	C_6H_6 + R-Cl & Heat → C_6H_5-R + HCl $AlCl_3$ catalyst An Arene	$R^{(+)}$
Acylation: Friedel-Crafts	C_6H_6 + RCOCl & Hheat → C_6H_5COR +HCl $AlCl_3$ catalyst An Aryl Ketone	$RCO^{(+)}$

Table 1-1. Commonly used Electrophilic Aromatic Substitution.

Nucleophilic aromatic substitution

A nucleophilic aromatic substitution is a substitution reaction in organic chemistry in which the nucleophile displaces a good leaving group, such as a halide on an aromatic ring. There are 6 nucleophilic substitution mechanisms with aromatic systems, which have been proposed and investigated[19]:

1. the S_NAr (addition-elimination) mechanism;
2. the aromatic S_N1 mechanism encountered with diazonium salts;
3. the benzyne mechanism;
4. the free radical SR_N1 mechanism;
5. the ANRORC (Addition of the Nucleophile, Ring Opening, and Ring Closure in nucleophilic attack on aromatic ring systems) mechanism;
6. vicarious nucleophilic substitution.

The most important of these is the S_NAr mechanism, where electron-withdrawing groups activate the ring towards nucleophilic attack, followed by departure of the leaving group. The general mechanism is shown in figure 1-16.

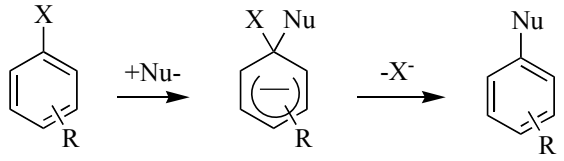


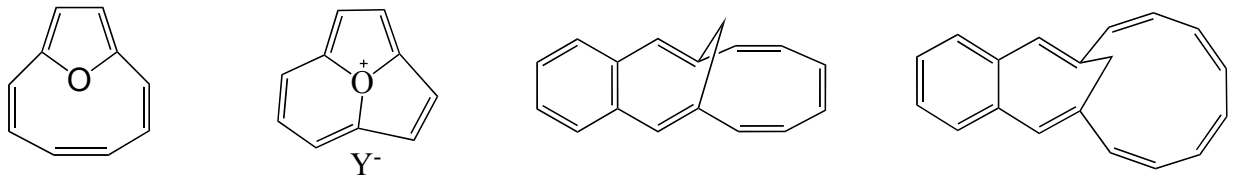
Figure 1-16. S_NAr mechanism for nucleophilic aromatic substitution.

In conclusion, annulene chemistry has attracted chemists' interest for more than 150 years, the field mature in the late 1980s. However, in the last decade of the 20th century, a number of synthetic discoveries, most notably ring-closing olefin metathesis and Pd-mediated cross-coupling reaction between sp- and sp^2- carbon centers, gave a "rebirth" of sorts to annulene chemistry. These synthetic methodologies made the previously laborious task of macro-annulene assembly now a quick and efficient process. In the next two chapters, I will discuss novel approaches and efforts to [12]annulene and [10]annulene via those methodologies respectively.

Chapter 2. The RCM approach toward selected bridged [10], [12]&[14] annulenes

2.1 Introduction

The characterization of [10]annulene (Hückel aromatic) and [12]annulene (Hückel antiaromatic) concentrated nearly exclusively on bridged derivatives due to facile low activation energy transannular cyclizations observed for the parent systems. Only limited structural data are known for these annulenes. Benzannulation is known to thermodynamically stabilize the [10] or [12]annulene ring, with the price of certain loss of the predicted aromaticity or antiaromaticity. In order to obtain accurate structural and spectral parameters, the first part of my project concentrates on the synthesis and investigation of the 10π, 12π and 14π systems. The key step in our general synthetic approach is the Ring Closing Olefin Metathesis (RCM), develop from earlier investigations in our group [20,21].



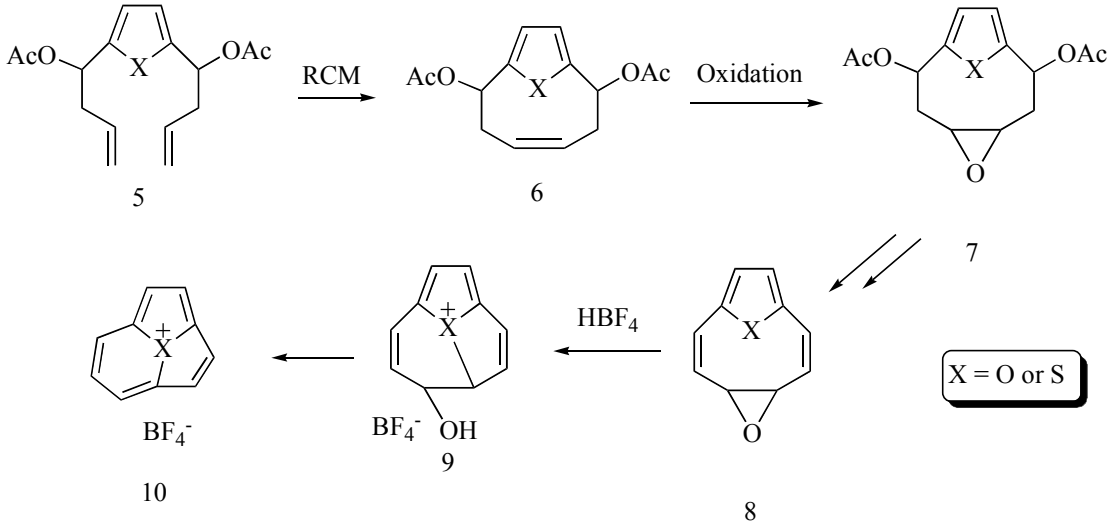
(X,X^+ = O or S) (Y^- = BF_4^- or ClO_4^-) 3 4

1 2

Figure 2-1. The target compounds

Compound (1) represents a 1,4 bridged [10]annulene (oxygen or sulfur) while compound (2), corresponds to the oxygen/sulfur cationic analogues of the known [3,2,2]cyclazines[22]. Compounds (3) and (4) are monobenz-annulated 1,6-methano [12] and [14]annulenes. We are interested in these compounds as to whether the non-benzenoid rings are planar and the degree of aromaticity or antiaromaticity they demonstrate.

From the X-ray result obtained from 3,4-benzo-1,6-methano[12]annulene (3) show that the molecule has a nearly planar structure. Its ^{1}H-NMR-data indicate a benz-annulated nearly planar 12π-system with the protons above the ring deshielded and the peripheral protons shielded. The methodology developed for the synthesis of 12π compound is extended to the synthesis of the 3,4-Benzo-1,6-methano[14]annulene (4) as outlined at scheme 2-6 page 35. The latest modification of this methodology for (3) & (4) represents a novel approach to a number of bridged or non-bridged annulenes currently under investigation in our group. One proposed route is shown below, the RCM of the readily available diacetate (5) is expected to give the strained meta-cyclophane (6). Oxidation of (6) is expected to give the epoxide (7), which is predicted to undergo a rapid transannular electrocyclization giving 11-substituted phenalenes (10), by using tetrafluoroboric acid via compound (9) long-sought after systems with a very rigid planar 10π-perimeter. (Scheme 2-1)



Scheme 2-1. The outline of our 10π strategy

2.2 Ring-Closing Metathesis

Ring-closing metathesis (RCM) of dienes is one of the most important methodologies now in use for the assembly of cyclic organic compounds. RCM represents a key step in many synthetic sequences: recent reviews describe its use in, inter alia, construction of synthetically valuable building blocks such as heterocyclic rings containing phosphorus, sulfur, oxygen or nitrogen including aromatic heterocycles, spirocyclic, cyclopane and polycyclic compounds[23]. While the common rings of 5-7 members have historically been dominant, owing in part to their greater ease of access, important advances have been made in the synthesis of medium and macrocyclic targets[24].

As with any other cyclization method, the synthetic efficiency of RCM is limited by the competition between intramolecular ring-closing and intermolecular oligomerization reactions. In the standard depiction (Figure 2-2), olefin metathesis is represented as a fully reversible set of [2+2] cycloaddition-cycloreversion equilibria, implying a thermodynamic distribution of "living" metathesis products[25]. The extent of reversibility in the various reaction manifolds in fact varies considerably, depending on the nature of the substrate and the extruded olefin, at the competence of the catalyst and the experimental conditions.

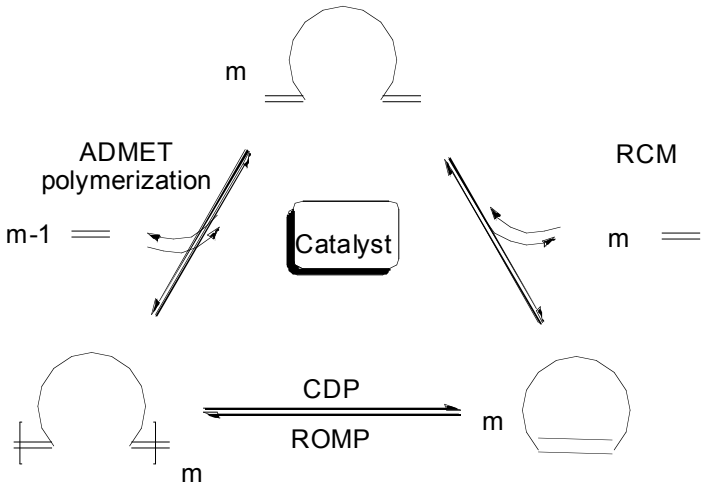


Figure 2-2. The competition of olefin metathesis and polymerization: ADMET = acyclic diene metathesis, RCM = ring-closing metathesis, ROMP = ring-opening metathesis polymerization, CDP = cyclodepolymerization.

In many cases, it will be seen that the diene RCM and oligomerization reactions are irreversible. Where the RCM and oligomeric products are not able to interconvert, these competing pathways are terminal, and a kinetic product distribution results. Under these circumstances, it is crucial to limit oligomerization yields are to be maximized. However, more and more cases are not terminal, because catalyst reactivity and lifetime suffice to enable sustained reaction at internal olefinic sites. A ring-chain equilibrium can then be established, involving cyclodepolymerization (CDP) of oligomers or polymers, or oligomerization of the intended RCM product. The development of relatively robust, highly active second generation **Ru-NHC** catalysts (NHC = *N*-heterocyclic carbene), has been a milestone in expanding the scope of RCM methodologies to previously intractable substrates, it led to fundamental changes arising from a greater tendency toward equilibrium processes. Thermodynamic control is

particularly relevant in the RCM synthesis of many medium-sized or macrocyclic targets *via* these catalysts[26].

2.2.1 Ring-Chain Equilibrium in RCM

In ROMP application, polymerization is typically driven by release of ring strain. Initiation of highly strained monomers is irreversible, though backbiting to form cyclic oligomers can occur. In RCM, no such enthalpic driver exists, barring strategies in which two reactions are coupled (e.g. ROM-RCM processes). RCM is thus entropy-driven, and the enthalpic costs that can be sustained are limited by the extent to which (in Gibbs-Helmholtz terms) the TΔS term can be maximized. The entropic benefit associated with release and volatilization of ethylene on metathesis of vinylic dienes is powerful but indiscriminate, driving both inter- and intramolecular reaction. Here we consider the thermodynamic role of substrate in controlling selectivity for cyclic *vs.* acyclic products and where the ring-chain equilibrium is accessible, how selectivity can be modulated[27].

2.2.2 Factors to Shift the Equilibrium in RCM (ERCM)

A fundamental difference between ROMP and most of RCM reactions lies in the nature of the catalyst resting state[27]. So the catalysts properties play a crucial role in ERCM reaction. When evidence for oligomerization is observed during intended ERCM reaction, the equilibrium in RCM can often be improved through the simple expedients of dilution, increasing reaction time or temperature. More details are discussed with selected examples.

Catalysts Properties and Catalysts Deactivation

As we mentioned previously, there is significant difference in performance of first- and second-generation **Ru** Catalysts. This demonstrates that the mechanistic pathway to RCM products can be controlled through choice of catalyst. The representatives of first and second-generation **Ru** catalysts are showing in figure 2-3. Other evidence suggests the possibility of influencing the position of the equilibrium.

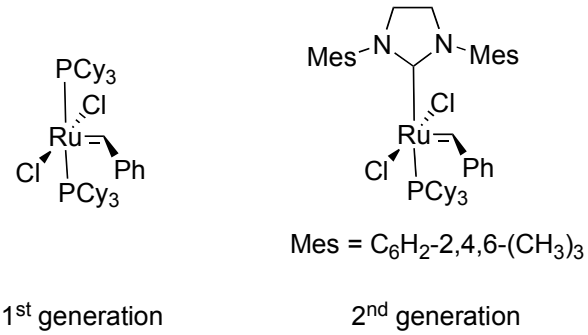


Figure 2-3. The representatives of first and second-generation **Ru** catalysts.

Besides the original properties of catalysts, another common feature to influencing the equilibrium in RCM reaction is catalyst deactivation: deactivation of the catalyst after complete consumption of substrate, but prior to equilibration, can result in isolation of polymeric material even if the reaction is carried out at appropriately high dilution (the influence of concentration on the equilibrium of RCM will be discussed in next section). Furthermore, the needs for high dilution cost a price in terms of reaction rates and productivity. First, the necessarily bimolecular reaction between substrate and catalyst means that rate of metathesis will decline as concentration decrease. Therefore, high temperature or long reaction time is required. Furthermore, the deleterious effect of adventitious contaminants becomes much more significant as catalyst concentration declines. The higher relative concentration of catalyst-noxious components, including “trace” air and water, is a particular risk for oxophilic, hydrolytically

sensitive catalysts based on the early and midtransition metals. Comparing with **W**- or **Mo**-catalysts, the Grubbs-class **Ru** metathesis catalysts are more robust and less sensitive to oxygen or water. However, they are still susceptible to deactivation through formation of stable chelate rings, particularly rings of five or six members[28]. Instances of sensitivity to alcohol or amine functionalities have also reported[29]. More details will be discussed in the discussion section 2.3.

Concentration

Concentration is one of the key experimental factors affecting ring-chain equilibrium in olefin metathesis[30] and one of the major tools available to manipulate product distribution in equilibrium of RCM. The lower concentration, the more intramolecular reaction is preferred than intermolecular reaction, which will lead to more RCM product is formed than polymerization product. The standard range of 0.2-8.5 mM was reported by Gradillas and Perez-Castells in a recent review of RCM macrocyclization[31]. As we mentioned previously, the high dilution comes at a cost. Besides the catalysts deactivation, it is not a viable solution to the challenges of ERCM from the industrial perspective. High costs of the large volumes of solvent is required, and further costs are associated with waste disposal, longer reaction time and the problems of product purification that commonly result from high catalyst loadings.

It is also worthy to mention that Danishefsky and co-workers examined use of Zieger "infinite dilution" methodologies[32] in RCM *via* **Ru**-catalyst[33]. Drop wise addition of diene over a 7-h period, to a solution of the catalyst in refluxing benzene had no effect on the yield of desired RCM product, relative to reactions in which all of the diene was added at the outset.

Reaction time

As we mentioned in previous two sections, when the high dilution is required, to maximize yields of ERCM reactions, sufficient time must be allowed for the CDP process to occur (presupposing operation in the appropriate concentration regime).

Temperature

Danishefsky and co-workers have commented on the potential to control product distribution in RCM macrocyclization reactions by increasing reaction temperature[33]. The proportions of the desired product vs the corresponding cyclic dimer were found to increase from ca. 1:2 at 40 ℃, to 1:1 at 80℃, at a constant dilution of 0.5 mM corresponding diene in benzene or toluene, respectively.

A similar effect was described by Grubbs and co-workers[29] during the synthesis of 14-membered macrolactone. They observed that dimerization competed with RCM at room temperature at diene concentrations as low as 3 mM. However, the desired RCM products was isolated in >75% yield in refluxing CH_2Cl_2. All these suggested that a higher reaction temperature favors intramolecular reaction products instead of undesired intermolecular products.

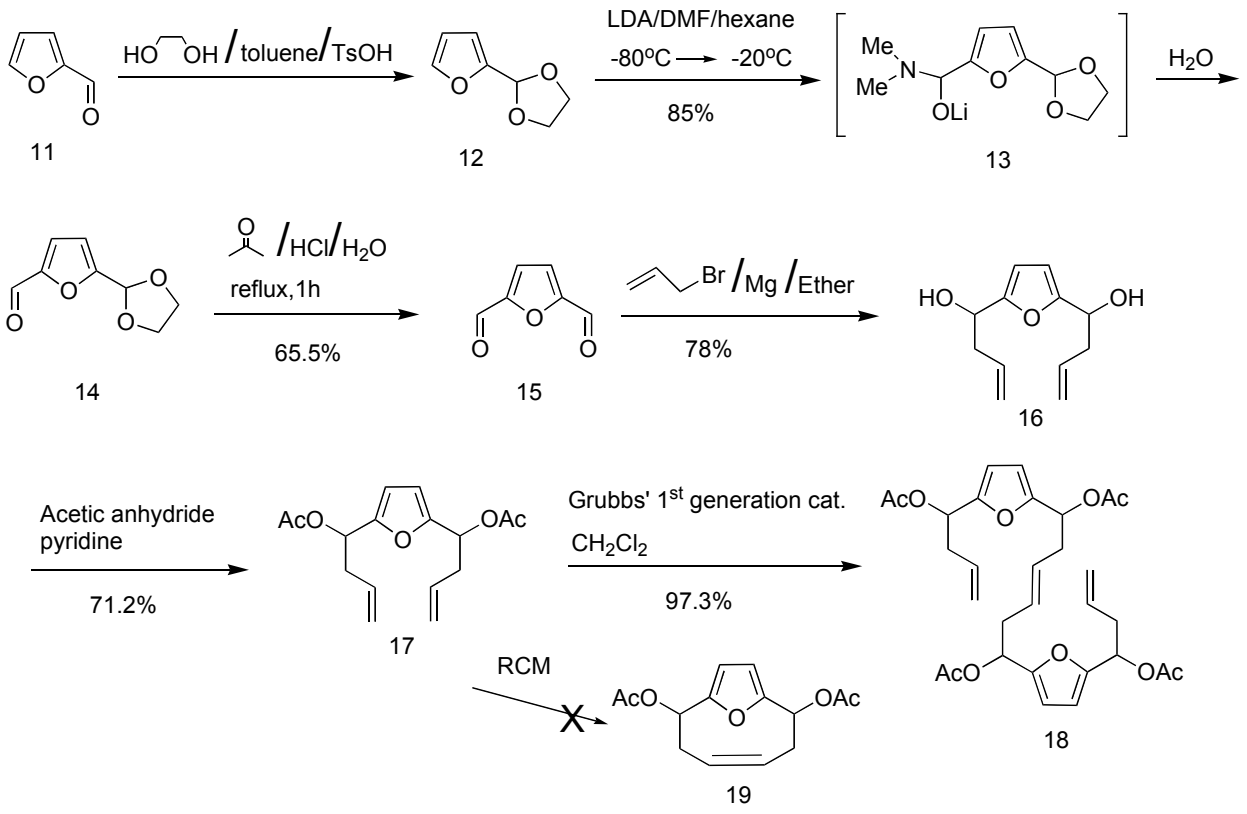
Further efforts to perturbing the equilibrium include addition of a more reactive catalyst, use of template agents and use of Lewis acid to reducing conformational motion. These topics are out of my research focus and will not be discussed in detail.

2.3 Synthesis of [10], [12], and [14]annulene

2.3.1 Synthesis of Ia, 2,5oxido[10]annulene

Furan-2,5-dicarboxaldehyde (15) was prepared in three steps from furfural according to the procedure reported by Feringa[34] (Scheme 2-2). The overall yield was around 50%. Furan-2,5-

dicarboxaldehyde (15) reacted with an excess of allylmagnesium bromide gave diol (16). The diol was converted into acetate (17) by using standard esterification procedures described in the experimental section of esterification. Compound (17) was treated with Grubbs' 1st generation catalyst to achieve the Ring Closing Olefin Metathesis (RCM). However, the ^{1}H-NMR spectrum of the RCM product, isolated in 97% yield, indicated that the structure was not the expected ring closed compound (19), but suggested the dimeric structure (18) cis or trans instead. Apparently the RCM reaction to the highly strained alkene (19) is thermodynamically unfavored therefore dimer (18) is observed. As we discussed in section 2.2 RCM reaction is very sensitive to catalyst activity. The catalyst also can be deactivated by forming a 5 or 6 membered ring chelation complex. The oxygen in furan has two lone-pairs of electrons, one pair of which can chelate with a **Ru** empty *d* orbital of the ruthenium to form a 6-membered ring (see page 35 Figure 2-8). It is also very sensitive to the reaction concentration. In order to avoid the formation of the intermolecular dimer, a lower reaction concentration and higher catalyst loading may be required to shift the equilibrium from polymerization to cyclization. Further investigation will be done to test this hypothesis.

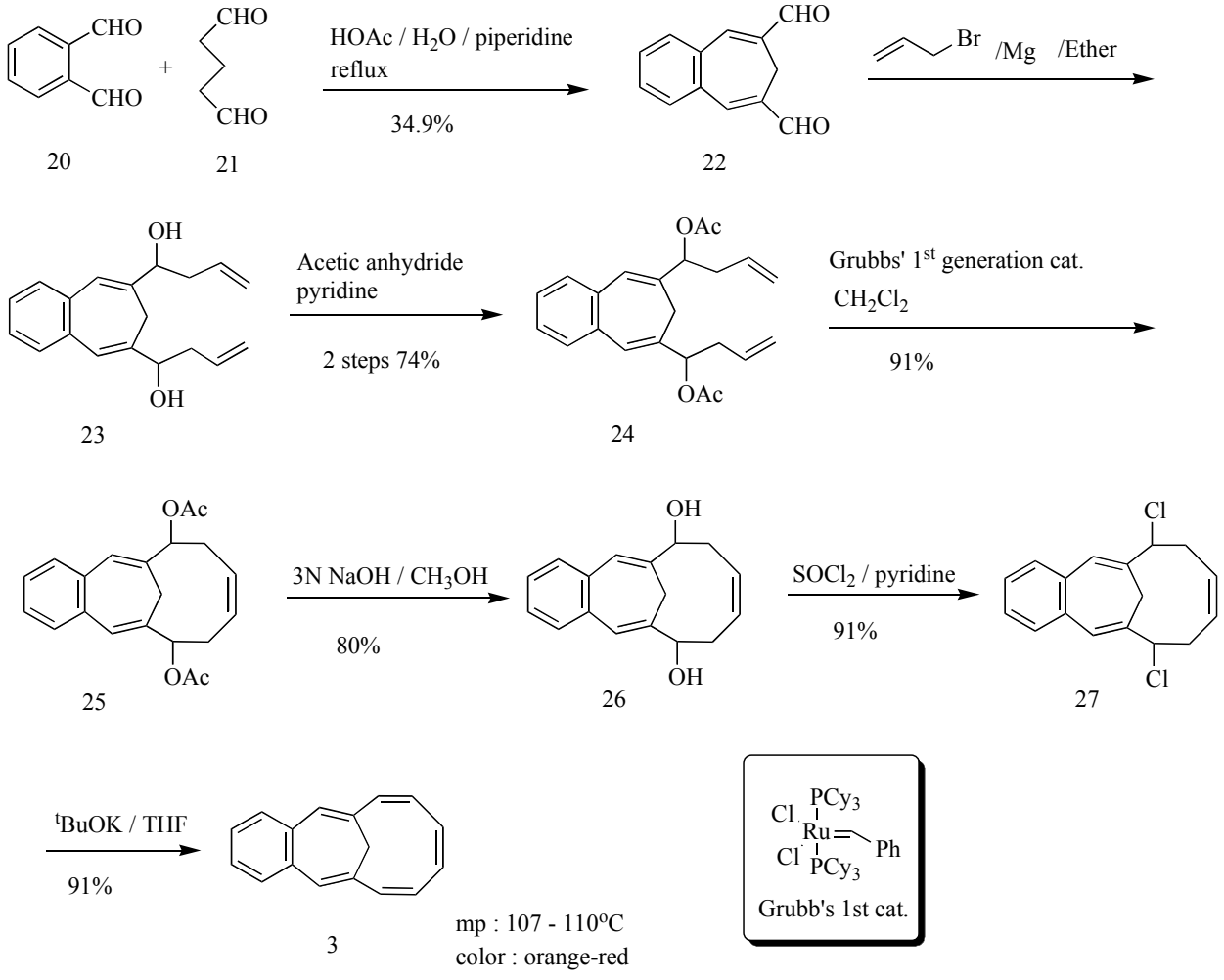


Scheme 2-2. Hetero[10]annulene approach

2.3.2 12π System: 3,4-Benzo-1,6-methano[12]annulene

Earlier work in our group (Ronnie Benshafrut and Shu-Ya Hsu) had successfully synthesized dialdehyde (22) by an Aldol condensation of *o*-phthaldehyde and glutaraldehyde (Scheme 2-3). Grignard reaction of dialdehyde (22) with allylmagnesium bromide gave diol (23), as a mixture of stereoisomers. The diol was converted into the acetate (24) by using standard procedures of esterification. Compound (24) was treated with Grubbs' 1st generation catalyst undergoing RCM to afford the ring closed diacetate (25) with 91% yield, the failure of RCM to afford 1,4-oxa[10]annulene compound (1), using the similar conditions that succeed for compound ring closed diacetate (25) provide strong evidence of the deactivating chelation possibility in the presence of **O** in the ring system of (17). The subsequent hydrolysis of the acetates gave diol

(26). Conversion of the diol into the dichloride (27), and subsequent treatment of the crude dichloride with t-BuOK in THF for four hours at reflux, followed by chromatography and recrystallization from hexane yielded orange-red crystals of (3), mp: 107-110, 91% yield, overall 44%yield from Ronnie's aldehyde (22). The ^{1}H NMR shown below has the bridge proton very deshielded as predicted for a paratropic 12π system. The room temperature ^{13}C NMR indicated the symmetry of the molecule, and also remains unchanged when repeated at in lower temperature (-60^{o}C). This suggests that the material exists as a single conformer and that the larger ring is not flipping.



Scheme 2-3. Synthesis of benz[12]annulene

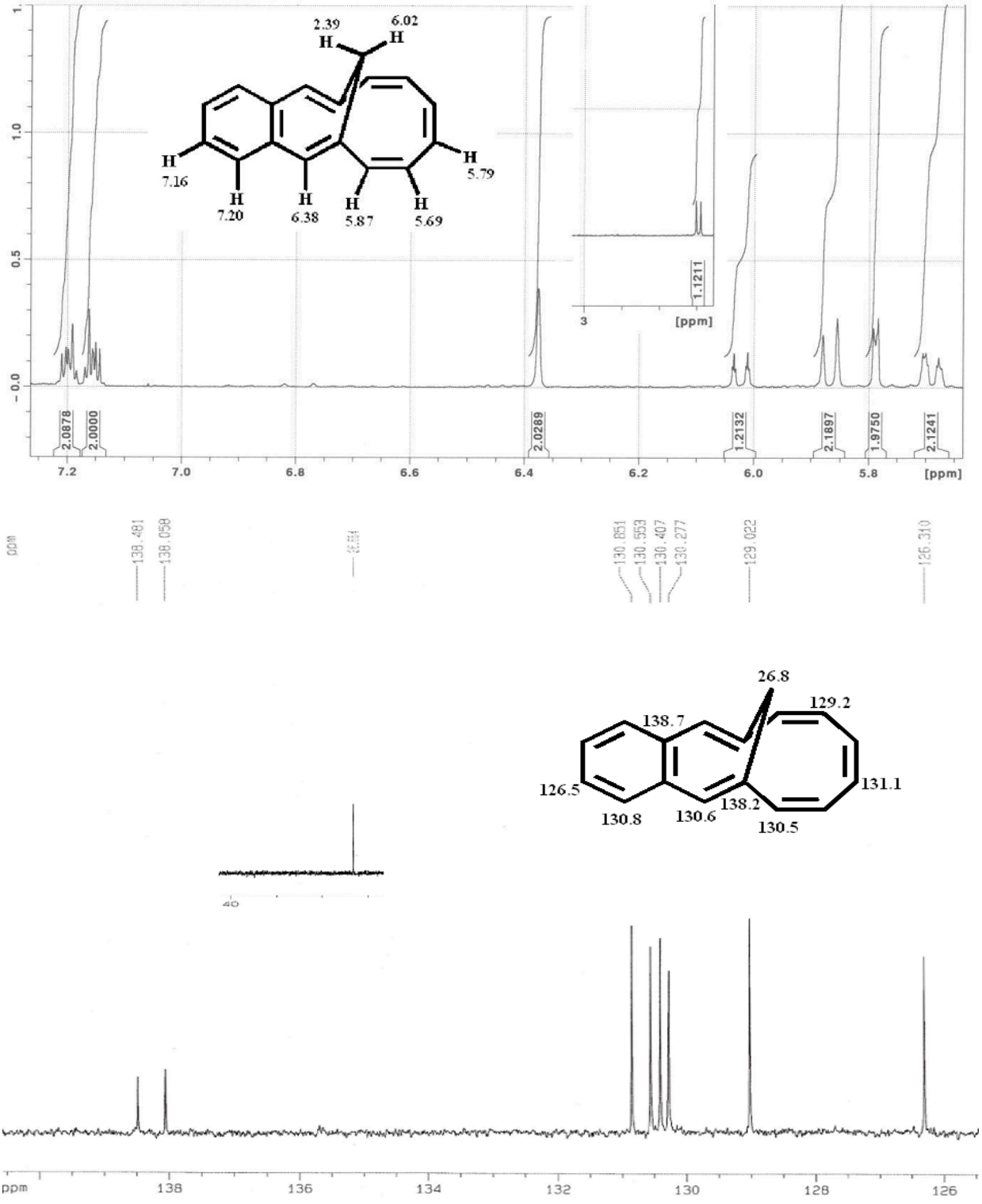


Figure 2-4. ^{1}H and ^{13}C NMR spectrum of the benz-bridge[12]annulene compound (3)

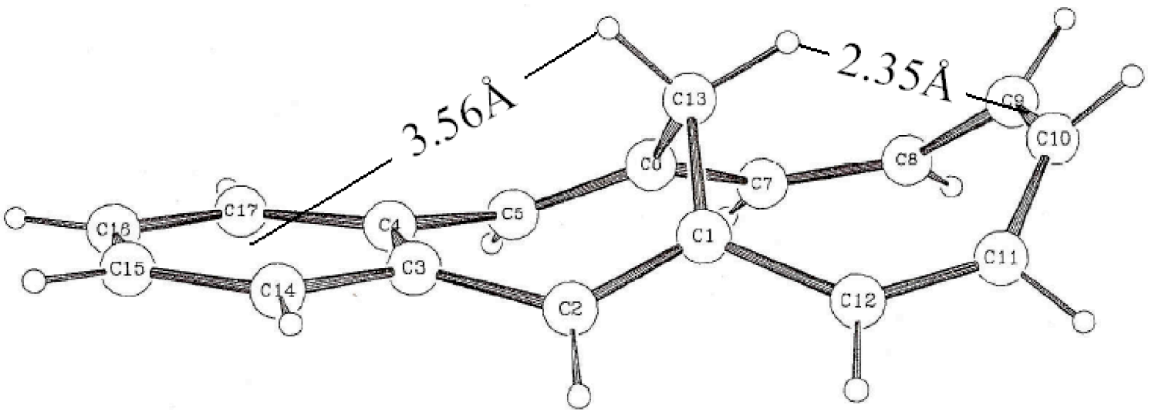


Figure 2-5. X-ray structure of benz-bridge[12]annulene compound (3)

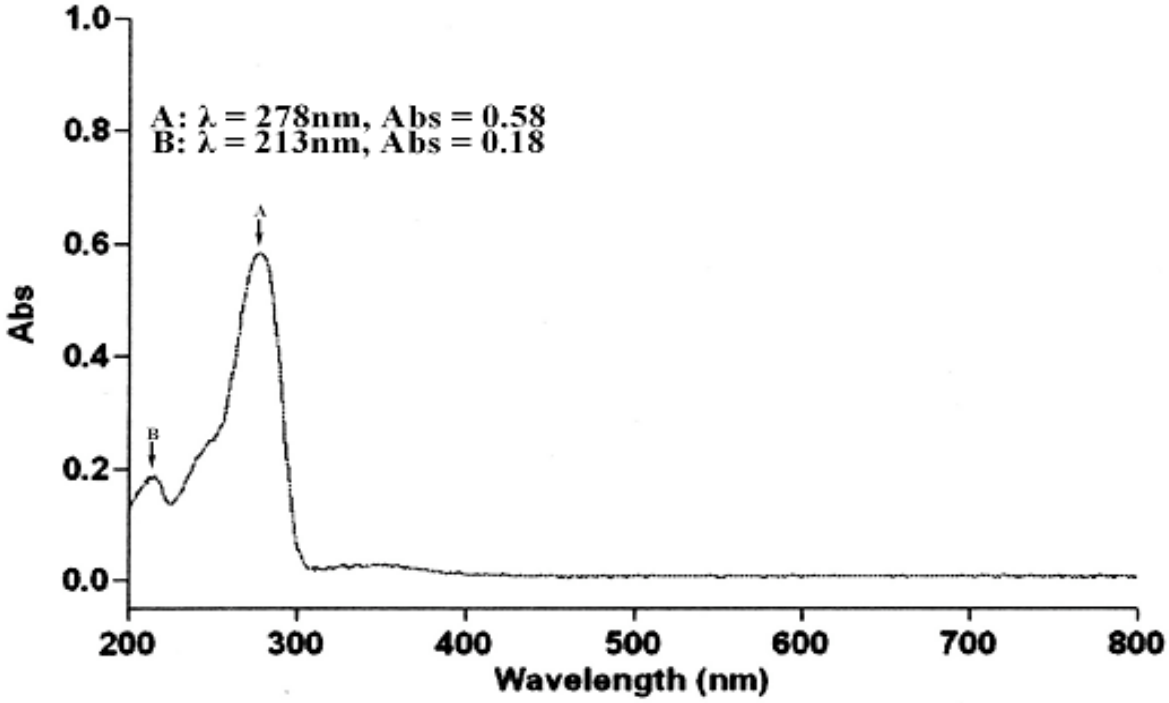
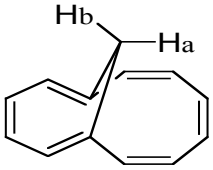
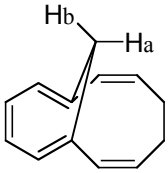
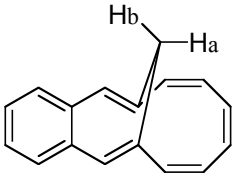
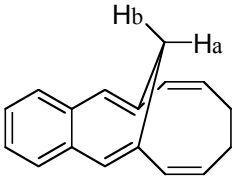


Figure 2-6. UV / Vis spectrum of benz-bridge[12]annulene (3)

2.3.3 Discussion

A new general approach toward methano bridged annulenes has been developed. The paratropic 12π system: 3,4-benzo-1,6-methano[12]annulene has been completely characterized

by. In ^{1}H NMR the $J_{7,8}$ is 12.3Hz and $J_{8,9}$ is 4.14Hz, ^{13}C NMR show only 9 different carbon, X-ray structure the bond length of $C_{7,8}$ is 1.344Å (C=C) and $C_{8,9}$ is 1.468Å (C-C), and UV spectra shown in figure 2-6 there is an small pick around 350nm that is the crystal color.

Compound	Ha	$\Delta\delta_{Ha}$	Hb	$\Delta\delta_{Hb}$
	7.02	3.89	2.79	1.22
	3.13		1.57	
	6.01	2.8	2.37	0.36
	3.21		2.01	

((2.8/3.89)*100% = 72%)

Table 2-1. Comparison of benz bridged[12] and bridged[12] annulene

Using the chemical shift change of the bridge protons between the completely conjugated 12π systems and the dihydro compounds (see table 2-1) one can estimate that the benzannulation in 3,4-benz-1,6-methano[12]annulene (3) reduces the paratropicity by about 28%. In other

words, compound (3) is about 72% antiaromatic compared to the Vogel's[35] 1,6-methano[12]annulene.

After we compare the ^{1}H NMR of non-fully conjugated benz[12]annulene with our benz[12]annulene (3) (Figure 2-7), we observe that the chemical shift of protons 3 and 4 on those two compounds are very different. Protons 3 and 4 on non-fully conjugated benz[12]annulene, is at the regular aromatic chemical shift down field from the chloroform peak. But for our benz[12]annulene (3) protons 3, 4 exhibit two peaks are shifted up field from the chloroform peak. This tells us the fully conjugated [12]annulene has antiaromatic behavior, and the benzene ring not only didn't decrease this compound's antiaromaticity but also is a part of it. Therefore we can see the fully conjugated benz[12]annulene compound as a fully conjugated [16]annulene.

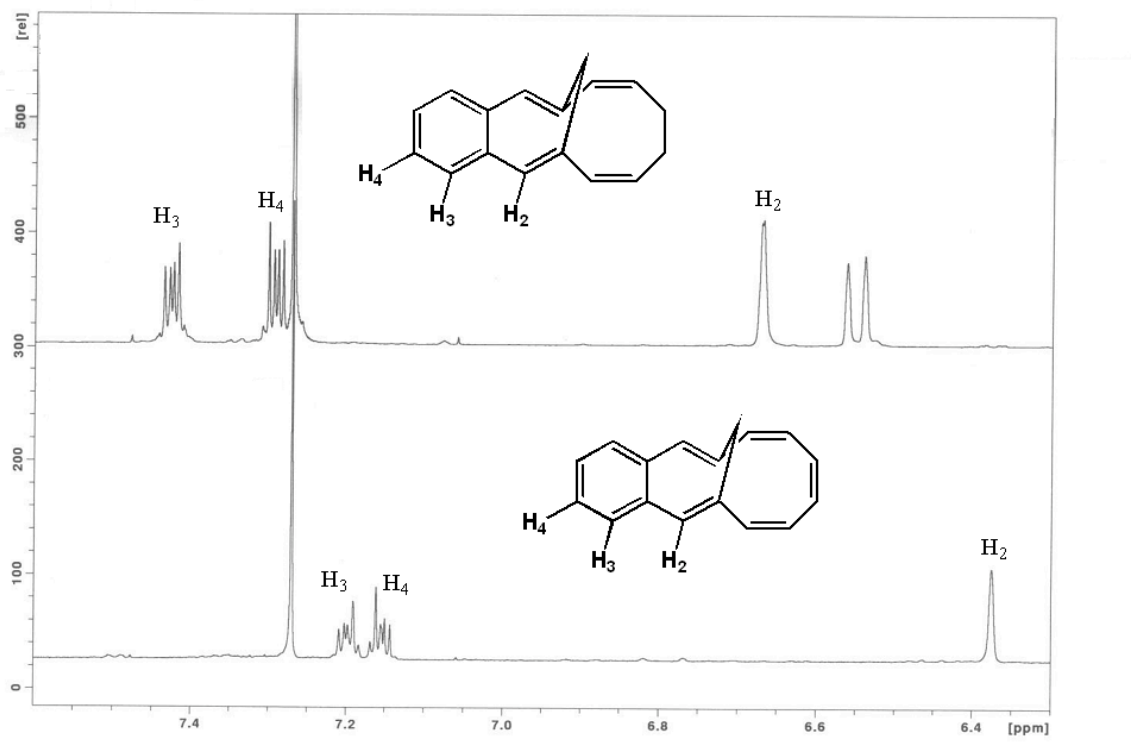
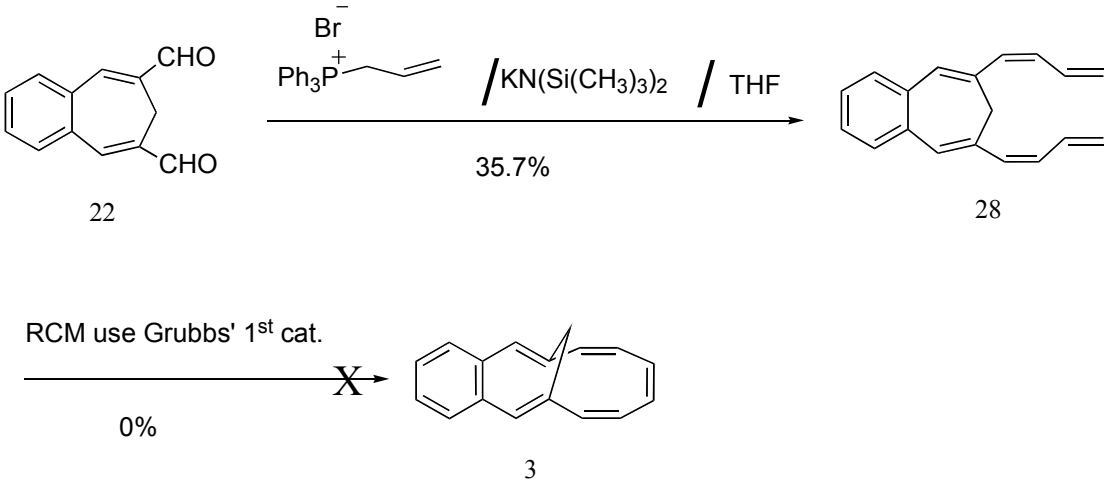


Figure 2-7. ^{1}H NMR of fully conjugated and dihydro benz[12]annulene

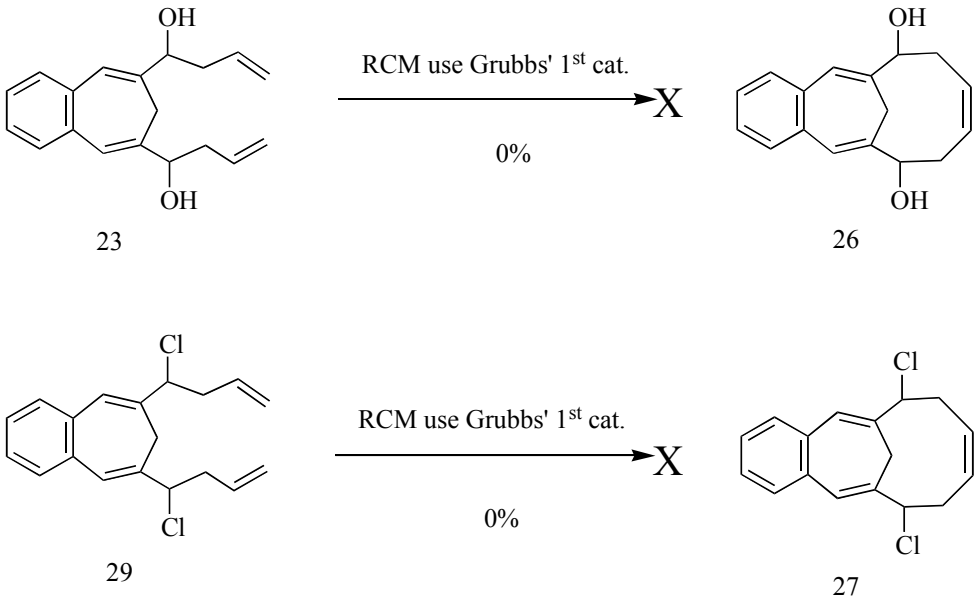
2.3.4 Shorten synthesis of benz[12]annulene (3)

In order to shorten the synthesis, we reacted the dialdehyde (22) with allyltriphenylphosphonium bromide, potassium bis(trimethylsilyl)amide, in THF giving the cis-conjugated diene (28). However, RCM reaction of diene (28) did not give the 12π system 3,4benzo-1,6-methano[12]annulene (3). In stead starting material was recovered and polymerization was observed. (Scheme 2-4)



Scheme 2-4. Two- step approach to the [12]annulene

Neither diol (23) nor dichloride (29) could undergo ring closed olefin RCM metathesis in our hands, and we did not recover any starting material back also. (Scheme 2-5)



Scheme 2-5. Different RCM approaches

The possible explanation is the formation of a 5-member ring chelate, which would decrease the catalyst activity (Figure 2-8). Grubbs also reported a low product conversion (about 23% yield)[32] due to the **OH** group.

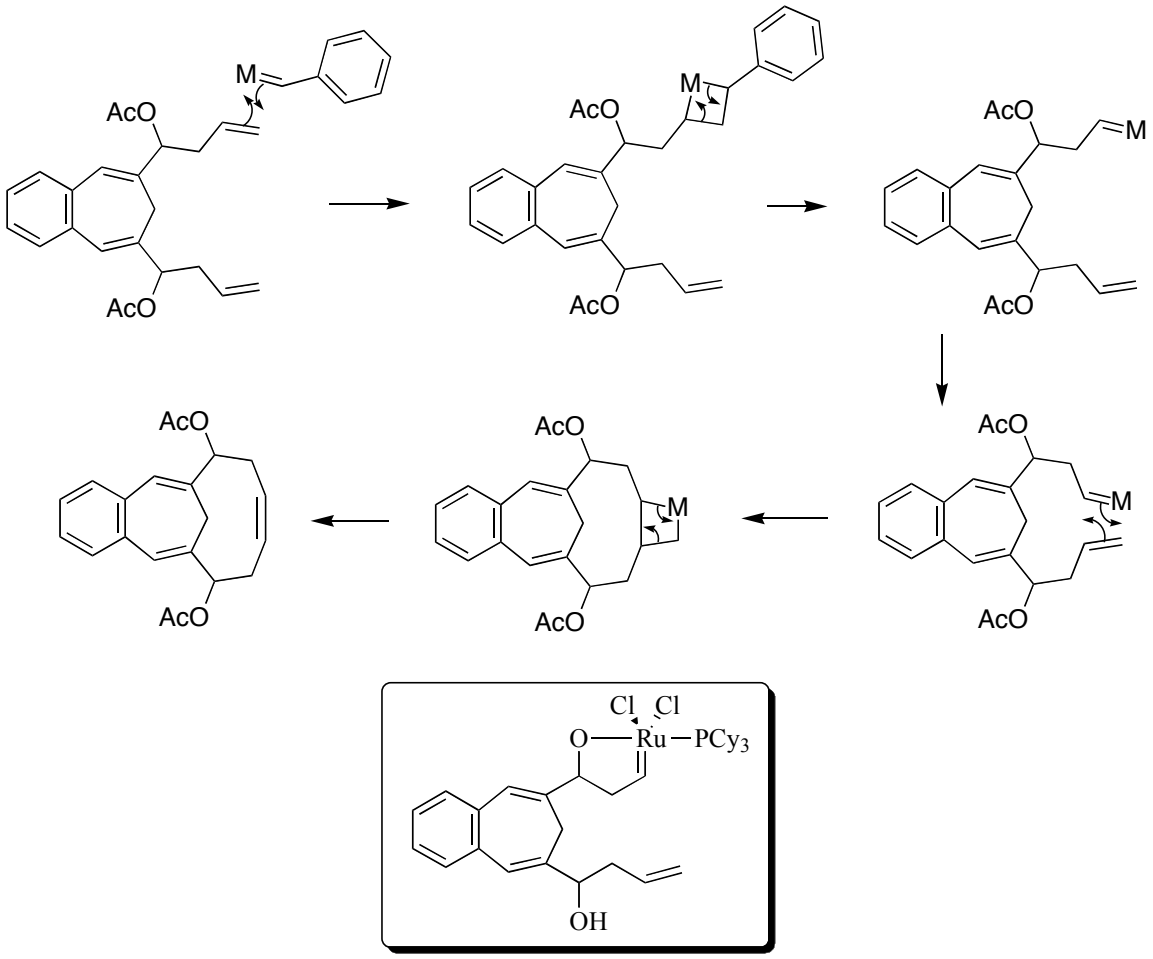


Figure 2-8. Grubbs' catalyzed RCM reaction mechanism and oxygen complex with Grubbs' catalyst.

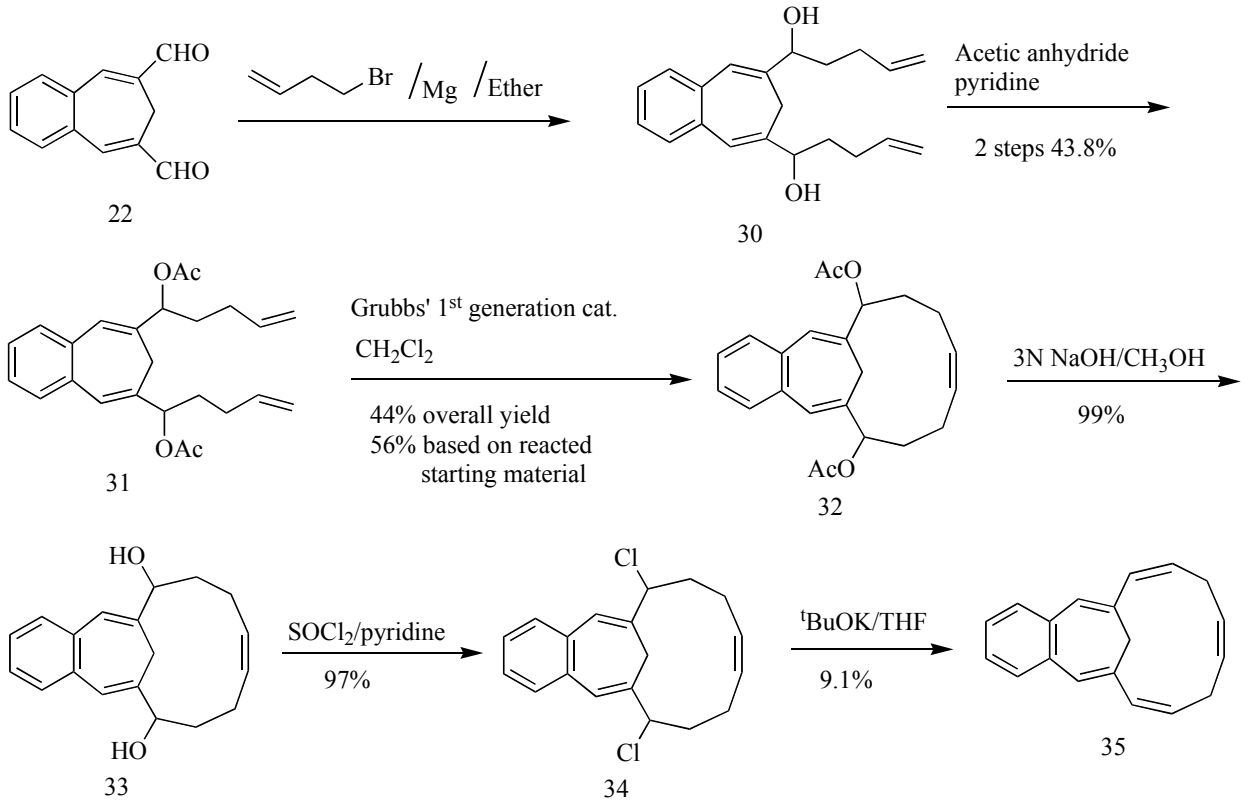
2.4 14π system

2.4.1 3,4-Benzo-1,6-methano[14]annulene

After the successful synthesis of benzo-bridged [12]annulene by using an RCM approach, we extended this method to the expected aromatic (diatropic) 14π system (4).

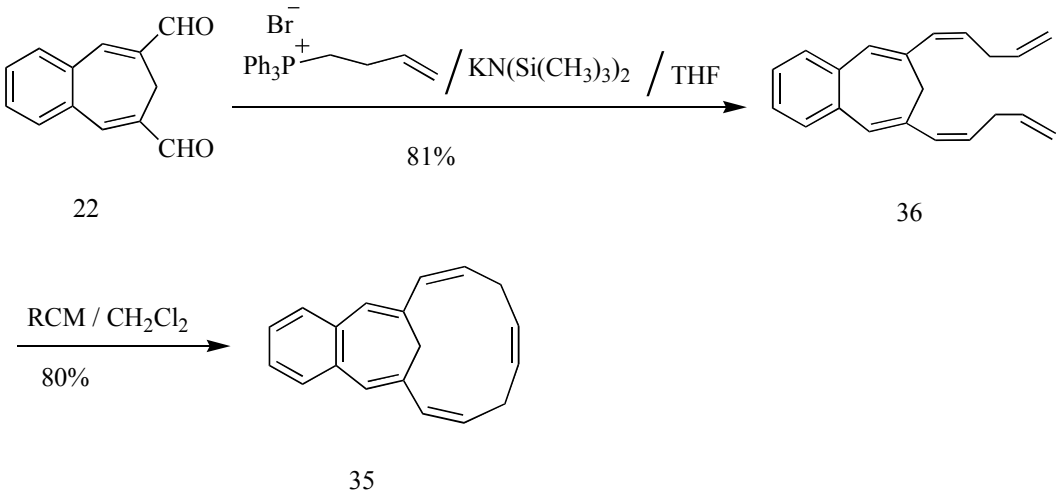
The known Grignard reagent derived from 4-bromo-1-butene was reacted with the dialdehyde (22) giving diol (30). The diol was converted into its diacetate (31) by using standard procedures. Compound (31) upon treatment with Grubbs' 1st generation catalyst under went

RCM to afford the ring- closed diacetate (32). Hydrolysis gave diol (33), which, upon conversion into the dichloride (34), and subsequent treatment of the crude dichloride with t-BuOK in THF for four hours at reflux, followed by chromatography gave the oily dihydro annulene (35) in 9% yield. (Scheme 2-6)



Scheme 2-6. Synthesis of [14]annulene

Due to the long synthesis and lower yield, we developed a new synthetic method by combining the Wittig and RCM approached. In this second approach, Wittig reaction of the dialdehyde with two equivalents of the known phosphonium salt derived from 4-bromo-1-butene gave the cis/cis isomer (36) with traces of the cis/trans isomer in 23% yield. Olefin metathesis of compound (36) gave the dihydro compound (35) identical with the compound obtained above in 80% yield. (Scheme 2-7)



Scheme 2-7. Wittig-RCM approach to the 9,12-dihydro [14]annulene

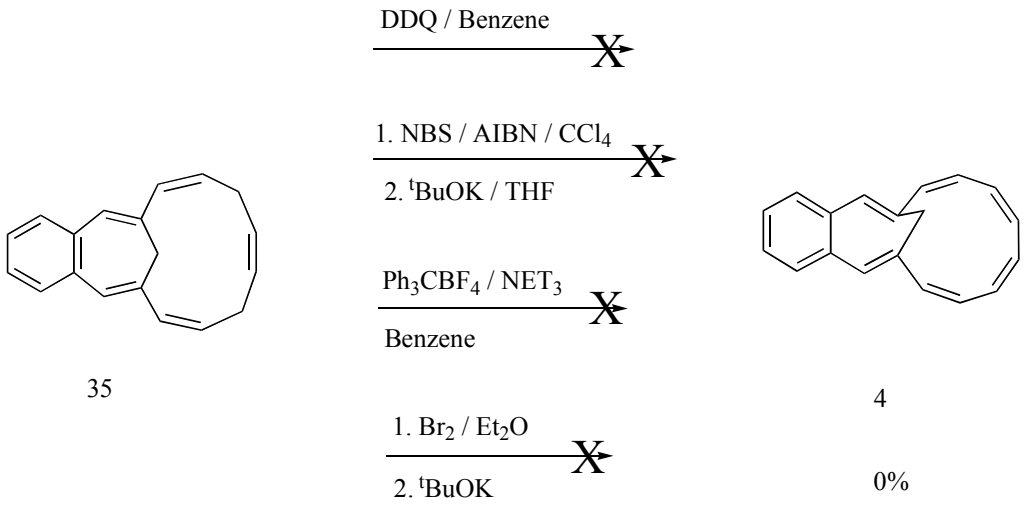
2.4.2 Aromatization of 9,12-dihydro-3,4-benzo-1,6-metheno[14]annulene (35)

Attempts to aromatize the 9,12-dihydro-3,4-benzo-1,6-metheno[14]annulene (30) led to decomposition of starting material and uncharacterizable products. Therefore, this approach has not succeeded so far. (Scheme 2-8)

a. DDQ / Benzene gave neither any identifiable product nor did we recover starting material.

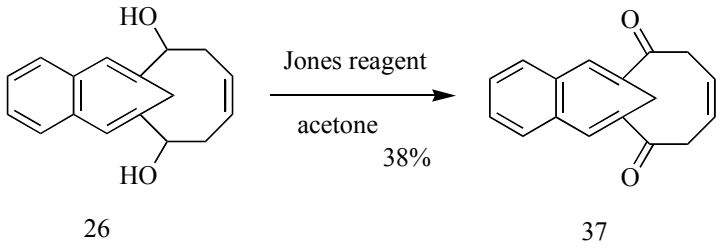
b. In a two-step sequence of bromination-dehydrobromination (Br_2/Ether then ^tBuOK/THF) led to an unidentifiable mixture,

c. NBS followed by ^tBuOK gave an unknown compound, which we have not structurally characterized at this time.



Scheme 2-8. Aromatization attempts with the 9,12-dihydro[14]annulene (35)

In order to reduce the ring flexibility of the [14]annulene, we started attempted to introduce two acetylenes at the 7 and 13 positions of [14]annulene. Therefore, we began with ring closed compound (26), oxidizing the alcohol with Jones reagent to give us diketone (37). The X-ray shows anti- conformation and NMR spectra show that compound (37) is a single conformer. (Figure 2-9 & 2-10)



Scheme 2-9. Oxidation of diol compound (26)

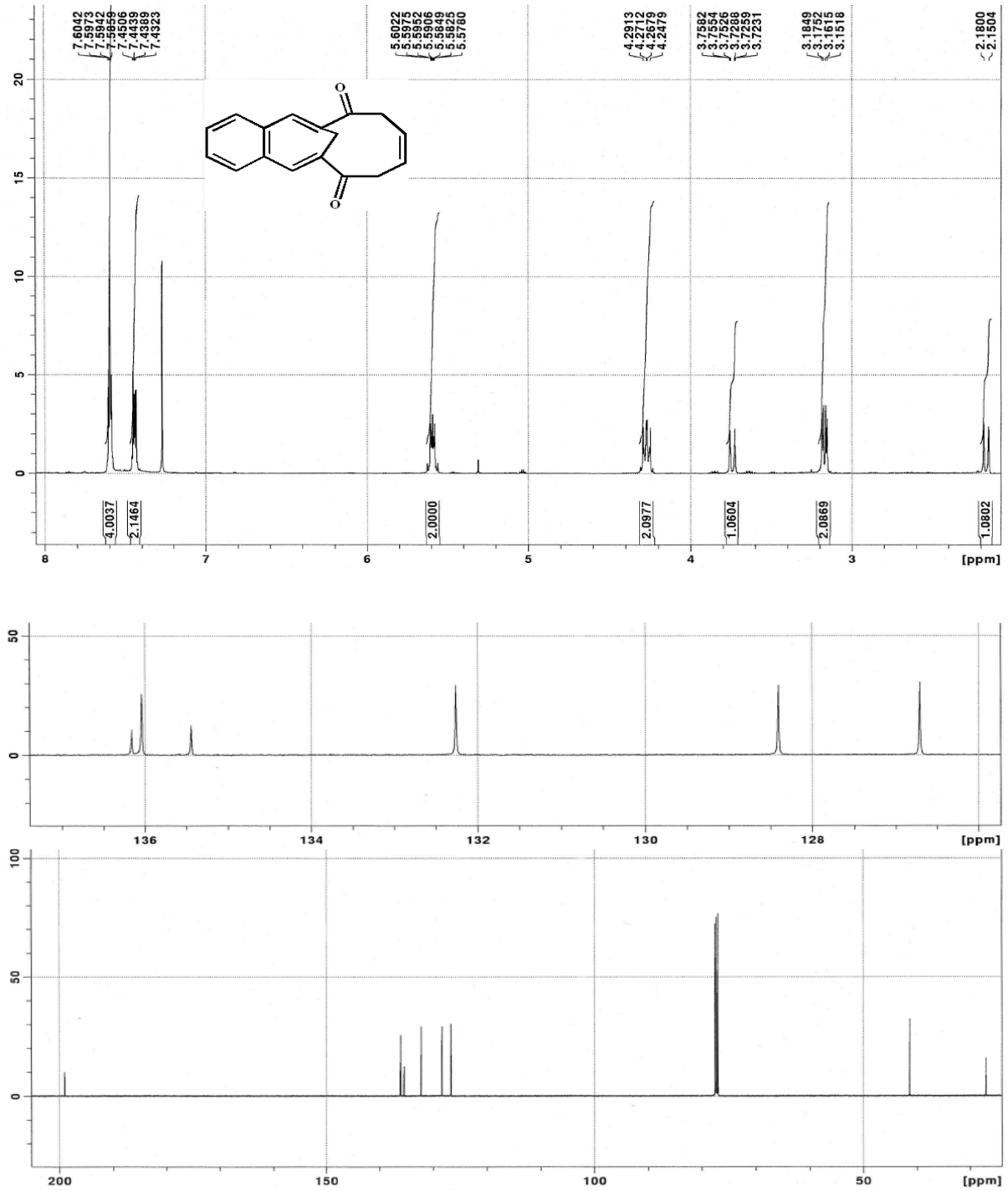


Figure 2-9. Diketone (37) ^{1}H and ^{13}C NMR spectrum of 7,11-diketone compound (37)

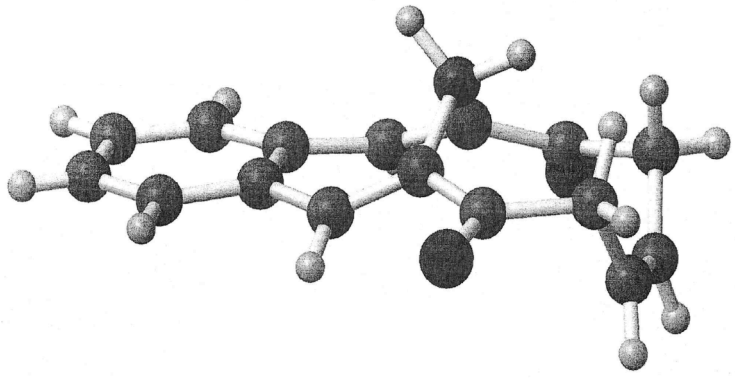
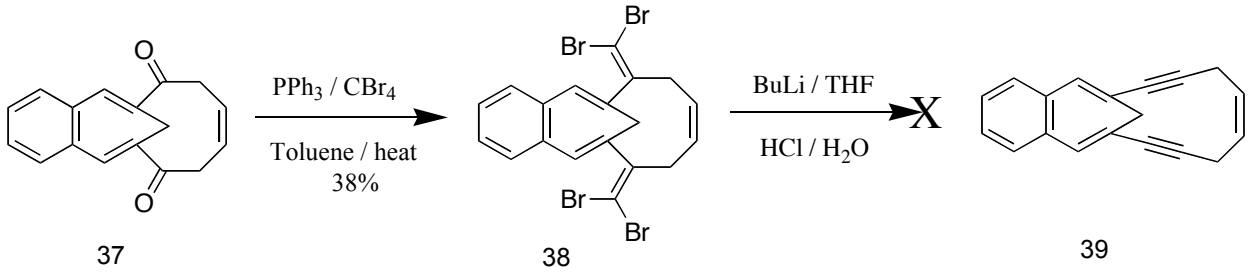


Figure 2-10. X-ray structure of 7,11-diketone compound (37)

We wanted to use dibromomethylene to see if it could be followed (Fritsch-Buttenburg-Wiechell rearrangement)[36] by elimination and carbon insertion with ring enlargement to produce the target diacetylene compound (39). But after our purification of the reaction mixture by using column chromatography, no useful product was detected (by flash chromatography and NMR spectroscopy). (Scheme 2-10)

The non- conjugated double bond of intermediate tetrabromide compound (38) can be syn or anti to the bridge (shown in the NMR spectrum figure 2-11), but the X-ray structure shows only the syn conformation (Figure 2-12).



