SYNTHETIC STRATEGY DIRECTED TOWARDS THE SYNTHESIS OF BICYCLO[3.3.0]OCTA-3,5,8-TRIENE-2,7-DIONE

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TANER ATALAR

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Approval of the graduate school of the Natural and Applied Sciences.

_____

Prof. Dr. Canan ÖZGEN
Director

I certify that thesis satisfies all the requirements as a thesis for the degree of Master of Sciences.

_____

Prof. Dr. Hüseyin ISÇI
Head of the Department

This is to certify that we have read this thesis and that in our opinion it is fully adequate, in scope and quality, as a thesis for the degree of Master of Science in Science Education.

_____

Prof. Dr. Metin BALCI
Supervisor

Examining Committee Members

Prof. Dr. Tarik PEKEL (Chairperson) _____

Prof. Dr. Metin BALCI _____

Prof. Dr. Cihangir TANYELI _____

Prof. Dr. Idris MECIDOGLU _____

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Taner ATALAR

ABSTRACT

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ATALAR, TANER

M.S. Deparment of Chemistry

Supervisor: Prof. Dr. Metin BALCI

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Although the chemistry of benzenoid and nonbenzenoid quinones have been the subject of extensive theoretical and experimental studies, the extent of our present understanding regarding the geometries and stabilities of quinones of pentalene is meager. After studying the existence of cyclopentadienone and its reactivity as a diene and dienophile in the literature, the study of some related species, particularly the ones with fully unsaturated pentalenic structures were started.

In this thesis, the elusive compound bicyclo[3.3.0]octa-3,5,8-triene-2,7-dione was tried to synthesize by using the synthetic strategy which was developed by us.

We used cycloheptatriene as the starting material. The bicyclic endoperoxiedes mixture obtained by the photooxygenation of cycloheptatriene was

treated with triethylamine to give tropone in high yield. Selective reduction of tropone afforded cyclohepta-3,5-dione which was converted by the way of photochemistry to the bicyclo[3.2.0]hept-6-en-3-one. After protection of the carbonyl group, dibromocarbene was added to the double bond to give desired bicyclic compound with pentalene skeleton. Substitution of the allylic bromide with hydroxyl group followed by PCC oxidation resulted in the formation of a diketone. All efforts to convert this diketone into fully conjugated system failed.

Keywords: Quinones of petalene, pentalene, aromaticity, singlet oxygen reactions.

ÖZ

BISIKLO[3.3.0]OKTA-3,5,8-TRIEN-2,7-DION'UN SENTEZINE YÖNELIK SENTETIK STRATEJI

ATALAR, TANER
Yüksek Lisans, Kimya Bölümü
Tez Yöneticisi: Prof. Dr. Metin BALCI

Temmuz 2004, 125 sayfa

Benzenoid ve nonbenzenoid kinonlarin kimyasi yaygin bir sekilde incelenmesine karsin pentalen kinon türevleri ile ilgili çalismalara literatürde fazla rastlanmamaktadir. Bundan dolayi da bu moleküllerin yapisal özellikleri ve kimyalari hakkinda fazla bilgi mevcut degildir. Litaratürde, siklopentadienonun sentezinden ve reaktivitesinin incelenmesinden sonra dien ve dienofil olarak, siklopentadienon türevleri ile ilgili çalismalar baslamistir, özelliklede konjuge pentalen türevleri ile ilgili bazi çalismalar mevcuttur. Bu bilesiklerin diger bir önemide dogal ürün sentezinde ara kademe olarak önemli rol oynamalaridir. Bunun yanisira bu bilesikler teorik incelemeler açisindan da önem srxetmektedirler.

Bu tezde, gerek deneysel ve gerekse teorik çaismalar kapsaminda son derece karasiz olmasi beklenilen bisiklo[3.3.0]okta-3,5,8-trien-2,7-dion' un sentezlenmesi hedeflenmistir.

Sikloheptatrien fotooksijenasyonu sonucu olusan endeperoksit karisiminin trietilamin ile reaksiyonu sonucu tropon yüksek verimle elde edilmistir. Troponun seçici olarak indirgenmesi sonucu olusan siklohepta-3,5-dienon'un fotokimyasal olarak bisiklo[3.2.0]hept-6-en-3-on'a çevrilmistir. Karbonil grubunun korunmasi sonucu, çift baga dibromokarben katilarak arzu edilen pentalen iskeleti elde edilmistir. Alilik brom atomunun alkol grubunun çevrilmesi ve akabinde oksidasyon sonucu diketon sentezlenmistir. Diketonun konjuge doymamis sisteme çevrilmesi için yapilan türlü denemeler sonuç vermemistir.

Anahtar kelimeler: Pentalen kinonlar, pentalen, aromatiklik, singlet oksijen reaksiyonlari.

To my family

ACKNOWLEDGEMENT

I would like to express my sincere feelings of gratitude and appreciation to my supervisor Prof. Dr. Metin Balci for directing me in this interesting study and for his skillful guidance, endless support, encoragement and patience throughout this tedious work. It has been a great honour for me to work with him.

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SCHEMES

LIST OF ABBREVIATIONS

Å	Amstrong (10^{-10} m)
COSY	correlation spectroscopy
FT	fourier transform
g	grams
h	hour(s)
HF	hartree-fock
HMBC	heteronuclear multibond coherence
HMO	Hückel's molecular orbital theory
HMQC	heteronuclear correlation
Hz	hertz
IR	infrared
J	coupling constant
MHz	megahertz
mL	mililitre
mmol	milimole(s)
NICS	nuclear independent chemical shift
NMR	nuclear magnetic resonance spectroscopy
ppm	parts per million
PQ	pentaloquinone
rt	room temperature
UV	ultra-violet
VBT	valence-bond theory

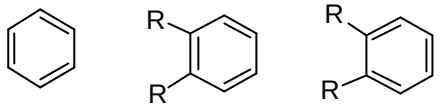
CHAPTER 1

INTRODUCTION

1.1 AROMATICITY

'Bicarburet of hydrogen' nowadays referred to as benzene (C_6H_6) continuously surprises the scientific community, since it was first isolated by Faraday in 1825. Despite its unsaturated character its properties differ from those of (conjugated) alkenes. In fact, benzene has a very distinct chemical reactivity.

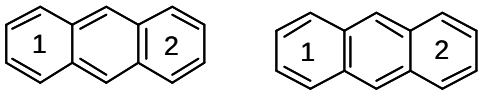
In 1858 August von Kekule [1] published a paper in which he clearly connected the carbon atoms to symbolyze a bond between these atoms. In this way it was possible to demonstrate that the C atom has four valences, which form the bonds. This method also predicted clearly the existence of isomeric compounds in which the C atoms are connected in different ways. In 1865 Kekule published his hexagon structure of benzene [2]. It brought an insight into the chemistry of aromatic substances and it enabled the principle of the four valences of carbon to be applied these cases. This formula contains three double bonds and therefore accounts correctly for the number of electrons in the system. However, the representation of a double bond by two single bonds does not properly describe the properties of a double bond.



1 **2** **3**

There should be two isomeric ortho-substituted derivatives (**2** and **3**), the first having one double bond between the substituents R and the second none. These could not be found. Kekule took account of this fact by the introduction of his oscillation hypothesis, which assumes that the positions of the double bonds are continuously changing.

The same diffuculty arises if rings are fused to the benzene ring (e.g. **4** and **5**). Thus ring **1** in formula **4** must be different from ring **2**. The same is true for formula **5** in which the double bonds in the central ring have changed places. Any difference between rings **1** and **2** cannot be found. The transition from benzene to naphthalene and anthracene is quite uniform as measured by the absorption spectra. This is called uniform annelation effect [3].

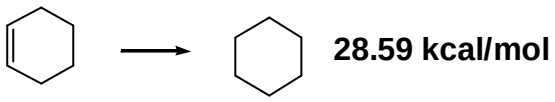


4 **5**

There are more facts incompatible with the presence of three true double bonds in benzene. The sum of the bond energies of the six C-H bonds plus three C-C bonds and three C = C bonds is 1286 kcal\mol. However, from the heat of combustion a value of 1323 kcal\mol is obtaned. The difference of 37 kcal/mol

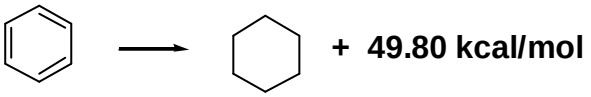
could therefore result from the interaction of the two Kekule structures. It is called resonance energy in the valence-bond (VB) theory [4].

The heat of hydrogenation can also be used to measure the interaction of the double bond structures. The heat of hydrogenation of cyclohexene to cyclohexane is 28.39 kcal\mol.



6 **7**

If there were three non-interacting double bonds in benzene three times this value should be obtained. However, the observed heat of hydrogenation of benzene is much smaller (49.80 kcal/mol).



1 **7**

The difference of 35.97 kcal/mol comes very near to the value obtained from the heat of combustion and must be result from aromatic interaction.

That such an interaction must take place is also shown by the X-ray analysis of benzene which results in regular hexagon with a side length of 1.39 A°. This excludes alternating single (1.54 Å) and double bonds (1.33 Å). If the aromatic

bonds were 50 per cent double bond in character one would expect a bond length of 1.435 Å. The compression of 0.045 Å for one bond is the result of the energy obtained by the aromatic interaction or delocalization of the p electrons.
Hückel's MO theory predicts [5] for benzene:

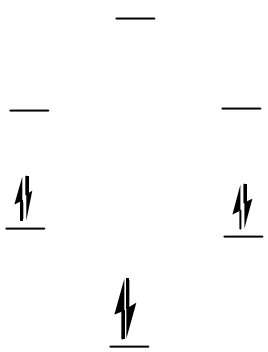
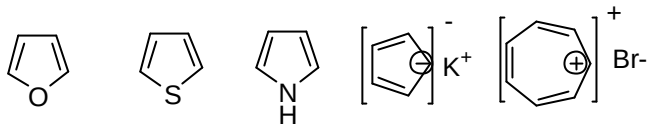


Figure 1 MO of benzene

The energy resulting from the delocalization of the p electrons is measured in terms of an energy unit β. This amounts to 18-20 kcal/mol and it is the energy obtained from one of the two-p electrons forming a double bond. A Kekule structure having three localized double bonds should have the energy of 6β. The MO treatment predicts an energy of 8β for the benzene molecule with delocalized double bonds. The excess energy 2β results, therefore, from the delocalizaion. The double bonds of the Kekule structures disappear in the ground state and are replaced by a new bond type with rather more than 50 per cent double bond character.

In Hückel's MO theory great importance is attached to the group of six (2+4n) p electrons, which gives stability to the ring system that would otherwise have an unsaturated character. Before the MO treatment Bamberger [6] had already

explained the stability of furan **(8)**, thiophene (**9**), and pyrrole (**10**), by the assuption of six potential valences, which Hückel later interpreted as a group of six π electrons in which the lone pair of electrons of the heteroatom participates. However, these systems have not the symmetry of benzene and there must be some limitation of the delocalization which mainly concerns the lone pair of the heteroatoms.



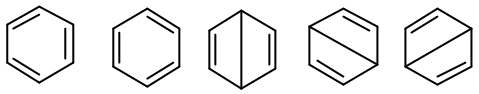
8 **9** **10** **11** **12**

The above group with six delocalized π electrons can be extended to the ionic compounds **11** and **12**. The K atom in cyclopentadienyl potassium **11** contributes one electron to the group of six. In cycloheptatrienyl bromide **12** the Br atom removes one electron from the seven p electrons of the ring thus forming the stable group of six.

Hückel's theory predicts particular stability for all cyclic systems, which have (2+4n) π electrons, n being integer. The main series of this kind is formed by the acenes, i.e. linearly benzene rings: benzene, naphthalane, anthracene, tetracene, pentacene, hexacene and heptacene. These have 6, 10, 14, 18, 22, 26, and 30 C atoms and π electrons, respectively. The higher members of this series are deeply coloured, highly reactive and very unstable. Hückel's rule does not discriminate between acenes and the angular annelated phenes which form the same series with (2+4n) π electrons but show a much greater stability. Moreover, it does not fit the series of the most stable hydrocarbons which are fully benzenoid and have

multiples of six π electrons. It is therefore obvious that Hückel's rule must be strictly limited to monocylic systems.

Another method of giving a quantitative description of the aromatic bond is the valence-bond (VB) method, which was induced by Pauling [7]. It uses classical structures: the two Kekule structures **2** and **3**. The interaction between these structures is called resonance. It results in a ground state, which cannot be represented by any Kekule structure but by a resonance hybrid which has a lower energy than a single Kekule structure.



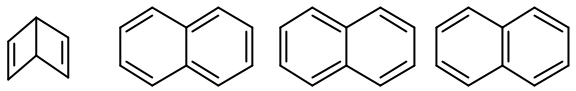
1 **13** **14** **15** **16**

This ground state does not contain double bonds. Besides the Kekule structures the three Dewar structures **14, 15** and **16** have to be considered. These are supposed to be less stable because of the long para bond. They contibute less to the ground state of benzene. The VB method gives the Kekule structures a contibution of 78 % and the Dewar structures 22 %. The resonance energy is calculated in units of α, the interaction energy of the two p electrons, which transforms the single bond into the double bond. The resonance energy calculated from the two Kekule structures is 0.9 a. This value increased to 1.11 α if the three Dewar structures are included.

Dewar benzene and a number of its derivatives were synthesized later [8]. However, their independent existence cannot be used as an argument against the resonance theory. Dewar benzene **17** is not planar and the para bond is single s

bond. Only the existence of a planar compound with a single para p bond would contradict the theory.

As with the MO theory the diffuculties begin with the annelated systems. An extension of the VB theory to naphthalene uses the three Kekule structures **18, 19** and **20**.



17 **18** **19** **20**

For anthracene there will be five Kekule structures. In addition to this, the Dewar structures have to be taken into account. The number of structures to be considered is thus rapidly increasing and the calculation is therefore enormously more complicated. There can be no doubt that mirror-like structures **18** and **19** have the same energy. However, this is not so certain for the structure **20**, which has a double bond between the two rings. This problem can be dealt with using NMR measurements [9].

The problem of aromaticity has always been one of the most diffucult and yet one of the most fascinating problems in chemistry. Ever since Kekule's intuitive idea on the structure of the benzene molecule 1 in 1865, aromatic chemistry [10] has been a challenge both to the theoretician and to the synthesist.

In recent years, the attention of those interested in aromaticity was directed mainly towards cyclic conjugated non-benzenoid aromatic compounds [11]. Some of them possessed features similar to those of benzene, a phenomenon which

derived this hydrocarbon of its unique status and tended to create the necessity for a new and broader defination of aromaticity. Even today, the concept of aromaticity is not defined unequivocally and is used with different meanings [12]. This vagueness is, due first of all to the fact that aromaticity has two meanings, which are basically different one from another: Classically, a compound is considered aromatic if it has a chemistry like benzene, while, according to the modern definition, a compound is aromatic if it has a low ground-state enthalpy [13].

Originally, the concept of aromaticity developed as a means characterizing a certain type of organic molecules that was inclined to substitution and disinclined to addition reactions and was thermally stable [14]. It is true that it has been known for some time that the aromatic compounds possess typical physical properties, such as the anisotropy of the diamagnetic susceptibility [15], but the emphasis has been on the chemical activity rather than on the physical properties in the ground state. Recently, it has been discovered that aromatic molecules possess very low enthalpy in the ground state [16]. With the advent of quantum chemistry, this emprical findings was given a theoretical grounding. Quantitative approximation methods, the valence bond method and the molecular orbital method were developed, and these permitted the calculation of the resonance energy of a conjugated system which is both a ground state property, and can also be measured experimentally [17].

This ambiguity in the concept of aromaticity is especially pronounced in the series of the non-benzenoid aromatics, e.g., the fulvenes. In the benzenoid aromatics, there is quite good correlation between the two definitions. However, the cyclopentadienyl anion, prepared by Thiele in 1900 [18] but not recognized as such, which is the prototype of the non-benzenoid aromatic compounds, possesses a low enthalpy in the ground state, but is very reactive chemically and very far from behaving like benzene.

The dichotomy is quite common and is most probably the source for the mushrooming of the various prefixes attached to the word aromaticity; to mention the most common:

1. Pseudo-aromaticity [19], which is a basic concept in Craig's rules, but in the broader sense refers to all non-benzenoid aromatic compounds.
2. Quasi-aromaticity [20]
3. Anti-aromaticity [21]
4. Non-aromaticity [22]
5. Homo-aromaticity [23]
6. Pseudo-anti-aromaticity [24]

These were attempts to modify the concept with the purpose of trying to bridge the gap between the two fundemental definations mentioned above.

The leading role in the theory of non-benzenoid aromatic compounds has been played by Hückel's rule. Contrary to the aromatic sextet of Armit [25] and Robinson [26] which was developed essentially as an emprical generalization; the Hückel rule was derived from theoretical considerations.

In contrast to the annulenes, the application of the Hückel's rule to the non-alternating hydrocarbons [27] in general, and to the simple non-alternant aromatic compound the monocyclic systems pentafulvene **21**, heptafulvene **22**, pentafulvalene **23**, sesquifulvalene **24** and heptafulvalene **25** and the bicyclic systems; pentalene **26**, azulene **27**, and heptalene **28** in particular, was only intuitive.

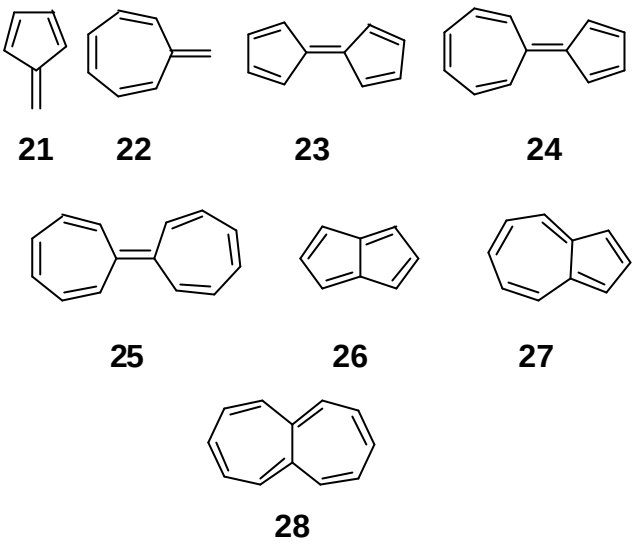
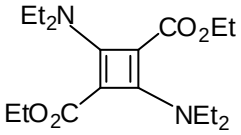


Figure 2 Monocyclic and bicyclic compounds

One attempt, based on Pople's method [28], was made by Fukui and his co-workers [29], who suggested guidelines for the synthesis of new aromatic compounds: they proposed to choose suitable substituents to be attached to the ring in such a way that the ring will acquire 4n+2 p electrons. The push-pull approach towards the synthesis of stable cyclobutadienes [30], e.g., diethyl 2,4-bis(diethylamino)-1,3-cyclo-butadiene-1,3-dicarboxylate 29 [31] was used.



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Among the theoretical concepts that constitute the rational basis of modern organic chemistry there are some controversial constructs, but, perhaps, none to such a degree as that of aromaticity. With all its versatility and usefulness for the systematization of various characteristics relating to structure, stability, reactivity and other chemical concepts, the idea of aromaticity lacks secure physical basis and is ill-defined and vague. Numerous attempts at the canonization of this concept have shown again that it could not be confined within any rigid framework whether it be of speculative or emprical nature [32, 33]. No wonder, unending debate has been going on for a considerable time whether the term “aromaticity” may at all be rightfully regarded as legitimate [34]. The following comment by Binsch [35] illustrates the intensity of the debate: “Aromaticity is just a name, and we are at liberty to continuously adapt its meaning to our changing needs for conceptualization...It is indeed suspicious how often magic rules had and have to serve as an alibi for creating an area of intellectual respectability for chemical research which is on the verge of turning stale.”

This is certainly forceful language. However, whatever guesswork and wrangling there is about the concept, the plain fact remains that it constitutes the basis for very useful classification of organic, inorganic and organometallic cyclic compounds, both qualitative and quantitative, into aromatic, antiaromatic or etc. With the quantitative degree of aromaticity (antiaromaticity) determined within each class.

One more factor that gives rise to the multitude of definations and criteria of aromiticity is the large variety of structural types (including nonclassical ones) of the compounds to which this concept is applied. As a result, there are many derivatives of the concept, some of which are shown in Figure 3:

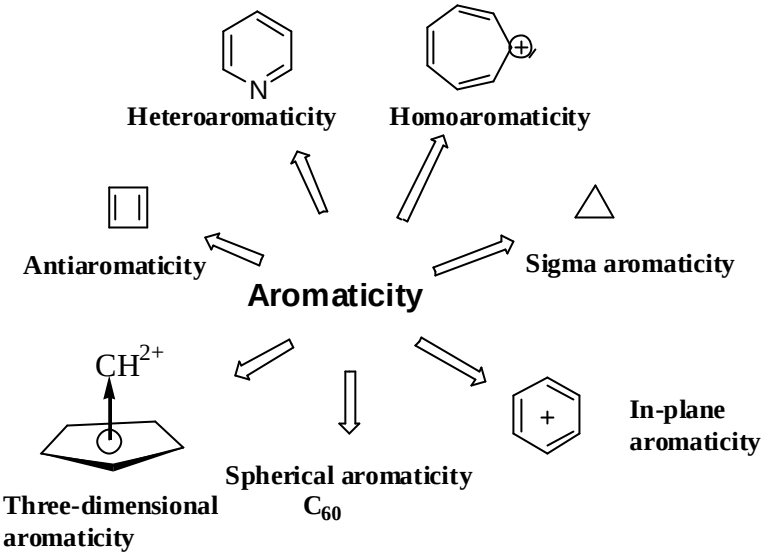
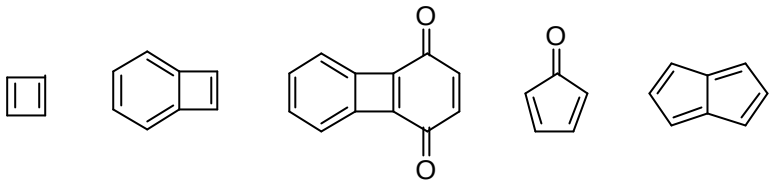


Figure 3 Outline of the aromaticity concept

Certain molecules have come to be described as “antiaromatic” which means that the molecules is described by the delocalization of the p-electrons in the same way as a conventional aromatic molecule thought to be stabilised by the delocalization of the p-electrons.

Cyclobutadiene and related compounds containing four membered rings have, over a span of many years, attracted the attention of workers in many areas. Cyclobutadiene is highly reactive molecule and is clearly recognized as an antiaromatic Hückel 4n p-electron system. Cyclobutadiene can only be subjected to spectroscopic studies at low temperature, with the aid of matrix isolation techniques [36]. According to the theoretical and experimental evidence, cyclobutadiene has a planar rectangular equilibrium with D_{2h} symmetry; the optimized square structure D_{4h} represents a transition state joining two equivalent minima on the potential energy surface [37].



30 **31** **32** **33** **26**

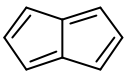
There are some antiaromatic compounds. It might be argued that a simpler definition of an antiaromatic molecule is one with a paramagnetic ring current as revealed by the NMR shifts and, less convincingly, by magnetic susceptibility measurements [38]. Historically, aromaticity has been a time-dependent phenomenon. Aromatic implies various features, properties, or behaviors to chemists with different backgrounds. While "benzene-like" still suffices for some, the "cyclic delocalization of mobile electrons" description now seems paramount. Its general implication for energies and structures, both geometrical and electronic, as well as magnetic and other properties, necessarily results in an ever increasing widening of the 19^{th} century aromaticity concept [39].

As a result, there is a huge amount of publications about this concept. This introduction just gives the overview of this aromaticity concept. Details of aromaticity concept is also out of our scope in this study.

1.2 PENTALENE

Pentalene (**26**) is generated for the first time in argon matrices by photocleavage of the corresponding dimer. It is found that the cleavage occurs in two distinct steps, the first of which leads presumably to a diradical. **26** is characterized by its electronic and vibrational absorption spectra which are assigned

and interpreted with reference to different quantum chemical calculations. These show that the first two excited states of pentalene involve a doubly excited configuration which had been ignored discussion of the electronic structure. Due to the antiaromatic nature of pentalene, the distortive force of the *p*-electrons which favor a *C*2*h* structure with localized single and double bonds predominates over the effect of the *s*-electrons which drive the molecule to a *D*2*h* structure.



26

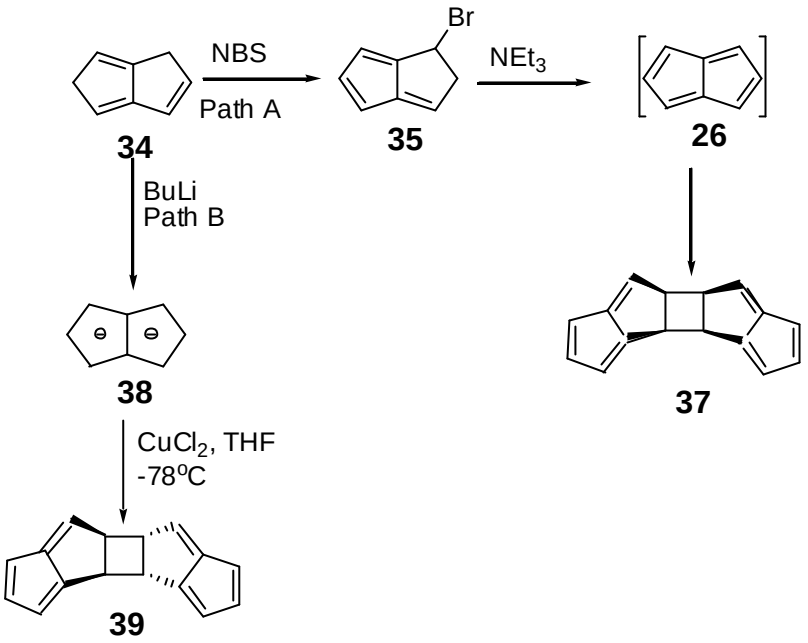
Pentalene (**26**) has fascinated synthetic as well as physical and theoretical organic chemists for more than four decades. In spite of this, convincing spectroscopic evidence for the parent system is still missing. So far, all pentalene derivatives which have been characterized or isolated were either sterically shielded or electronically stabilized. Thus, hexaphenylpentalene was the first simple pentalene which was isolated in 1962 by Le Goff, [40] whereas push-pull substituted pentalenes such as 1,3-bis(dimethylamino)pentalene [41] or 1,4-diamino-3,6-dimethylpentalene- 2,5-dicarbonitrile [42] did not allow unambiguous conclusions with regard to the properties of the electronically unperturbed system.

In the 1970's experimental evidence for thermally unstable alkylpentalenes began to appear, starting with the trapping and UV characterization of 1-methyl-, 2-methyl-, and 1,3-dimethylpentalene, and culminating with the successful isolation and spectroscopic as well as structural characterization4e of 1,3,5-tri-*tert*-butylpentalene which was recently re-subjected to detailed scrutiny by electronic and vibrational spectroscopy. Thermally induced 8*p* cyclization of 8

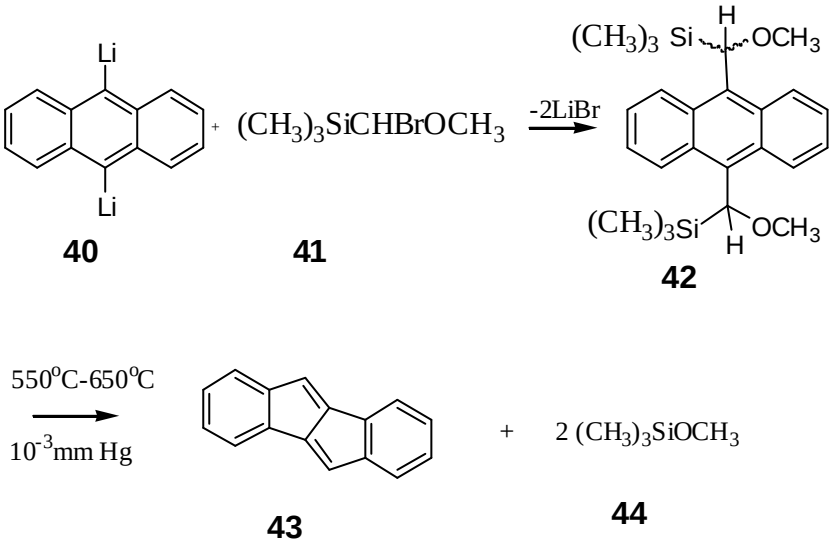
[(dialkylamino) vinyl]fulvenes proved to be a very useful synthetic route to pentalenes which also led to the isolation of the parent pentalene dimer (**37**) and cycloaddition products with cyclopentadiene in cases where pentalene **(26)** was formed as a reactive intermediate.

Parent pentalene has been the subject of numerous Hückel-type or semiempirical theoretical studies which focussed primarily on the reason for and the extent of the bond alternation in this formally antiaromatic species or on its excitation energies.

Recently found two straightforward synthetic pathways to pentalene dimers **37** and **39**, starting with the dihydropentalene **34.** Whereas the bromination dehydrobromination series **34? 35 ? 26** yields exclusively the *syn-cis* dimer **37** (besides polymers and byproducts), twofold deprotonation **34** ? **39** and $CuCl_2$ induced oxidative coupling of pentalene dianion **6** gives a diastereomeric mixture of **37** and **39** (Scheme 1) [43]. Although the yields are very moderate in both cases , pure samples of crystalline pentalene dimers **37** and **39** are easily accessible by simple "one-pot" reactions. Similar to the dimers of methylpentalenes, **37** and **39** undergo photochemical [2 + 2] and thermal [8 + 2] cycloreversions.



Scheme 1 Synthetic pathways to pentalene dimer



Scheme 2 Thermolysis method to synthesize pentalene dimer

Thermolysis of **42** (Scheme 2) to give pentalene derivative **33** [44].

As we know that pentalene, which is predicted to have in the ground state the polyolefin structure is unstable. One of the most interesting aspects of the development of organometallic chemistry has been the discovery that transition metals can form stable complexes with oganic molecules which are unstable under normal conditions. A classic example provided by the work of Petit and his coworkers on cyclobutadiene [45]. Due to this fact, pentalene and pentalene derivatives are important molecules in the oganometallic chemistry. Also, in the past two decades a substantial effort has been devoted to the search of semiconducting polymers that have a small band gap. Antiaromatic molecules, such as pentalene, are ideally suited to construct polymers that have a small band gap [46]. As a result, pentalene and pentalene derivatives has received great attention due to their relation to the concept of aromaticity.

1.3 QUINONES OF PENTALENE

From the earliest days of modern structural theory of organic chemistry, quinones have been intimately associated with the chemistry of aromatic compounds. Their importance in dye industry, in medicinal chemistry, in biological electrontransport processes, and in other fields has been documented over the years. Although the chemistry of benzenoid and nonbenzenoid quinones have been the subject of extensive theoretical and experimental studies, the extent of our present understanding regarding the geometries and stabilities of quinones of pentalene (‘pentaloquinones’ or PQs) is meager. Pentalene quinones are defined as the fully unsaturated derivatives of the various isomeric bicyclo[3.3.0]octanediones. The numbering system for pentalene and four possible pentalene quinones that can be constructed with two carbonyl groups and three double bonds are shown in Figure

4. Two pentalene quinones related to metabenzoquinone are also shown here. For ease of reference, abbreviated names rather than arbitrary numbers will be used for the pentalene quinones throughout this thesis. Thus, for example, 1,2-pentaloquinone will be referred to simply as1, 2-PQ (see Figure 4).

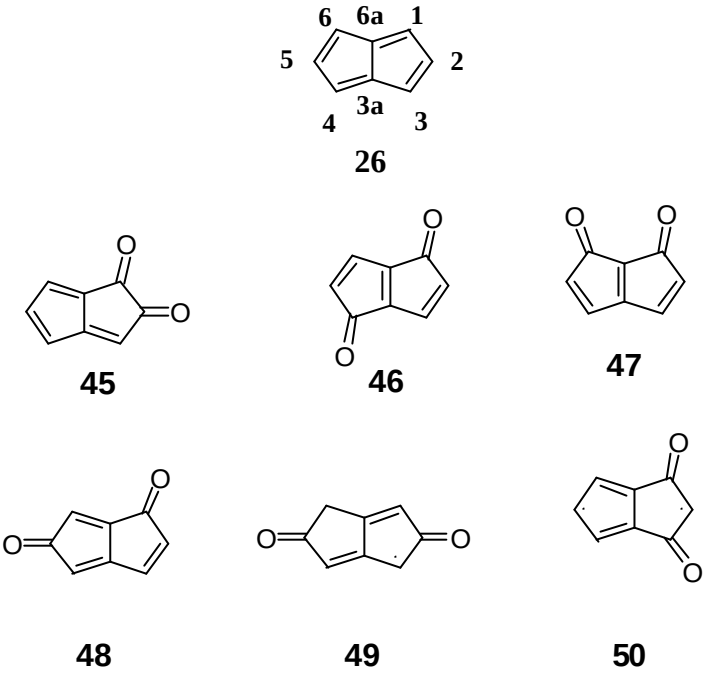


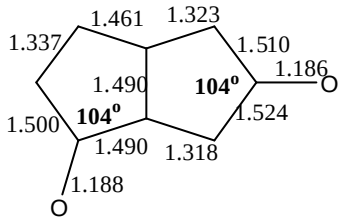
Figure 4 Pentalene and pentaloquinones (PQs)

After studying the existence of cyclopentadienone and its reactivity as a diene and dienophile, it has been started the study of some related species, particularly the ones with fully unsaturated pentalenic structures as pentaloquinones. The presence of the second condensed ring of cyclopentadienone may remarkably affect the stability of such species and their reactivity in Diels-Alder processes. The study of such species has received no attention up to recently, although partially saturated

structures similar to pentaloquinones have shown to be very useful synthons for the synthesis of natural products and other compounds of theoretical interests.

Even though pentaloquinones are not presently available for more studies, it is possible to carry out ab initio calculations at the Hartree–Fock level, from which many properties and structures can be obtained with an accuracy that is competitive with experiment. Since the theoretical results are free from intermolecular interactions, they are a valuable tool for systematic study of structural effects in simple organic molecules. Yavari et al. [47] studied to investigate the structural optimization of pentaloquinones shown in Figure 4. The results of semiempirical and ab initio calculations for pentaloquinones (PQs) are given in their paper. The most interesting conclusion from the calculations is that 1,5-PQ **48** should be the most stable isomer of the pentaloquinones. 1,2-PQ **45** is predicted, by all methods, to be the next stable isomer. As shown in their results, 1,2-PQ **45** is 6.48 kJ mol^{-1} less stable than 1,5-PQ **48**. The calculated energies for 1,6- PQ **47** and 1,4-PQ **46** are 47.51 and 50.27 kJ mol^{-1} higher than that for 1,5-PQ **48**. The two pentaloquinones related to meta-benzoquinone, named 1,3-PQ **50** and 2,5-PQ **49**, are also investigated. For both isomers, the singlet (S) electronic configuration is 150–185 kJ mol^{-1} more stable than the triplet (T). The 2,5- isomer is calculated to be about 60 kJ mol^{-1} more stable than 1,3-PQ **50**.