Scheme 2-10. First synthetic approach to didehydro [14]anulene

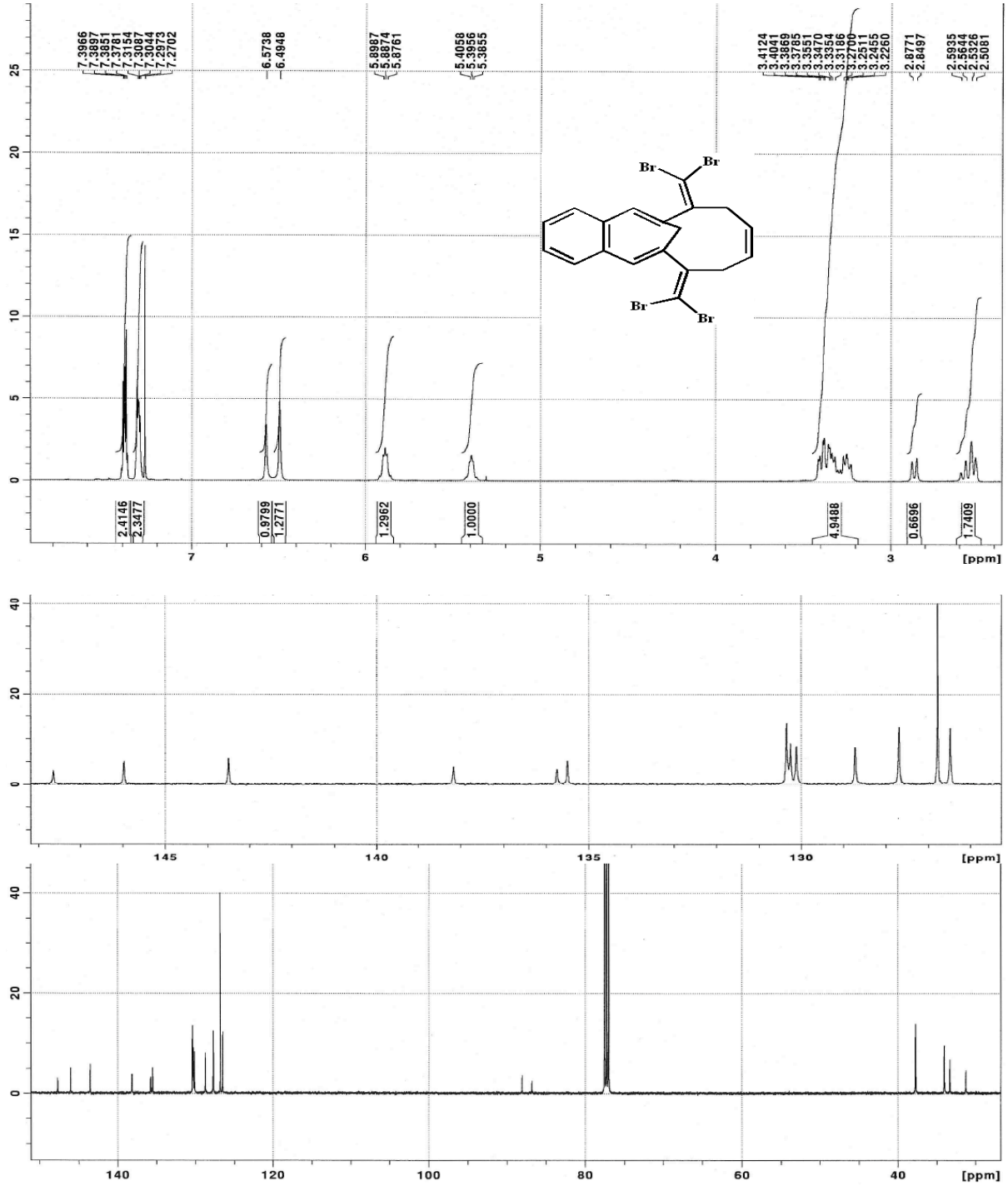


Figure 2-11. ^{1}H and ^{13}C NMR spectra of tetra-bromide compound (38)

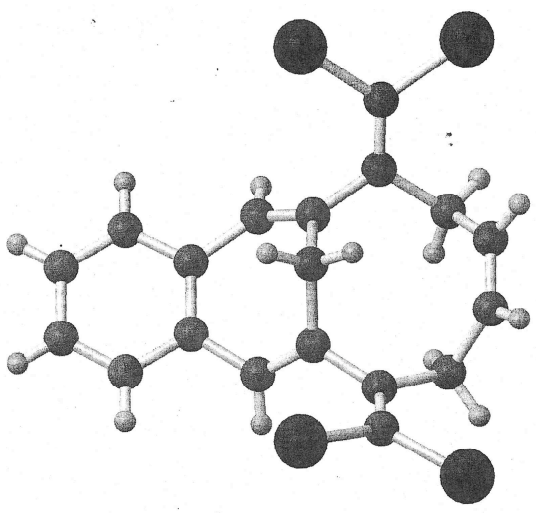
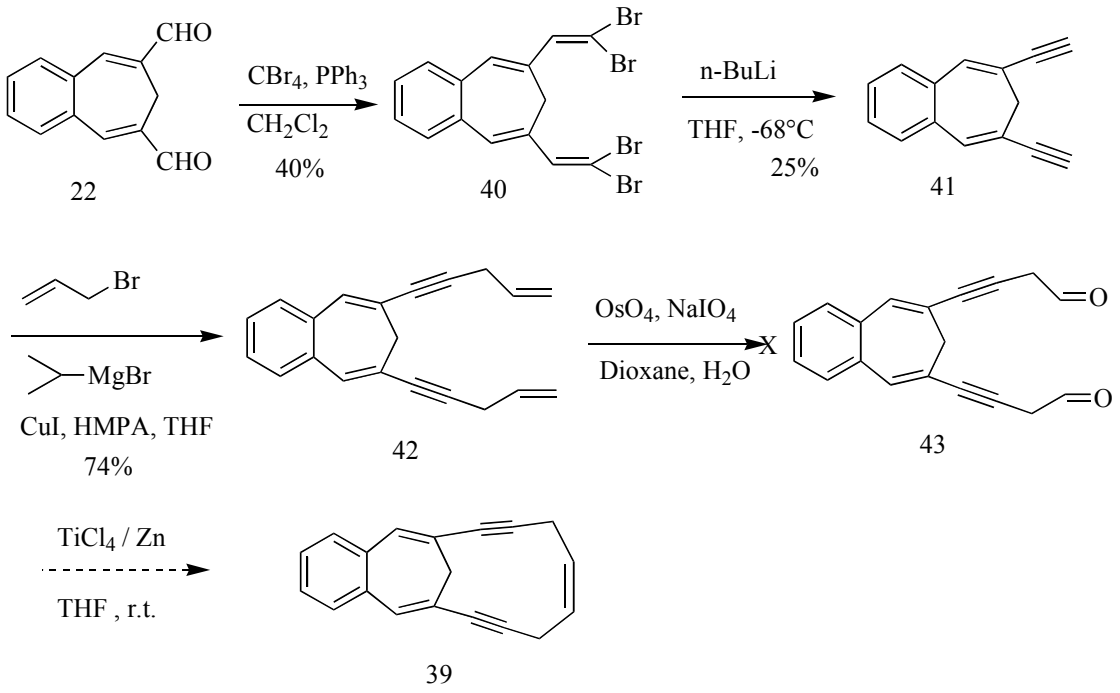


Figure 2-12. The X-ray structure of tetra-bromide compound (38)

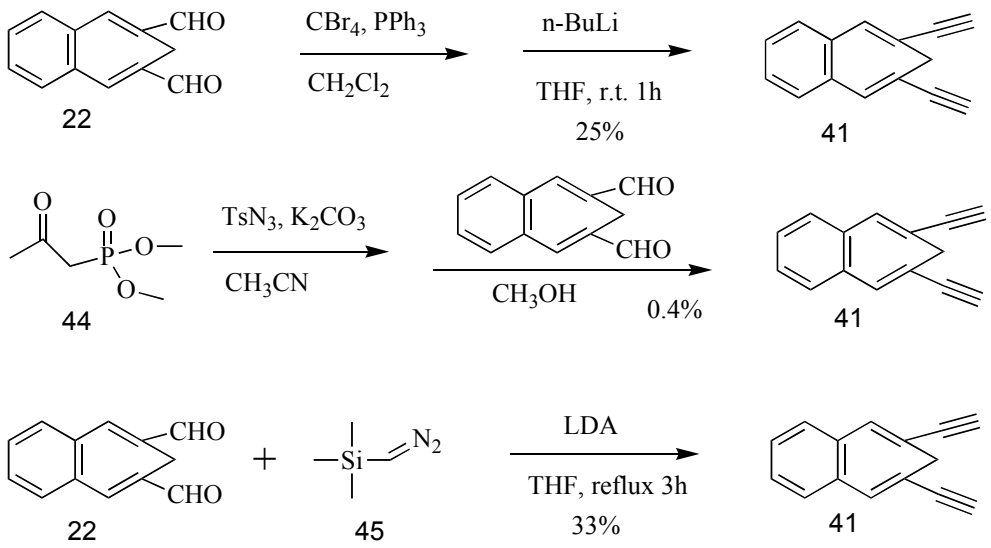
2.4.3 The McMurry approach to Bisdehydro[14]annulene

In order to explore a different approach to the synthesis of bisdehydro[14]annulene (39), we start from Ronnie's aldehyde (22), Wittig reaction followed by elimination gave 1,6-diacetylene (36) which was extended by three carbons by treating with allyl bromide to form compound (42). In order to use the McMurry reaction to yield ring system (39), we oxidized compound (42) to the dialdehyde, but we were unable to isolate compound (43). (Scheme 2-11)



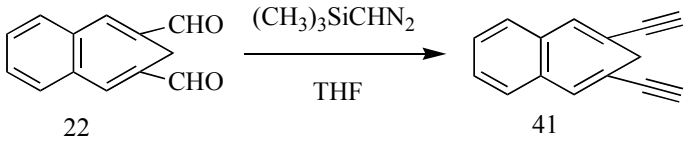
Scheme 2-11. McMurry approach to the 7,13-didehydro [14]annulene

In this McMurry approach, we had tried three additional different procedures to prepare the key intermediate diacetylene (41) shown in (Scheme 2-12). Of the three methods for making the diacetylene[37] (41). Only the Shiori procedure afforded a higher yield in 33% of 1,6-diethynyl-3,4-benzocycloheptatriene compound (41). The second method by Gerald et al. had been applied to azulene-1-carbaldehyde and did not produce the azulene-1-acetylene product.



Scheme 2-12. Alternate syntheseis of diacetylene compound (41)

However, all the efforts to optimize this methodology were unsuccessful. Thus, the original conditions gave us our best result. (Table 2-2) (Scheme 2-13)



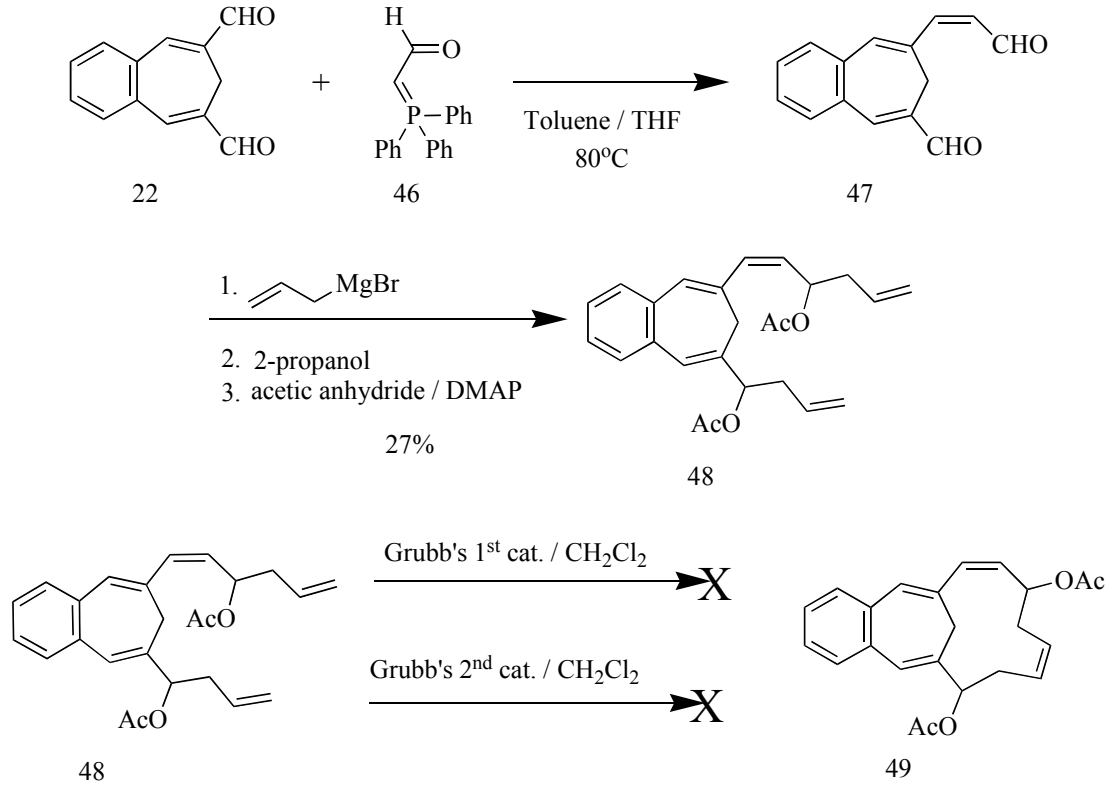
Scheme 2-13. Optimization of the synthesis of key intermediate diacetylene (41)

LDA, reflux, 3h	33%
LDA, r.t. 20h	19%
LDA, ^{t}BuOK, r.t. 2h	10%
LDA, reflux, 2h	33%
LDA, reflux, 3h	22%
n-BuLi, reflux, 3h	14%

Table 2-2. Optimization of the synthesis of key intermediate diacetylene (41)

2.4.4 Asymmetry approach to the benz[14]annulene

Next, we tried a stepwise asymmetric method approach to reach the compound (4). In order to introduce a double bond extension on one side of Ronnie's dialdehyde (22), we started with the Wittig reaction by using Ronnie's aldehyde and reacted it with 1 equivalent of (formylmethylene)triphenylphosphorane. Then this was followed by allyl Grignard reaction on both aldehydes of compound (47), immediately followed by protection of the diol by the acetic anhydride to form diacetate (48). This was followed by RCM reaction in dry dichloromethane to hopefully form ring closed compound (49), but nether Grubb's 1st nor Grubb's 2nd generation catalyst gave us the desired ring closed compound (49). More investigation will be done in the future. (Scheme 2-14)



Scheme 2-14. Asymmetric strategy for [14]annulene

One possible reason for why we cannot get the desired the product ring closed diacetate compound (49) from ring opened diacetate compound (48) by using RCM reaction, on the compound (48) has three double bonds. Thus, the catalyst can select any two of them to do the RCM reaction[32]. Then we will get a serious mixture of products.

2.5 conclusion of the bridge proton chemical shift

It appears the shielding effect of the double bond is very small as the data in figure 2-13 indicate. The proton point to the double bond is no change even in 9,10-dihydro[12]annulene, only a little deshield in doketone compound (37) and deshield by antiaromatic in [12]annulene (3).

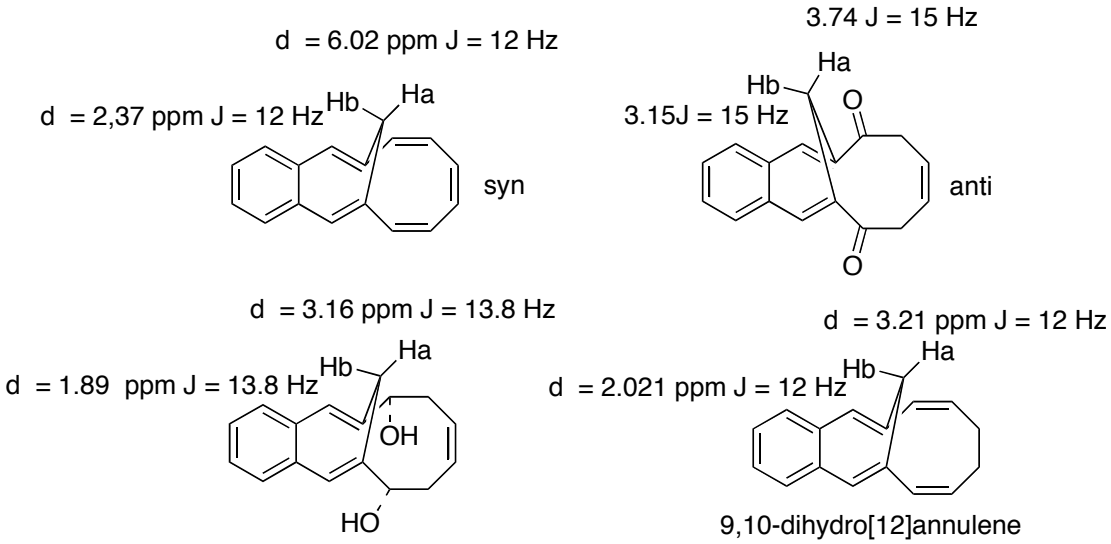
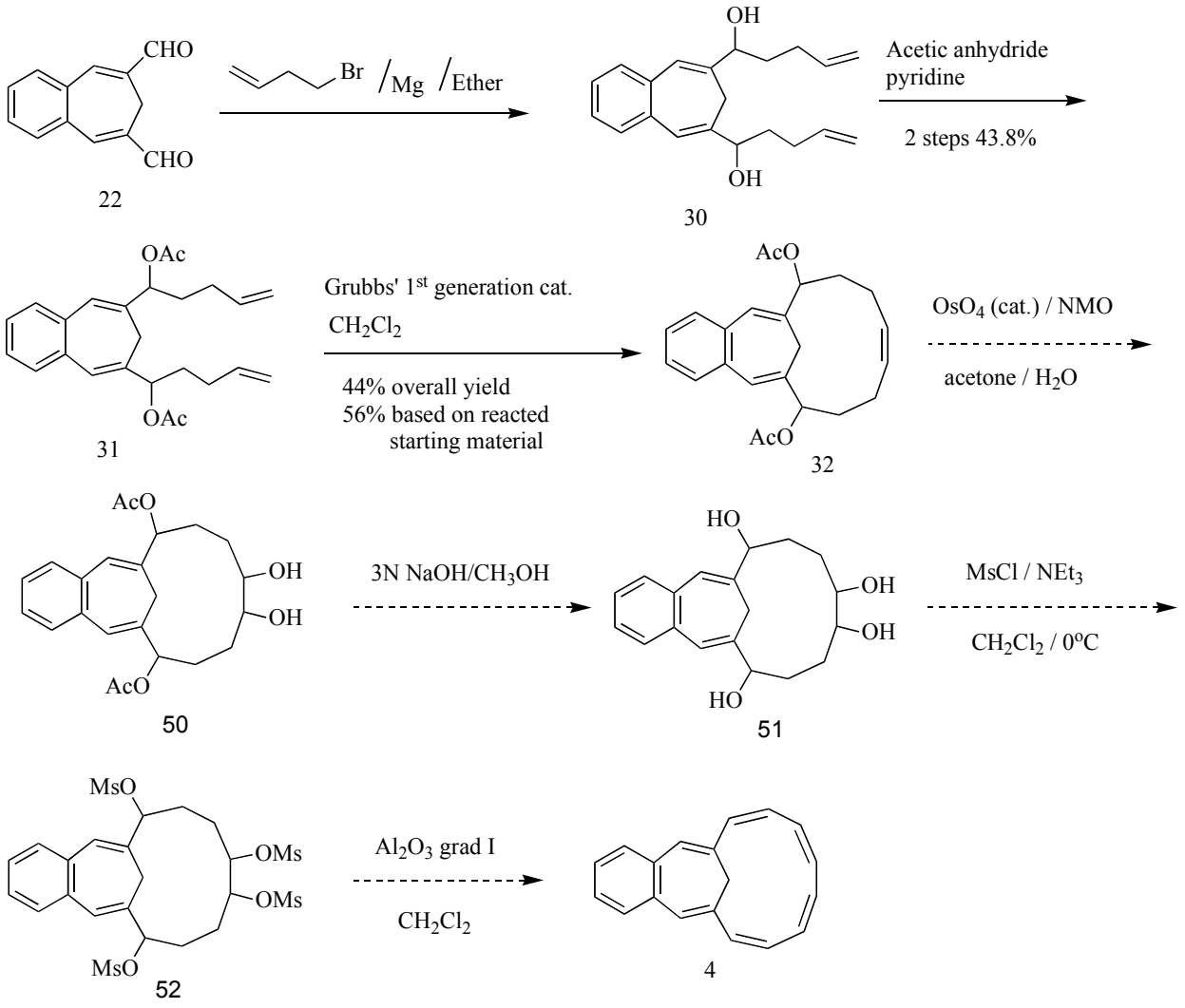


Figure 2-13. Chemical shift of bridge proton point to double bond

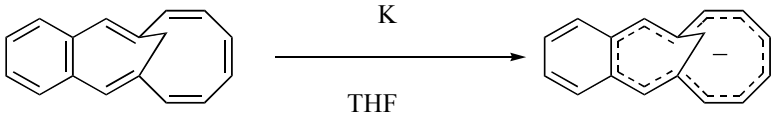
2.6 Plans for further experimentation

For the unsuccessful efforts of our 14π synthesis, the following modifications of the synthesis method are proposed. First, use the successful method for preparing the ring closed compound (32). After that we then propose use of osmium tetraoxide to oxidize the non-conjugated double bond, to afford the diol (50), followed by deprotection of the acetate groups, f to form tetraol compound (51). Then mesylation of the tetraol followed by elimination gives us the desired target compound (4). (Scheme 2-15)



Scheme 2-15. Future work for the synthesis of [14]annulene

Conversion of compound (3) from 12π into the aromatic 14π anion by using K in THF solution.



12π
(4n)π, antiaromatic

14π-anion
(4n+2)π, aromatic

Scheme 2-16. Conversion 12π to 14π

Chart 3. Synthesis of enediyne [10] annulene

3.1. Introduction

The discovery of the "enediyne" antitumor antibiotics calicheamicin γ_1 and esperamycin A1 (Figure 3-1) has provided both new possibilities for the treatment of cancer and a challenge to synthetic chemists to construct the highly strained bicyclo[7,3,1]tridecenediyne unit present as a common feature in the aglycone portion of each molecule. Although enediynes posses potent anti-tumor activity, their clinical use has been limited because of their modest selectivity for cancer cells. Besides anti-cancer activity, these compounds exhibit cytotoxicity against various cell lines, protein degradation activity, topoisomerase inhibitory activity[38]. In order to improve the biological activity of the enediynes, efforts are being made to synthesize analogous compounds with better efficacy as well as developing general methodologies for the enediyne motif.

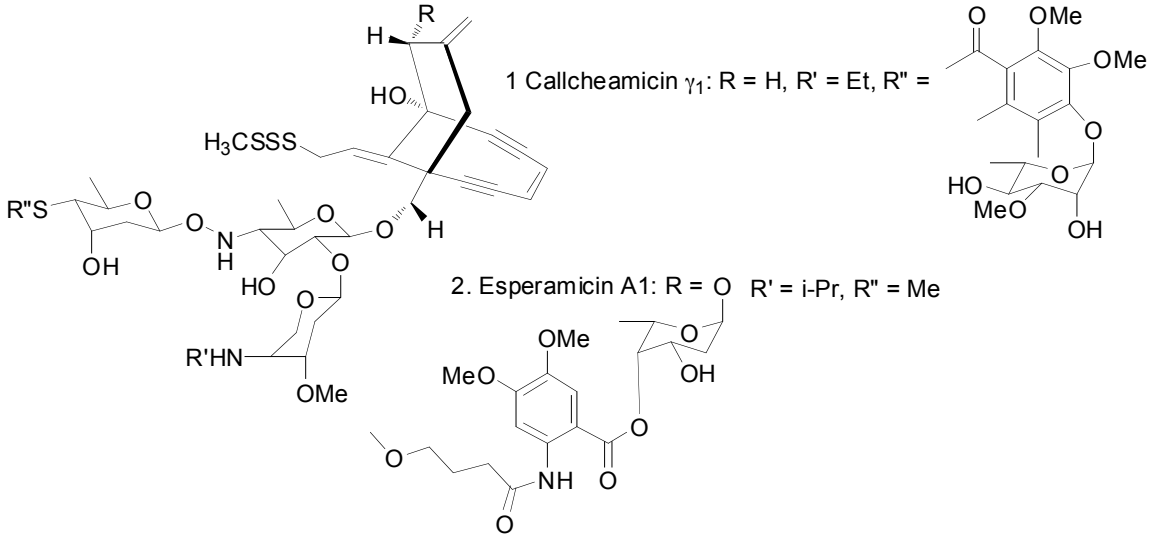
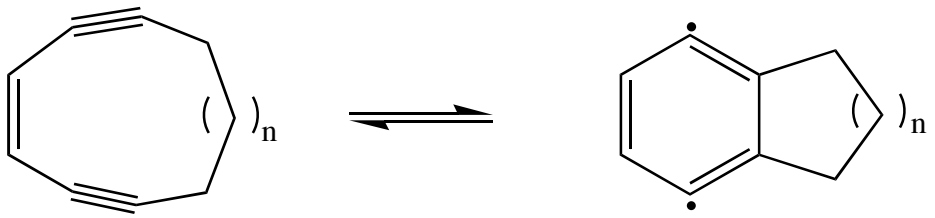


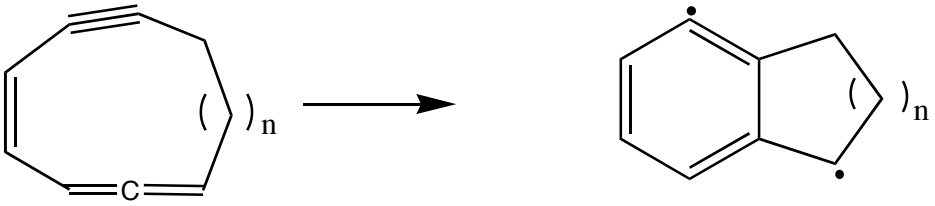
Figure 3-1. "enediyne" antitumor antibiotics.

Originally, enediynes are a class of bacterial products and usually have 9 or 10 member rings containing two triple bonds separated by a double bond. Enediyne chemistry has been the subject

of intense study in recent years due to its applications in medicinal and pharmaceutical chemistry. The anti-cancer activity of those compounds is due to the presence of the highly unsaturated 1,5-diyne-3-ene unit that undergoes Bergman cyclization (Figure 3-2) generating a benzene-1,4-diradical, which cleaves DNA[39].



Bergman cyclization



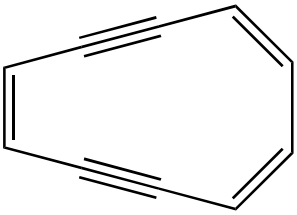
Myers-Saito cyclization

Figure 3-2. Bergman[40] and Myers-Saito[41] cyclization

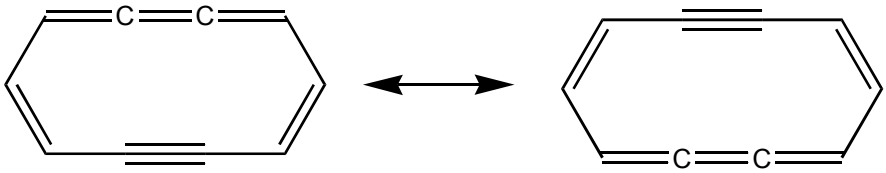
With macro annulene systems ($n \geq 10$), ring flexibility can be reduced by introducing a triple bond into the ring system. The less flexibility, the more planar structure can be maintained. As we mentioned in chapter 1, one of the criteria of classical aromaticity is planar structure. Here we only focus on the classical aromaticity and antiaromaticity, and did not consider the modern concept of aromaticity in transannulene and Mobius ring systems. In order to explore aromaticity and antiaromaticity present in the [10] annulene system, as well as to develop novel methodology to make enediyne systems, Investigated the synthesis of bisdehydro[10]annulene: possibility and extension.

3.2. Bisdehydro[10]annulene

There are two possible bisdehydro[10]annulene structures, one is 1,5-bisdehydo[10]annulene, the other is 1,6-bisdehydro[10]annulene. Only 1,6-bisdehydro[10]annulene has its resonance form to stabilize this structure (Figure 3-3).



1,5-Bisdehydro[10]annulene



1,6-Bisdehydro[10]annulene

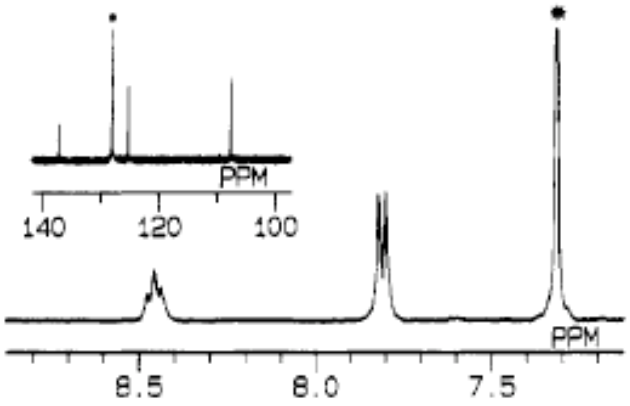
Figure 3-3. 1,5- and 1,6-bisdehydro[10]annulene[40,41]

The 1,6-didehydro[10]annulene is a monocyclic, planar hydrocarbon, it exhibits the ring current anisotropy expected for a 4n+2 annulene. This remarkable compound (Figure 3-5) was synthesized recently by chemists at the California Institute of Technology.[41] The planar configuration required for aromaticity was maintained by introducing two new C-C-π-electron units as alkyne or cumulene groups on opposite sides of the ring. Unfortunately, two π-bonds, orthogonal to the annulene π-electron ring, interact unfavorably across the ring (magenta colored orbitals). Calculations suggest this repulsion leads to a slight distortion of bond angles, as shown. Although the transannular orbital overlap provides a low activation energy pathway for

decomposition, the compound is sufficiently stable at low temperature to permit NMR measurements. At –90ºC the ^{13}C and ^{1}H NMR spectra[42] display the characteristic signals listed in the shaded box.

1,6-didehydro[10]annulene NMR:

^{13}C : 137, 125, 107.5 ppm, ^{1}H : 7.81 (d,4H), 8.45 (t, 2H).



^{1}H NMR spectrum of **1** (2:1 THF-d_8/CD_2Cl_2, −75 °C, 400 MHz): δ 8.45 (t, 2 H, J = 8.3 Hz, H5 and H10), 7.81 (d, 4 H, J = 8.3 Hz, H1, H4, H6, H9). Inset: ^{13}C NMR spectrum of **1** (CD_2Cl_2, −90 °C, ^{1}H-decoupled, 100 MHz): δ 137.1 (2 C, C5, and C10), 125.1 (4 C, C2, C3, C7, and C8), 107.5 (4 C, C1, C4, C6, and C9). Assignments verified by selective ^{1}H-decoupled ^{13}C NMR.

Figure 3-4. ^{1}H and ^{13}C NMR of 1,6-bisdehydro[10]annulene[42]

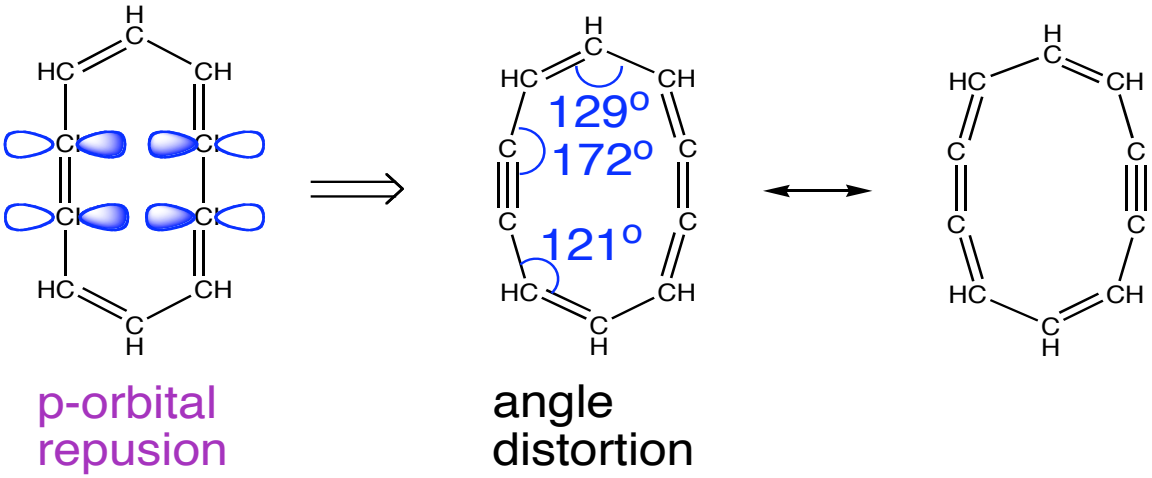


Figure 3-5. The angle of 1,6bisdehydro[10]annulene

The paradox of an aromatic hydrocarbon (by NMR criteria) is thermally unstable. At temperatures above –60º C, its structure identified by NMR, and the nature of its instability is recognized. During warming in solution, 1,6-didehydro[10]annulene is converted to naphthalene (Figure 3-6). The hydrogens at positions 1 & 5 in the naphthalene originate from the solvent; this was proved by using deuterated solvent. As shown in figure 3-6, Hydrogen or deuterium abstraction by the diradical was found at position 1 & 5. The normal chemical stability and low reactivity generally observed for aromatic compounds, is due to the high activation energy associated with disruption of the aromatic π-electron system when sigma-bonded intermediates are formed by addition of electrophilic species. In the present case, the transannular bonding that converts 1,6-didehydro[10]annulene to a naphthalene diradical takes place in the nodal plane, and does not disrupt the [10]annulene aromatic system. Consequently, the aromatic stabilization of the 10 π-electron ring is maintained throughout the reaction.

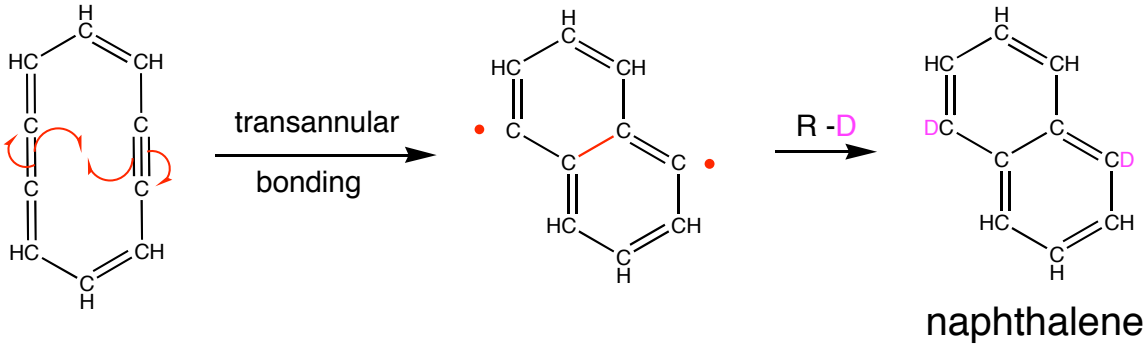
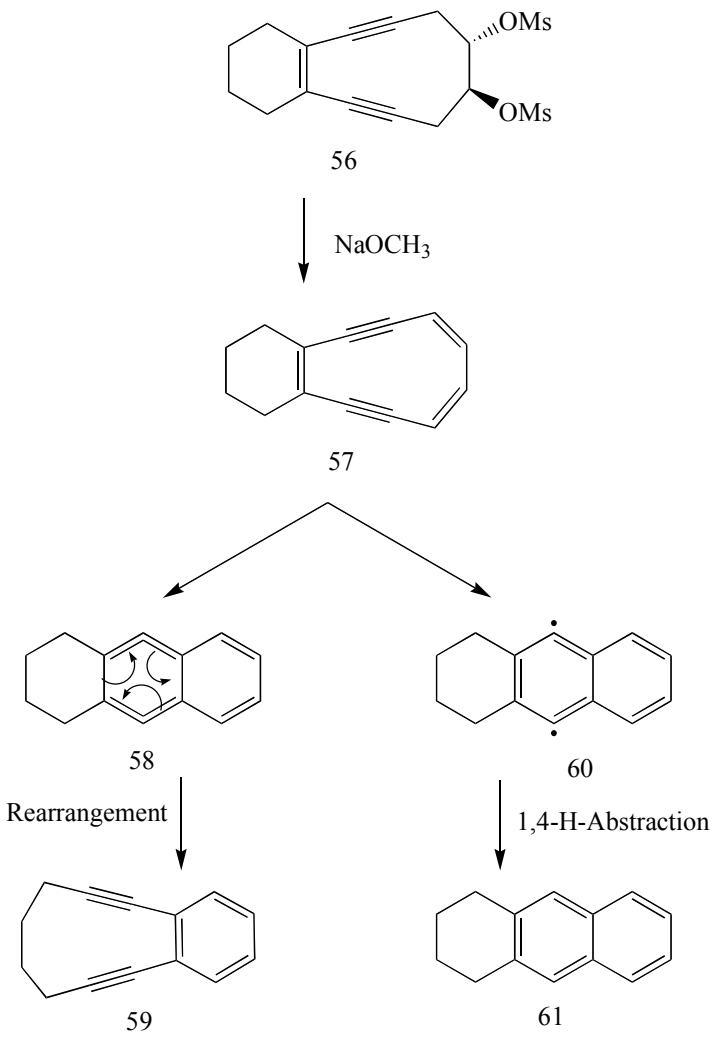


Figure 3-6. Electron cyclization and hydride abstraction

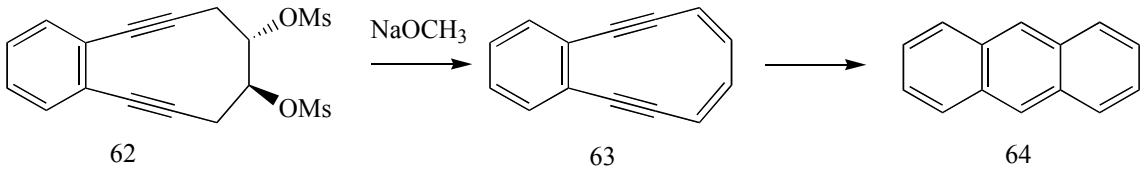
3.2.1 Earlier work on 1,5-bisdehydro[10]annulene

In earlier work of the S. Masamune group to make the 1,5-bisdihydro[10]annulene[43] they used the dimesylate compound (56) to effect elimination Compound (57) was treated with sodium methoxide to give elimination product (57). After purification, they only isolated compound (59) and (61). Therefore, they proposed two mechanisms to define their result (Scheme 3-1). Compound (57) converted to compound (60), followed by 1,5-hydride abstractions to give 5,6,7,8-tetrahydroanthracene (61). A second route proposes that compound (57) is converted to compound (58), followed by rearrangement to afford compound (59).



Scheme 3-1. 1,5-bisdehydro[10]annulene

Further efforts were conducted in Masamune's group[43] based on these unusual results, they designed benzene to replace cyclohexene to make the 1,5-bisdehydro[10]annulene. However it did not lead to the expected product, they only isolated anthracene (64) instead.



Scheme 3-2. Benz-1,5-bisdehydro[10]annulene

One year after Masamune published their unusual result, Bergman[44] published the rearrangement shown in figure 3-7, it shows a 1,4-benzyne intermediate and then to another 3-hexene-1,5diyne. This rearrangement is known as Bergman rearrangement.

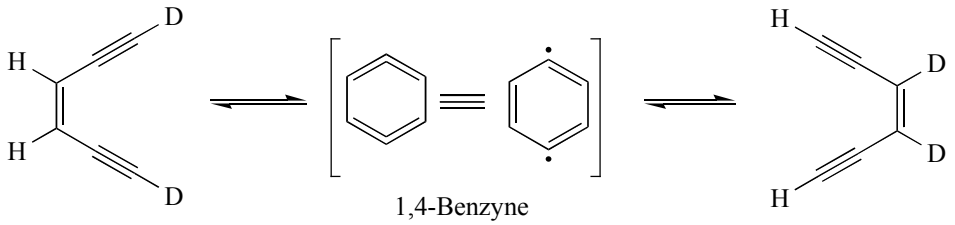


Figure 3-7. Bergman rearrangement

3.2.2 Our approach to the 1,5-bisdehydro[10]annulene system

Compounds (53) and (54) are the annulenes that interest us since both can be viewed as a [14]annulene. These two compounds can't undergo Bergman Rearrangement; since they do not have the required enediyne structure, compared to the Masamune's group 1,5-bisdehydro[10]annulene. However, if we treat compound (54) with a dieneophile, such as acetylene compounds, to undergo low temperature Diels Alder reaction, it will provide the required enediyne structure 1,5-bisdehydro[10]annulene (55), which can undergo Bergman Rearrangement to form naphthalene derivative at room temperature. This is why we plan to use low temperature Diels-Alder reaction in the NMR tube, in order to avoid the undesired Bergman Rearrangement and to maintain [10]annulene structure. The naphthalene annulated 1,5-bisdehydro[10]anulene (100) was included in this investigated since for this molecule a higher activation energy for the Bergmann rearrangement is expected thus possible allowing its isolation.

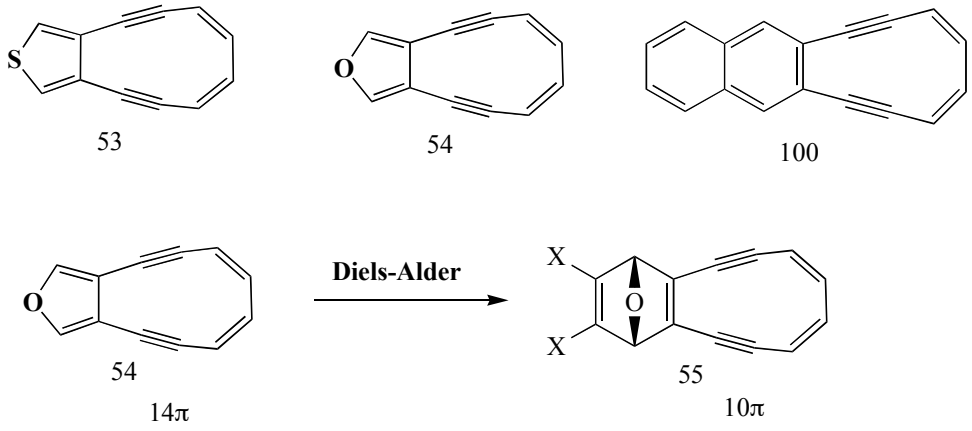
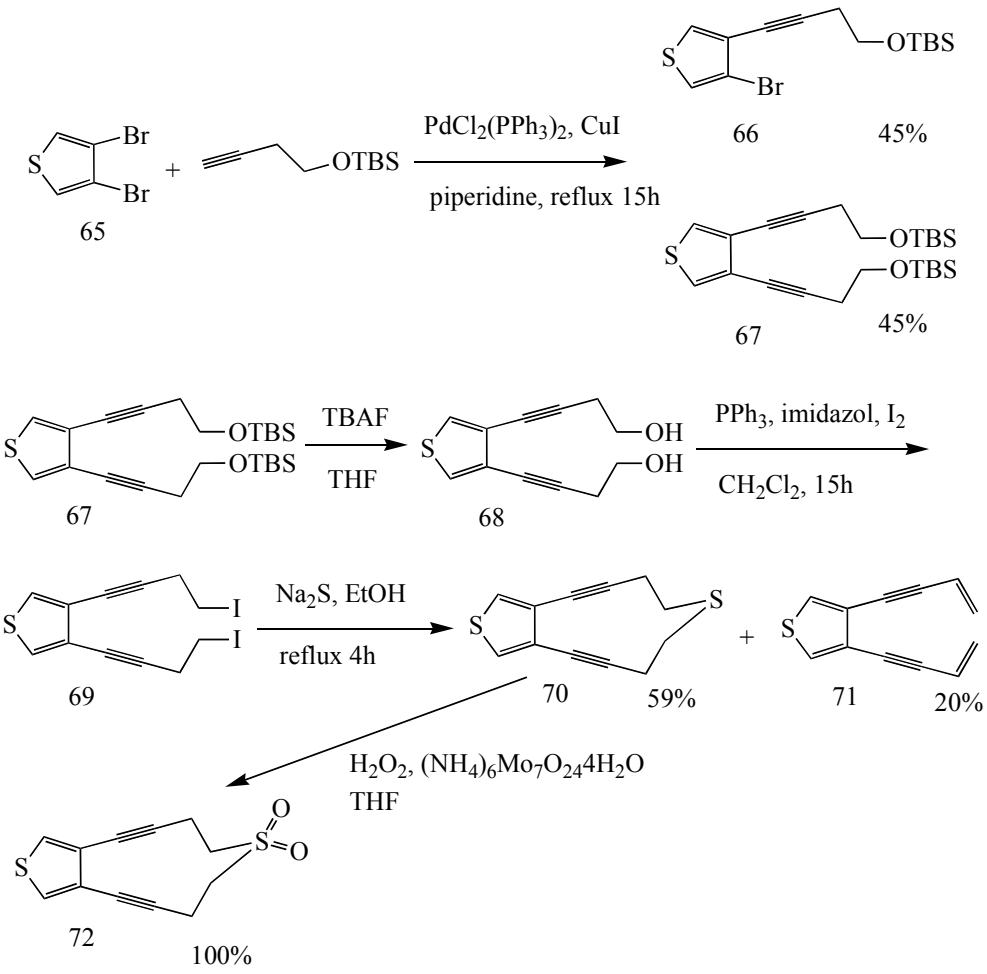


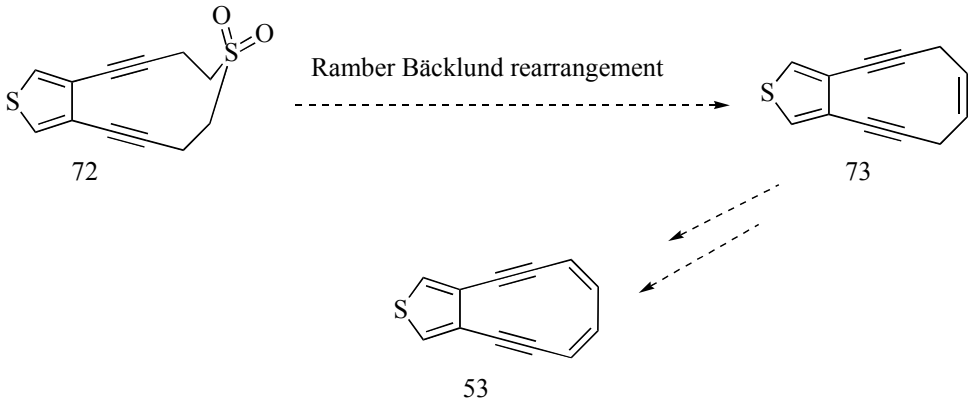
Figure 3-8. Target compounds of the [10]annulene system

Starting from 3,4-dibromothiophene (65) and TBS protected 3-butyne-1-ol, Sonogashira coupling[45] gave a 1:1 mixture of mono and bis substituted products (66) and (67). Deprotection of the TBS group, and conversion of hydroxyl to iodide gave compound (69). Then sodium sulfide was reacted with compound (69) to give major ring closed sulfide compound (70) in 59% yield and elimination product (71) in 20% yield. Oxidation of sulfur to sulfone by using hydrogen peroxide gave compound (72).



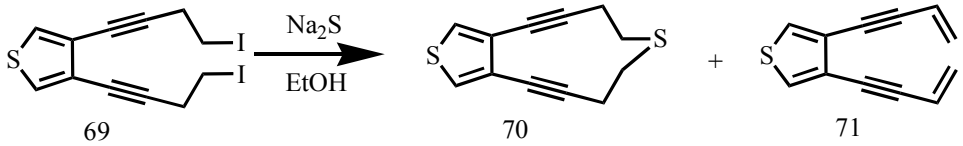
Scheme 3-3. First approach to compound (53)

Compound (72) could undergo Ramberg-Bäcklund rearrangement to form 10 member enediyne ring (73), which may further aromatize to afford our target dienediynecompound (53).



Scheme 3-4. Ramberg-Bäcklund rearrangement and expected aromatization

However the step of making intermediate compound (70) is very sensitive, and compound (69) is so labile to basic condition, it is more favored to undergo elimination than cyclization. Efforts to optimize this reaction were not successful; the crucial factor to determine the reaction chemoselectivity is still under investigation.



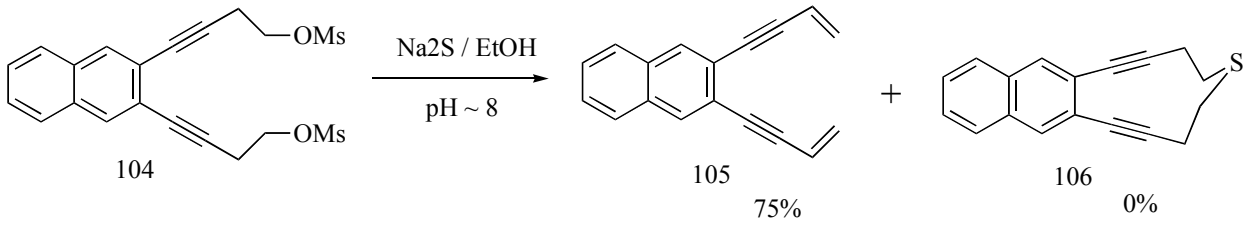
69 70 71

Scheme 3-5. Efforts to make the thioether ring

Reaction condition	Compound 48	Compound 49
75-80°C, 3h	0%	80%
Reflux 3h	0%	82%
0 to r.t. then r.t. 15h	0%	67%
r.t. 15h then reflux 7h	0%	30%
Reflux 15h	0%	70%
Quench reaction immediately	0%	65%
Reflux 3h	5%	88%

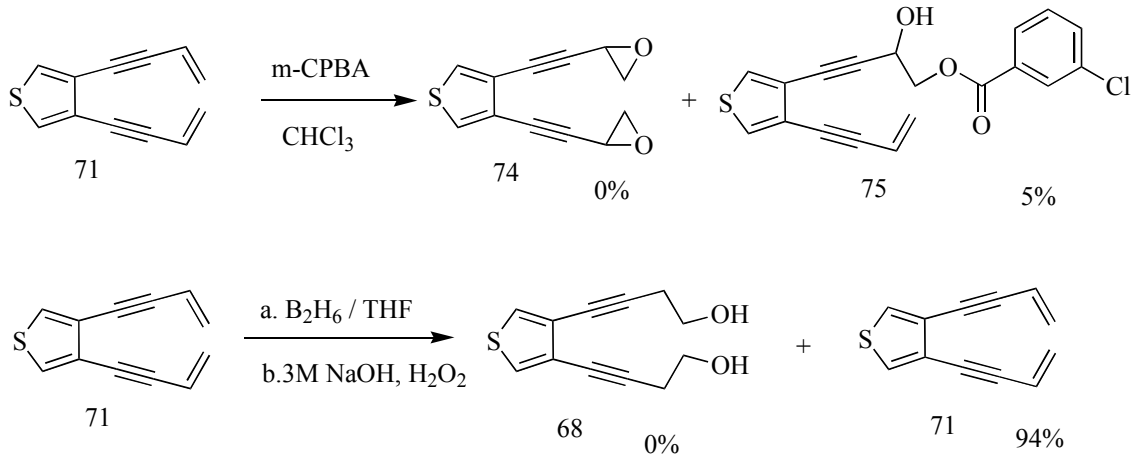
Table 3-1. Efforts to make the sulfur ring

The same results were obtained from Professor Grohmann's work by using naphthalene diyne (104). He observed elimination in preference to S_N2 products. Only isolated elimination product (105) and no cyclic sulfide compound was observed.



Scheme 3-6. Attempted use of a naphthalene to make cyclic sulfide

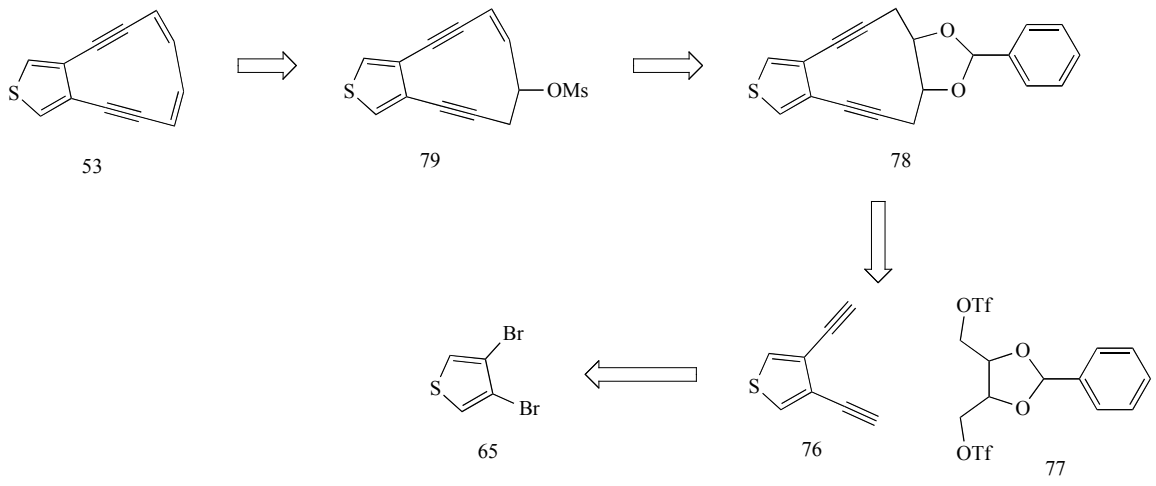
Because of the difficult accessibility of compound (70), we switched our interest to more accessible compound (71). First effort was conducted to oxidize the alkenes (71) to the epoxide (74) by using m-CPBA at room temperature for three hours, also 50^{o}C for four hours, but with the exception of a trace amount of mono addition product (75), no desired epoxide was isolated. We also found compound (71) is not reactive with standard hydroboration-oxidation[46] conditions. After treatment with B_2H_6 at 0^{o}C for two hours, we added 3M $NaHCO_3$ and H_2O_2 at 0^{o}C then stirred the mixture at room temperature for two hours. No desired compound (68) was identified, only starting material (71) was recovered (Scheme 3-7). Possible explanation for the failure is that the conjugated double bond may need more forcing conditions to perform hydroboration-oxidation than an isolated double bond.[47]



Scheme 3-7. Oxidation of the alkene (71)

3.2.3 New Approach to the 1,5-bisdehydro[10]annulene

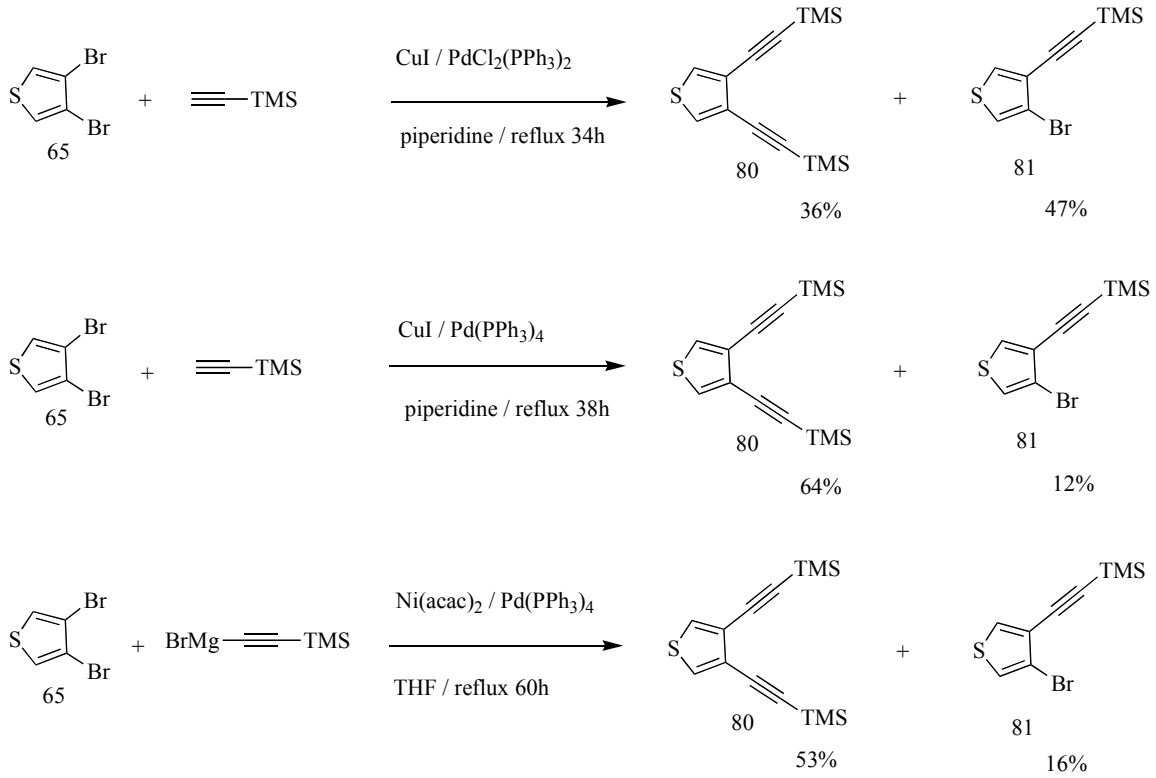
An alternative approach to our target product was conducted in order to avoid the difficulty of forming the sulfur ring required for the Ramberg-Backlund approach. The idea is to follow Masamune's approach to making our target compound. We started out from 3,4-dibromothiophene to make the 3,4-bis ethynylthiophene, and then to react (76) with triflate (77) give ten membered ring (78). This would be followed by deprotection and elimination to afford final product (53).



Scheme 3-8. Retro-synthesis of compound (53)

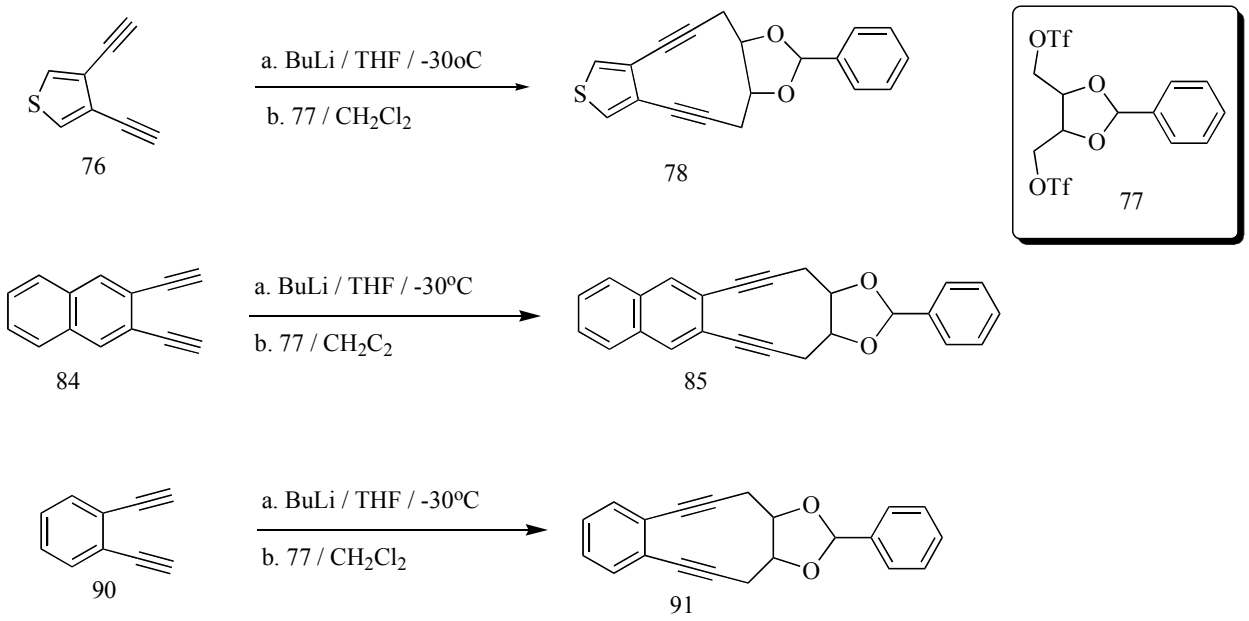
Our first effort was to make the bis ethynylthiophene (80) as a precursor of compound (76). The Sonogashira coupling of compound (65) with TMS acetylene by using **Pd^0** gave us a mixture of disubstituted compound (80), and monosubstituted compound (81). Efforts to optimize the chemoselectivity of this reaction were not successful (Scheme 3-8). $Ni(acac)_2$

catalyst also afforded the diacetylene compound (80), but the result was not as good as Sonogashira coupling[45].



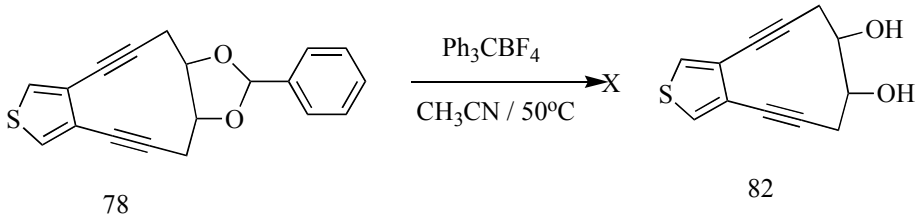
Scheme 3-9. Synthesis of bis-3,4- ethynylthiophene

For our next strategy we applied the Masamune[43] et al. approach. After making the protected bis ethynylthiophene (80), this was followed by deprotection of the silyl group to afford the bis acetylene (76). The diacetylene (76) was reacted with freshly prepared diol-protected bis triflate compound (77) to afford ten member ring (78). The 1,2-bisethynylbenzene and 2,3-bisethynylnaphthalene also use the same reagent and procedure to making ten member ring (85) and (91).



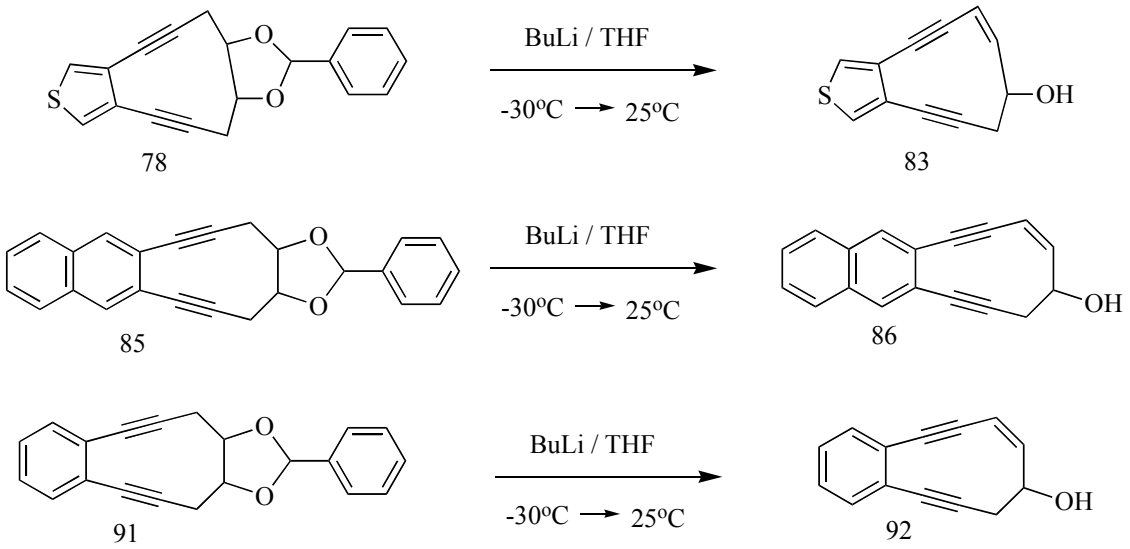
Scheme 3-10. Making the ten member ring

After we got the ten member ring then we followed literature by using mild condition to deprotect the acetal group, but we did not get any of compound (82) only the starting material (78) back.



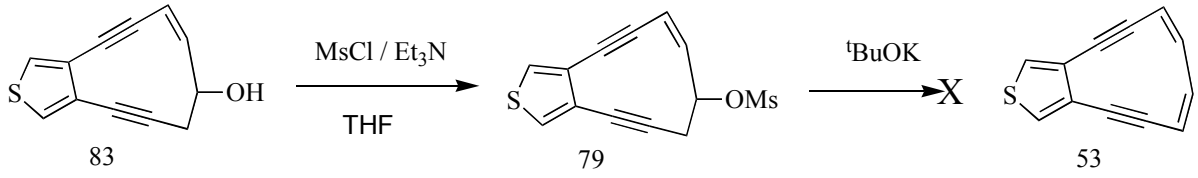
Scheme 3-11. Deprotection by using triphenylcarbenium tetrafluroborate

After we tried the literature procedure and did not get desired product, then we discovered novel conditions for deprotection of this stable benzylidene acetal group. Using strong base n-Butylithium in THF under -30°C for 2 hours, we got allylic alcohols (83), (86), (92).



3-12. Novel method to remove benzylidene acetal group[47]

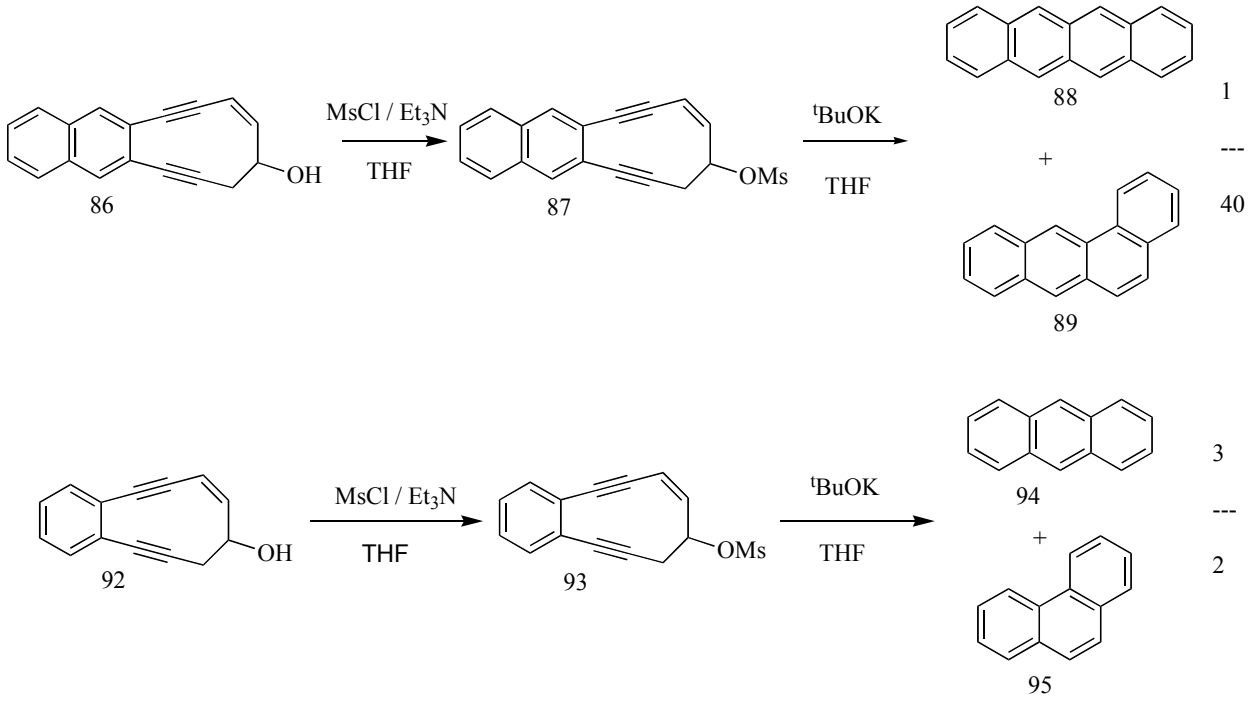
In order to introduce the last double bond we carried out the mesylation of the allylic alcohol, follow by potassium tert-butoxide to effect the elimination of mesylate to give fully conjugated ring system compound (53). But after purification we were unable to isolate compound (53).



3-13. Approach target compound (53)

In order to increase the enediyne stability, to make it possible for us isolate and characterize the final compound under less harsh conditions such as low temperature and inert atmosphere, we introduced naphthalene into the enediyne structure to construct didehydro [10]annulene. By applying the same strategy described in scheme 3-13, we[48] isolated two major compounds after final elimination. They are tetracene and benz(a)anthracene in 1 to 40 ratio (Scheme 3-14). This

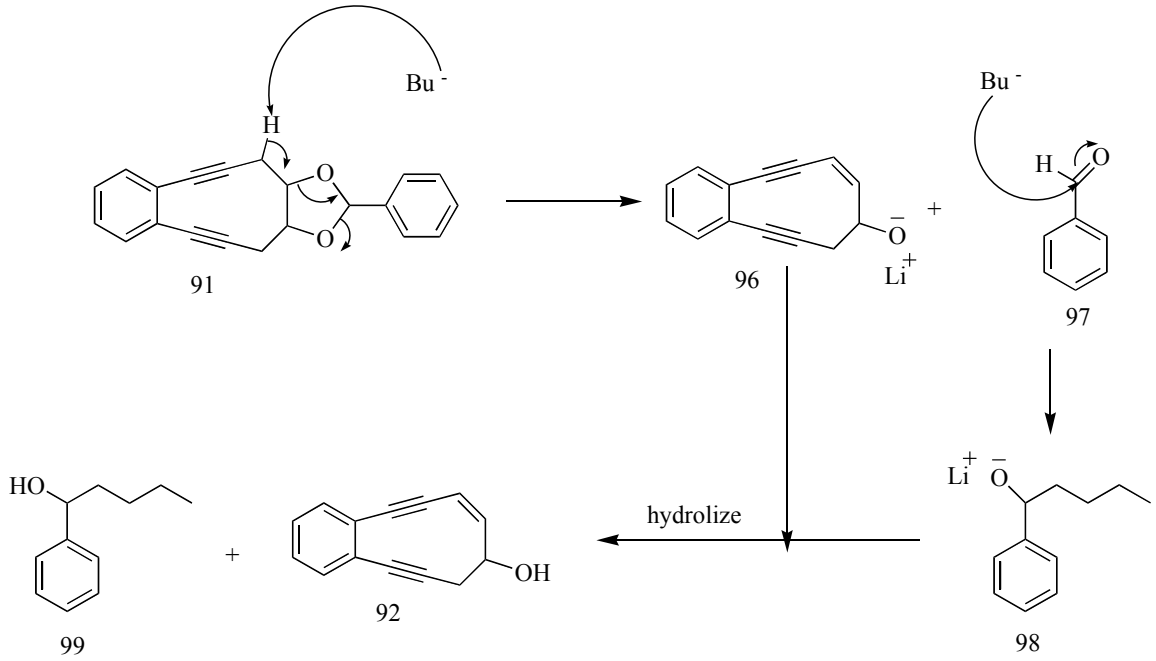
unusual result shows that the compound (87) can form allene compound (102) (Scheme 3-17) under basic conditions and undergo Myers-Saito cyclization, followed by two hydride abstractions and elimination of OMs group to give the compound (89). A minor pathway is Bergman cyclization to form tetracene (88). In the benzene didehydro [10]annulene, we got more Bergman cyclization product (94) then the Myers-Saito cyclization product (95) in the ratio of 3 to 2.



Scheme 3-14. Synthesis of naphthalene and benzenz didehydro[10]annulene[48]

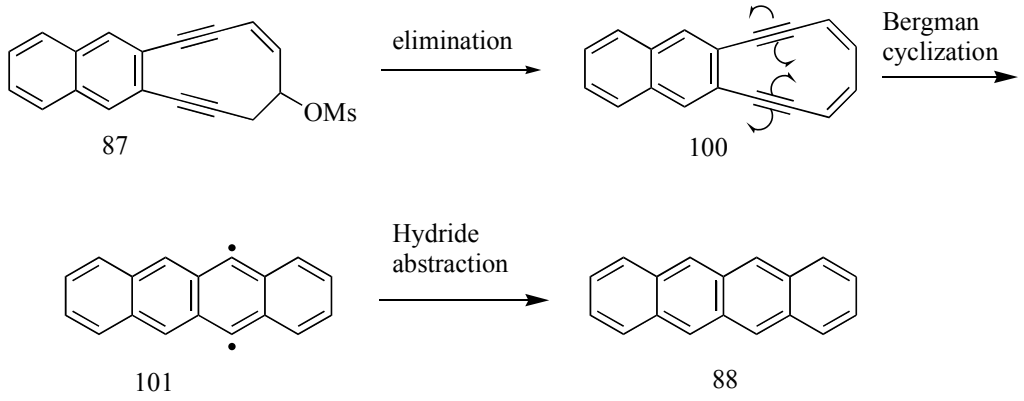
3.2.4 Mechanisms

Shown below is the possible mechanism for cleavage of benzylidene acetal group. We were able to cleave the 10 membered ring diyne acetals with two equivalents of n-Butyllithium at -20 to -30^{o}C. This novel fragmentation converts the acetals into an allylic alcohol and n-butylphenylcabinol as shown below. This reaction proceeds in 65% to 75% yield. (Scheme 3-15)



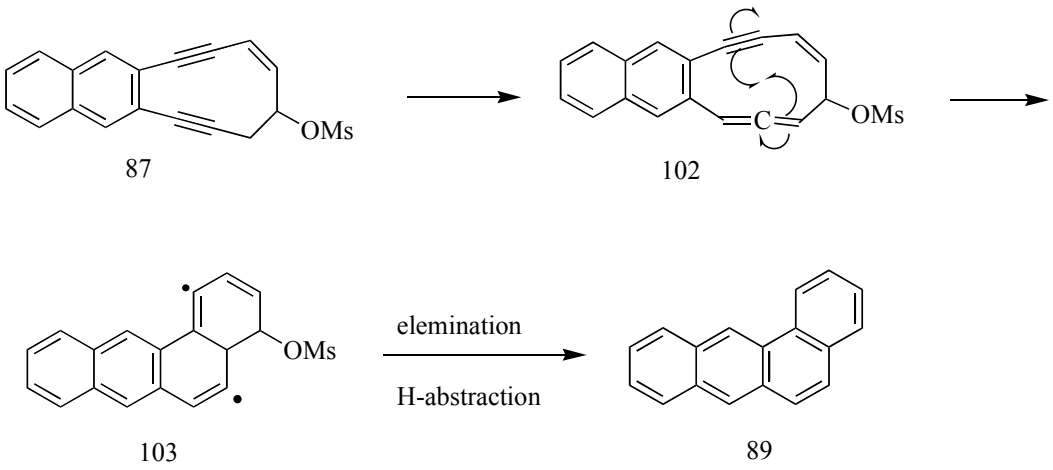
Scheme 3-15. Mechanism of the elimination of benzylidene acetal group

The cyclizations to form aromatic hydrocarbons begins with the process of elimination of the OMs group to form dienediyne, followed by Bergman cyclization to afford a diradical intermediate[48], which, after hydride abstraction gives tetracene. (Scheme 3-16)



Scheme 3-16. Mechanism of Bergman cyclization

Another possible sequence proposed is that: the compound forms an allene first, and then undergoes Myers-Saito cyclization to afford the diradical intermediate, followed by hydride abstraction to afford benz(a)anthracene and concludes with the elimination of OMs group to afford the observed product. (Scheme 3-17)



Scheme 3-17. Mechanism of Myers-Saito cyclization

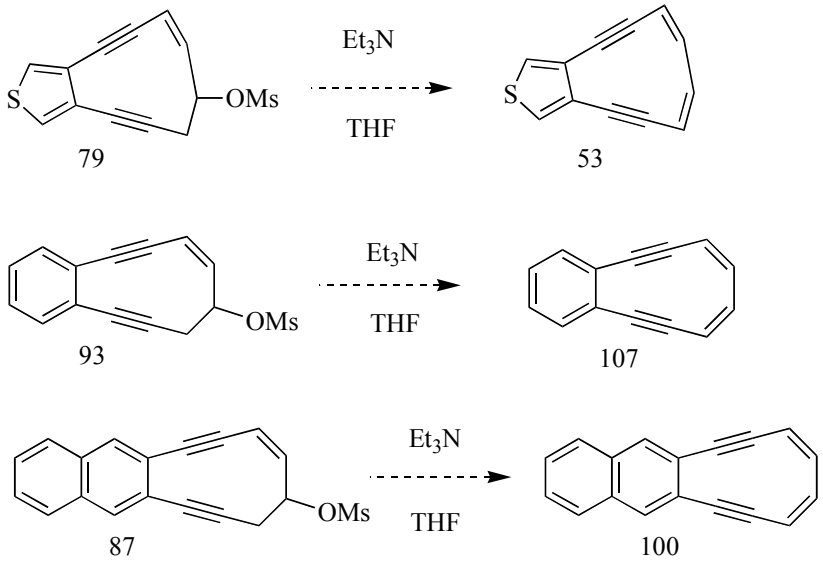
3.3 Summary

Because of its extended aromatic system (thiophene), compound (53) was expected to be stable at room temperature; the thiophene motif in compound (53) should block Bergman cyclization to form the cyclized compound. But all our efforts did not lead to the final product (53), which means only thiophene compound is not strong enough to prevent the unwanted reaction. Further effort will invole doing the elimination reaction inside the NMR tube at the low temperature see if we are able obtain the evidence for the formation of the final compound (53) in situ. By contrast, the efforts to make didehydro [10]annulene derivatives of naphthalene and benzene provided more useful results. The naphthalene didehydro [10]annulene reaction have less Bergman cyclization product tetracene (88) and more Myers-Saito cyclization product benz(a)anthracene (89). By contrast, to the benz didehydro [10]annulene, the Bergman

cyclization product anthracene (94) is major product, and Myers-Saito cyclization product phenathrene (95) is minor. The results tell us that extended aromatic system favors Myers-Saito cyclization since Bergman cyclization may need more energy to disturb the aromaticity in extended system.

3.4 Plans for further experimentation

In the reaction of forming mesylate compound (93), we detected some anthracene by the NMR spectrum. Therefore, we think if we use a weak base like triethylamine, that we maybe could isolate our target product compound (53), (100) and (107).



Scheme 3-18. Use of mild conditions for the elimination

Chapter 4. Experimental section

4.1 General procedures

All glassware used in moisture or air sensitive reactions was oven-dried at over 100^{o}C overnight, then assembled as described in each individual experiment and flushed with nitrogen or argon. A common set-up consisted of a three-necked round bottom flask fitted with a pressure equalizing dropping funnel and a condenser attached to a three-way connecting tube for inert atmosphere inlet and a calcium dichloride and potassium hydroxide drying tube. Stirring was achieved by the use of a magnetic stirrer. Acid or basic neutralization was accomplished by the addition of a suitable aqueous solution, usually saturated sodium bicarbonate for acid neutralization, and dilute hydrochloric acid or saturated ammonium chloride for basic neutralization. Standard work-up included quenching with a suitable cold aqueous solution, extraction with a suitable organic solvent, drying over magnesium sulfate and removal of organic solvent by rotary evaporation in vacuum at a water aspiration pressure of about 11 torr.

4.2 Spectroscopy

Proton and carbon magnetic resonance spectra (^{1}H and ^{13}C NMR) were collected by a Bruker 500 MHz spectrometer. All samples were prepared by dissolving a suitable amount of compound in a properly deuterated solvent, usually $CDCl_3$ (99% D, 0.05%V/V tetramethylsilane). Chemical shifts are reported in part per million (ppm) downfield from the TMS internal standard δ =0, and are expressed in the following order: chemical shift (ppm); multiplicities (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad); coupling constant (J in Hz).

Gas chromatography / mass spectra were determined by either electron impact (EI) ionization or chemical ionization (CI) using argon as the carrier gas on a Hewlett-Packard 5890 series II GC / 5989A mass spectrometer.

X-ray crystal structure determinations were measured on an Enraf-Nonius CAD4 diffractometer (graphite-monochromated Mo Kα radiation, ω -2θ scans).

Melting points were determined by using a Melt-temp II instrument in glass capillaries to measure.

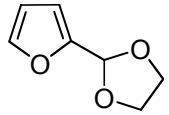
Thin-layer chromatography was performed using pre-coated glass plates of silica gel, with a thickness of 0.25mm, supplied by Merck. UV active compounds were observed by 254 nm UV lamp. Non-UV active compounds were observed by phosphomolybdic acid in ethanol (0.5g / 100mL).

Column chromatography was performed using silica gel 60 for ether regular or flash chromatography.

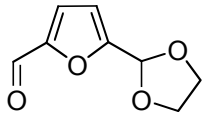
4.3 Solvents were ACS reagent grade and purified as follows

Hexane	distilled over calcium hydride
Ethyl acetate	distilled over calcium hydride
Dichloromethane	distilled over calcium hydride
Acetonitrile	distilled over calcium hydride
Toluene	distilled over calcium hydride
Pyridine	distilled over calcium hydride
Piperidine	distilled over calcium hydride
Tetrahydrofuran	distilled twice over sodium
Triethylamine	distilled over sodium

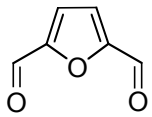
4.4 Experimental procedures



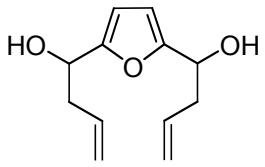
2-(2-Formyl)-1,3-dioxolane (12) : Prepared following the known procedure with slight modifications (toluene as solvent and pyridinium tosylate as catalyst)



2-(5-Formyl-2-furanyl)-1,3-dioxolane (14) : To a solution of butyllithium (30mL, 0.075mol) in hexane, diisopropylamine (11.2mL, 0.08mol) was added drop wise at -20℃ under Argon. The resulting mixture was stirred for 15 minutes. Then, THF (60mL) was added, the solution was cooled to -80℃, followed by the dropwise addition of 2-(2-furanyl)-1,3-dioxolane (7.5g, 0.0536mol) in THF (25mL). After continuous stirring for 30 minutes under this temperature, DMF (50mL) was added, and the reaction mixture was stirred for 12h, allowing the temperature gradually to rise to 20℃. After that ether (200mL) was added to the mixture which was then washed with H_2O (3 X 150mL), separated and dried over ($MgSO_4$). After evaporation, the residue was purified by vacuum distillation to afford the desire product as colorless oil (7.6g, 85% yield).

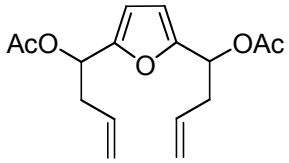


Furan-2,5-dicarboxaldehyde (15) : Compound (14) (2.42g, 0.0144mol) was dissolved in a mixture of acetone (150mL) and 6N HCl (10mL), the resulting solution was stirred under reflux for 1h. The major part of the solvent was removed, and the residue was diluted with CH_2Cl_2 (150mL). After washing with 15%aq K_2CO_3 (3 X 100mL),and drying over $MgSO_4$ and the remaining solvent was removed. The residue was purified by flash chromatography (Hexane/Ethyl acetate 2:1 v/v ratios) to afford off white solid compound (10) (1.16g, 65% yield).

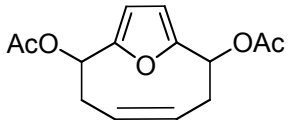


1,5-bis(1-hydroxybutenyl)furan (16) : Magnesium metal (0.999g, 0.042mol) was treated with ether(120mL) followed by dropwise addition of allyl bromide (4.87g, 0.04mol) at 0℃ under argon, and the mixture was stirred at room temperature for 1 hr. Then, a solution of furan-2,5-dicarboxaldehyde (1.17g, 0.009mol) in ether (50mL) was added dropwise, the resulting mixture was stirred overnight at room temperature. When the reaction was complete, ice-cold 3N HCl (50mL) was added in to mixture at 0℃, followed by addition of ice-cold brine (150mL). After

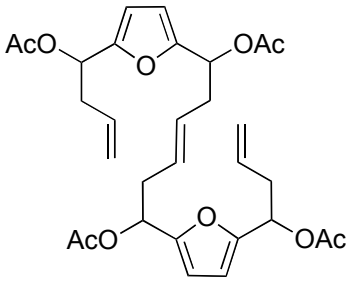
two phases was separated, the aqueous layer was extracted with ether (2 X 150mL), the combined organic layer was washed with ice-cold saturated sodium bicarbonate (1 X 150mL) and dried over $MgSO_4$. After solvent removal, compound (16) was obtained as a colorless oil (1.53g, 78%), and used in next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.35(m, 2H), 5.83(m, 2H), 5.71(m, 2H), 5.46(m, 2H), 5.07(m, 2H), 4.85(m, 1H), 4.10(m, 1H), 3.52(m, 1H), 2.89(m, 2H)



1,5-bis(acetoxybutenyl)furan (17) : To a solution of compound (11) (1.53g, 0.0074mol) in freshly distilled acetic anhydride (20mL), pyridine (1 mL)was added dropwise at 0℃, After stirring overnight, the reaction was quenched by adding ice-cold 0.2N HCl (150mL), then it was extracted with ether (2 X 130mL), each ether fraction was washed with ice-cold saturated sodium bicarbonate (150mL), and dried over $MgSO_4$, and evaporated. After column chromatography, compound (17) was obtained as light yellow solid (1.23g, 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.28 (d, *J* = 4.9Hz, 2H), 5.88 (t, *J* = 5.3Hz, 2H), 5.71 (m, 2H), 5.13 (dd, *J* = 17.1, 1.5 Hz, 2H), 5.08 (d, *J* = 10.2, 2H), 2.72 (t, *J* = 3.4 Hz, 2H), 2.08 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.1, 152.2, 132.6, 118.3, 109.1, 67.9, 37.0, 21.0

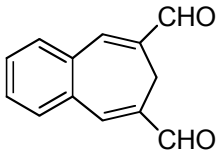


(19)



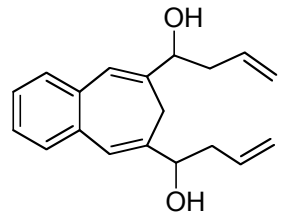
(18)

(Z)-11-oxa-bicyclo[6.2.1]undeca-1,4,8-triene-2,7-diyl diacetate (19) : To a solution of 1,5-bis(acetoxybutenyl)furan (1.0g, 0.0034mole) in CH_2Cl_2 (20mL), was added Grubbs' 1st generation catalyst (150mg, 0.00018mol) at room temperature and the solution was allowed to stand for four days. Evaporation of solvent followed by chromatography yielded dimer compound in 0.88g (97%) (18), not the RCM product (19).

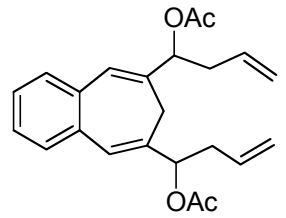


3,4-benzocycloheptatriene-1,6-dialdehyde (22) : At room temperature, glacial acetic acid (6mL) and water (3mL) were placed in 100mL round bottom flask, followed by addition of (10 drops) piperidine and o-phthalaldehyde (10g, 74.5mmol). Under stirring, 50% aqueous 1,5-glutaric dialdehyde (15.2mL, 12.6g, 126mmol) was added as one portion, and the resulting thick solution was refluxed under stirring for 4 hours. During the reaction progress, the solution color was changed to a dark orange and solid precipitates were formed. Quenched reaction with water, and diluted with CH_2CL_2 until all the precipitates were dissolved. The aqueous layer was separated

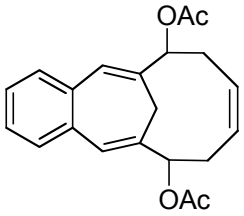
and extracted with CH_2Cl_2 (3 X 50mL). The combined organic layer was washed with saturated sodium bicarbonate solution (50mL), dried over $MgSO_4$ and evaporated, the residue was re-dissolved in a minimum of CH_2Cl_2 and titrated slowly with hexane until no more light yellow precipitate was formed. After filtration, the filtrate was further evaporated, dissolved in a minimum of CH_2Cl_2 and titrated again. The cycle was repeated 4 times in total, collecting all the pale yellow precipitates. Recrystallization from methanol and sublimation (120℃, 0.1 torr) was conducted to afford compound (22) as a pale yellow solid (4.95g, 34% yield). mp: 178-179℃.



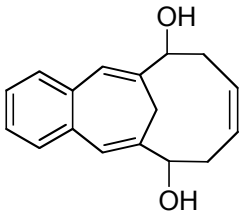
3,4-benz-1,6bis-(1-hydroxybutenyl)-1,3,5-cycloheptatriene (23) : 3,4-benzocycloheptatriene-1,6-dialdehyde (22) (4.02g, 30mmol) was dissolved in anhydrous THF (80mL). Then, a THF solution 2.0M allyl magnesium chloride (50mL, 100mmol) was added to the magnetically stirred mixture under argon at 0℃. After further stirring overnight at room temperature, the reaction mixture was quenched by saturated NH_4Cl solution and extracted with diethyl ether (2 X 100mL). The organic layer was washed with water, dried over $MgSO_4$ and evaporated to obtain a pale yellow residue. Chromatography purification on silica gel (hexane : ethyl acetate = 4:1) afforded a clear oily mixture of two isomers, which was used in the next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.31 (m, 2H), 7.26 (m, 2H), 6.60 (s, 2H), 5.88 (m, 2H), 5.19 (m, 4H), 4.38 (m, 2H), 2.91 (d, *J* = 21.5 Hz, 1H), 2.54 (m, 4H), 2.26 (d, *J* = 15.3 Hz, 1H); ^{13}C-NMR (125MHz, $CDCl_3$): δ = 143.7, 136.1, 134.7, 130.3, 126.4, 125.6, 118.4, 75.7, 40.9, 27.0; MS (EI / 70 eV) m/z M^+ 281, 246, 155.



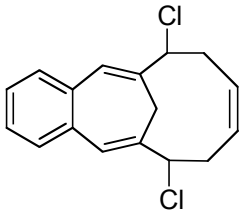
3,4-benz-1,6-bis(1-acetoxybutenyl)-1,3,5-cycloheptatriene (24) : To a suspension of 3,4-benz-1,6-bis-(1-hydroxybutenyl)-1,3,5-cycloheptatriene (18) in acetic anhydride (30mL) at 0℃. pyridine (3mL) was added slowly into the reaction, then the ice bath was removed and the reaction mixture was stirred at room temperature overnight. The reaction was quenched by diluted HCl (120mL) and extracted with diethyl ether (3 X 100mL). The organic layer was washed with saturated $NaHCO_3$ solution and water (100mL), the organic layer was dried over $MgSO_4$ and evaporated to afford colorless residue. The residue was purified by chromatography (hexane : ethyl acetate = 8:1) to afford a white solid mixture of two isomers, in two steps (8.125g, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.30(m, 2H), 7.25(m, 2H), 6.61(s, 2H), 5.76(m, 2H), 5.49(m, 2H), 5.13(dd, *J* = 17.1, 1.6 Hz, 2H), 5.09(dd, *J* = 11.0, 0.9 Hz, 2H), 2.58 (m, 3H), 2.42(d, *J* = 14.6 Hz, 1H), 2.11(s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.3, 138.5, 135.7, 133.5, 130.1, 128.2, 126.5, 118.2, 76.9, 38.2, 27.6, 21.4



3,4-benzo-7,12-diacetoxy-7,8,11,12-tetrahydro-1,6-methano[12]annulene (25) : 3,4-benz-1,6-bis(1-acetoxybutenyl)-1,3,5-cycloheptatriene (0.16g, 0.53mmol) was dissolved in freshly distilled dichloromethane (20mL) at room temperature under argon, followed by addition of bis(tricyclopentylphosphine)benzylidine ruthenium(IV) dichloride (19.6mg, 0.026mmol), the reaction mixture was stirred at room temperature for 48 hours. It was then further stirred under refluxing for 24 hours. After evaporation of solvent, the residue was purified by column chromatography (hexane : ethyl acetate = 8:1) to obtain compound (25) as an off white solid mixture of two isomers (0.16g, 91% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.34(m, 2H), 7.25(m, 2H), 6.64(s, 2H), 5.67(dd, *J* = 10.9, 6.4 Hz, 2H), 5.42(m, 2H), 3.08(d, *J* = 14.2 Hz, 1H), 2.97(m, 2H), 2.49(m, 2H), 2.10(s, 6H), 1.94(d, *J* = 14.3 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.4, 137.3, 136.0, 131.6, 130.5, 128.0, 126.6, 79.7, 30.2, 22.6, 21.7

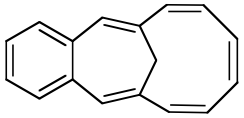


3,4-benzo-7,12-dihydroxy-7,8,11,12-tetrahydro-1,6-methano[12]annulene (26) : 3,4-benzo-7,12-diacetoxy-7,8,11,12-tetrahydro-1,6-methano[12]annulene (0.24g, 0.88mmol) was treated with methanol (15mL), and 3N $NaOH_{(aq)}$ (2mL) under nitrogen and stirred at 0℃ for 1.5 hours. The reaction mixture was quenched by ice-cold brine (30mL) and extracted with diethyl ether (50mL). Then the organic layer was further washed with ice-cold brine (30mL), dried over $MgSO_4$ and evaporated to afford a white solid residue. The residue was recrystallized from dichloromethane to obtain colorless crystals (0.179g, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.32(m, 2H), 7.24(m, 2H), 6.49(s, 2H), 5.39(m, 2H), 4.58(dd, *J* = 10.5, 6.2 Hz, 2H), 3.16(d, *J* = 13.9 Hz, 1H), 2.93(q, *J* = 12.3, 10.7 Hz, 2H); 2.45(m, 2H), 1.89(d, *J* = 13.9 Hz, 1H)

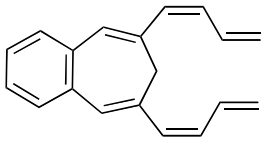


3,4-benzo-7,12-dichloro-7,8,11,12-tetrahydro-1,6-methano[12]annulene (27) : 3,4-benzo-7,12-dihydroxy-7,8,11,12-tetrahydro-1,6-methano[12]annulene (50mg, 0.26mmole) and thionyl chloride (0.32mL, 4.4mmol) were mixed in a 5mL round bottom flask under argon. Pyridine (0.25mL) was added slowly into the reaction mixture kept in an ice bath. After 90 minutes of stirring, the ice bath was removed and the reaction mixture was stirred at room temperature for

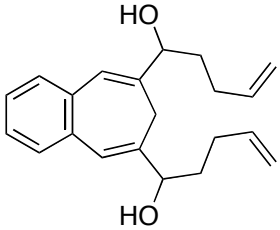
additional 30 minutes. Then, the reaction mixture was quenched by ice-cold brine and extracted with dichloromethane. The organic layer was washed with water and evaporated to afford yellow oil residue. The residue was carried on to the next step without further purification.



3,4-benzo-1,6-methano[12]annulene (3) : To a solution of compound (27) in (20mL) of THF was added potassium tert-butoxide (0.12g, 1.07mmol) at 0^{o}C. After 40 minutes of stirring, the solution was moved to a refrigerator (-4^{o}C) and allowed to sit overnight. Then, the reaction mixture was slowly warmed up to room temperature and quenched by ice-cold brine (50mL). Then it was extracted with dichloromethane (2 X 50mL), the organic layer was washed with ice water, dried over $MgSO_4$ and evaporated to obtain an oil residue which was then purified by column chromatography on aluminum oxide using hexane as eluent to afford orange-red crystal compound (3) (91% yield). Mp: 107-110℃. ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.19(m, 2H), 7.15(m, 2H), 6.37(s, 2H), 6.02(d, *J* = 11.8 Hz, 1H), 5.86(d, *J* = 12.3 Hz, 2H), 5.78(d, *J* = 4.1 Hz, 2H), 5.68(d, *J* = 11.3 Hz, 2H), 2.39(d, *J* = 11.8 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 138.6, 138.2, 130.9, 130.7, 130.5, 130.4, 129.1, 126.4, 26.8

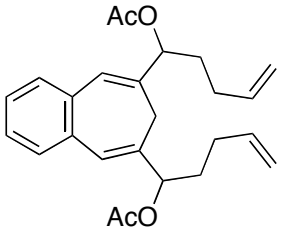


3,4-benz-1,6bis-(1,3-butadiene)-1,3,5-cycloheptatriene (28) : Dissolved allyltriphenylphosphonium bromide (4.82g, 12.6mmol) in THF (50mL), under argon and stirred at -78^{o}C. Drop in 0.6M SHMDS (8.4mL, 5.04mmol) to the reaction, after drop finish let reaction warm to room temperature for an hour. Then cool to -78^{o}C and drop in dialdehyde (22) (0.96g, 4.86mmol) in THF (30mL). Let reaction stirred at room temperature for two hour. Quench reaction by using HCl (1mL) in ice-cold salt solution (100mL). Extracted with ether (2 X 100mL). Dried over $MgSO_4$ and evaporated ether. After column chromatography get product (28) (0.426g, 35.7% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.35(m, 2H), 7.25(m, 2H), 6.66(m, 2H), 6.45(m, 4H), 6.10(m, 2H), 5.31(m, 2H), 5.14(m, 2H), 2.72(s, 1H), 2.35(s, 1H); MS (EI / 70 eV) m/z M^{+} 246, 215, 165.

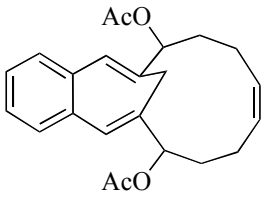


3,4-benz-1,6bis-(1-hydroxypentenyl)-1,3,5-cycloheptatriene (30) 3,4-benzocycloheptatriene-1,6-dialdehyde (22) (1.584g, 8mmol) was dissolved in anhydrous THF (50mL). 50ml n-butylmagnesium bromide ethyl ether solution (20mmol) was added to the magnetically stirred mixture under argon at 0℃. After further stirring overnight at room temperature, the reaction mixture was quenched by saturated NH_4Cl solution and extracted with diethyl ether (2 X 100mL). The organic layer was washed with water, dried over $MgSO_4$ and evaporated to obtain

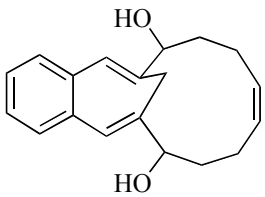
pale yellow residue. Chromatography purification on silica gel (hexane : ethyl acetate = 4:1) afforded a clear oil mixture of two isomers, and used in next step without further purification.



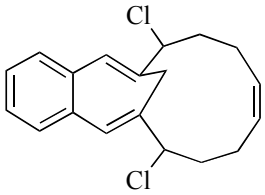
3,4-benz-1,6-bis(1-acetoxypentenyl)-1,3,5-cycloheptatriene (31) : To a suspension of 3,4-benz-1,6bis-(1-hydroxypentenyl)-1,3,5-cycloheptatriene (30) in acetic anhydride (30mL) at 0℃, pyridine (3mL) was added slowly into the reaction, then ice bath was removed and the reaction mixture was stirred at room temperature overnight. The reaction was quenched by diluted HCl (120mL) and extracted with diethyl ether (3 X 100mL). The organic layer was washed with saturated $NaHCO_3$ solution and water (100mL), the organic layer was dried over $MgSO_4$ and evaporated to afford colorless residue. The residue was purified by chromatography (hexane : ethyl acetate = 8:1) to afford a white solid mixture of two isomers, in two steps (1.39g, 44% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.29(m, 2H), 7.24(m, 2H), 6.59(s, 2H), 5.84(m, 2H), 5.43(t, *J* = 6.6 Hz, 2H), 5.03(m, 2H), 2.63(d, *J* = 14.3 Hz, 1H), 2.35(d, *J* = 14.3 Hz, 1H), 2.11(m, 10H), 1.90(m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.0, 138.7, 137.4, 135.5, 130.5, 127.0, 126.2, 115.3, 76.9, 32.6, 28.7, 26.9, 21.2



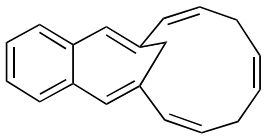
3,4-benzo-7,14-diacetoxy-7,8,9,12,13,14-hexahydro-1,6-methano[14]annulene (32) : 3,4-benz-1,6-bis(1-acetoxypentenyl)-1,3,5-cycloheptatriene (1.39g, 3.53mmol) was dissolved in fresh distilled dichloromethane (150mL) at room temperature under argon, followed by addition of bis(tricyclopentylphosphine)benzylidine ruthenium(IV) dichloride (290mg, 0.35mmol), the reaction mixture was stirred at room temperature for 48 hours and further stirred under refluxing for 24 hours. After evaporation of solvent, the residue was purified by column chromatography (hexane : ethyl acetate = 8:1) to obtain compound (32) as an off white solid mixture of two isomer (0.567g, 44% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.88(m, 2H), 7.86(m, 2H), 7.48(m, 2H), 6.29(m, 2H), 5.60(br s, 2H), 2.23(m, 12H), 1.87(m, 2H), 1.72(m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.3, 137.2, 133.2, 129.9, 127.9, 126.4, 70.2, 66.0, 60.5, 35.3, 22.9, 21.4



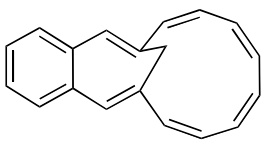
3,4-benzo-7,14-dihydroxy-7,8,9,12,13,14-hexahydro-1,6-methano[14]annulene (33) : 3,4-benzo-7,14-diacetoxy-7,8,9,12,13,14-hexahydro-1,6-methano[14]annulene (0.54g, 1.47mmol) was treated with methanol (34mL), and 3N $NaOH_{(aq)}$ (4.5mL) under nitrogen and stirred at 0℃ for 3 hours. The reaction mixture was quenched by ice-cold brine (30mL) and extracted with diethyl ether (100mL). Then the organic layer was further washed with ice-cold brine (100mL), dried over $MgSO_4$ and finally evaporated to afford a white solid residue. The residue was recrystallized from dichloromethane to obtain colorless crystals (0.415g, 99% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.26 (m, 2H), 6.63(br s, 2H), 5.51(br s, 2H), 4.34(br s, 2H), 2.46(br s, 2H), 1.98(br m, 8H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 175.1, 141.9, 136.2, 130.2, 126.1, 124.6, 79.5, 53.4, 28.6, 20.7



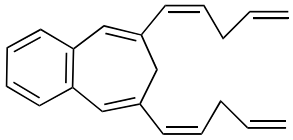
3,4-benzo-7,14-dichloro-7,8,9,12,13,14-hexahydro-1,6-methano[14]annulene (34) : 3,4-benzo-7,14-dihydroxy-7,8,9,12,13,14-hexahydro-1,6-methano[14]annulene (33) (0.415g, 1.47mmole) in dichloromethane (5mL) was treated with thionyl chloride (2mL, 10.4mmol) in a 15mL round bottom flask under argon. Pyridine (1.5mL) was added slowly into the reaction mixture with ice bath cooling. After 90 minutes of stirring, the ice bath was removed and the reaction mixture was stirred at room temperature for additional 30 minutes. Then, the reaction mixture was quenched by ice-cold brine and extracted with dichloromethane. The organic layer was washed with water and evaporated to afford a yellow oil residue. The residue was carried on the next step without further purification.



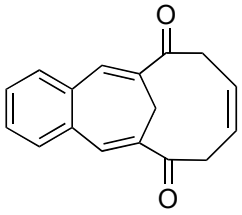
3,4-benzo-1,6-methano-9,12-dihydro[14]annulene (35) : To a solution of compound (34) (0.455g, 1.4mmol) in (50mL) THF was added potassium tert-butoxide (0.12g, 1.07mmol) at 0^{o}C. After 40 minutes of stirring, the reaction mixture was slowly warmed up to room temperature and quenched by ice-cold brine (50mL). Then it was extracted with dichloromethane (2 X 50mL), and the organic layer was washed with ice water, dried over $MgSO_4$ and evaporated to obtain an oil residue which was then purified by column chromatography on aluminum oxide using hexane : ethyl acetate (10 : 1) as eluent to afford the light yellow product (35) in 31mg, 9%yield. ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.47(m, 2H), 7.30(m, 2H), 6.50(d, J = 1.4 Hz, 2H), 6.15(dd, J = 10.1, 1.5 Hz, 2H), 5.55(m, 2H), 5.44(m, 2H), 2.82(t, J = 6.5 Hz, 4H), 2.32(s, 2H)



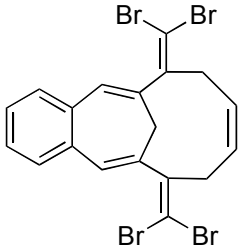
3,4-benzo-1,6-methano[14]annulene (4) : (a) To a solution of 3,4-benzo-1,6-methano-9,12-dihydro[14]annulene (1.17g, 4.76mmol) in carbon tetrachloride (150mL) under nitrogen, was added N-bromosuccinimide (1.31g, 7.36mmol) and azobisisobutyronitrile (97mg, 0.59mmol). The reaction was stirred at reflux for 1.5h, cooled to room temperature, then filtered and evaporated. The crude was dissolved in THF (50mL), under nitrogen and stirred at 0^oC, with added potassium tert butoxide (1.05g, 9.4mmol). Stirring continued at 0^oC for 1.5h. Then it was warmed up to room temperature for additional 1h. The reaction was quenched by addition of HCl (1mL) in ice-cold salt solution (200mL), extracted with ether (3 X 100mL), which was dried over $MgSO_4$ and evaporated. Flash column chromatography didn't yield any useful compound.



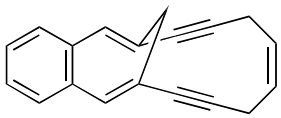
3,4-benz-1,6-bis(1,4-pentadiene)-1,3,5-cycloheptatriene (36) : Dissolved butenetriphenylphosphene bromide (3.51g, 8.84mmol) in THF (50mL), under nitrogen and stirred at -75^oC. Then drop in 0.6M SHMDS (14mL, 8.4mmole), after drop finish let reaction warm to room temperature for an hour. Cool to -75^oC and dropwise added dialdehyde (22) (0.799g, 4mmol) in THF (30mL), drop finish let reaction warm to room temperature for 2 hours. Quench reaction by using HCl (1mL) in ice-cold salt solution (100mL). Extracted with ether (2 X 100mL). Dried over $MgSO_4$ and evaporated ether. After column chromatography get product (36) (770mg, 70% yield). ^1H NMR (500 MHz, $CDCl_3$) : δ = 7.31(m, 2H), 7.21(m, 2H), 6.56(s, 2H), 6.12(d, J = 11.5 Hz, 2H), 5.81(m, 2H), 5.55(m, 2H), 5.01(m, 4H), 2.97(m, 4H), 2.53(s, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 136.9, 136.6, 136.2, 131.8, 130.3, 129.3, 128.1, 125.7, 115.2, 35.3, 33.1; MS (EI / 70 eV) m/z M^+ 274, 178.



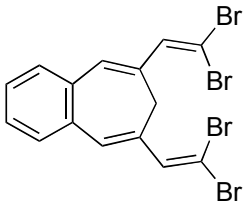
3,4-benzo-1,6methano-7,12-diketon-8,11-dihydro[12]annulene (37) : Dissolved diol compound (37) (1.45g, 5.7mmol) in dry acetone (100mL), under nitrogen and stirred at room temperature. Added Jones reagent (16.3mL, 22.8mmol) drop wise to the reaction, and stirred for 1h. Quench by added isopropanol (10mL), then added ice-cold salt solution (200mL) and extracted with ether (3 X 150mL). Dried ether layer over $MgSO_4$, and evaporated solvent. Gave yellow solid (720mg). After column gave colorless crystal (540mg, 38% yield). Mp: 218-220℃. ^1H NMR (500 MHz, $CDCl_3$) : δ = 7.56(m, 4H), 7.41(m 2H), 5.56(m, 2H), 4.26(m, 2H), 3.72(d, J = 14.7 Hz, 1H), 3,14(dd, J = 11.7, 4.8 Hz, 2H), 2.13(d, J = 14.8 Hz, 1H); ^{13}C-NMR (125MHz, $CDCl_3$): δ = 198.9, 136.1, 136.0, 135.4, 132.2, 128.4, 126.7, 41.3, 26.9; MS (EI / 70 eV) m/z M^+ 250, 140



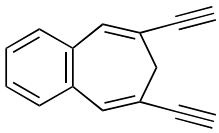
3,4-benzo-1,6-methano-7,12-bisdibromomethylene-8,11-dihydro[12]annulene (38) : Dissolved the triphenylphosphine (2.83g, 10.8mmol) in toluene (20mL), under nitrogen and stirred at room temperature. Then added carbon tetra bromide (1.793g, 5.4mmol) in THF (10mL) drop wise. And let reaction stirred for 1h. Then drop in diketone (0.54g, 2.16mmol) in THF (20mL). After drop finish, let reaction reflux for 18h. Then stirred at room temperature for 116h. Quench by added ice-cold salt solution (200mL), extracted with ether (3 X 100mL). Dry over $MgSO_4$, and evaporated solvent yield yellow crude 4g. Column chromatography gave colorless crystal (520mg, 43% yield). Mp: 208-210℃. ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.38(m, 2H), 7.30(m, 2H), 6.57(s, 2H), 5.39(m, 2H), 3.33(m, 4H), 2.87(d, *J* = 13.7 Hz, 1H), 2.59(d, *J* = 14.3 Hz, 1H); ^{13}C-NMR (125MHz, $CDCl_3$): δ = 1147.7, 143.5, 138.1, 135.7, 130.3, 128.7, 126.7, 88.0, 37.7, 31.2



3,4-benzo-1,6-methano-7,13-didehydro-9.12-dihydro[14]annulene (39) : The tetrabromide (38) (800mg, 1.42mmol) was dissolved in THF (100mL), kept under nitrogen, and stirred at -78^{o}C. Then it was treated with n-butyllithium 2.5M in hexane (3.5mL, 8.75mmol) drop wise over a period of 8 minutes. After addition was complete, the reaction was stirred at -78 for additional 1h. Then the reaction was allowed to warm to room temperature for an additional 2h. Hydrolysis with HCl (2mL) in ice-cold salt solution (100mL) was followed by extraction with dichloromethane (2 X 100mL), drying over $MgSO_4$ and evaporation to yield 200mg crude. Column chromatography did not afford any identifiable material.



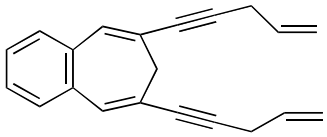
3,4-benzocycloheptatriene-1,6-bisdibromomethylene (40) : Triphenylphosphine (48.03g, 0.18mol) was dissolved in dry dichloromethane (250mL), kept under nitrogen and stirred at 5℃. Then, CBr_4 (32.21g, 0.097mol) was added in dry dichloromethane (50mL) and stirred for 5 min. followed by dialdehyde 22 (9.35g, 0.047mol) in dry dichloromethane (100mL). Stirring continued for an additiional 10min. at which time the reaction was quenched with ice-cold salt solution (250mL), extracted with dichloromethane (2 X 100mL), Dried with $MgSO_4$ and evaporated. Column chromatography of the crude product afforded colorless crystals (8g, 33% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.38(m, 2H), 7.32(m, 2H), 7.21(s, 2H), 6.95(s, 2H), 2.86(s, 2H); MS (EI / 70 eV) m/z M^+ 510, 350, 189.



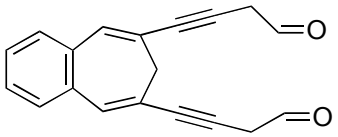
1,6-diethynyl-3,4-benzocycloheptatriene (41) : (a) Tetrabromide compound 40 (4g, 7.8mmol) was dissolved in THF (250mL), kept under nitrogen and stirred at -68℃. It was then treated with n-butyllithium 2.5M in hexane solution (14mL, 35mmol) in a dropwise manner over 40min. and then stirred for an hour. The reaction was quenched with HCl (2mL) in ice-cold salt solution (200mL), extracted with dichloromethane (2 X 100mL), which was dried over $MgSO_4$ and evaporated. After column chromatography of the crude yielded product (41) in (0.47g, 31% yield).

(b) Dimethyl 2-oxopropylphosphonate (2.0g, 12mmol), p-toluenesulfonyl azide (2.4g, 12mmol), and potassium carbonate (4.14g, 30mmol) were dissolved in dry acetonitrile (150mL), kept under nitrogen and stirred at room temperature for 3hrs. Compound (22) (0.99g, 5mmol) was added in THF (30mL)/methanol (30mL) mix solvent and the reaction was allowed to stir at room temperature for 19 hrs. Stirring was continued at 58℃ for an additional 24hrs at which time the reaction was quenched by addition of ice-cold salt solution (200mL) The aquueous layer was extracted with ether (2 X 50mL)which was dried over $MgSO_4$, and evaporated to afford brown crude 2g. After column chromatography, product (41) was obtained. (4mg, 0.4% yield).

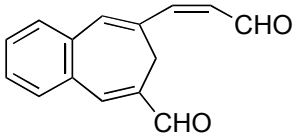
(c) A solution of Trimethylsilyl) diazomethane (2.0M in Ethyl ether, (6mL, 12mmol) was added drop wise to a solution of LDA, prepared from diisopropylamine (1.444g, 14mmol), and n-butyllithium (2.5M hexane solution, 5.7mL, 14mmol) in THF (10mL) at -78℃ under nitrogen and stirred for 30 minutes. A solution of aldehyde (22) (0.99g, 5mmol) in THF (30mL) was then added drop wise at -78^{o}C for 1 hr. then heated under reflux for 3 hrs. After a quench with ice-cold salt solution, the mixture was extracted with ether. The organic layer was dried over $MgSO_4$ and evaporated. The residue was purified by column chromatography to gave product (41) (310mg, 33% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.31(m, 4H), 7.03(s, 2H), 3.00(s, 2H), 2.80(s, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 136.7, , 135.8, 130.7, 127.4, 119.7, 85.8, 75.9, 35.6; MS (EI / 70 eV) m/z M^{+} 189, 163, 94.



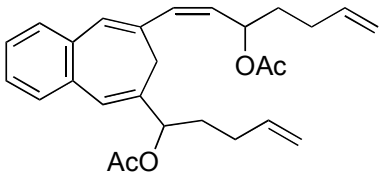
3,4-benz-1,6-bis(pentenyl-1-yne)-1,3,5-cycloheptatriene (42) : Diacetylene (41) (0.395g, 2.1mmol)was dissolved in THF (40mL), kept under nitrogen and stirred at 0^{o}C. There was added drop wise isopropylmagnesium bromide solution 2M in THF (3mL, 6mmol), and copper iodide (0.19g, 1mmol), and allyl bromide (0.7g, 5.8mmol) in THF (10mL). After addition was complete, the reaction was allowed to warm-up to room temperature and then it was refluxed for 1h. It was then stirred overnight at room temperature. Quenching of the reaction with HCl (1mL) in ice-cold salt solution (100mL). was followed by extraction with ether (3 X 100mL), drying over $MgSO_4$ and evaporation of solvent. Crude product 0.9g. was subjected to column chromatography to afford oily product (0.269g, 74% yield).



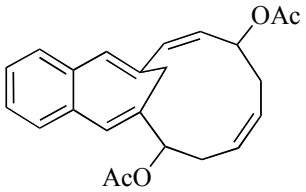
3,4-benz-1,6-bis(4-butylaldehyde-1-yne)-1,3,5-cycloheptatriene (43) : Compound (42) (0.2694g, 1mmol) was dissolved in a mixed solvent of freshly distilled 1,4-dioxane (150mL) and deionized water (50mL), and stirred at room temperature. Osmium tetroxide 2.5 wt% in t-butyl alcohol (0.6mL, 0.6mmol) was then added and the mixture was then stirred until the solution turned black (about 30 minutes). Then sodium periodate (0.909g, 4.2mmol) was added in small portions and the reaction temperature was kept between 26 to 28^{o}C. Half an hour after the last portion was added, stirring was stopped and the white precipitate was filtered off. The solution was diluted with ether (300mL) and washed with 30% sodium thiosulfate until the washings were free of precipitate and color. Did not get any product after wash.



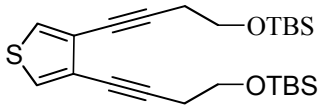
Formylmethyltriphenylphosphorane (3.34g, 11mmol) was dissolved in toluene (120mL), followed by dropwise addition of aldehyde compound (22) (2g, 10mmol) in THF (50mL). The reaction was kept under nitrogen and stirred at 80^{o}C overnight. Quenching was done with an ice-cold salt solution (200mL) of brine and the aqueous layer was extracted with ethyl acetate (200mL). The organic layer was dried over $MgSO_4$ and evaporated to give 2g. Of crude product. After column chromatography, the desired compound was obtained (0.6g, 27% yield), along with recovered starting material (1g, 50% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 9.69(d, *J* = 7.4 Hz, 1H), 9.62(s, 1H), 7.57(d, *J* = 7.2 Hz, 1H), 7.48(m, 4H), 7.24(m, 1H), 7.04(s, 1H), 6.72(dd, *J* = 15.6, 7.4 Hz, 1H), 3.05(s, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 193.7, 191.2, 152.9, 147.3, 139.4, 138.2, 136.8, 136.7, 134.7, 132.1, 131.9, 129.7, 129.6, 128.5, 21.2



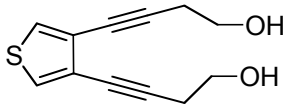
Dissolved compound (47) (1g, 4.5mmol) in THF (20mL), under nitrogen and stirred at -70^{o}C. Add allyl magnesium bromide (1.0M, 13.6mL, 13.6mmol) drop wise, and stirred for 100 minuets. Then add isopropanol (1mL), and stirred for additional 20 minuets. Add the acetic anhydride (3.5mL, 32mmol), and DMAP (0.5g, 4mmol) in THF (5mL), let reaction stirred over night, the temperature from -70℃ worm up to room temperature. Quench by add ice-cold ammonia chloride solution, and aqua layer extracted with ether (2 X 100mL). Dried over $MgSO_4$ and evaporated solvent get crude 1.72g. After column chromatography get product (470mg, 27% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.23(m, 2H), 7.25(m, 2H), 6.63(d, *J* = 15.4 Hz, 2H), 6.46(dd, *J* = 15.7, 5.3 Hz, 1H), 5.99(dd, *J* = 15.7, 7.5 Hz, 1H), 5.79(m, 1H), 5.65(m, 1H), 5.46(m, 2H), 5.08(m, 4H), 2.79(dd, *J* = 13.9, 6.0 Hz, 1H), 2.50(m, 5H), 2.09(m, 6H);



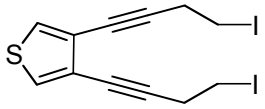
3,4-benzo-1,6-methano-9,14-diacetate-10,13-dihydro[14]annulene (49) : Compound (48) (230mg, 059mmol) in dry dichloromethane (100mL), under nitrogen and stirring at room temperature was treated with the Grubb's first generation catalyst (24.7g, 0.03mmol). The reaction was stirred for 2 days. Solvent removal and flash chromatography did not permit isolation of any useful product.



3,4-bis(4-(tert-butyldimethylsilyloxy)-1-butynyl)thiophene (67) : A solution of 3,4-dibromothiophene (65) (2.42g, 20mmol), $PdCl_2(PPh_3)_2$ (562mg, 0.8mmol), and CuI (152mg, 0.8mmol) in piperidine (40mL) was stirred under argon at room temperature. TBS protected 3-butyne-1-ol (11.04g, 60mmol) was then added drop wise . After addition was complete, the color changed to brown, and the reaction was refluxed for 20h. Quenching by addition of HCl (20ml) in ice cold water (100mL) was followed by extraction with ether (3 X 100mL) which was dried over $MgSO_4$ and evaporated to afford a brown oil. Flash column chromatography gave product (67) as a yellow oil (4.29g, 48% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.29(s, 2H), 3.82(t, *J* = 14.8 Hz, 4H), 2.65(t, *J* = 14.8 Hz, 4H), 0.91(s, 18H), 0.08(s, 12H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 127.6, 125.4, 89.1, 75.7, 62.2, 26.1, 24.1, 18.5, -5.1

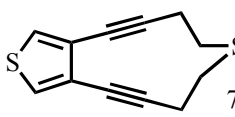


3,4-bis(3-butynyl-1-ol)thiophene (68) : Dissolved TBS protacted alcohol (67) (4.29g, 9.6mmol) in THF (10mL) under nitrogen, stir. Then added TBAF 1.0M in THF (7.83g, 30mmol). Let reaction stir at room temperature for 2 hours. Quench reaction by add HCl (2mL) in ice-cold water (100mL), extracted with ether (3 X 100mL), the ether layer was washed with cold brine (100mL), dried over $MgSO_4$ and evaporated. Column chromatography gets colorless oil compound (68) (1.5g, 71%yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.33(s, 2H), 381(t, *J* = 11.8 Hz, 4H), 2.72(t, *J* = 11.8 Hz, 4H), 2.18(s, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 127.7, 125.1, 89.1, 77.0, 60.9, 24.1; MS (EI / 70 eV) m/z M^+ 281, 220, 171, 115.



3,4-bis(3butynyl-1-iodo)thiophene (69) : To a cold solution of triphenylphosphine (3.93g, 15mmol), imidazole (2.04g, 30mmol) in dichloromethane (30mL), iodine (3.81g, 15mmol) was added under nitrogen and the mixture was stirred for 30 minutes, at which time a yellow cloudy

solution forms. The dialcohol compound (68) (1.5g, 6.8mmol) was then added in dichloromethane (13mL) drop wise. Let reaction was stirred for 7 hours. It was then quenched by addition of ice-cold water (100mL), followed by extraction with ether (3 X 100mL), drying over $MgSO_4$, evaporation, and finally column chromatography, to afford yellow oil diiodo compound (69) (0.3g, 10% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.35(s, 2H), 3.33(t, *J* = 14.6 Hz, 4H), 3.04(t, *J* = 14.6 Hz, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 127.7, 125.2, 89.1, 77.1, 60.9, 24.1; MS (EI / 70 eV) m/z M^+ 440, 281, 207.



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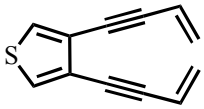

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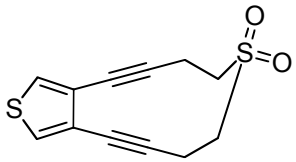
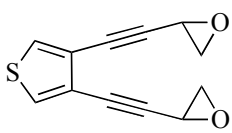
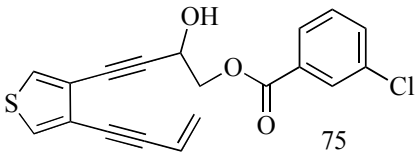
6,7(3,4thiophene)-1-thiocycloundeca-4,5,8,9-diyne (70) : To a solution of diiodo compound (69) (0.308g, 0.7mmol) in100% ethanol (10mL) was added dropwise a solution of sodium sulfide nonahydrate (360mg, 1.5mmol) in ethanol (10mL). The reaction was kept under nitrogen and stirred for 1 hour. Then it was quenched with water and extracted with ethyl acetate. The solvent was removed, followed by column chromatography to afford elimination product (71) (43mg, 0.23mmole, 33% yield) and cyclic sulfide (70) (90mg, 0.41mmole, 59% yield). Compound (70) ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.23(s, 2H), 2.95(t, *J* = 7.5 Hz, 4H), 2.68(t, *J* = 7.5 Hz, 4H); MS (EI / 70 eV) m/z M^+ 218, 171; Compound (71) ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.39(s, 2H), 6.03(dd, *J* = 17.5, 11.5 Hz, 4H), 5.75(dd, *J* = 17.5, 2 Hz, 2H), 5.56(dd, *J* = 11.5, 2.5 Hz, 2H);



6,7-(3,4-thiophene)-1-(s,s-dioxide)thiocycloundeca-4,5,8,9-diyne (72) : A solution of the cyclic sulfide (70) (90mg, 0.4mmol), $(NH_4)_6Mo_7O_{24}$- $4H_2O$ (188mg, 0.15mmol), and a suspension of silica gel (50mg) in dry THF (5mL) under nitrogen was stirred at 0^{o}C. A 30% H_2O_2 in H_2O (0.5mL, 4.8mmol) reagent was then added dropwise, followed by stirring at room temperature for 2h. Quenching the reaction by filtration through filter paper yielded a clear solution. After evaporation of solvent, there was obtained an off-white solid product (100mg, 100% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.24(s, 2H), 3.54(t, *J* = 5.4 Hz, 4H), 3.03(t, *J* = 5.4 Hz, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 126.6, 125.0, 96.3, 92.3, 54.7, 14.7



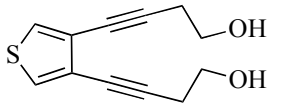
74



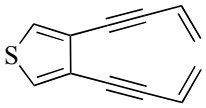
75

3,4-bis(2-ethynyloxirane)thiophene (74) : Compound (71) (400mg, 2.17mmol)was dissolved in dry chloroform (10mL)., kept under nitrogen and stirred at 0^{o}C. Dropwise addition of m-CPBA (1.1g, 6.4mmol) in chloroform (15mL) was followed by a TLC analysis which shoed incomplete reaction. The solution was allowed to warm to room temperature and an additional portion of m-CPBA (0.5g, 3.0mmol) in chloroform (10mL) was introduced. The reaction was stirred at room

temperature for 3 hours and then allowed to stand at -4°C overnight. Again, the reaction was warmed to room temperature and a further batch of m-CPBA (1g. 5.6mmol) in chloroform (10mL) was added and the reaction was stirred for an additional 4 hours. Finally, it was quenched by adding ice-cold saturated sodium bicarbonate (100mL), and followed by extraction with ether (3 X 100mL) which was dried over $MgSO_4$ and evaporated. Column chromatography gave no desired compound (74) and only get starting material was recovered along with a small amount of compound (75) (39mg, 5% yield).

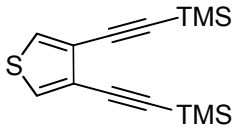


68

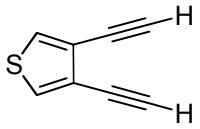


71

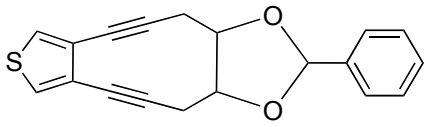
3,4-bis(3-butynyl-1-ol)thiophene (68) : A solution of compound (71) (420mg, 2.3mmol) in dry THF (20mL), under nitrogen was stirred at 0°C and treated with diborane (23.5mg, 1.68mmol) via dropwise addition.. The reaction was stirred at room temperature for 2 hours. For workup, it was cooled to 0°C, and sodium hydroxide (1.5mL of a 3M solution) and 30% hydrogen peroxide (1.5mL) were added drop wise. Then the solution was warmed to room temperature and stirred for 2 hours. The reaction was then treated with ice-cold sodium bicarbonate (50mL), and extracted with ether (3 X 50mL) which was dried over $MgSO_4$ and evaporated. Column chromatography gave 400mg of recovered starting material (71), and nothing more.



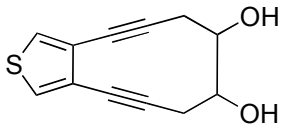
3,4-Bistrimethylsilylethynylthiophene (80): A mixture of CuI (78mg, 0.4mmol), $PdCl_2(PPh_3)_2$ (284mg, 0.4mmol), TMSA (2.94g, 30mmol), and 3,4-dibromothiophene (2.42g, 10mmol) in a 50 mL round bottom flask was stirred under nitrogen. Then piperidine (20mL) was added and the reaction was refluxed for 17 hours. Quenching by addition of HCl (16mL) in water (100mL)was followed by extraction with ethyl ether (3 X 100mL).After drying and solvent removal the crude was subjected to flash chromatography to afford colorless oil compound (80) (1.3g, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.40(s, 2H), 0.26(s, 18H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 129.1, 125.3, 98.2, 96.9, 0.2; MS (EI / 70 eV) m/z M^+ 276, 261, 73.



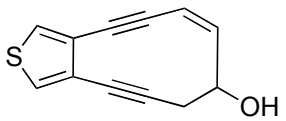
3,4-diethynylthiophene (76): Compound (80) (1.3g, 4.7mmol) was dissolved in methanol (40mL)and then treated with K_2CO_3 (1.56g, 11mmol) in 6ml water, and stirred for 1hour. Then, the reaction was quenched by addition of ice cold water (50mL) and extracted with ethyl ether (3 X 50mL) which was then dried over $MgSO_4$ and evaporated. Flash column chromatography afforded a colorless oil compound (76) (0.61g, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.49(s, 2H), 3.22(s, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 130.1, 124.1, 79.7, 77.4; MS (EI / 70 eV) m/z M^+ 132



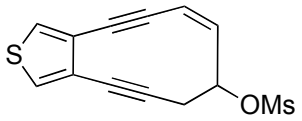
3,4-(3,4-thiopheno)-cyclodeca-1,2,5,6-diyne-8,9-diol-benzylidenacetal (85) : A solution of thiophene-3,4-diacetylene (76) (0.66g, 5mmol) in THF (200mL), under nitrogen and stirred at -30^{o}C was treated with n-butyllithium (1.6M in hexane, 8mL, 12.8mmol) and stirred for 30 minutes at which time HMPTA (4mL, 23mmol) was added and stirring was continued for an additional 10 minutes. The, compound (77) (3.13g, 6.6mmol) in THF (60mL) was added dropwise and the reaction was stirred overnight. Quenching was done with with ice-cold salt solution (100ml), and the aqueous solution was extracted with ether (2 X 100mL). The ether layer was dried over $MgSO_4$ and evaporated, and then column chromatography of the residue gave benzylidene product 78 (324mg, 21% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.50(m, 2H), 7.41(m, 3H), 7.20(dd, *J* = 8.4, 2.9 Hz, 2H), 5.90(s, 1H), 4.45(m, 2H), 3.06(dd, *J* = 16.7, 3.1 Hz, 1H), 3.01(dd, *J* = 16.5, 3.4 Hz, 1H), 2.85(dd, *J* = 16.6, 10.8 Hz, 1H), 2.70(dd, *J* = 16.7, 10.5 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 136.2, 129.7, 128.5, 127.8, 126.6, 123.3, 123.1, 102.6, 92.7, 91.8, 82.2, 81.1, 80.3, 80.2, 26.1, 25.3; MS (EI / 70 eV) m/z M^+ 307



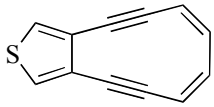
3,4-(3,4-thiopheno)-cyclodeca-1,2,5,6-diyne-8,9-diol (82) : A solution of benzylidene compound (78) (140mg, 0.46mmol) in dry acetonitrile (50mL), under nitrogen and stirred at 50^{o}C was treated with triphenylcarbenium tetrafluoroborate (0.445g, 1.38mmol) and then stirred overnight. Quenching with ice-cold salt solution (100mL), extraction with ether (2 X 100mL), drying the ether layer over $MgSO_4$ and evaporation gave crude material.. After column chromatography, only starting material (100mg, 71%) was recovered.



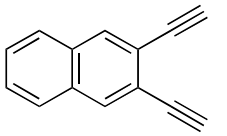
3,4-(3,4-thiopheno)-cyclodeca-1,2,5,6-diyne-7-ene-9-ol (83) : A solution of benzylidene compound (78) (324mg, 1.06mmol) in dry THF (80mL) was stirred under nitrogen at -70^{o}C. Then, n-butyllithium 1.6M in hexane solution (2.5mL, 4mmol) was added dropwise, and the reaction was stirred for 1 hour. The solution was allowed to warm to 0^{o}C and it was stirred for an additional 1hr. It was then quenched by an acidified ice-cold salt solution (HCl 0.35mL), and extracted with ether (3 X 100mL). The organic layer was dried over $MgSO_4$ and evaporated followed by column chromatography to yield recovered starting material (25mg, 8%) and the enediyne alcohol product (83) (71mg, 33% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.31(d, *J* = 2.9 Hz, 1H), 7.23(d, *J* = 2.9 Hz, 1H), 6.14(dd, *J* = 11.6, 6.2 Hz, 1H), 5.86(dd, *J* = 11.6, 1.4 Hz, 1H), 4.91(s, 1H), 2.77(m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 145.6, 129.8, 129.5, 123.9, 122.7, 110.4, 96.9, 93.8, 80.8, 28.8



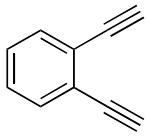
3,4-(3,4-thiopheno)-cyclodeca-1,2,5,6-diyne-7-ene-9-methanesulfonate (79) : A solution of the enediyne alcohol (83) (62mg, 0.31mmol) in dry dichloromethane (20mL), sirring under nitrogen at 0°C was treated with triethylamine (0.13mL, 0.93mmol), and then methanesulfonyl chloride (0.18mL, 2.33mmol) in dry dichloromethane (10mL) dropwise over a period of 40 minutes. The reaction was stirred for an additional 1hr. It was then quenched by adding ice-cold salt solution (100mL) acidified with HCl (0.15mL). Then it was extracted with dichloromethane (20mL) which was dried over $MgSO_4$. Evaporation of solvent, gave crude 64 mg. Which was used directly in the next step without purification. ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.35(d, *J* = 2.8 Hz, 1H), 7.26(d, *J* = 2.9 Hz, 1H), 6.12(dd, *J* = 11.5, 6.2 Hz, 1H), 5.97(dd, *J* = 11.5, 1.5 Hz, 1H), 5.71(m, 1H), 3.04(s, 3H), 1.36(t, *J* = 7.3 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 139.2, 129.2, 124.6, 112.6, 95.5, 94.1, 81.9, 52.7, 46.4, 39.5, 31.7, 27.8, 9.5



3,4-(3,4-thiopheno)-cyclodeca-1,5-diyne-7,9-diene (53) : A solution of mesylate (79) (64mg, 0.23mmol) in THF (30mL), was stirred under nitrogen at 0°C and treated with DBU (0.17mL, 1.15mmol), and then stirred for 1 hour. The reaction was then heated up to 50°C for 2 hour. After TLC showed no reaction,, the solution was cooled to 0°C and then treated with solid potassium tert-butoxide (52mg, 0.46mmol) and stirred for 30 minutes. Quenching with HCl (0.2mL) in ice-cold salt solution (50mL), extraction with ether (2 X 50mL), drying the organic layer over $MgSO_4$ and evaporation gave crude material, which after column chromatography afforded no characterizable material.

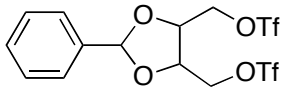


84



90

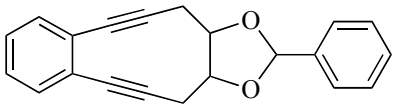
2,3-Diethynylnaphthalene[50] (84) and 1,2-Diethynylbenzene[51] (90) were synthesized according to the literature procedures.



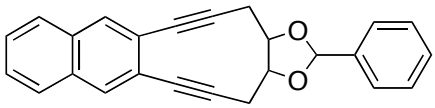
2,3-O-Benzylidene-1,4-O-trifluoromethanesulfonyl-D-threitol[52] (77) : 2,3-O-Benzylidene-1,4-O-trifluoromethanesulfonyl-D-threitol[51] (77) : A dried 250mL RBF was charged under argon with 2,3-O-benzylidene-1,4-D-threitol (4.62g, 22mmol), freshly distilled pyridine (4.6mL, 46mmol) and dry dichloromethane (90mL). The reaction was cooled to -30°C to -35°C. A solution of freshly distilled (from P_2O_5) trifluoromethanesulfonic anhydride (12.7g, 45mmol) in dichloromethane (80mL) was added slowly over a period of 70 minutes. The temperature was maintained at -30°C. Stirring was continued while allowing the temperature to rise to 0°C. Hydrolysis with ice water (100mL) and washing the reaction with an additional portion of ice water (150mL) and drying the organic layer over $MgSO_4$ gave the crude solution of the triflate. It

was filtered and the solvent was carefully evaporated on a good rotary evaporator. Anhydrous benzene was added twice and each time evaporated at 4 torr with no heat. The dry triflate was a colorless oil. Its NMR was identical with that reported by Funk.
It was dissolved in anhydrous THF (100mL) and divided into two equal parts.