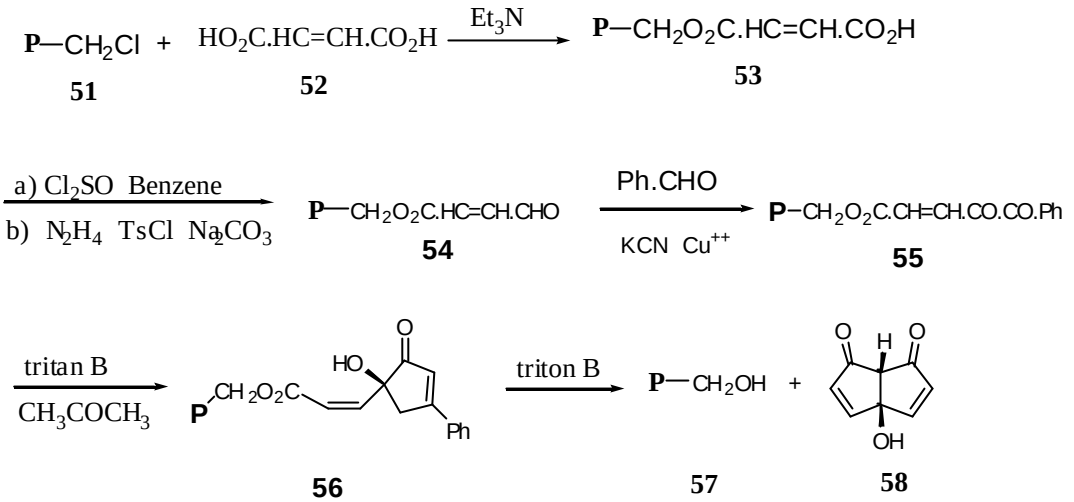
According to the computational studies, calculated bond lengths (in Å) and bond angles (in ^{o}) for 1,5-Pentaloquinone **48**:



1,5-PQ
48

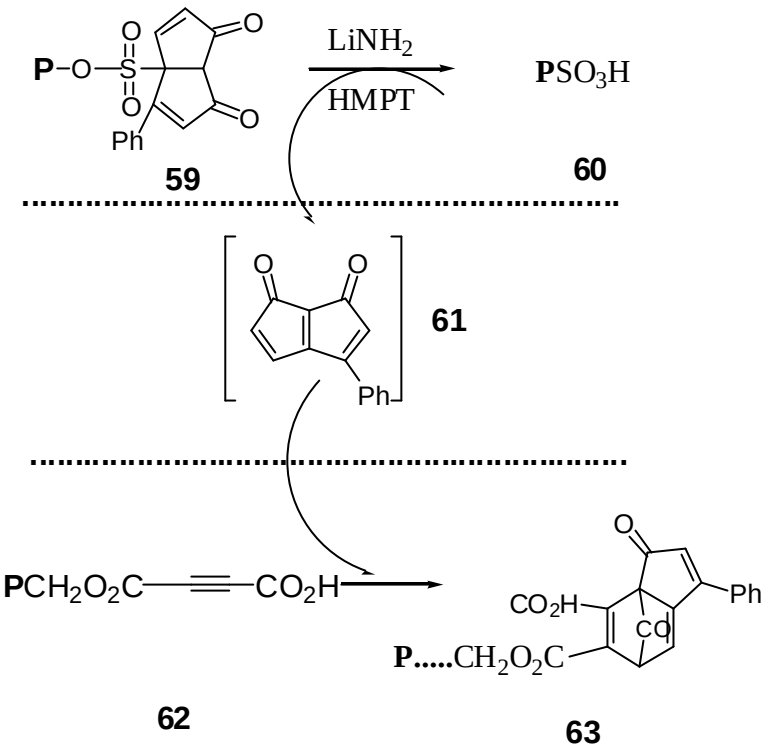
All structures of pentaloquinones are planar. In summary, ab initio calculations provide a picture of geometries of pentaloquinones from both structural an energeticpoints of view and 1,5-PQ is the most stable isomer. Also, geometries and bond orders, chemical hardness, and NICS values gave no definite indication for aromatic or antiaromatic character [48]. However, homodesmotic ring-opening rections to give acyclic analogues indicated that 1,5-PQ is nonaromatic. Nucleus-independent chemical shift (NICS) values do not always reflect aromaticity. In 1996, Schleyer *et al.* proposed a new magnetic criterion for aromaticity: NICS, which is defined as the negative of the magnetic shielding at some selected point in space, e.g., at a ring center. Positive and negative NICS values indicate paratropicity and diatropicity, respectively, and hence have been referred to as indicators of local aromatic character. However, recently noticed that NICS values do not always represent the local aromaticities of polycyclic p-systems [49, 50].

Francisco Gavina *et al.* [51] have reported that the elusive ketone 4-phenylbicyclo[3.3.0]octa-1(5),3,6-triene-2,8-dione **(61)** has been generated from an insoluble polymeric precursor which was synthetized from chlorosulfonated macromolecular resin and 5-hydroxy-4- phenylbicyclo[3.3.0]octa-3,6-diene-2,8-dione **(58)**. Their synthetic methods are shown in Scheme 3 and 4.The liberated diketone can act as a diene but not as a dienophile in the assayed pericyclic reactions.



Scheme 3 Synthesis of Precursor **58**

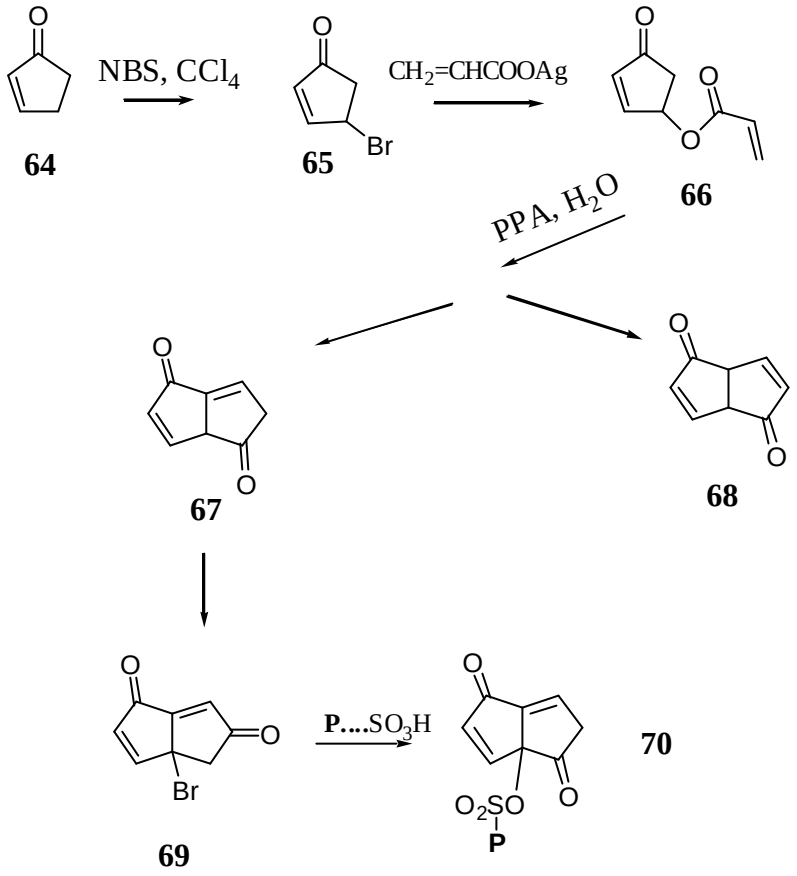
Synthesis of Precursor **58,** the synthesis of compound **58** was carried out as shown in Scheme 3 by using techniques of synthesis on solid supports [52]. These techniques present the advantage of an easier separation between the principal and side products, which can be very useful in processes with a high number of steps.Three-phase test the existence and reactivity of 4-phenylbicyclo[3.3.0]octa-1(5), 3,6-triene-2,-dione (**61**) was established by using the three-phase test. A suitable polymeric precursor for **61** was prepared by reaction of chlorosulfonated macromolecular resin with the alcohol **58** to yield the polymeric tosylate **59** (Scheme 4**).**



Scheme 4 Synthesis of ketone 4-phenylbicyclo[3.3.0]octa-1(5),3,6-triene-2,8-dione**(61)**

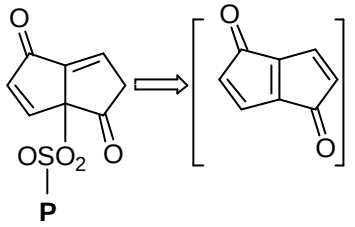
Francisco Gavina et al.[53] studied synthesis of bicyclo[3.3.0]-octa-1(5),3,7-triene-2,6-dione **(46)**. Evidence is presented the existence of free bicyclo[3.3.0]octa-1(5),3,7-triene-2,6-dione, which through an elimination process has been generated from an insoluble polymeric precursor. The diketone can act either as a diene or as a dienophile in pericyclic reactions.

Synthesis of precursor **70.** The synthesis of compound **70** was carried out as outlined in Scheme 5**.** Cyclopent-2-en-1-one was brominated by NBS**,** yielding the 4-bromo derivative, which reacted with the silver salt of acrylic acid to give the ketonic ester **70.**



Scheme 5 Synthesis of precurser **70**

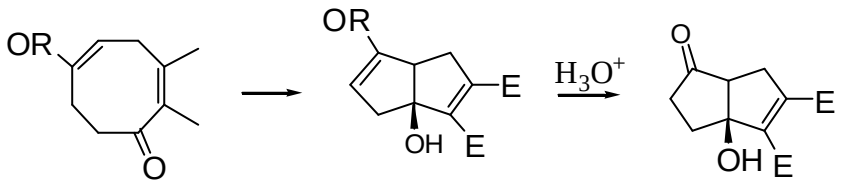
Attempts to isolate **46** in solution, from precursor **70,** led to a mixture of carbonyl products. The same behavior has been observed in the case of annulenone **61,** showing their instability facing polymerization or decarbonylation. As a dienophilic trapping agent, the polymeric monoester of acetylenedicarboxylic acid was used.



70 **46**

The present trapping results support the conclusion that the pentalenic ketone bicyclo[3.3.0]octa-l(5),3,7-triene-2,6-dione (**46**) can exist in solution as a highly reactive species. Reactivity of this compound differs from the one of another pentalenic ketone, 4-phenylbicyclo[3.3.0]octa-1(5),3,6-triene-2,8-dione (**61**), since this does not seem able to act as a dienophile in such cases.

Paul A. Wender and coworkers [54] obtained the skeleton of bicyclic compounds by using the transition metal-catalyzed [5+2+1] cycloaddition reaction (Scheme 6).



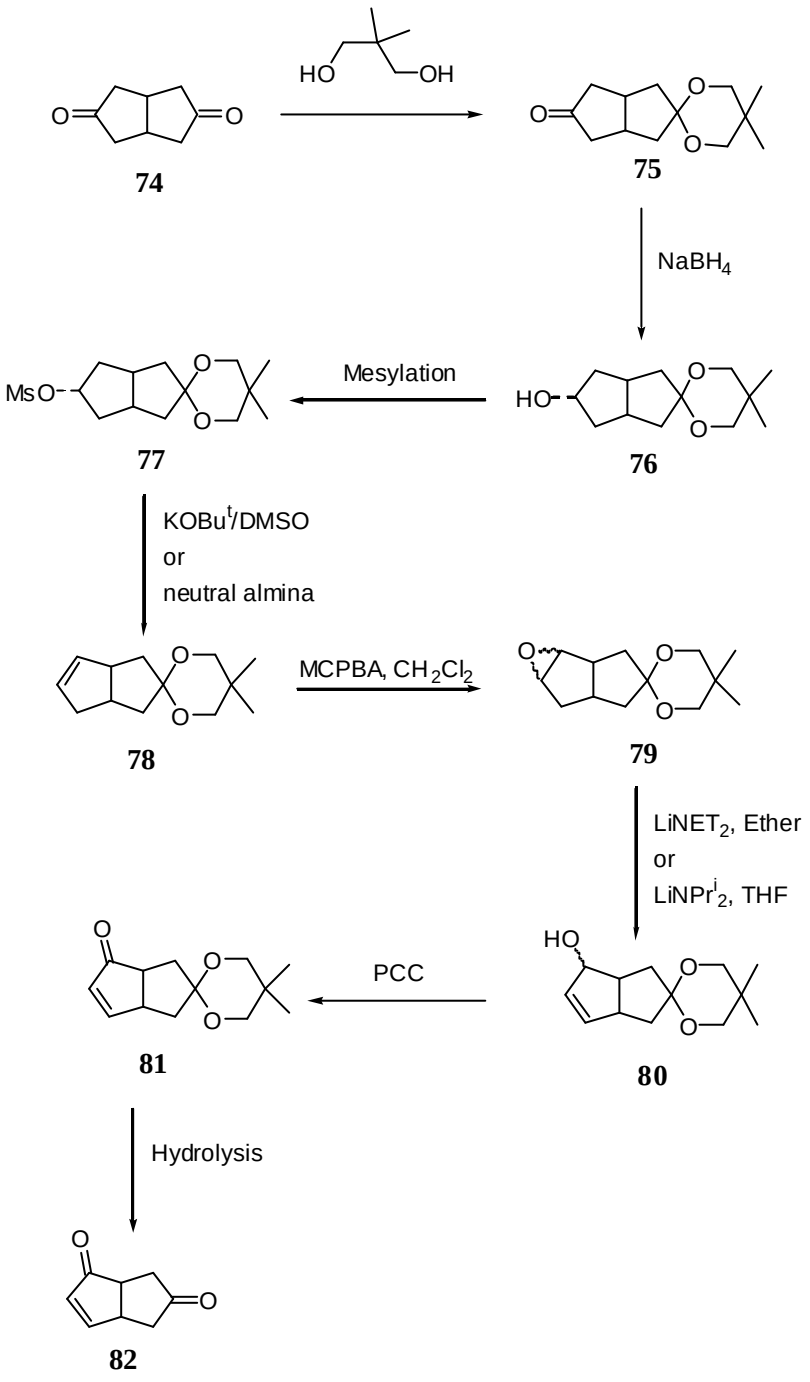
71 **72** **73**

Scheme 6

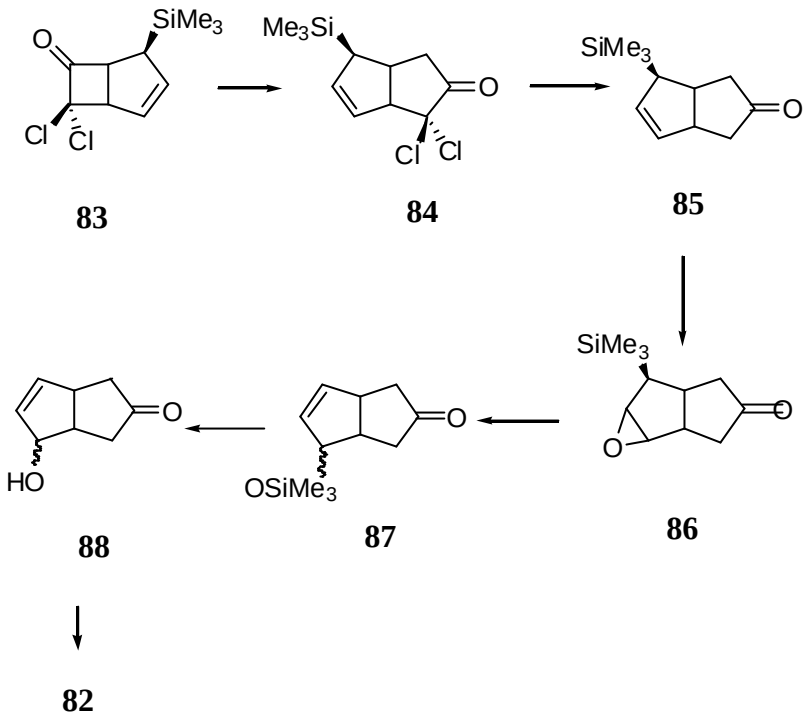
Recently, organometallic regents are also very usefull tools for synthetic organic chemistry. Using Pauson-Khand rection, this bicylic skelotons are easily obtained. Kunio Hiroi and coworkers studied for synthesis of this type of structures [55].

Cis-bicyclo[3.3.0]oct-3-ene-2,7-dione **(82)** is an intersting synthetic intermediate in which all eight carbon atoms are properly activated and ready to undergo a series of chemo, regio, and stereoselective reactions very useful for the synthesis of either natural or non natural polyfused cyclopentanoid systems.

Carceller and coworkers [56] stynthesized cis-bicyclo[3.3.0]oct-3-ene-2,7-dione **(82)** either from cis-bicyclo[3.3.0]octane-3,7-dione **(74)** or the [2+2] cycloadduct of 5-trimetylsilylcyclopentadiene with dichloroketene **83,** Scheme 7 and 8.



Scheme 7 Synthesis of cis-bicyclo[3.3.0]oct-3-ene-2,7-dione **(82)**

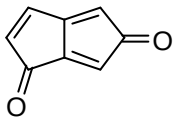


Scheme 8 Synthesis of cis-bicyclo[3.3.0]oct-3-ene-2,7-dione **(82)**

1.4 AIM OF THE STUDY

Quinones of pentalene have facinated synthetic as well as physical and theoretical organic chemists for more then two decades. These compounds have been the subject of numerous Hückel-type or semiemprical theoretical studies. Unfortunately, the extent of our present understanding regarding the geometries and stabilities of quinones of pentalene (pentaloquinones) is meager.

In this study, we will try to develop a new synthetic strategy leading to the synthesis of bicyclo[3.3.0]octa-3,5,8-triene-2,7-dione **(48)**.

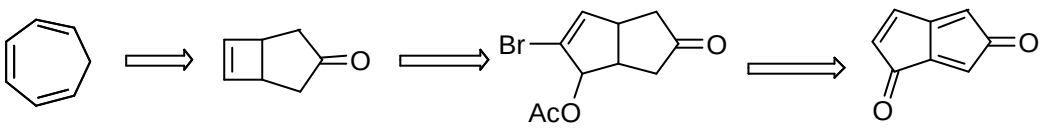


48

CHAPTER 2

RESULTS AND DISCUSSION

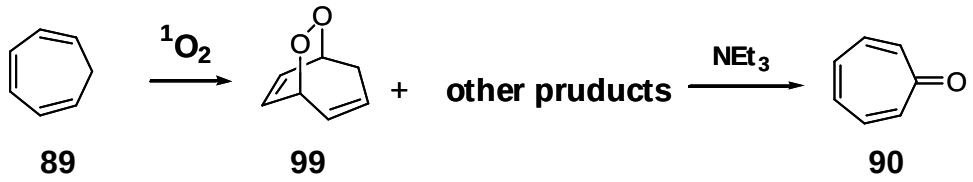
As mentioned before, the aim of this work was the synthesise of bicyclo[3.3.0]octa-3,5,8-triene-2,7-dione **(48)**. For that reason commercially available and inexpensive cycloheptatriene **89** was choosen as the starting material. The synthetic strategy is summarized below:



89 **92** **96** **48**

2.1 THE SYNTHESIS OF TROPONE 90

There exist some numerous routes leading to the synthesis of tropone **90** in the literature [57]. Among these, the most efficient one is the treatment of endoperoxides, which are produced in the photooxidation of cyclohepatriene, with base such as triethylamine [58].



89 **99** **90**

Tropone was synthesized by the photooxygenation of cycloheptatriene and followed by triethylamine treatment, in quantitative yield. Chaaracterization of the tropone **90** was based on the IR, ^{1}H- and ^{13}C-NMR spectral data, which was also consistent with the literature data.

Kende and Chu have reported evidence that the oxidation of tropilidene by photochemically generated singlet oxygen gave ($4\pi+2\pi$) cycloadducts and hydroperoxides [59]. In this thesis, we prefered to use singlet oxygen reactions due to its widespread use and great utility in organic syntheses nowadays.

2.1.1 SINGLET OXYGEN [60]

Although the existence of singlet molecular oxygen has been recognized since 1924, its chemistry has developed dramatically during the last four decades. Not only have chemists contributed to the exponentially growing chemistry of singlet oxygen, but other scientists such as biologists and biochemists have also shown substantial interest in this field. This interest has grown considerably since the recognition of the biochemical roles of the excited state of oxygen in certain blood diseases, in cancer-inducing mechanisms, in a possible free-radical-like aging mechanism, in the role of bacterial activities of phagocytes, and in metabolic hydroxylation. In addition to investigations into the role of singlet oxygen in these phenomena and the mechanism of its reactions, its synthetic applications have also been explored and their utility has been demonstrated.

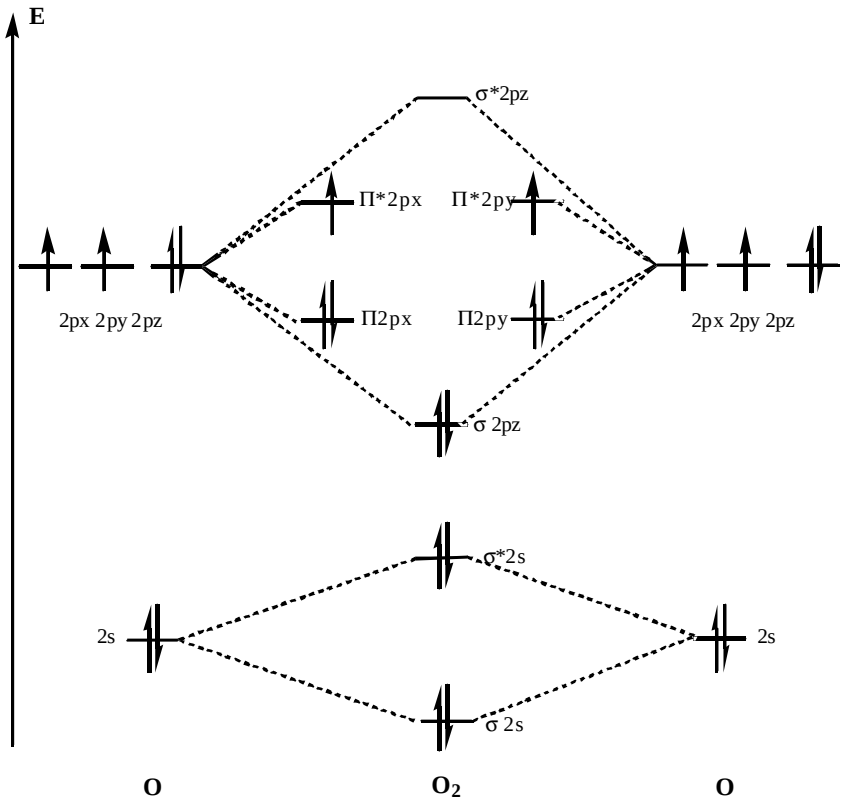


Figure 5 The Molecular Orbital of Diatomic Oxygen Molecule

The reactivity of a molecule is closely related to its electronic structure so the scientists concern with the Molecular Orbital Theory to describe the various electronic configuration of molecular oxygen (Fig 5). Thus the molecular oxygen in its ground state has two unpaired electron with parallel spin and in the degenerated p*2p orbitals so oxygen can be shown as $^3O_2$ in the ground state.

The unpaired electrons in parallel spins in the ground state of the oxygen impart the paramagnetism, which so facilitates the measurement of gaseous oxygen. More importantly, these parallel electron spins forbid the direct entry of paired electrons and allow the reaction include one-electron step. As a result, while the

reaction of oxygen is exothermic, the barrier of spin allows the reaction between triplet oxygen and molecule ground state singlet. The other two lowest electronic states of molecular oxygen known as *singlet oxygen* have electrons with antiparallel spins and can be generated by an input of energy.

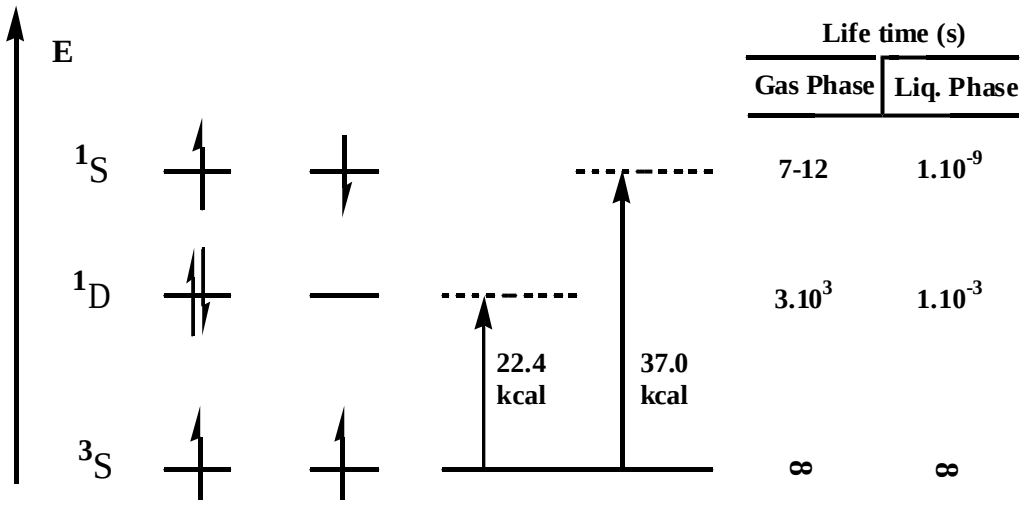


Figure 6 Energy Diagrams and Life Time of Singlet and Triplet Oxygen States

The $^1?_g$ state has energy 22.4 kcal above the ground state. It is not a radical; there are no unpaired electrons. The $^1\Sigma_g$ state is even more reactive, 37.5 kcal above the ground state and electrons are in p*2p orbitals in antiparallel spins (Fig 6). In both forms of singlet oxygen the spin restriction is removed and so the oxidizing ability is greatly increased.

The life times estimated by integrated absorption measurements are 45 minute for the $^1?_g$ state, and 7.1 second for the $^1S^+_g$ state at a zero pressure, but even at 1 atm pressure intermolecular collisions change the transition mechanism to electric

dipole, with much shortened life times. The life times in solution for the singlet molecular oxygen states becomes drastically shortened, with estimates of 10^{-3} sec for the $^1?_g$ state and 10^{-9} sec for the $^1S^+_g$ state in water due to deactivation of molecule with increasing intermolecular collisions. Generally, the reactions made in solvent are concerned, the $^1?_g$ state is in more intense as active singlet oxygen due to long lifetime considering to S^+_g state.

Singlet oxygen is most often generated in laboratory by *photosensitization reactions*. If certain molecules are illuminated with light of a given wavelength they absorb it and the energy raises the molecule into an excited state. The excitation energy can then be transferred onto an adjacent oxygen molecule, converting it to the singlet state whilst the photosensitizer molecule returns to the ground state.

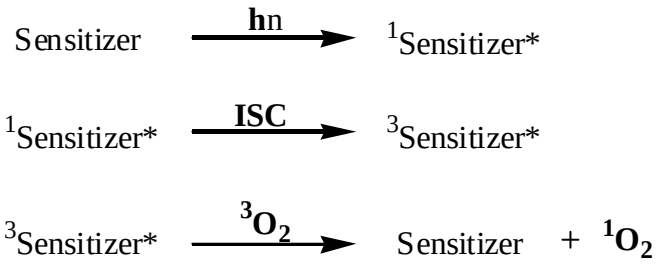


Figure 7 Formation of Singlet Oxygen with Sensitizer

Popular sensitizers of singlet oxygen formation include the dyes *acridine orange, methylene blue, rose bengal, meso-tetraphenlyporphyne* and *toluidine blue*; but any compounds found *in vivo* are also effective, such as the water-soluble vitamin *riboflavin* and its derivatives, *chlorophylls* a and b, the bile pigment *bilirubin, retinal* and various *porphyrins*, both free and bound to proteins. The polycyclic aromatic hydrocarbons can also be used as sensitizer. The most

important step in the formation of singlet oxygen by energy transfer is annihilation of triplet oxygen with triplet sensitizer and it is called as *triplet-triplet annihilation.* The sensitizers must have lower ability to the oxidation with themselves and its triplet energies (30-70 kcal) must be bigger than the energies of the two states of singlet oxygen.

There are some other chemical methods for generating singlet oxygen in solution including the reaction of hydrogen peroxide with sodium hypochlorite, the thermolysis of triaryl phosphite ozonides, and the decomposition of 9,10-diphenylanthracene peroxide.

2.1.1.1 REACTIONS OF SINGLET OXYGEN

The three most common modes of reaction of singlet oxygen with olefins are the ene reaction leading to a hydroperoxide, the Diels-Alder type of cycloaddition forming an endoperoxide, and the direct addition of $^1O_2$ to an activated double bond resulting in the formation of a 1,2-dioxetane (Fig 8). All three types of singlet oxygen reactions have been utilized in organic synthesis for the regiospecific and stereospecific oxidation of olefins.

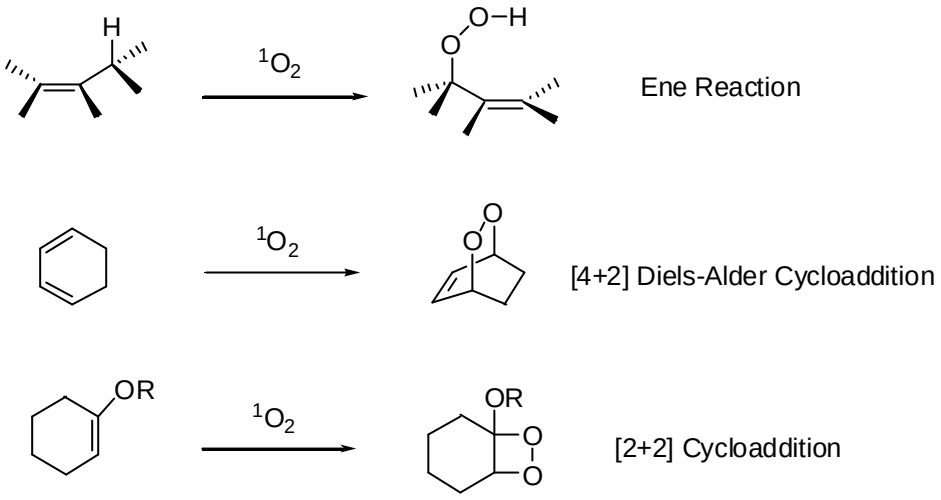
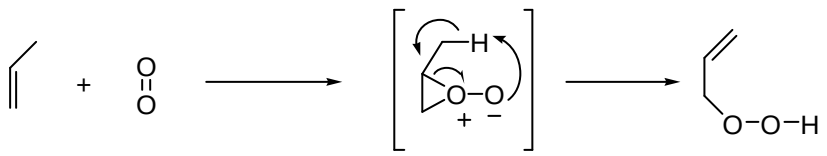


Figure 8 The Types of Singlet Oxygen Reactions

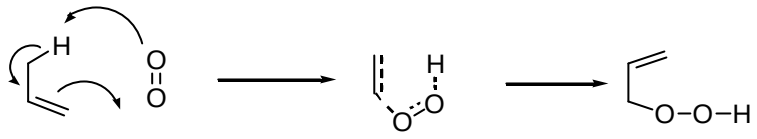
A) Ene Reaction:

The ene reaction, by far the most widely investigated singlet oxygen reaction, involves the formation of an allylic hydroperoxide from an olefin by a process involving abstraction of an allylic proton along with migration of the carbon-carbon double bond. Ene-product formation is strongly dependent on the stereoelectronic and steric effects exerted by the olefin on the attacking electrophilic singlet oxygen. Unlike the Diels-Alder reaction, the mechanism for ene-reaction remains controversial. There are some possible mechanisms for ene-reactions but two of them are considered to be more important.

i) Perepoxide mechanism



ii) Concerted Mechanism



B) [4+2] Diels-Alder Cycloaddition Reaction:

[4+2] Cycloaddition reaction of singlet oxygen is observed with conjugated dienes and yields endoperoxides.

The rate constant for these reactions of $^1O_2$ are very much higher than those for the corresponding Diels-Alder reactions, principally because of the much lower activation energies for the singlet oxygen reactions. The effect of substituents on the diene in these reactions is very similar to that reported for the same reactions in solution and for the normal Diels-Alder reaction. It has therefore been assumed by most workers that a "product like" 6-center cyclic transition state occurs in all such reactions and these reactions go through concerted mechanism like Diels-Alder reactions.

The lowering the activation energy for the reaction when electron donating groups are placed on the diene can then be accounted for by considering the interactions between the highest occupied molecular orbital (HOMO) on the diene and the lowest unoccupied molecular orbital (LUMO) on oxygen. Such an interaction can give rise to a polar transition state and hence account for the big difference between the gap phase and solution reaction rates. However, in Diels-Alder reaction, this big difference is not observed between two phases. Also, the endo selectivity is lost in singlet oxygen reaction. These results remove the

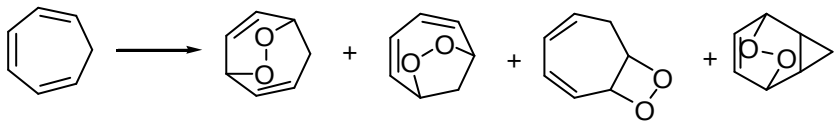
similarities between normal Diels-Alder and [4+2] cycloaddition reaction of singlet oxygen.

C) [2+2] Cycloaddition Reaction:

The formation of 1,2-dioxetanes by singlet oxygen [2+2] cycloaddition to double bonds is usually limited to highly strained or electron-rich olefins such as vinyl sulfides, enol ethers, enamines or alkyl substituted alkenes which do not take part in an "ene" reaction.

These unstable peroxides normally decompose on warming to form carbonyl products resulting from the oxidative cleavage of the original carbon-carbon double bond. Because of the restriction of this type of oxygenation to specific types of olefinic systems, applications of the dioxetane-singlet oxygen reaction in synthesis have been limited.

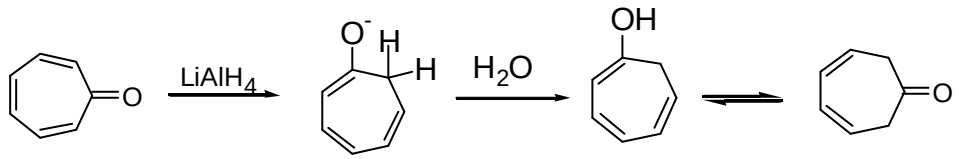
The photooxygenation of cycloheptatriene performed by Balci and Adam [61] is a very good example including all kind of reactions of singlet oxygen at the same time.



89 **99** **100** **101** **102**

2.2 THE SYNTHESIS OF THE CYCLOHEPTA-3,5-DIENONE (91) [62]

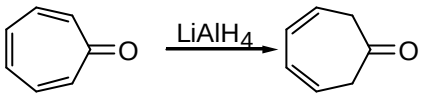
In the literature, the synthesis of **91** from cyclohexanone was used as described by Parham [64] and his coworker. The material as obtained was impure the recovery was poor. The procedure was found to be tedious and a shorter route was sought. Chapman, et *al.,* had reported that lithium aluminum hydride reduction of tropone gave mixtures of 3,5-cycloheptadienone **(91)** and 3,5-cycloheptadienol [65]. Schuster investigated this interesting reaction and reported that the reaction proceeds in three steps. Conjugated addition of hydride to tropone **90** gives the enolate **103,** which gives ketone **91** on hydrolysis. The alcohol is formed predominantly if not totally by reduction of ketone **91** with residual hydride during the hydrolysis work-up procedure. The yield of ketone **91** was substantially increased relative to that of alcohol by inverse addition of the hydride reaction mixture to acetic acid with rapid stirring in the hydrolysis step. An even better procedure gives ketone **91** almost totally free of alcohol. The procedure is simple, can be carried out on a large scale, and gives ketone **91** in high purity after a single distillation.



90 **103** **104** **91**

There exist some numerous routes as mentioned above leading to the synthesis of the compound **91** in the literature. Among these, the most efficient one

is the treatment of the tropone with lithium aliminum hydride at room temperature in diethyl ether [63].



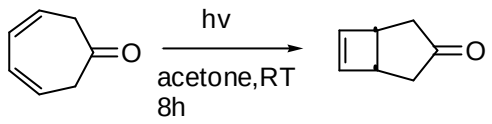
90 **91**

Characterization of the dienone **91** was based on IR, ^{1}H- and ^{13}C-NMR spectral data, which was also consistent with the literature data.