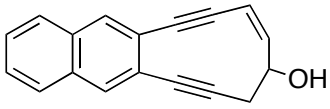
The cyclization of the bis-triflate (77) with 1,2diethynylbenzene and 2,3-dethynylnaphthalene was carried out as reported by Funk et al.



3,4-benzo-cyclodeca-1,2,5,6-diyne-8,9-diol-benzylidenacetal (91) : In a 500mL RBF under argon, the 1,2-diethynylbenzene (900mg, 7.14mmol) was dissolved in freshly distilled THF (250mL). At -35^{o}C a 1.6M solution of n-BuLi inhexane (10mL) were added rapidly via a syringe. The solution was allowed to warm to -10^{o}C and freshly distilled HMPTA (6mL) were added. The solution was warmed up to 15^{o}C and the prepared triflate about (50mL) diluted with an additional anhydrous THF (100mL) added over a period of 2 hours. The reaction mixture was hydrolyzed in an ice bath with ice water (15mL). Most of the THF was removed at room temperature on a rotary evaporator. The dark oily residue was washed with cold brine (150mL) and extracted with ether (2 X 150mL). TLC (9:1) showed three major spots.
Chromatography on silica gel 60 with hexane / ethyl acetate (95:5) gave 160mg an oily as mixture of recovered diacetylene and compound identified as (99), followed by 1.07g of the 10-membered ring diacetylene (91) as a white crystalline solid (49%). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.51(m, 2H), 7.42(m, 3H), 7.34(m, 2H), 7.25(m, 2H), 5.90(s, 1H), 4.43(m, 2H), 3.07(m, 2H), 2.86(m, 1H), 2.70(m, 1H)

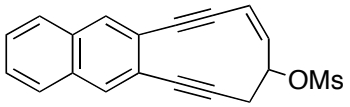


using 2,3-Diethynylnaphthalene in an analogous sequence gave compound (85) in 45% yield. ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 783(d, *J* = 7.7 Hz, 2H), 7.76(m, 2H), 7.50(m, 6H), 7.42(m, 3H), 5.93(s, 1H), 4.47(m, 2H), 3.11(m, 2H), 2.88(m, 1H), 2.75(m, 1H)

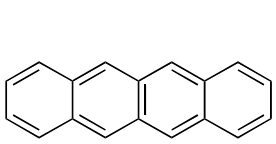


3,4-(2,3-naphthol)-cyclodeca-1,2,5,6-diyne-7-ene-9-ol (86) : A solution of acetal compound (85) (260mg, 0.74mmol) in dry THF (50mL), under argon was stirred at -70^{o}C and treated with butylithium 1.6M in hexane (2mL, 3.2mmol) added dropwise. The reaction was stirred for 45 min and then warmed to 0^{o}C and stirred for an additional 40 min. The reaction was quenched with HCl (0.3mL) in cool brine (90mL), extracted with ether (2 X 100mL). dried over MgSO4 and the organic layer was evaporated. Column chromatography afforded compound (86) (90mg, 49.8% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.89(d, *J* = 11.7 Hz, 2H), 7.79(m, 2H), 7.51(m, 2H), 6.23(dd, *J* = 11.5, 6.0 Hz, 1H), 5.91(dd, *J* = 11.5. 1.4 Hz, 1H), 5.06(br s, 1H), 2.87(m, 2H),

2.39(br s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 146.3, 132.8, 128.2, 127.9, 127.5, 126.0, 111.5, 98.2, 85.2, 29.2



3,4-(2,3-naphthol)-cyclodeca-1,2,5,6-diyne-7-ene-9-methanesulfonate (87) : A solution of compound (86) (90mg, 0.37mmol) in dry CH_2Cl_2 (25mL), under argon and stirred at 0^{o}C was treated with triethylamine (0.15g, 1.4mmol) and MsCl (0.127g, 1.1mmol) in CH_2Cl_2 (15mL). After addition was complete, stirring was continued for 1h. Work-up was done by washing with ice water (2 X 75mL) acidified with HCl (0.1mL). Drying and evaporation of solvent gave a crude material which without further purification was used in the following experiment. ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.89(d, *J* = 19.4 Hz, 2H), 7.79(m, 2H), 7.51(m, 2H), 6.18(dd, *J* = 11.5, 6.0 Hz, 1H), 6.00(dd, *J* = 11.5, 1.6 Hz, 1H), 5.87(m, 1H), 3.07(s, 3H), 3.05(m, 2H)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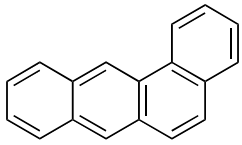
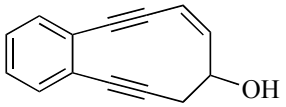
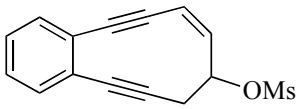

89

Tetracene (88) : Mesylate (87) was dissolved in THF (30mL), kept under argon and stirred at 5^{o}C. Solid ^{t}BuOK HOW MUCH// was added and the reaction was stirred for 35 min. at which time it was quenched with ice-cold brine (2 X 75mL), and extracted with ether (2 X 80mL). The organic layer was dried over MgSO4 and evaporated. Column chromatography of the crude yielded 50mg of an inseparable mixture of compounds (88) and (89) in a ratio is 1 to 40 as measured by a proton NMR spectrum.

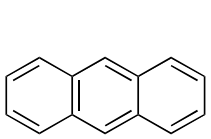


3,4-(1,2-benzo)-cyclodeca-1,2,5,6-diyne-7-ene-9-ol (92) : A solution of benzylidene compound (91) (460mg, 1.53mmol) in THF (80mL), under argon and stirred at -60^{o}C was treated with butyllithium 1.6M in hexane (2.6mL), for a period of 25 min. The reaction was then warmed to 0^{o}C for 2h. Quenching the reaction with HCl (1mL) in ice-cold brine (100mL), extraction with ether (2 X 100mL) drying the organic layer and evaporation gave a crude material which was subjected to column chromatography to afford compound (92) (210mg, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.39(m, 2H), 7.27(m, 2H), 6.17(dd, *J* = 11.6, 6.0 Hz, 1H), 5.85(dd, *J* = 11.6, 1.4 Hz, 1H), 5.01(br s, 1H), 2.84(dd, *J* = 17.3, 10.1 Hz, 1H), 2.75(dd, *J* = 16.2, 2.1 Hz, 1H);^{13}C-NMR (125 MHz, $CDCl_3$): δ = 145.9, 130.0, 128.7, 128.0, 127.9, 110.4, 98.3, 97.5, 85.2, 28.8



3,4-(1,2-benzo)-cyclodeca-1,2,5,6-diyne-7-ene-9-methanesulfonate (93) : A solution of compound (86) (210mg, 0.77mmol) in dry CH_2Cl_2 (50mL), under argon and stirred at 0^{o}C. was treated with triethylamine (282mg, 2.8mmol) and MsCl (184mg, 1.6mmol) in CH_2Cl_2 (15mL). After addition was complete the reaction was stirred for 1h. Work-up consisted of washing with

ice water (2 X 75mL) acidified by HCl (0.1mL). Drying and evaporation of solvent gave crude material which without further purification was used in the following experiment.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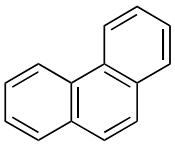

95

Anthracene (94) : Mesylate (93) was dissolved in THF (30mL), kept under argon and stirred at 5^{o}C. Solid ^{t}BuOK was added and the reaction was stirred for 35 min. It was quenched with ice-cold brine (2 X 75mL), and extracted with ether (2 X 80mL), which was dried and evaporated. Column chromatography afforded 90mg of an inseparable mixture of compounds (94) and (95) in a ratio of 3 to 2 as measured by a proton NMR spectrum.

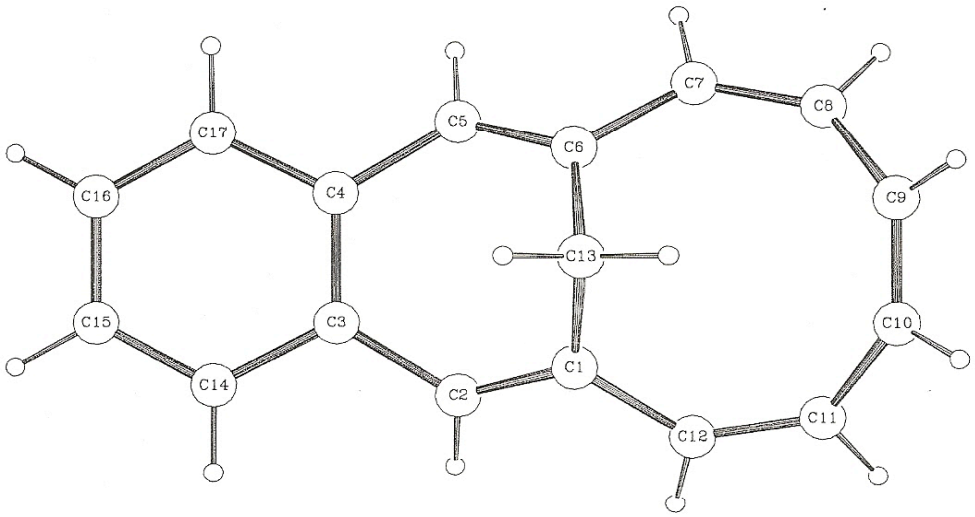


Figure 1. X-ray structure of a molecule of YY-1 at 100 K

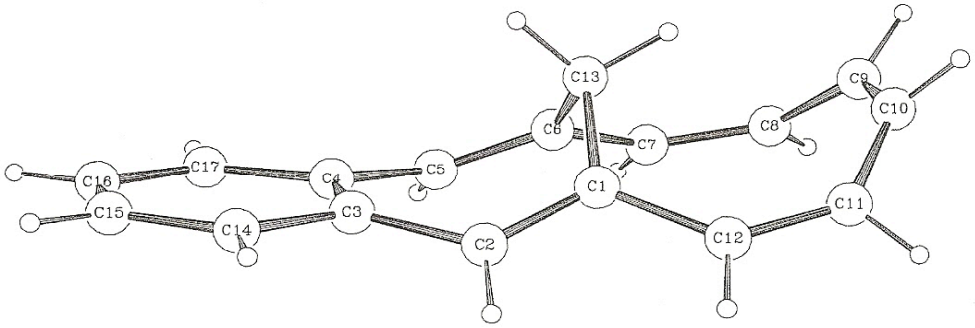
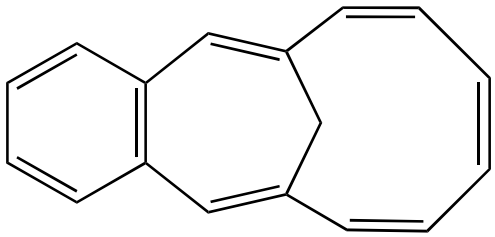


Figure 2. X-ray structure of a molecule of YY-1 at 100 K



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              Prepared by SDP2BL on   5 Oct 05 at 11:28 by TODARO
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 10 C11   C12   C13   C14   C15   C16   C17   H2A   H5A   H7A

 20 H8A   H9A   H10A  H11A  H12A  H13A  H13B  H14A  H15A  H16A

 30 H17A

Function: 501 1 15 3 3 4
Function: 421 1 -31
   31 atoms in array
Function: 55

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Function: 350
   Error in input--no atoms found
   No centroid calculated
Function: 340 9 10
   Error in input:  move atoms   9 -  10 to follow atom   0
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   C10             0.669
Name of centroid (A6): MIDB
MIDB   is atom  32
Function: 350 3 4 14 -17
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   C4              1.417
   C14             1.378
   C15             1.399
   C16             1.392
   C17             1.379
Name of centroid (A6): MIDA
MIDA   is atom  33
Function: 33

 33 atoms in file

       1     2     3     4     5     6     7     8     9    10

  0 C1    C2    C3    C4    C5    C6    C7    C8    C9    C10

 10 C11   C12   C13   C14   C15   C16   C17   H2A   H5A   H7A

 20 H8A   H9A   H10A  H11A  H12A  H13A  H13B  H14A  H15A  H16A

 30 H17A  MIDB  MIDA

Function: 121 27 27 32 32 5

H13B    MIDB       2.352  *

Function: 121 26 26 33 33 5
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H13A     MIDA        3.559
H13A     MIDA        4.579   56501

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C13      H13B        0.990
C13      C6          1.502
C13      C1          1.503

H13A     C13      H13B       108.89    0.99  0.99    1.61
H13A     C13      C6         110.85    0.99  1.50    2.07
H13A     C13      C1         110.85    0.99  1.50    2.07
H13B     C13      C6         110.85    0.99  1.50    2.07
H13B     C13      C1         110.85    0.99  1.50    2.07
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Function:
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x1538l: Bond Distances and Bond Angles

Bond	Distance		Bond	Angle
C1 - C2	1.350(2) Å		C2 - C1 - C12	120.1(1)°
C1 - C12	1.456(2) Å		C2 - C1 - C13	118.1(1)°
C1 - C13	1.503(2) Å		C12 - C1 - C13	121.7(1)°
C2 - C1	1.350(2) Å		C1 - C2 - C3	125.2(2)°
C2 - C3	1.464(2) Å			
C3 - C2	1.464(2) Å		C2 - C3 - C4	122.8(2)°
C3 - C4	1.422(3) Å		C2 - C3 - C14	118.4(2)°
C3 - C14	1.408(2) Å		C4 - C3 - C14	118.4(1)°
C4 - C3	1.422(3) Å		C3 - C4 - C5	122.3(1)°
C4 - C5	1.463(3) Å		C3 - C4 - C17	118.2(2)°
C4 - C17	1.407(2) Å		C5 - C4 - C17	119.2(2)°
C5 - C4	1.463(3) Å		C4 - C5 - C6	125.9(2)°
C5 - C6	1.350(2) Å			
C6 - C5	1.350(2) Å		C5 - C6 - C7	121.1(2)°
C6 - C7	1.451(3) Å		C5 - C6 - C13	118.2(2)°
C6 - C13	1.502(2) Å		C7 - C6 - C13	120.5(1)°
C7 - C6	1.451(3) Å		C6 - C7 - C8	130.0(2)°
C7 - C8	1.344(2) Å			
C8 - C7	1.344(2) Å		C7 - C8 - C9	134.0(2)°
C8 - C9	1.468(3) Å			
C9 - C8	1.468(3) Å		C8 - C9 - C10	133.9(2)°
C9 - C10	1.341(3) Å			

C10 - C9	1.341(3) Å	C9 - C10 - C11 133.6(2)°
C10 - C11	1.465(2) Å	
C11 - C10	1.465(2) Å	C10 - C11 - C12 133.5(2)°
C11 - C12	1.343(2) Å	
C12 - C1	1.456(2) Å	C1 - C12 - C11 130.1(2)°
C12 - C11	1.343(2) Å	
C13 - C1	1.503(2) Å	C1 - C13 - C6 104.5(1)°
C13 - C6	1.502(2) Å	
C14 - C3	1.408(2) Å	C3 - C14 - C15 122.0(2)°
C14 - C15	1.381(2) Å	
C15 - C14	1.381(2) Å	C14 - C15 - C16 119.3(2)°
C15 - C16	1.387(3) Å	
C16 - C15	1.387(3) Å	C15 - C16 - C17 120.2(2)°
C16 - C17	1.379(3) Å	
C17 - C4	1.407(2) Å	C4 - C17 - C16 121.8(2)°
C17 - C16	1.379(3) Å	

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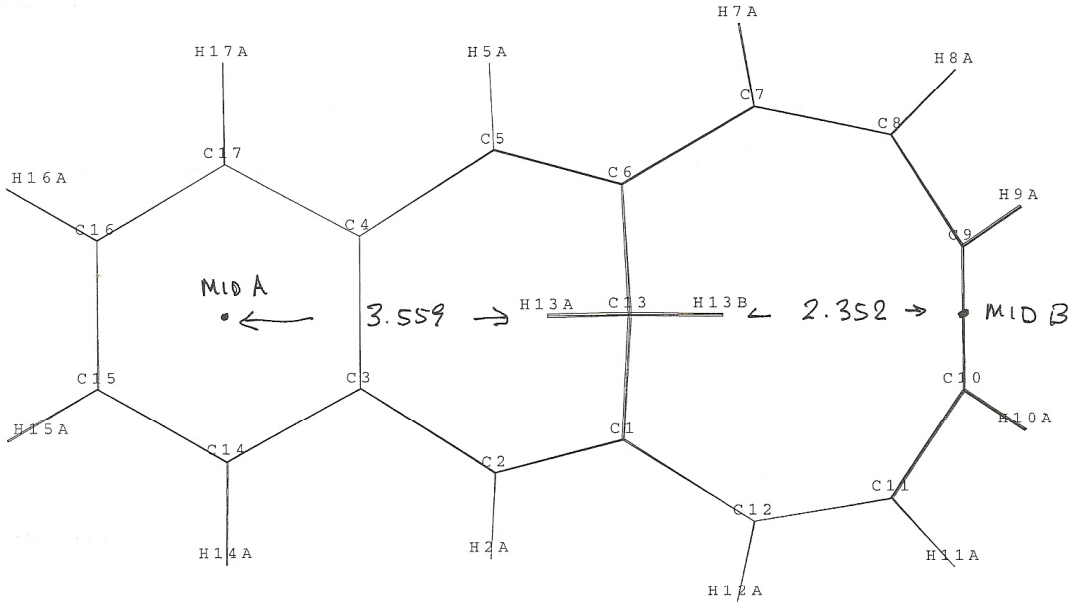
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H5A
H8A
C7
C8
C5
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C6
H16A
H9A
C16
C4
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H13A
C13
H13B
2.352
MID B
C15
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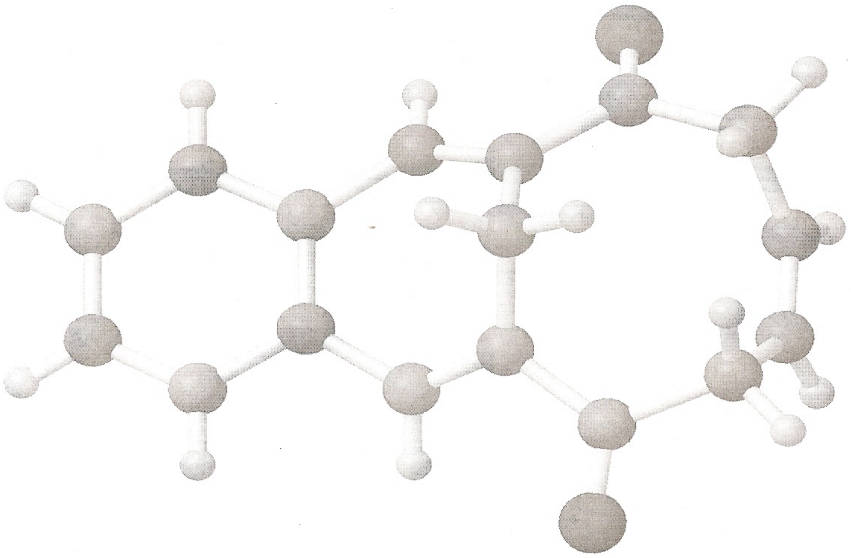

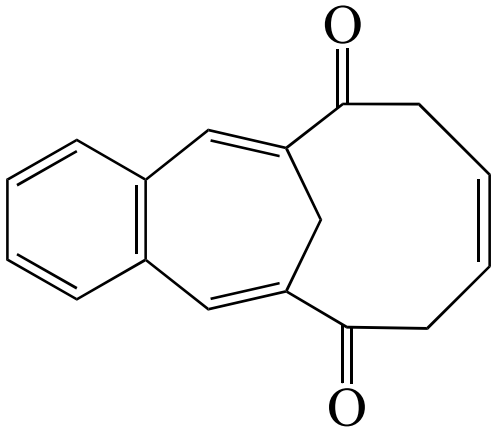
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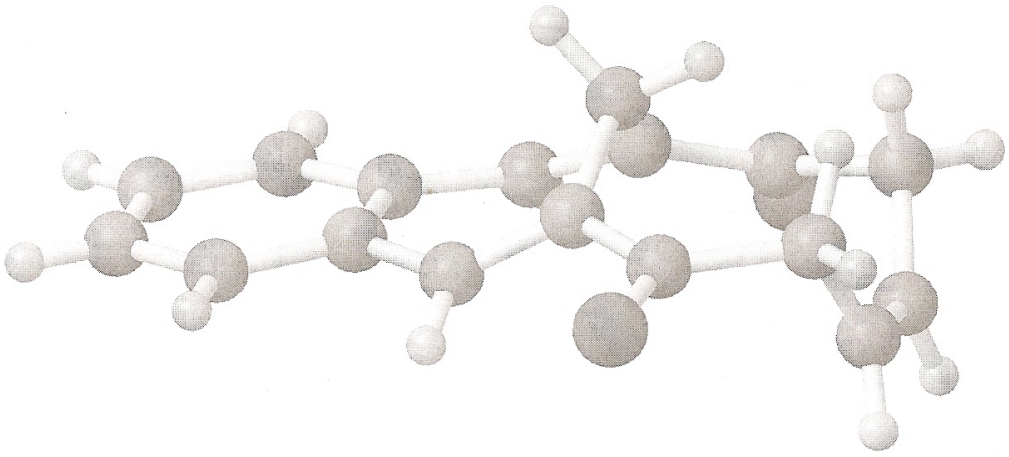
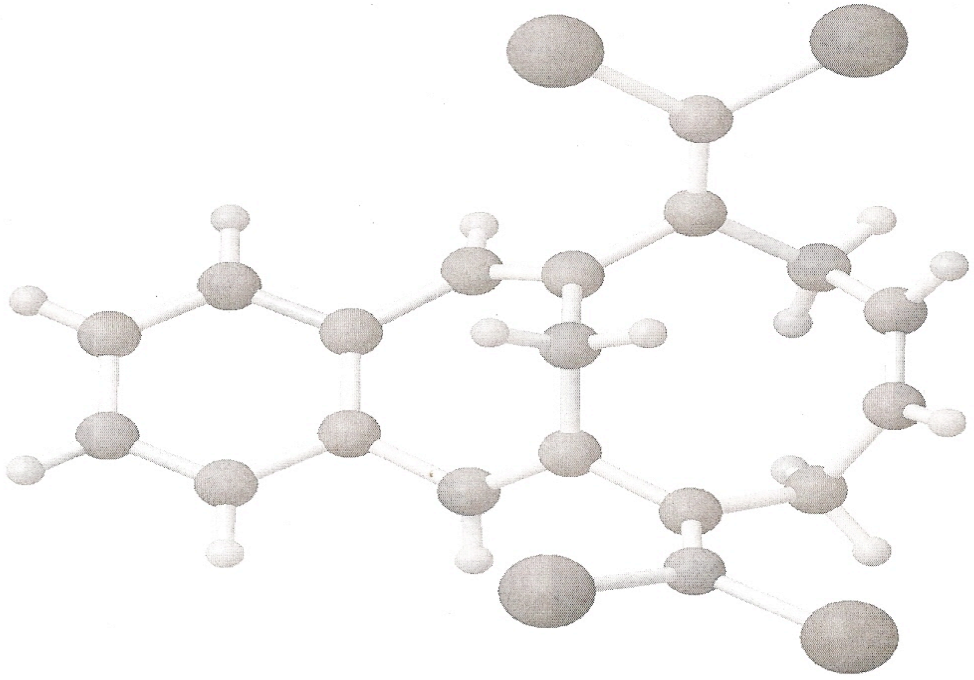
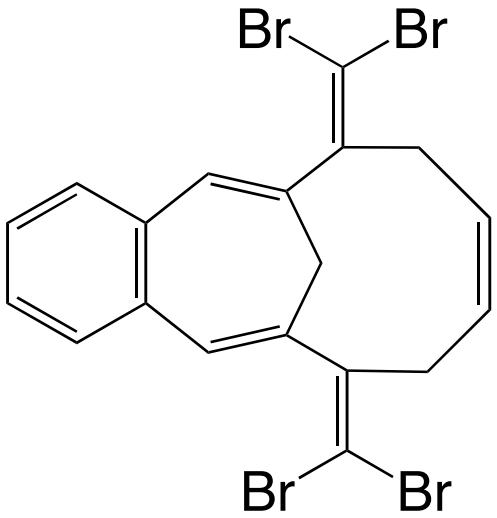


X1616L: Bond Distances and Bond Angles at 100 K

Bond	Distance	Bond	Angle
O7 - C7	1.220(3) Å		
O12 - C12	1.216(3) Å		
C1 - C2	1.343(2) Å	C2 - C1 - C12	119.7(2)°
C1 - C12	1.494(3) Å	C2 - C1 - C13	119.4(2)°
C1 - C13	1.506(3) Å	C12 - C1 - C13	120.9(2)°
C2 - C1	1.343(2) Å	C1 - C2 - C3	127.3(2)°
C2 - C3	1.460(3) Å		
C3 - C2	1.460(3) Å	C2 - C3 - C4	125.1(2)°
C3 - C4	1.415(3) Å	C2 - C3 - C16	116.7(2)°
C3 - C16	1.411(3) Å	C4 - C3 - C16	118.1(2)°
C4 - C3	1.415(3) Å	C3 - C4 - C5	123.0(2)°
C4 - C5	1.461(3) Å	C3 - C4 - C19	118.5(2)°
C4 - C19	1.403(2) Å	C5 - C4 - C19	117.8(2)°
C5 - C4	1.461(3) Å	C4 - C5 - C6	126.8(2)°
C5 - C6	1.341(2) Å		
C6 - C5	1.341(2) Å	C5 - C6 - C7	118.3(2)°
C6 - C7	1.499(3) Å	C5 - C6 - C13	118.7(2)°
C6 - C13	1.500(3) Å	C7 - C6 - C13	122.9(2)°
C7 - O7	1.220(3) Å	O7 - C7 - C6	121.2(2)°
C7 - C6	1.499(3) Å	O7 - C7 - C8	120.0(2)°
C7 - C8	1.522(3) Å	C6 - C7 - C8	118.4(2)°
C8 - C7	1.522(3) Å	C7 - C8 - C9	106.8(1)°
C8 - C9	1.502(3) Å		
C9 - C8	1.502(3) Å	C8 - C9 - C10	128.7(2)°
C9 - C10	1.331(4) Å		
C10 - C9	1.331(4) Å	C9 - C10 - C11	128.3(2)°
C10 - C11	1.509(3) Å		
C11 - C10	1.509(3) Å	C10 - C11 - C12	108.6(2)°
C11 - C12	1.526(3) Å		
C12 - O12	1.216(3) Å	O12 - C12 - C1	121.2(2)°
C12 - C1	1.494(3) Å	O12 - C12 - C11	120.2(2)°
C12 - C11	1.526(3) Å	C1 - C12 - C11	118.5(2)°
C13 - C1	1.506(3) Å	C1 - C13 - C6	110.6(1)°
C13 - C6	1.500(3) Å		
C16 - C3	1.411(3) Å	C3 - C16 - C17	121.7(2)°
C16 - C17	1.377(3) Å		
C17 - C16	1.377(3) Å	C16 - C17 - C18	119.9(2)°
C17 - C18	1.384(3) Å		
C18 - C17	1.384(3) Å	C17 - C18 - C19	119.5(2)°
C18 - C19	1.374(3) Å		
C19 - C4	1.403(2) Å	C4 - C19 - C18	122.2(2)°
C19 - C18	1.374(3) Å		

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Br
Br
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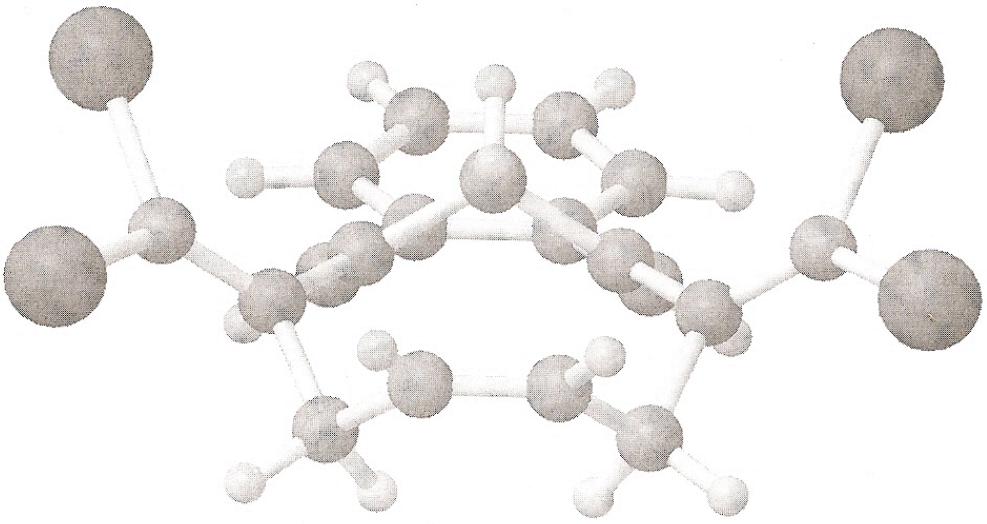

X1615L: Bond Distances and Bond Angles at 100 K

Bond	Distance	Bond	Angle
Br1 - C14	1.901(4) Å		
Br2 - C14	1.895(5) Å		
C1 - C2	1.334(6) Å	C2 - C1 - C12	123.6(4)°
C1 - C12	1.489(7) Å	C2 - C1 - C13	120.9(5)°
C1 - C13	1.501(5) Å	C12 - C1 - C13	115.5(4)°
C2 - C1	1.334(6) Å	C1 - C2 - C3	123.9(4)°
C2 - C3	1.474(7) Å		
C3 - C2	1.474(7) Å	C2 - C3 - C16	117.7(5)°
C3 - C16	1.407(7) Å	C2 - C3 - C3	124.0(4)°
C3 - C3	1.427(8) Å	C16 - C3 - C3	118.3(4)°
C10 - C11	1.510(6) Å	C11 - C10 - C10	126.0(4)°
C10 - C10	1.328(8) Å		
C11 - C10	1.510(6) Å	C10 - C11 - C12	109.9(3)°
C11 - C12	1.528(6) Å		
C12 - C1	1.489(7) Å	C1 - C12 - C11	115.9(4)°
C12 - C11	1.528(6) Å	C1 - C12 - C14	122.4(4)°
C12 - C14	1.319(7) Å	C11 - C12 - C14	121.3(4)°
C13 - C1	1.501(5) Å	C1 - C13 - C1	111.8(3)°
C13 - C1	1.501(5) Å		
C14 - Br1	1.901(4) Å	Br1 - C14 - Br2	112.1(2)°
C14 - Br2	1.895(5) Å	Br1 - C14 - C12	123.4(4)°
C14 - C12	1.319(7) Å	Br2 - C14 - C12	124.3(4)°
C16 - C3	1.407(7) Å	C3 - C16 - C17	122.2(5)°
C16 - C17	1.374(7) Å		
C17 - C16	1.374(7) Å	C16 - C17 - C17	119.3(5)°
C17 - C17	1.416(8) Å		

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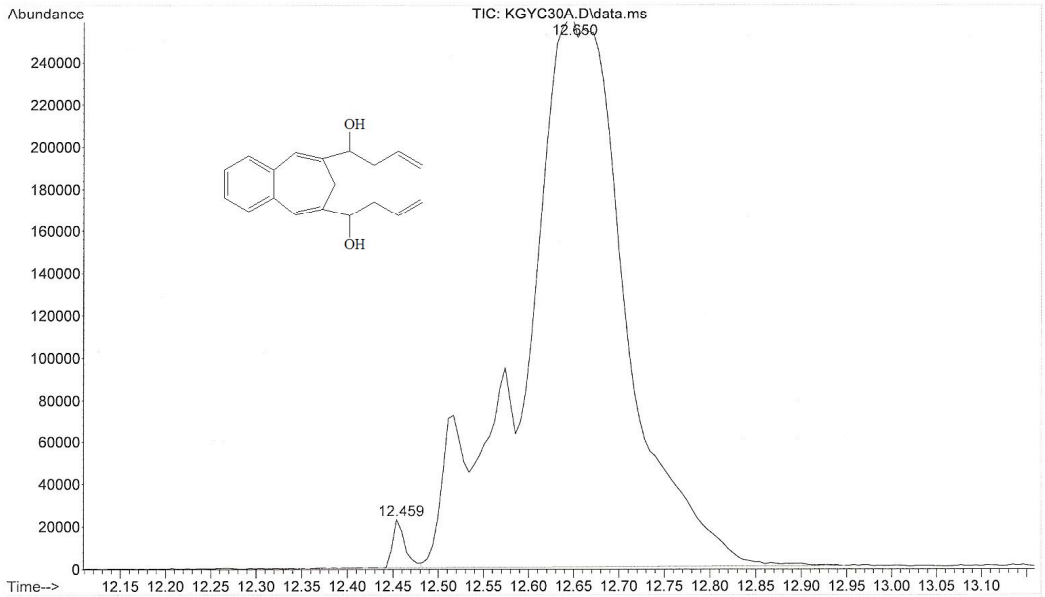

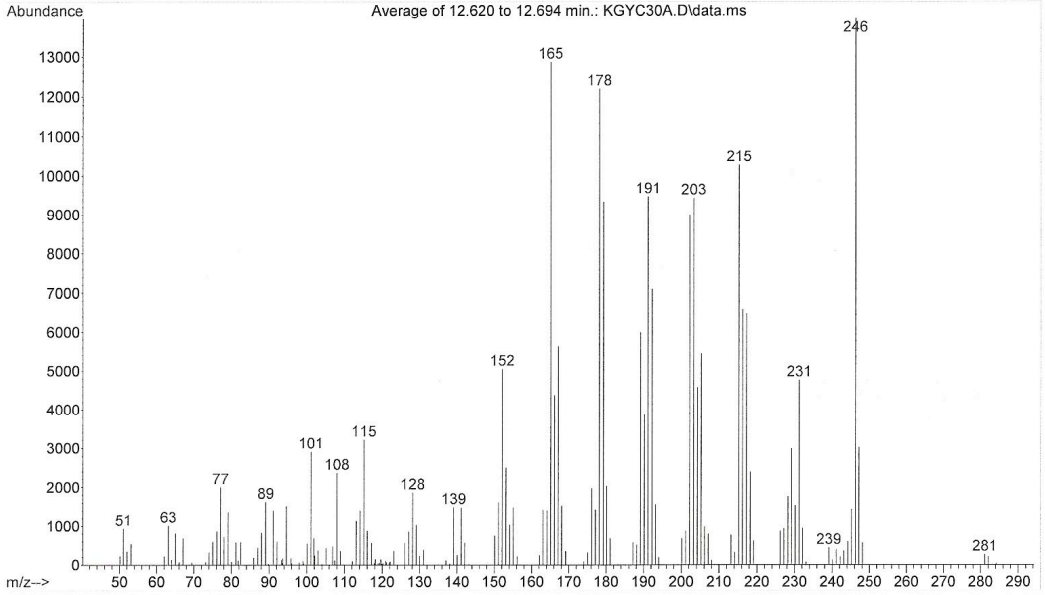

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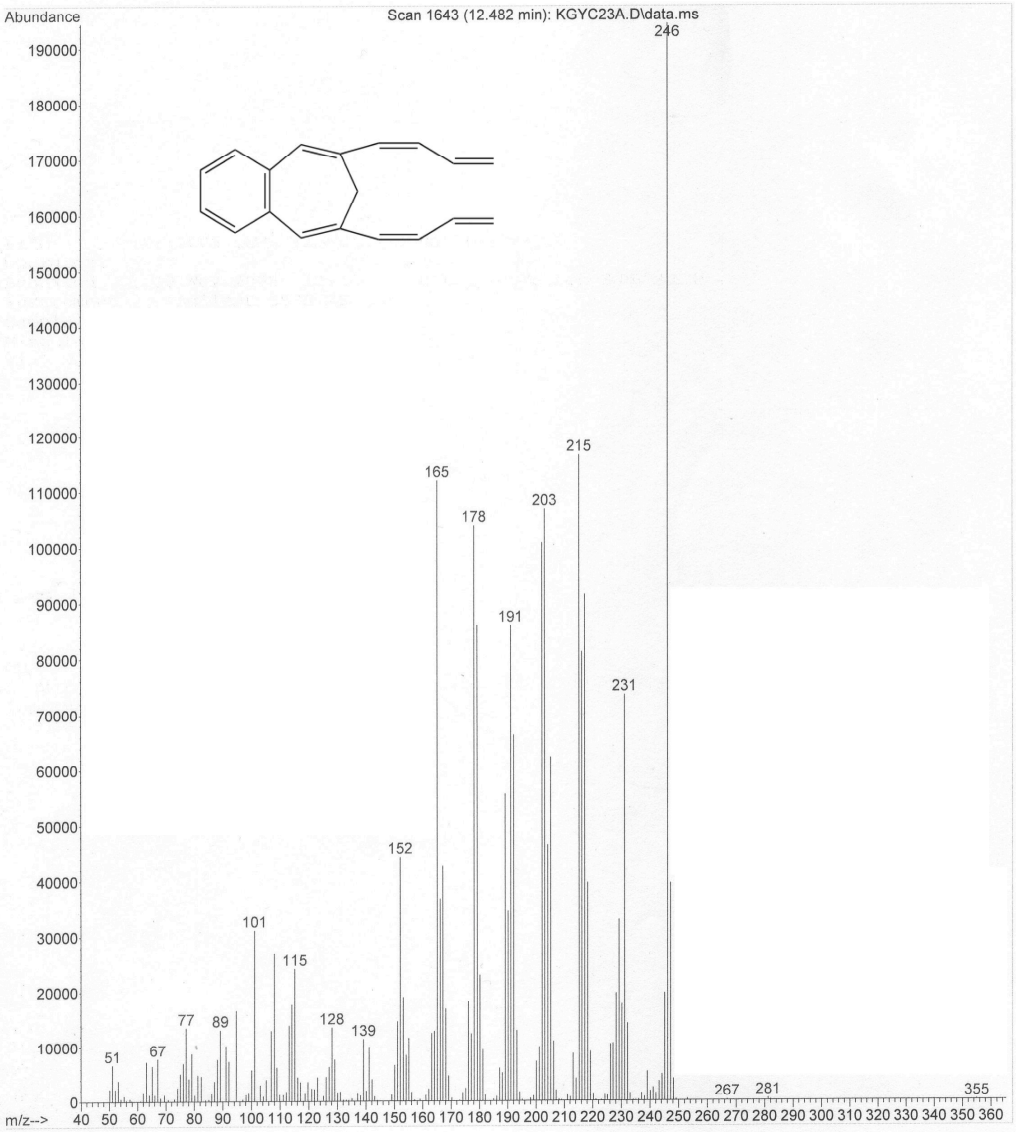

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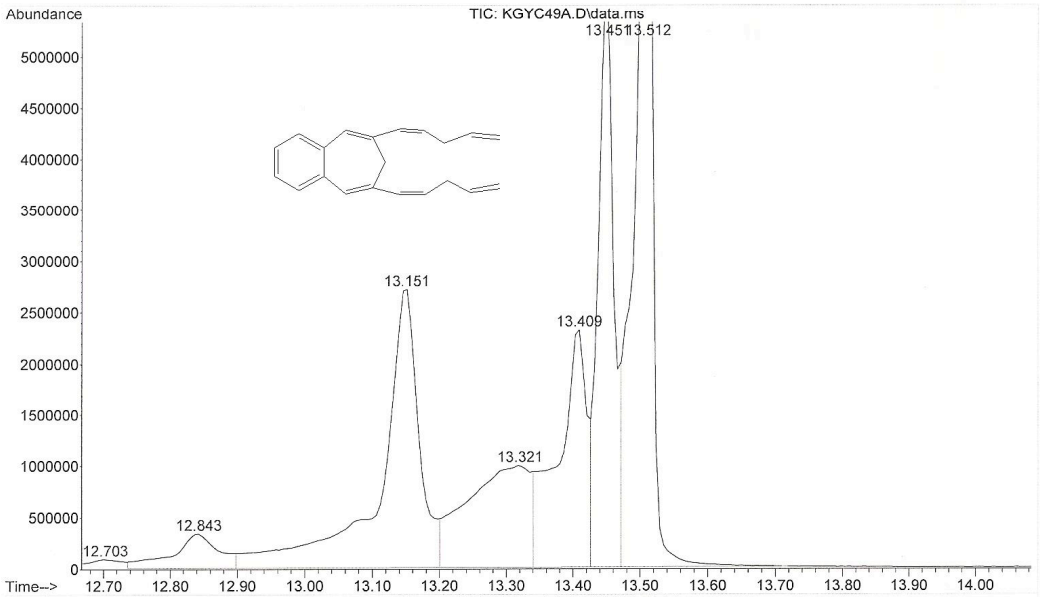

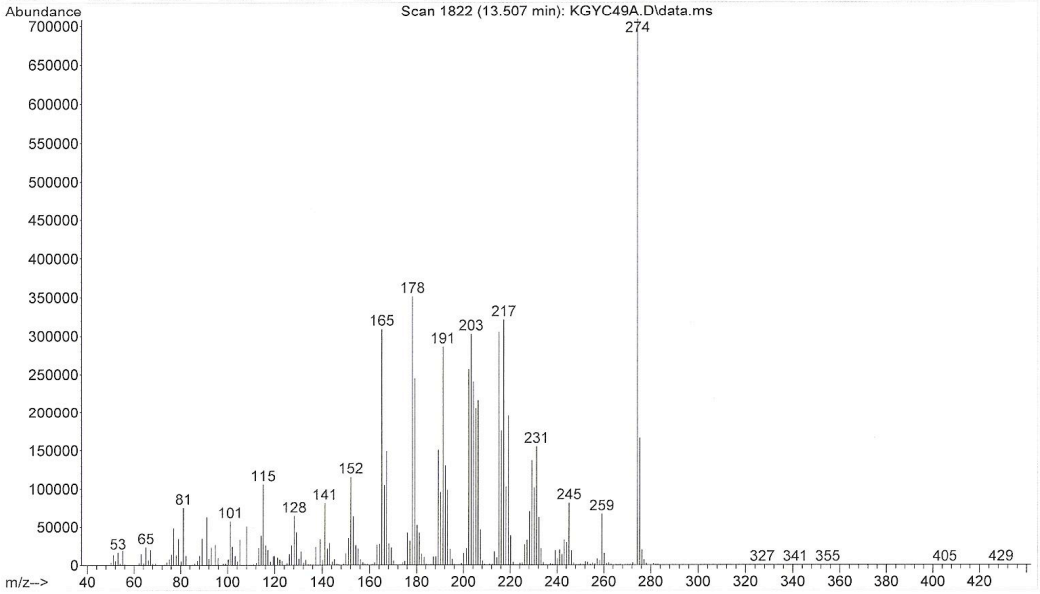

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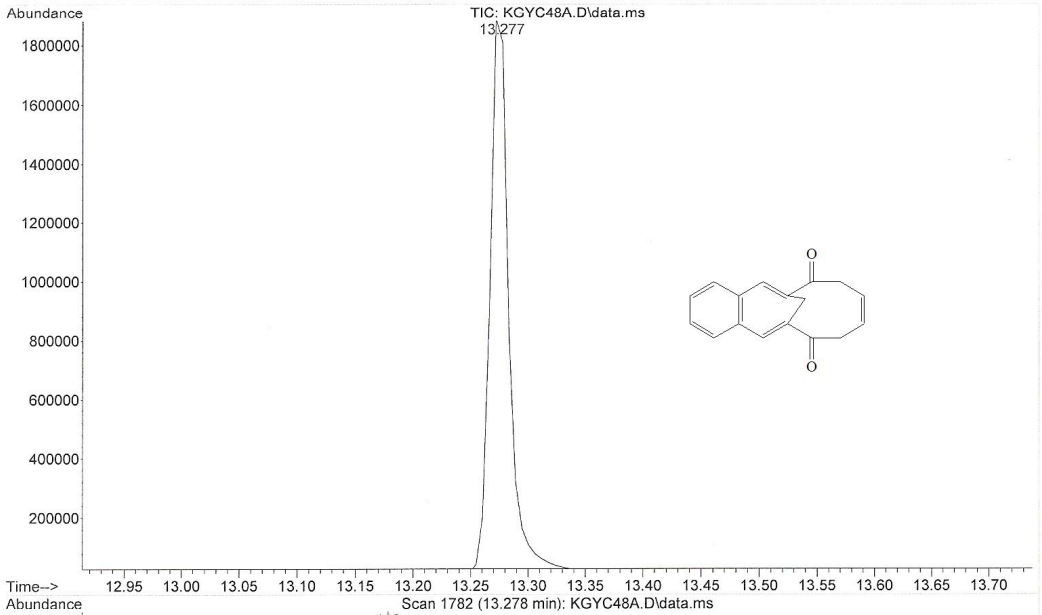

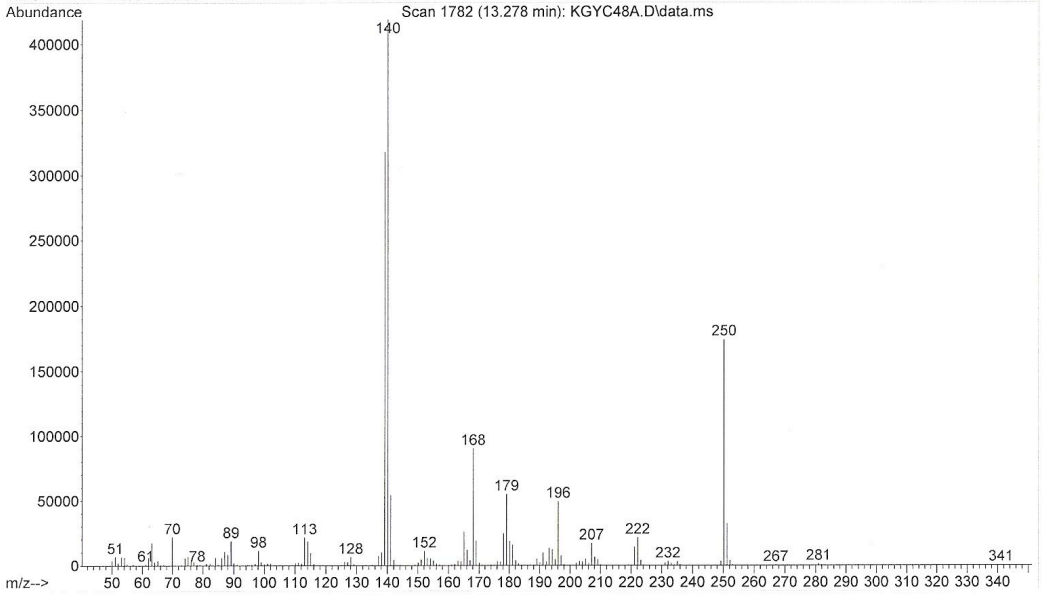

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Vial Number: 7
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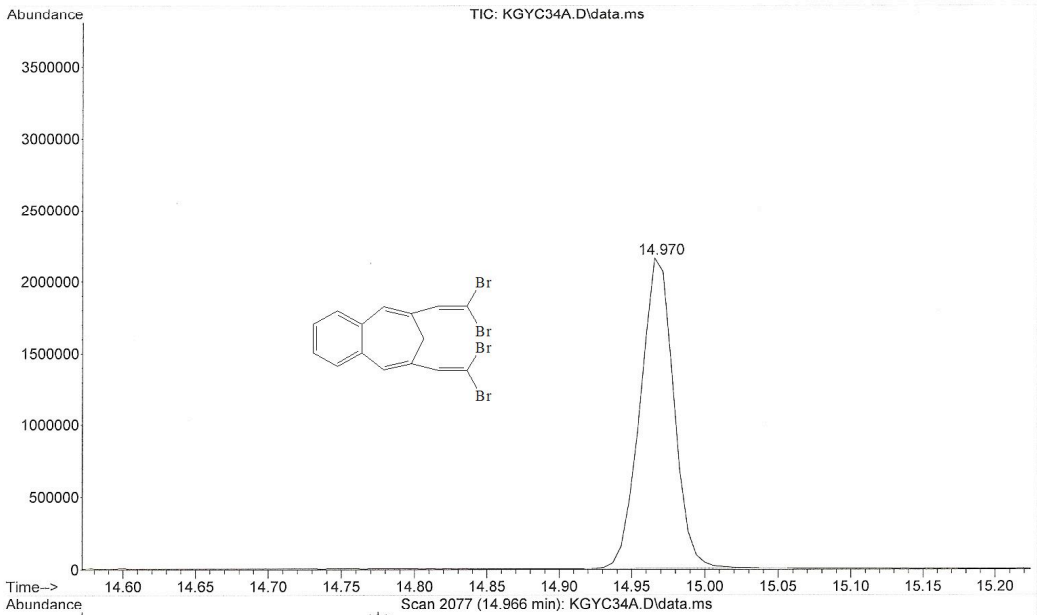
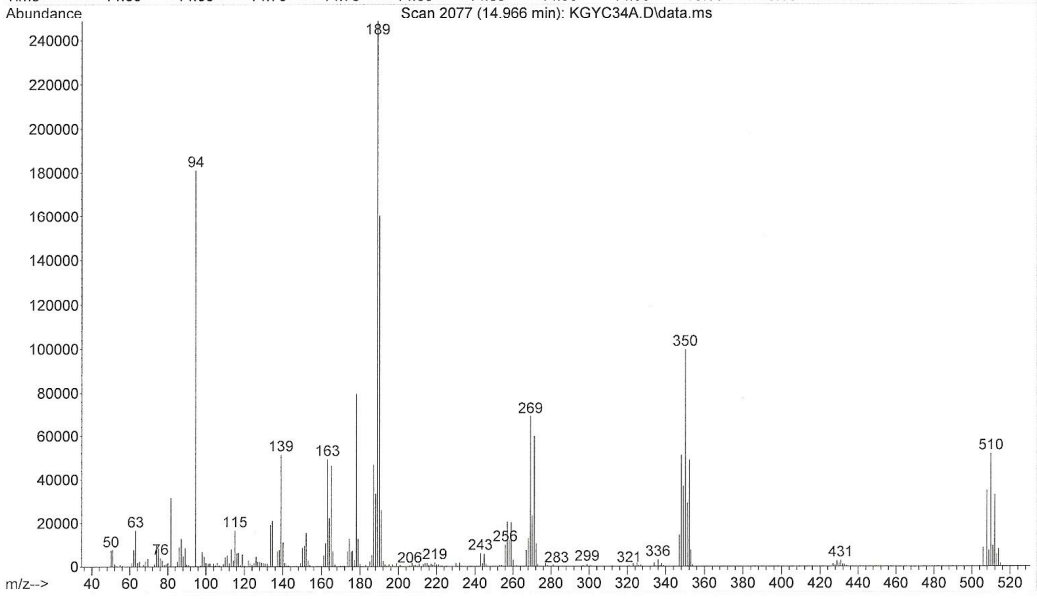
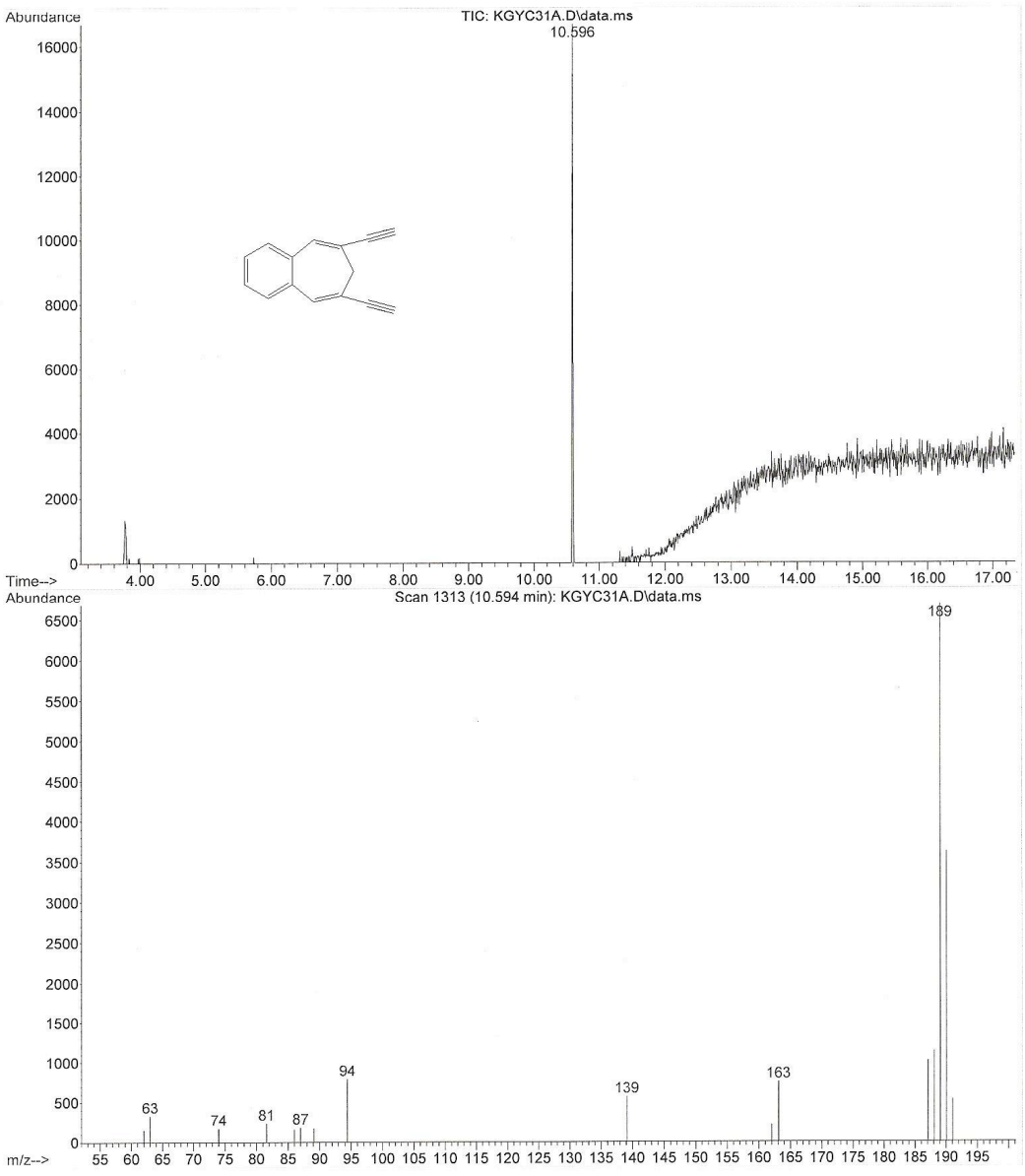
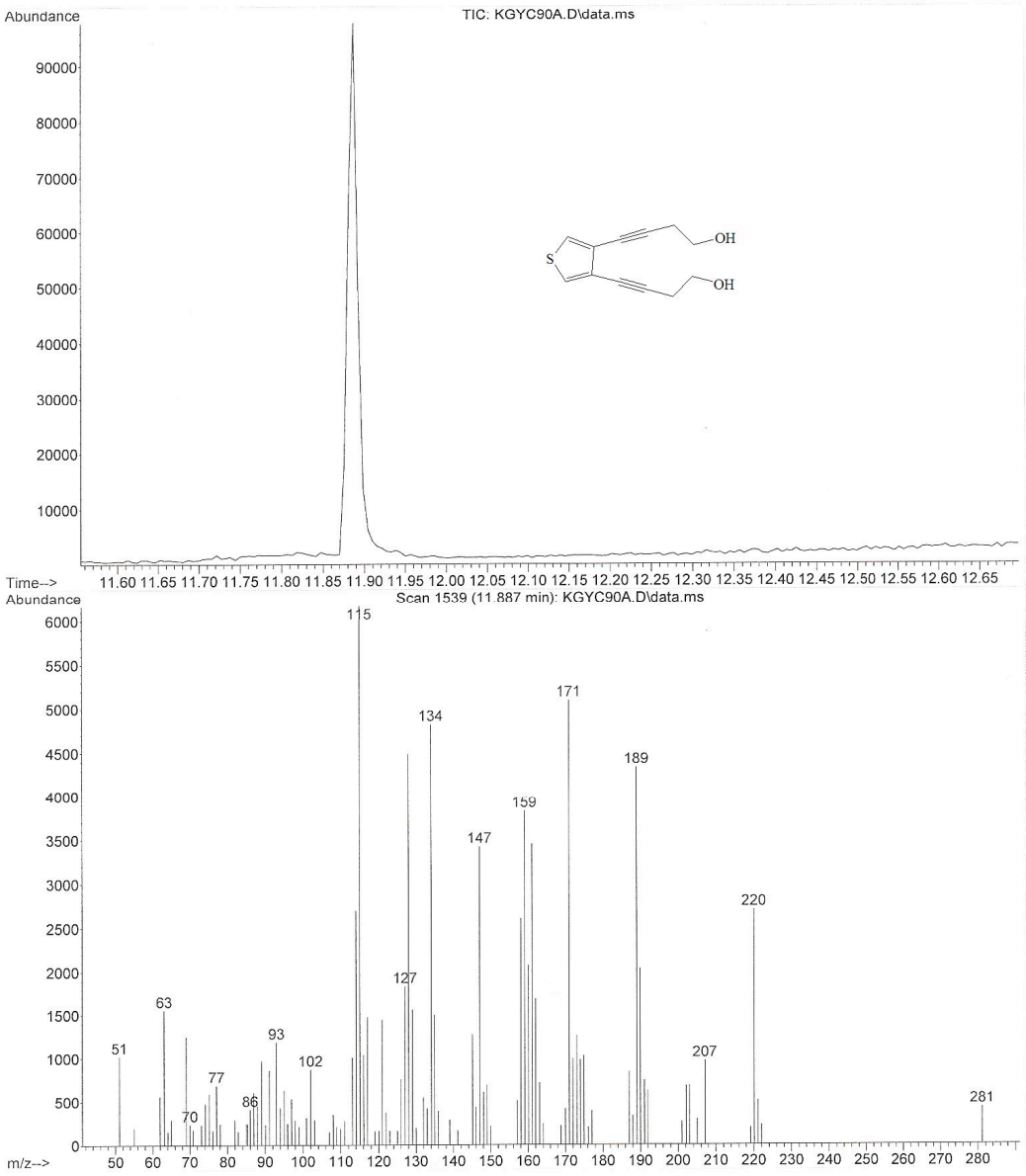




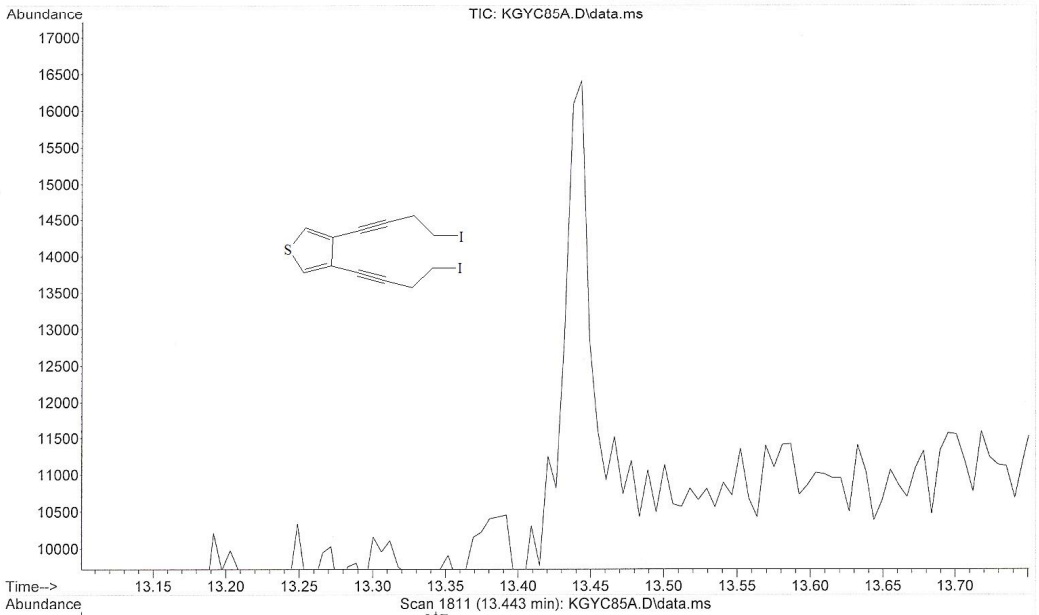
```
File       :D:\2006 GCMS Files\KGYC31A.D
Operator   :
Acquired   :  2 Jun 2006  13:53     using AcqMethod HUNTER1.M
Instrument :    Agilent 5975 MS
Sample Name: MS-198-12
Misc Info  : MW=190 SM=
Vial Number: 4
```

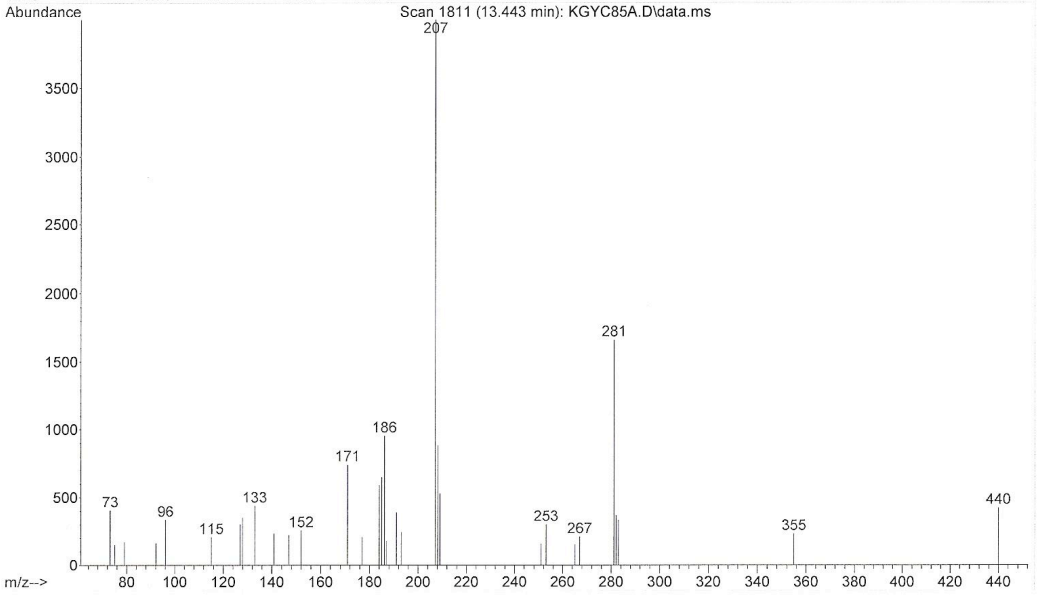


```
File       :D:\2008 GCMS Files\KGYC90A.D
Operator   :
Acquired   : 15 Jul 2008  15:58     using AcqMethod HUNTER1.M
Instrument :    Agilent 5975 MS
Sample Name: YY-02-93-16
Misc Info  :
Vial Number: 3
```

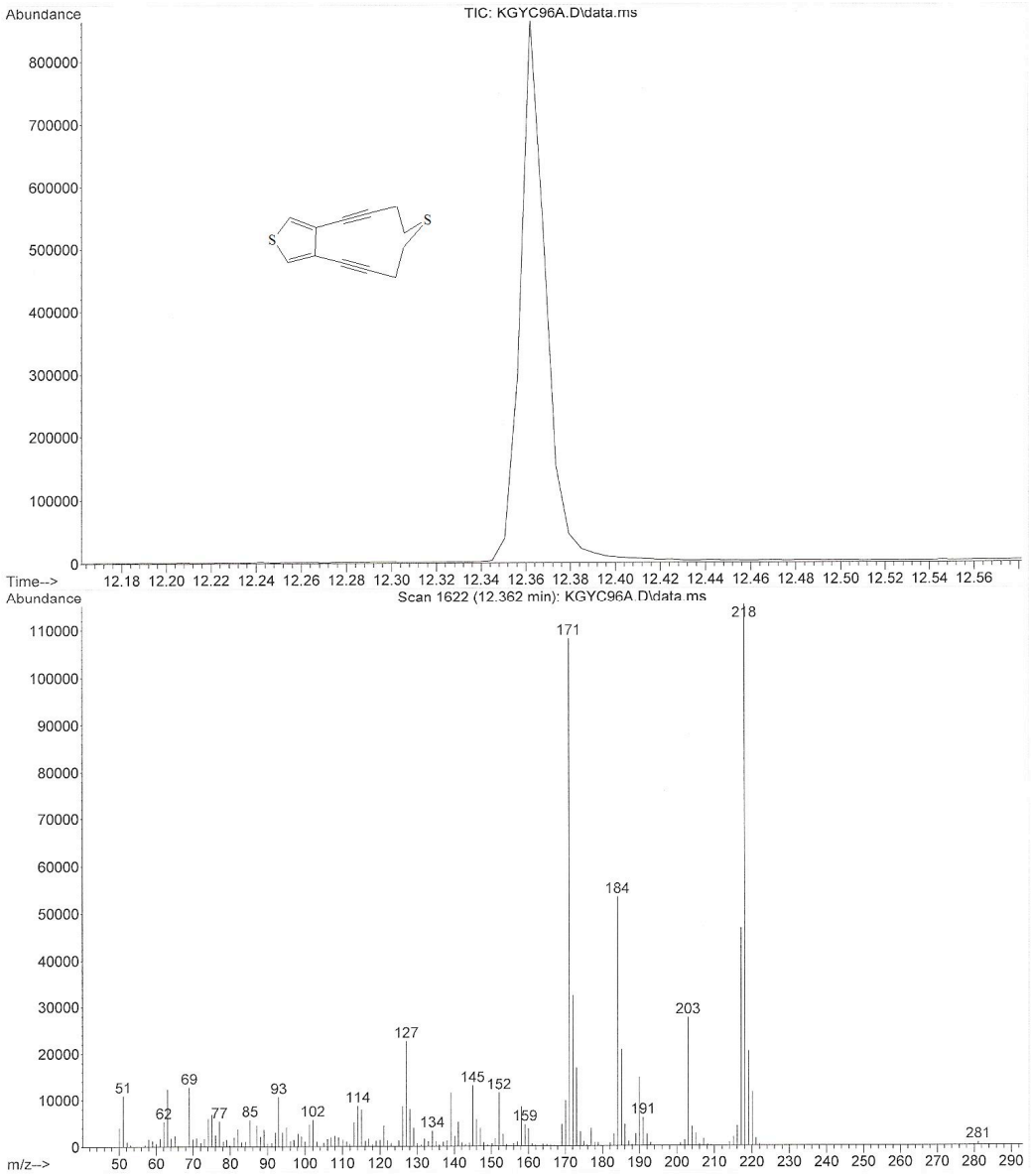


```
File       :D:\2008 GCMS Files\KGYC85A.D
Operator   :
Acquired   : 16 May 2008  11:08     using AcqMethod HUNTER1.M
Instrument :    Agilent 5975 MS
Sample Name: YY-02-73
Misc Info  :
Vial Number: 3
```