2.3 THE SYNTHESIS OF BICYLO[3.2.0]HEPT-6-EN-3-ONE (92) [66]

When a conjugated homoannular diene is irradiated in solution with ultraviolet light, it is transformed into valence tautomoric structure, i.e. only carbon-carbon bonds and not carbon-hydrogen bonds are involved in the reaction. Depending on the structure of the starting diene ring cleavage of intramolecular cyclization occurs. These kinds of transformations are known as electrocyclic reactions, and the steric course of these reactions is determined by the symmetry of the highest occupied molecular orbital of the open-chain partner [67].

Direct irradiation at 254 nm cyclohepta-3,5-dienone **(91)**, in solution with a mercury arc for 8 hours at room temperature gave photo isomer **92**.



91 **92**

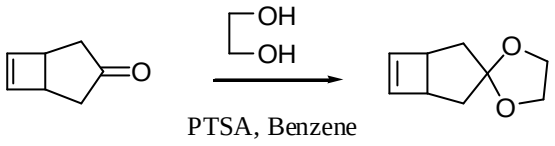
The formation of **92** can be explained with the [2+2] disrotatory ring closure, which is a photochemically allowed process according to Woodward-Hoffmann rules.

Characterization of bicyclic ketone **92** was based on the IR, ^{1}H, ^{13}C-NMR spectral data, which was also consistent with the literature data.

After the synthesis of olefin **92,** we tried to add dibromo carbene to the compound **92**, however, it did not work. Then we decided to protect functionality in ketone and we added carbene again we observed that carbene addition takes place.

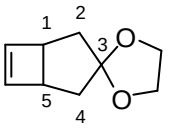
2.4 PROTECTION OF THE BICYLO[3.2.0]HEPT-6-EN-3-ONE (92)

In the literature, there are many reagents for protection of ketones and many reaction routes exist for this reason [68]. Among these, one of the most efficient methods is the protection of ketones with ethylene glycol. Treatment of the compound **92** with ethylene glycol and p-toluenesulfonic acid monohydrate in benzene at reflux temperature of the solvent for 28 hours afforded ketal **93** in quantitative yield.



92 **93**

Characterization of ketal **93** was based on the NMR spectral data. In the proton NMR spectrum of this compound **93**, olefinic protons resonate at 5.99 ppm as singlet which indicates that there is no coupling with the cyclobutene protons. However, cyclobutene protons (H_1 and H_5) gives triplet at 3.20 ppm with a coupling constant of 3.2 Hz arising from the interaction with methylenic protons of the five membered ring. The methylenic protons H_2 and H_4 resonate as broad singlet at 1.76 ppm. The methylenic protons of ketal give AA'BB' system between 3.69 and 3.88 ppm.



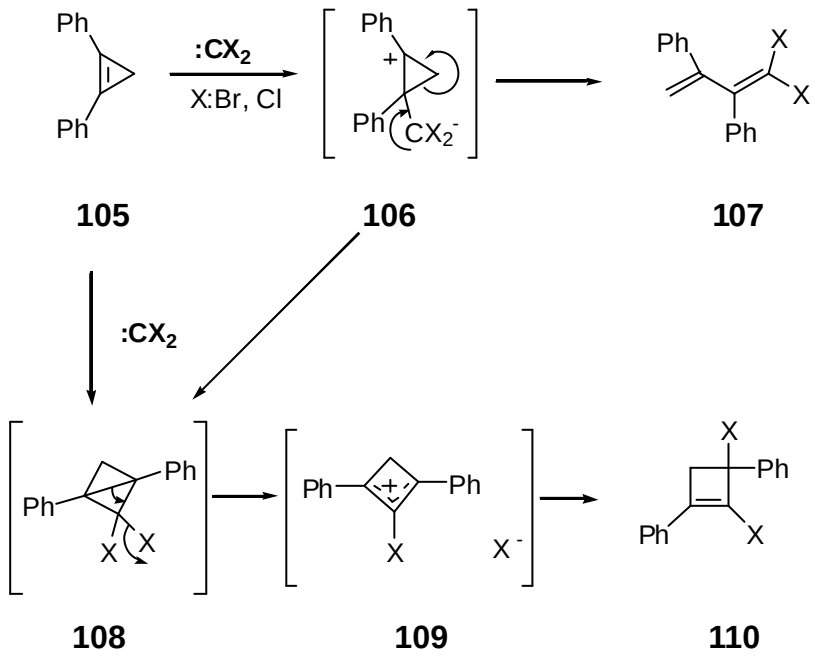
93

The ^{13}C-NMR spectrum of the compound **93** consists of six lines due to symmetry in the molcule as expected. Olefinic carbons resonate at 140.0 ppm and quaternary carbon which is attached two oxygen atoms at 119.5 ppm. The methylenic carbons in the ring resonate at 38.8 ppm and methyne carbons of cyclobutene resonate at 46.1 ppm. The ketal carbons resonates at 63.6 and 65.12 ppm.

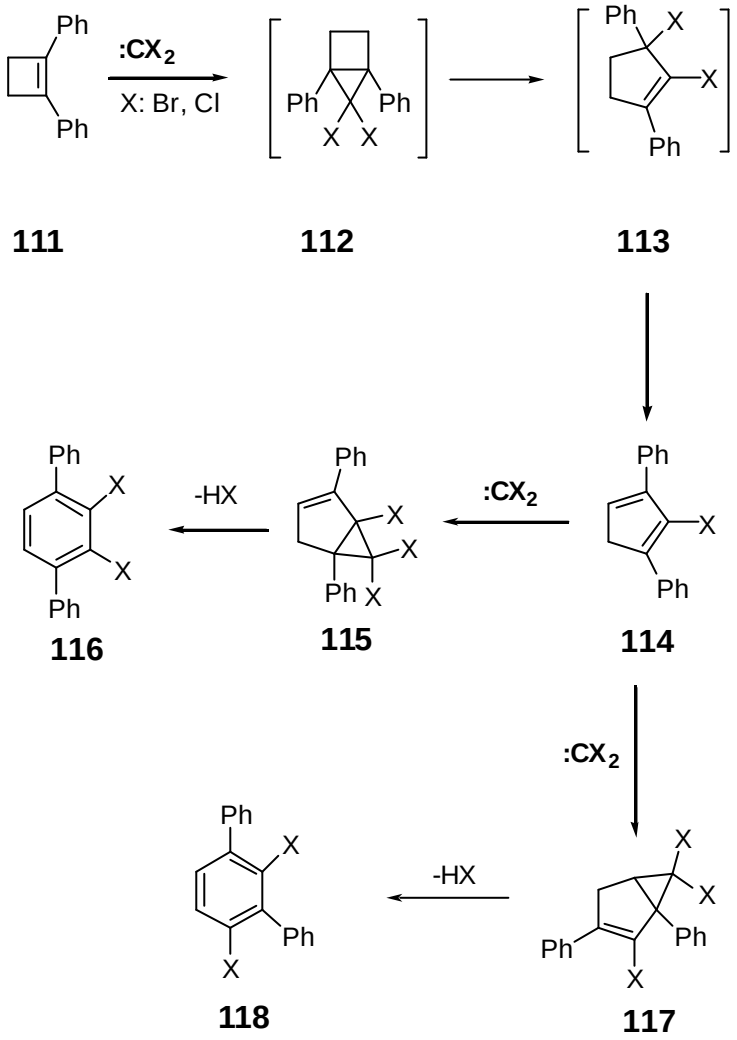
2.5 DIBROMOCARBENE ADDITION REACTION [69]

The most common and throughly investigated reactions of carbene is the addition to carbon-carbon double bonds. Since dihalocarbenes are electrophilic reagents they can easily undergo addition reactions with electrophilic rich double bonds even at low temperatures to give cyclopropane derivatives. Although vast literature concerning dihalocarbene reactions with open chain and cyclic alkenes larger than four membered rings exist, only a few studies with small-ring have been reported [70].

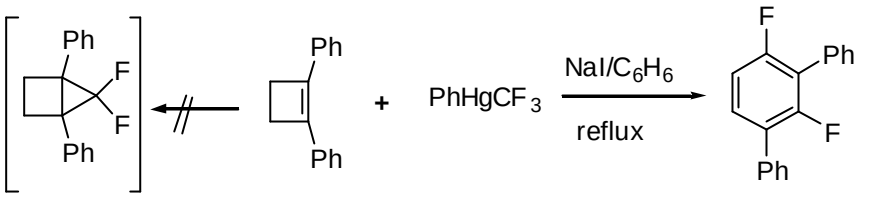
Brinker and Weber [71] have reported the reactions of dihalocarbens with 1,2-diphenylpropene **(105)** which resulted in the formation of 1,3-butadiene **107** and cyclobutene **110**. Further they have suggested a two step mechanism involving dipolar or polarized activated complex, such as **106.**



To provide further evidence for the proposed mechanism, 1,2-diphenyl cyclobutene **111** was treated with dibromo and dichlorocarbene which were generated by three different ways and the reaction resulted in the formation of cyclopentadiene **114**, besides aromatic compounds **116** and **118**.

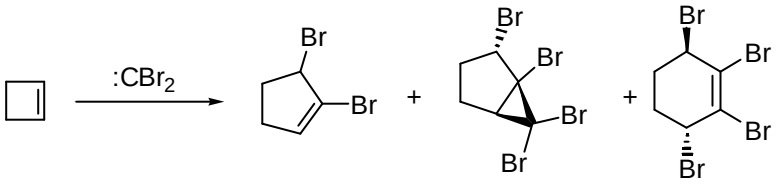


Similar results were found with the difluorocarbene in another study by Lewis et. al [71c].



119 **120** **121**

Balci et. al. [90] have isolated dibromo **123,124** and terabromo **125** from the reaction of dibromocarbene and cyclobutene **122**.



122 **123** **124** **125**

Skell and Sandler [72] have reported that the reaction of geminal dihalocyclopropanes results in the formation of alkanes via the ring expansion. Moreover the reactions of these compounds with electrophilic reagents and/or heat resulted in allyl derivatives, whereas the reaction with Mg, Na or alkyllithiums resulted in the formation of allenes.

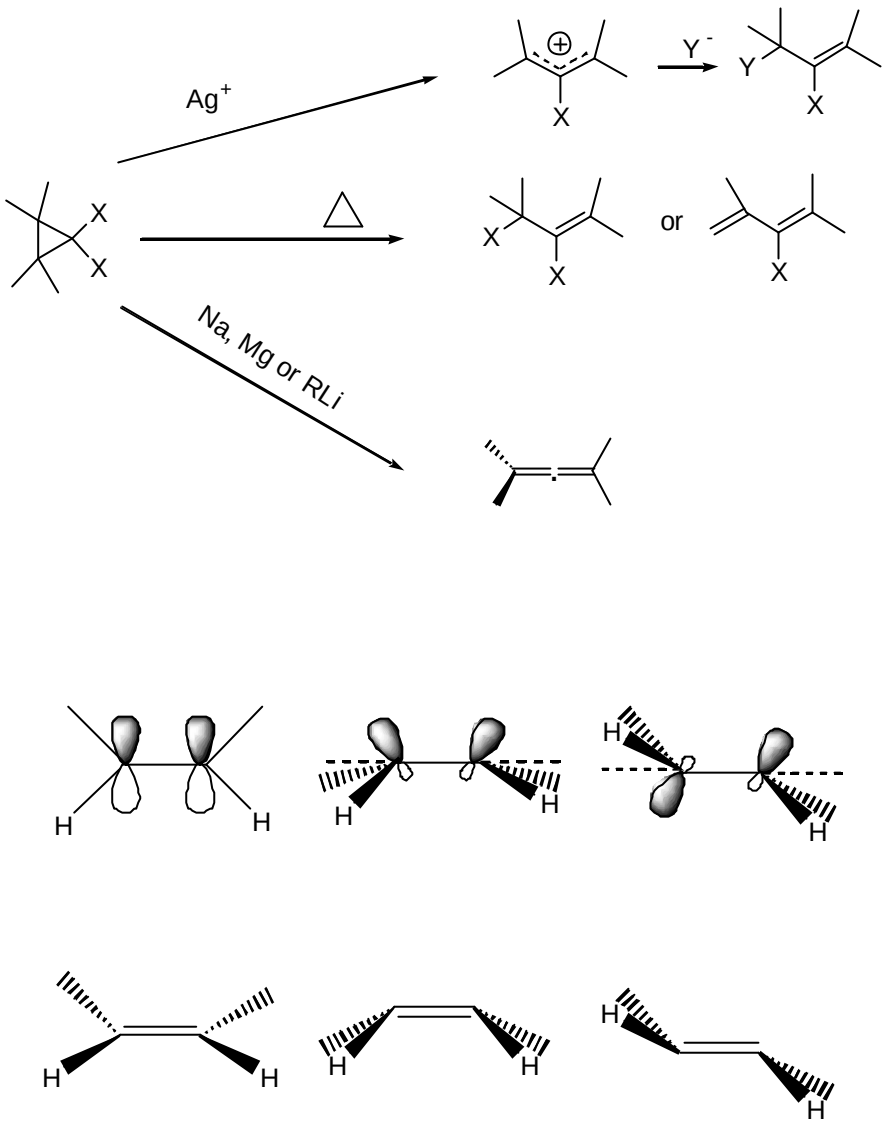
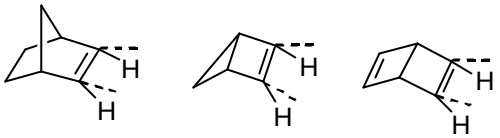


Figure 9. Planar double bond, pyramidalized double bonds, nonplanar.

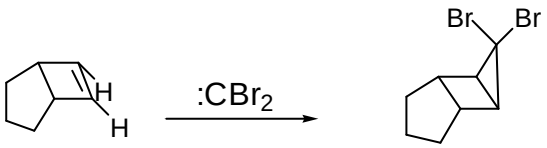
Since the alkenes are normally planar, the addition of the carbene to an alkene can take place from the both side of the double bond as well. But there are some cases in which the double bonds are distorted from the planarity. The distortion is defined as π pyramidalization in the literature [73] (Fig. 9).

The direction of pyramidalization depends on the molecular geometry of the compound. Some *endo*-pyramidalized alkenes to which the *exo* addition are favored are given below.



126 **127** **128**

Previous model calculations [73a] in bicylic alkenes suggest the *endo*-pyramidalization of the double bond in **129** which in terms favors the exo-attack of dibromocarbene to **129**. Furthermore the stereochemistry of allylic bromide defines the stereochemistry of carbene addition. The exo-configuration of bromide implies *exo*-addition of dibromocarbene to **129**.



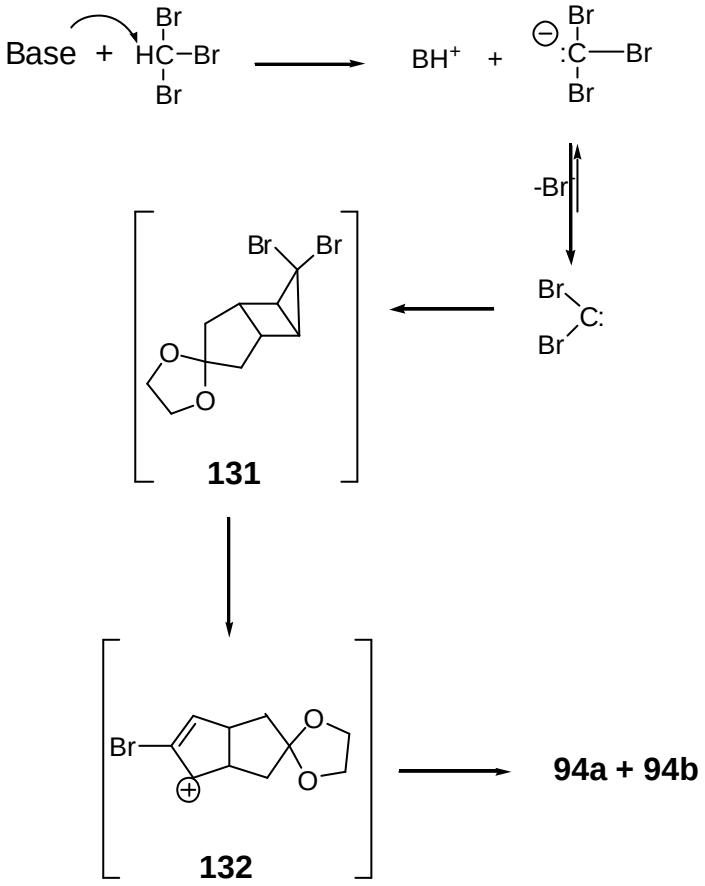
129 **130**

Figure 10 *Endo*-pyramidalization in alkene **129** and *exo*-addition of carbene**.**

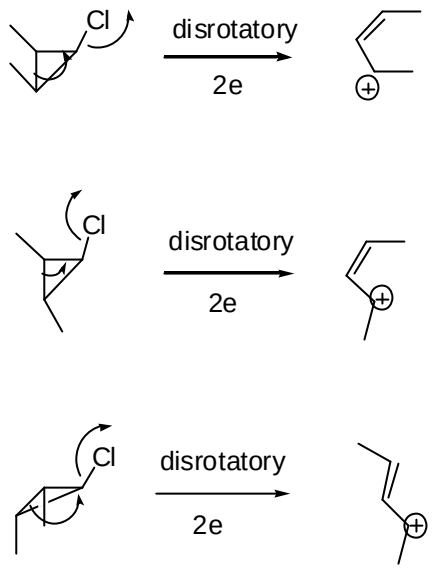
The mechanism leading to the formation of the products is as follows: first the proton abstraction from bromoform by base takes place, the formed tribromo intermediate is in equilibrium with the dibromocarbene of which the exo-addition

to the double bond shifts the equilibrium towards the carbene. The formed intermediate, gem-dihalocyclopropane derivative **131**, immediately undergoes 2 electrons disrotatory ring opening reaction which is a thermally allowed process according to the Woodward-Hoffmann rules to give dibromo compound [74a]. Moreover this process is supported by bromine being a good leaving group.

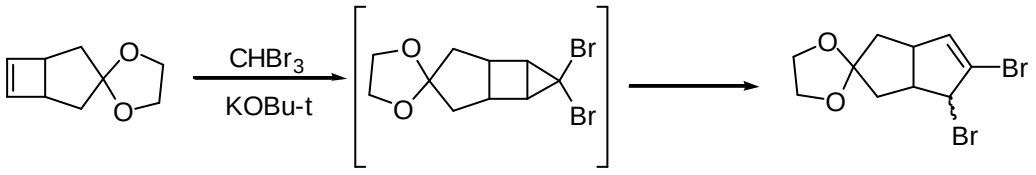
It is well-established that the departing halide is the one which is in the *endo*-position.



Some various examples of this kind of 2 electrons thermal disrotatory rearrengements have been shown in the literature [73b].



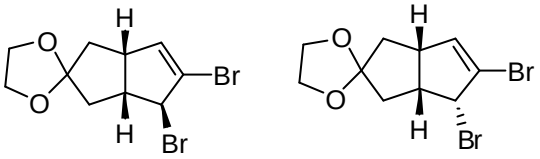
In the light of these literature data, we applied the carbene addition to ketal **93** to synthesize the corresponding carbene addition product **94**. Dibromo carbene addition was performed at -10 °C to give the isomeric mixtures of allylic bromides **94** in a moderate yield.



93 **131** **94**

Actually, we were not able to isolate the expected product **131**. However, analysis of the reaction mixture revealed the formation of two isomeric ring-opening products **94**.

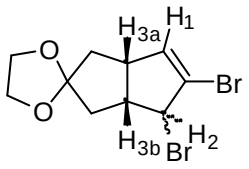
The ^{1}H-NMR data of the major isomer **94a** was extracted from the mixture NMR spectrum of **94a** and **94b.**



94a **94b**

The structure of dibromide **94** has been elucidated on the basis of NMR spectral data. The olefinic proton resonates at 5.93 ppm as doublet with coupling constant of 2.1 Hz. The proton H_2 resonates at 4.62 ppm as a broad singlet. The protons of the ring junction (H_{3a}, H_{3b}) give complex signals between 3.0 and 3.5 ppm. The methylenic protons of five membered ring resonate between 1.55 and 2.06 ppm as mutiplet. Methylenic protons of ketal resonate at 3.79 ppm as a broad singlet.

We have determined the *exo* configuration of the bromide by measuring the coupling constant between the proton H_2 and H_{3b}. On the basis of the *exo*-configuration of the bromide we suggest that the carbene addition occures from the *exo*-face of the molecule. The endo isomer **94b** is probably a secondary product which is formed by the isomerization of **94a**.

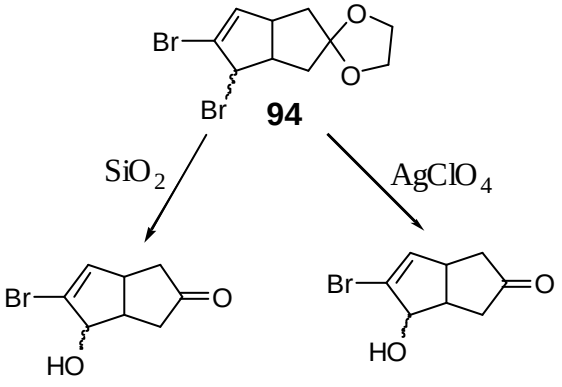


94

In the ^{13}C-NMR spectrum of **94**, we observed ten signals as a result of the unsymmetrical structure of the compound. There are two olefinic carbons at 140.4 ppm and 122.7 ppm. The carbon atom attached to the ketal oxygens resonates at 117.4 ppm and the carbon atom attached to the bromine resonates at 65.2 ppm.

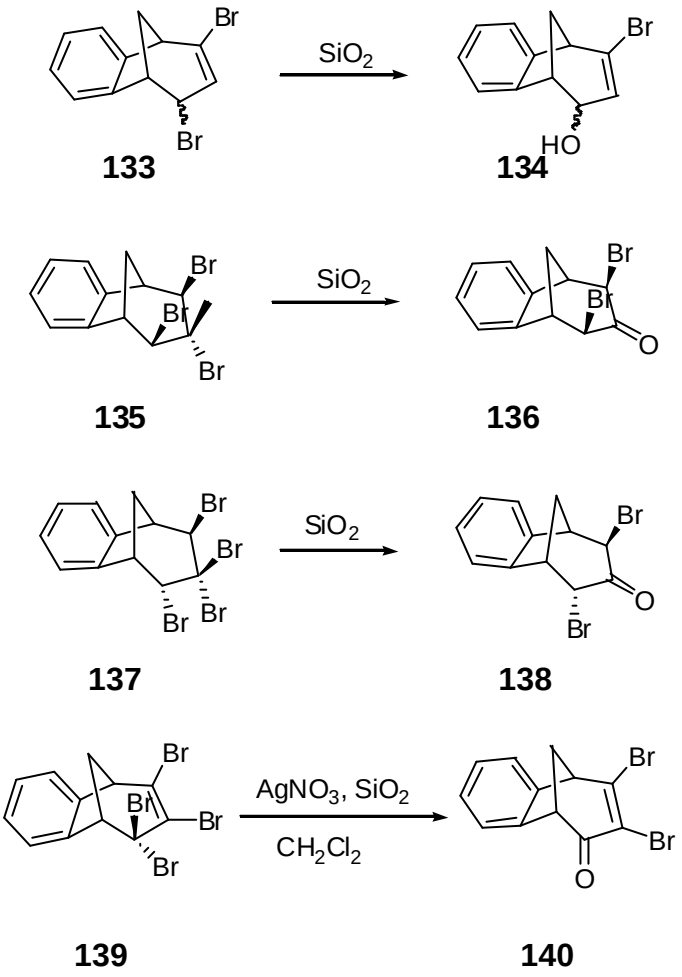
2.6 THE SYNTHESIS OF THE 5-BROMO-4-HYDROXY-3,3a,4,6a-TETRAHYDRO-1H-PENTALEN-2-ONE (95)

There exist some numerous routes leading to the synthesis of alcohols in the literature. For example, displacement of primary or secondary halides by hydroxide ion leads to alcohols, although elimination rections complicate the process.

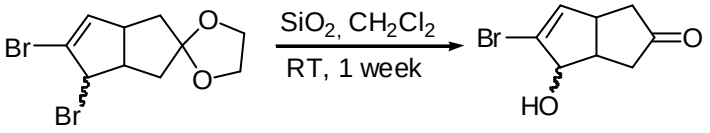


94 **95** **95**

Also the dibromo compounds having an allylic bromine can easily hydrolysed to hydroxy bromine derivatives in silica gel column. Even in some cases dibromo compounds were hydrolysed to ketone derivatives in silica gel column [76].

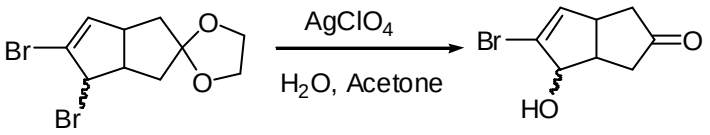


However, silica gel-assisted hydrolysis of allylic bromides requires longer times in our system. Treatment of **94** with silica gel for one week provided the partial conversion of the bromide **94** into **95**.



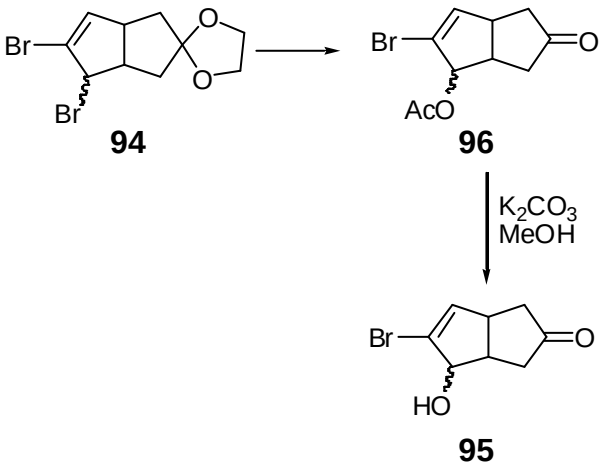
94 **95**

In the literature, many methods are described for conversion of alkyl halides to alcohols. Therefore, we have reacted **94** with $AgClO_4$, it is a widly used reaction in this type of conversions [77].



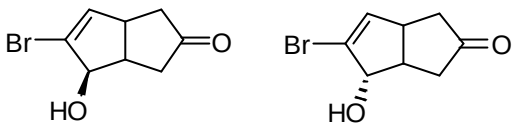
94 **95**

The yield of alcohol was low. So we decided to use different strategy to synthesize this alcohol **95**. We converted the compound **94** into acetylated form **96** which was easily converted to the corresponding alcohol **95** in quantitative yield.



94 **96** **95**

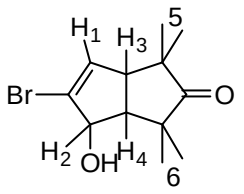
Actually we obtained two alcohols due to the configuration of the hydroxy group either exo or endo from this synthetic pathway. The isomeric alcohols were not separated, since they were converted directly to the ketone **98**. However, careful inspection of the NMR spectrum of the mixture revealed the chemical resonances of the individual isomers.



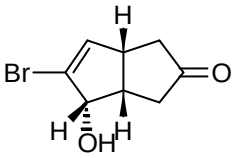
95a **95b** .

Characterization of the alcohol **95** was based on the IR, ^{1}H-NMR, and ^{13}C-NMR spectral data. The structures of these alcohols are also proved chemically by the oxidation to ketone **98** with pyridinium chloro chromate (PCC).

We took the NMR spectra of the mixture for this reason. In the ^{1}H-NMR specrum of the alcohol **95**, olefinic proton (H_1) resonates at 6.07 ppm as a doublet. The H_2 proton resonate different for each isomer, however. For one isomer it resonates 4.77 ppm as a doublet with a coupling constant of 7.3 Hz due to the interaction of the one of the ring junction proton (H_4). For another isomer it resonates at 4.46 ppm as abroad singlet. If we look at the structure of the molecules, dihedral angle between H_2 and H_4 is around 0° for **95b** so according to the Karplus-Conroy graph [78], coupling constant is high for at this diheral angle. There is a coupling for one isomer clearly and this isomer should be **95b**.



95



95b

The ring junction protons (H_3 and H_4) resonate between 3.0 and 3.6 ppm as multiplet. Due to the methylenic protons two AB system exist, these AB system peaks observed for four multiplet peaks between 2.1 and 2.7 ppm. In the ^{13}C-NMR spectrum shows sixteen peaks due to two ismers of the alcohol **95.** According to the NMR spectral data and IR spectrum (chracteristic OH stretching frequency), structure of the compound is assigned clearly.

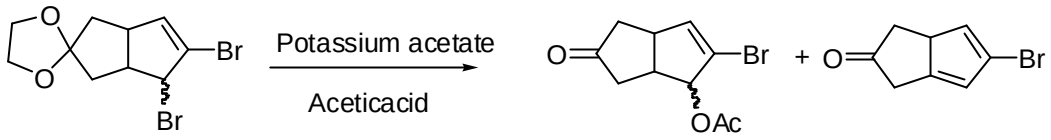
2.7 SYNTHESIS OF THE 2-BROMO-5-OXO-1,3a,4,5,6,6a-HEXAHYDRO-PENTALENE-1-YL-ACETATE (96)

Acetyl functionality is a useful moiety that can have a potential of being converted to many other functional groups suh as alcohols, etc. Here we aimed to obtain an ester group which will then converted into a hydroxyl group in our synthetic strategy. In the literature, there are many publications about acetylation [75].

For the conversion of the isomeric dibromides into the corresponding acetates we have choosen nucleophilic substitution reaction with potassium acetate.

We performed the acetylation using sodium acetate in acetic acid at reflux temperature of acetic acid for sixteen hours. Three products were obtained at the end of this recation; acetylated products, *2-bromo-5-oxo-1,3a,4,5,6,6a-hexahydro-*

pentalen-1-yl-acetate **(96)** and elimination product, *3-Bromo-3,3a-dihydro-1H-pentalen-2-one* **(97)**.

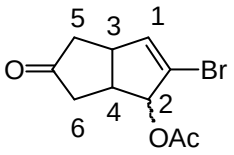


94 **96** **97**

Because of the applied high temperature during acethylation reaction, some part of **96** underwent elimination reaction to give **97**, which was easily separated by column chromotography. When reaction temperature was decreased, it was noticed the formation of **97** was completely supressed.

The structures of these compounds **96** and **97** have been elucidated on the basis of NMR spectral data. In the proton NMR spectrum of compound **96** the olefinic proton resonates at 6.10 ppm as a doublet with a coupling constant of 1.9 Hz. The proton in the position 2 resonates at 5.33 ppm as a broad singlet. The ring junction protons (position 3 and 4) gave multiplet at 3.60 and 3.35 ppm. In the position 5 and 6 (the methylenic protons), two AB system presents separately. The methyl group of the acetate resonates at 2.06 ppm as a singlet.

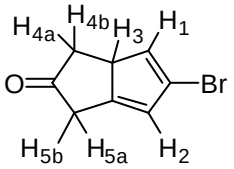
In the ^{13}C-NMR specrum of **96**, we observed ten signals due to the unsymmetrical shape of the molecule. The carbonyl carbon resonates at 216.6 ppm and one ester carbon resonates at 170.8 ppm. There are two olefinic carbons at 141.4 and 122.0 ppm. The carbon attached to the oxygen atom resonates at 87.2 ppm as expected. Other carbons resonate 45.0, 43.0, 42.0, 38.2, 21.3 ppm.



96

Characterization of olefin **97** was based on the NMR spectral data. In the proton NMR spectrum two olefin protons were observed. One resonates at 6.83 ppm as a broad singlet and the other olefinic proton resonates at 5.79 ppm as a doublet with a coupling constant of 1.8 Hz. Analysis of HMBC spectrum reveals that the proton resonating at 7.79 ppm is the proton H_1. Ring junction proton resonats at 3.55 ppm as triplet with a coupling constant of 5.6 Hz. Also there are two AB systems arising from methylenic protons. A part of the first AB system and B part of the second AB system overlapped.

In the ^{13}C-NMR, there are eihgt signals. DEPT-90 spectrum shows the presence of 3 CH carbon atoms as expected. Two of them are olefinic carbons resonating at 129.8 and 118.0 ppm and other carbon is the ring junction carbon resonating at 47.3 ppm. Remaining saturated sp^3 carbons are clearly seen in the DEPT-135 spectrum at 45.1 and 41.9 ppm.



97

2.8 2-BROMO-3a, 4, 6, 6a-TETRAHYDROPENTALENE-1,5-DIONE (98)

There exist some numerous routes for the oxidation of the secondary alcohols to ketones in the literature. Simple 1º and 2º-alcohols in the gaseous state lose hydrogen when exposed to a hot copper surface. This catalytic dehydrogenation reaction produces aldehydes (as shown below) and ketones, and since the carbon atom bonded to the oxygen is oxidized. Gas phase dehydrogenations of this kind are important in chemical manufacturing, but see little use in the research laboratory. Instead, alcohol oxidations are carried out in solution, using reactions in which the hydroxyl hydrogen is replaced by an atom or group that is readily eliminated together with the alpha-hydrogen.

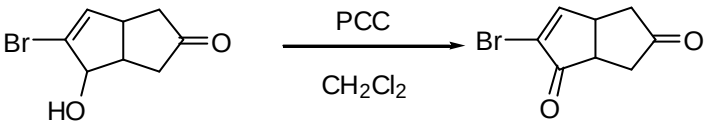
$$RCH_2\text{–}OH + \text{hot Cu} \longrightarrow RCH{=}O + H_2$$

$$RCH_2\text{–}O\text{–}Cl + \text{base} \longrightarrow RCH{=}O + H\text{–}Cl$$

The most generally useful reagents for oxidizing 1º and 2º-alcohols are chromic acid derivatives. Two such oxidants are Jones reagent (a solution of sodium dichromate in aqueous sulfuric acid) and pyridinium chlorochromate ($C_5H_5NH^{(+)}CrO_3Cl^{(-)}$), commonly named by the acronym PCC and used in methylene chloride solution. In each case a chromate ester of the alcohol substrate is believed to be an intermediate, which undergoes an E2-like elimination to the carbonyl product. The oxidation state of carbon increases by 2, while the chromium decreases by 3 (it is reduced). Since chromate reagents are a dark orange-red color (VI oxidation state) and chromium III compounds are normally green, the progress of these oxidations is easily observed. The following equations illustrate some oxidations of alcohols, using the two reagents defined here. Both reagents effect the oxidation of 2º-alcohols to ketones, but the outcome of 1º-alcohol oxidations is different. Oxidation with the PCC reagent converts 1º-alcohols to aldehydes; whereas Jones reagent continues the oxidation to the carboxylic acid product.

Pyridinium chlorochromate was first described by Corey and Suggs in 1975. Their article was entitled "Pyridinium Chlorochromate. PCC, an Efficient Reagent for Oxidation of Primary and Secondary Alcohols to Carbonyl Compounds" [79].

In our synthetic strategy, we use PCC as oxidation agent in order to synthesize the bromo diketone **98** and the oxidation of isomeric alcohols **95** was completed in quantitative yield.

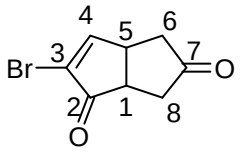


95 **98**

Characterization of bromodiketone **98** was done by using NMR spectral data and IR spectroscopy.

In the ^{1}H-NMR spectrum, olefinic proton resonates at 7.8 ppm as a doublet (J=3 Hz). Due to the configuration of the double bond with the adjacant carbonyl group, the chemical shift of this olefinic proton appears at unusual low-field. Ring junction protons resonate at 3.7 and 3.3 ppm as multiplet and quintet (J: 5.9 Hz) respectively. Moreover, two AB system exist in this molecule and A parts of them are overlapped at 2.8 ppm. One of the B part of the AB system resonates at 2.5 ppm as doublet of doublets with coupling constants of 4.2 and 19.7 Hz. The other B part of the AB system resonates at 2.3 ppm as doublet of doublets with coupling constants of 4.6 Hz, 19.7 Hz.

The ^{13}C-NMR spectrum shows the presence of seven signals. The compound must have eight resonance signals. From the higher intensity of the resonance signal at 41.1 ppm we assume that two carbon signals are overlapped. Two carbonyl carbons appear at 212.7 ppm and 201.1 ppm. The presence of two double bond carbons and four sp^3 carbons are in agreement with the proposed structure. It is expected that the carbonyl carbon peaks do not correlate with any proton signal. On the other hand, the carbon resonance at 162.7 ppm correlates with the proton resonance at 7.7 ppm arising from the olefinic proton. We can assign the carbon resonance at 162.7 to the carbon atom C-4, whereas the carbon resonance at 127.1 ppm to the quaternary carbon atom C-3. the remaining methine and methylene protons correlate with the carbon resonances appearing between 44.1 and 40.2 ppm.



98

The HMBC spectrum of the bromodiketone **98** seems similar to the HETCOR spectrum. The ^{13}C-NMR spectrum is plotted along the v_2 axis and the ^{1}H-NMR spectrum is plotted along the v_1 axis. Interpretation of HMBC spectra requires a degree of flexibility, because we can not always find what it is expect. For example, in some cases the three-bond correlations can not be found.

We begin with the carbonyl carbon resonances. It can be easily recognized that the carbonyl carbons shows many correlations. For examle, a line drawn paralle to the v_1 axis (^{1}H-NMR spectrum) starting from the carbonyl carbon resonance at 201.1 ppm, this line will intersect four cross peaks at 7.7, 3.1, 2.7, and 2.4 ppm,

respectively. From the structure we expect that this carbonyl carbon can correlate with the methine protons (H_1 and H_5) and methylene protons H_8 and the neighbouring olefinic proton H_4. On the basis of these correlations we can assign the cross peak at 3.1 ppm to the proton H_1. A correlation with the proton H_5 is not observed in this case. The three bond correlations can be absent occasionally, whereas the two bond correlations are always present. The other cross peaks belong to the methylene protons. The diastereotopic methylene protons (H_8) give rise to an AB-system, whereas the A-part appears doublets of doublets at 2.7 ppm. On the other hand, a parallel line drawn from the carbon resonance at 212.7 ppm intersects five cross peaks. This carbon resonance correlates with the entire proton resonances appear between 2.4 and 3.6 ppm. Careful examination of the cross peak shows that this peak consists actually of the different cross peaks indicating the overlapping of the methylene protons (H_6 and H_8). Another useful example can be found by drawing a parallel line from the carbon resonance at 162.7 ppm. There are correlations to the tertiary protons H_1 and H_5 as expected. Furthermore, it correlates with the proton resonances at 2.4 and 3.6 ppm. With this observation we can assign those proton resonances to the diastereotopic methylene protons H_6. The carbon atom C-4 cannot correlate with the methylene protons attached to the carbon C-8. Other assignments can be performed in the same way. The HMBC spectrum of this bromoketone **98** allows one to completely confirm the suggested structure with the help of long-range carbon-proton connectivities.

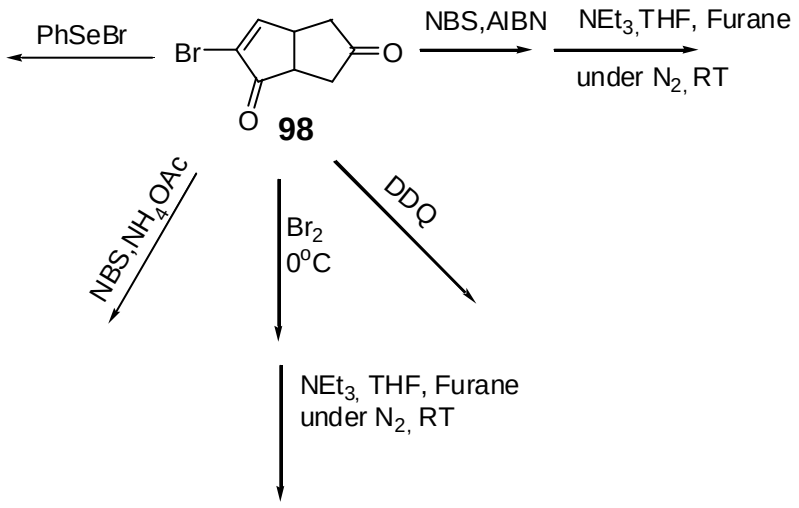
2.9 ATTEMPTS TO SYNTHESIZE THE ELUSIVE COMPOUND 1,5-PENTALOQUINONE 48

Pentalene quinones are defined as the fully unsaturated derivatives of the various isomeric bicyclo[3.3.0]octanediones. Even though pentaloquinones are not presently available for more studies due to the unstable nature of these compounds

like smaller members of the strained allenes [80], we attempted to synthesize this elusive compound **48** by using our synthetic strategy however all attemts were failed.

In the literature some of the isomers of this compound were catched by using special methods like polymer supported solid phase. Attempts to isolate these annlenones in solution always lead to a complex mixture of carbonylic products. This behaviour closely corresponds to that observed for the parent compound cyclopentadienone, the stability of which is so small that it can only be isolated as its dimer or as its decarbonylation products [81].

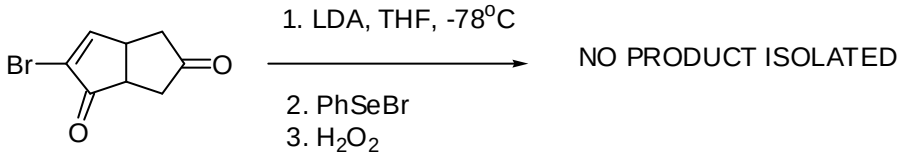
To synthesize this elusive compound **48** we applied different chemical reaction pathways as shown below:



The most straightforward method is the dehydrogenation of carbonyl compounds. There are a number of methods for performing this conversion [82], the most important of which is the α-bromination-dehydrobromination method.

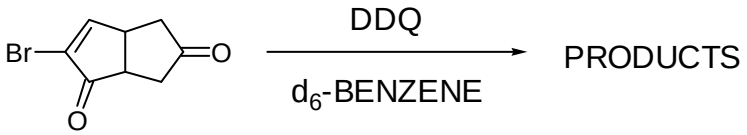
Direct dehydrogenations can be performed by a number of reagents including selenium dioxide [83], dichlorodicyanoquinone (DDQ) [84], periodic acid [85], oxygen in the presence of transition metal catalysts [86].

Sharpless and Lauer first used selenoxide eliminations synthetically in the conversion of epoxides to allyl alcohols. Then several groups have explored the reaction for the dehydrogenation of ketones. However, one pot transformations of ketones to enones using this reagent is prone to side reactions because of the sensitivity of the selenoxide function. In our system this organo selenium reagents didn't work, we couldn't isolate any product.



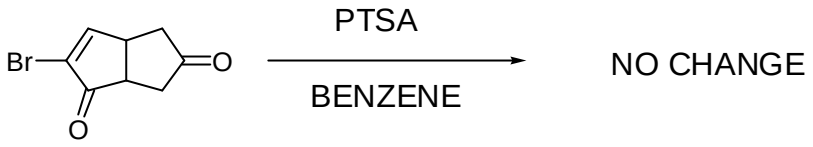
98

We decided to use 2,3-dichloro –5,6-dicyano-1,4-benzoquinone (DDQ). The reactions of DDQ have been reviewed by D. Walker and J. D. Hiebert, [84]. We used this reagent in different conditions and we observed some products however we couldn't achieve characterization. DDQ-oxidation of **98** produced a mixture consisting of unstable and inseperable products.



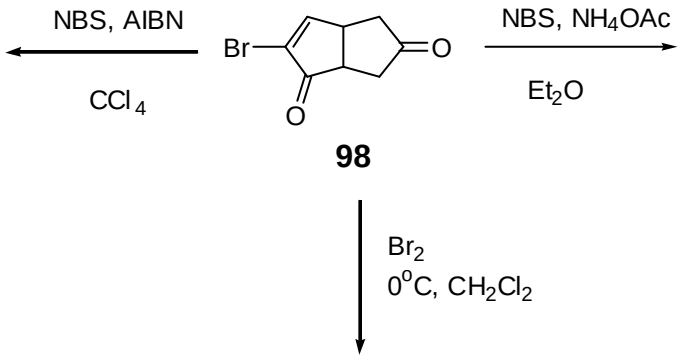
98

We have tried to achieve an inter molecular condensation product with **98**. Even though we heated the bromoketone **98** in p-toluene sulfonic acid in benzene for two days and we didn't observe any isomerization of this compound.



98

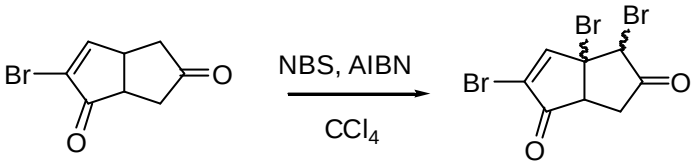
Bromination-dehydrobromination reactions have been well studied in the literature by many groups. We turned back to this classical method and firstly performed the bromination of the bromodiketone **98** by using molecular bromine in the dichloromethane and also bromination performed by NBS (N-bromosuccinimide) with AIBN (α,α^{i} –azobisisobutyronitrile) or NH_4OAc as a catalyst [87].



98

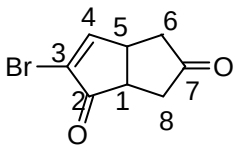
As a result of these rections some products were obtained however characterization of these procducts were not succeded completely. Bromination attempts to bromodiketone by using NBS with NH_4OAc as a catalyst didn't give any product.

Indeed we achieved the characterization of one of the products obtained by bromination of the bromodiketone rection with NBS (assisted with AIBN).



98 **141**

Actually according to this reaction one can expect eight possible products as shown below (without considering streoisomers like configuration of the bromine atoms e.g. *exo* or *endo*).



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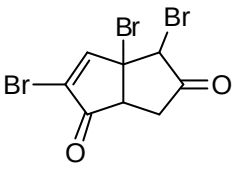
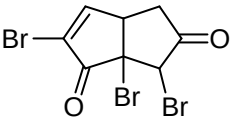
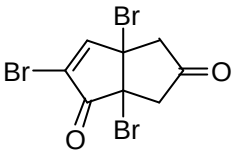


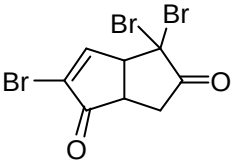
141



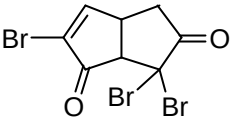
142



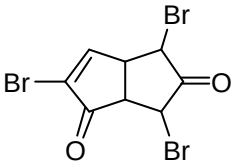
143



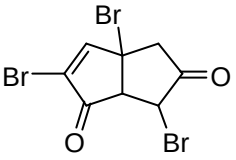
144



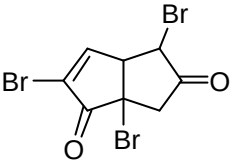
145



146



147



148

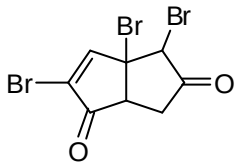
The structure of bromination product of bicyclic bromodiketone **141** has been elucidated on the basis of ^{1}H-NMR and ^{13}C-NMR spectra. The proton NMR spectrum of the compound indicated that the olefinic proton (H_4) resonates at 8.08 ppm as a singlet because it doesn't interact with the allylic position (we can eliminate **142**, **144**, **145**, **146**, **148**). Also a proton resonance at 6.05 ppm as a doublet with a coupling counstant of 1.9 Hz with any adjacant proton, that proton attached a carbon atom bearing a bromine atom.According to finding, it can be eliminated the three possible products; **143**, **144** and **145**.

By careful inspection of the ^{1}H-NMR spectrum one can easily reveal that this product has only one ring junction proton resonating at 3.74 ppm as triplet with a coupling constant of 7 Hz. So we can eliminate some possible products; **143**, **144**, **145**, and **146**. Furthermore, the presence of AB system with a coupling constant of

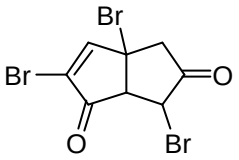
17.6 Hz clearly indicates the presence of methylene group attached directly to a carbonyl group. Now, the isomer **146** can also be excluded.

Also we see an AB system and seen as dublet of dublet coupling constants of 7 Hz and 17.6 Hz. This proves that a methylene adjacant to the carbonyl group, now we can eliminate **146** easily.

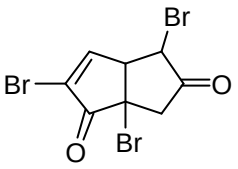
Remaining possible three isomers are **141**, **147** and **148.**



141



147



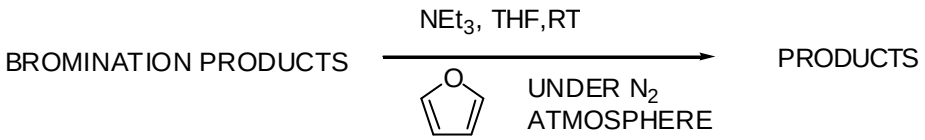
148

If we look at the small coupling constant of AB system and coupling constant of ring junction protons, we will see that the coupling constants are equal. This means that ring junction protons are close to the AB system. So we can eliminate **147** and **148** easily. In conclusion, bromination product of bicyclic bromodiketone is the compound **141**.

After the bromination of this bromodiketone **98** by using either molecular bromine or NBS, elimination reactions [88] were carried on and some products were obtained, whereas characterization of these products have not been achieved so far.

In order to obtain fully unsaturated derivatives of bicyclo[3.3.0]octadienone **(48)**. The isolated three-bromide **141** was isolated from the different bromination

reactions (bromination with NBS and bromination with molecular bromine). Bromination products were submitted to HBr elimination reaction with NEt_3.



The addition of triethylamine caused a spontaenously the formation of black gum which could not be characterized.

CHAPTER 3

CONCLUSION

In the literature, many scientists studied the existence of cyclopentadienone, and some of the scientists have studied of some related species, particularly the ones with fully unsaturated pentalenic structure as pentaloquinones. The presence of the second condensed ring of cyclopentadienone may remarkably affect the stability of such species and their reactivity in Diels-Alder processes. The study of such species has received no attention up to last two decades, although partially saturated structures similar to **98** have shown to be very useful synthons for the synthesis of natural products and other compounds of theoretical interests.

Quinones of pentalene have fascinated synthetic as well as physical and theoretical organic chemists for more then two decades. These compounds have been the subjects of numerous Hückel-type or semiemprical theoretical studies. Unfortunately, the extent of our present understanding regarding the geometries and stabilities of quinones of pentalene (pentaloquinones) is meager.

Synthetic route, starting from cycloheptatriene **83**, led to the formation of bicyclo [3.2.0] hept-6-en-3-one **(92)** via the photoloysis of cyclohepta-3,5-dienone **(91)**. Then the protection of the carbonyl group was applied in order to add dibromocarbene to the double bond of **93**. Carbene addition product **94** was converted directly alcohol **98** by using silver perchlorate, whereas in this reaction

also rearrangements have occurred and these byproducts have lowered the yields of this reaction. The dibromo compounds possessing an allylic bromine can be easily hydrolyzed to hydroxyl bromine derivatives in silica gel column [76]. Therefore, alcohol **98** was synthesized by using silica gel however in this case reaction time was so long that it was not a suitable method for our synthetic strategy. Acethoxylation reaction was applied to dibromocarbene addition product **94.** Hydrolysis of **96** gave alcohol **95** in quantitative yield. Meanwhile an elimination product **97** was obtained during the acethoxylation reaction. Also this compound is interesting in terms of the structure of this compound. Oxidation of alcohol **95** with PCC produced the dibromodiketone **98**.

This bromodiketone **98** is an interesting synthetic intermediate in which all eight-carbon atoms are properly activated and ready to undergo a series of chemo-, regio-, and stereoselective reactions, very useful for the synthesis of either natural or nonnatural polyfused cyclopentanoid systems.

After synthesizing this bromodiketone **98**, we attempted to convert this compound into fully unsaturated systems, which formally can be considered as constituted of two condensed structures of cyclopentadienone. Unfortunately, all reactions were failed.

Consequently, the target molecule **48** could not synthesized. However, obtained dibromodiketone can be used as a key compound for the synthesis of versatile compounds.

CHAPTER 4

EXPERIMENTAL

4.1 General Consideration

Nuclear Magnetic Resonance (^{1}H, ^{13}C and 2-D) spectra were recorded on a Bruker Instruments Avance Series-Spectoskopin DPX-400, Ultra Shield (400 MHz), High Performance digital FT-NMR spectrometer. Chemical shifts are reported in parts per million (δ) downfield from an internal tetramethylsilane (TMS) reference and deuterochloroform, $CDCl_3$ as the solvent. Coupling constants (J values) are repoted in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (duplet), t (triplet), q (quartet), and m (multiplet). Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer by using chloroform, $CHCl_3$ as a solvent. Band positions are reported in reciprocal centimeters (cm^{-1}).

Column chromotographic separations were performed by using Fluka Slicagel 60 (particle size 0.063-0.170 mm). The relative proportions of solvents refer to volume: volume ratio. Routine thin layer chromotography (TLC) was performed by using precoated 0.25 mm silicagel plates purchased from Fluka. All the solvent purifications were done as stated in the literature [89].

4.2 The synthesis of tropone 90

Sensitized Photooxidation of Cycloheptatriene. A 250 mL of CCl_4 solution of 130.4 mmol cycloheptatriene (12 g.) and 240 mg tetraphenylporphyrin (TPP) sensitizer at room temperature was irradiated with a General Electric 150-W sodium street lamp while passing continuously a slow stream of dry oxygen gas. The progress of photooxygenation was monitored by ^{1}H-NMR until essentially complete consumption of the starting material. Usually within 16 hours, singlet oxygenation was completed. At the end of this reaction, endeperoxides were obtained quntitatively.

After obtaining the endoperoxide mixture, 200 mL of cold methanol solution were stirred at 0℃ and then to this solution 6 ml of triethylamine was dropwise added in 10 minutes. After the addition was completed, the reaction was stirred for one day at 0°C. The solvent was removed under reduced pressure. The product was purified by vacuum distillation (Kp_{15}: 113°C) and the liquid product was obtained (6.5 g., 130.4 mmol) in 46% yield.

^{1}H-NMR d **ppm:** 6.89 (m, 2H), 6.79 (m, 4H)
^{13}C-NMR d **ppm:** 134.8, 136.0, 142.6, 187.9
IR : 1706, 1636, 1576, 1250, 894, 771, 574.

4.3 The synthesis of the cyclohepta-3,5-dienone (91) [62]

To a suspension of 1.41 g. (0.037 mol) of $LiAlH_4$ in 100 mL dry ether was added dropwise 5 g. (0.047 mol) of tropone **90** in 50 mL of ether with vigorous stirring. The mixture was stirred rapidly at rt for 2 hours. Then the mixture was taken into a dropping funnel and dropwise added to 50 mL of glacial acetic acid with rapid stirring. The organic layer was washed with 10 % $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated. Vacuum distillation gave 2.7 g. (0.025 mol, 68% yield) of cycloheptadienone **91** at 70 °C at 25 mmHg.

^{1}H-NMR d **ppm:** 6.43 (d, J=10.3 Hz, 2H), 6.00 (m, 2H), 3.20 (d, J= 5.9Hz, 4H)
^{13}C-NMR d **ppm:** 209.9, 129.8, 124.9, 45.4.
IR : 3666, 3408, 3017, 2926, 1708, 1655, 1595, 1410, 1226, 1042, 777, 686.

4.4 The synthesis of bicyclo[3.2.0]hept-6-en-3-one (92) [66]

A magnetically stirring solution of 1.7 g (0.0157 mol) of cyclohepta-3,5-dienone **(91)** in 350 mL of acetone was irradiated at 254 nm for 8 hours with a mercury arc lamp at room temperature under the stream of nitrogen. The solvent was removed by simple distillation to give 1.5 g (0.014 mol, 88% yield) of crude product **92** which was used in the next step after the purification. Purification of the product **92** was performed by using vacuum distillation and yellow liquid product was obtained purely (Kp_{13} 45°C).

^{1}H-NMR d **ppm:** 6.0 (s, 2H), 3.4 (d, J= 8.4 Hz, 2H), 2.3 (dd, A part of the AB system, J= 8.4-18 Hz, 2H), 2.1 (d, B part of the AB system, J=18 Hz, 2H).
^{13}C-NMR d **ppm:** 216.3, 140.4, 43.0, 41.3
IR: 3452, 3017, 2953, 1734, 1401, 1237, 1090, 882, 781, 741.

4.5 The synthesis of the spiro[bicyclo[3.2.0]hept-6-ene-3,2'-[1,3]dioxolane] (93)

Bicyclo[3.2.0]hept-6-en-3-one (5 g, 0.046 mol), ethane-1,2-diol (5.7 g, 0.09 mol), catalytic amount of *p*-toluene sulphonic acid and anhydrous benzene (50 mL) were placed in a round-bottomed flask fitted with a Dean- Stark water separator and a reflux condenser. The reaction mixture was heated until no more, water collected. The reaction was also monitored by TLC. The mixture was cooled, the ethylene glycol layer was separated, and the benzene layer was washed succesively with saturated sodium bicarbonate solution and sodium chloride solution and dried over calcium chloride. Removal of solvent gave the product **93** with 5.6 g. (0.037 mol) a yield of 80 %.

^{1}H-NMR d **ppm:** 6.0 (s, 2H), 3.7-3.9 (AA'BB' system, 4H), 3.2 (t, J=3.2 Hz, 2H), 1.8 (bs, 4H).
^{13}C-NMR d **ppm:** 38.8, 46.1, 63.6, 65.1, 119.5, 139.9.
IR: 3035, 2933, 1741, 1425, 1334, 1273, 1177, 1123, 1075, 1051, 1013, 762,555.

4.6 The synthes of the 4',5'-dibromo-3', 3a', 4', 6a'-tetrahydro-1'H-spiro[1,3-dioxolane-2,2'-pentalene] (94)

A solution of 9.17 g (36 mmol) $CHBr_3$ in hexane (20 mL) was dropwise added to a mixture of 5 g (33mmol) ketal **93** and 4.41 g (39 mmol) potassium tert-butoxide in hexane (80 mL), with stirring below 0°C over a period of 6 hours. The organic layer was washed with water and dried over calcium chloride. The residue was characterized as dibromo compounds **94** (due to the configuration of the allylic bromine two isomers were produced). When silica gel (50 g) column chromotography was performed to purify the compound **94** with hexane as eluent; dibromo compound (solid) and a new product, which was identified as the alcohol

95 were isolated. The NMR data of the major isomer **94a** and minor isomer **94b** were extracted from the mixture NMR spectrum of **94a** and **94b**.

Major isomer NMR data (94a)

^{1}H-NMR d **ppm:** 5.93 (d, J= 2.1 Hz, 1H), 4.62 (bs, 1H), 3.79 (bs, 4H), 3.28-3.36 (m, 1H), 3.18 (q, J= 8.4 Hz, 1H), 1.94-2.06 (m, 2H), 1.55-1.64 (m, 2H).

Minor isomer NMR data (94b)

^{1}H-NMR d **ppm:** 5.77 (d, J= 2.1 Hz, 1H), 4.49 (bs, 1H), 3.79 (bs, 4H), 3.28-3.36 (m, 1H), 3.00 (q, J= 7.5 Hz, 1H), 1.94-2.06 (m, 2H), 1.55-1.64 (m, 2H).

^{13}C-NMR d **ppm:** 140.5, 122.7, 117.4, 65.2, 64.5, 64.0, 50.9, 46.3, 41.3, 39.1.
IR: 2885, 1742, 1602, 1430, 1334, 11092, 1089, 1016, 947, 795, 723, 436.

4.7 The synthesis of 2-bromo-5-oxo-1, 3a, 4, 5, 6, 6a-hexahydro-pentalen-1-yl acetate (96)

5 g (0.0154 mol) of carbene addition product **94** and 2.3 g. (0.0169 mol) of sodium acetate were dissolved in 15 mL of glacial acetic acid. The mixture was refluxed for 14 hours. When the reaction was completed, the reaction mixture was poured into a saturated sodium bicarbonate solution in order to neutralize the acetic acid. After the neutralization process, the reaction mixture was extracted with diethylether or dichloromethane (3×30 mL) and then organic layer was dried over anhydrous magnesium sulphate. Solvent is evaporated and crude product was obtained. Then silica gel (50 g) column chromotography was performed to purify

the compound **98** with hexane: ethyl acetate (5%) as eluent mixture. The acethoxylated compound was purely obtained in 3.12g (0.012 mol) a yield of 78%.

^{1}H-NMR d **ppm:** 6.10 (d, J= 1.9 Hz, 1H), 5.33 (bs, 1H), 3.60 (m, 1H), 3.33-3.39 (m, 1H), 2.82 (m, A part of AB system, 1H), 2.61 (dd, B part of AB system, J= 10.8-19.3 Hz, 1H), 2.42 (dd, A part of AB system, J= 10.1-19.0 Hz, 1H), 2.18 (m, B part of AB system), 2.06 (s, 3H).
^{13}C-NMR d **ppm:** 216.6, 170.9, 141.4, 122.1, 87.3, 44.9, 42.9, 42.0, 38.2, 21.3.

4.8 The synthesis of 3-bromo 3, 3a, -dihydro-1H-pentalen-2-one (97)

Following the procedure outlined in the synthsis of the 2-bromo-5-oxo-1, 3a, 4, 5, 6, 6a-hexahydro-pentalen-1-yl acetate **(96)**. After the column chromotography (silica gel, 65 g) with hexane: ethy lacetate (3%) as eluent mixture to give compound **97** in a yield of 21 %. Actually yield of this prodoct **97** depends on the reaction temperature because this is an elimination reaction. If the reaction temperature is kept lower enough, the elimination product is not observed.

^{1}H-NMR d **ppm:** 6.83 (bs, 1H), 5.79 (d, J= 1.8 Hz, 1H), 3.55 (t, J= 5.6 Hz, 1H), 3.00 (dd, A part of AB system, J= 7.3-16.8 Hz, 1H), 2.68 (m, B part of first AB system and A part of the second AB system, 2H), 2.34 (dd, B part of the second AB system, J= 5.1-17.1 Hz, 1H).
^{13}C-NMR d **ppm:** 208.5, 184.2, 142.2, 129.8, 118.0, 47.7, 45.1, 41.9.
IR: 3460, 1694, 1604, 1544, 1271, 1147, 913, 823, 743.

4.9 The synthesis of 5-bromo-4-hydroxy-3, 3a, 4, 6a-tetrahydro-1H-pentalen-2-one (95)

4.9.1 The synthesis of the alcohol 95 by using SiO_2

200 mg (0.617 mmol) of the compound **94** was added to 20 mL of silica gel and dichloromethane mixture and then the reaction mixture was stirred for one five days at room temperature. The reaction was monitored by TLC. At the end of this time partial conversion to alcohol **95** was obseved.

4.9.2 The synthesis of the alcohol 95 by using $AgClO_4$

1.41 g (6.79 mmol) $AgClO_4$ was dissolved in 40 ml of acetone and 30 mL of water at room temperature. A solution of 2 g (6.17 mmol) of the compound **94** in 30 mL of acetone was added slowly to a magnetically stirring $AgClO_4$ solution. The mixture was stirred for 2 hours at room temperature. Precipitated AgBr was filtered and removed. The solution was extracted three times with 150 mL of diethylether and combined organic phase were washed three times with 30 mL of water. Then organic phase was dryed over magnesium sulphate. After removal of solvent with a rotary evaporator, the alcohol **95** was obtained in a yield of 68 %. However, the reaction was prone to the rearrangements and byproducts lowered the yield.

4.9.3 The synthsis of the alcohol 95 from hydrolysis of the acethoxylated compound 96

1.07 g (7.72 mmol) unhydrous potassium carbonate and 2 g (7.72 mmol) of acethoxylated compound **96** were dissolved in 30 ml of methanol at room temperature. The mixture was stirred for 1 hour at room temperature. The reaction was monitored by TLC. The reaction mixture was extracted three times with 30 mL

of ethyl acetate and then organic layer was dryed over unhydrous magnesium sulphate, the solvent was removed by rotary evaporator. The mixture of alcohols **95** was obtained in (6.176 mmol, 1.34 g) a yield of 80%.

^{1}H-NMR d **ppm:** 6.07 (d, J= 1.7 Hz, 1H), 6.05 (d, J= 2.1 Hz, 1H), 4.77 (d, J= 7.3 Hz, 1H), 4.47 (bs, 1H), 3.6 (m, 1H), 3.3 (m, 1H), 3.2 (m, 1H), 3.0 (m, 1H), 2.1-2.7 (m, 4 AB systems overlapped).
^{13}C-NMR d **ppm:** 218.1, 135.9, 126.4, 85.9, 45.9, 44.0, 43.1, 37.3.
IR:3399, 2921, 2847, 1732, 1613, 1398, 1314, 1165, 1058, 822.

4.10 The synthesis of 2-bromo-3a, 4, 6, 6a-tetrahydro-pentalene-1,5-dione (98)

To a magnetically stirring solution of 2.7 g (0.0126 mol) PCC in 30 mL dichloromethane at 0 °C, 2.50 g (0.0115 mol) of alcohol **95** in 20 mL of dichloromethane was dropwise added in 15 minutes. The reaction was monitored with TLC. After stirring for additional 5 hours, the reaction mixture was filtered in order to remove inorganic precipitates and then filtrated liquid part was extracted with dichloromethane and dried over sodium sulphate. After the removal of solvent with a rotary evaporator, the residue was filtered on a short silica gel (20 g) column eluted with dichloromethane to give (7.6 mmol, 1.63 g) 60% yield.

^{1}H-NMR d **ppm:** 7.8 (d, J= 3.0 Hz, 1H), 3.7 (m, 1H), 3.3 (q, J= 5.9 Hz, 1H), 2.8 (m, A parts of the two AB systems overlapped, 2H), 2.5 (dd, B part of the AB system, J= 4.2-19.7 Hz, 1H), 2.3 (dd, B part of the AB system, J= 4.6-18.9 Hz, 1H).
^{13}C-NMR d **ppm:** 212.7, 201.1, 162.8, 127.1, 44.1, 41.1, 40.2.
IR: 1738, 1274, 1259, 909, 762, 747.

4.11 The synthesis of the 2, 3a, 4,-tribromo-3a, 4, 6, 6a-tetrahydro-pentalene-1,5-dione (141)

0.5 g (2.33 mmol) of bromodiketone **95** was dissolved in 75 mL of carbontetrachloride. Magnetically stirred solution was heated and then 0.83 g (4.66 mmol) of NBS was added to the solution. When the reflux started catalytic amount of AIBN was added to the reaction mixture. Rection was monitored by TLC. Within the 16 hours the reaction was completed. When it was cooled to the room temperature the reaction mixture was filtered. Filtrated liquid part was extrcated with carbontetrachloride and organic layer was dried over magnesium sulphate, the solvent was removed by using rotary evaporator and then a short silica gel (25 g) column chromotography was performed to purify the compound **141**.

^{1}H-NMR d **ppm:** 8.08 (s, 1H), 6.05 (d, J= 1.9, 1H), 3.74 (t, J= 7, 1H), 2.7 (dd, J= 7.7-17.6, 1H), 2.5 (dd, J= 6.5-17.6, 1H).

^{13}C-NMR d **ppm:** 206.9, 204.0, 170.0, 146.9, 135.3, 123.0, 50.4.

IR: 2918, 1710, 1610, 913, 743.