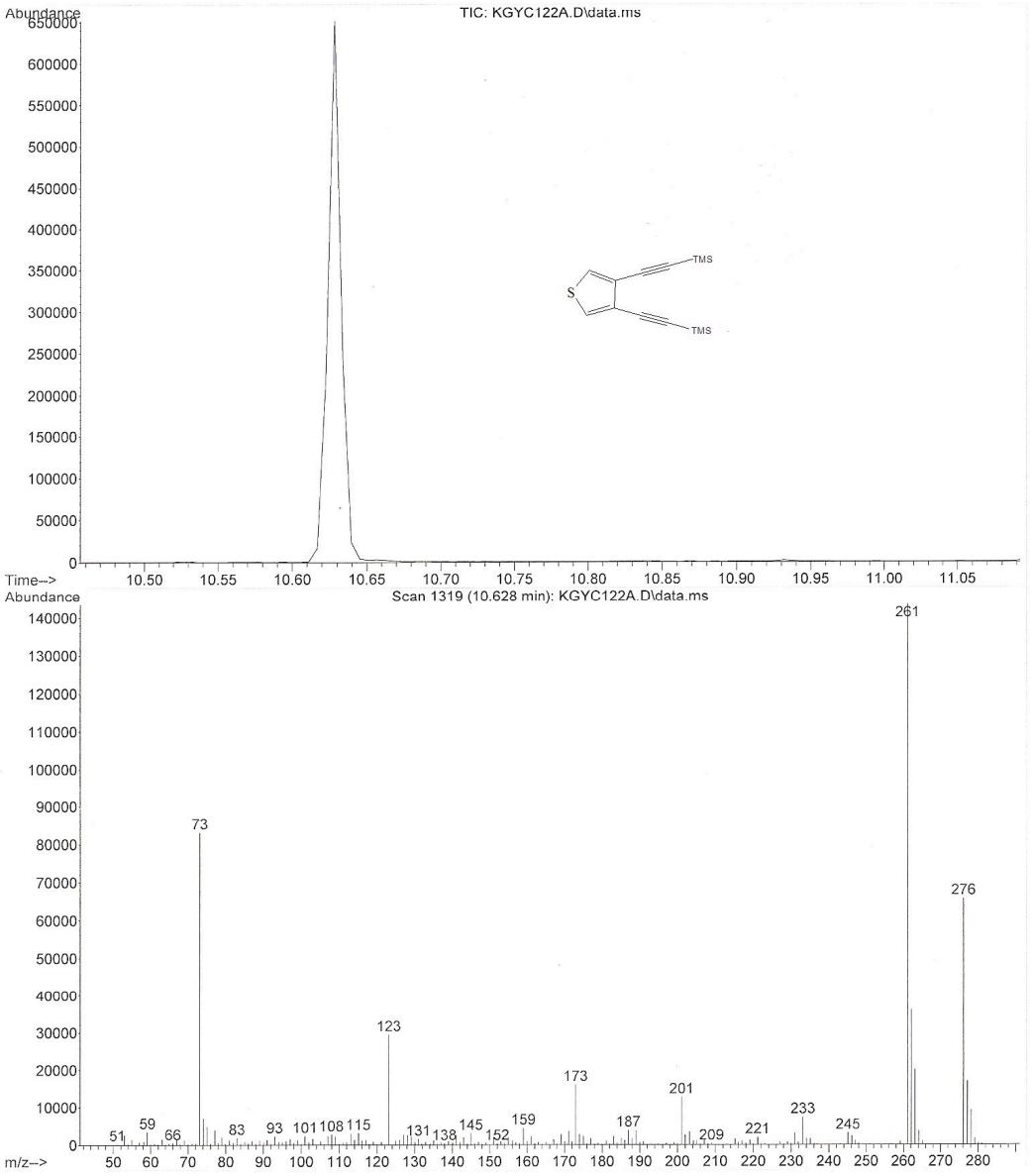




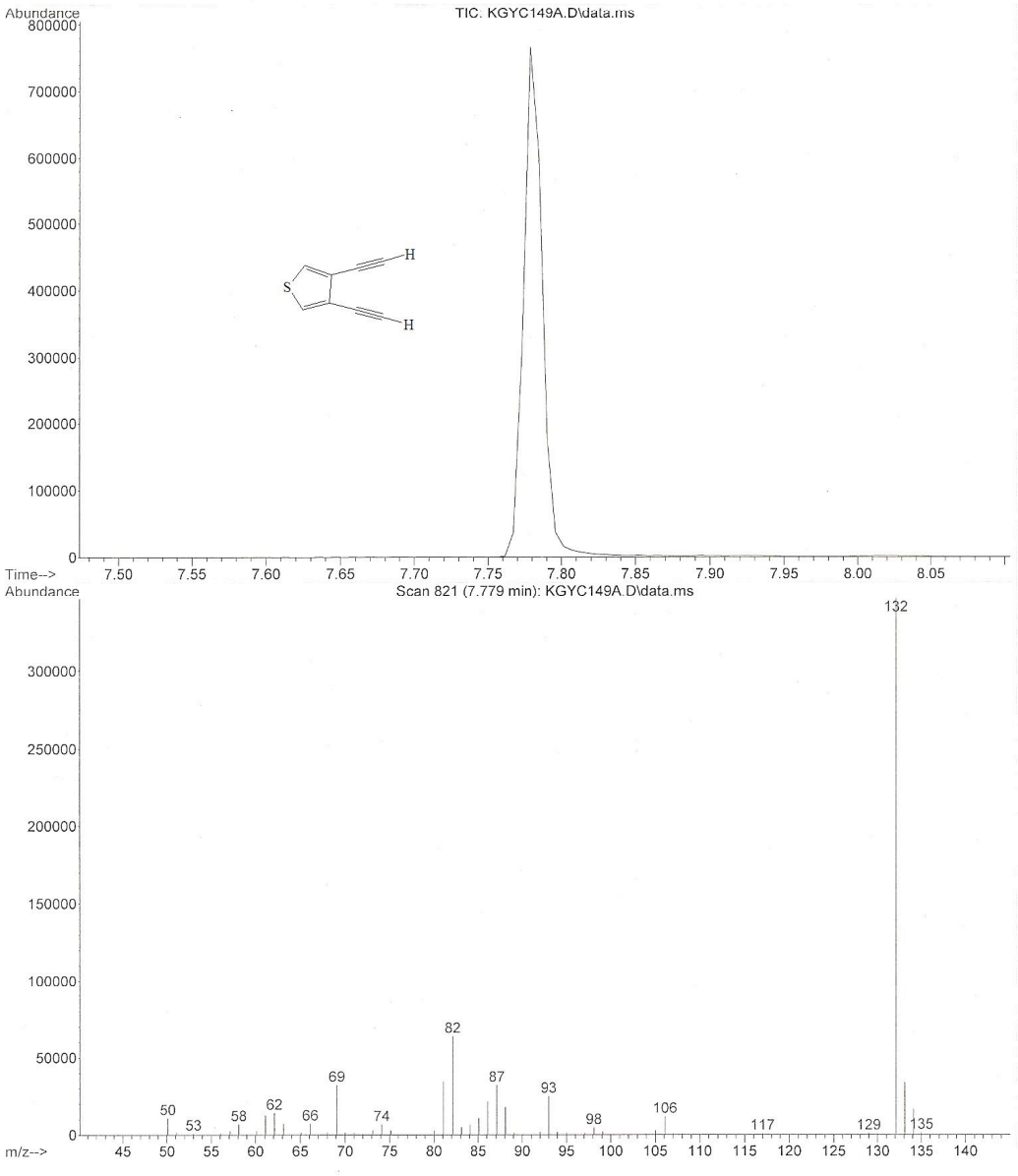
```
File       :D:\2008 GCMS Files\KGYC96A.D
Operator   :
Acquired   :  4 Aug 2008  16:29     using AcqMethod HUNTER1.M
Instrument :    Agilent 5975 MS
Sample Name: YY-02-103-4
Misc Info  :
Vial Number: 6
```



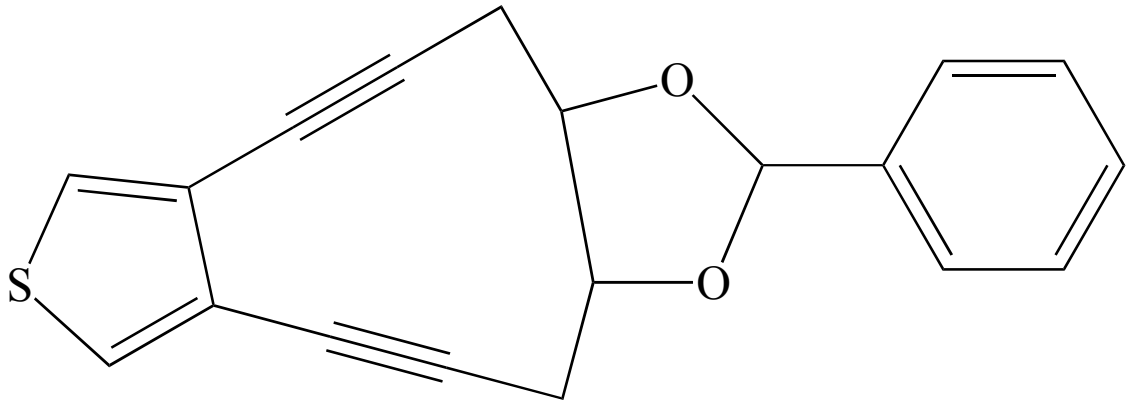
```
File       :D:\2008 GCMS Files\KGYC122A.D
Operator   :
Acquired   :  7 Oct 2008  11:52     using AcqMethod HUNTER1.M
Instrument :    Agilent 5975 MS
Sample Name: yy-02-127-18
Misc Info  :
Vial Number: 5
```



```
File       :D:\2009 GCMS Files\KGYC149A.D
Operator   :
Acquired   :  2 Jul 2009  16:51     using AcqMethod HUNTER1.M
Instrument :    Agilent 5975 MS
Sample Name: yy-02-197
Misc Info  :
Vial Number: 3
```



HighResolution Electrospray Mass Spectrum for Compound 78



$C_{19}H_{14}O_2S$ theor. mass 306.0715

m/z for M+H = 307.01875

Qualitative Compound Report

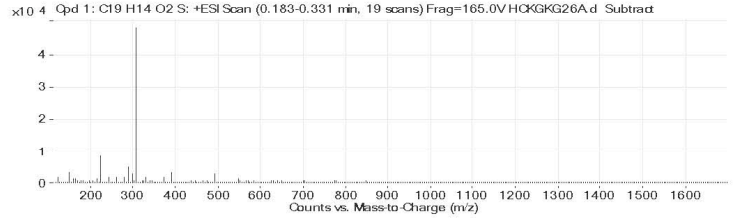
Data File	HCKGKG26A.d	Sample Name	KGYYC-6
Sample Type	Sample	Position	P1-A1
Instrument Name	Instrument 1	User Name	
Acq Method		IRM Calibration Status	Success
DA Method	HCEmpirical1.m	Comment	EM=306 M=HC ESI Pos Small Molecule No HPLC.m

Compound Table

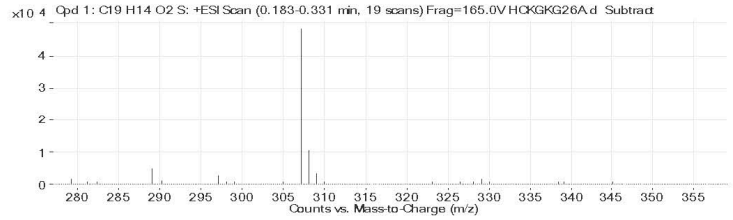
Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	MFG Diff (ppm)
Cpd 1: C19 H14 O2 S	0.24	306.0713	48172	C19 H14 O2 S	306.0715	-0.37	C19 H14 O2 S	0.37

Compound Label	RT	Algorithm	Mass
Cpd 1: C19 H14 O2 S	0.24	Find By Formula	306.0713

MS Spectrum



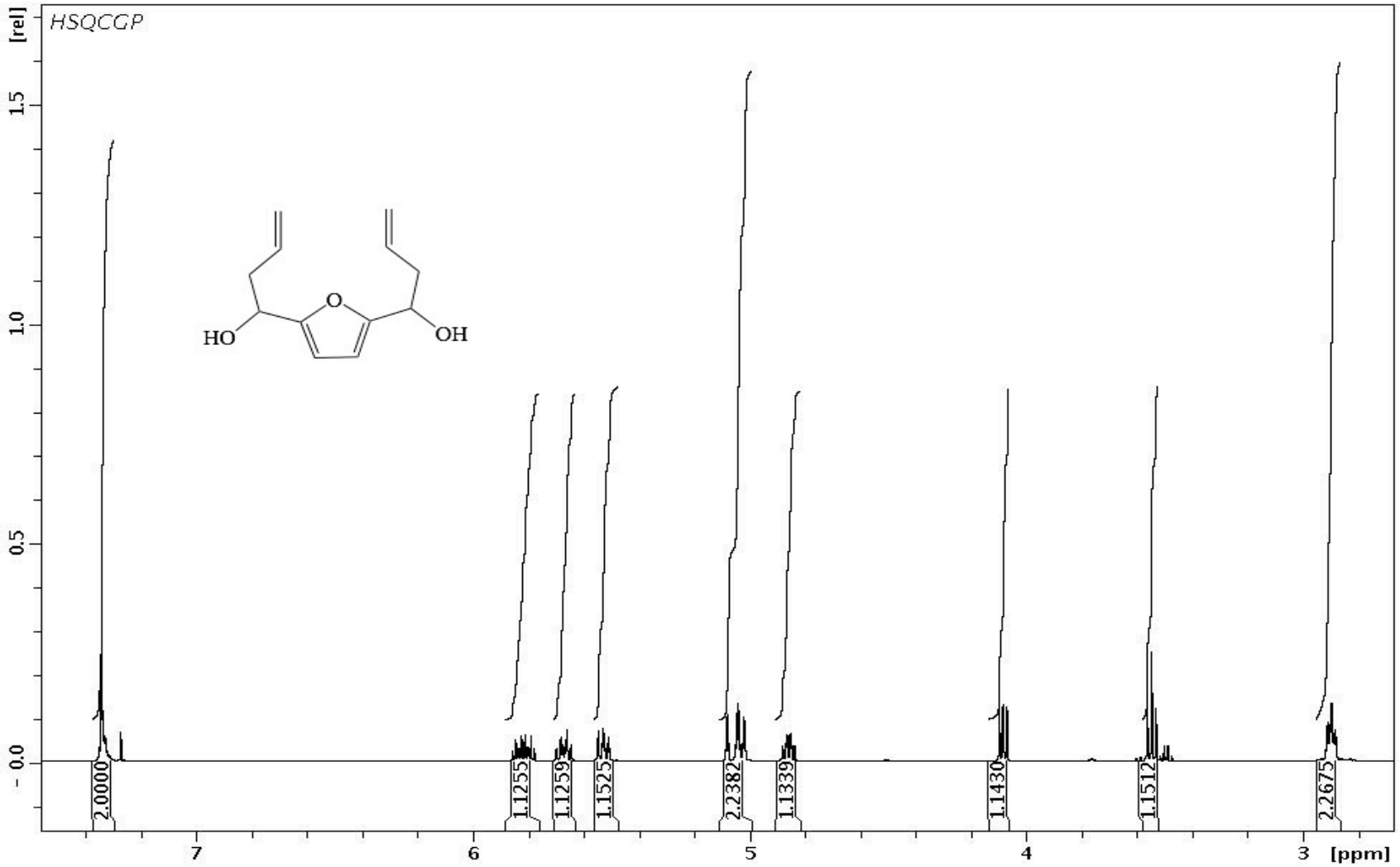
MS Zoomed Spectrum

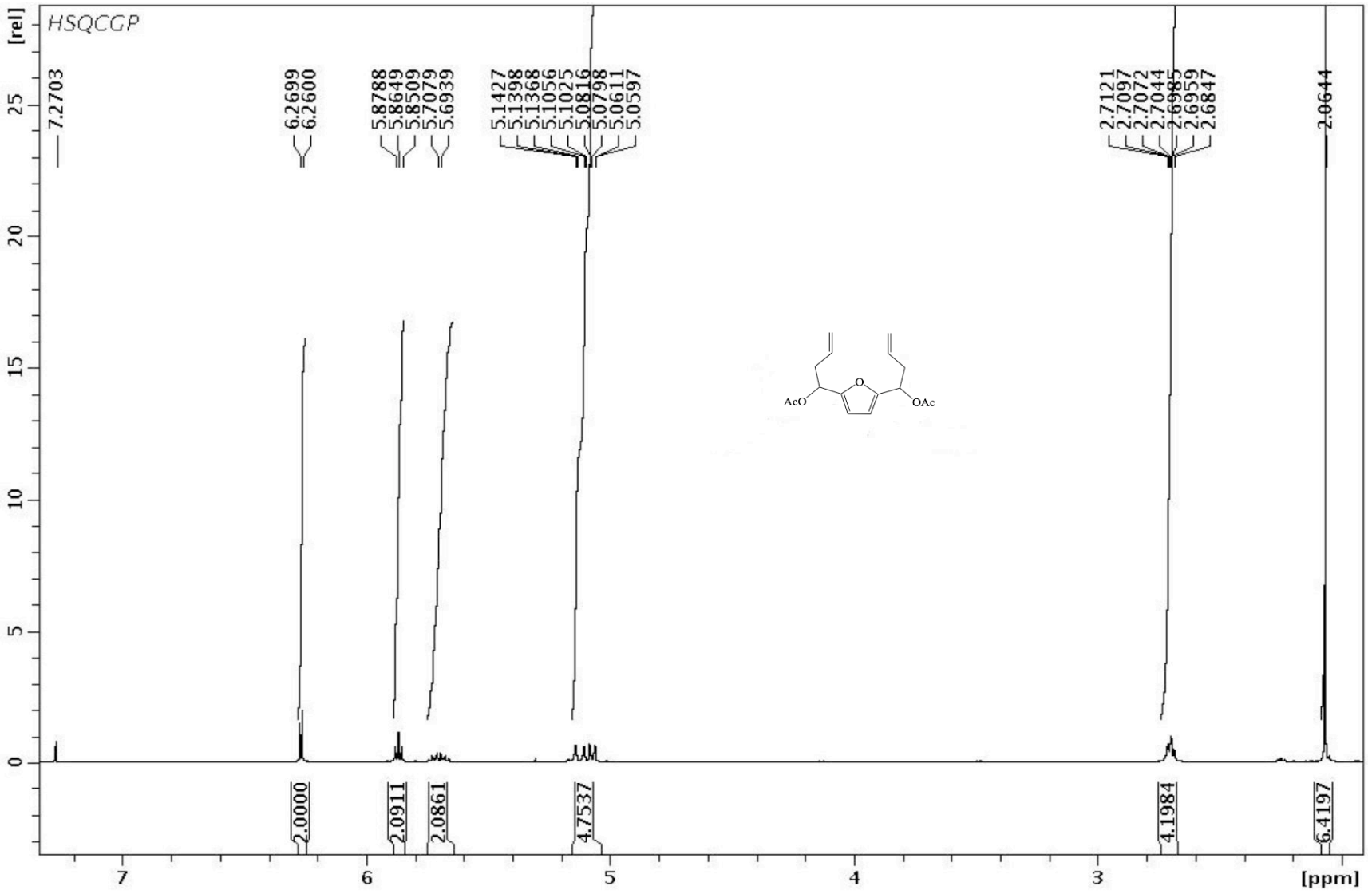


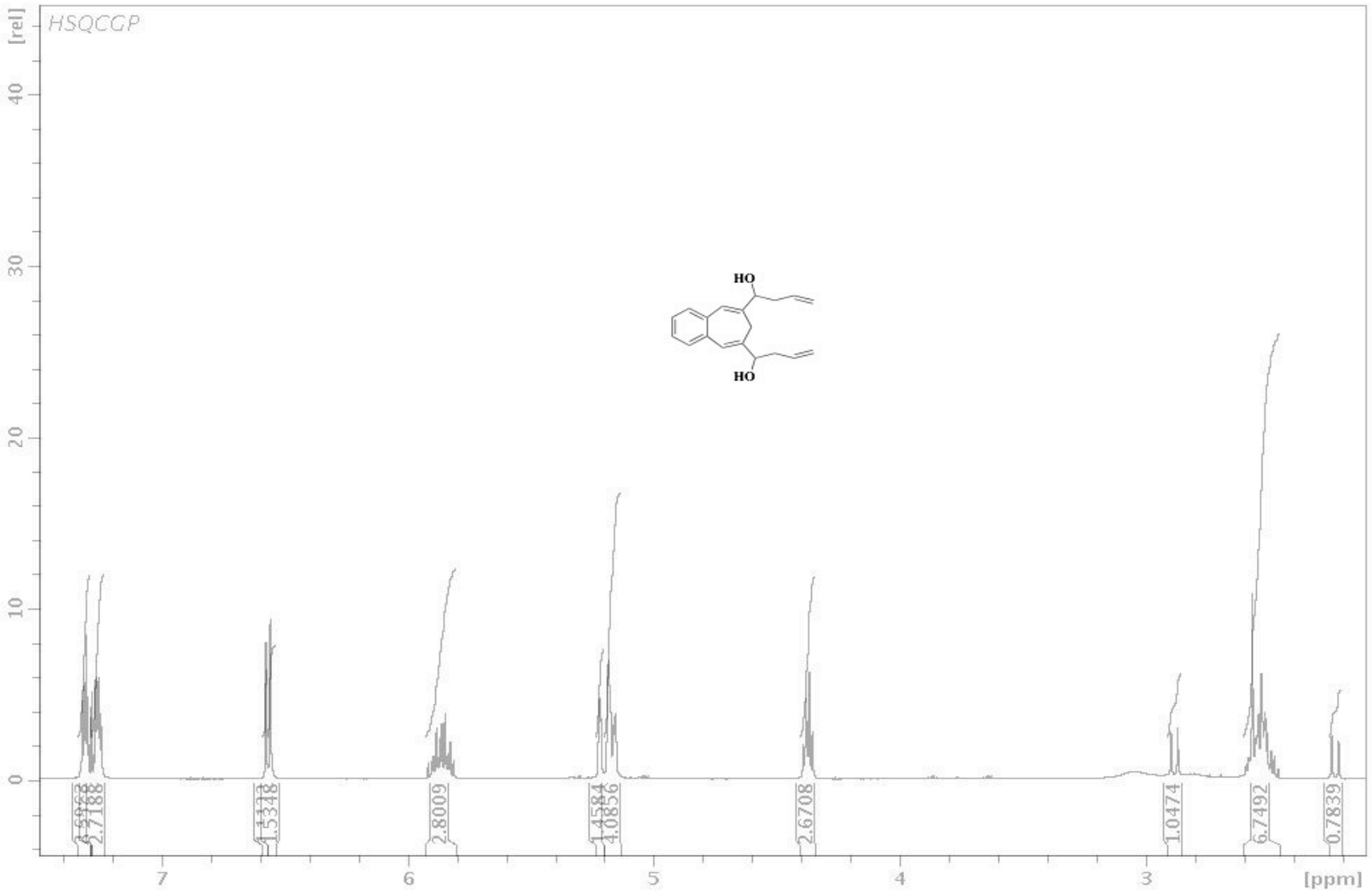
MS Spectrum Peak List

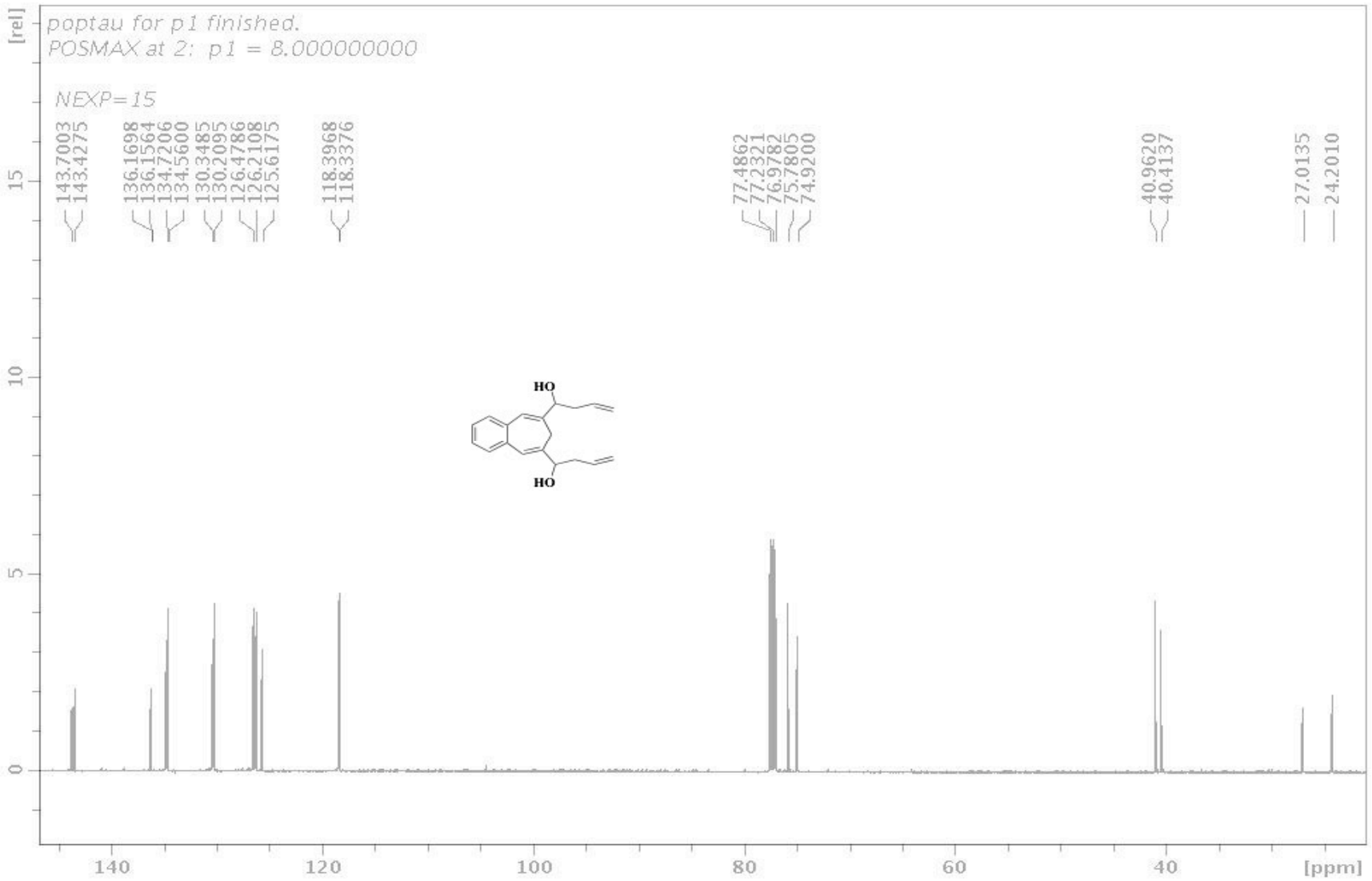
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
149.0232			1	3496		
223.0634			1	8389		
289.0679			1	4705		
307.0786	307.0787	-0.36	1	48172	C19 H15 O2 S	(M+H)+
308.0818	308.082	-0.65	1	10404	C19 H15 O2 S	(M+H)+
329.0606	329.0607	-0.18	1	1880	C19 H14 Na O2 S	(M+Na)+
391.284			1	3434		

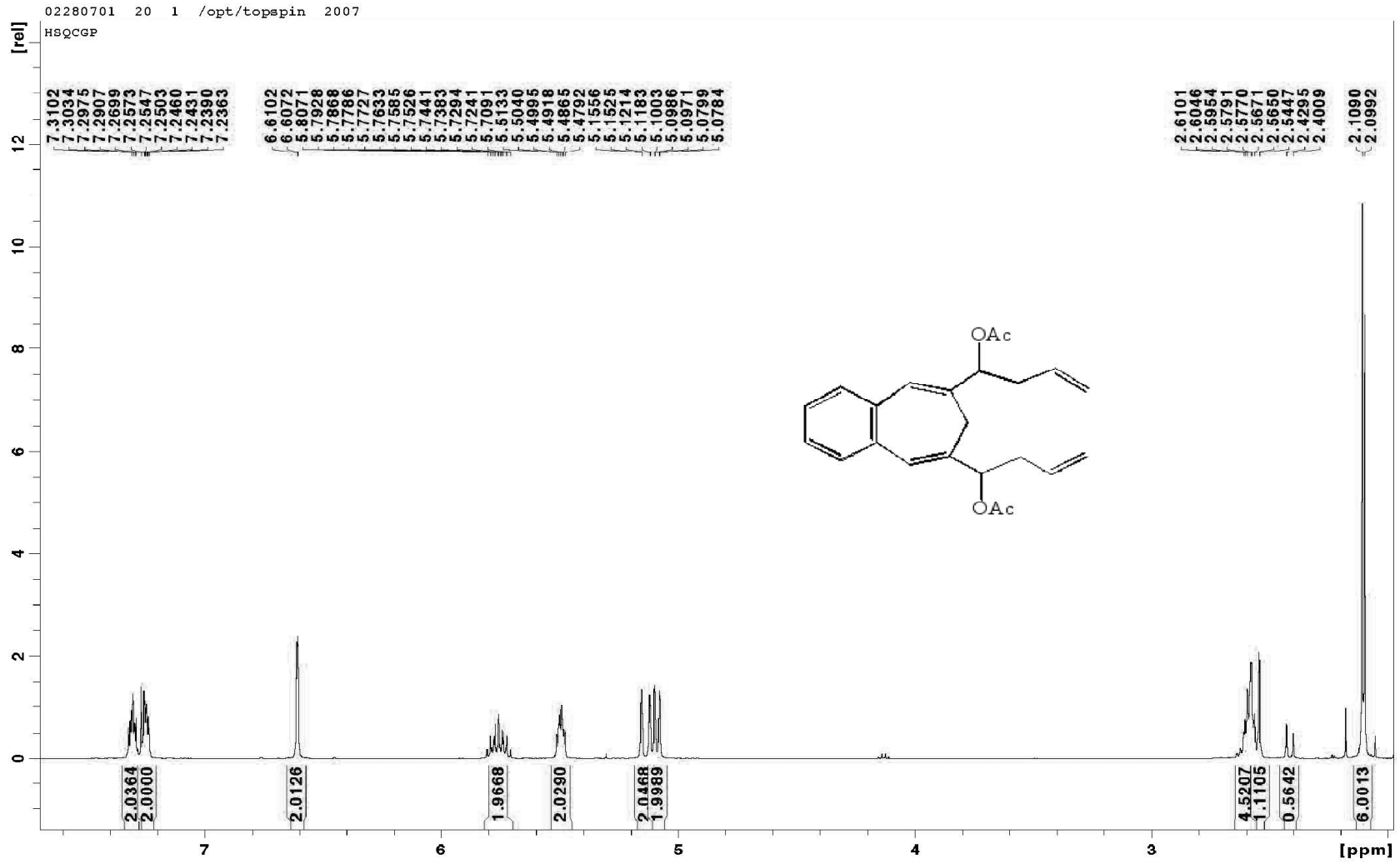
--- End Of Report ---

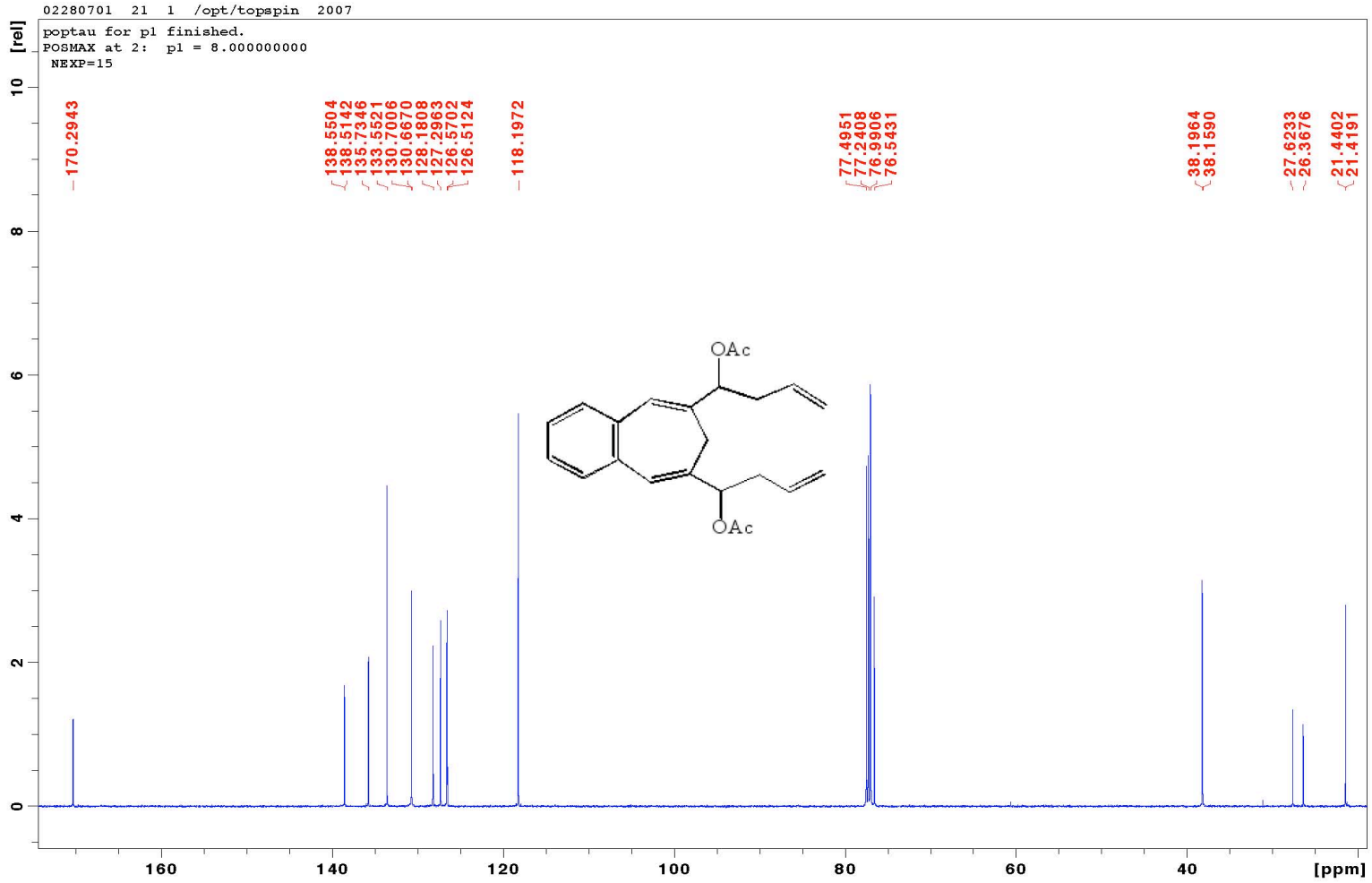

HSQCGP
[rel]
1.5
1.0
0.5
- 0.0
HO
O
OH
2.0000
1.1255
1.1259
1.1525
2.2382
1.1339
1.1430
1.1512
2.2675
7
6
5
4
3
[ppm]

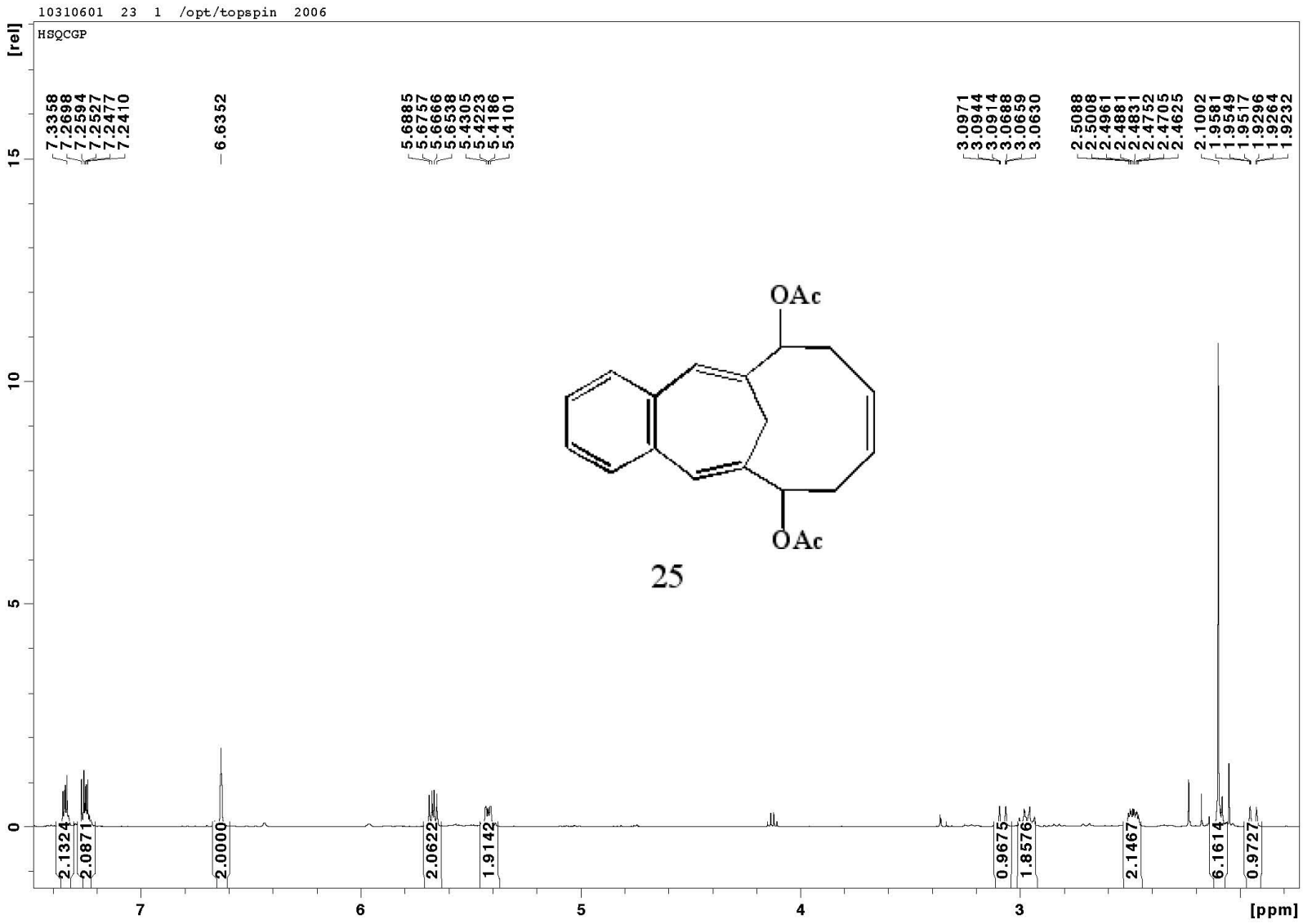

HSQCGP
[rel]
7.2703
6.2699
6.2600
5.8788
5.8649
5.8509
5.7079
5.6939
5.1427
5.1398
5.1368
5.1056
5.1025
5.0816
5.0798
5.0611
5.0597
2.7121
2.7097
2.7072
2.7044
2.6985
2.6959
2.6847
2.0644
AcO
OAc
2.0000
2.0911
2.0861
4.7537
4.1984
6.4197
[ppm]

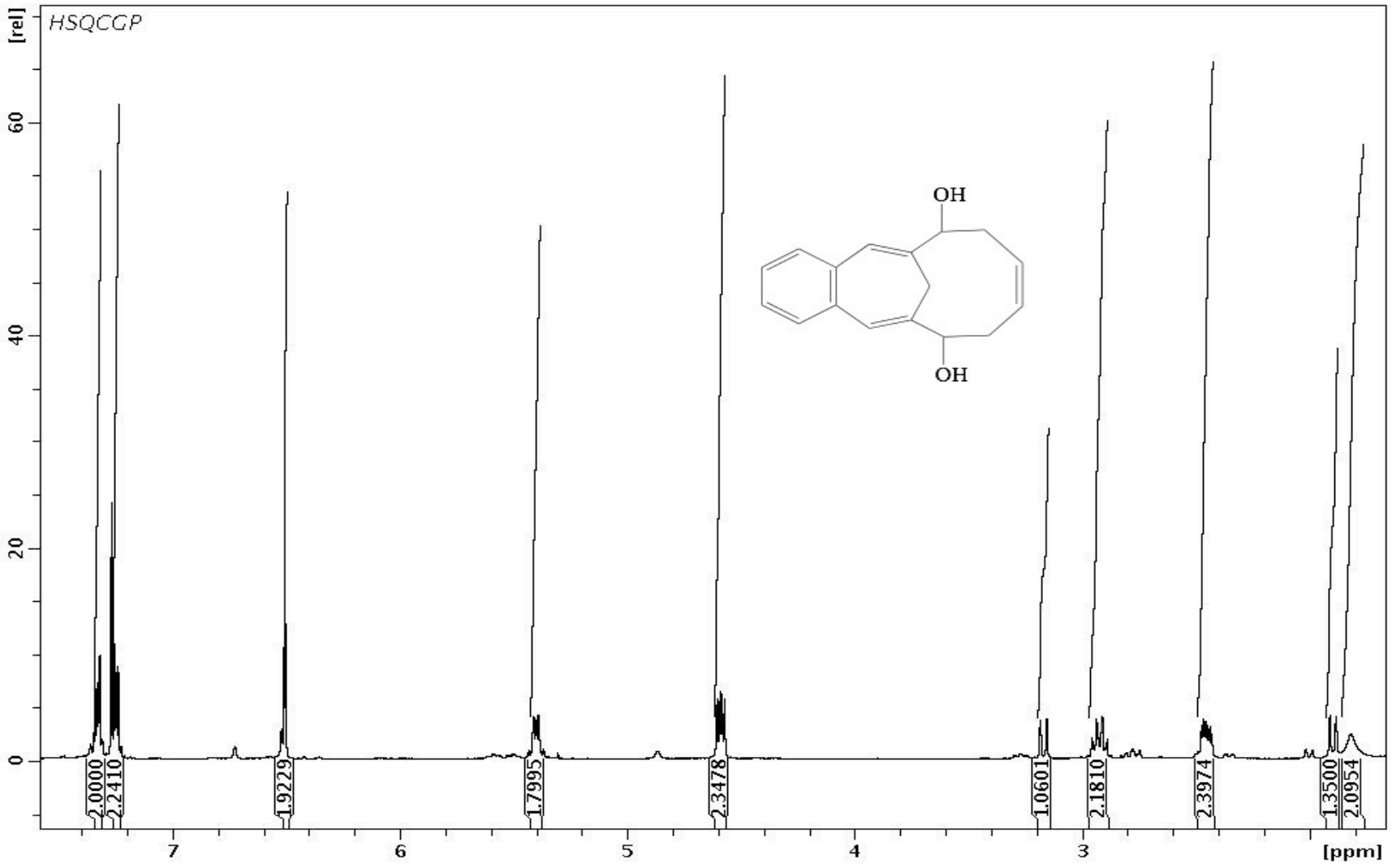

HSQCGP
[rel]
40
30
20
10
0
HO
HO
2.7188
1.5348
2.8009
1.4584
4.0856
2.6708
1.0474
6.7492
0.7839
7
6
5
4
3
[ppm]


poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
143.7003
143.4275
136.1698
136.1564
134.7206
134.5600
130.3485
130.2095
126.4786
126.2108
125.6175
118.3968
118.3376
77.4862
77.2321
76.9782
75.7805
74.9200
40.9620
40.4137
27.0135
24.2010
HO
HO
[rel]
15
10
5
0
140
120
100
80
60
40
[ppm]


02280701 20 1 /opt/topspin 2007
HSQCGP
[rel]
7.3102
7.3034
7.2975
7.2907
7.2699
7.2573
7.2547
7.2503
7.2460
7.2431
7.2390
7.2363
6.6102
6.6072
5.8071
5.7928
5.7868
5.7786
5.7727
5.7633
5.7585
5.7526
5.7441
5.7383
5.7294
5.7241
5.7091
5.5133
5.5040
5.4995
5.4918
5.4865
5.4792
5.1556
5.1525
5.1214
5.1183
5.1003
5.0986
5.0971
5.0799
5.0784
2.6101
2.6046
2.5954
2.5791
2.5770
2.5671
2.5650
2.5447
2.4295
2.4009
2.1090
2.0992
OAc
OAc
2.0364
2.0000
2.0126
1.9668
2.0290
2.0468
1.9989
4.5207
1.1105
0.5642
6.0013
[ppm]


02280701 21 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
[rel]
170.2943
138.5504
138.5142
135.7346
133.5521
130.7006
130.6670
128.1808
127.2963
126.5702
126.5124
118.1972
77.4951
77.2408
76.9906
76.5431
38.1964
38.1590
27.6233
26.3676
21.4402
21.4191
OAc
OAc
[ppm]


10310601 23 1 /opt/topspin 2006
HSQCGP
[rel]
7.3358
7.2698
7.2594
7.2527
7.2477
7.2410
6.6352
5.6885
5.6757
5.6666
5.6538
5.4305
5.4223
5.4186
5.4101
3.0971
3.0944
3.0914
3.0688
3.0659
3.0630
2.5088
2.5008
2.4961
2.4881
2.4831
2.4752
2.4705
2.4625
2.1002
1.9581
1.9549
1.9517
1.9296
1.9264
1.9232
OAc
OAc
25
2.1324
2.0871
2.0000
2.0622
1.9142
0.9675
1.8576
2.1467
6.1614
0.9727
[ppm]


HSQCGP
[rel]
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40
20
0
OH
OH
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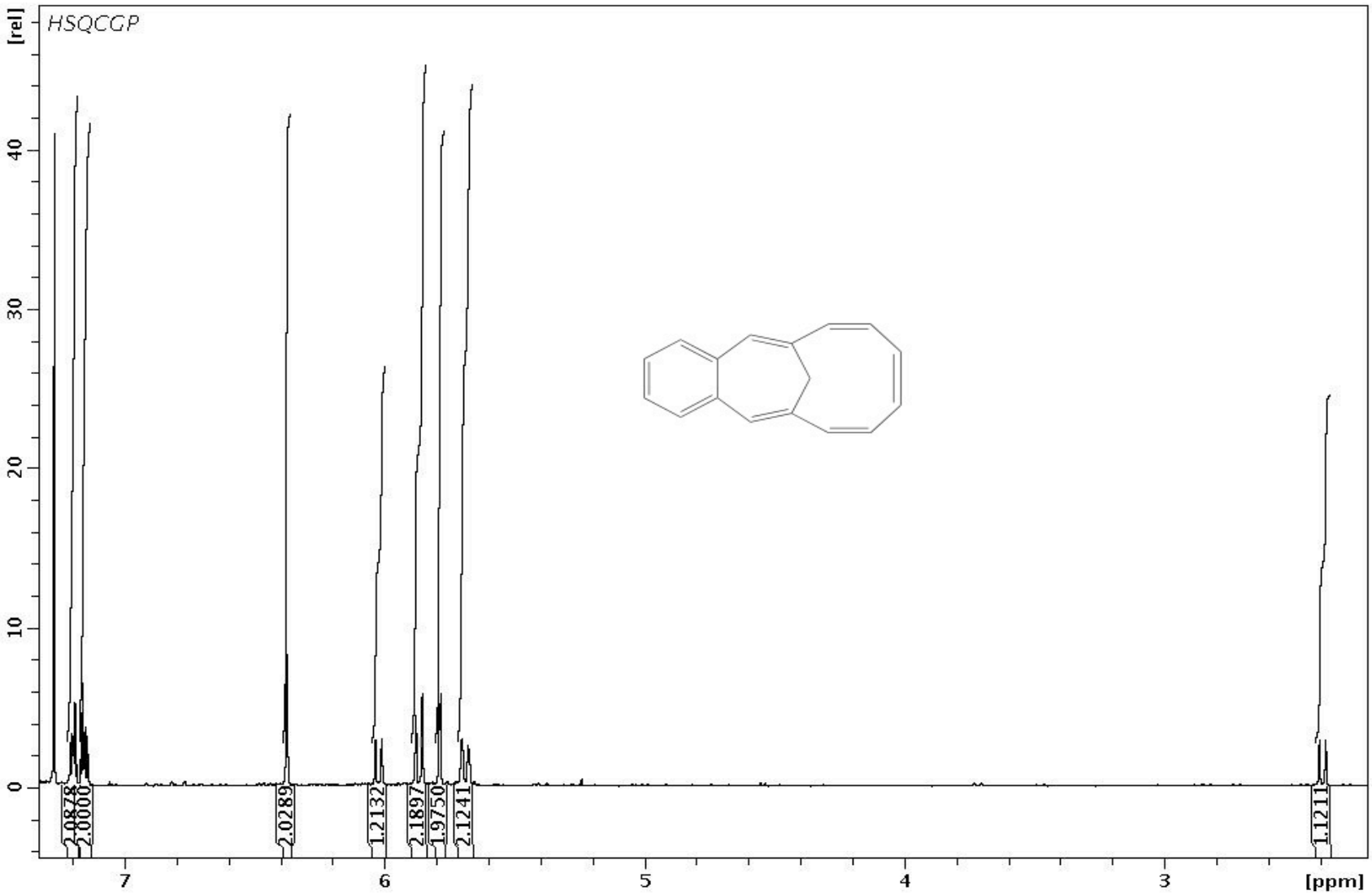
1.9229
1.7995
2.3478
1.0601
2.1810
2.3974
1.3500
2.0954
7
6
5
4
3
[ppm]


HSQCGP
[rel]
0
10
20
30
40
7
6
5
4
3
[ppm]
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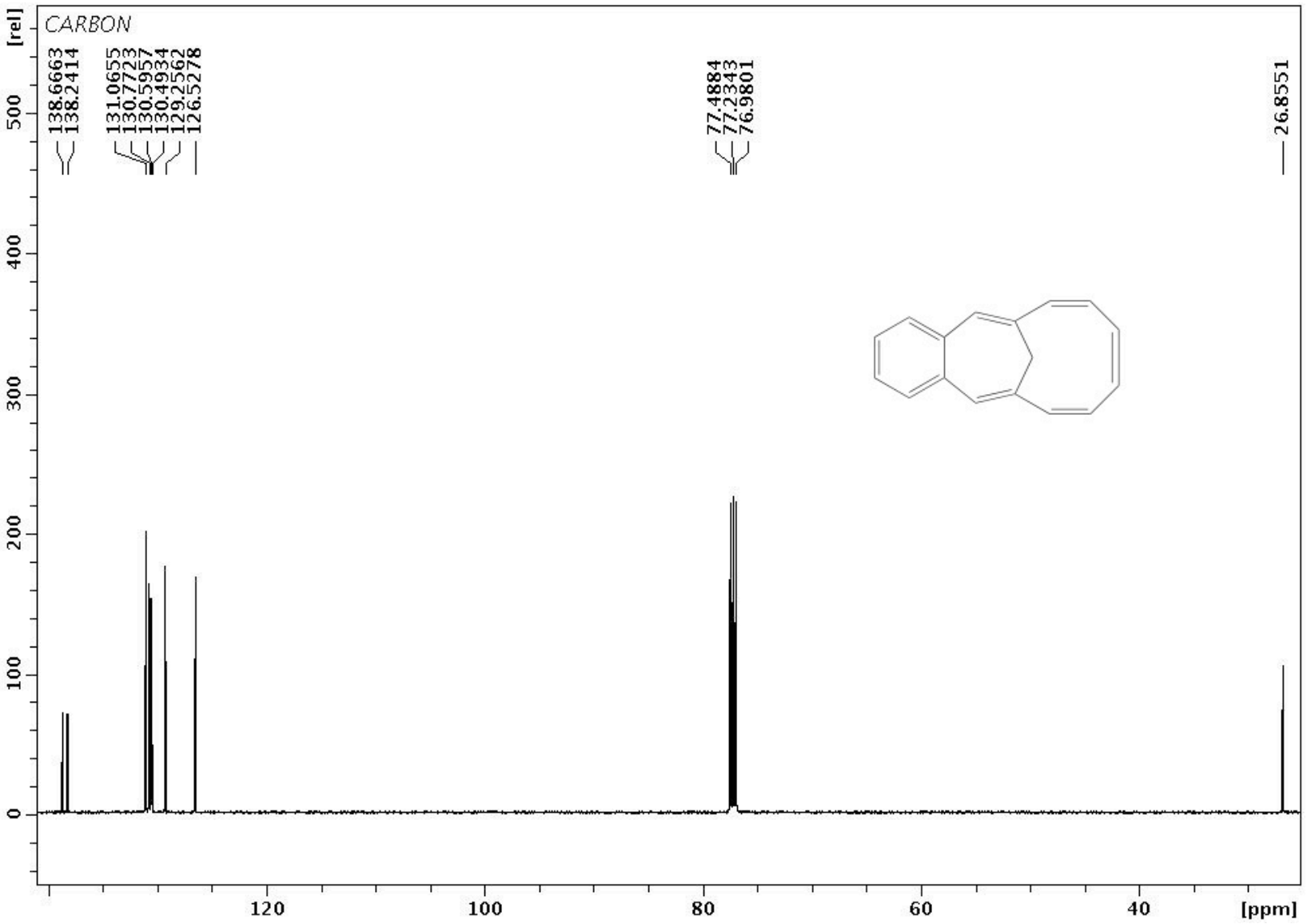
2.0000
2.0289
1.2132
2.1897
1.9750
2.1241
1.1211


CARBON
[rel]
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400
300
200
100
0
138.6663
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131.0655
130.7723
130.5957
130.4934
129.2562
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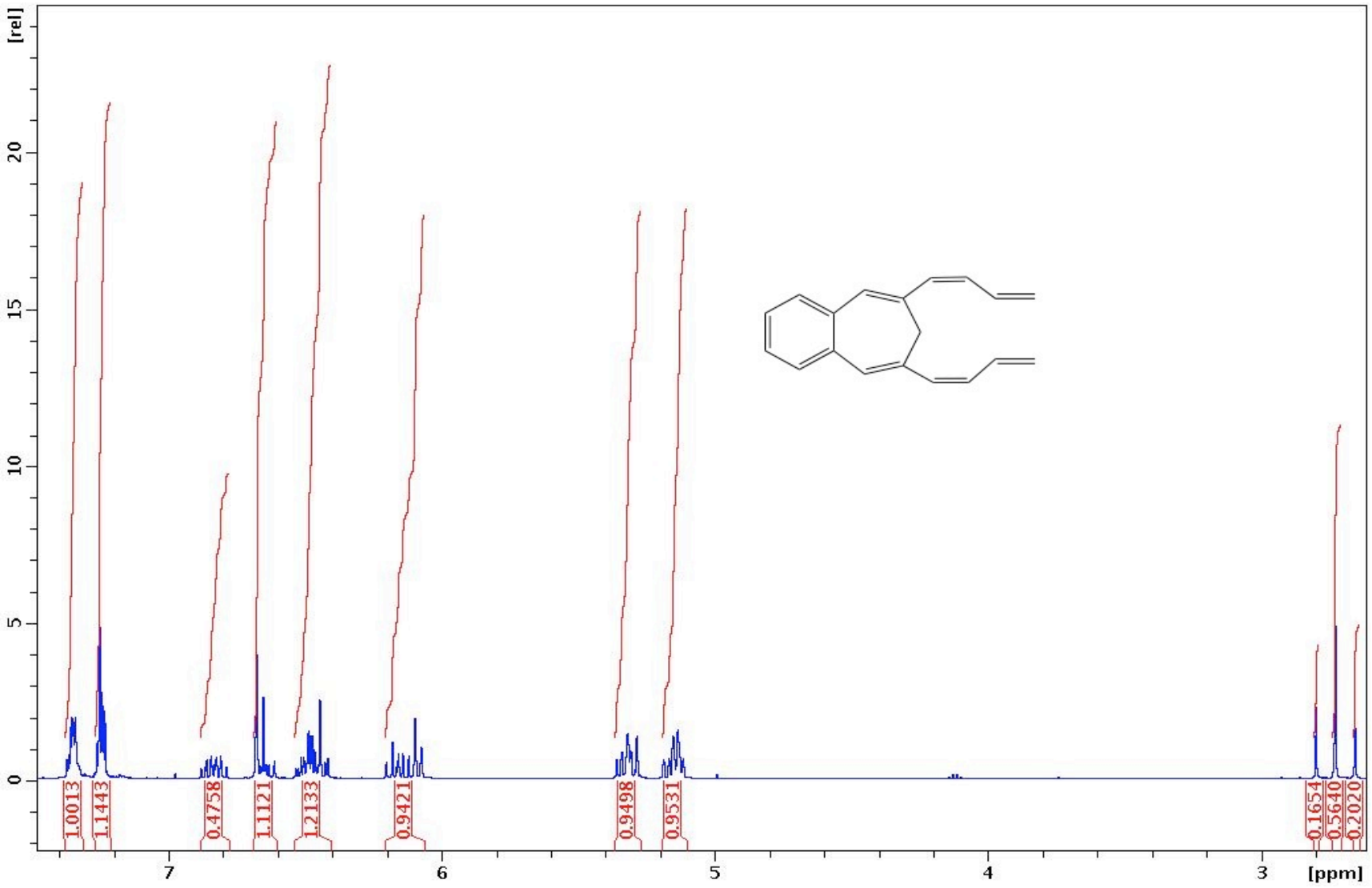
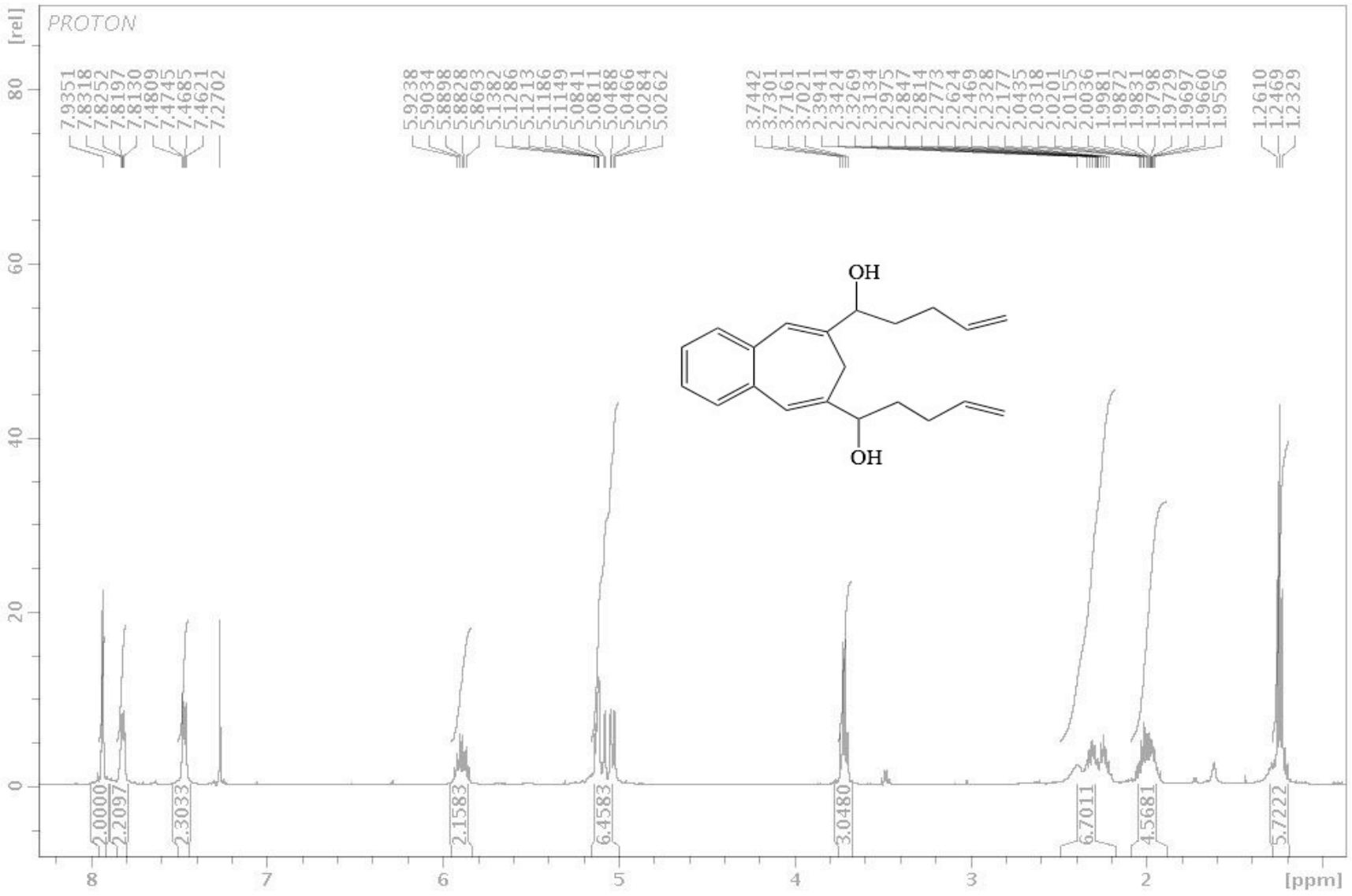
77.4884
77.2343
76.9801
26.8551
120
100
80
60
40
[ppm]


[rel]
20
15
10
5
0
1.0013
1.1443
0.4758
1.1121
1.2133
0.9421
0.9498
0.9531
0.1654
0.5640
0.2020
7
6
5
4
3
[ppm]


PROTON
[rel]
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60
40
20
0
7.9351
7.8318
7.8252
7.8197
7.8130
7.4809
7.4745
7.4685
7.4621
7.2702
5.9238
5.9034
5.8898
5.8828
5.8693
5.1382
5.1286
5.1213
5.1186
5.1149
5.0841
5.0811
5.0488
5.0466
5.0284
5.0262
3.7442
3.7301
3.7161
3.7021
3.3941
2.3424
2.3269
2.3134
2.2975
2.2847
2.2814
2.2773
2.2624
2.2469
2.2328
2.2177
2.0435
2.0318
2.0201
2.0155
2.0036
1.9981
1.9872
1.9831
1.9798
1.9729
1.9697
1.9660
1.9556
1.2610
1.2469
1.2329
OH
OH
2.0000
2.2097
2.3033
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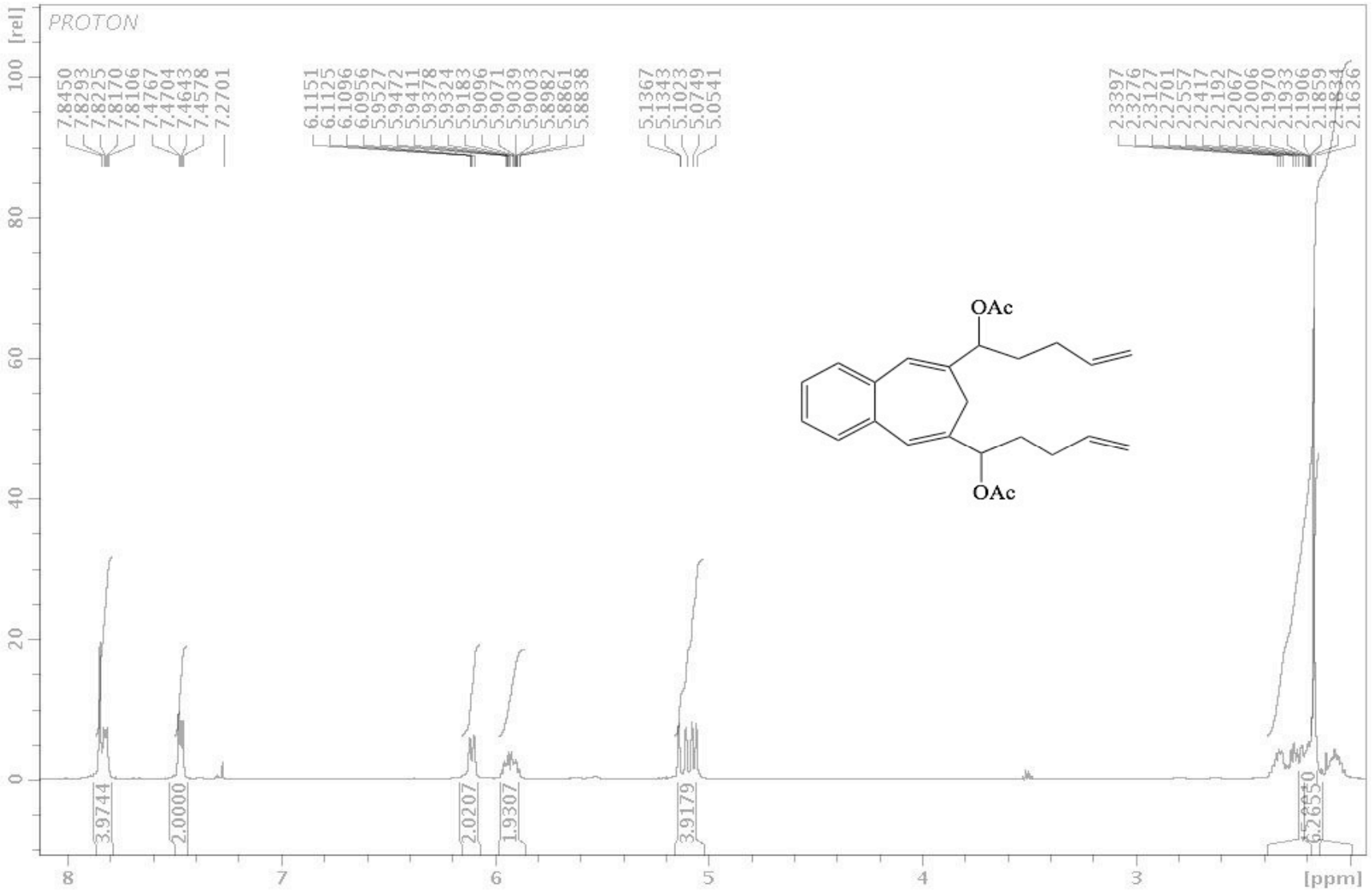
6.4583
3.0480
6.7011
4.5681
5.7222
8
7
6
5
4
3
2
[ppm]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80
60
40
20
0
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7.8106
7.4767
7.4704
7.4643
7.4578
7.2701
6.1151
6.1125
6.1096
6.0956
5.9527
5.9472
5.9411
5.9378
5.9324
5.9183
5.9096
5.9071
5.9039
5.9003
5.8982
5.8861
5.8838
5.1367
5.1343
5.1023
5.0749
5.0541
2.3397
2.3276
2.3127
2.2701
2.2557
2.2417
2.2192
2.2067
2.2006
2.1970
2.1933
2.1906
2.1859
2.1834
2.1636
OAc
OAc
3.9744
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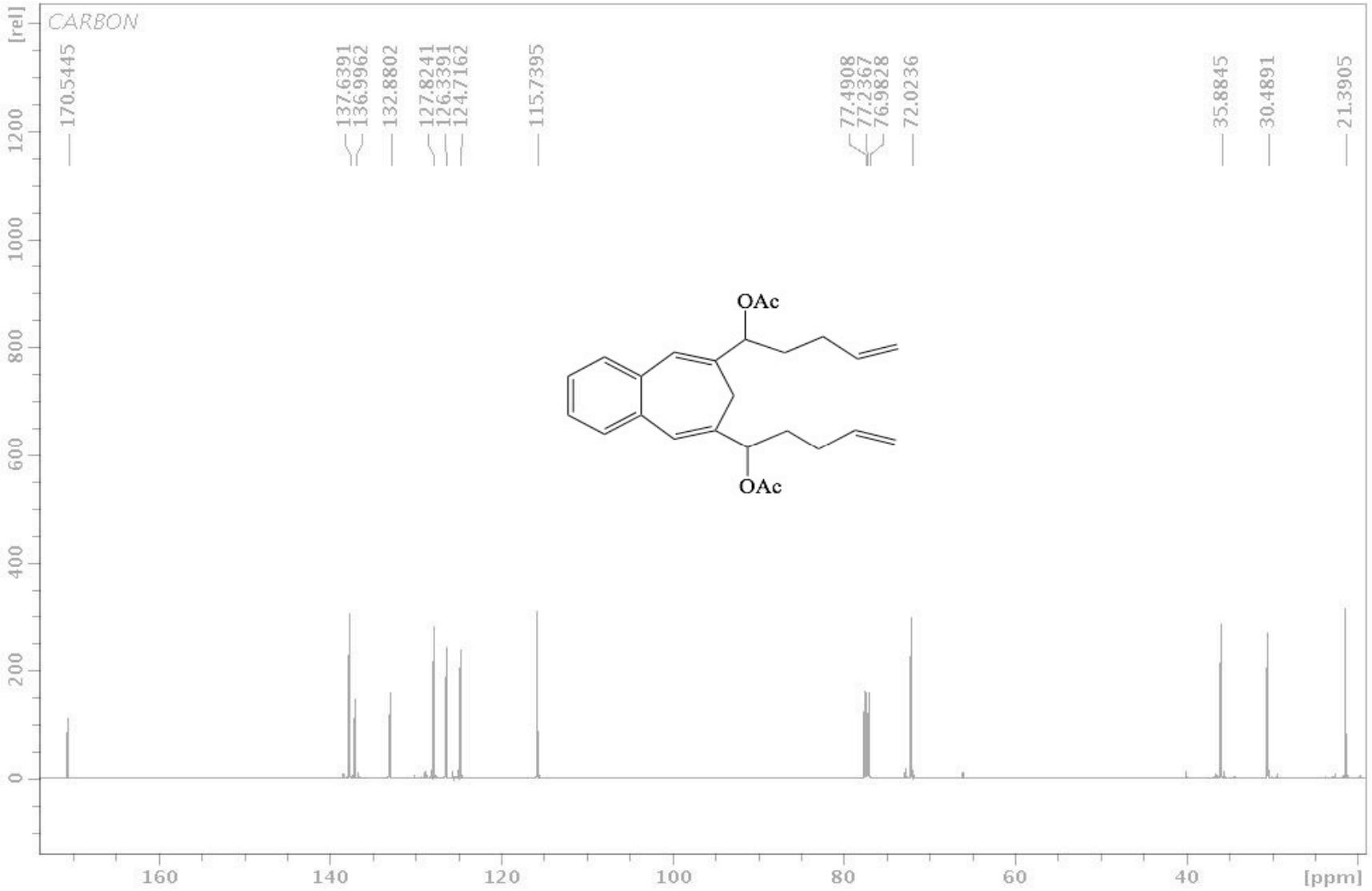
2.0207
1.9307
3.9179
6.2655
8
7
6
5
4
3
[ppm]