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APPENDIX A

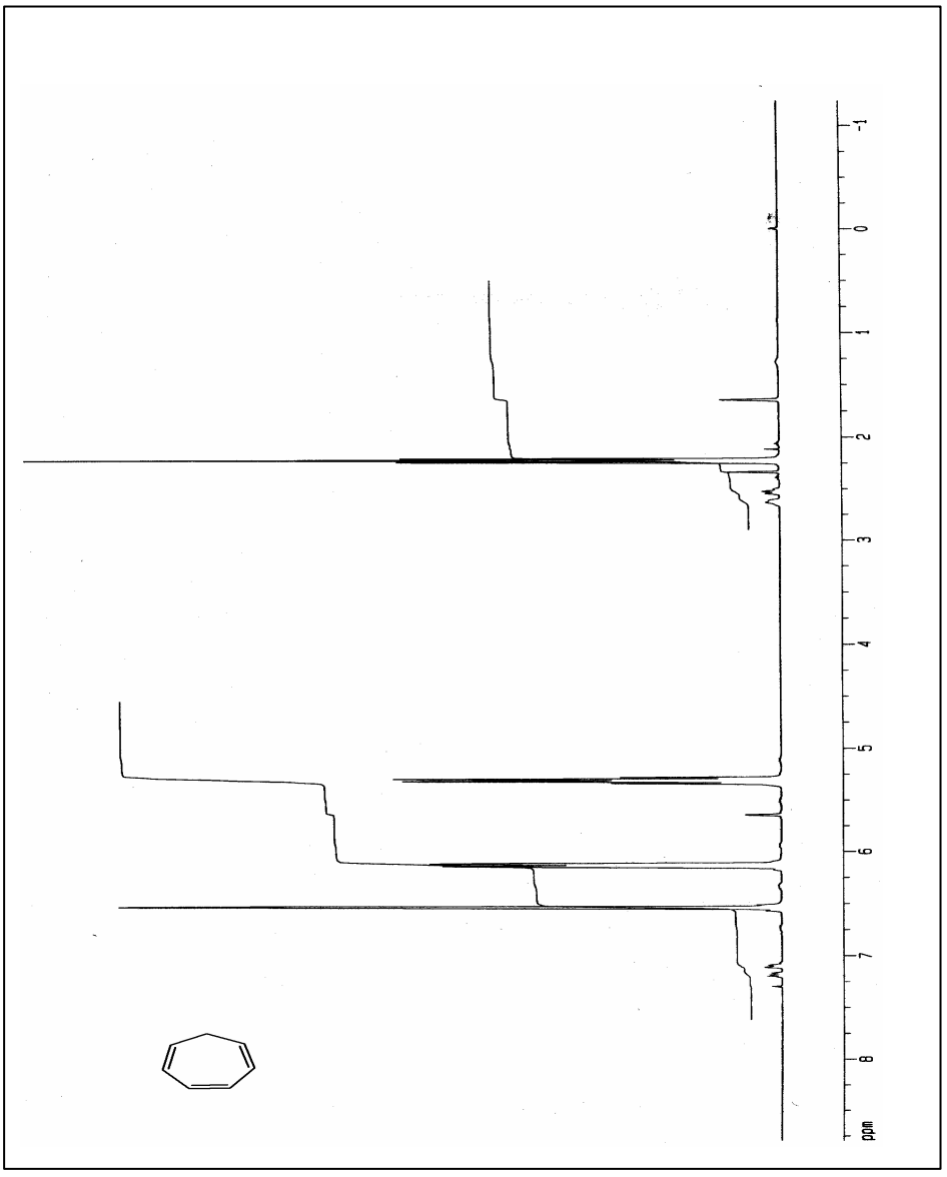


Figure 11: ^{1}H-NMR Spectrum of compound **83**

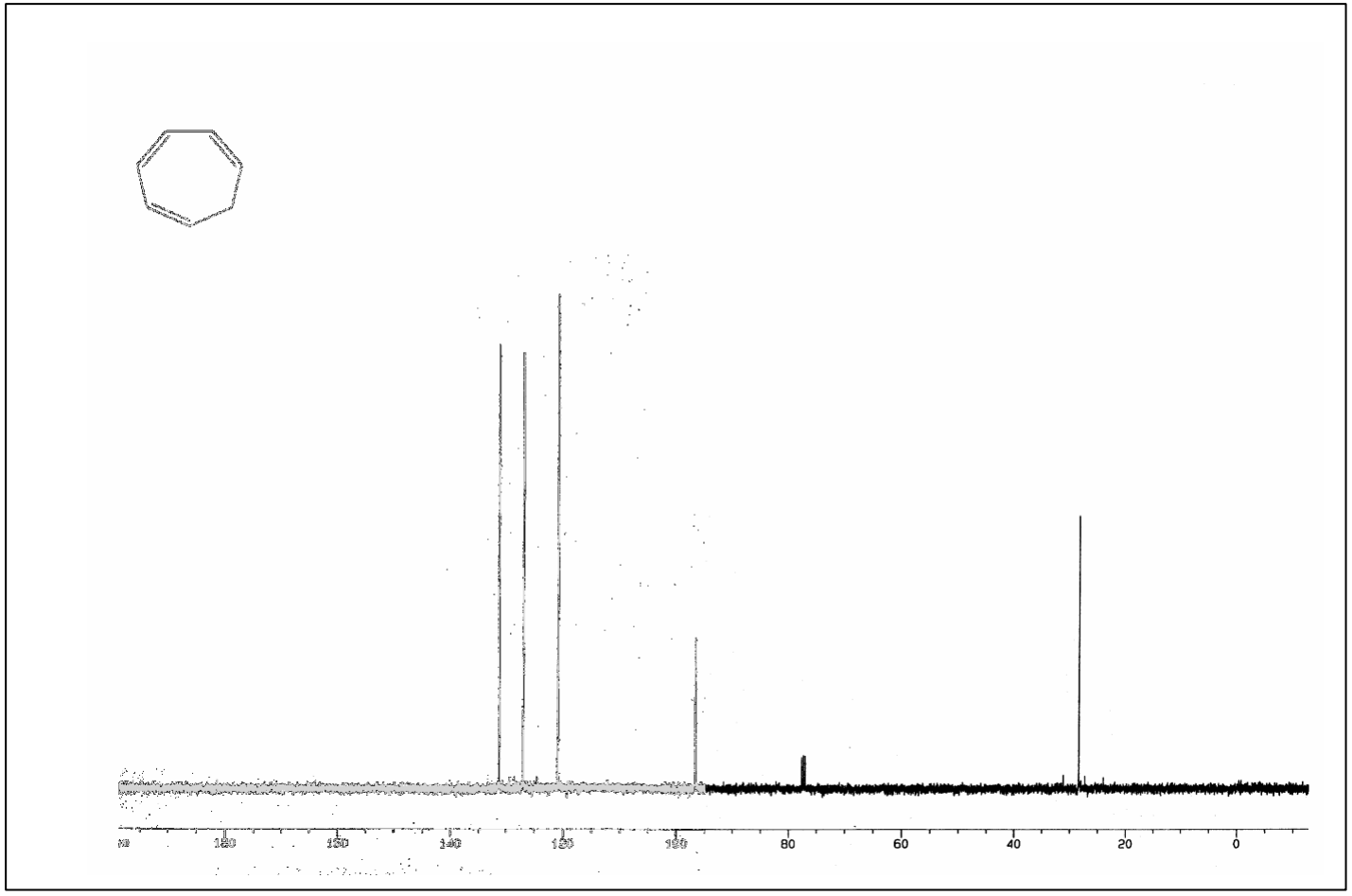


Figure 12: ^{13}C-NMR Spectrum of compound **83**

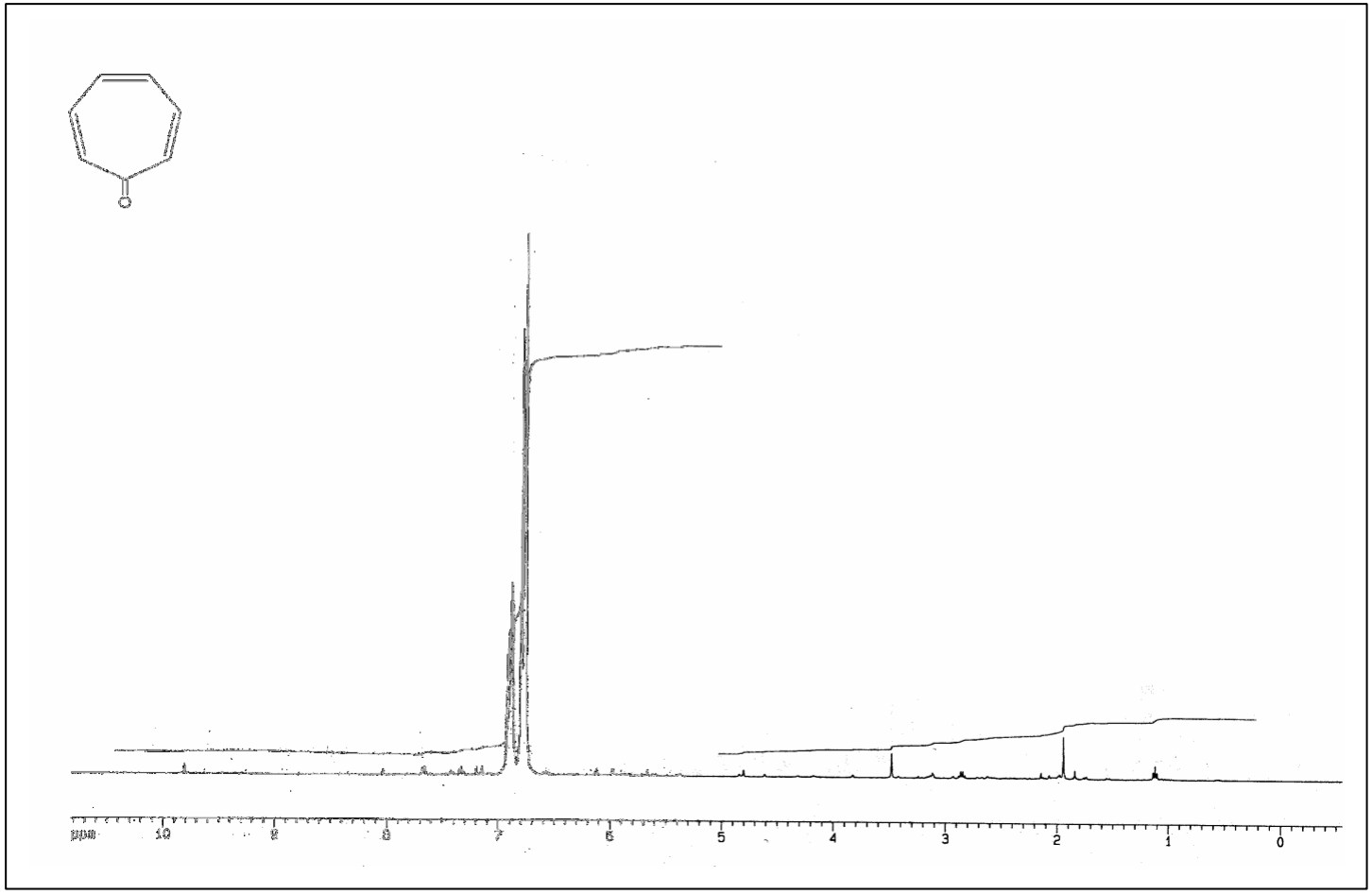


Figure 13: : ^{1}H-NMR -Spectrum of compound **90**

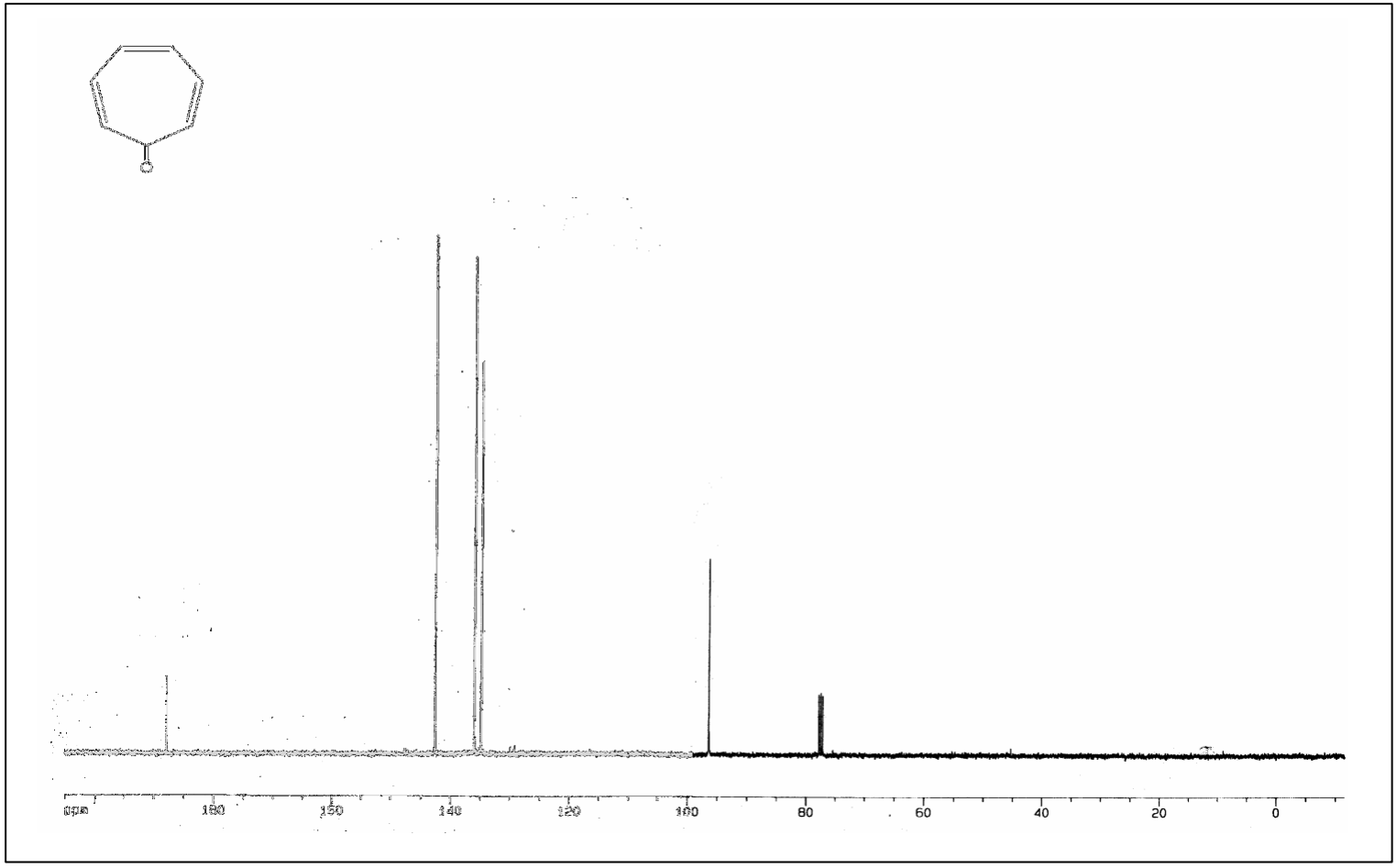


Figure 14: ^{13}C-NMR Spectrum of compound **90**

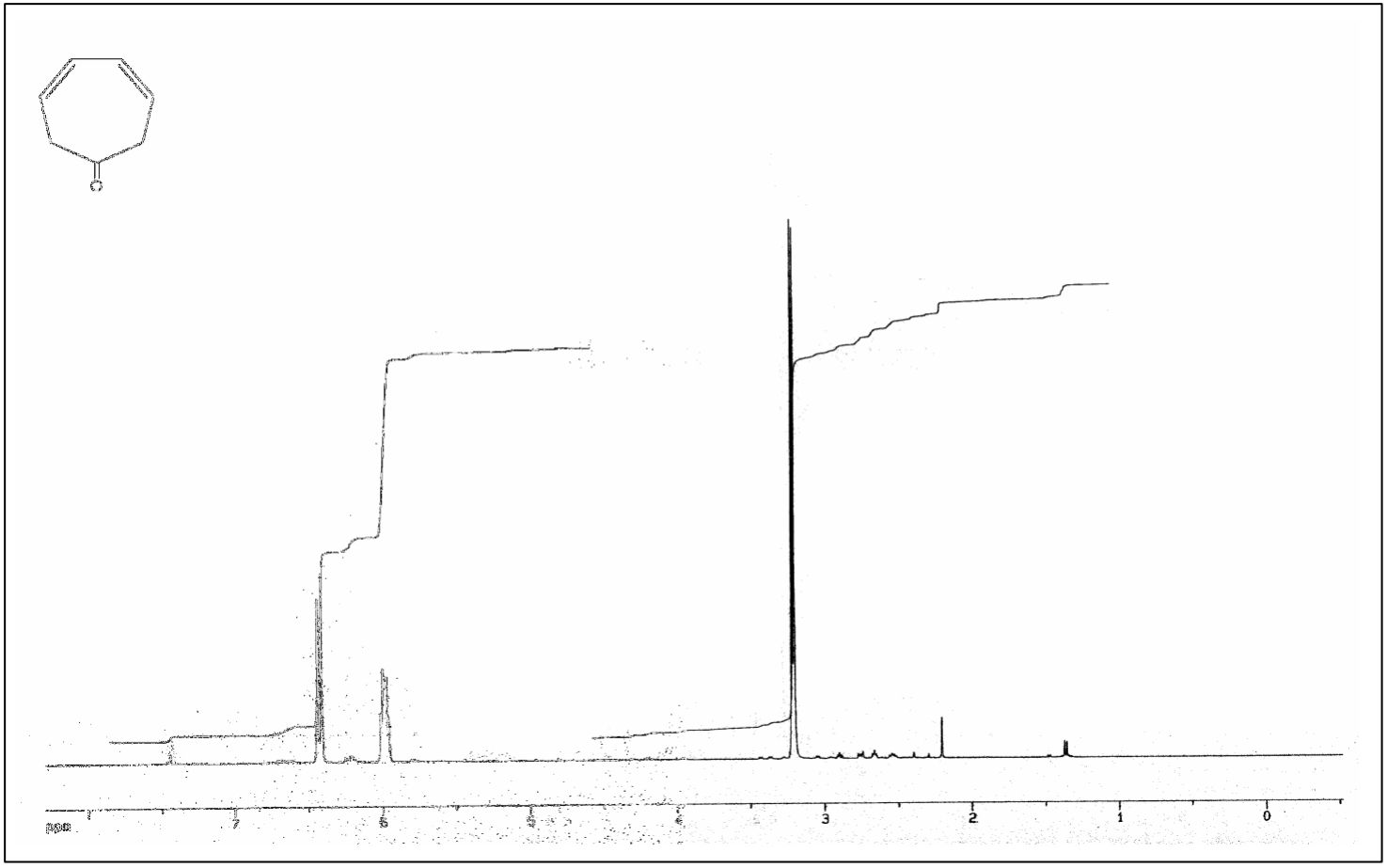


Figure 15: ^{1}H-NMR -Spectrum of compound **91**

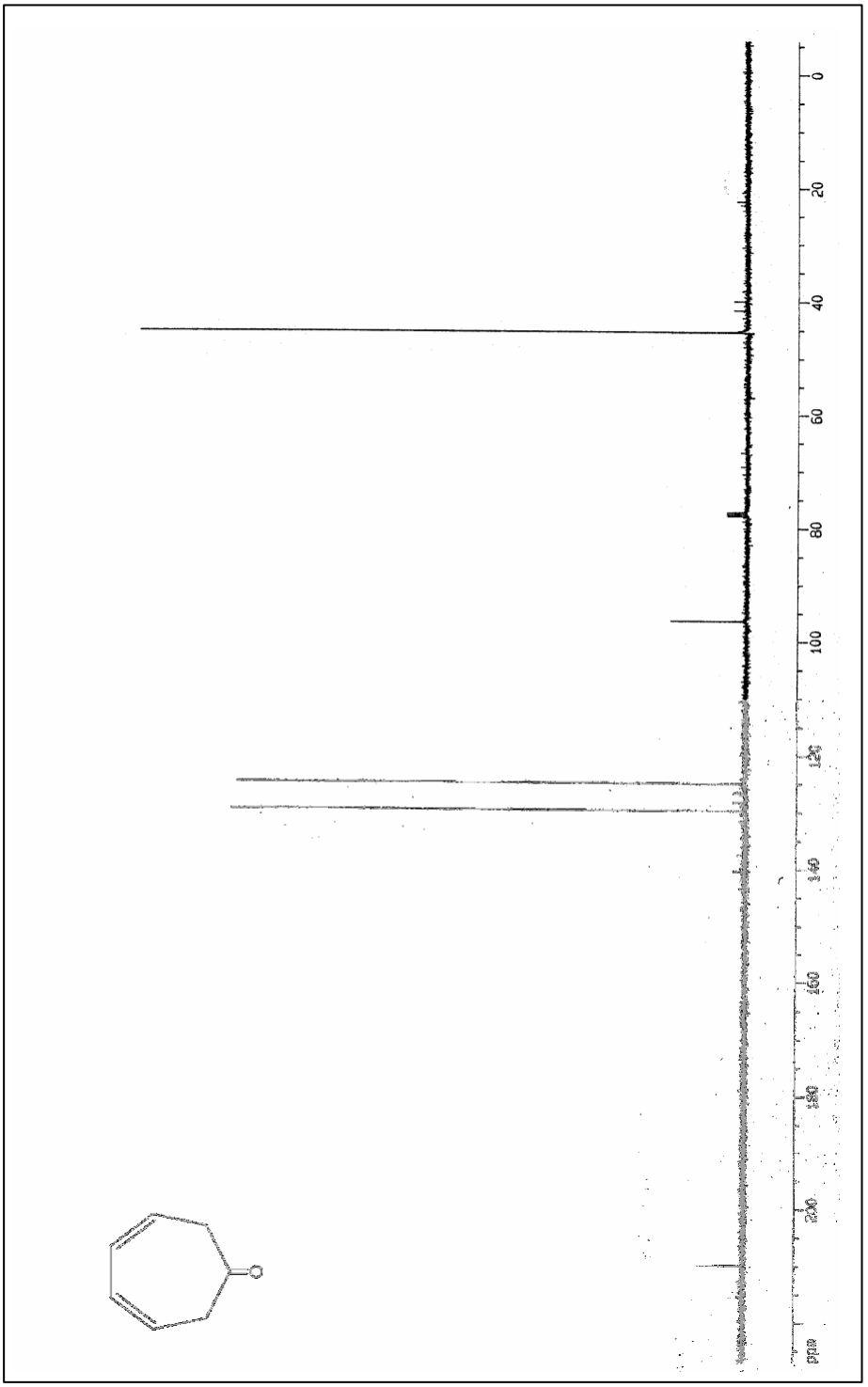


Figure 16: ^{13}C-NMR Spectrum of compound **91**

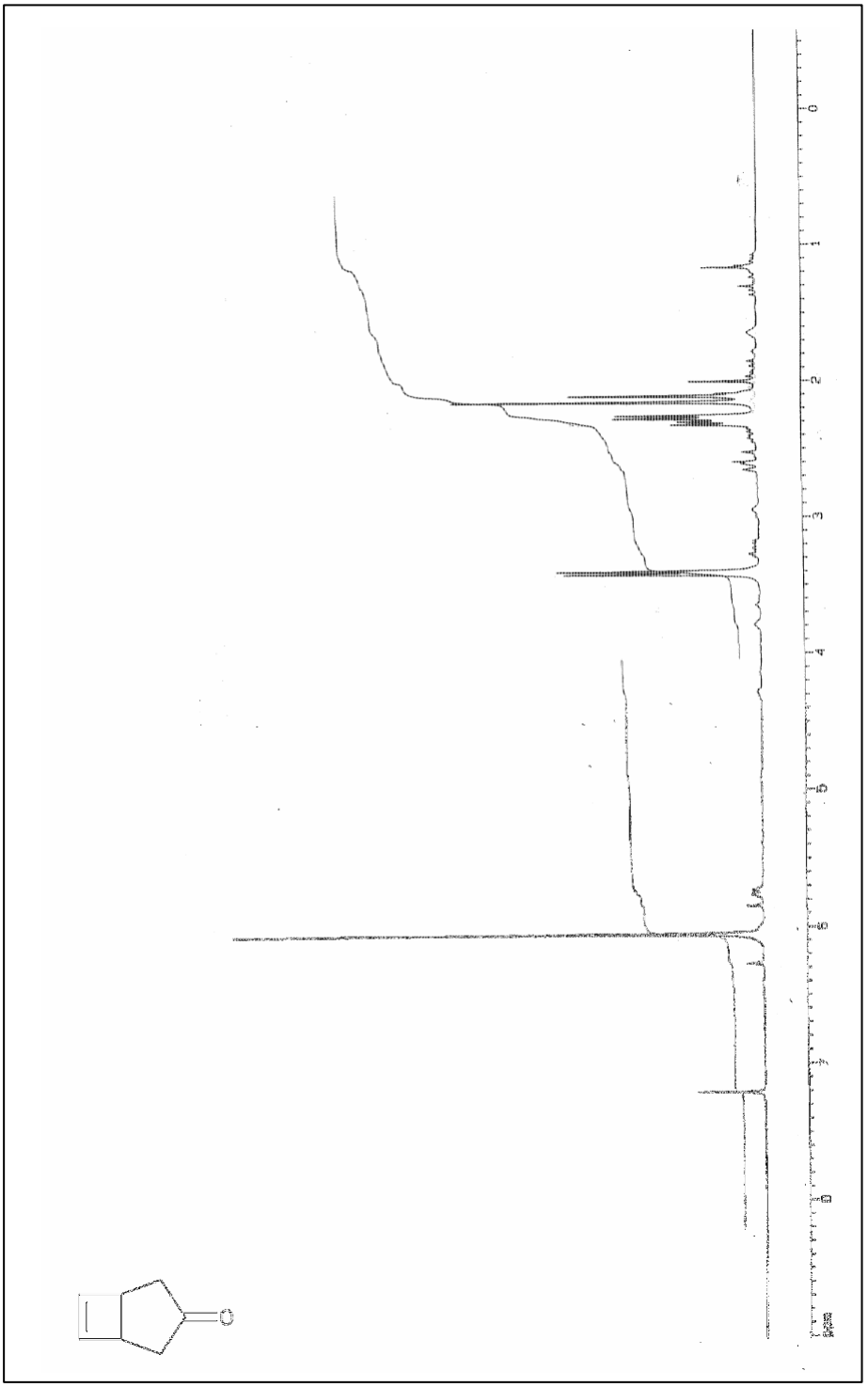


Figure 17: ^{1}H-NMR -Spectrum of compound **92**

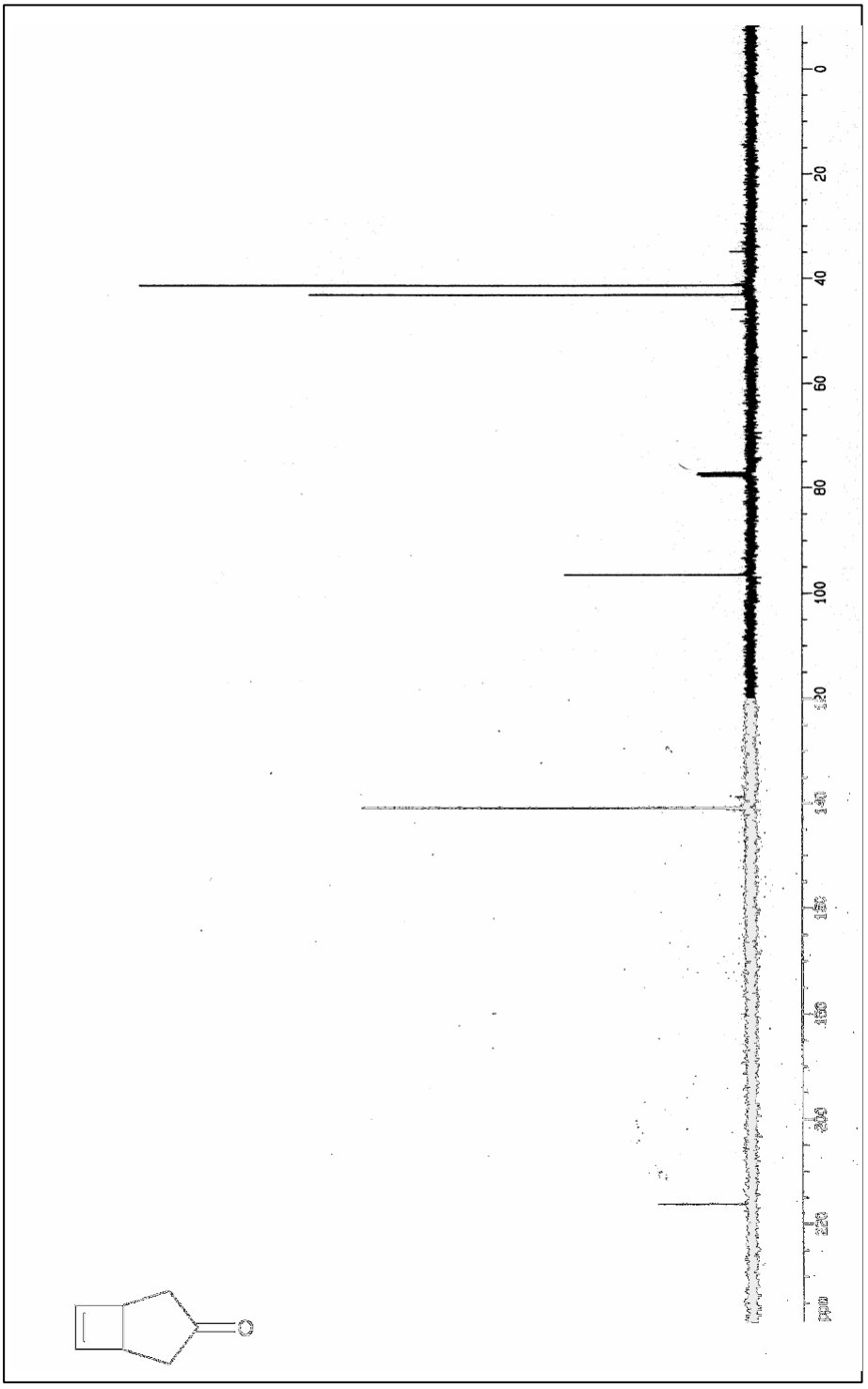


Figure 18: ^{13}C-NMR Spectrum of compound **92**

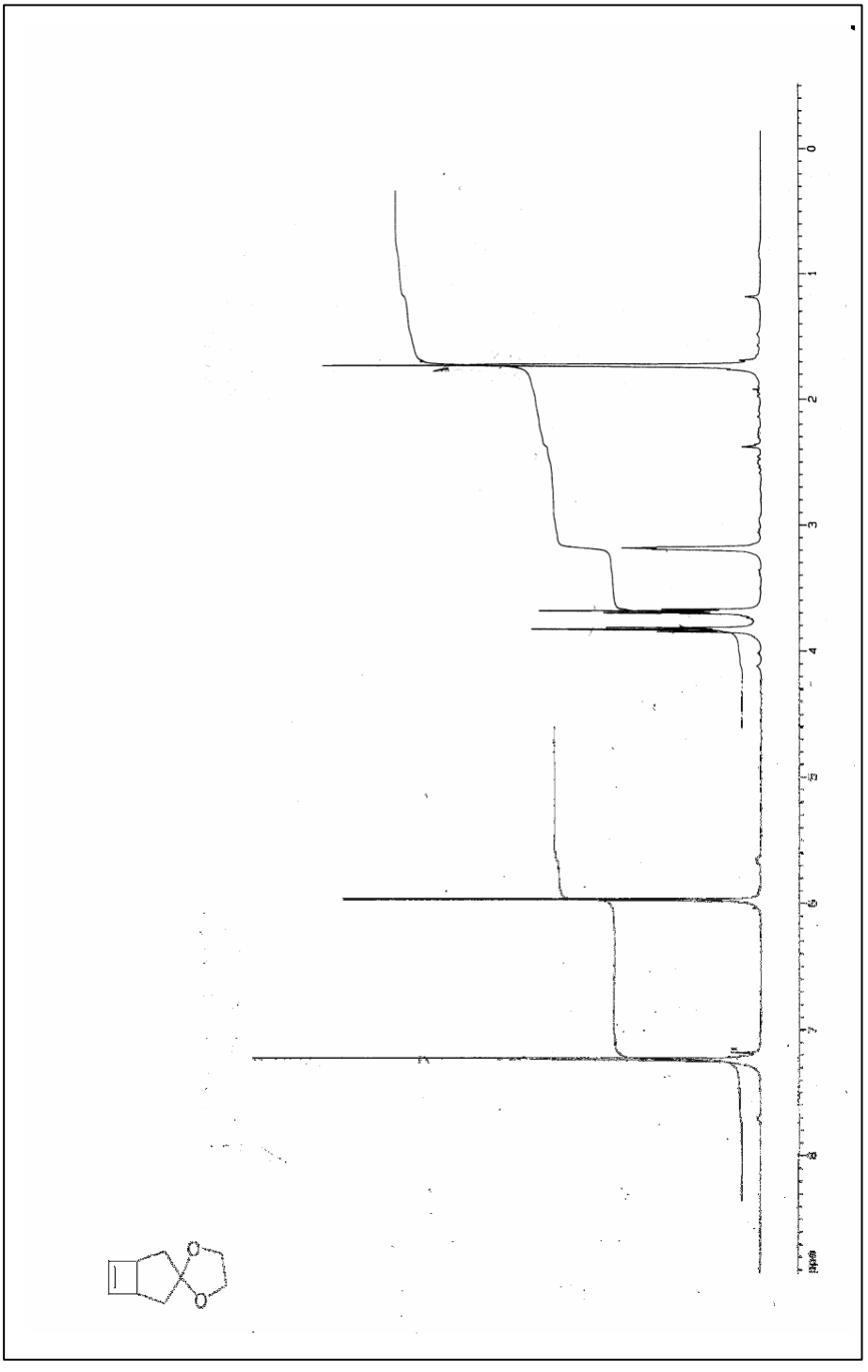


Figure 19: ^{1}H-NMR -Spectrum of compound **93**

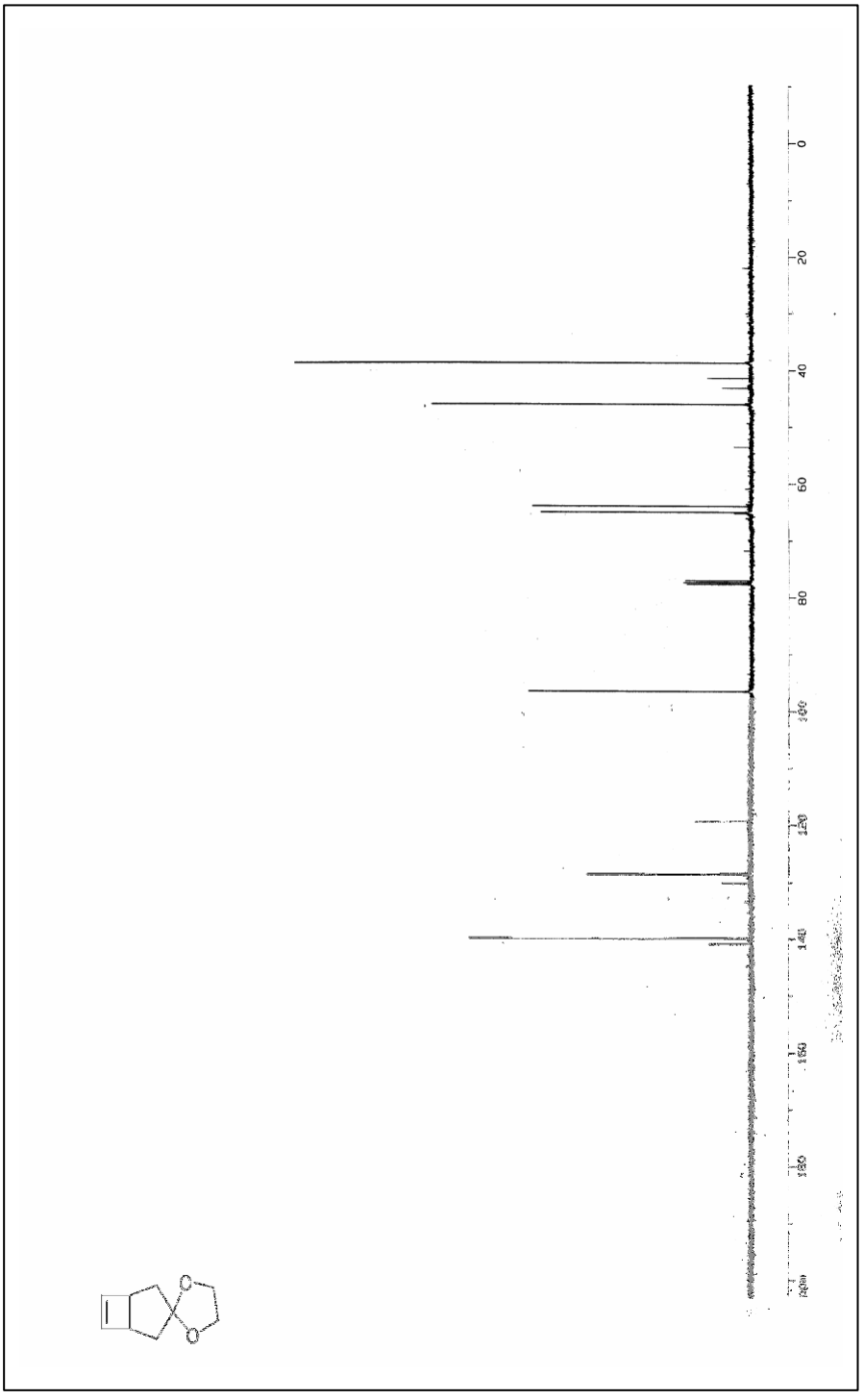


Figure 20: ^{13}C-NMR Spectrum of compound **93**

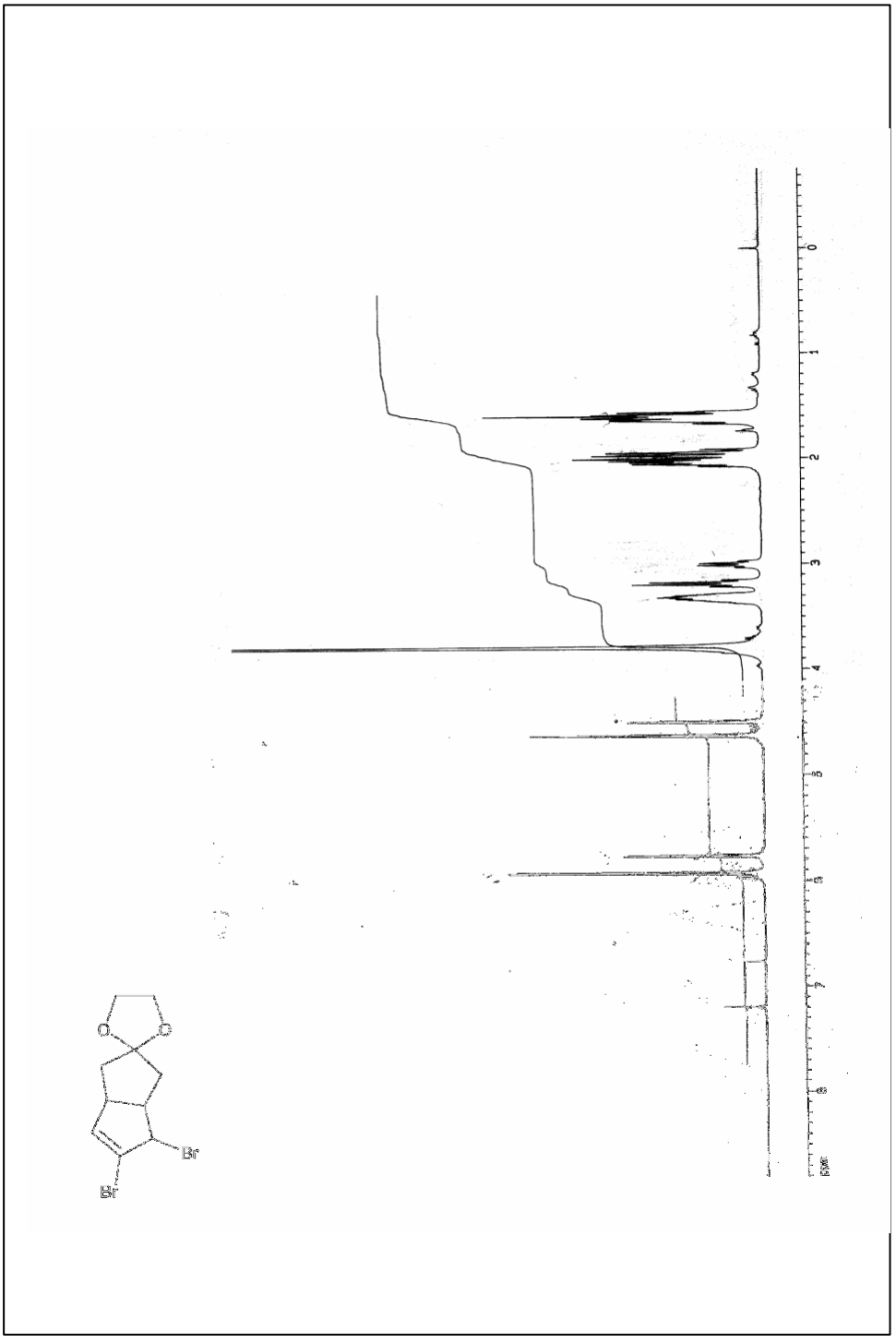


Figure 21: ^{1}H-NMR -Spectrum of compound **94**

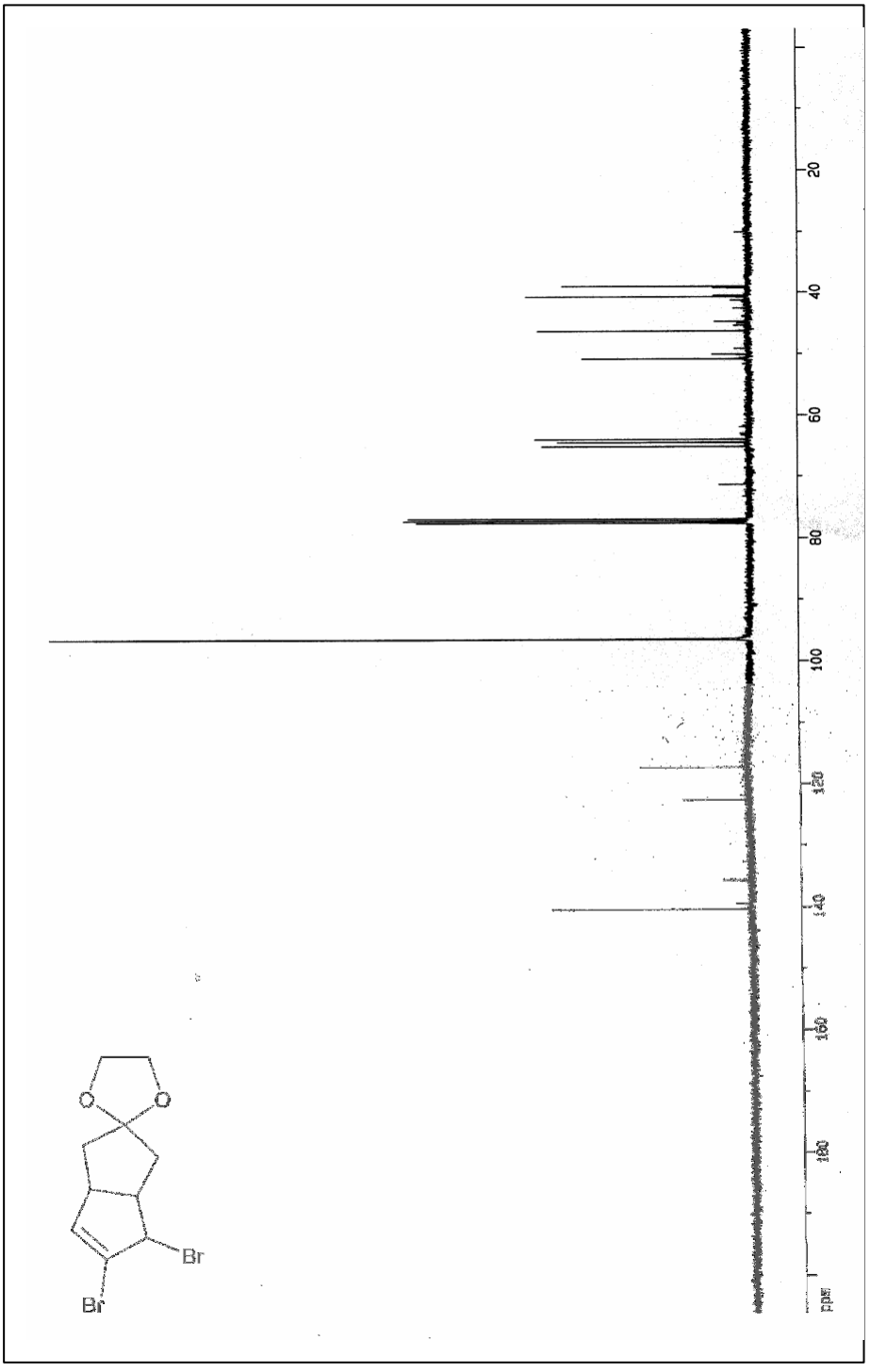


Figure 22: ^{13}C-NMR Spectrum of compound **94**

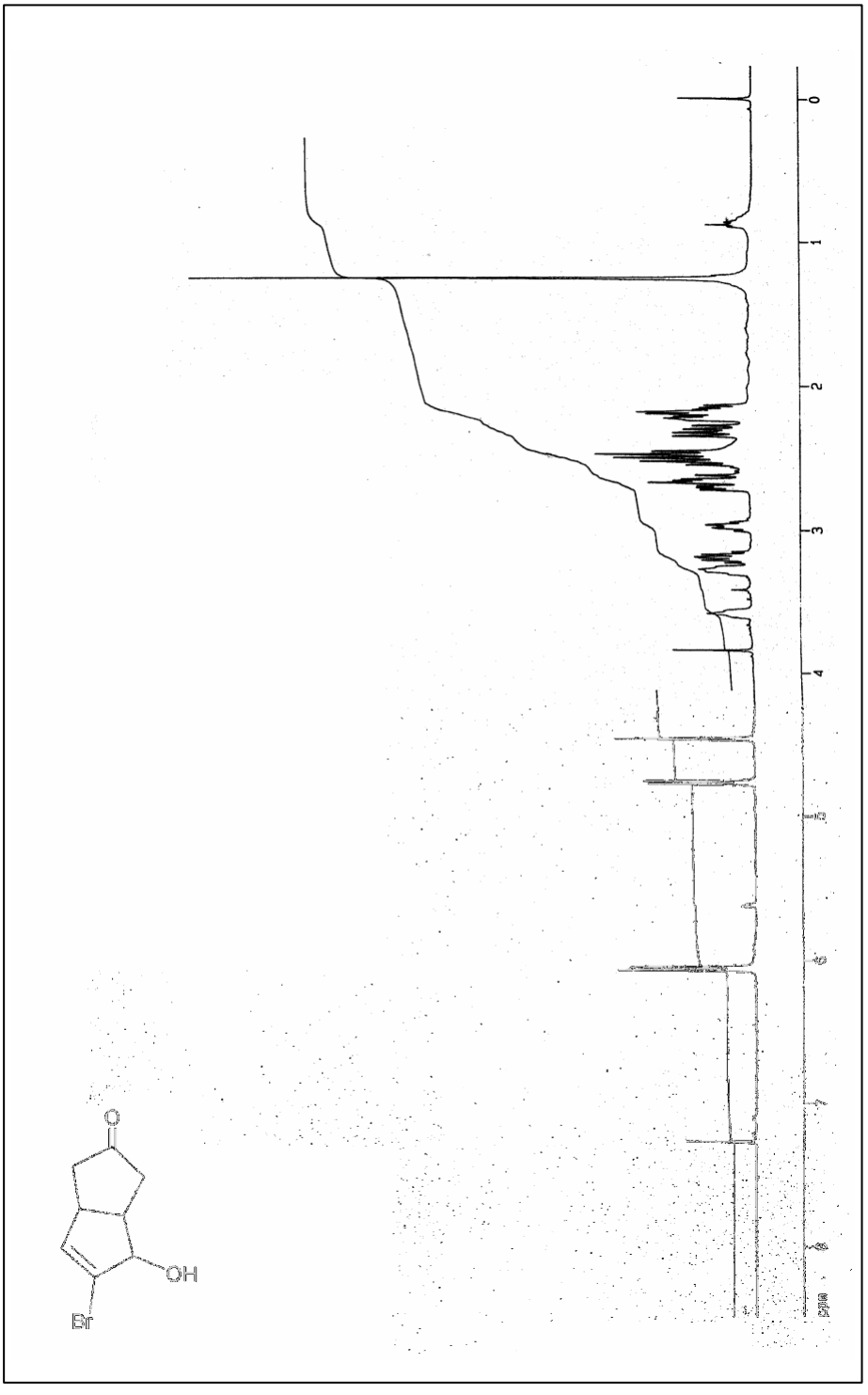


Figure 23: ^{1}H-NMR -Spectrum of compound **95**

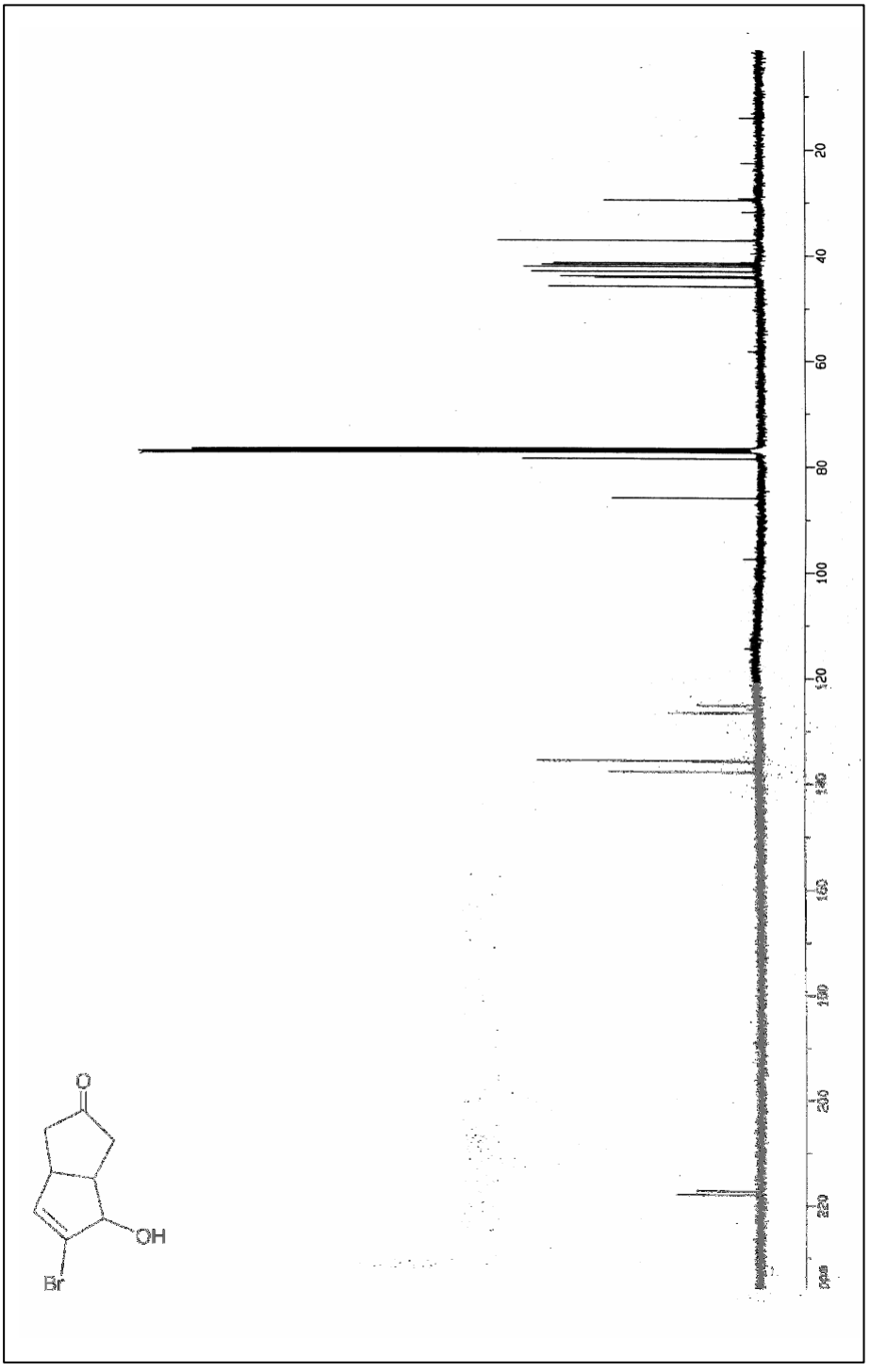


Figure 24: ^{13}C-NMR Spectrum of compound **95**

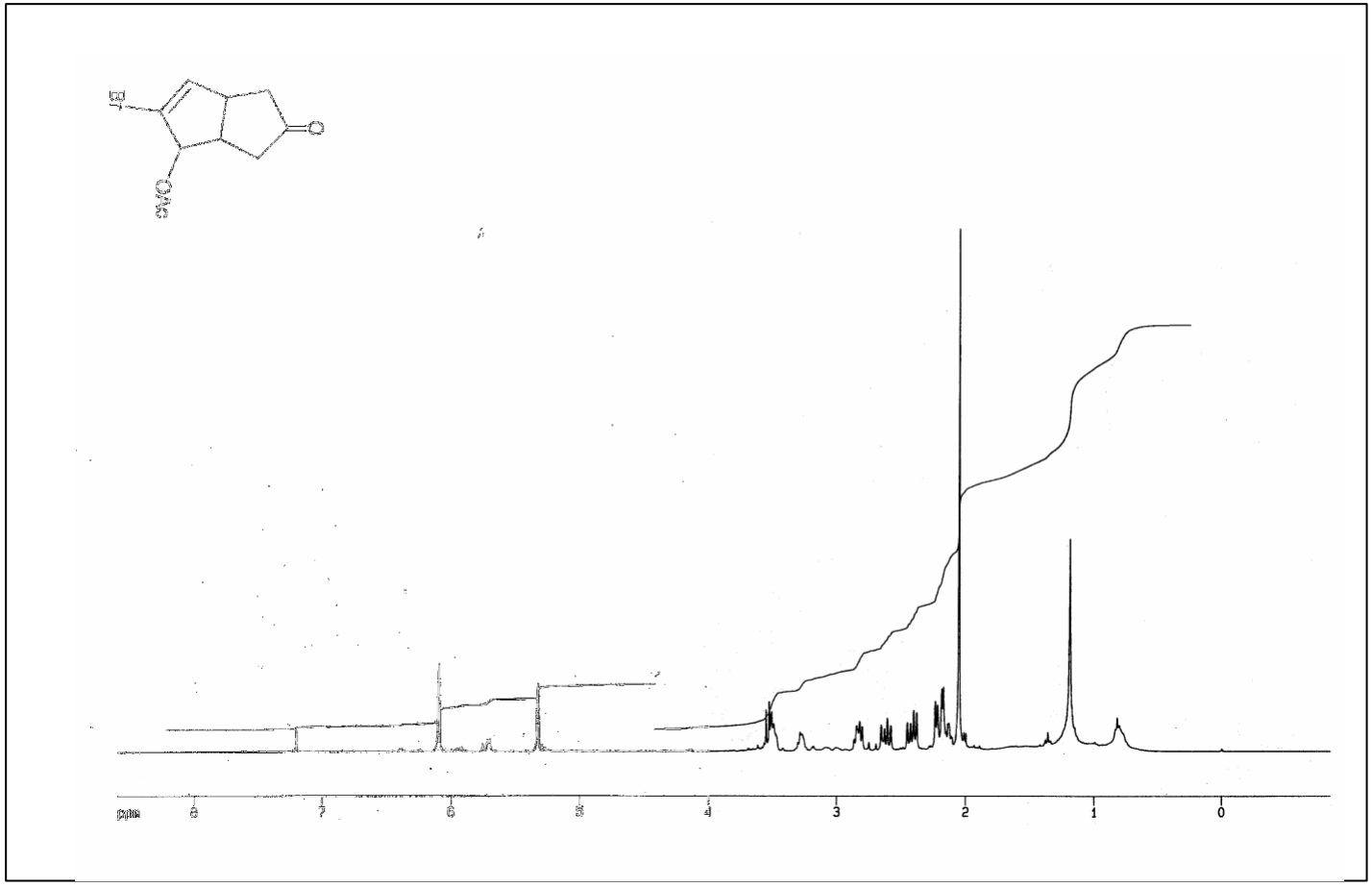


Figure 25: ^{1}H-NMR -Spectrum of compound **96**

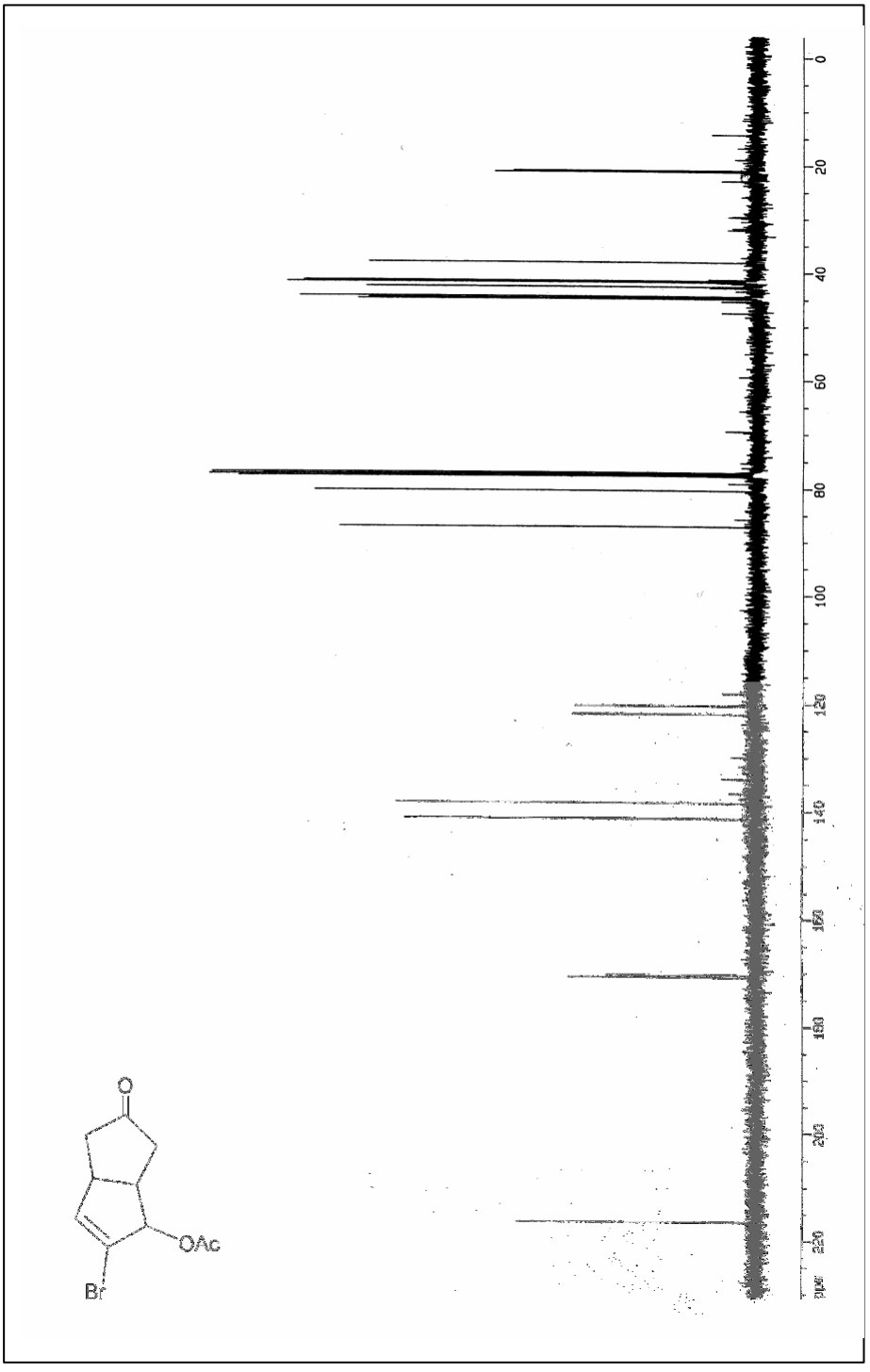


Figure 26: ^{13}C-NMR Spectrum of compound **96**

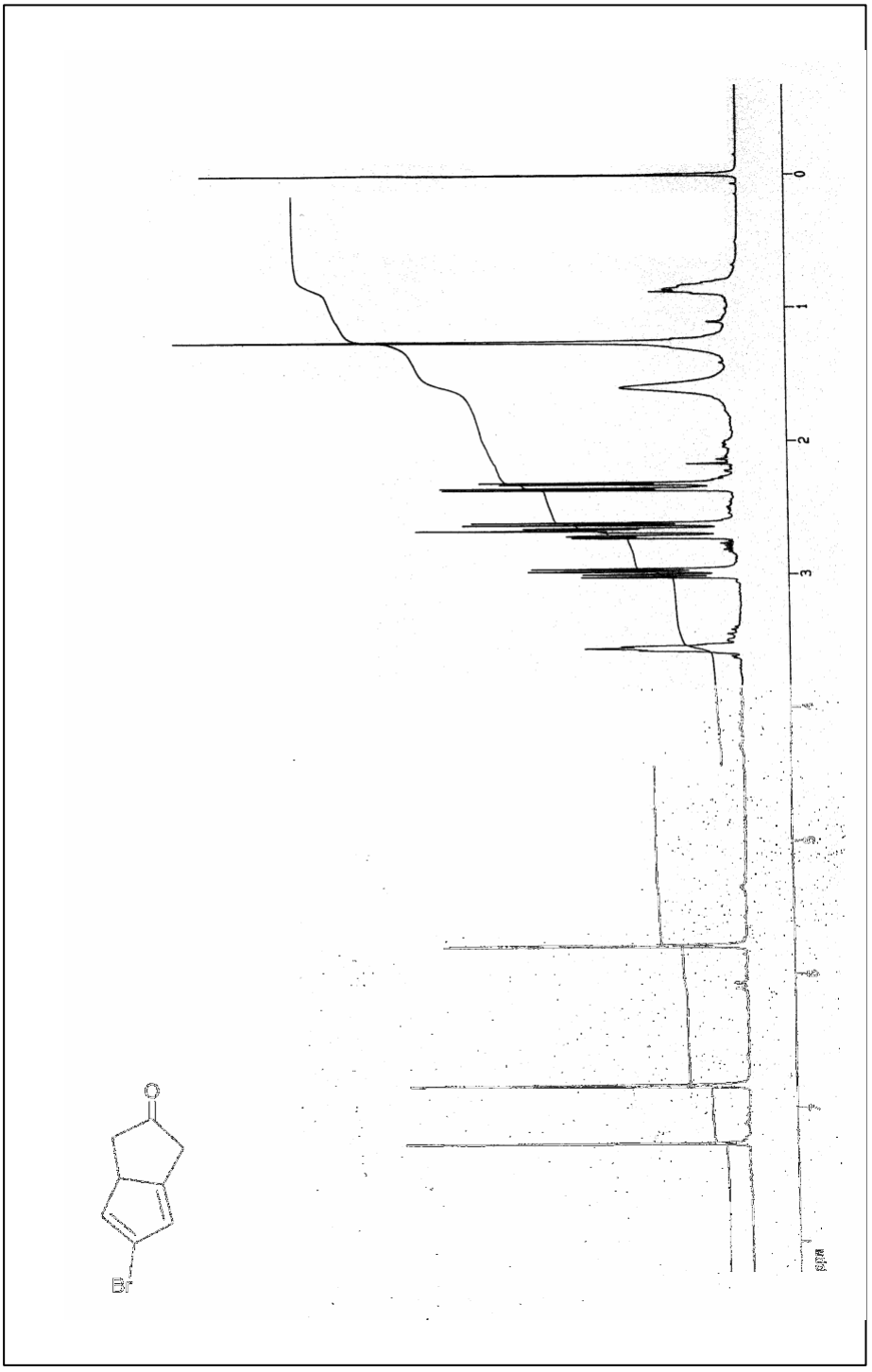


Figure 27: ^{1}H-NMR -Spectrum of compound **97**

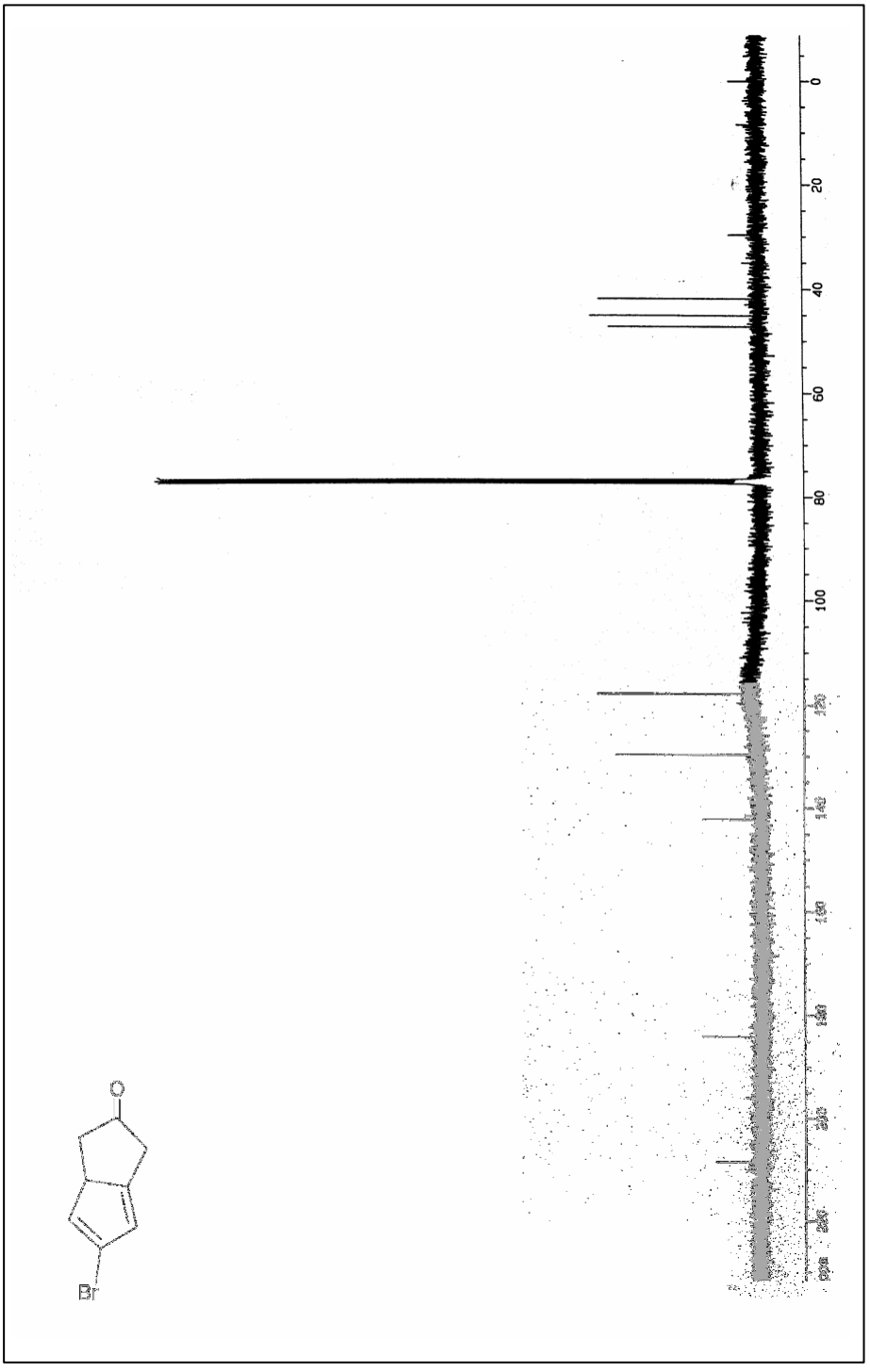


Figure 28: ^{13}C-NMR Spectrum of compound **97**

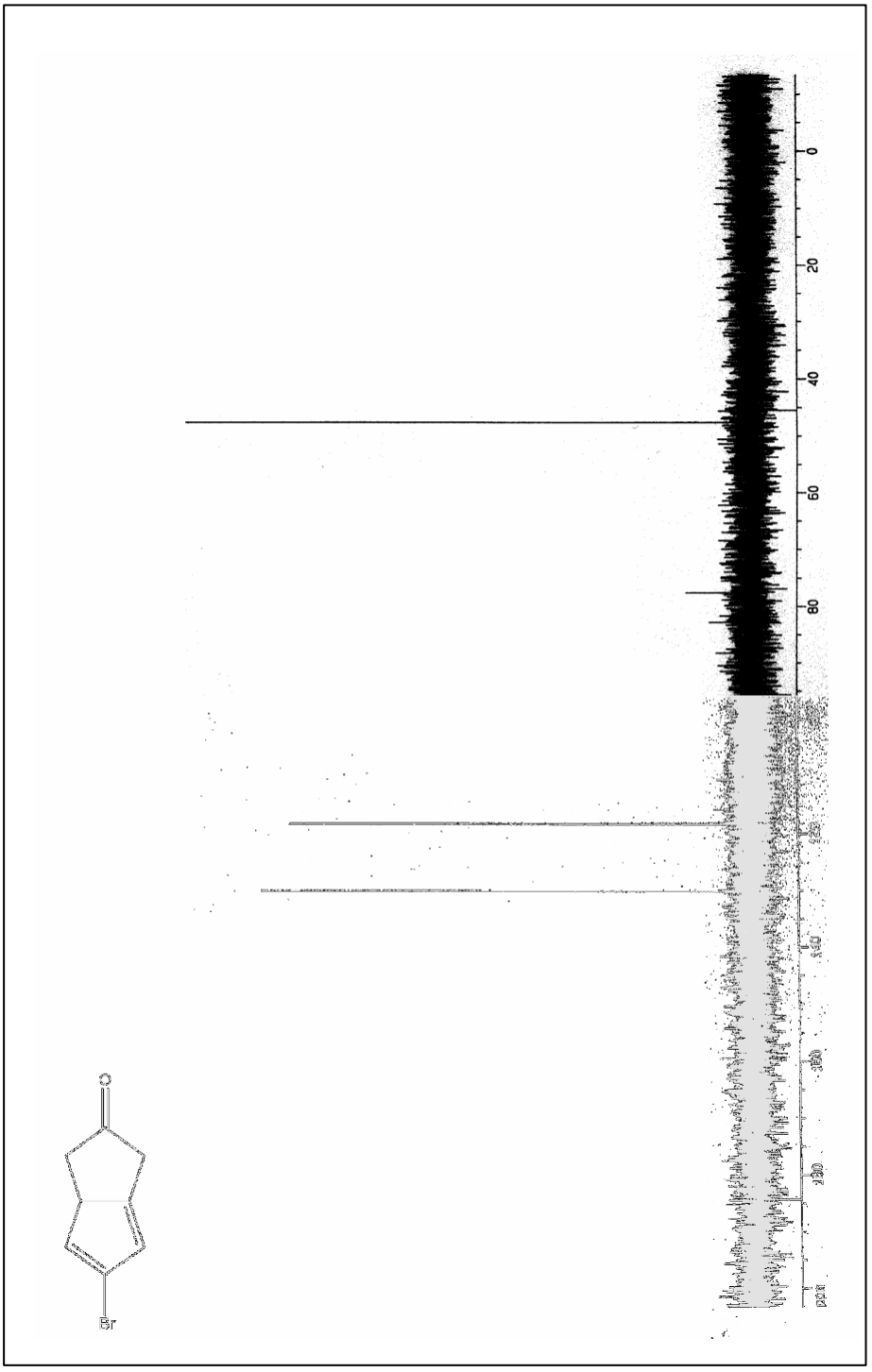


Figure 29: DEPT-90 spectrum of compound **97**

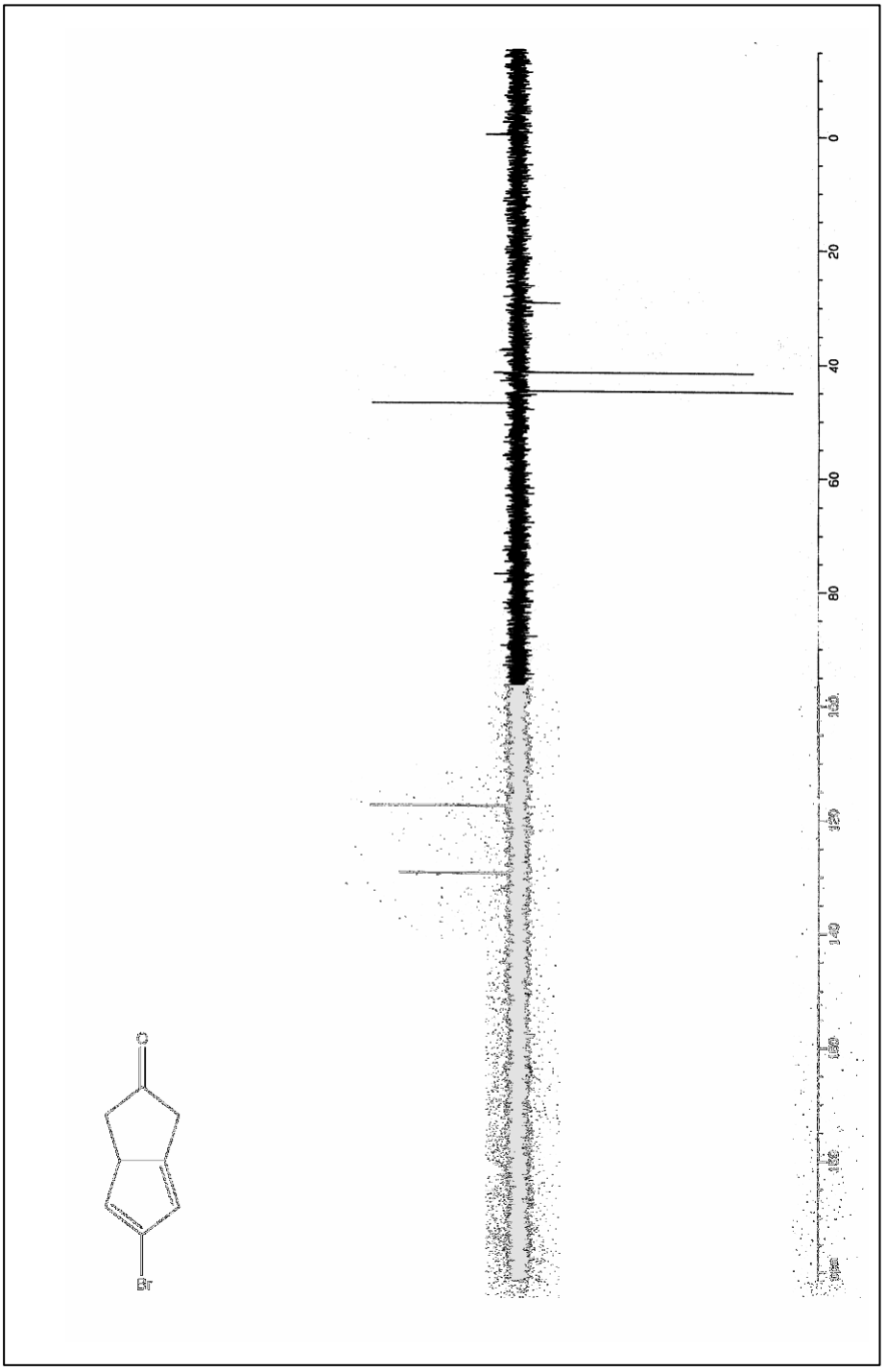
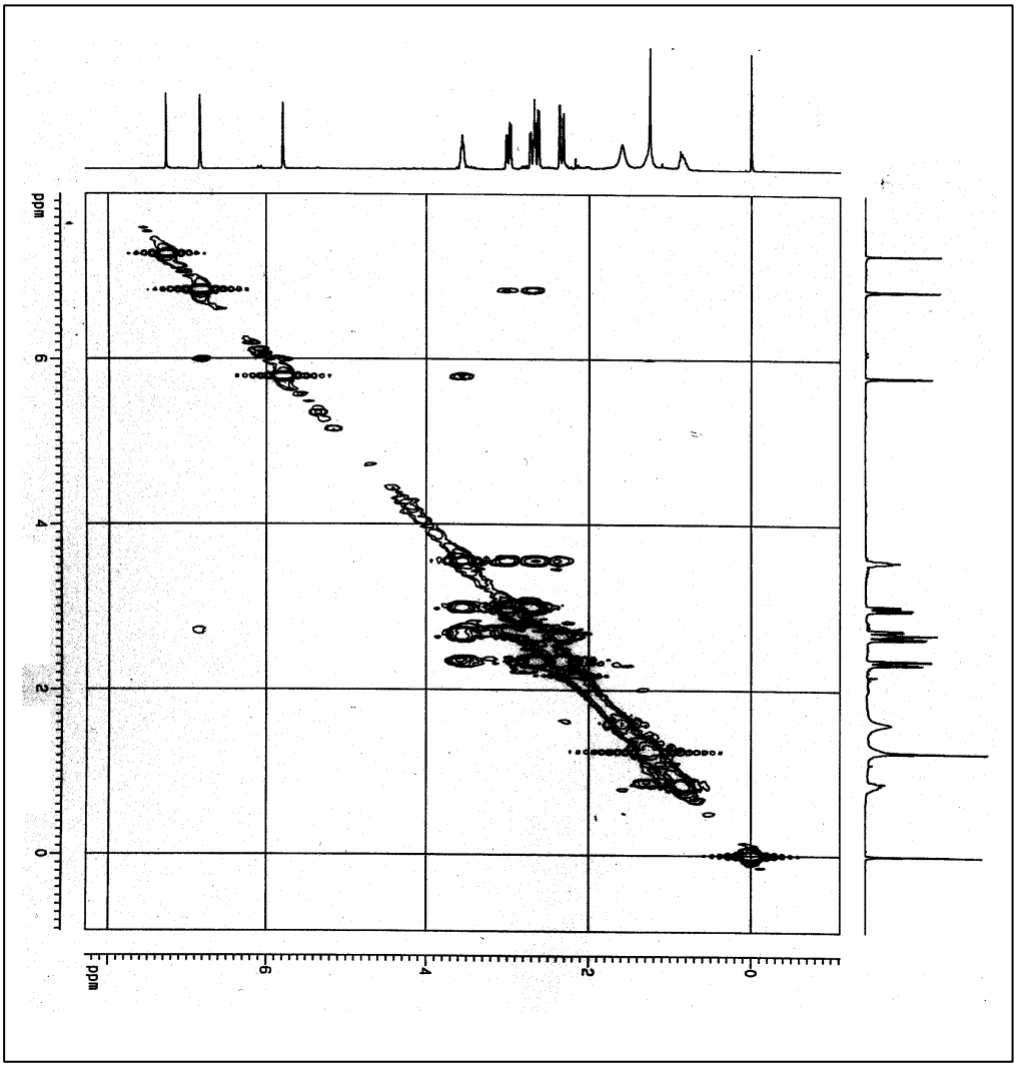