CARBON
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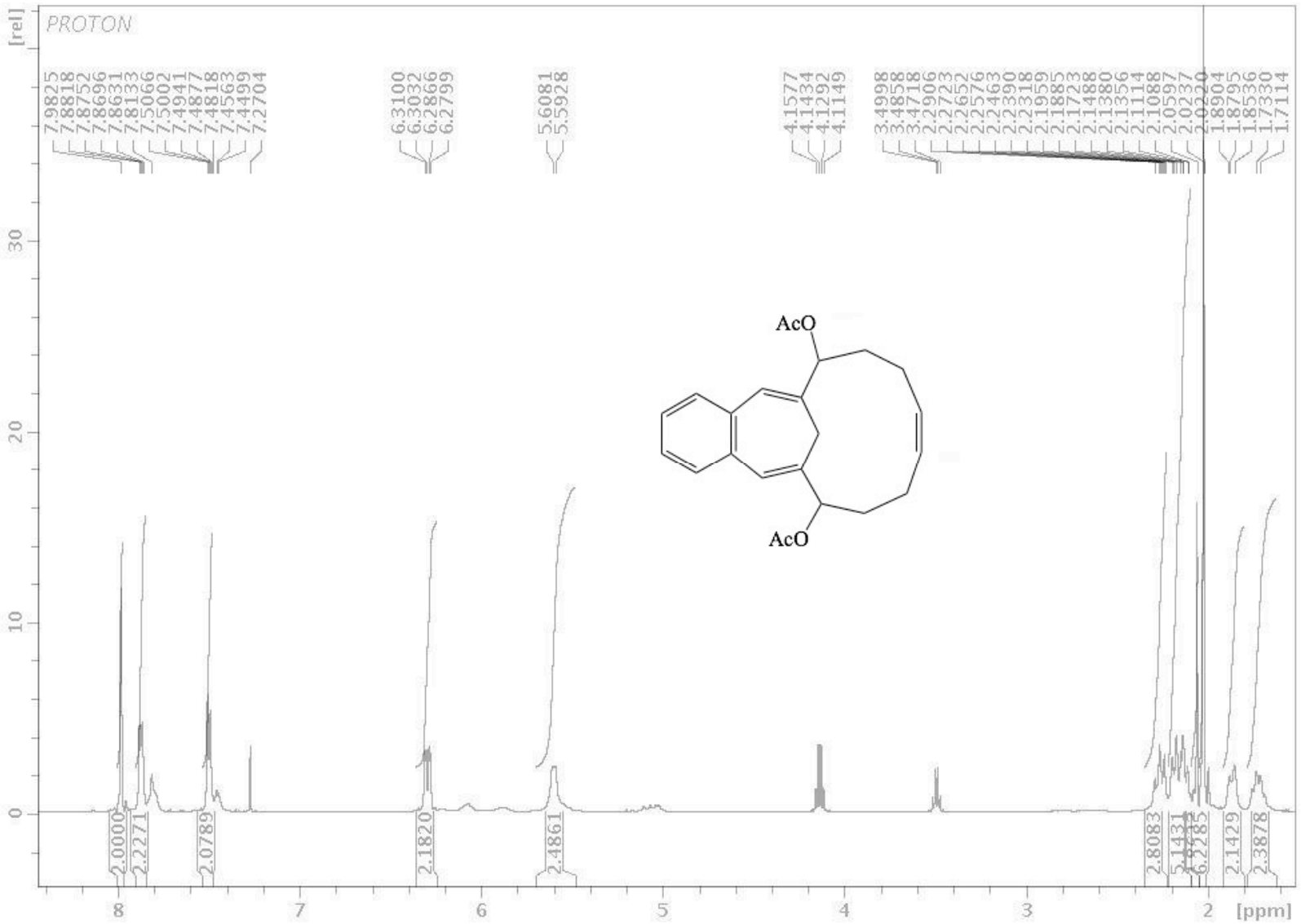
136.9962
132.8802
127.8241
126.3391
124.7162
115.7395
77.4908
77.2367
76.9828
72.0236
35.8845
30.4891
21.3905
OAc
OAc
0
200
400
600
800
1000
1200
160
140
120
100
80
60
40
[ppm]


PROTON
[rel]
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7.8818
7.8752
7.8696
7.8631
7.8133
7.5066
7.5002
7.4941
7.4877
7.4818
7.4563
7.4499
7.2704
6.3100
6.3032
6.2866
6.2799
5.6081
5.5928
4.1577
4.1434
4.1292
4.1149
3.4998
3.4858
3.4718
2.2906
2.2723
2.2652
2.2576
2.2463
2.2390
2.2318
2.1959
2.1885
2.1723
2.1488
2.1380
2.1356
2.1114
2.1088
2.0597
2.0237
2.0220
1.8904
1.8795
1.8536
1.7330
1.7114
AcO
AcO
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2.0789
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5.1431
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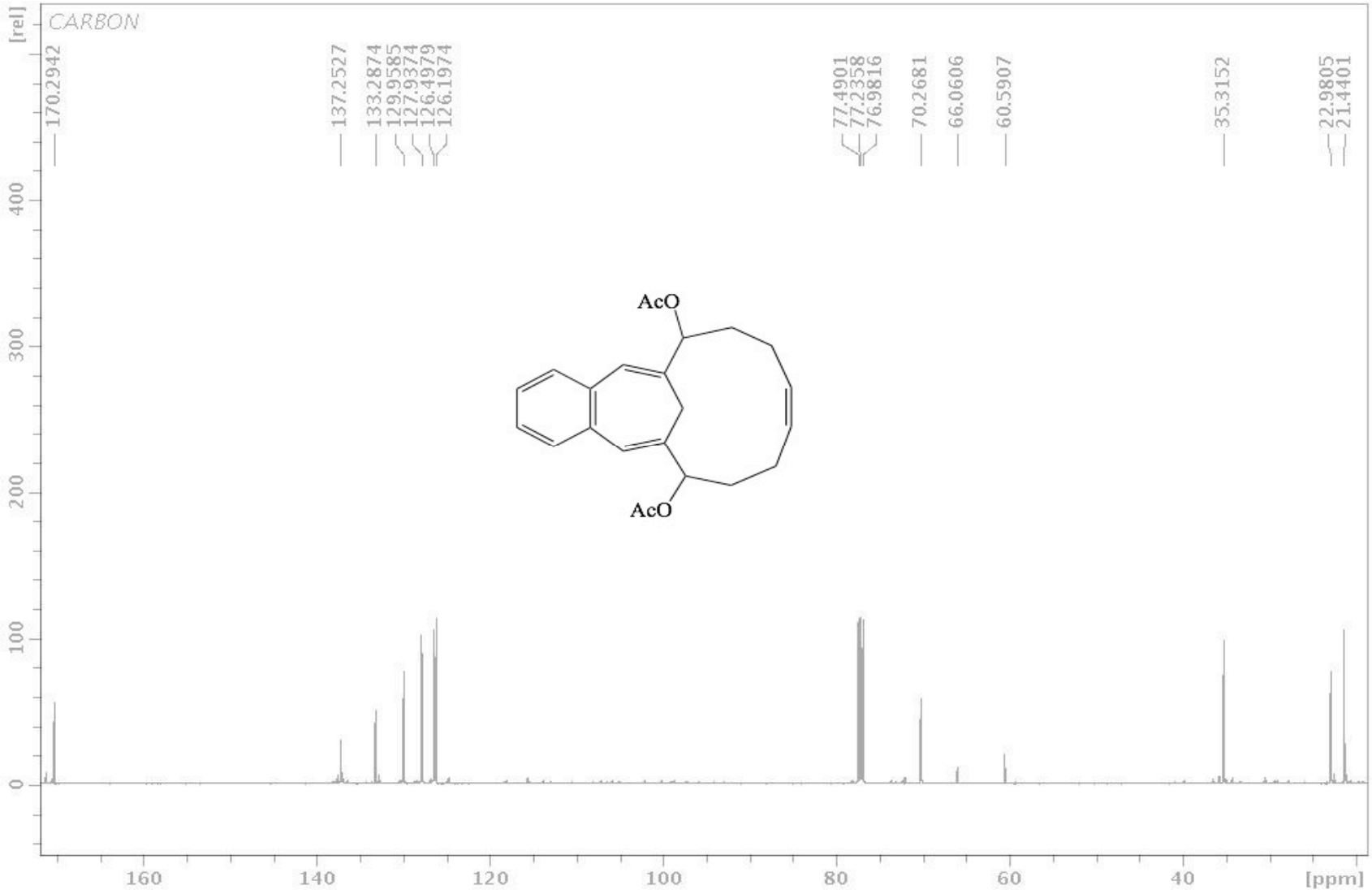
[ppm]


CARBON
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133.2874
129.9585
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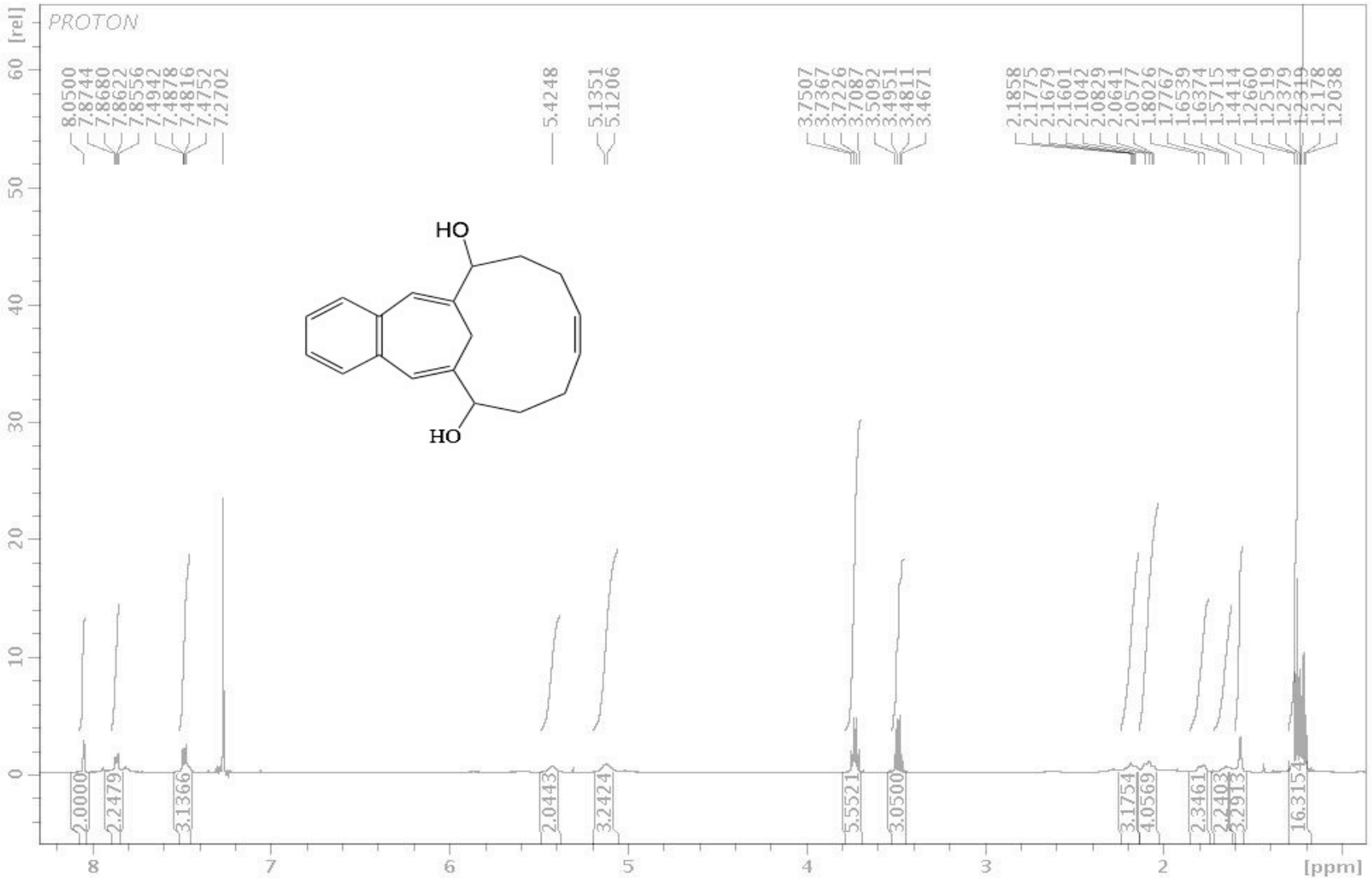
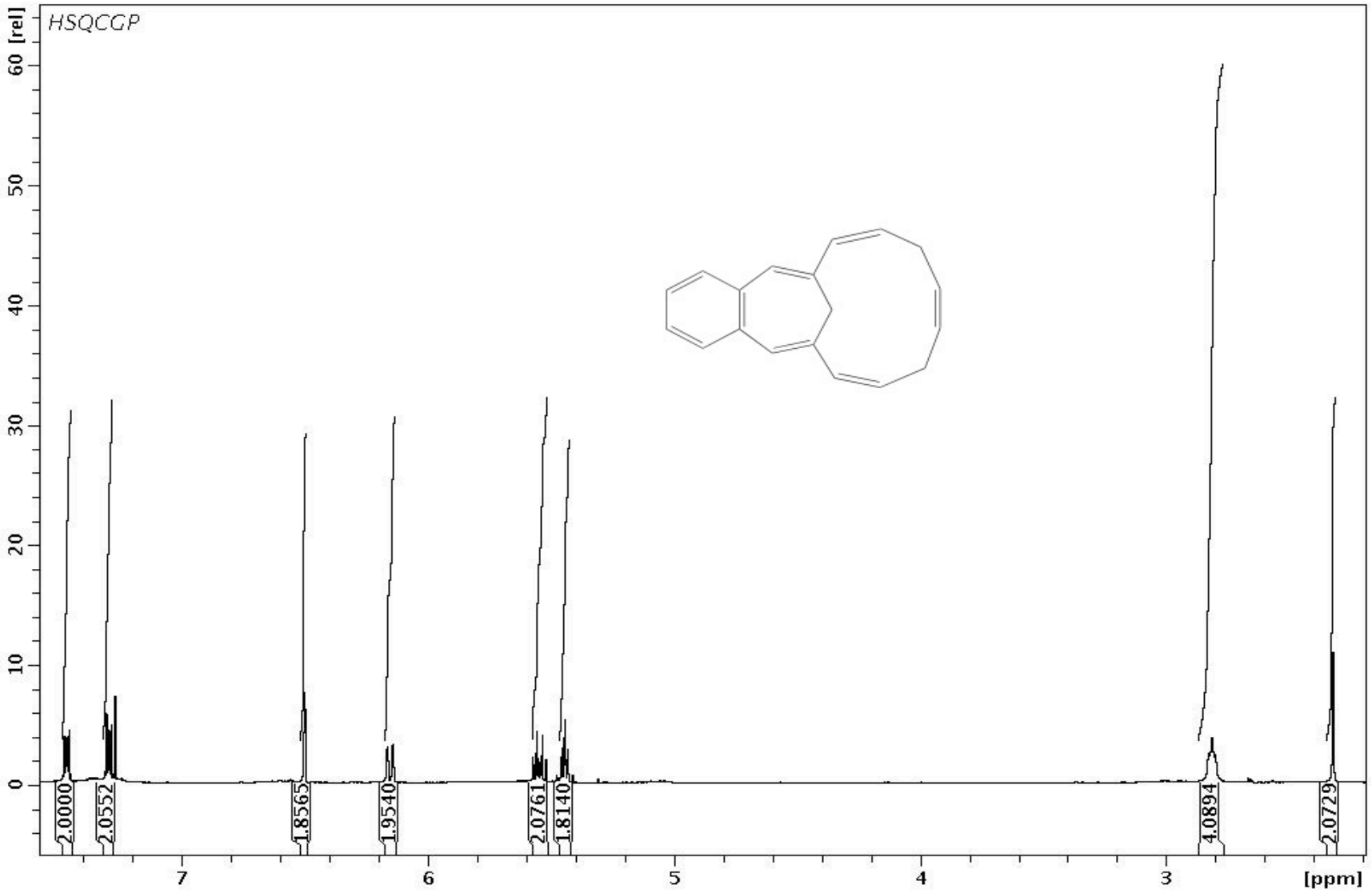
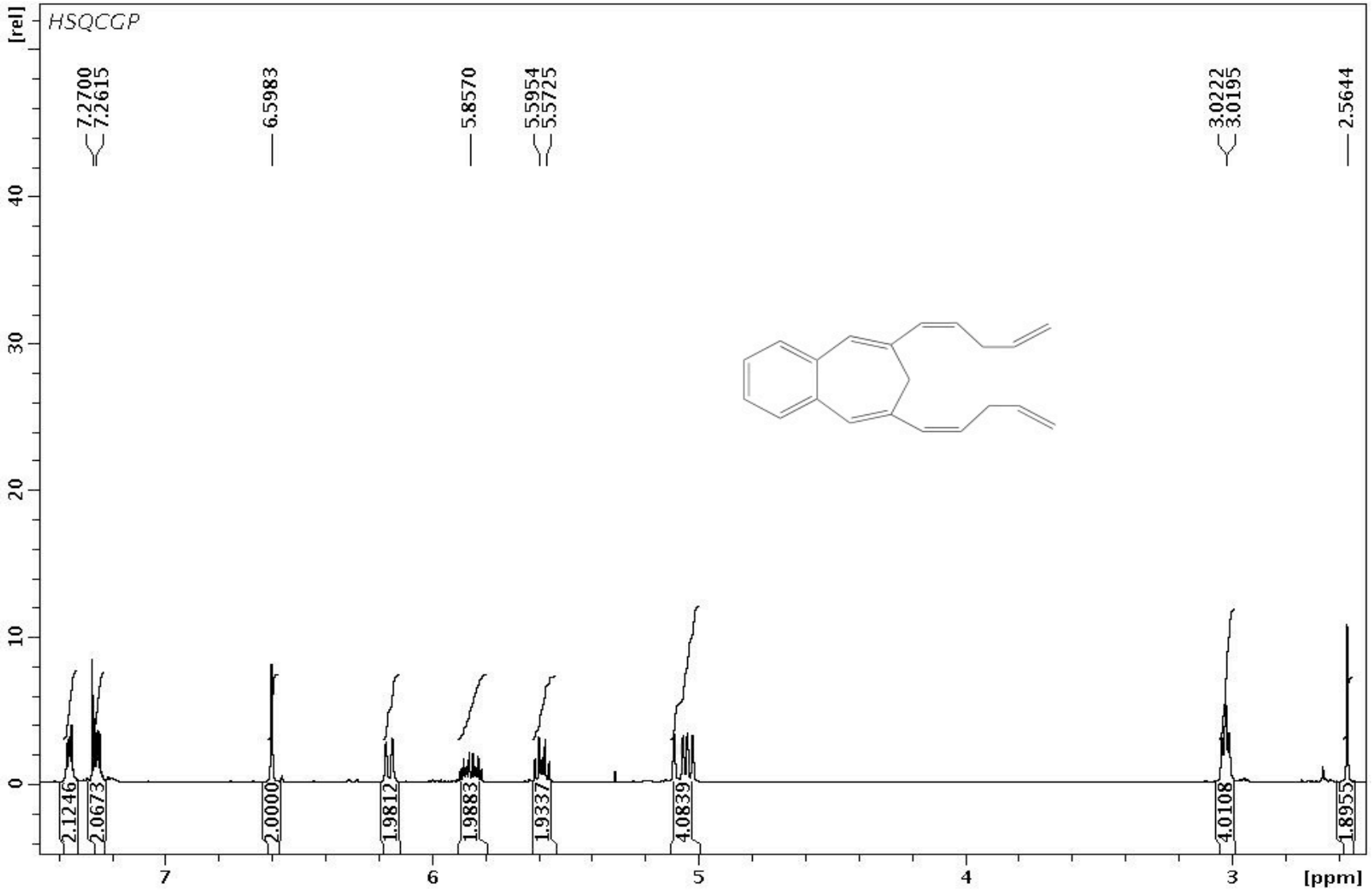
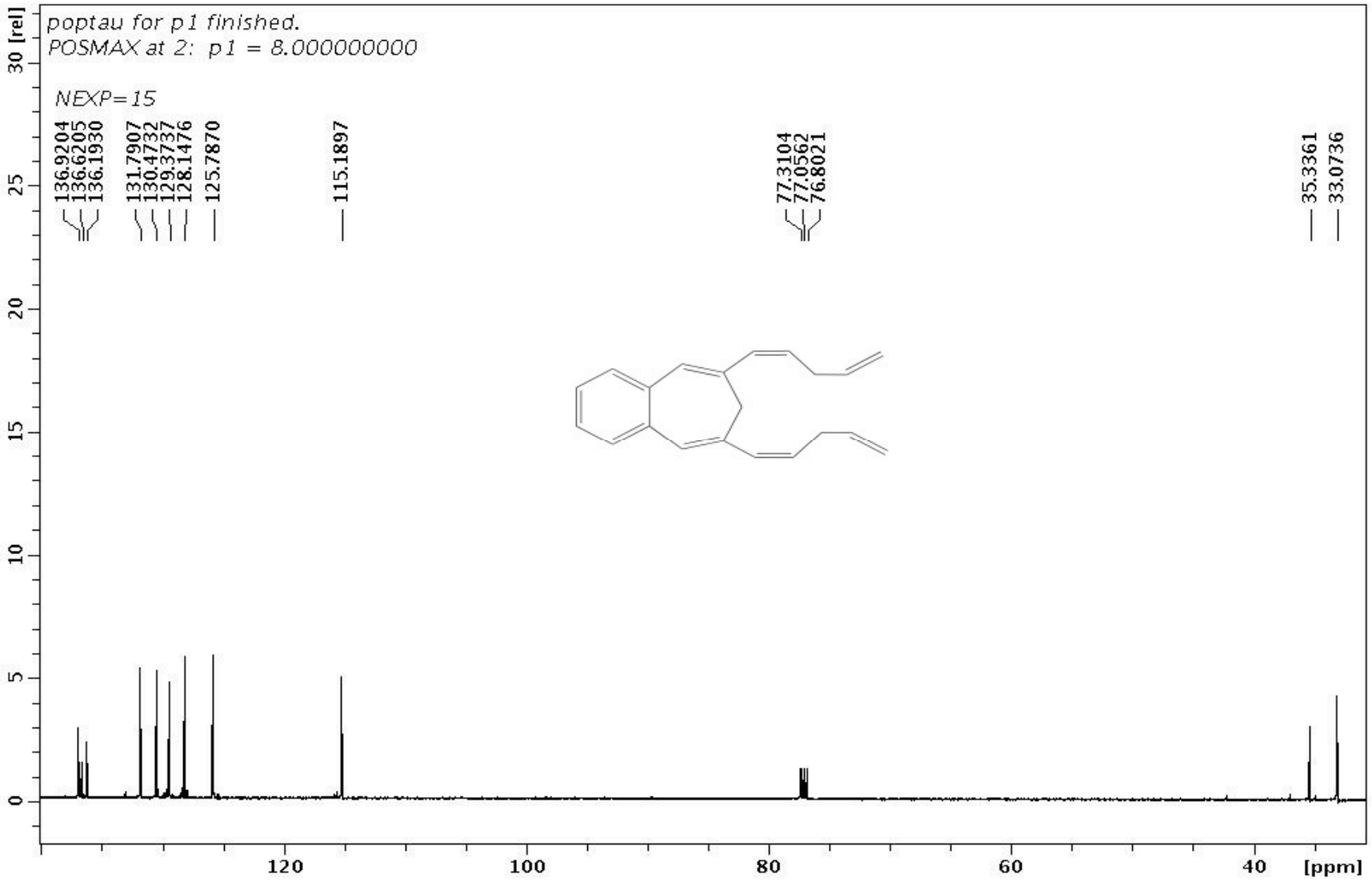
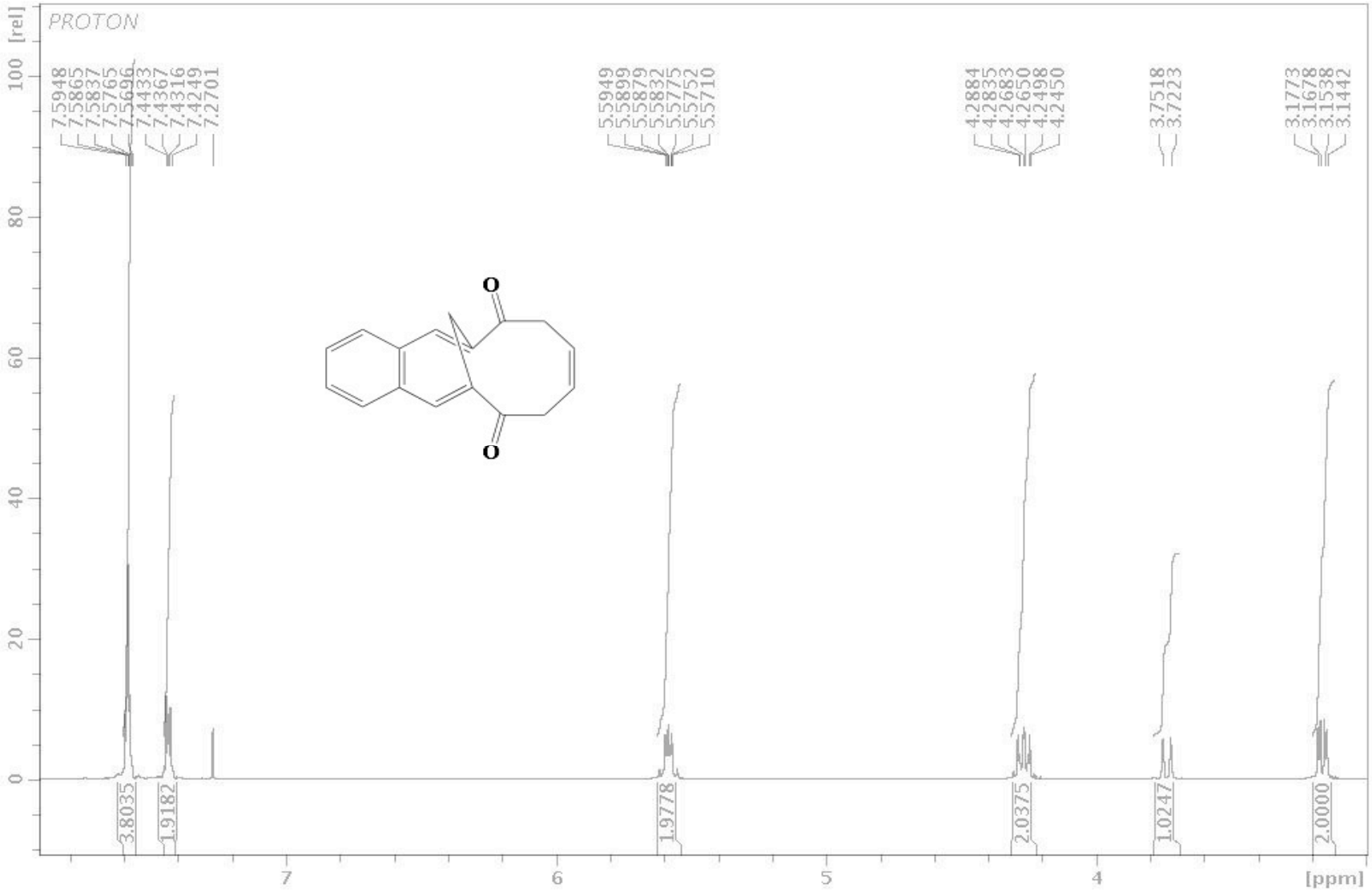
126.4979
126.1974
77.4901
77.2358
76.9816
70.2681
66.0606
60.5907
35.3152
22.9805
21.4401
AcO
AcO
0
100
200
300
400
160
140
120
100
80
60
40
[ppm]

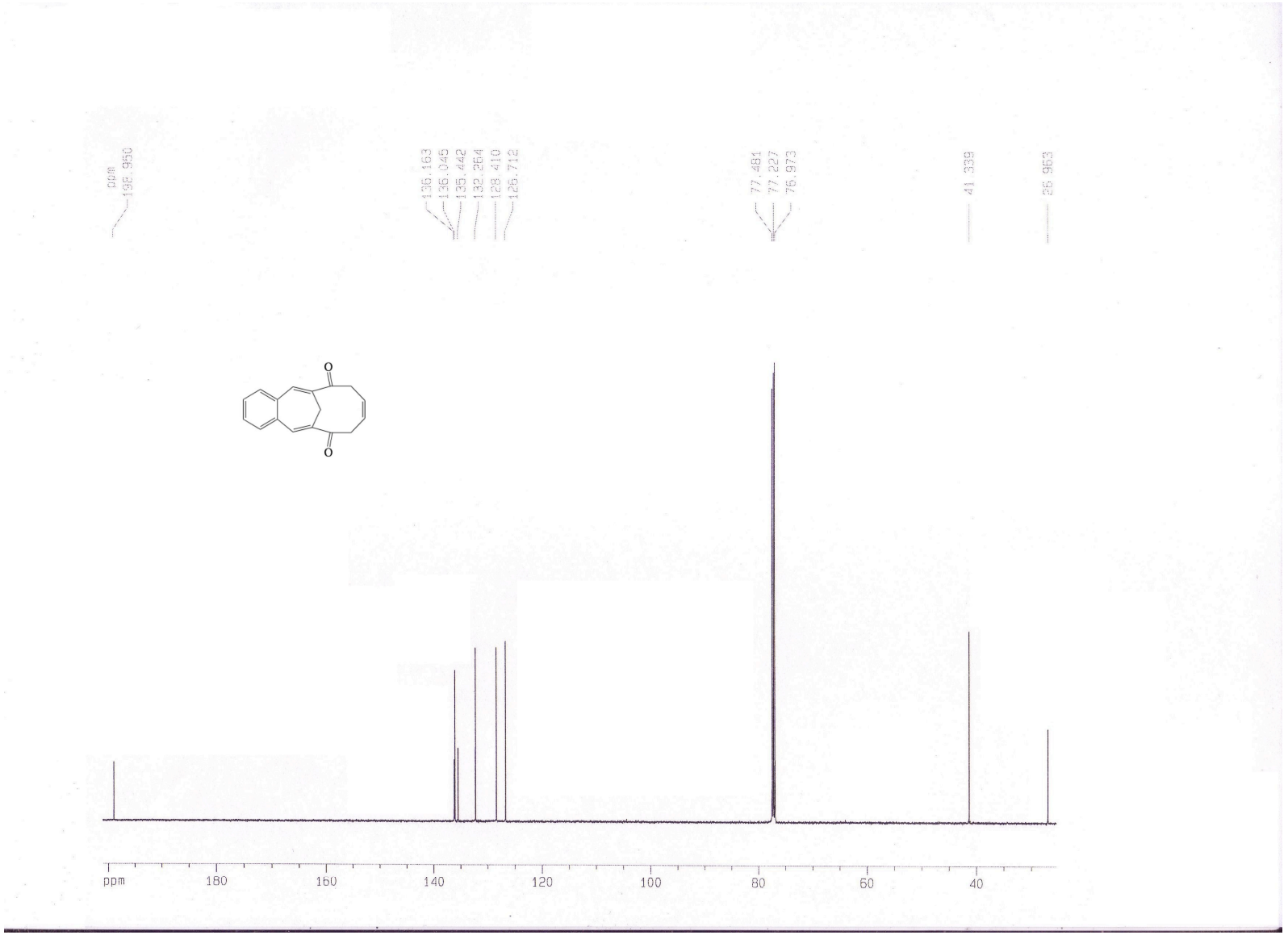

PROTON
[rel]
8.0500
7.8744
7.8680
7.8622
7.8556
7.4942
7.4878
7.4816
7.4752
7.2702
5.4248
5.1351
5.1206
3.7507
3.7367
3.7226
3.7087
3.5092
3.4951
3.4811
3.4671
2.1858
2.1775
2.1679
2.1601
2.1042
2.0829
2.0641
2.0577
1.8026
1.7767
1.6539
1.6374
1.5715
1.4414
1.2660
1.2519
1.2379
1.2319
1.2178
1.2038
HO
HO
2.0000
2.2479
3.1366
2.0443
3.2424
5.5521
3.0500
3.1754
4.0569
2.3461
2.2403
3.2913
16.3154
[ppm]

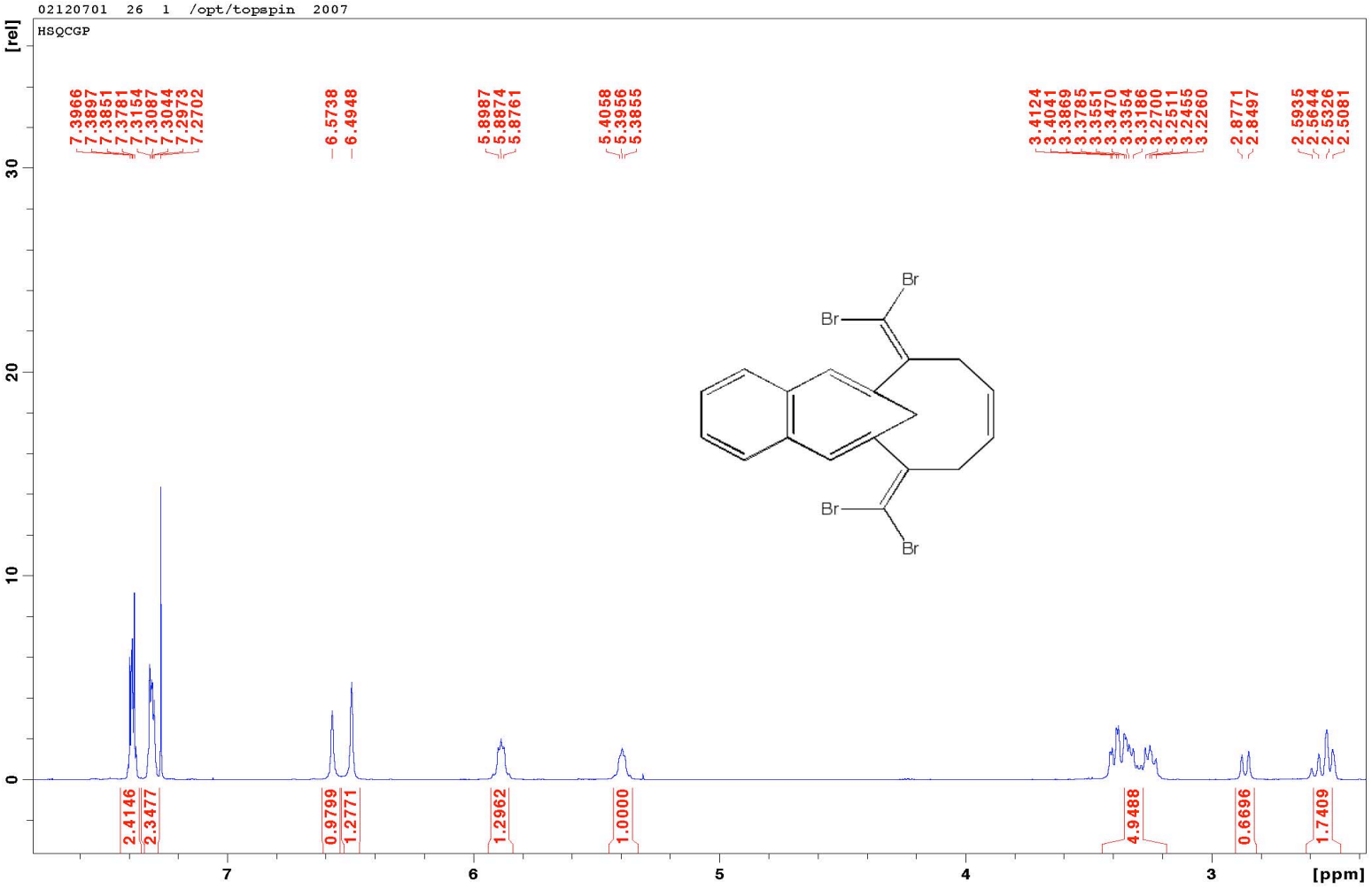

HSQCGP
60 [rel]
50
40
30
20
10
0
2.0000
2.0552
1.8565
1.9540
2.0761
1.8140
4.0894
2.0729
7
6
5
4
3
[ppm]

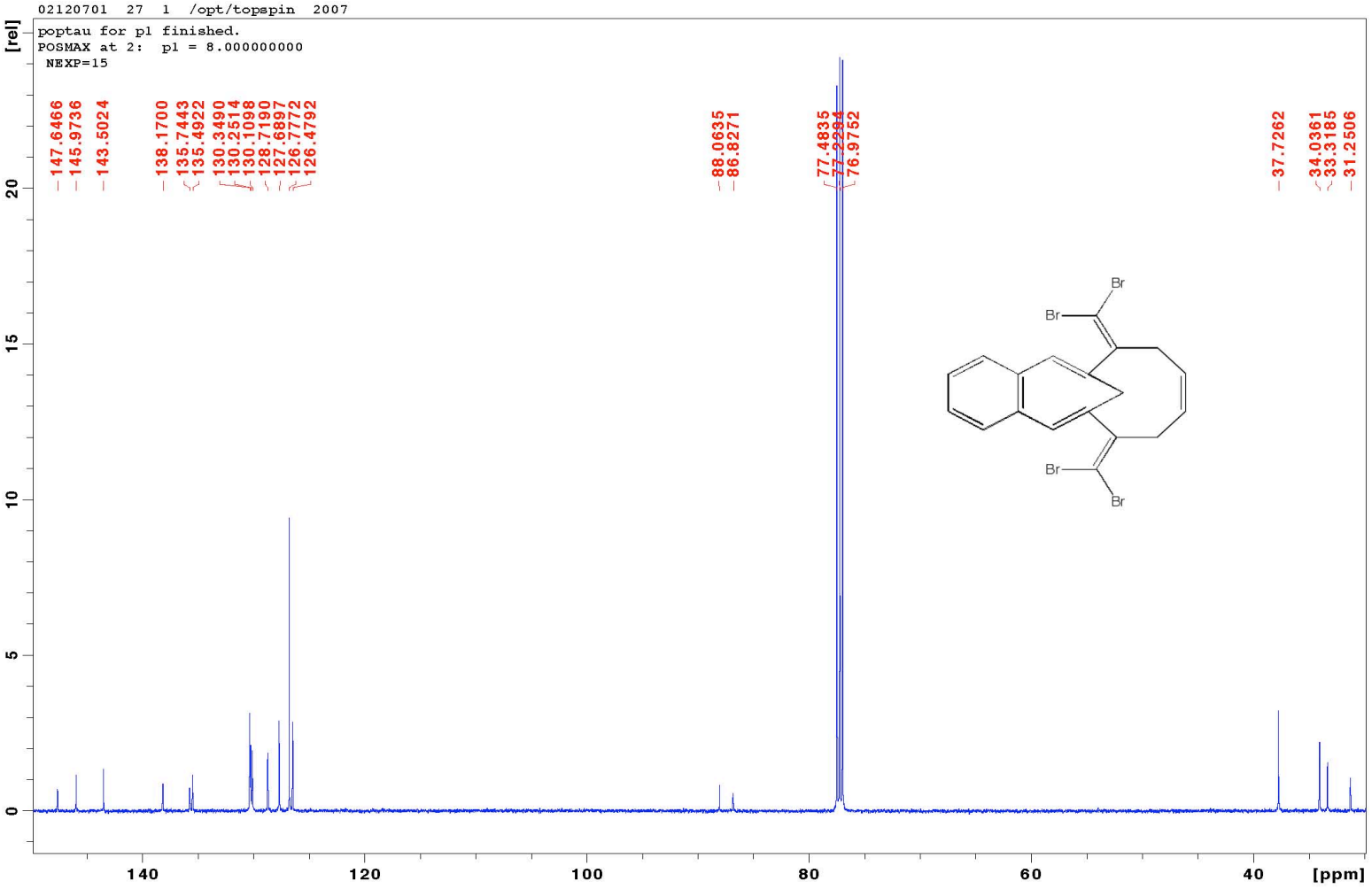

HSQCGP
[rel]
7.2700
7.2615
6.5983
5.8570
5.5954
5.5725
3.0222
3.0195
2.5644
2.1246
2.0673
2.0000
1.9812
1.9883
1.9337
4.0839
4.0108
1.8955
[ppm]

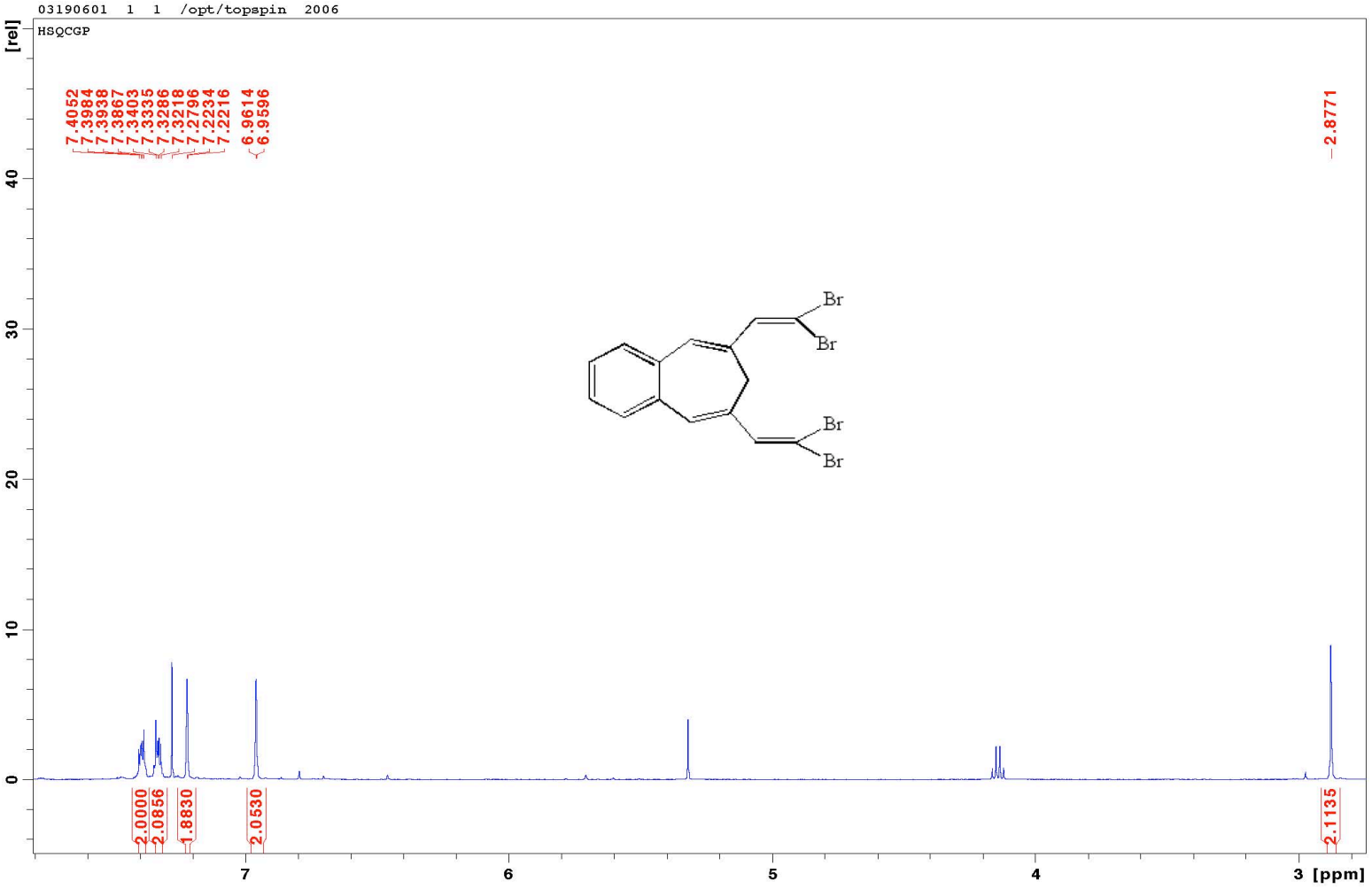

poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
136.9204
136.6205
136.1930
131.7907
130.4732
129.3737
128.1476
125.7870
115.1897
77.3104
77.0562
76.8021
35.3361
33.0736
30 [rel]
25
20
15
10
5
0
120
100
80
60
40
[ppm]

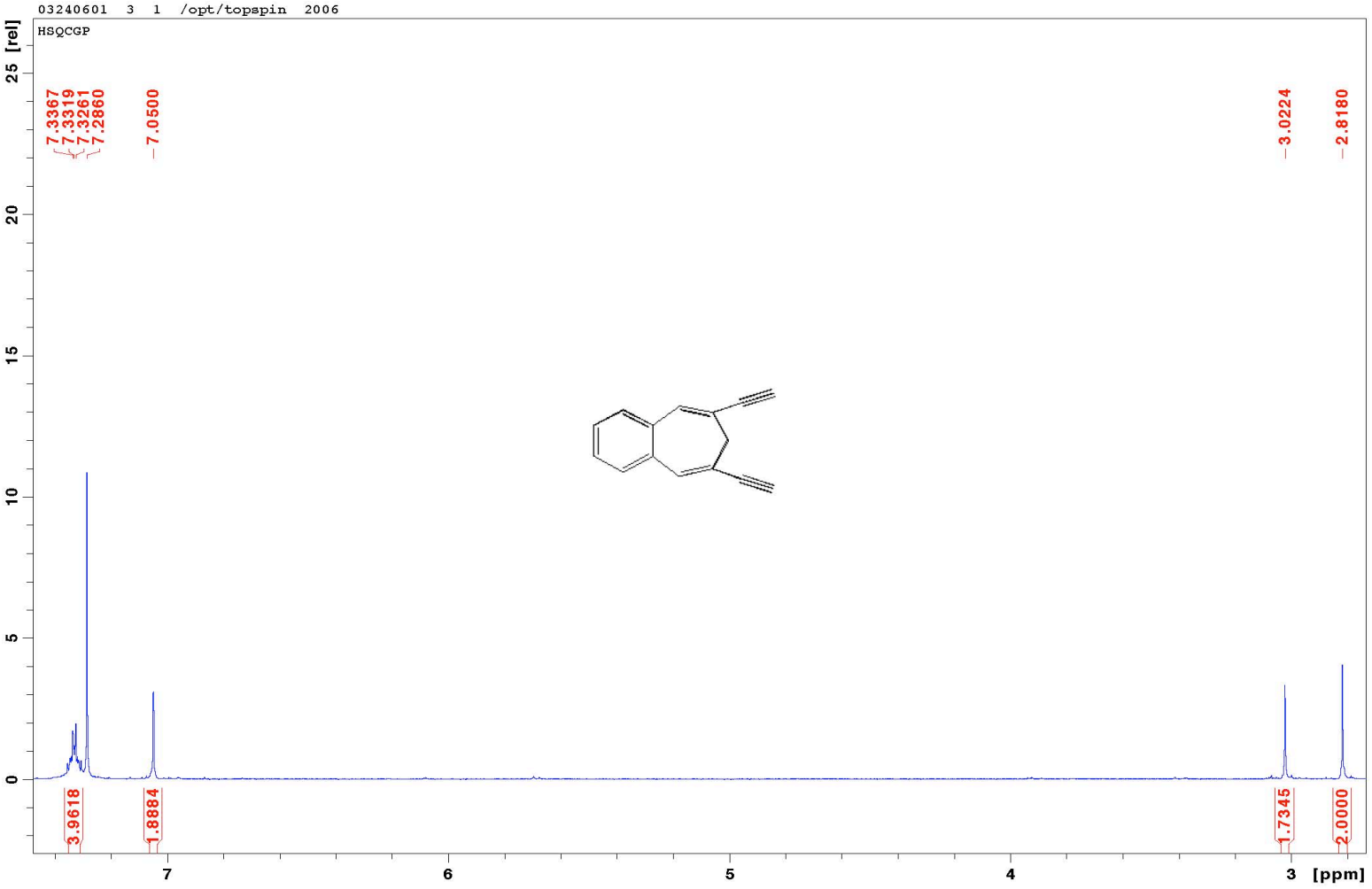

PROTON
100 [rel]
80
60
40
20
0
7.5948
7.5865
7.5837
7.5765
7.5696
7.4433
7.4367
7.4316
7.4249
7.2701
5.5949
5.5899
5.5879
5.5832
5.5775
5.5752
5.5710
4.2884
4.2835
4.2683
4.2650
4.2498
4.2450
3.7518
3.7223
3.1773
3.1678
3.1538
3.1442
O
O
3.8035
1.9182
1.9778
2.0375
1.0247
2.0000
7
6
5
4
[ppm]

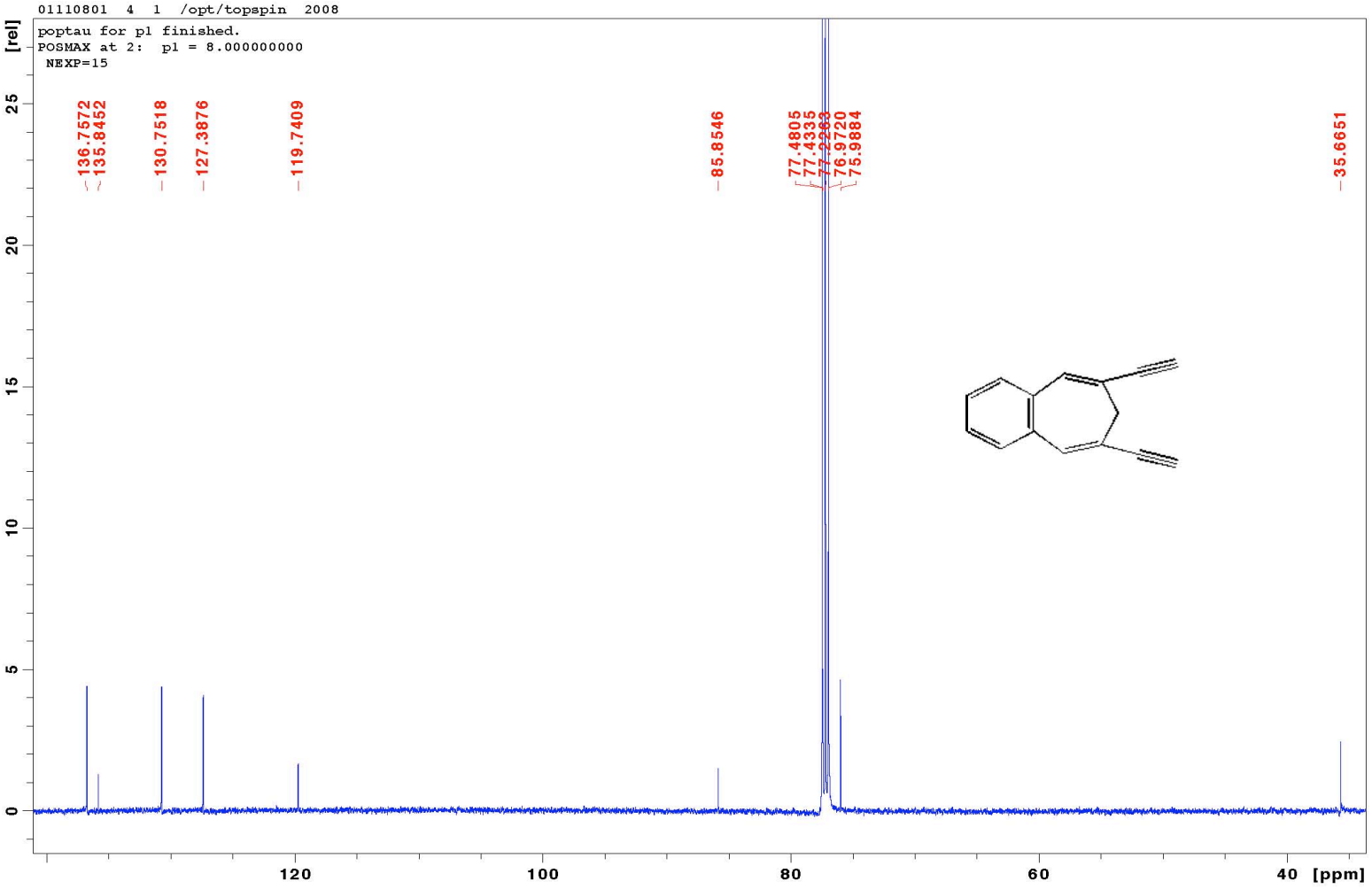

ppm
198.950
136.163
136.045
135.442
132.264
128.410
126.712
77.481
77.227
76.973
41.339
26.963
O
O
ppm
180
160
140
120
100
80
60
40

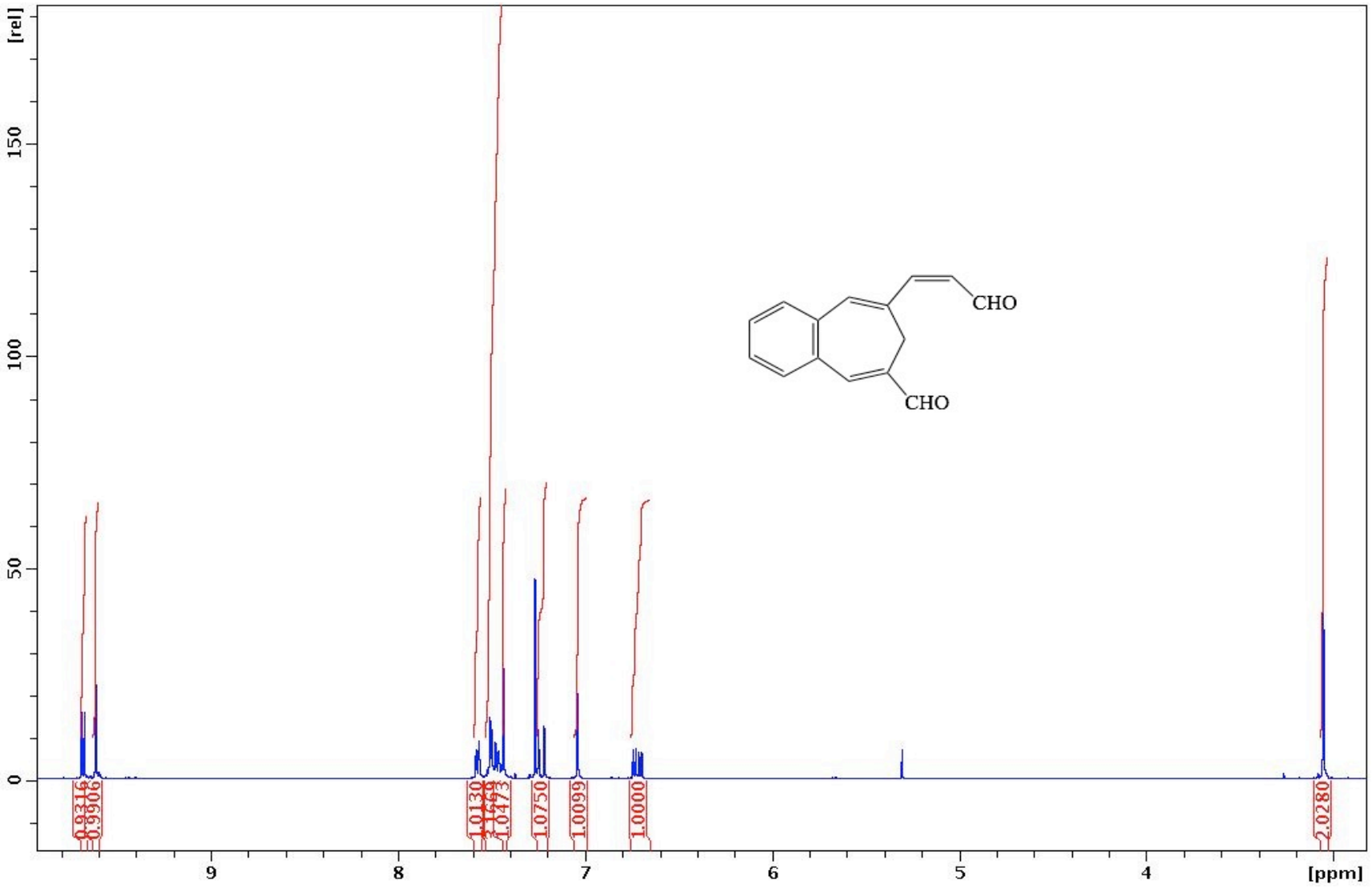

02120701 26 1 /opt/topspin 2007
HSQCGP
[rel]
7.3966
7.3897
7.3851
7.3781
7.3154
7.3087
7.3044
7.2973
7.2702
6.5738
6.4948
5.8987
5.8874
5.8761
5.4058
5.3956
5.3855
3.4124
3.4041
3.3869
3.3785
3.3551
3.3470
3.3354
3.3186
3.2700
3.2511
3.2455
3.2260
2.8771
2.8497
2.5935
2.5644
2.5326
2.5081
Br
Br
Br
Br
2.4146
2.3477
0.9799
1.2771
1.2962
1.0000
4.9488
0.6696
1.7409
[ppm]

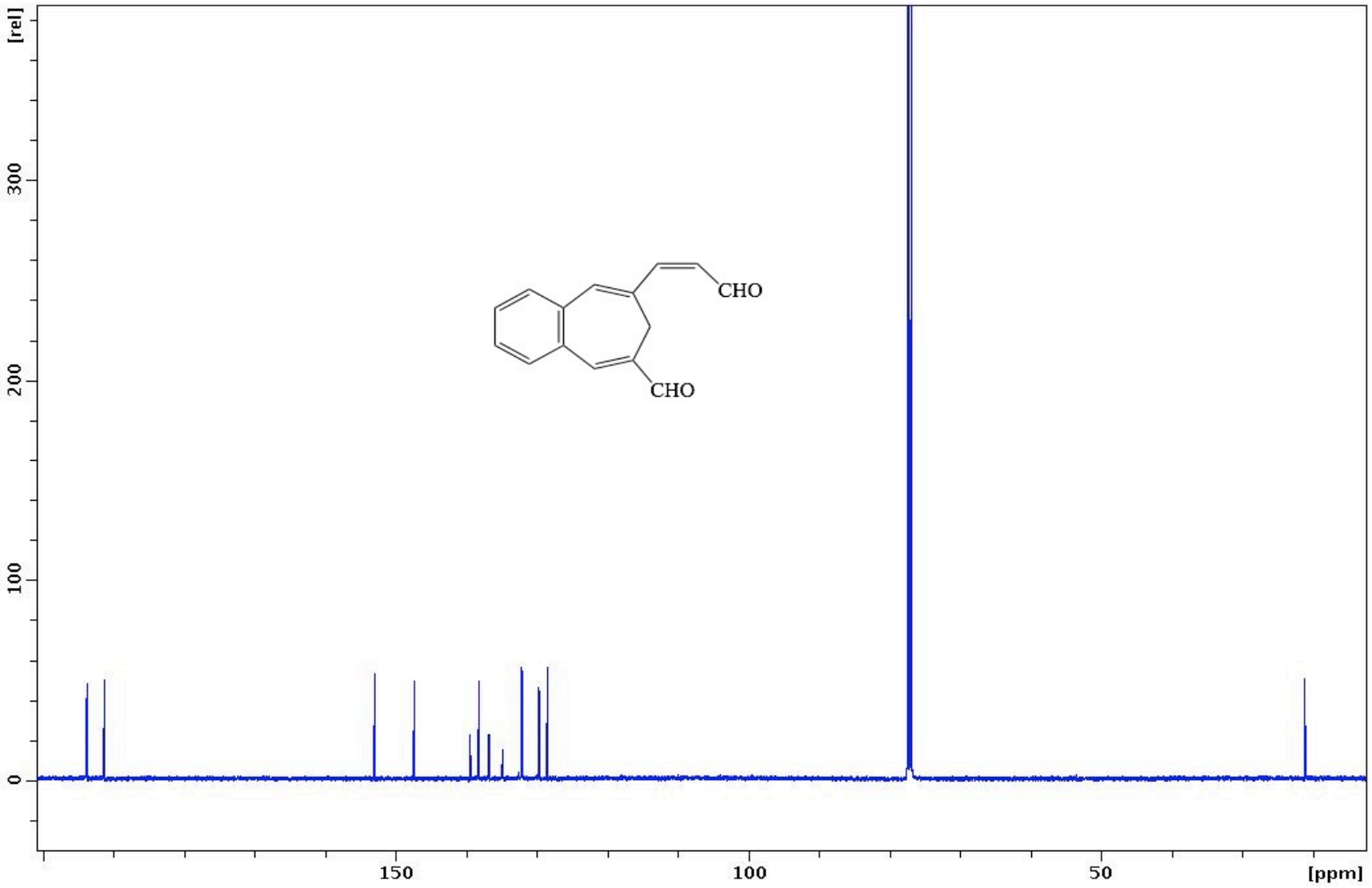

02120701 27 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
147.6466
145.9736
143.5024
138.1700
135.7443
135.4922
130.3490
130.2514
130.1098
128.7190
127.6897
126.7772
126.4792
88.0635
86.8271
77.4835
77.2284
76.9752
37.7262
34.0361
33.3185
31.2506
[rel]
0
5
10
15
20
140
120
100
80
60
40
[ppm]
Br
Br
Br
Br

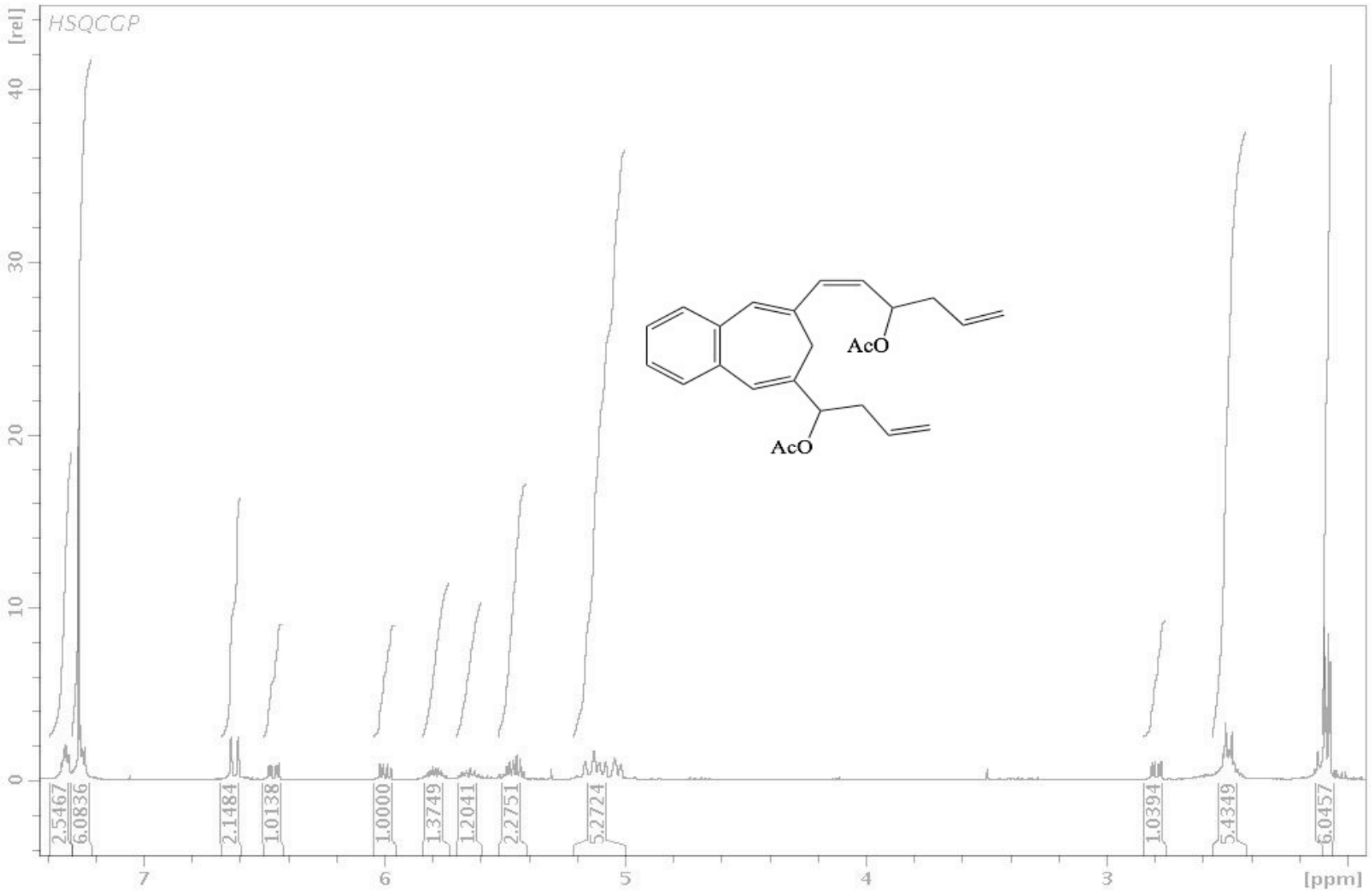

03190601 1 1 /opt/topspin 2006
HSQCGP
[rel]
7.4052
7.3984
7.3938
7.3867
7.3403
7.3335
7.3286
7.3218
7.2796
7.2234
7.2216
6.9614
6.9596
2.8771
Br
Br
Br
Br
2.0000
2.0856
1.8830
2.0530
2.1135
7
6
5
4
3 [ppm]

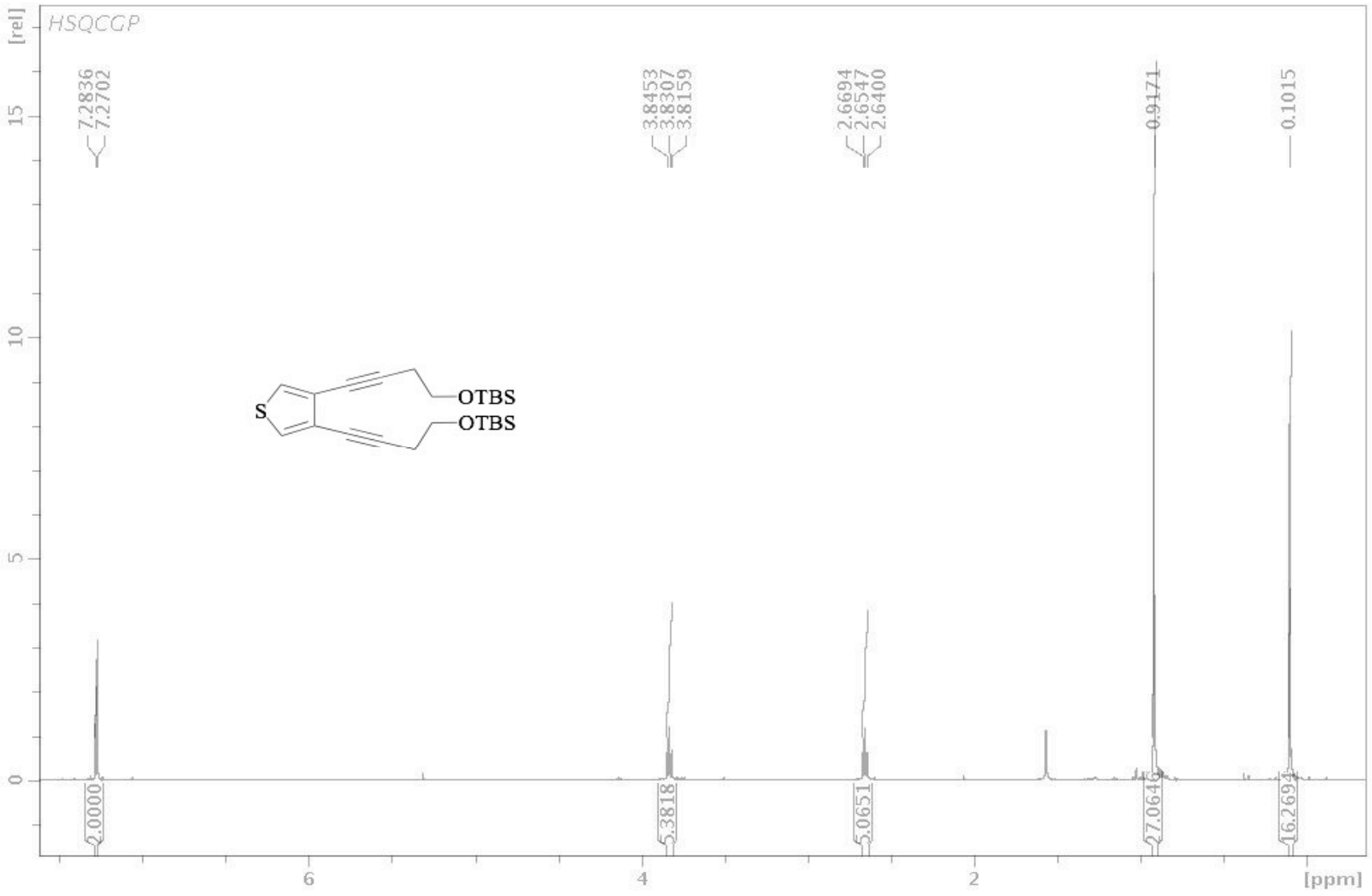

03240601 3 1 /opt/topspin 2006
HSQCGP
25 [rel]
20
15
10
5
0
7.3367
7.3319
7.3261
7.2860
7.0500
3.0224
2.8180
3.9618
1.8884
1.7345
2.0000
7
6
5
4
3
[ppm]

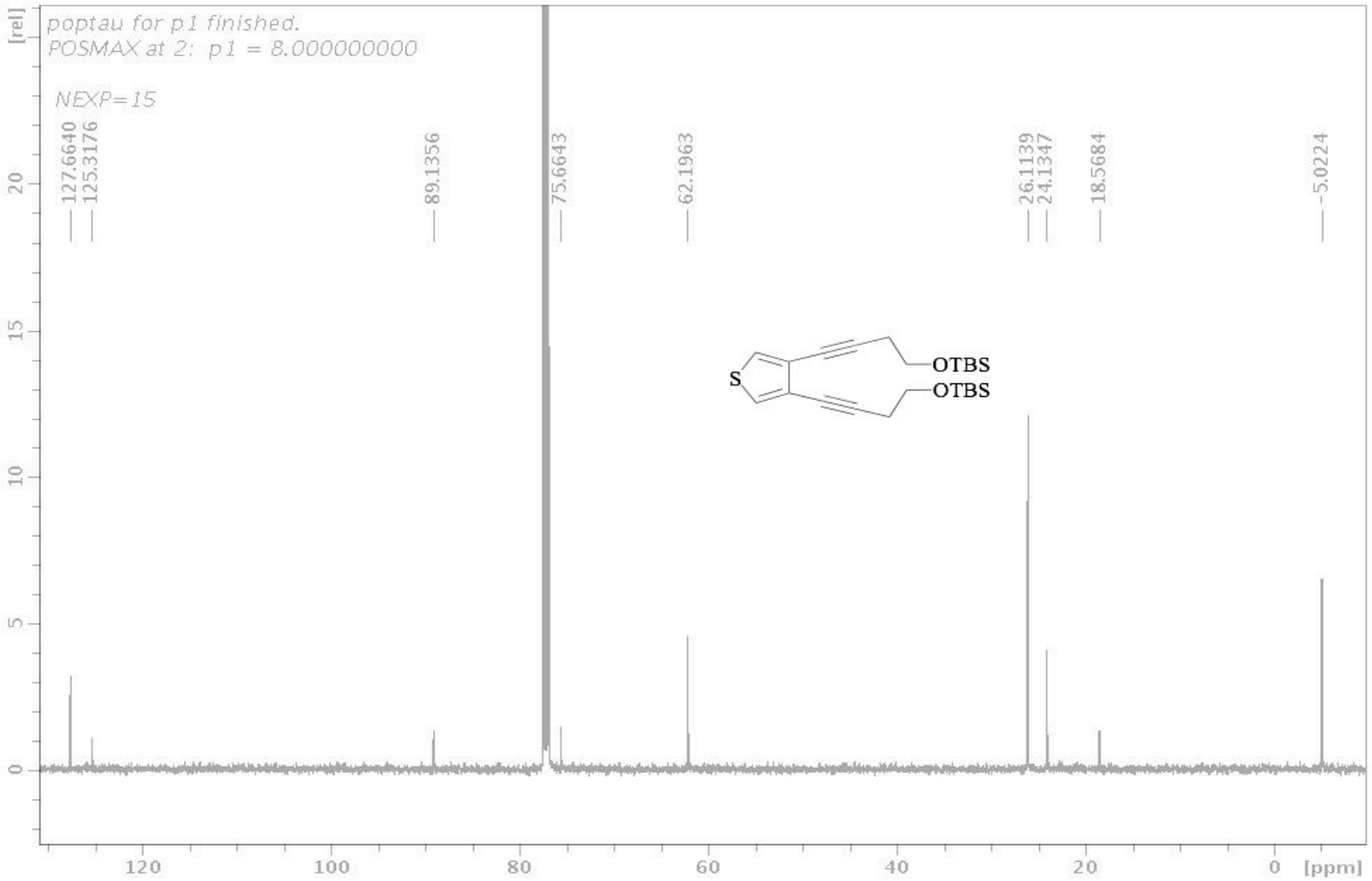

01110801 4 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
136.7572
135.8452
130.7518
127.3876
119.7409
85.8546
77.4805
77.4335
77.2263
76.9720
75.9884
35.6651
[rel]
0
5
10
15
20
25
120
100
80
60
40
[ppm]

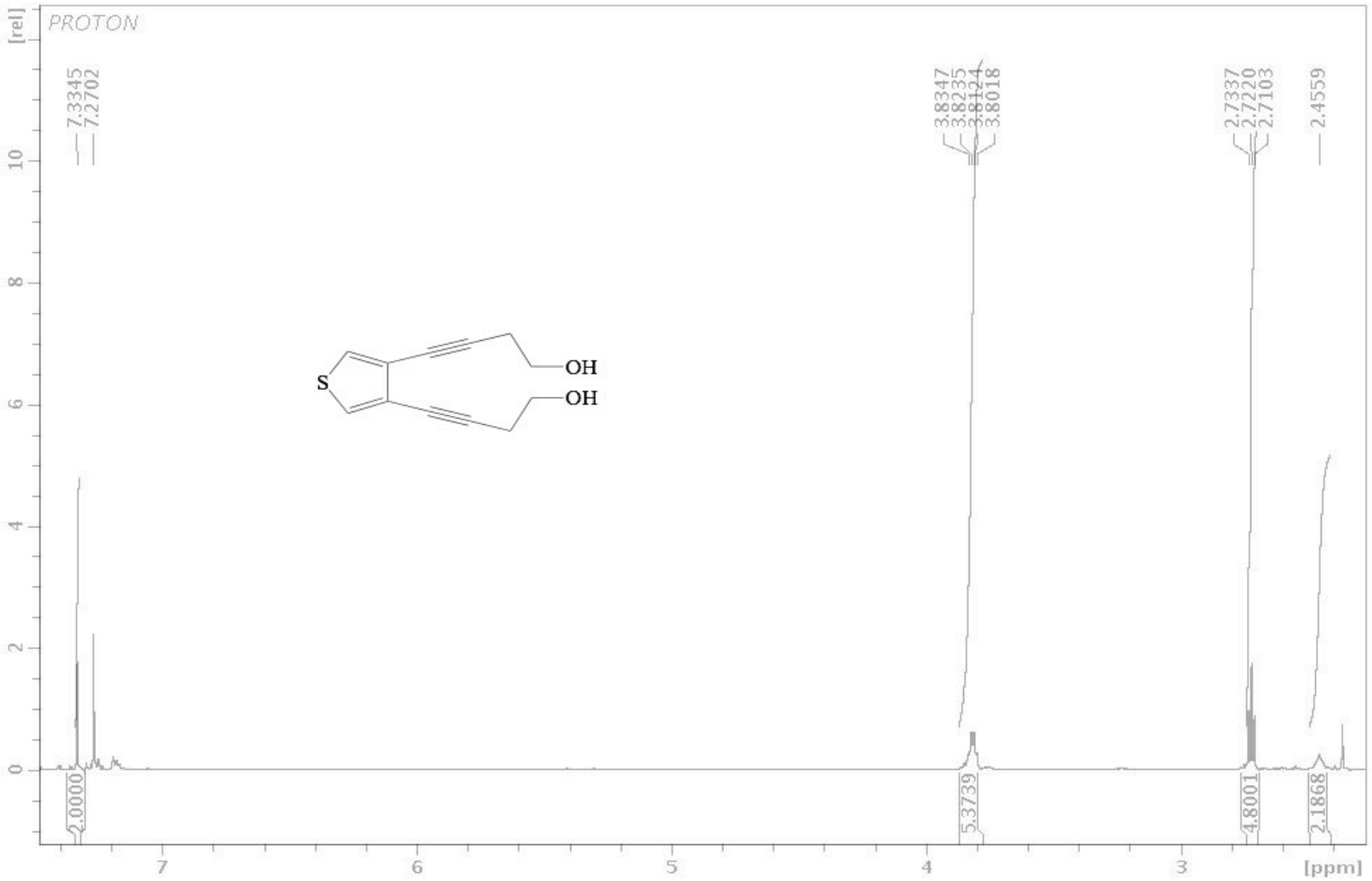

[rel]
150
100
50
0
9
8
7
6
5
4
[ppm]
CHO
CHO
0.9316
0.9906
1.0130
1.1669
1.0473
1.0750
1.0099
1.0000
2.0280

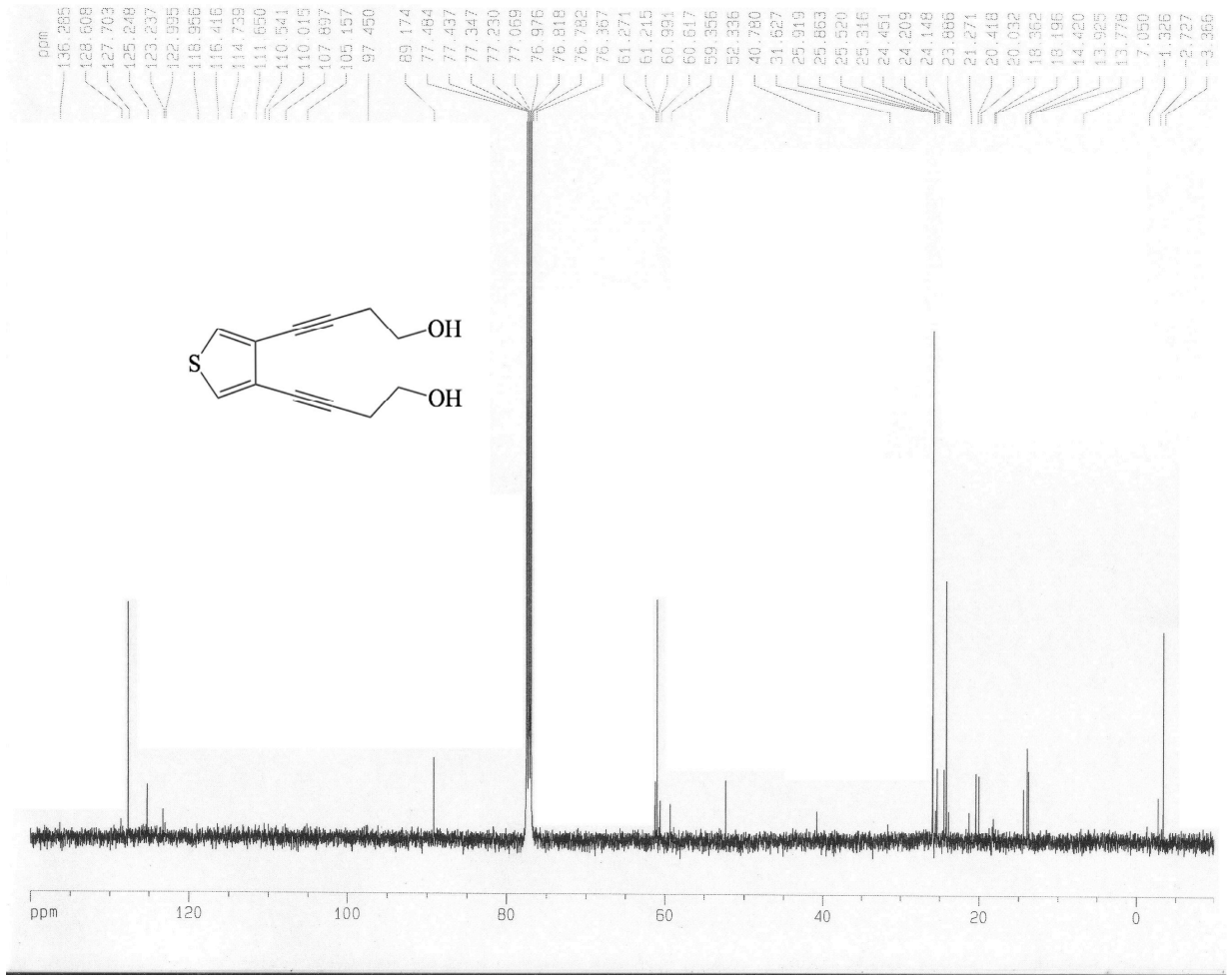

[rel]
300
200
100
0
CHO
CHO
150
100
50
[ppm]

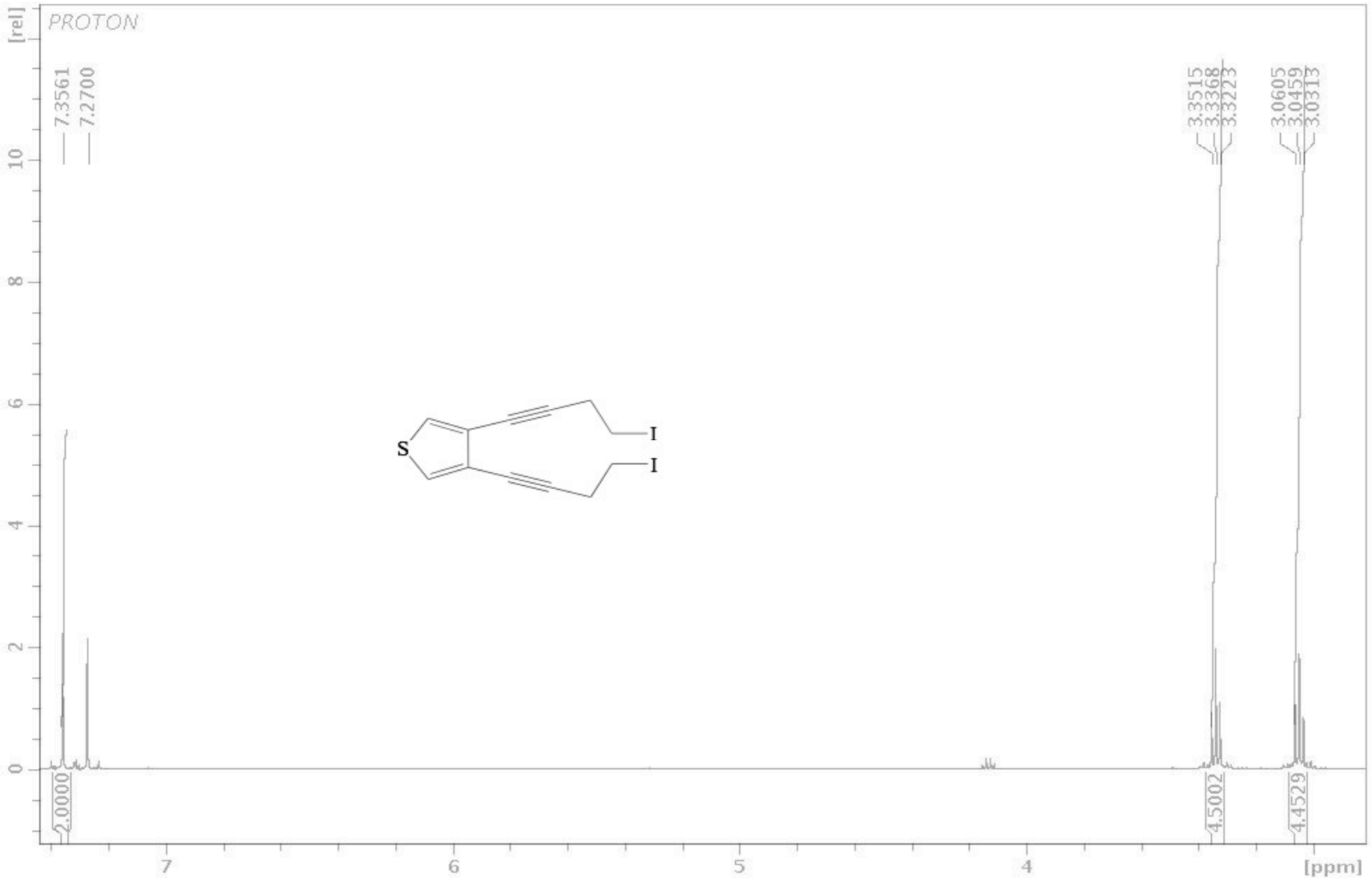

HSQCGP
[rel]
40
30
20
10
0
AcO
AcO
2.5467
6.0836
2.1484
1.0138
1.0000
1.3749
1.2041
2.2751
5.2724
1.0394
5.4349
6.0457
7
6
5
4
3
[ppm]

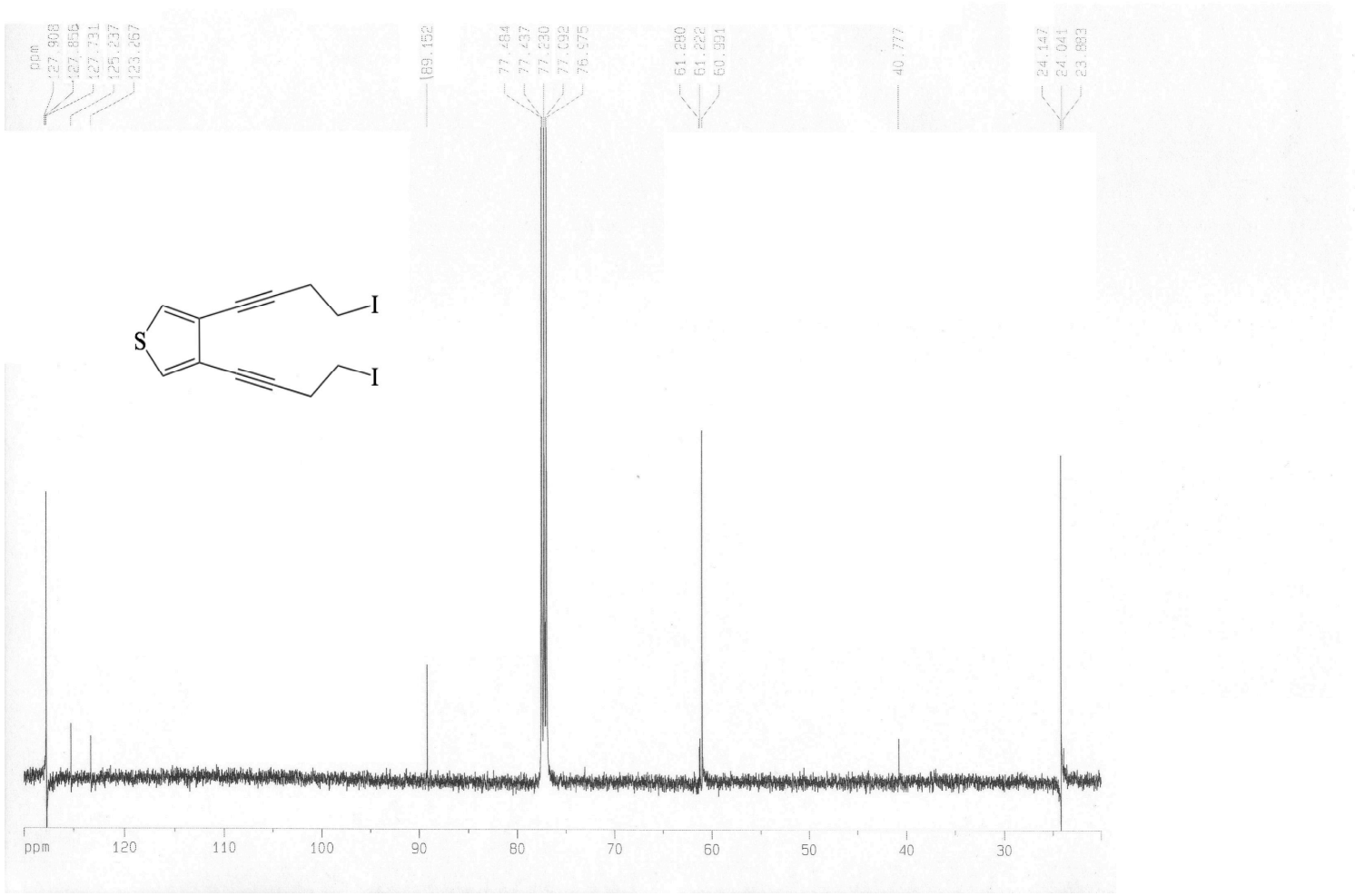

HSQCGP
[rel]
15
10
5
0
7.2836
7.2702
3.8453
3.8307
3.8159
2.6694
2.6547
2.6400
0.9171
0.1015
S
OTBS
OTBS
2.0000
5.3818
5.0651
27.0646
16.2694
6
4
2
[ppm]

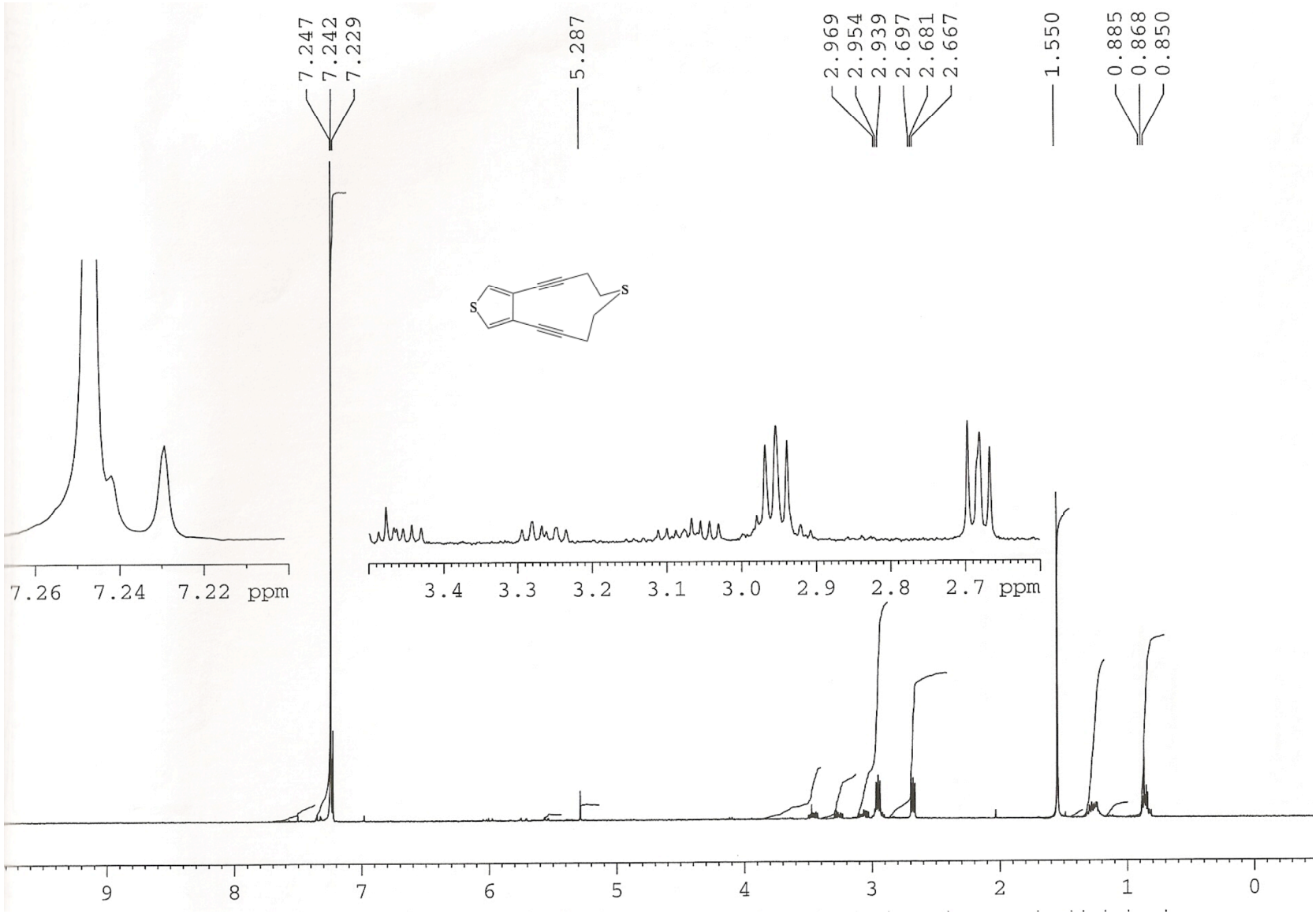

poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
127.6640
125.3176
89.1356
75.6643
62.1963
26.1139
24.1347
18.5684
-5.0224
S
OTBS
OTBS
[rel]
0
5
10
15
20
120
100
80
60
40
20
0
[ppm]

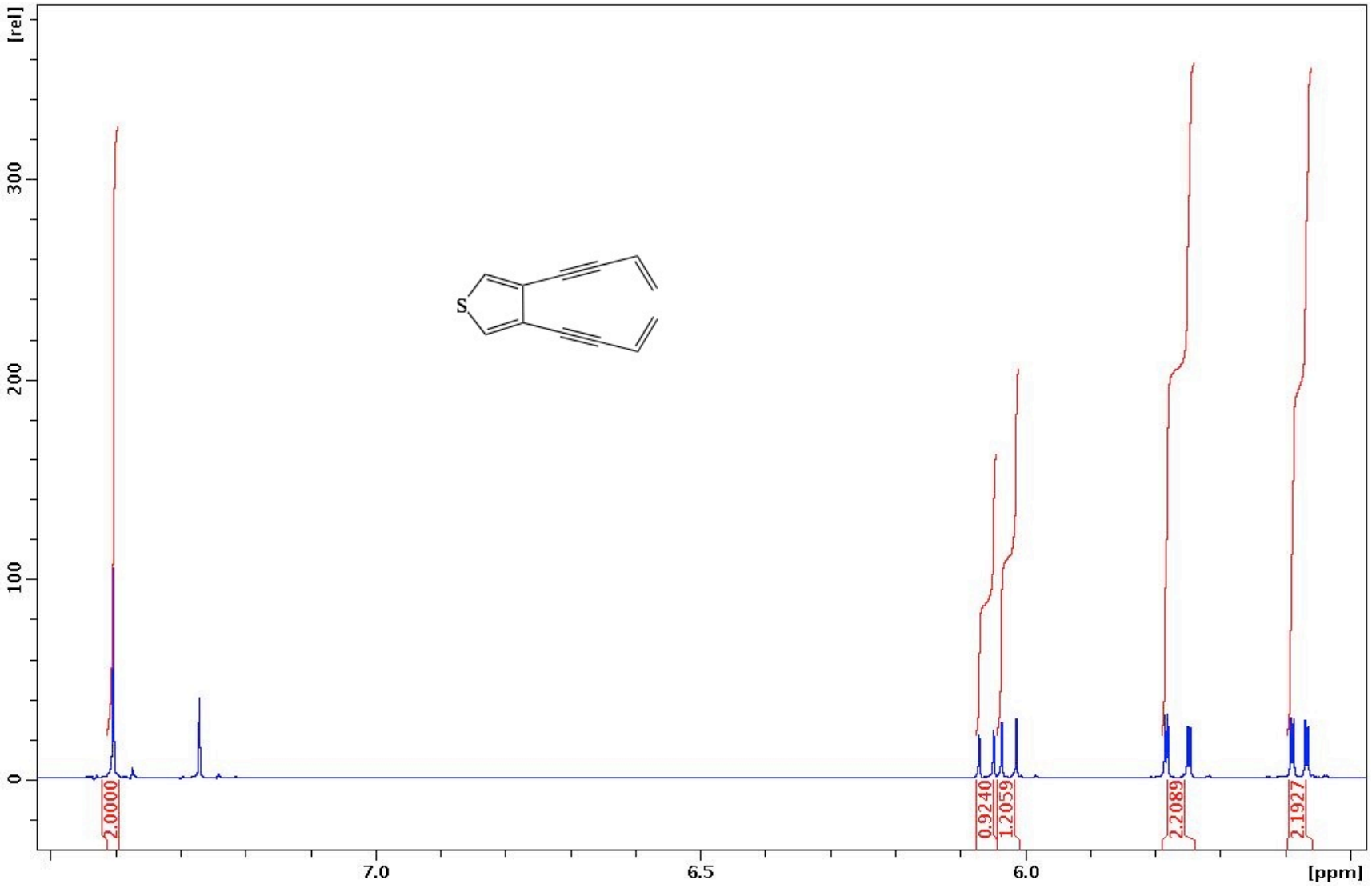

PROTON
[rel]
7.3345
7.2702
3.8347
3.8235
3.8124
3.8018
2.7337
2.7220
2.7103
2.4559
S
OH
OH
2.0000
5.3739
4.8001
2.1868
[ppm]

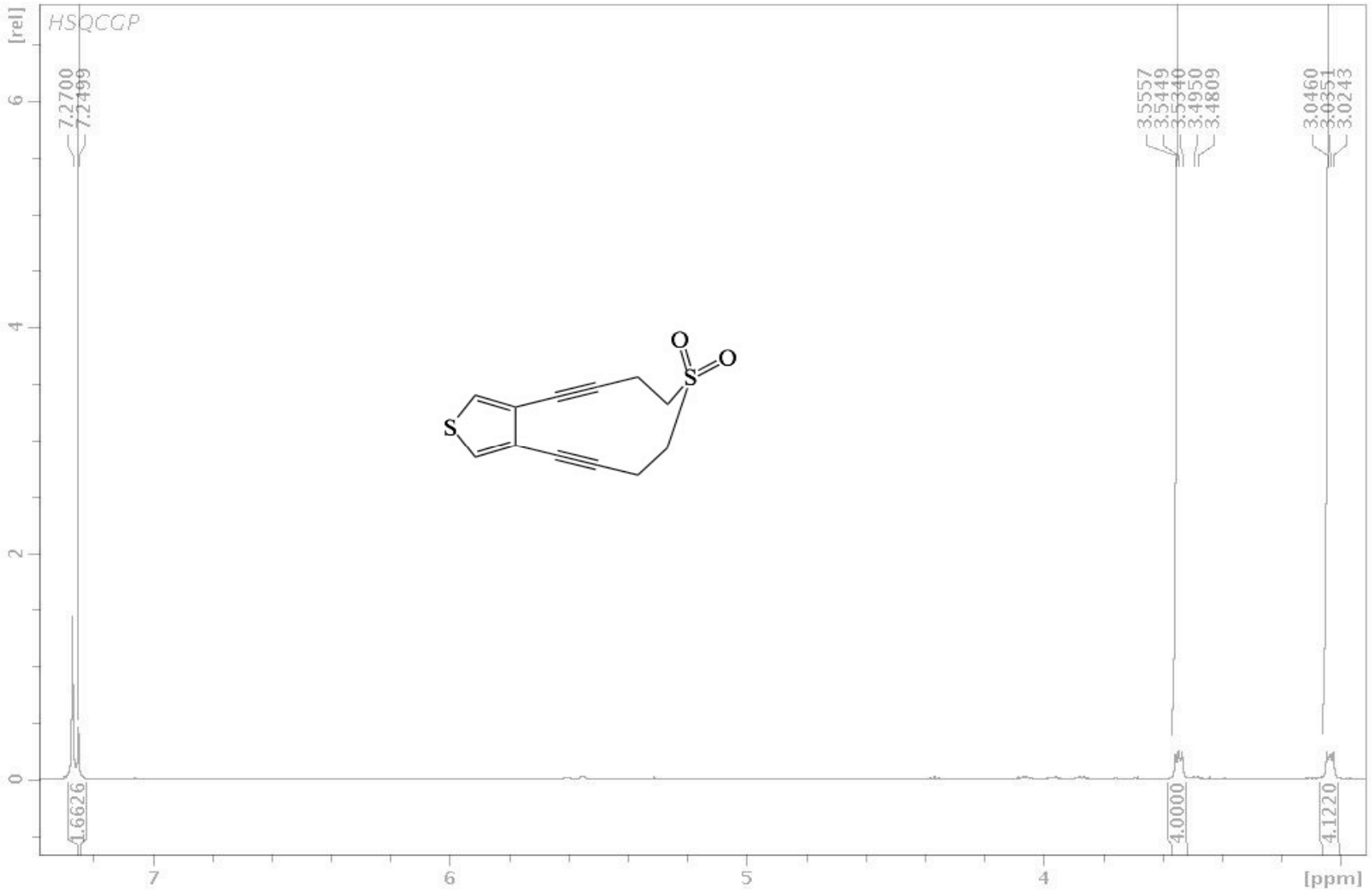

ppm
136.285
128.608
127.703
125.248
123.237
122.995
118.956
115.416
114.739
111.650
110.541
110.015
107.897
105.157
97.450
89.174
77.464
77.437
77.347
77.230
77.069
76.976
76.818
76.782
76.367
61.271
61.215
60.991
60.617
59.356
52.336
40.780
31.627
25.919
25.863
25.520
25.316
24.451
24.209
24.148
23.866
21.271
20.418
20.032
18.362
18.196
14.420
13.925
13.778
7.050
-1.326
-2.727
-3.366
S
OH
OH
ppm
120
100
80
60
40
20
0

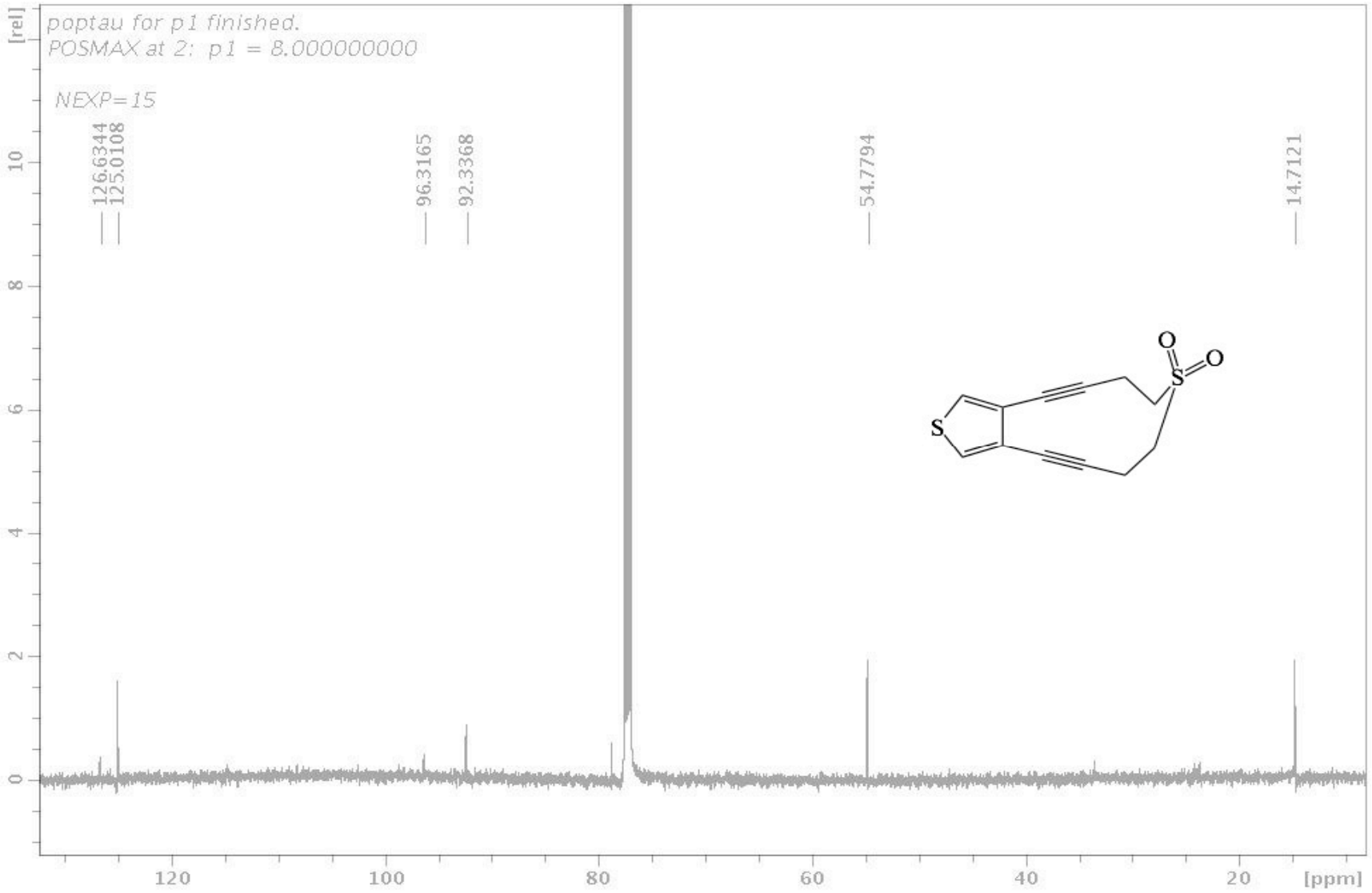

PROTON
[rel]
7.3561
7.2700
3.3515
3.3368
3.3223
3.0605
3.0459
3.0313
S
I
I
2.0000
4.5002
4.4529
0
2
4
6
8
10
7
6
5
4
[ppm]

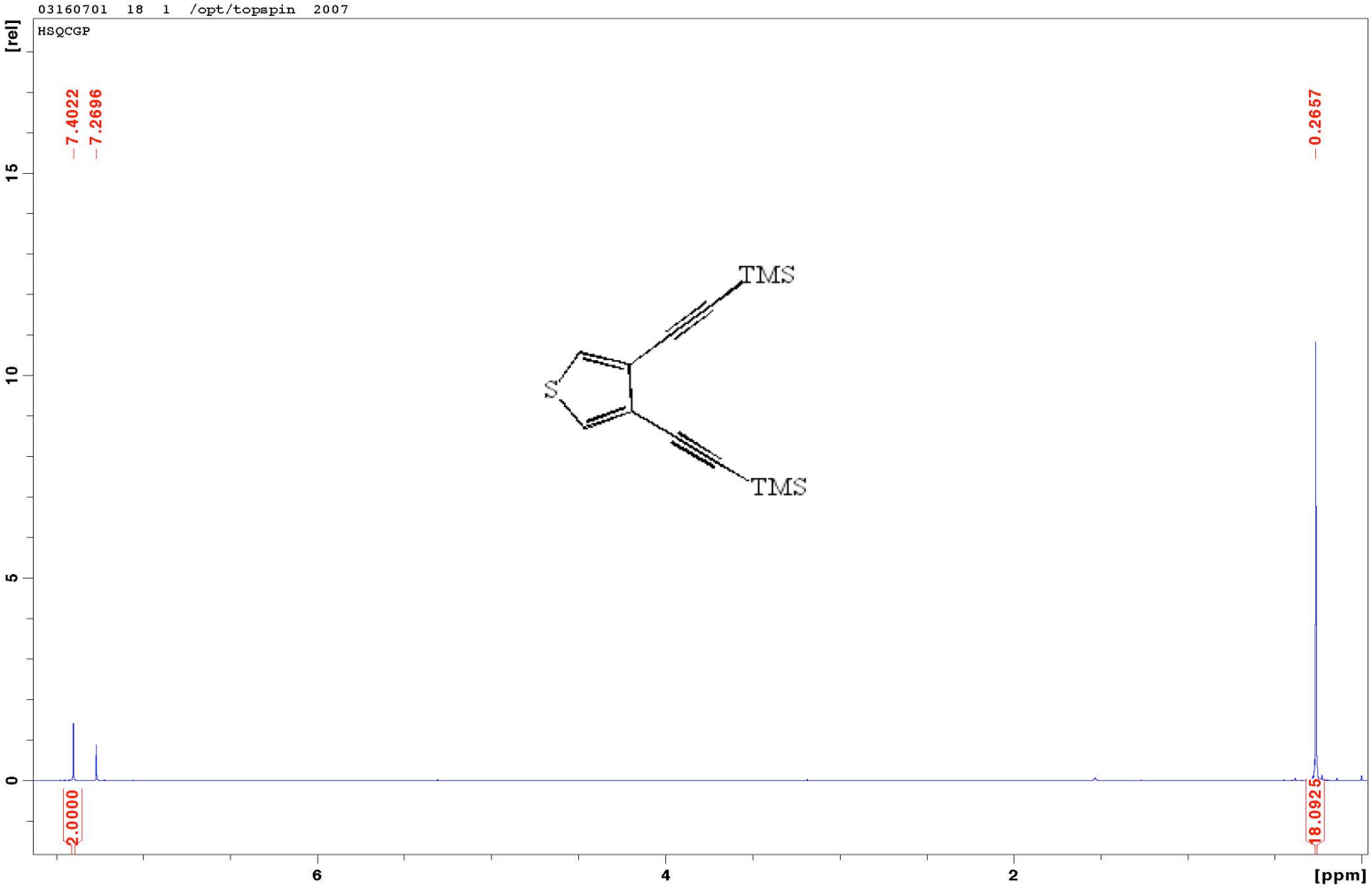

ppm
127.908
127.856
127.731
125.237
123.257
89.152
77.484
77.437
77.230
77.092
76.575
61.280
61.222
60.931
40.777
24.147
24.041
23.883
S
I
I
ppm
120
110
100
90
80
70
60
50
40
30

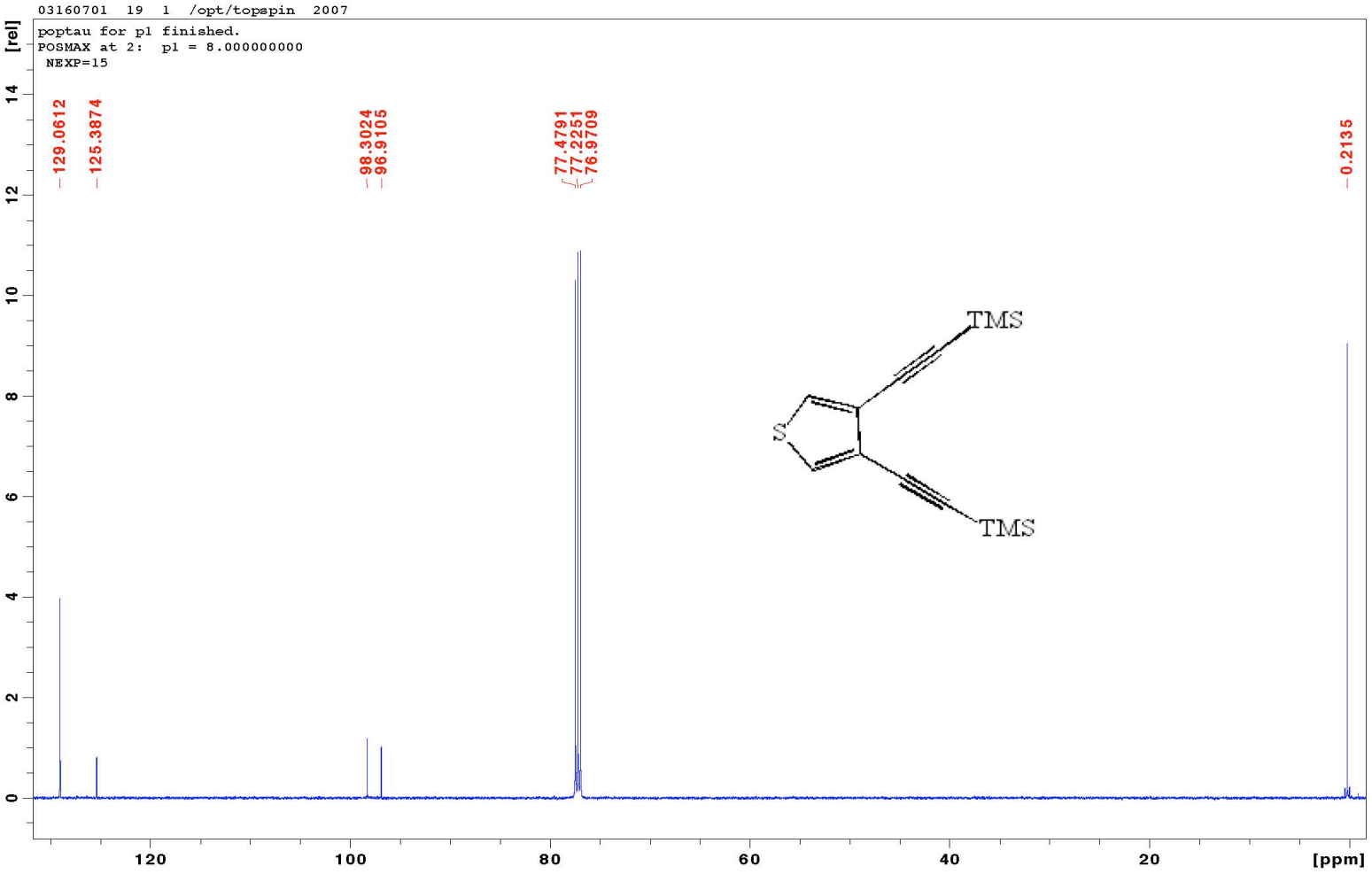

7.247
7.242
7.229
5.287
2.969
2.954
2.939
2.697
2.681
2.667
1.550
0.885
0.868
0.850
S
S
7.26 7.24 7.22 ppm
3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 ppm
9 8 7 6 5 4 3 2 1 0

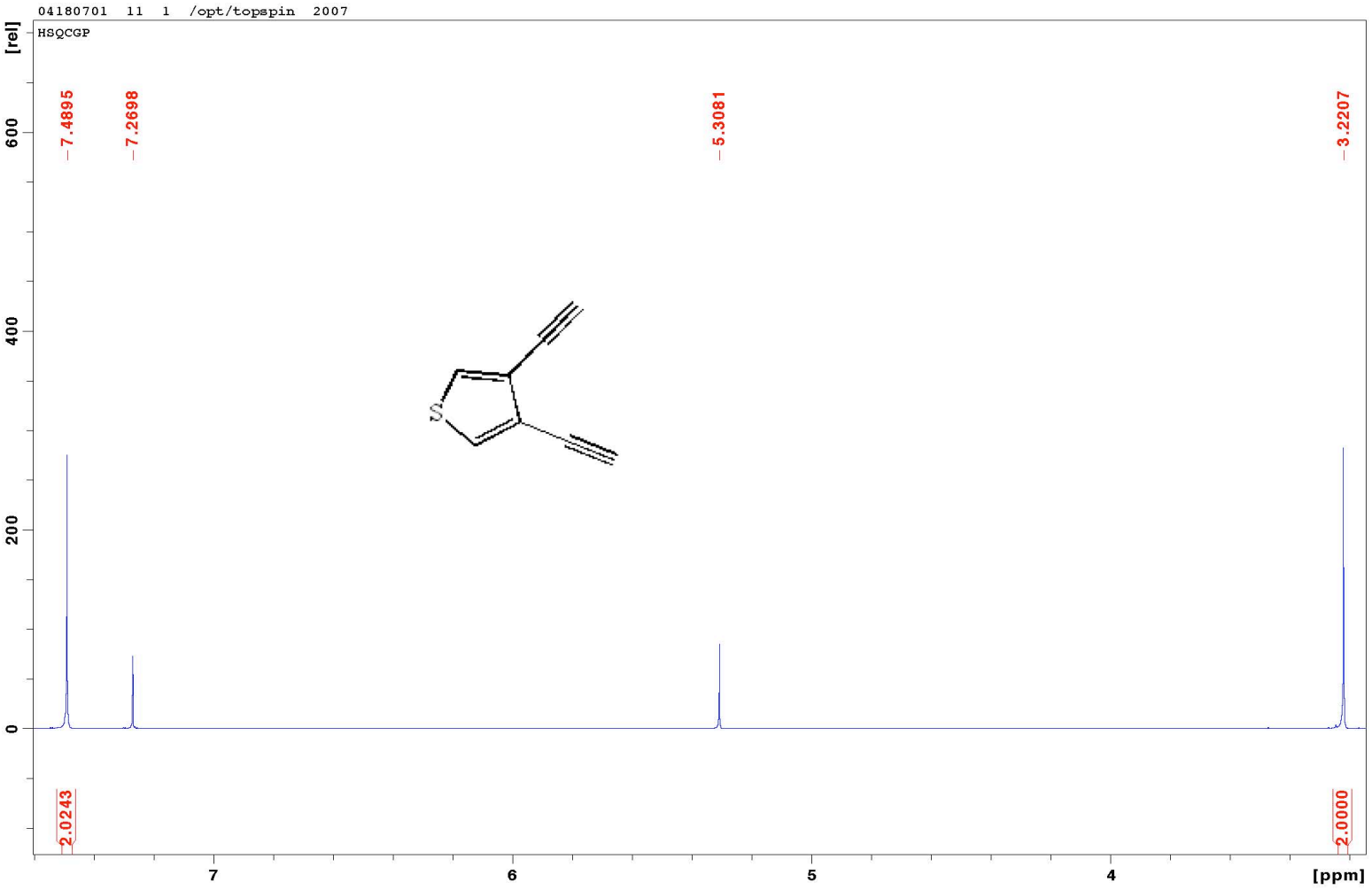

[rel]
300
200
100
0
S
2.0000
0.9240
1.2059
2.2089
2.1927
7.0
6.5
6.0
[ppm]

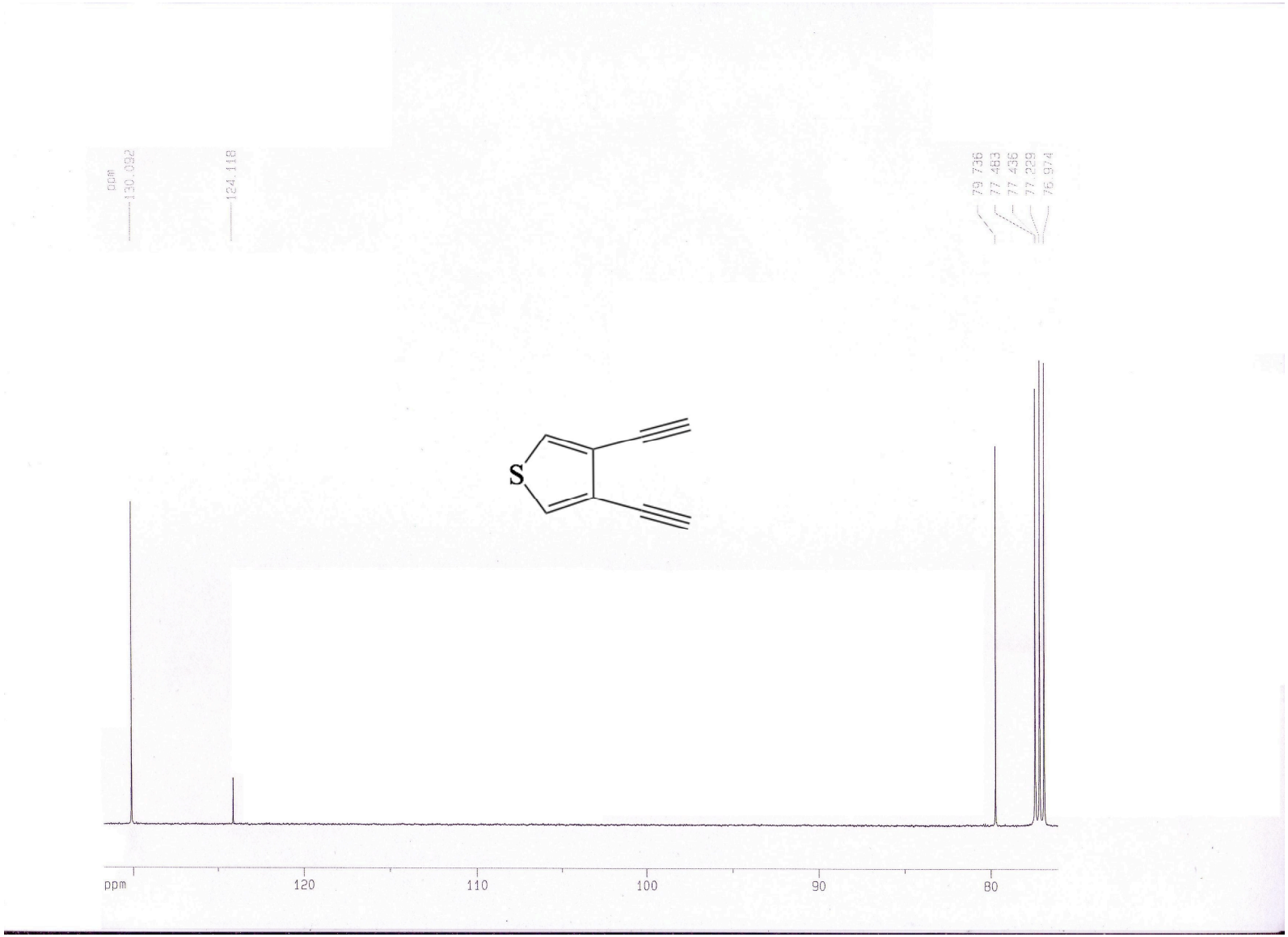

HSQCGP
[rel]
7.2700
7.2499
3.5557
3.5449
3.5340
3.4950
3.4809
3.0460
3.0351
3.0243
1.6626
4.0000
4.1220
[ppm]

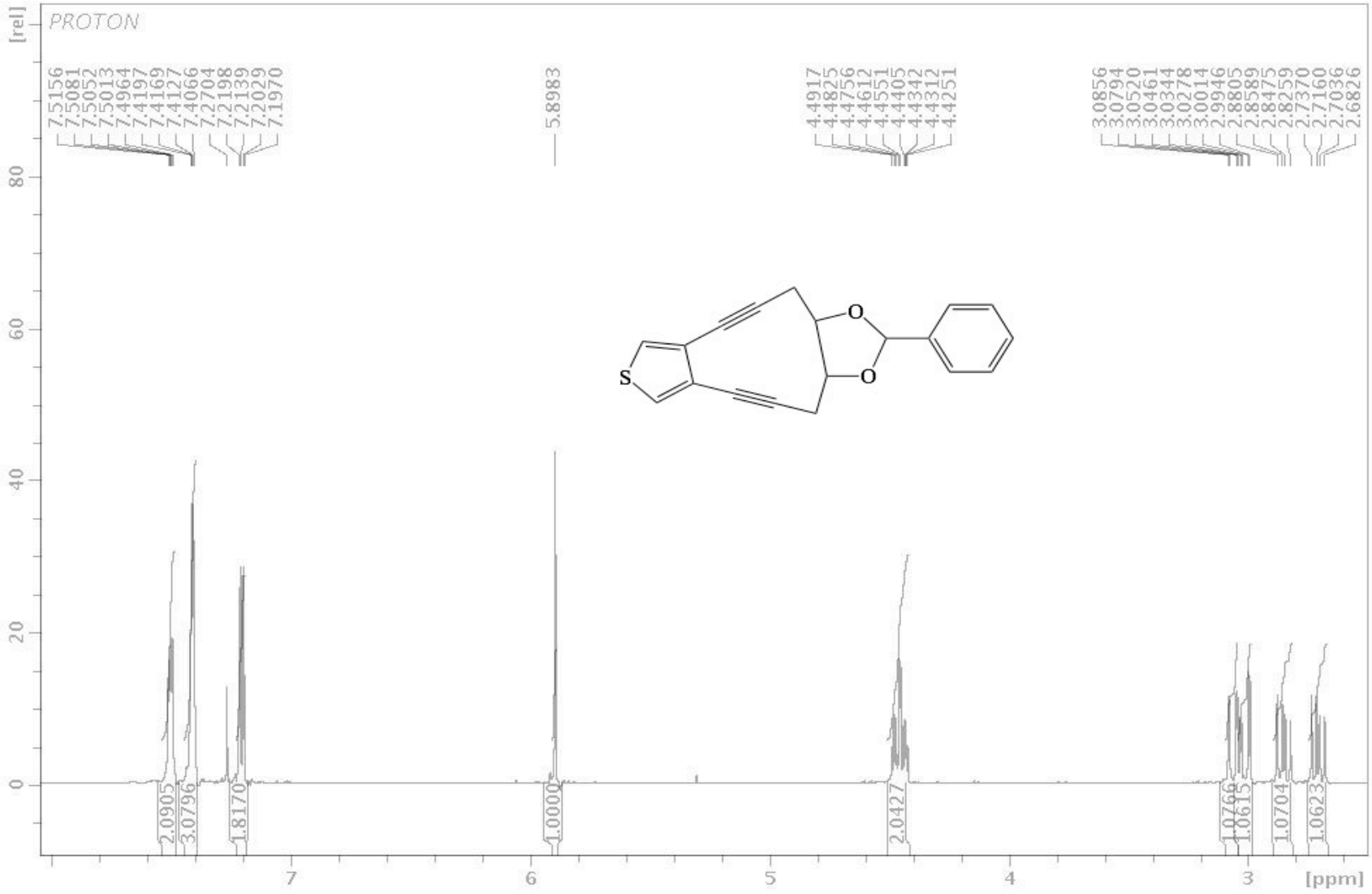

poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
126.6344
125.0108
96.3165
92.3368
54.7794
14.7121
[rel]
[ppm]
120
100
80
60
40
20
O
O
S
S


03160701 18 1 /opt/topspin 2007
HSQCGP
[rel]
7.4022
7.2696
0.2657
TMS
S
TMS
2.0000
18.0925
6
4
2
[ppm]


03160701 19 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
129.0612
125.3874
98.3024
96.9105
77.4791
77.2251
76.9709
0.2135
[rel]
0
2
4
6
8
10
12
14
120
100
80
60
40
20
[ppm]
TMS
S
TMS


04180701 11 1 /opt/topspin 2007
HSQCGP
[rel]
600
400
200
0
7.4895
7.2698
5.3081
3.2207
2.0243
2.0000
7
6
5
4
[ppm]


130.092
124.118
79.736
77.483
77.436
77.229
76.974
S
ppm
120
110
100
90
80


PROTON
[rel]
7.5156
7.5081
7.5052
7.5013
7.4964
7.4197
7.4169
7.4127
7.4066
7.2704
7.2198
7.2139
7.2029
7.1970
5.8983
4.4917
4.4825
4.4756
4.4612
4.4551
4.4405
4.4342
4.4312
4.4251
3.0856
3.0794
3.0520
3.0461
3.0344
3.0278
3.0014
2.9946
2.8805
2.8589
2.8475
2.8259
2.7370
2.7160
2.7036
2.6826
O
O
S
2.0905
3.0796
1.8170
1.0000
2.0427
1.0766
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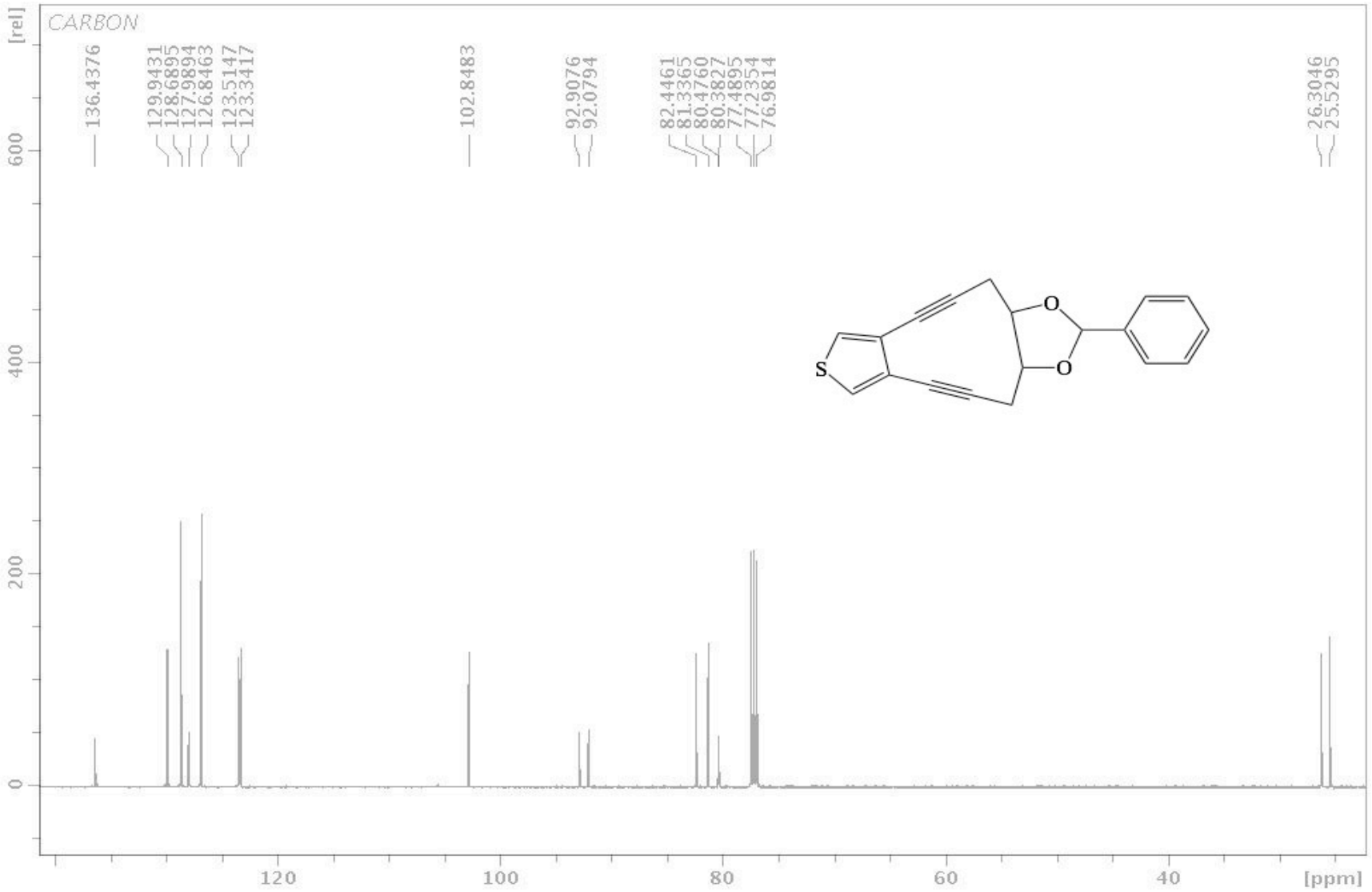
1.0704
1.0623
0
20
40
60
80
7
6
5
4
3
[ppm]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400
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123.5147
123.3417
102.8483
92.9076
92.0794
82.4461
81.3365
80.4760
80.3827
77.4895
77.2354
76.9814
26.3046
25.5295
O
O
S
120
100
80
60
40
[ppm]