Figure 30: DEPT-135 spectrum of compound **97**



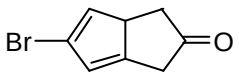
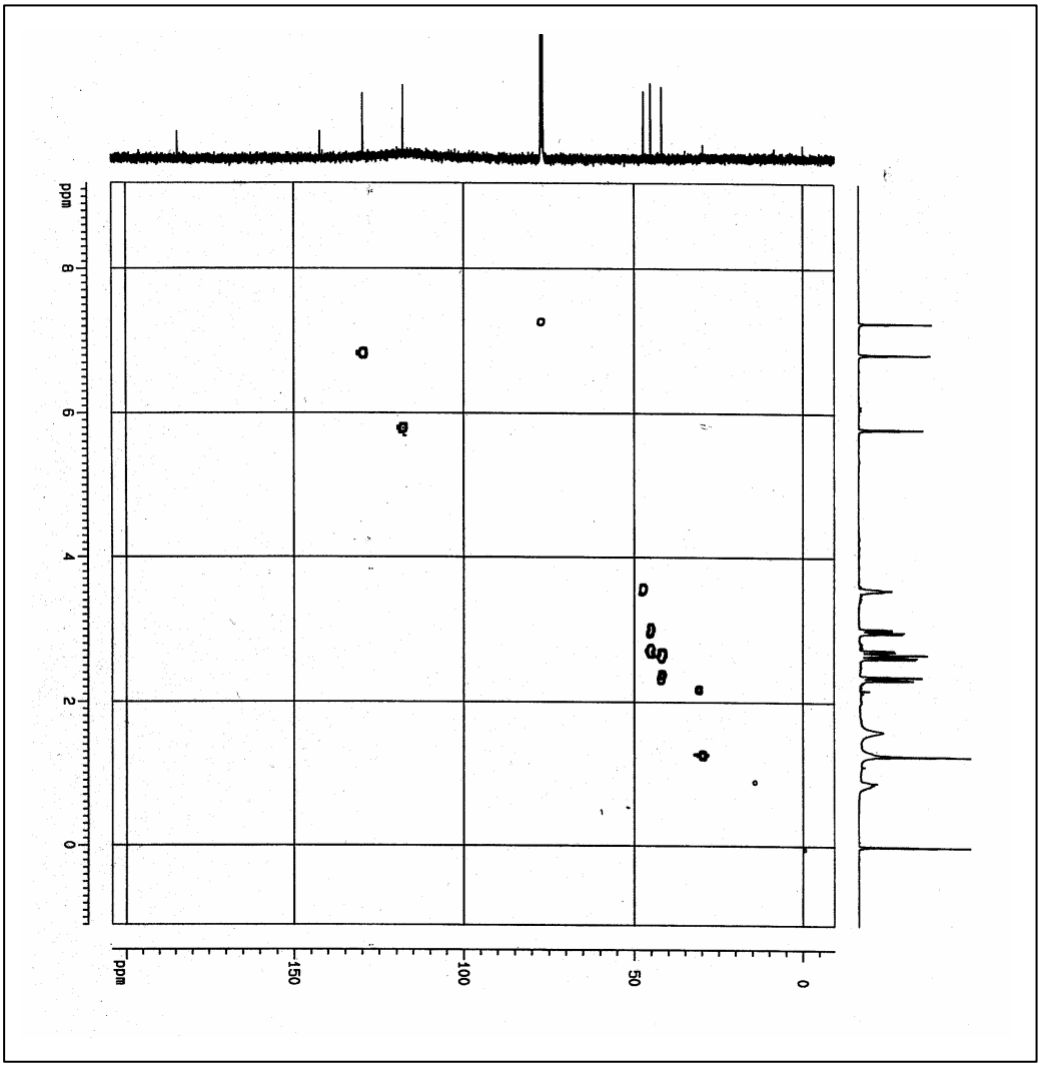


Figure 31: COSY spectrum of compound **97**



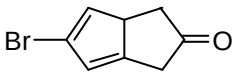
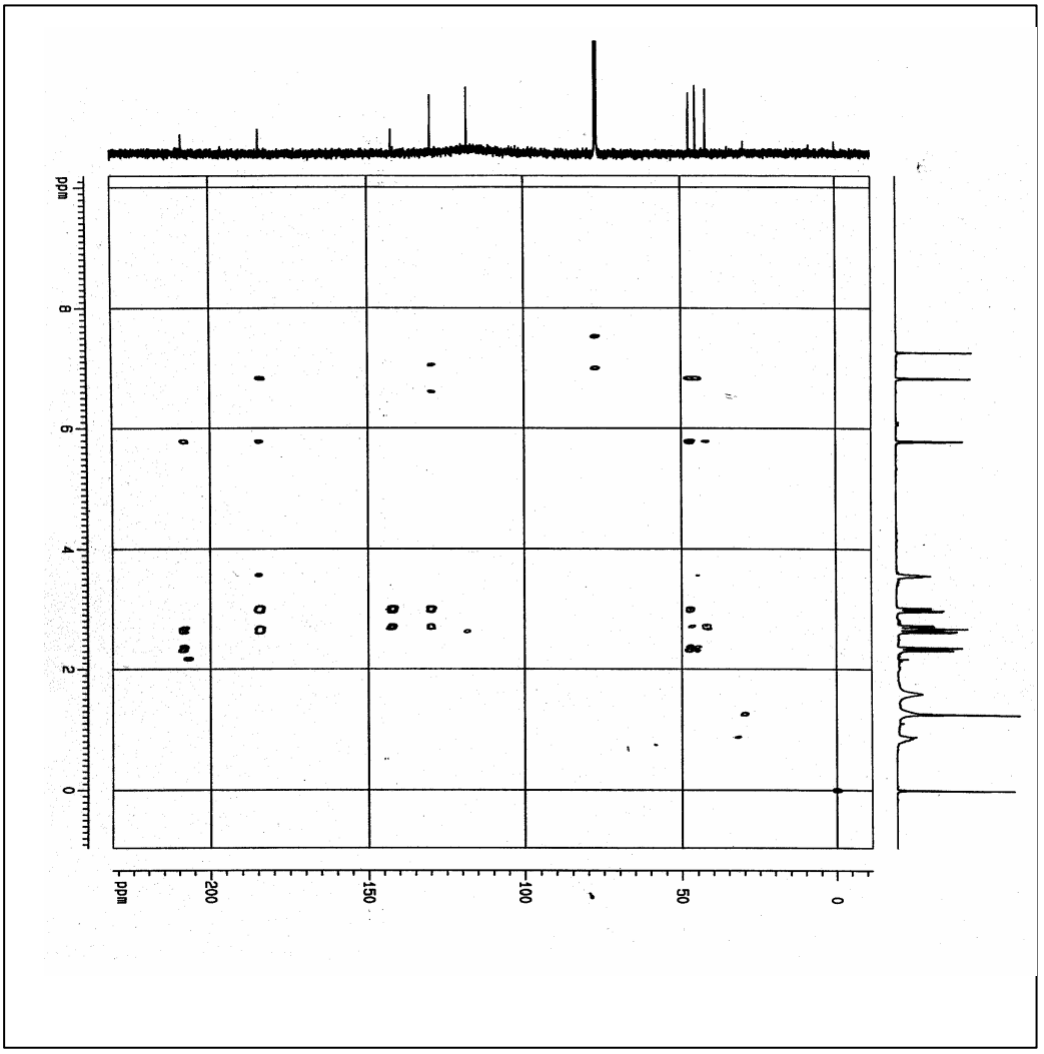


Figure 32: HMQC spectrum of compound **97**



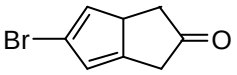


Figure 33: HMBC spectrum of compound **97**

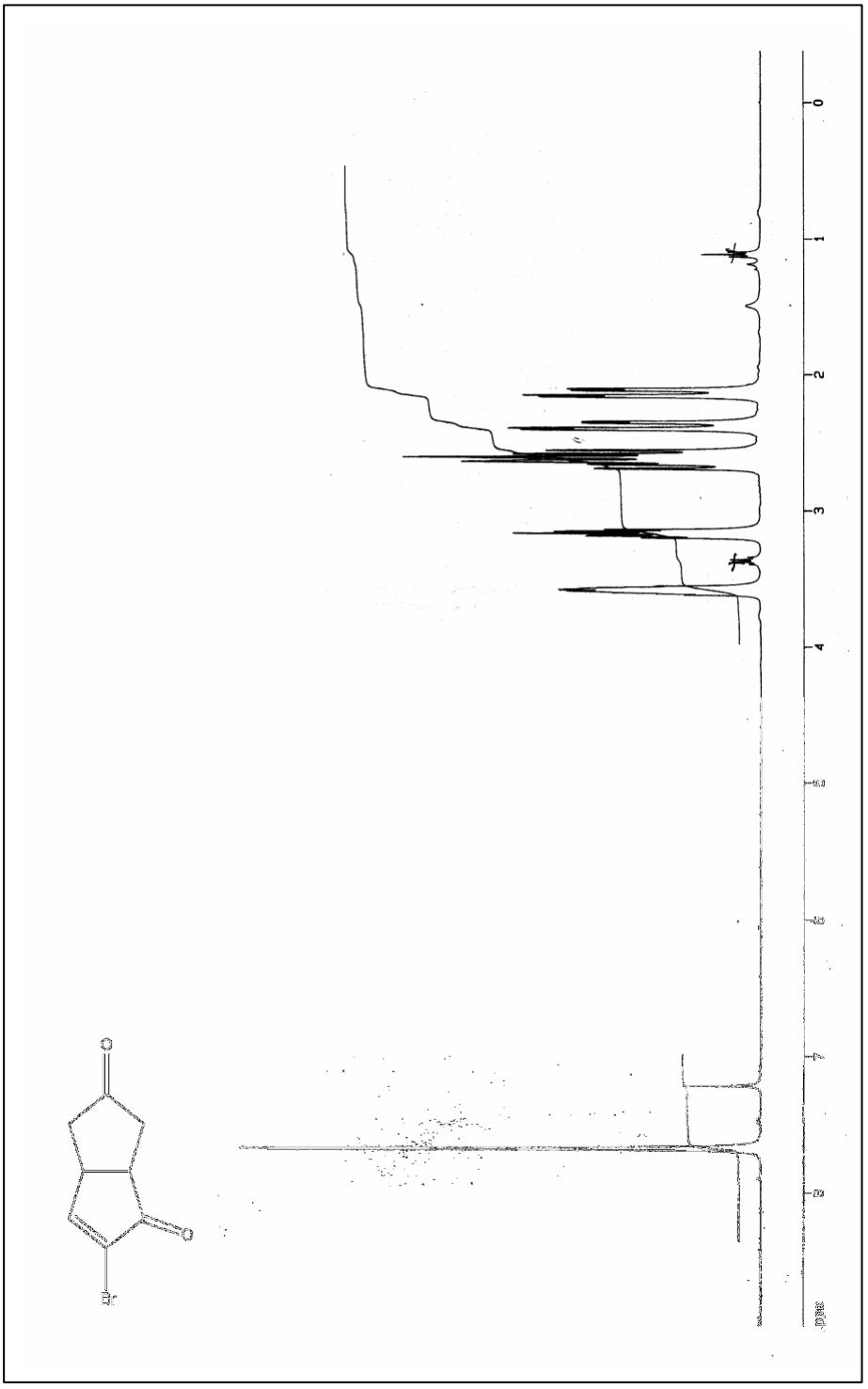


Figure 34: ^{1}H-NMR -Spectrum of compound **98**

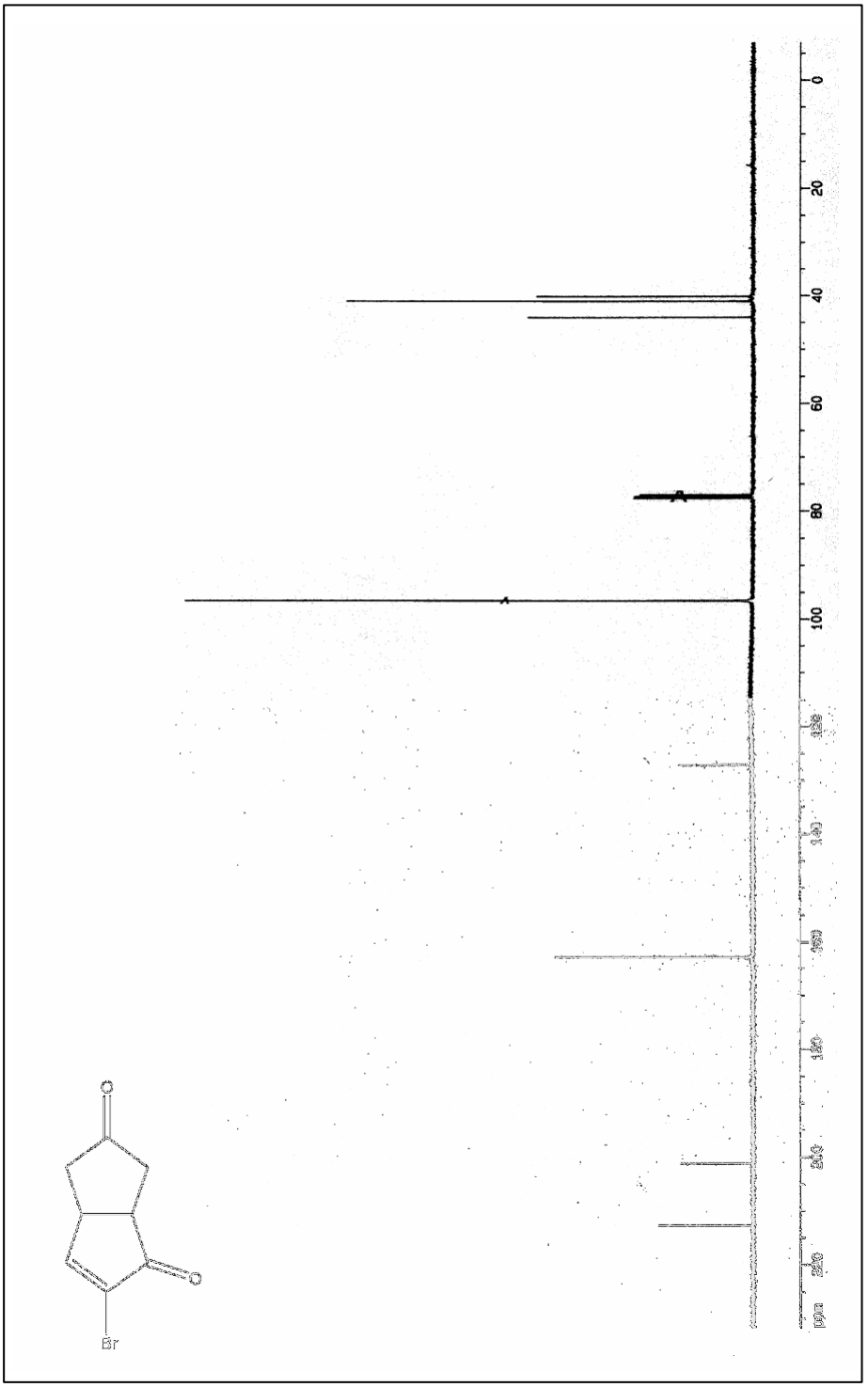


Figure 35: ^{13}C-NMR Spectrum of compound **98**

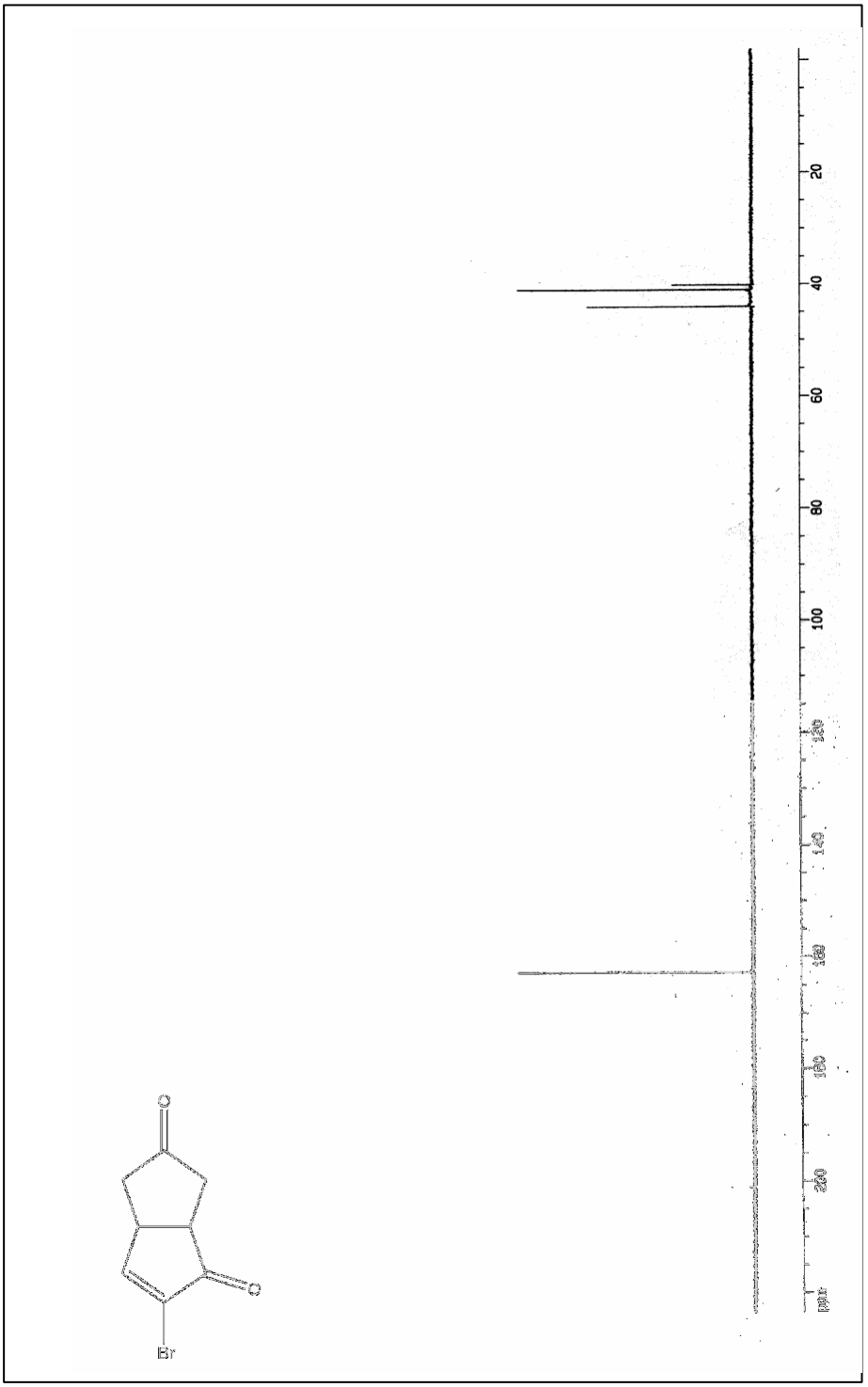


Figure 36: DEPT-90 spectrum of compund **98**

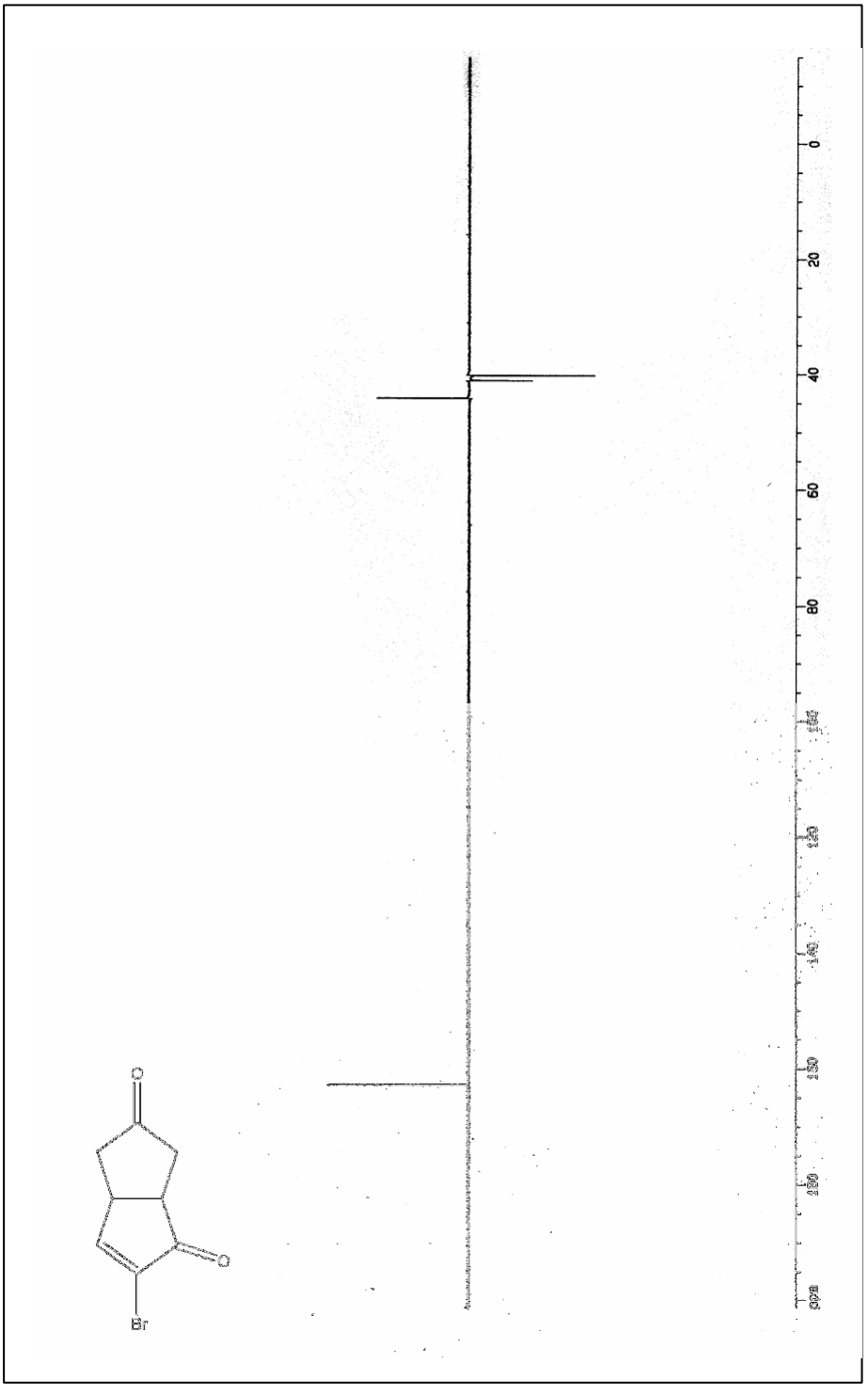
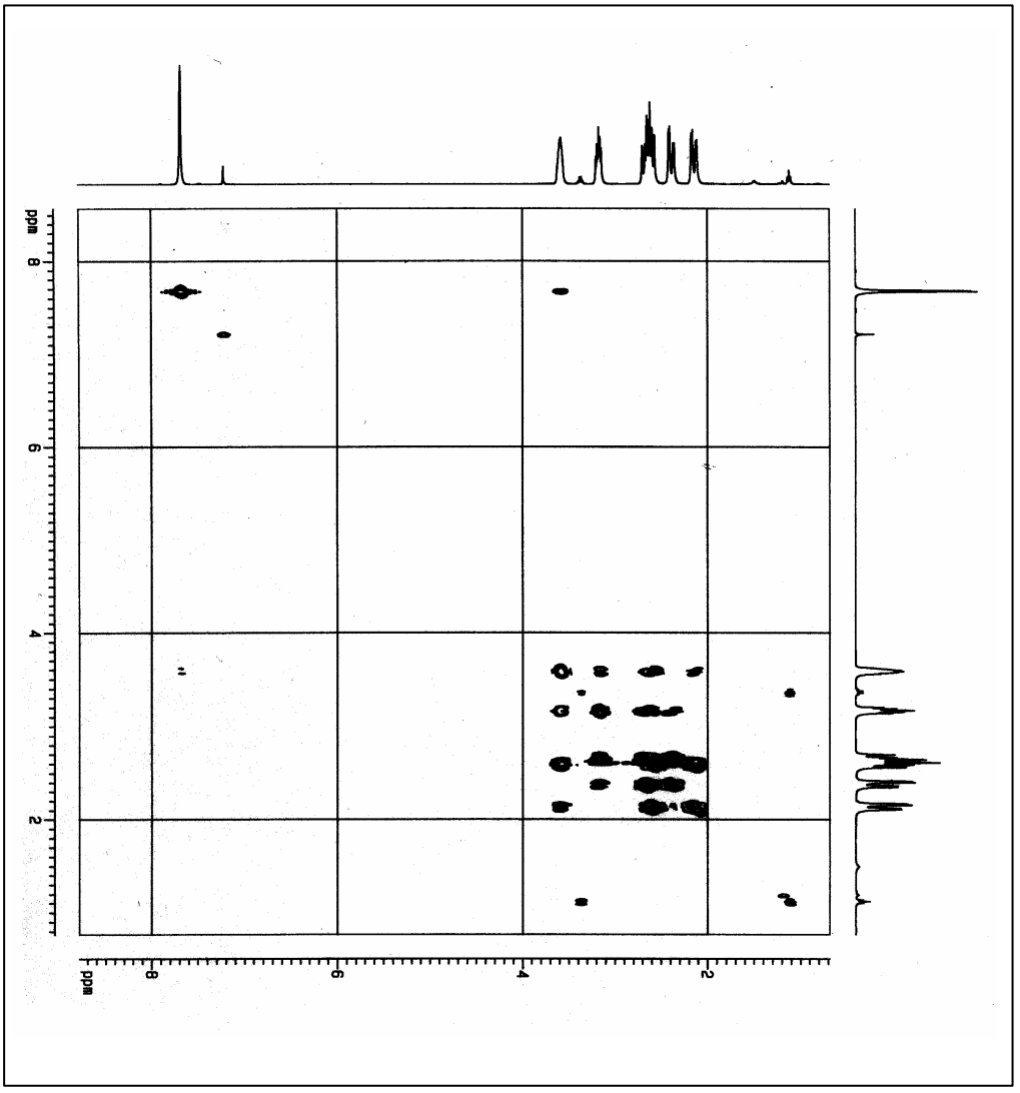


Figure 37: DEPT-135 spectrum of compound **98**



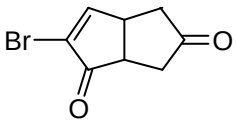
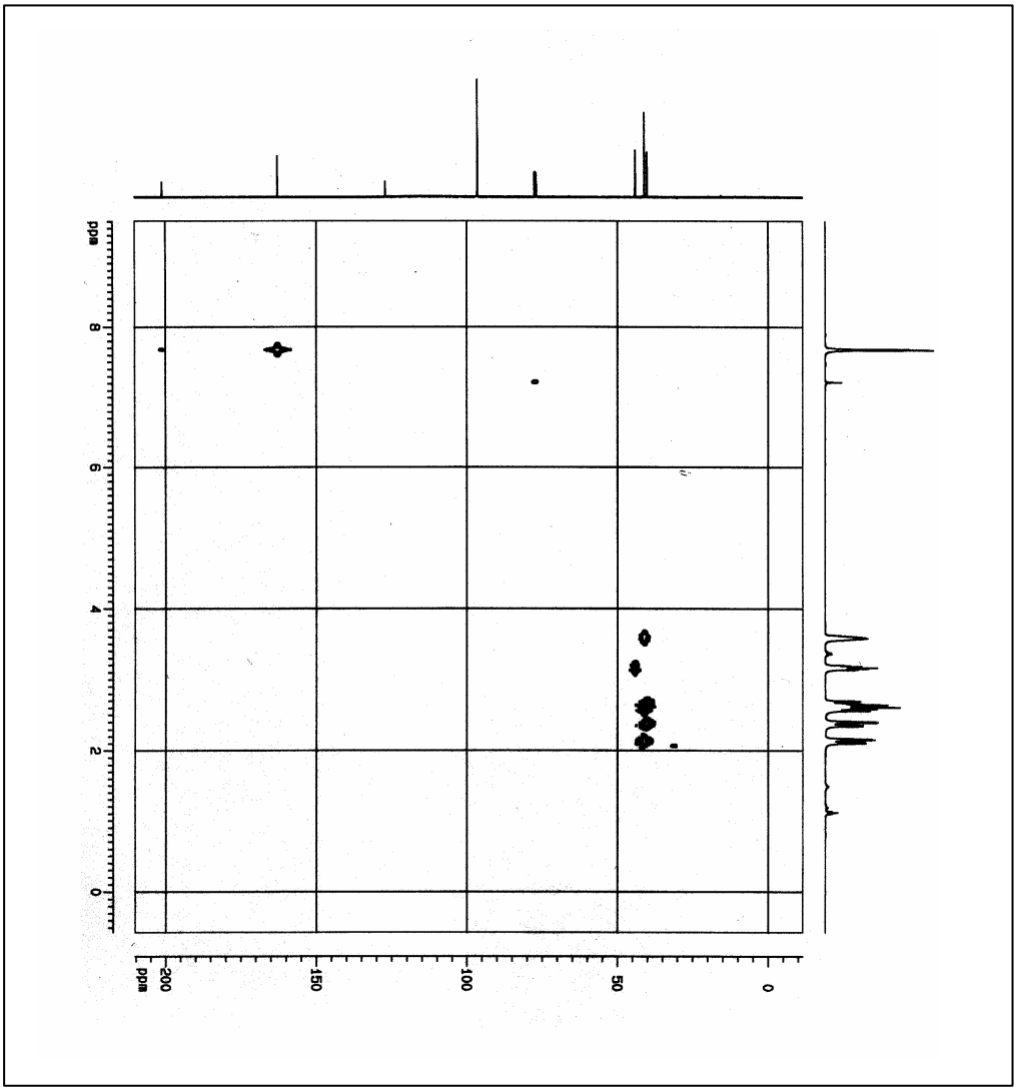