PROTON
[rel]
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7.3096
7.2702
7.2366
7.2308
6.1623
6.1499
6.1391
6.1268
5.8748
5.8720
5.8516
5.8489
4.9090
2.8317
2.8130
2.7973
2.7786
2.7669
2.7618
2.7466
2.7327
2.7277
S
OH
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2.3612
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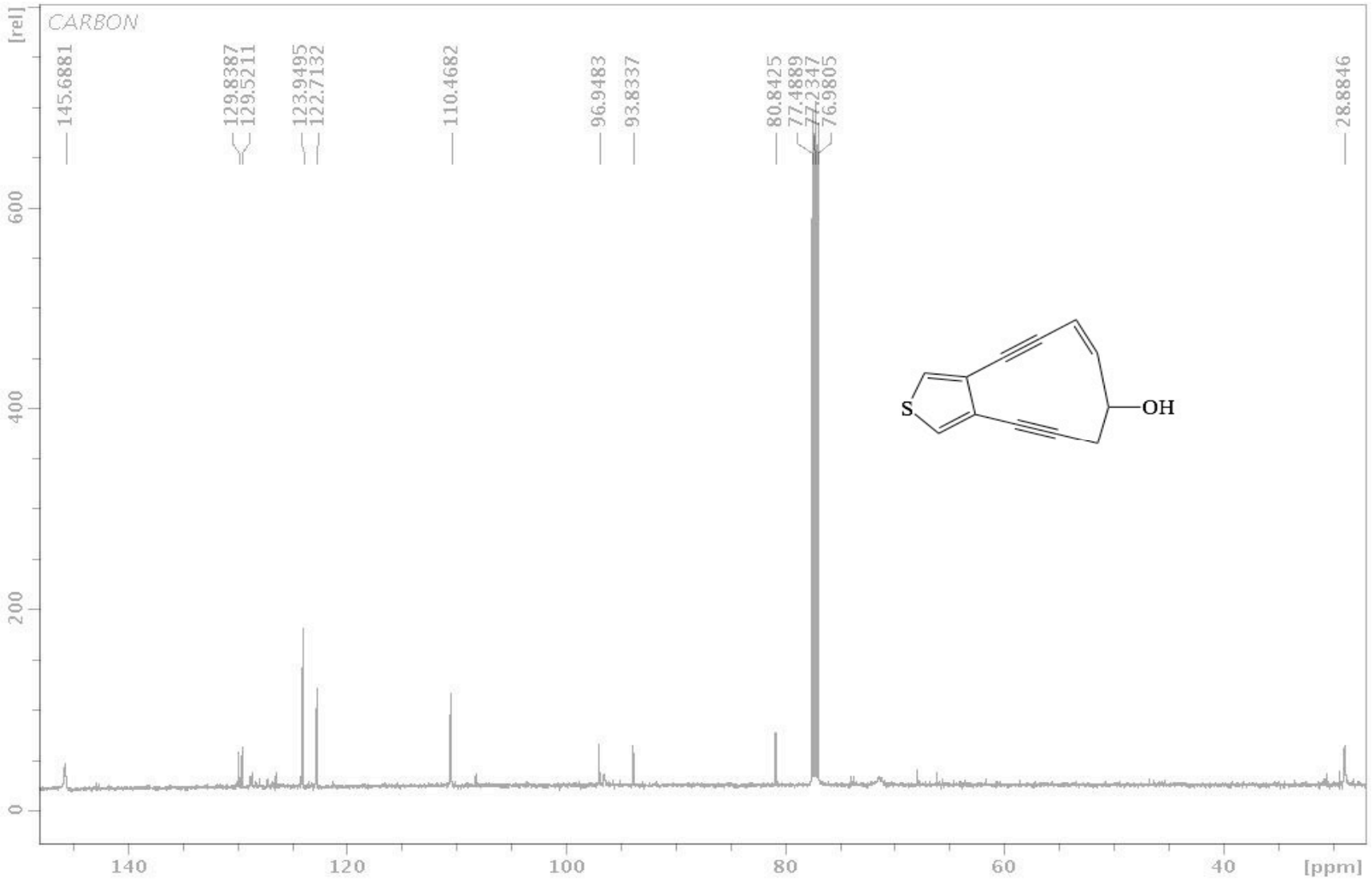
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80.8425
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28.8846
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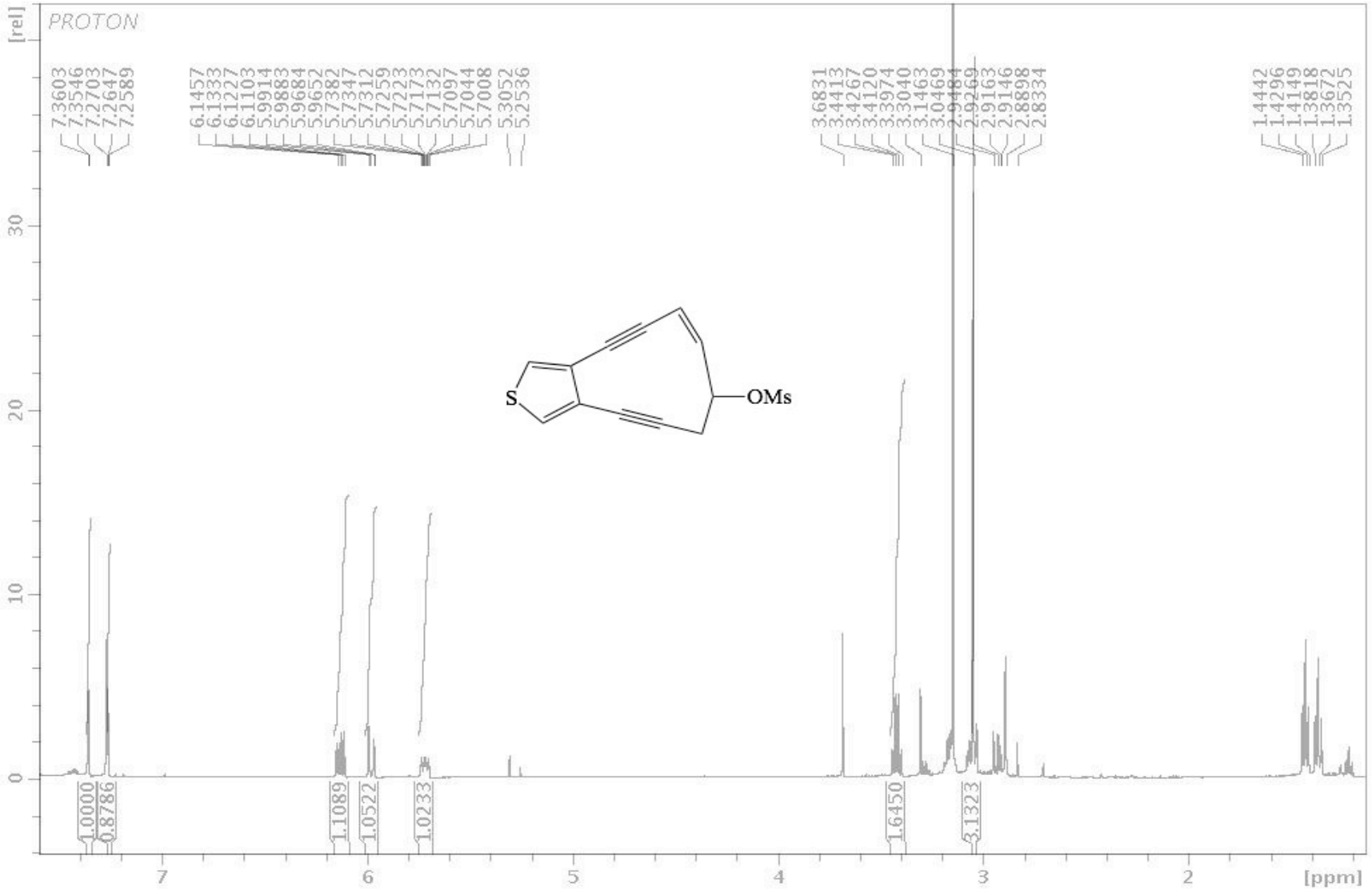
200
400
600
140
120
100
80
60
40
[ppm]
S
OH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7.2647
7.2589
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6.1333
6.1227
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5.9914
5.9883
5.9684
5.9652
5.7382
5.7347
5.7312
5.7259
5.7223
5.7173
5.7132
5.7097
5.7044
5.7008
5.3052
5.2536
3.6831
3.4413
3.4267
3.4120
3.3974
3.3040
3.1463
3.0469
2.9484
2.9269
2.9163
2.9146
2.8898
2.8334
1.4442
1.4296
1.4149
1.3818
1.3672
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OMs
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1.0233
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3.1323
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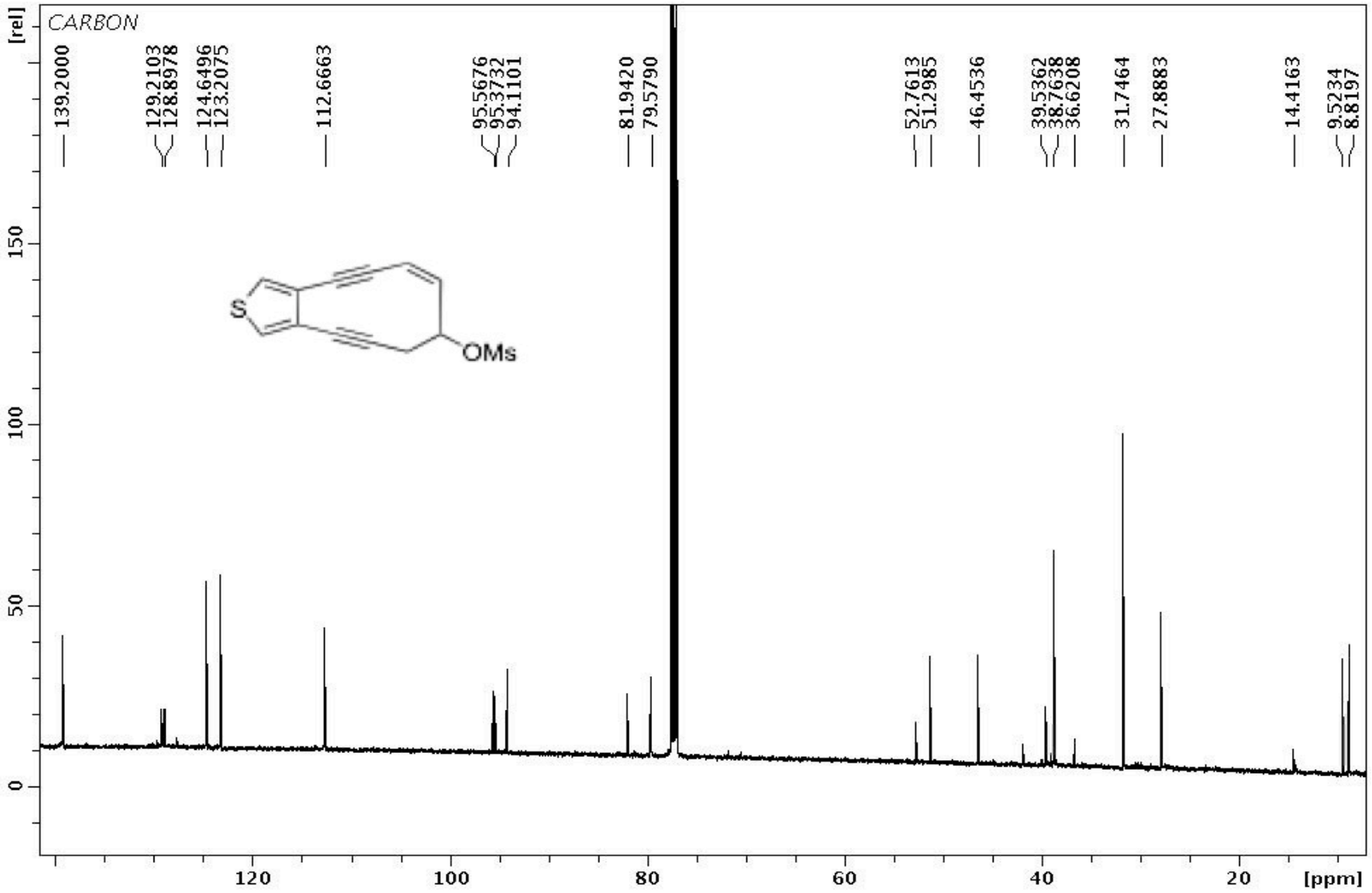
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81.9420
79.5790
52.7613
51.2985
46.4536
39.5362
38.7638
36.6208
31.7464
27.8883
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8.8197
S
OMs
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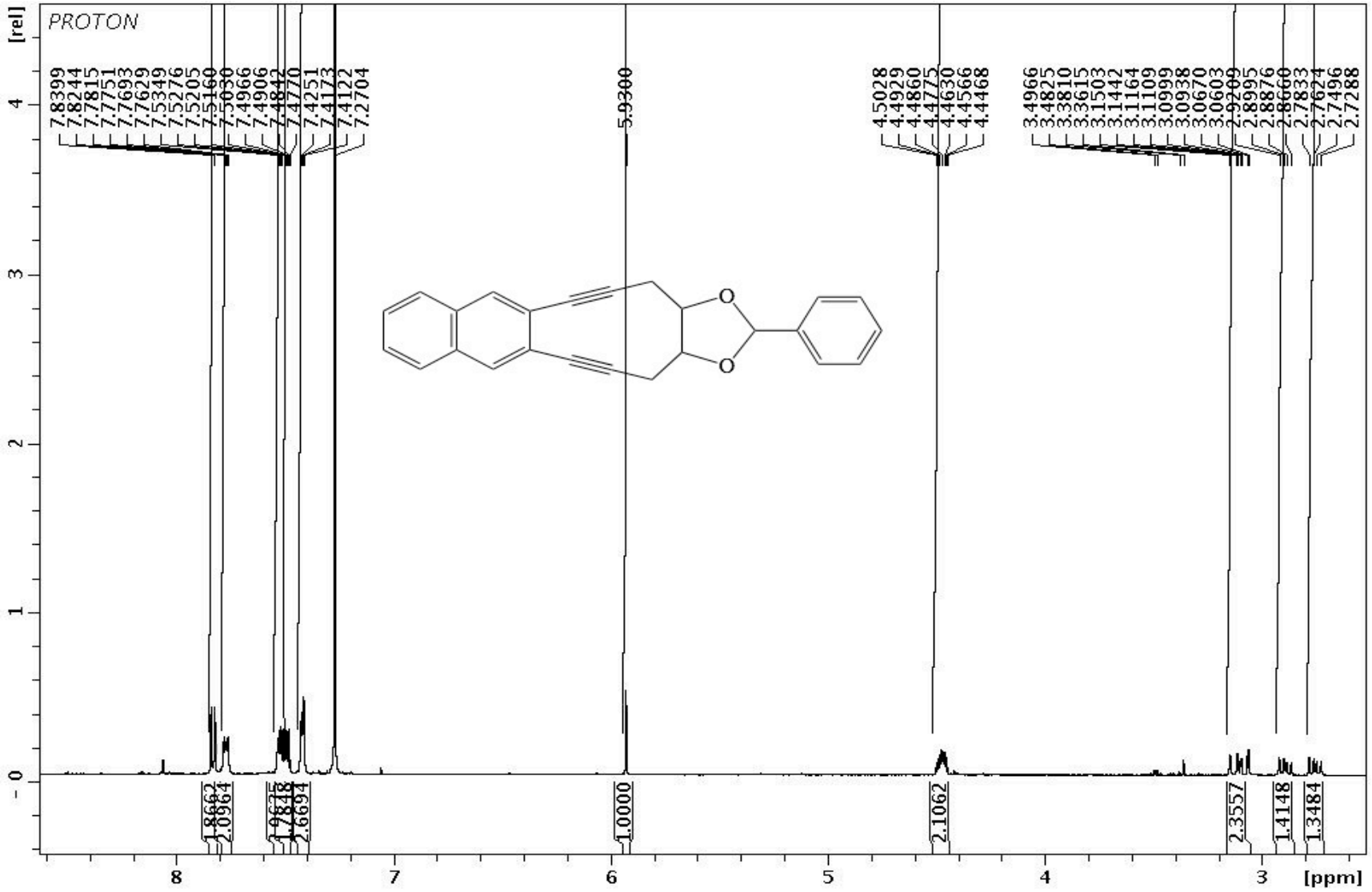
100
50
0
120
100
80
60
40
20
[ppm]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7.5205
7.5160
7.5030
7.4966
7.4906
7.4842
7.4770
7.4251
7.4173
7.4122
7.2704
5.9300
4.5028
4.4929
4.4860
4.4775
4.4630
4.4566
4.4468
3.4966
3.4825
3.3810
3.3615
3.1503
3.1442
3.1164
3.1109
3.0999
3.0938
3.0670
3.0603
2.9209
2.8995
2.8876
2.8660
2.7833
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2.1062
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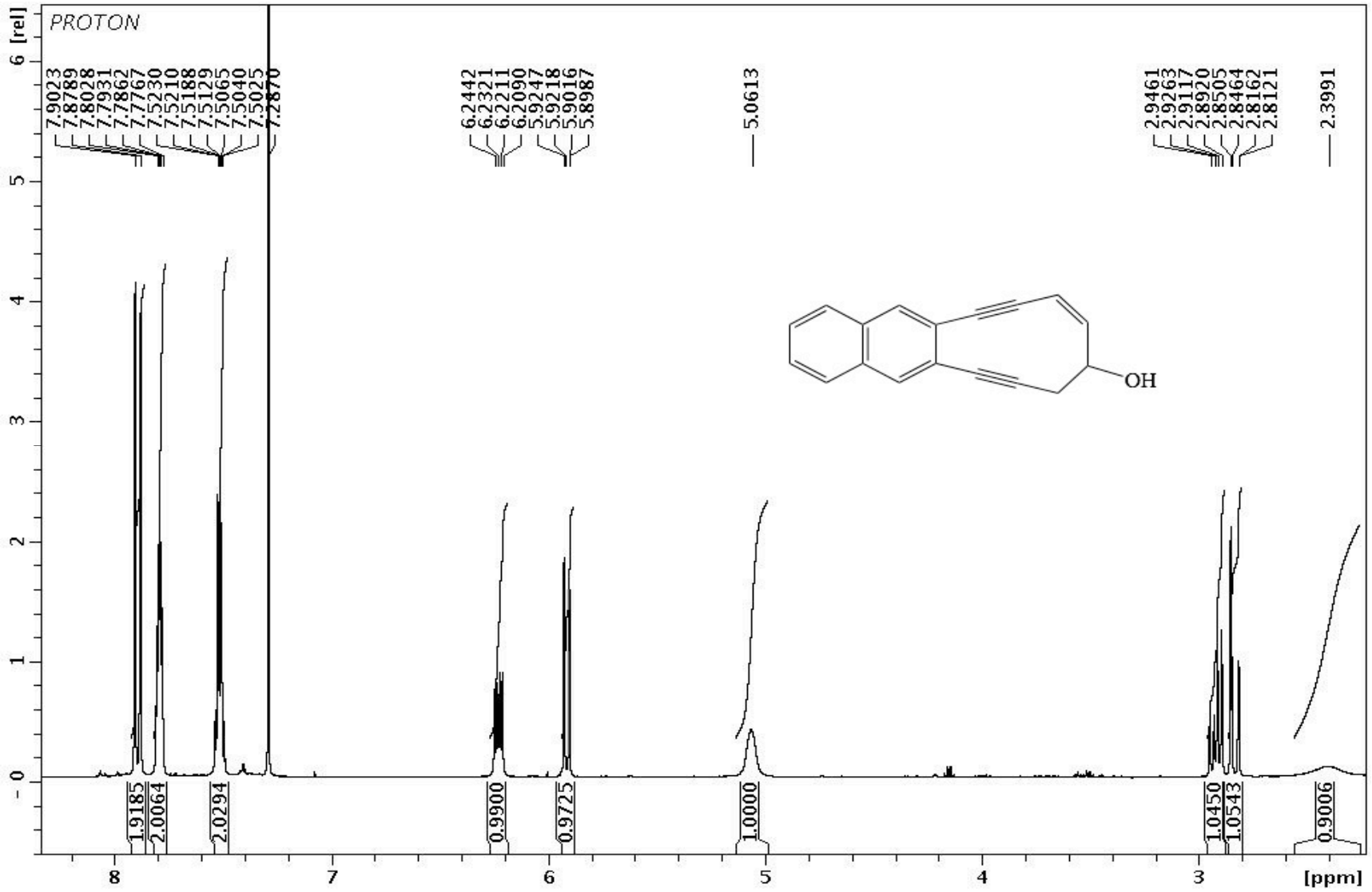
1.3484


PROTON
6 [rel]
5
4
3
2
1
- 0
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7.7931
7.7862
7.7767
7.5230
7.5210
7.5188
7.5129
7.5065
7.5040
7.5025
7.2870
6.2442
6.2321
6.2211
6.2090
5.9247
5.9218
5.9016
5.8987
5.0613
2.9461
2.9263
2.9117
2.8920
2.8505
2.8464
2.8162
2.8121
2.3991
OH
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2.0064
2.0294
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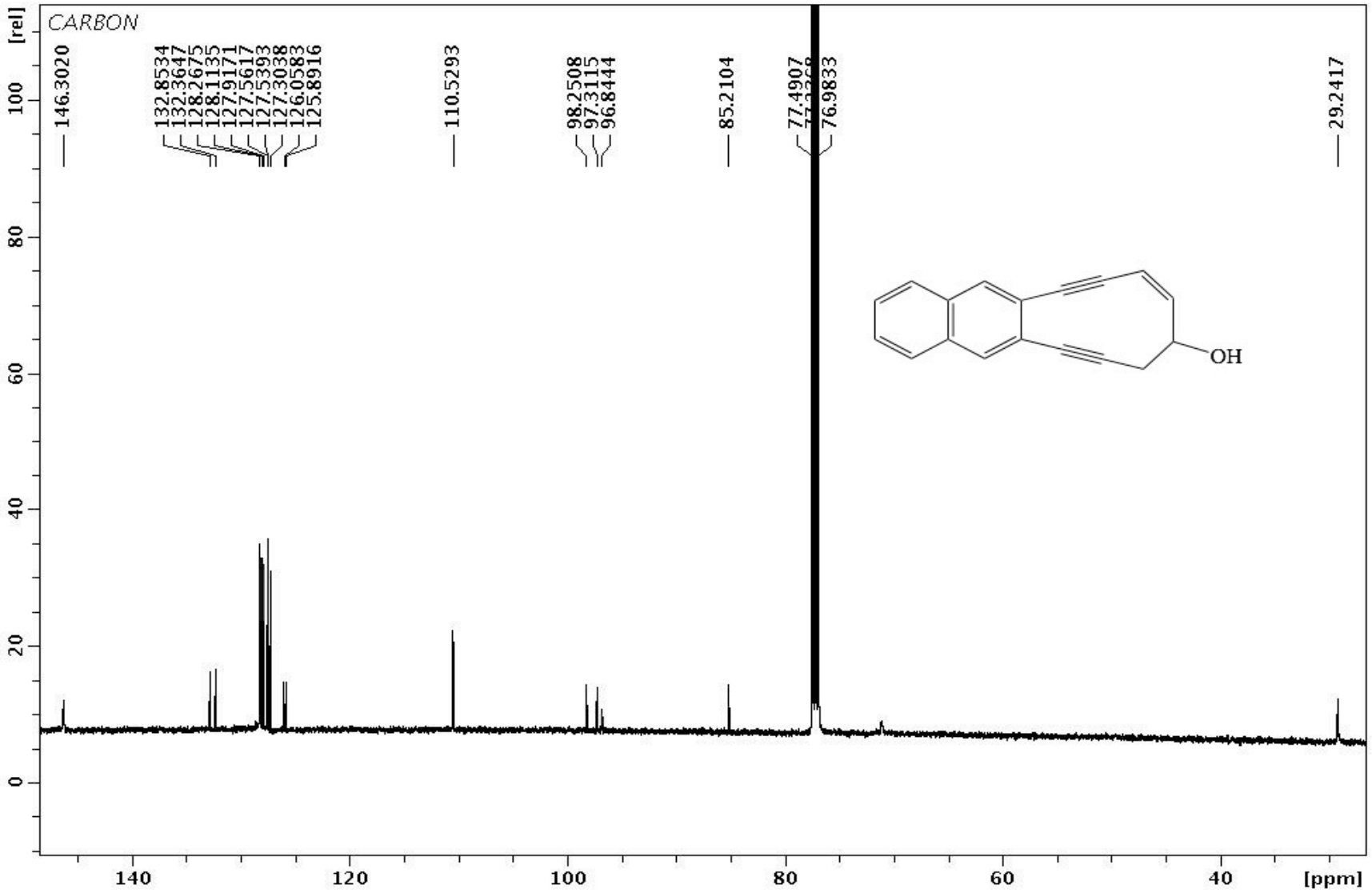
1.0000
1.0450
1.0543
0.9006
8
7
6
5
4
3
[ppm]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127.3038
126.0583
125.8916
110.5293
98.2508
97.3115
96.8444
85.2104
77.4907
76.9833
29.2417
OH
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80
60
40
20
0
140
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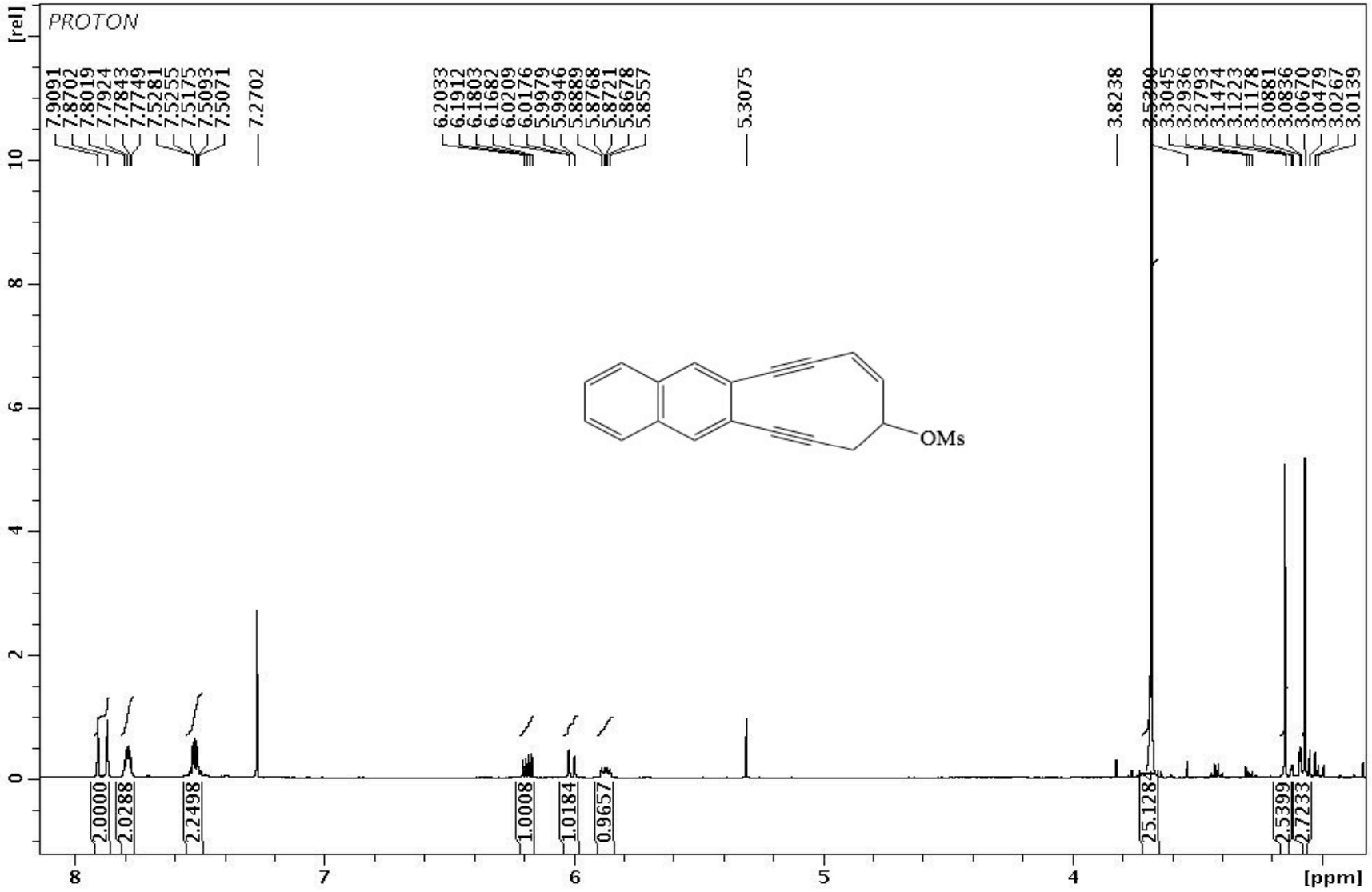
100
80
60
40
[ppm]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7.5093
7.5071
7.2702
6.2033
6.1912
6.1803
6.1682
6.0209
6.0176
5.9979
5.9946
5.8889
5.8768
5.8721
5.8678
5.8557
5.3075
3.8238
3.3045
3.2936
3.2793
3.1474
3.1223
3.1178
3.0881
3.0836
3.0670
3.0479
3.0267
3.0139
OMs
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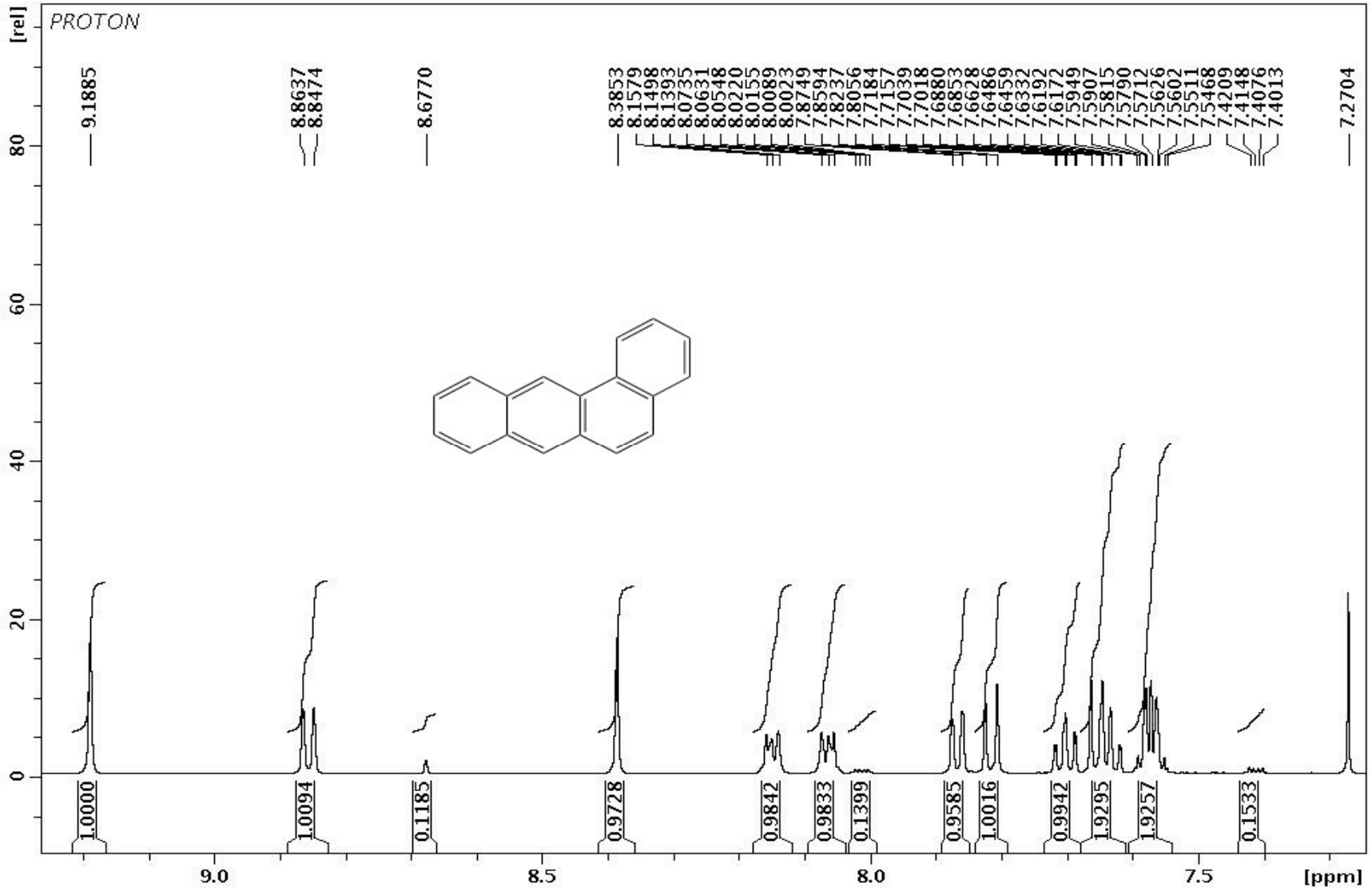
[ppm]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8.1393
8.0735
8.0631
8.0548
8.0220
8.0155
8.0089
8.0023
7.8749
7.8594
7.8237
7.8056
7.7184
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7.7039
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7.6628
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7.6332
7.6192
7.6172
7.5949
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7.5815
7.5790
7.5712
7.5626
7.5602
7.5511
7.5468
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1.0000
1.0094
0.1185
0.9728
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0.9585
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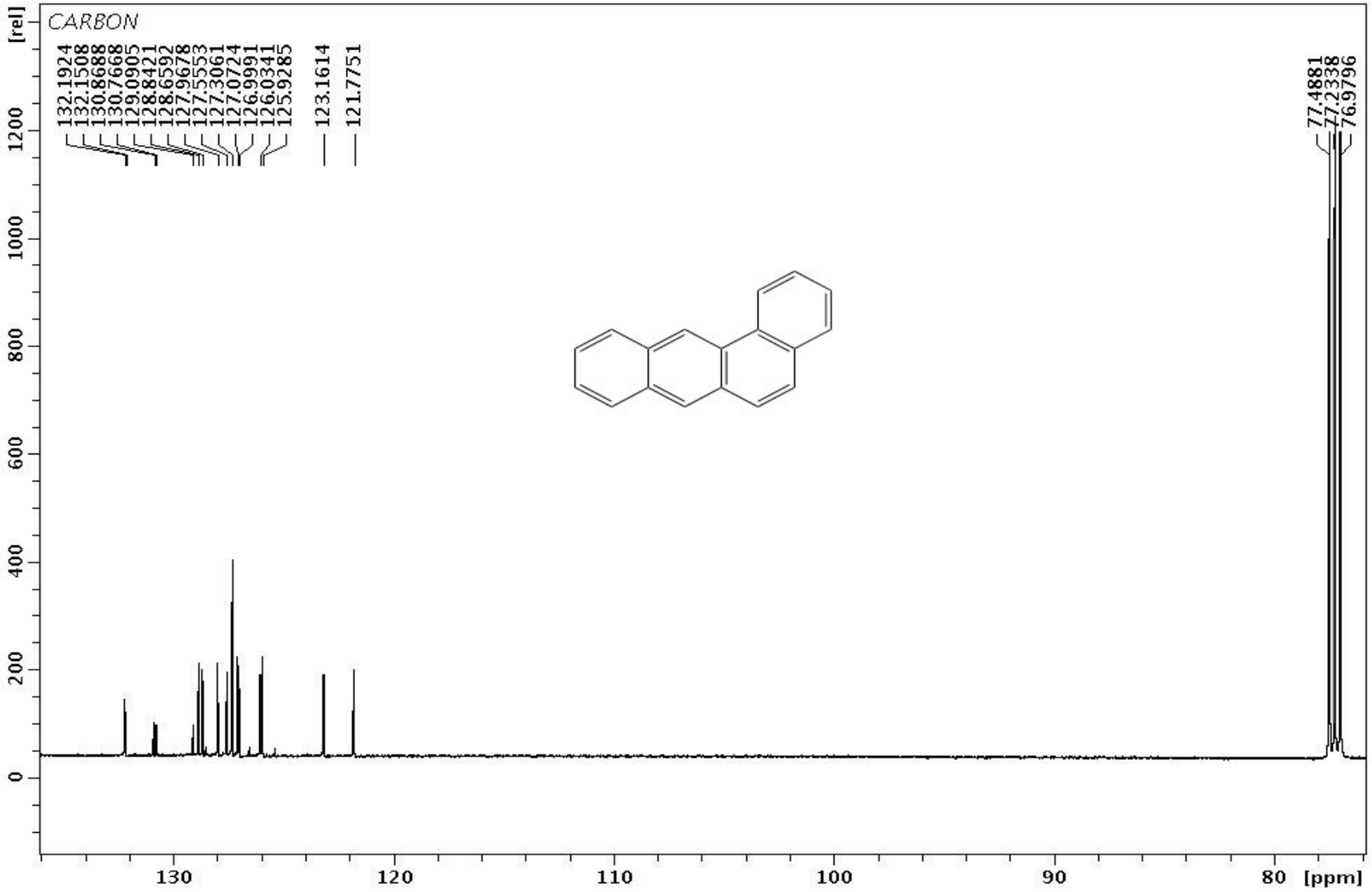
0.1533
[ppm]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127.5553
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126.9991
126.0341
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77.2338
76.9796
130
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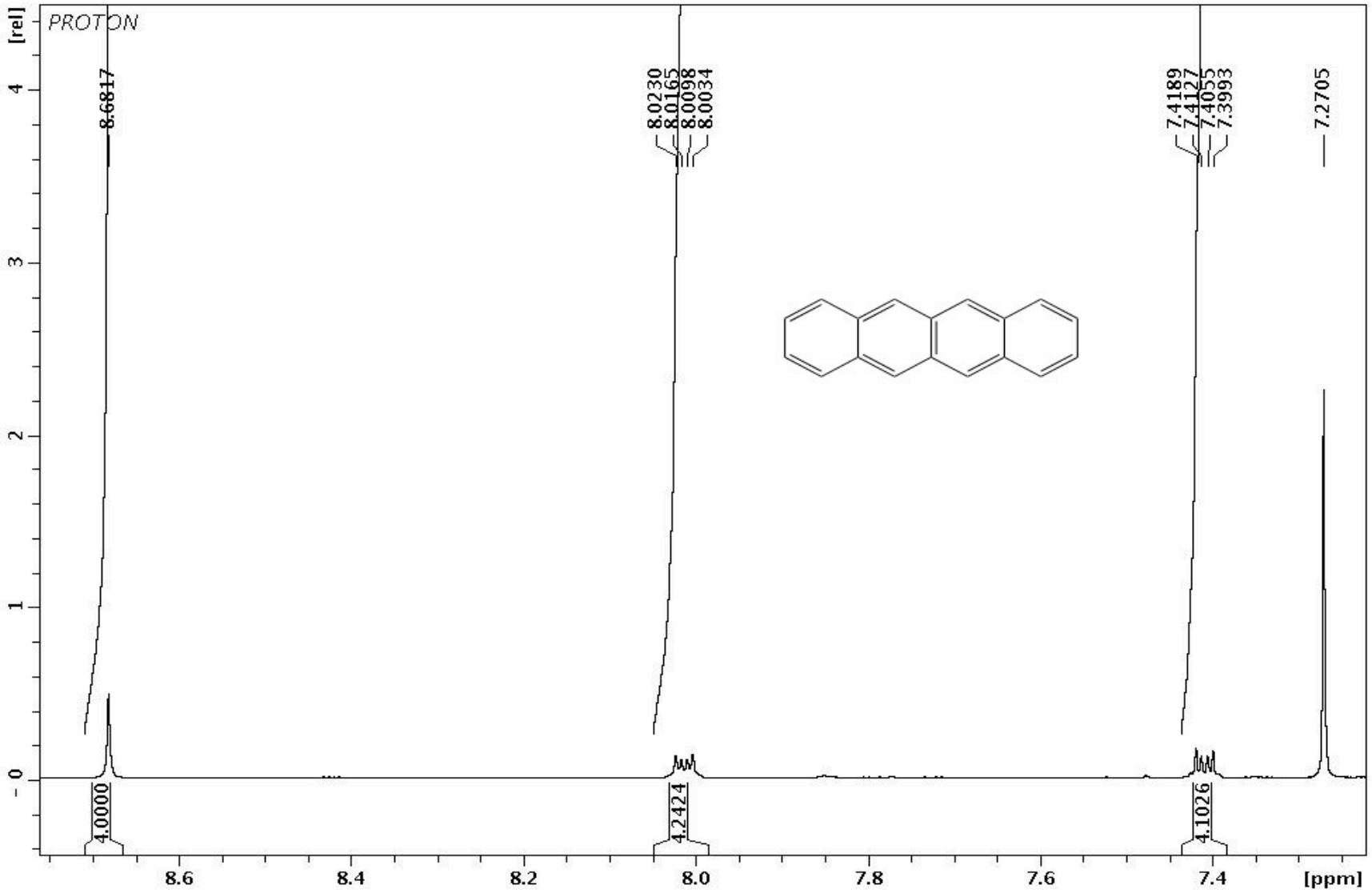
110
100
90
80
[ppm]


PROTON
[rel]
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3
2
1
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8.0165
8.0098
8.0034
7.4189
7.4127
7.4055
7.3993
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4.0000
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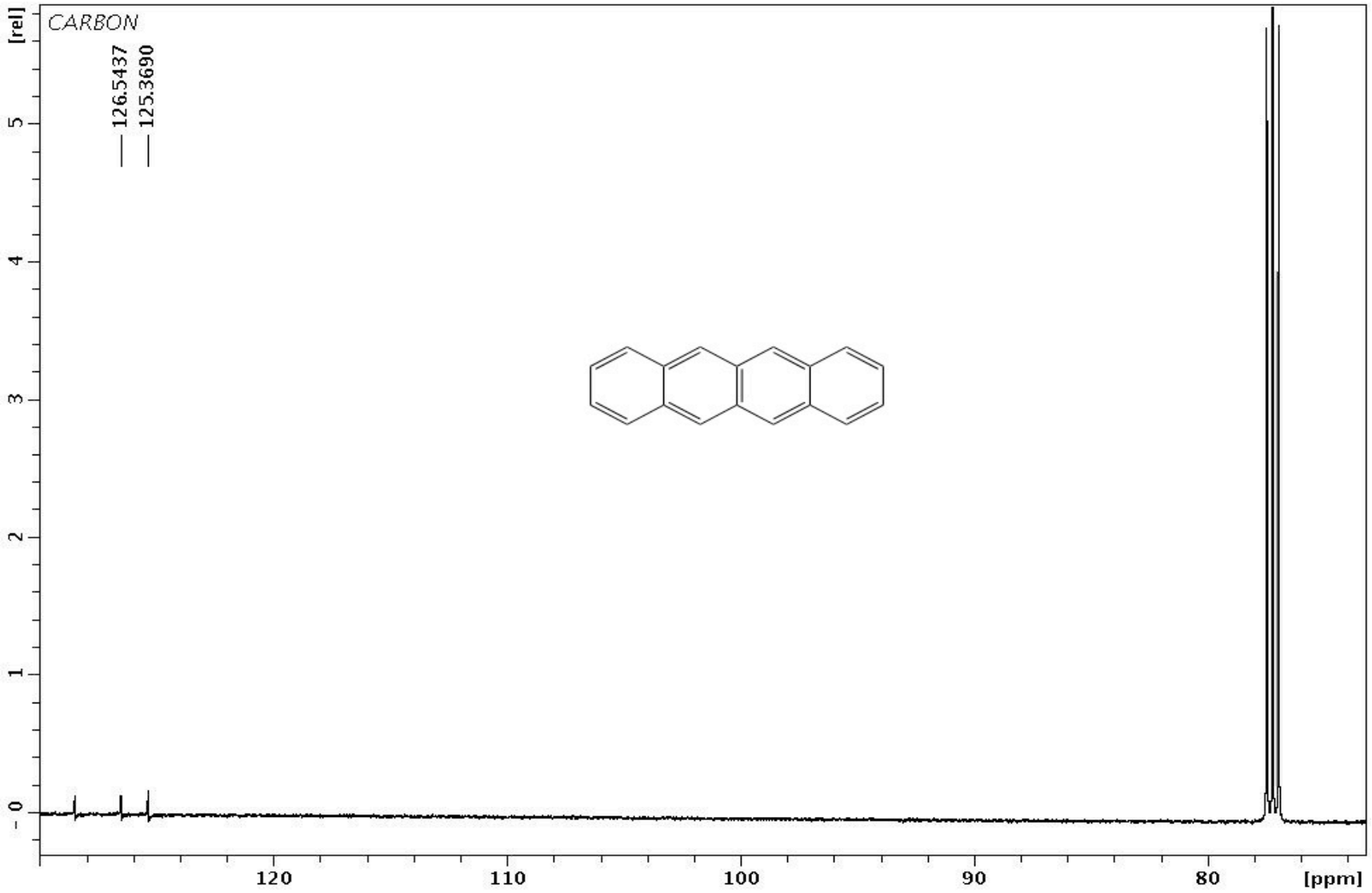
4.1026
8.6
8.4
8.2
8.0
7.8
7.6
7.4
[ppm]


CARBON
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125.3690
[rel]
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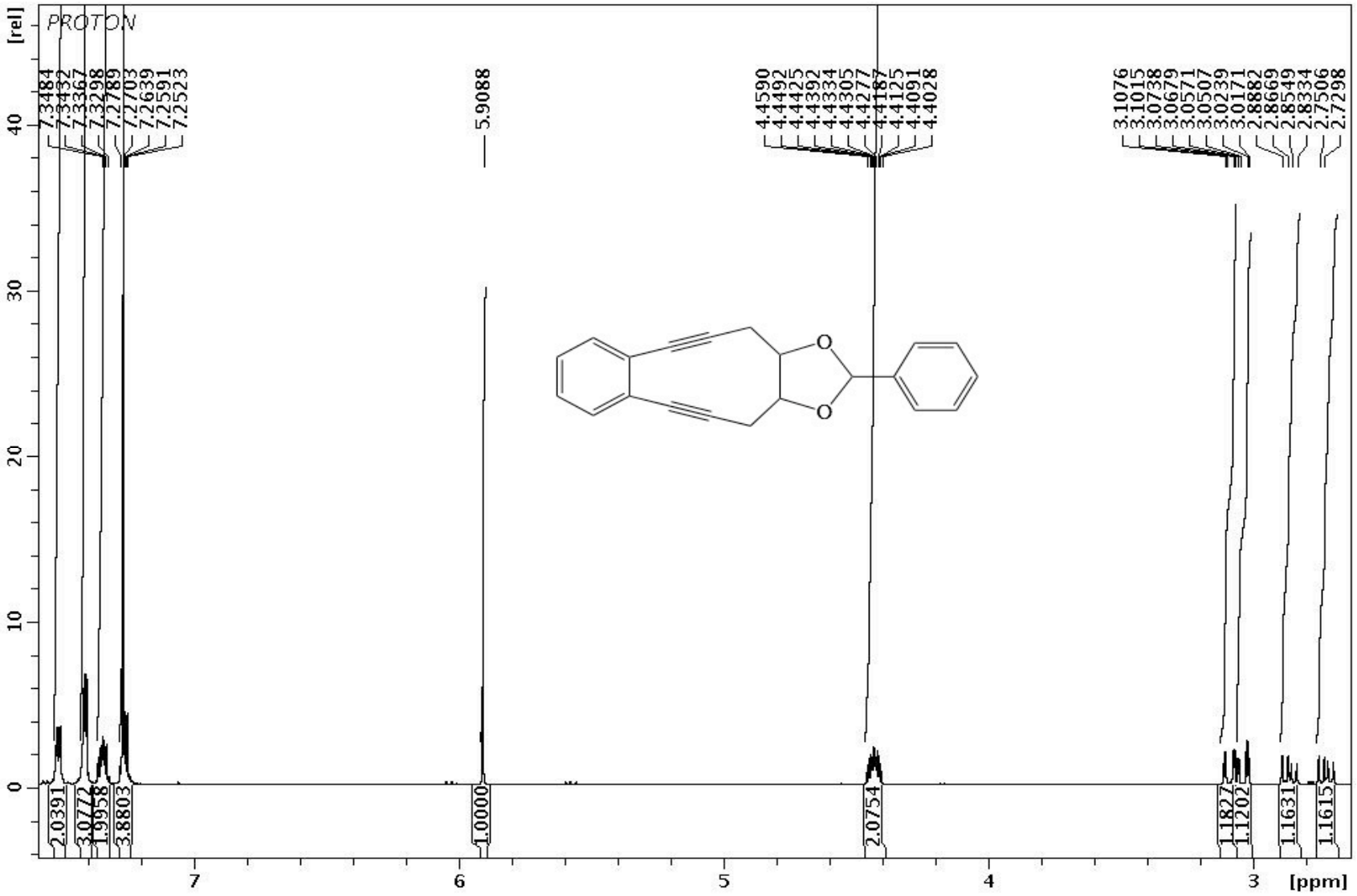
4
3
2
1
0
120
110
100
90
80
[ppm]


PROTON
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7.2591
7.2523
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4.4492
4.4425
4.4362
4.4334
4.4305
4.4277
4.4167
4.4125
4.4091
4.4028
3.1076
3.1015
3.0738
3.0679
3.0571
3.0507
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2.8669
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2.0391
3.0772
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1.1631
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O
O
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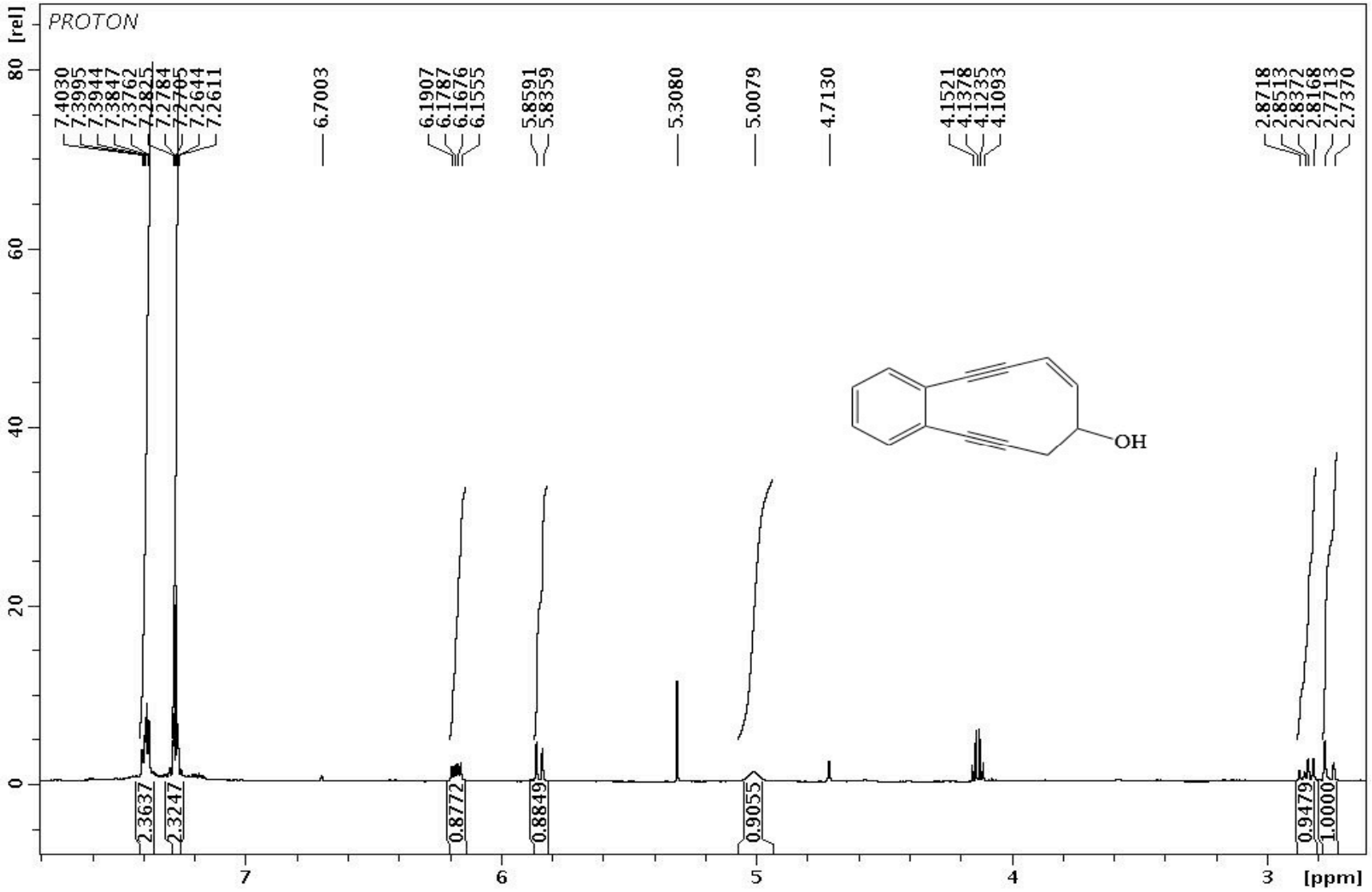
PROTON
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20
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7.2611
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6.1555
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4.1378
4.1235
4.1093
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2.8513
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2.7713
2.7370
OH
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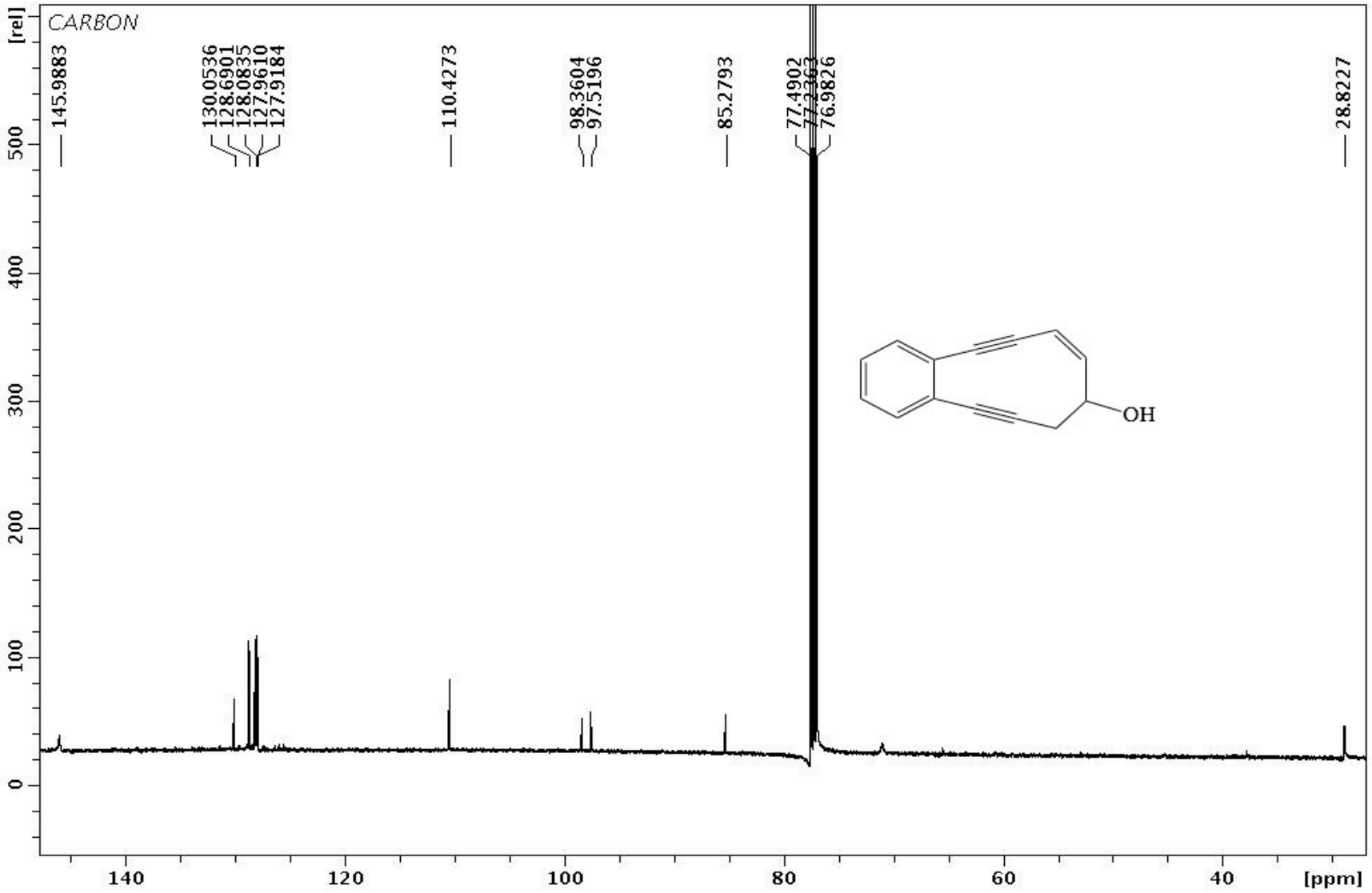
4
3
[ppm]


CARBON
[rel]
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400
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200
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127.9184
110.4273
98.3604
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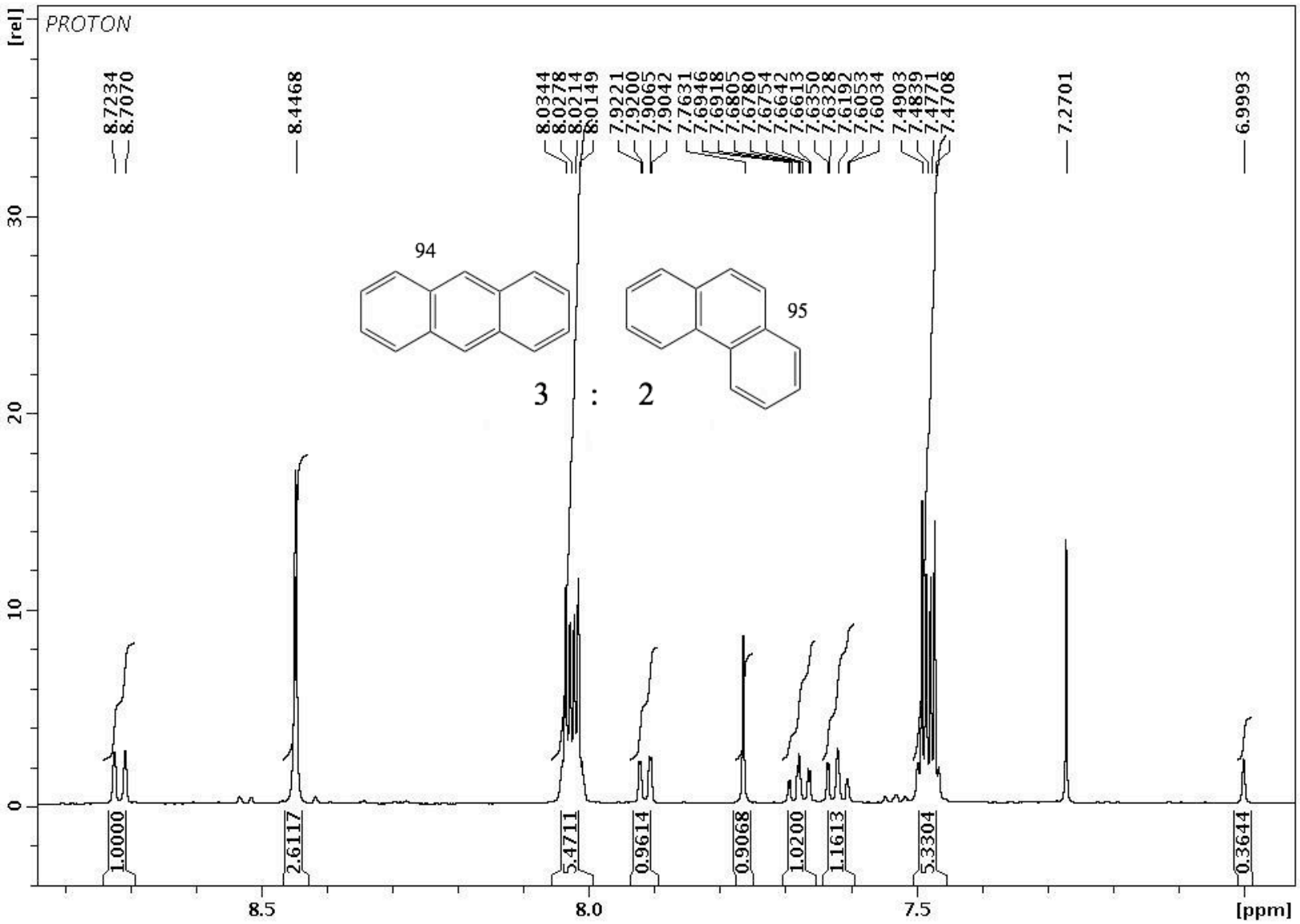
77.2363
76.9826
28.8227
OH
140
120
100
80
60
40
[ppm]


PROTON
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7.9065
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7.6946
7.6918
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7.6350
7.6328
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7.4839
7.4771
7.4708
7.2701
6.9993
94
95
3 : 2
1.0000
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0.9068
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1.1613
5.3304
0.3644
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7.5
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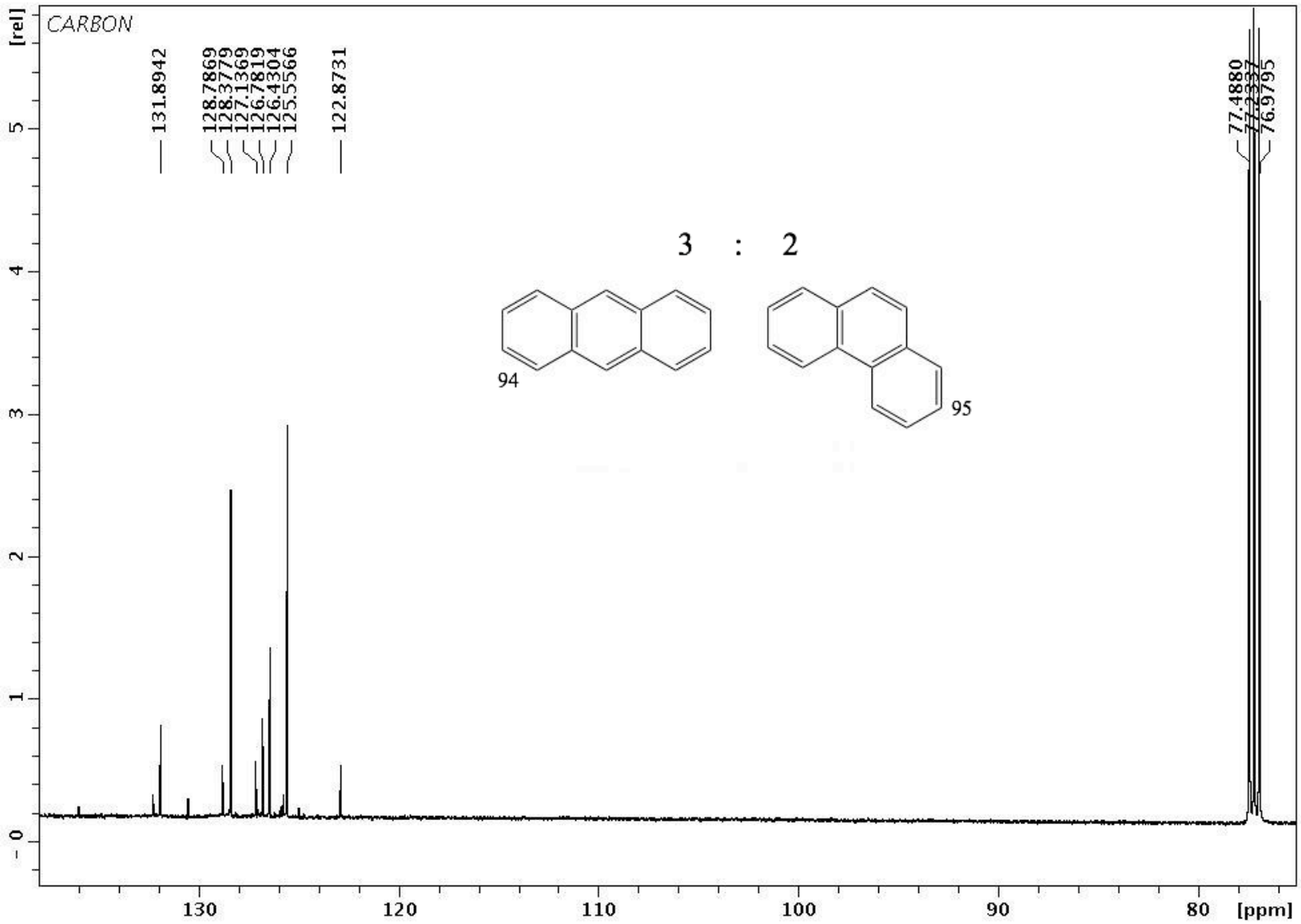
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77.4880
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76.9795
3 : 2
94
95
[ppm]

References

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