Figure 38: COSY Spectrum of compound **98**



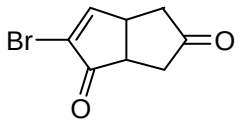
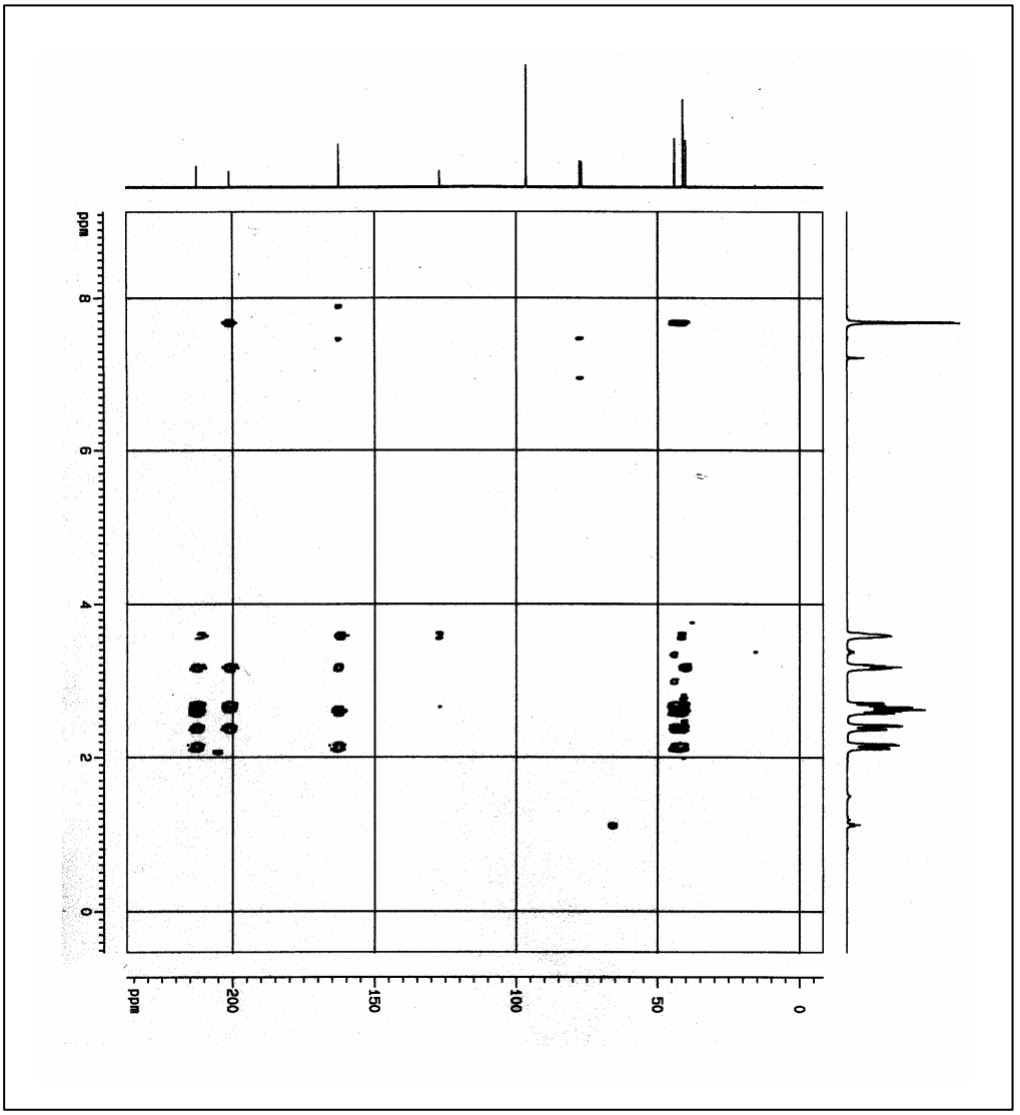


Figure 39: HMQC Spectrum of the compound **98**



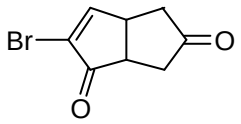


Figure 40: HMBC Spectrum of the Compound **98**

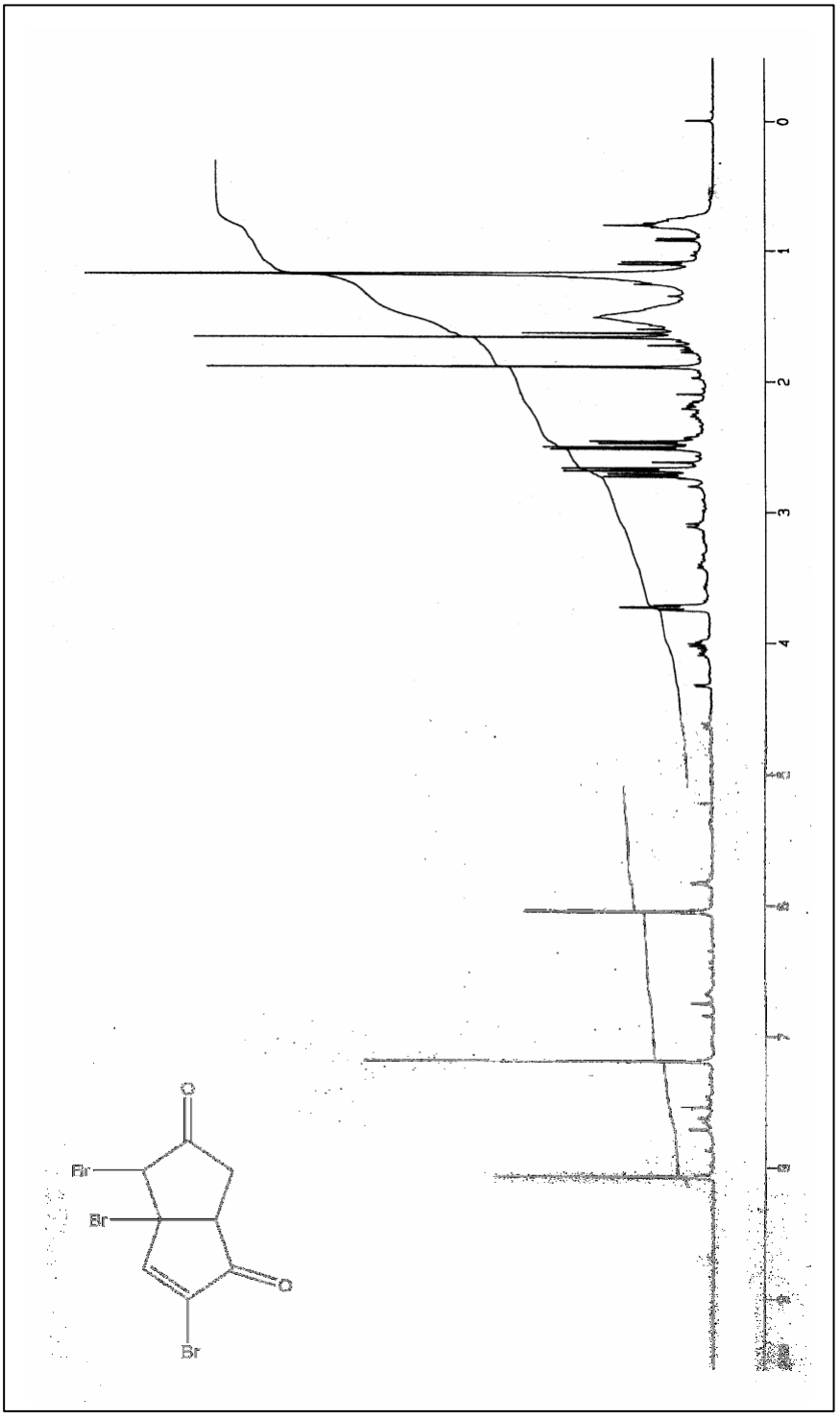


Figure 41: ^{1}H-NMR -Spectrum of compound **141**

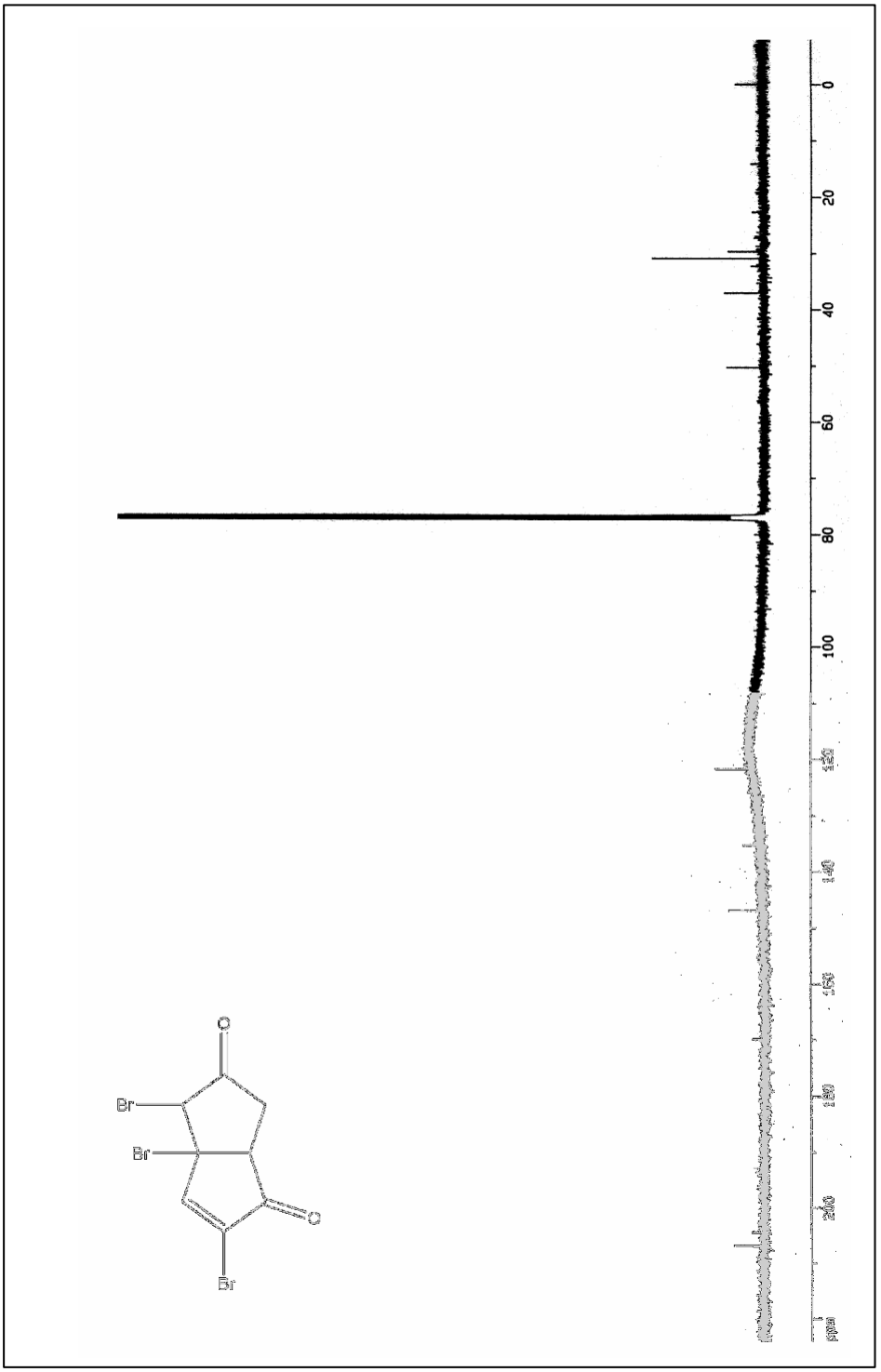
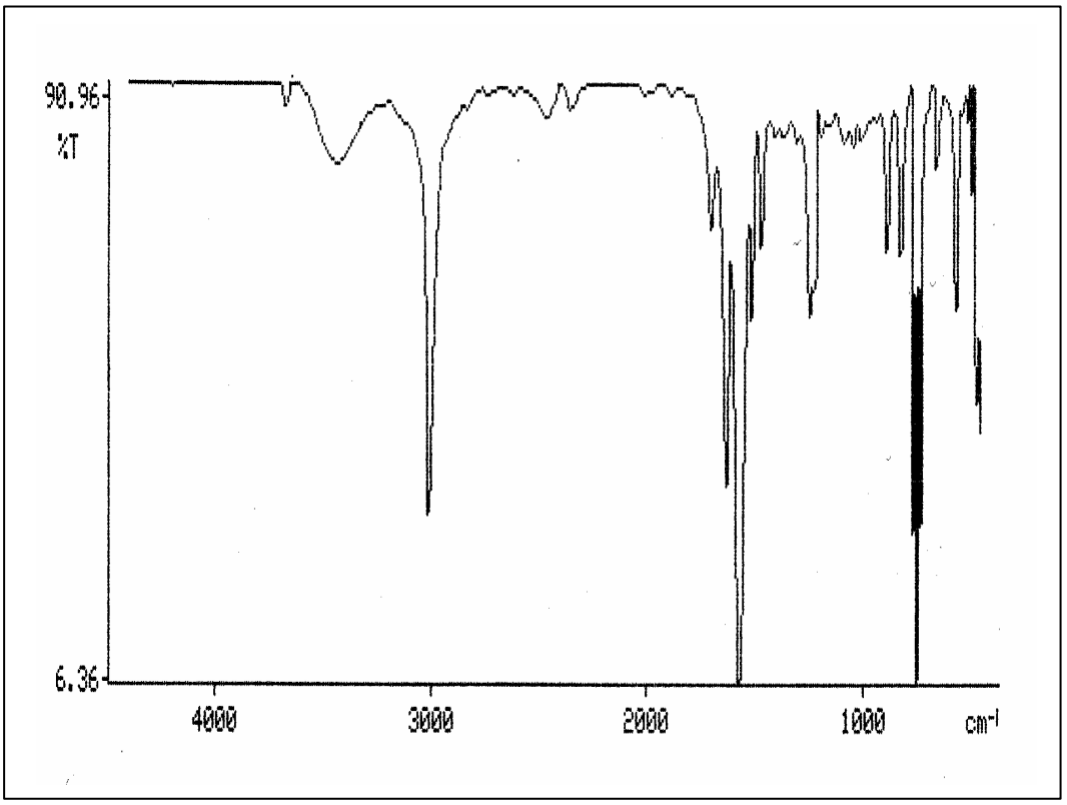


Figure 42: ^{13}C-NMR Spectrum of compound **141**

APPENDIX B



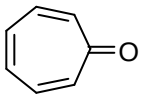
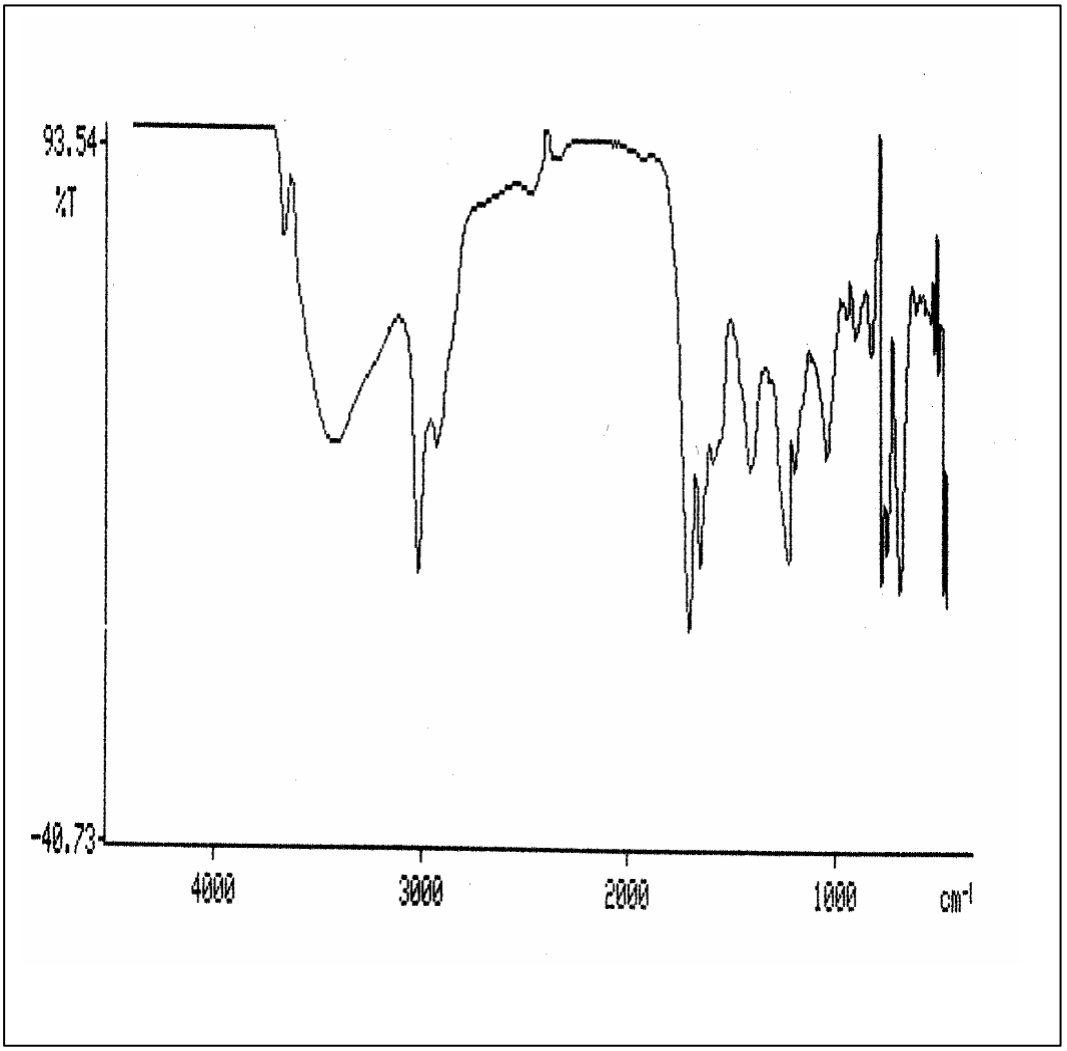


Figure 43: IR Spectrum of compound **90**



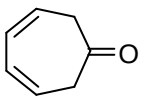
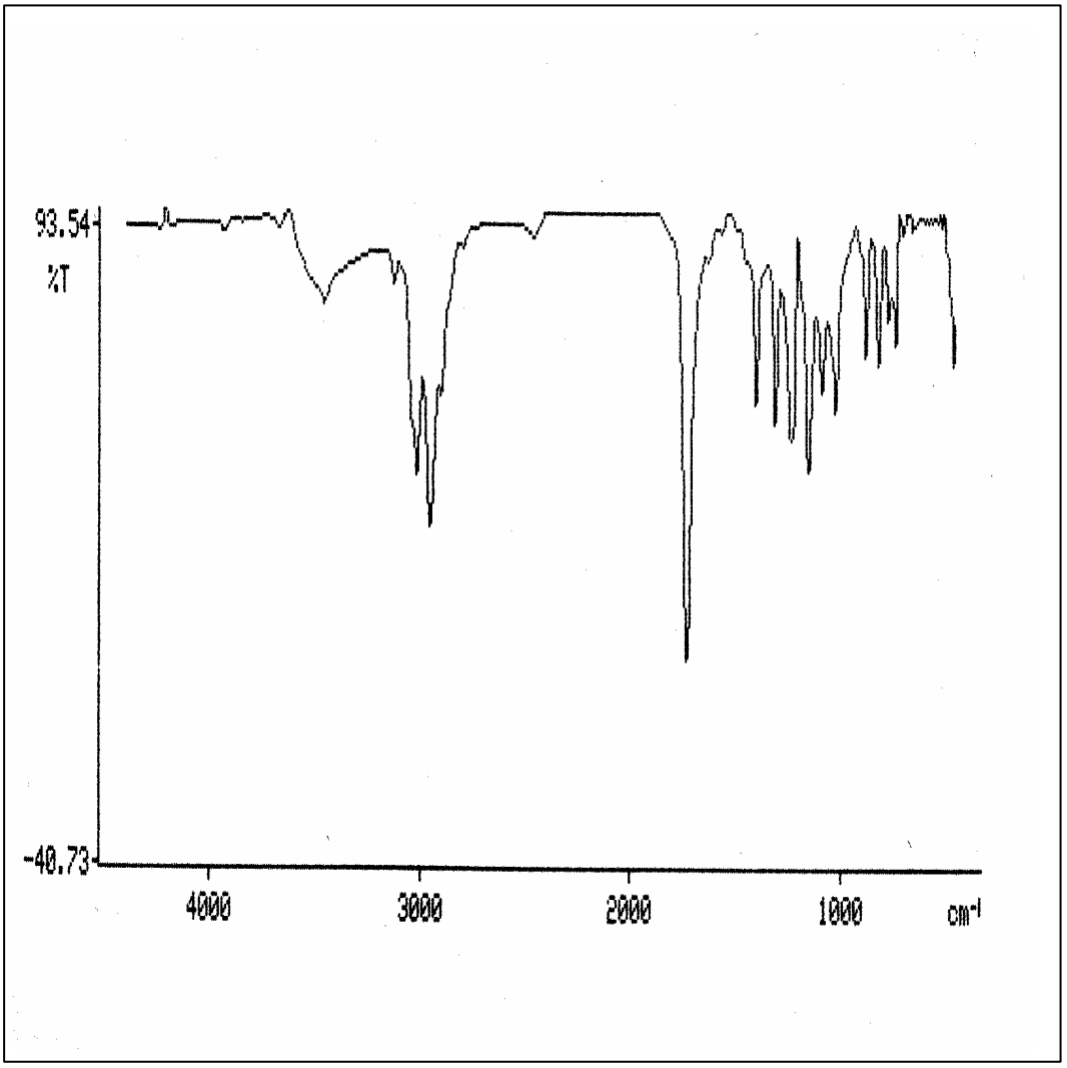


Figure 44: IR Spectrum of compound **91**



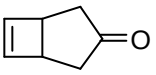
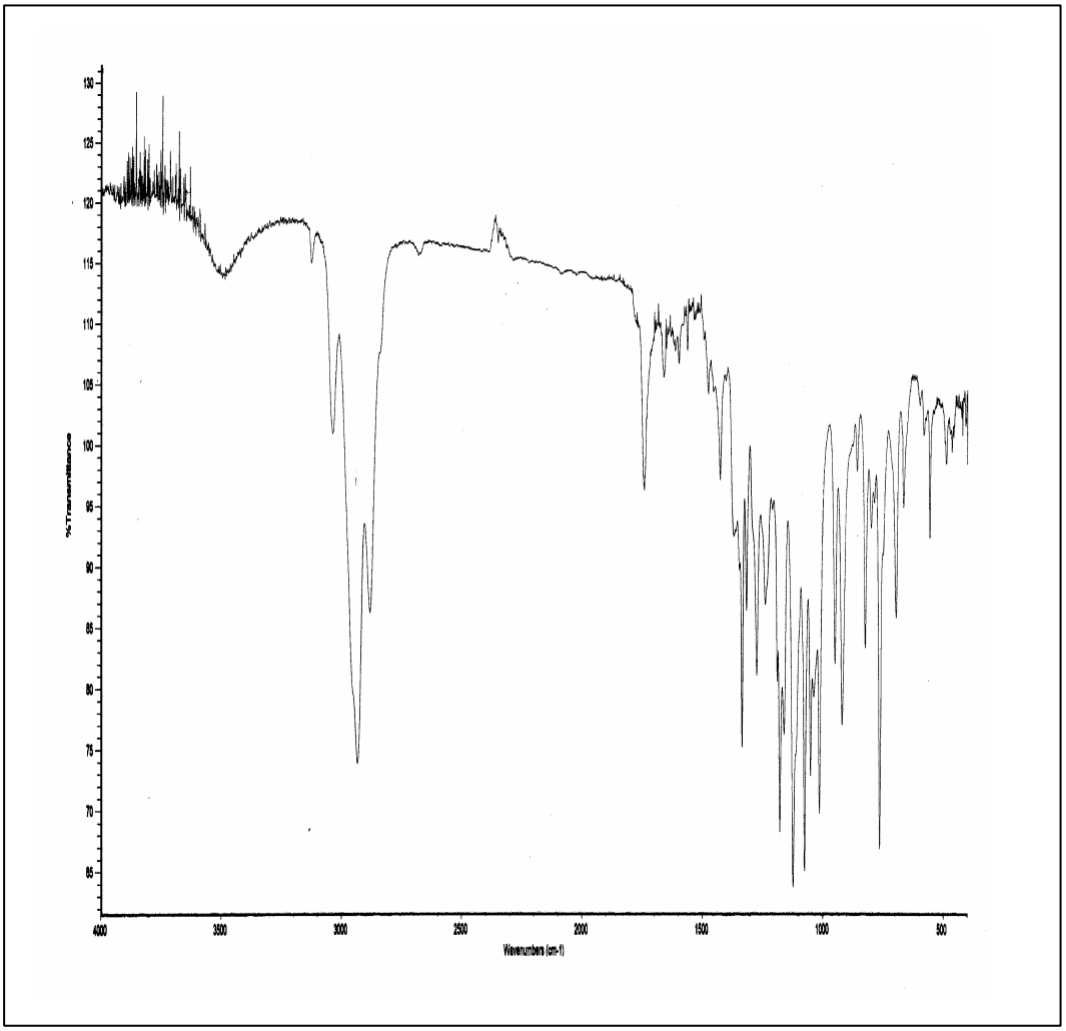


Figure 45: IR Spectrum of compound **92**



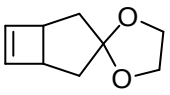
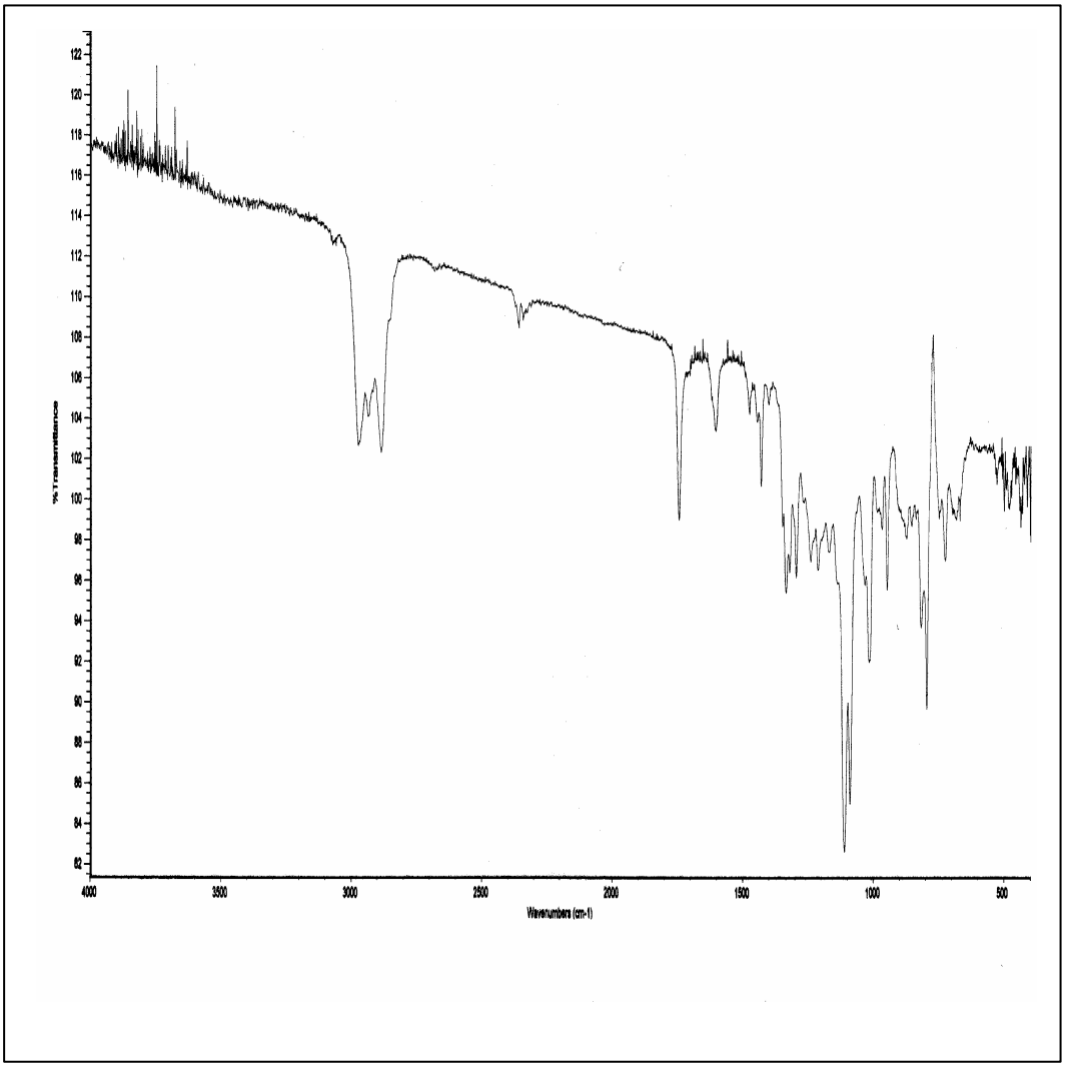


Figure 46: IR Spectrum of compound **93**



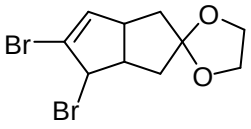
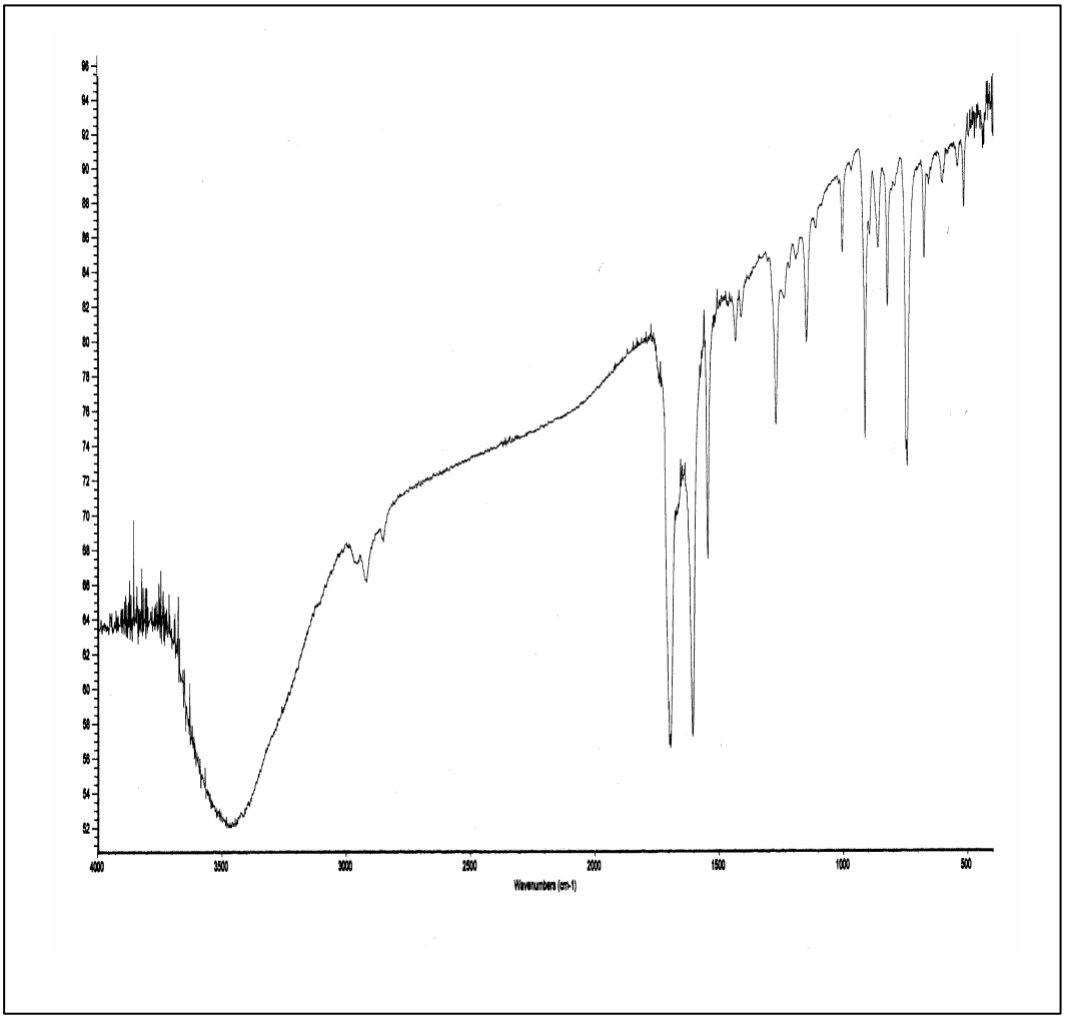


Figure 47: IR Spectrum of compound **94**



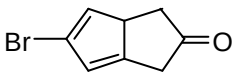
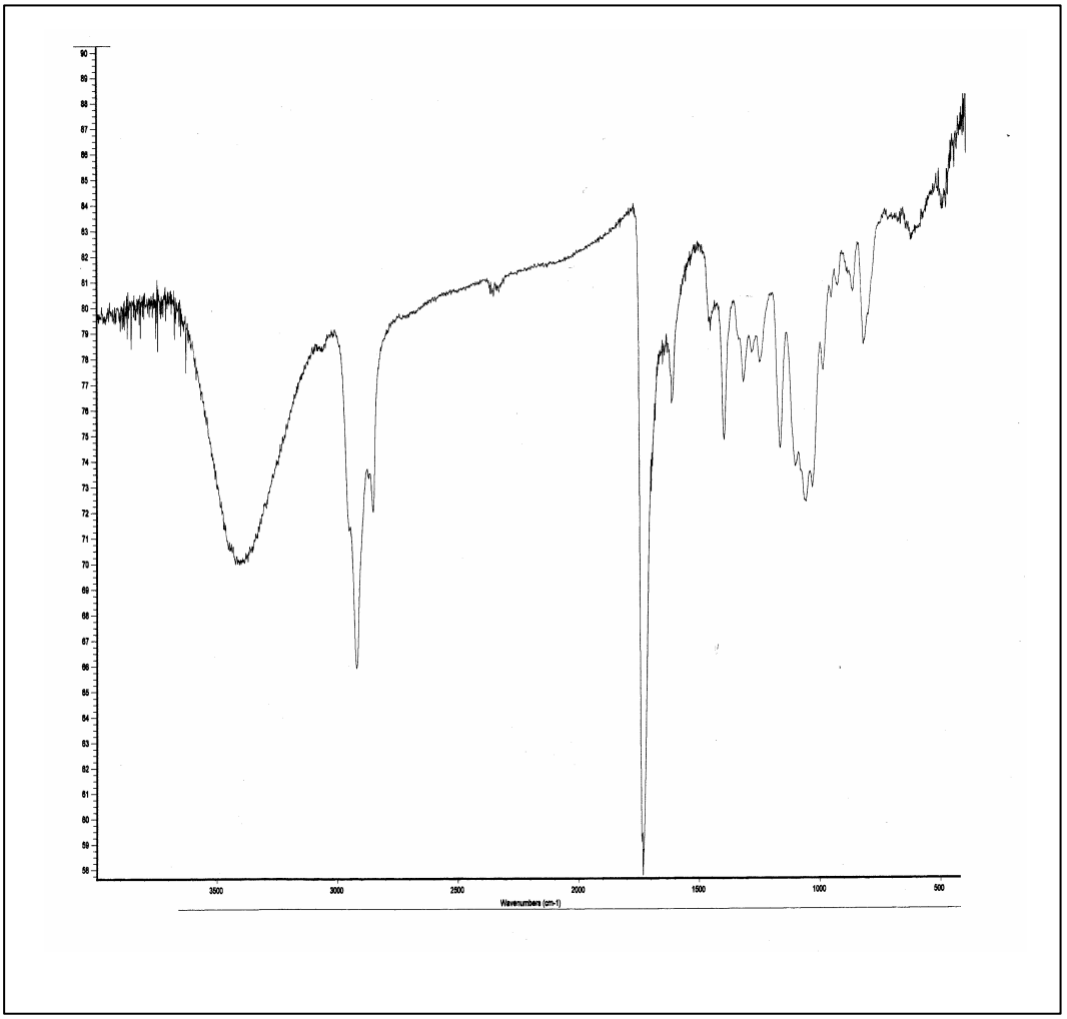


Figure 48: IR Spectrum of compound **97**



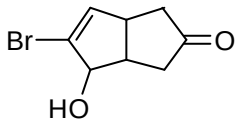
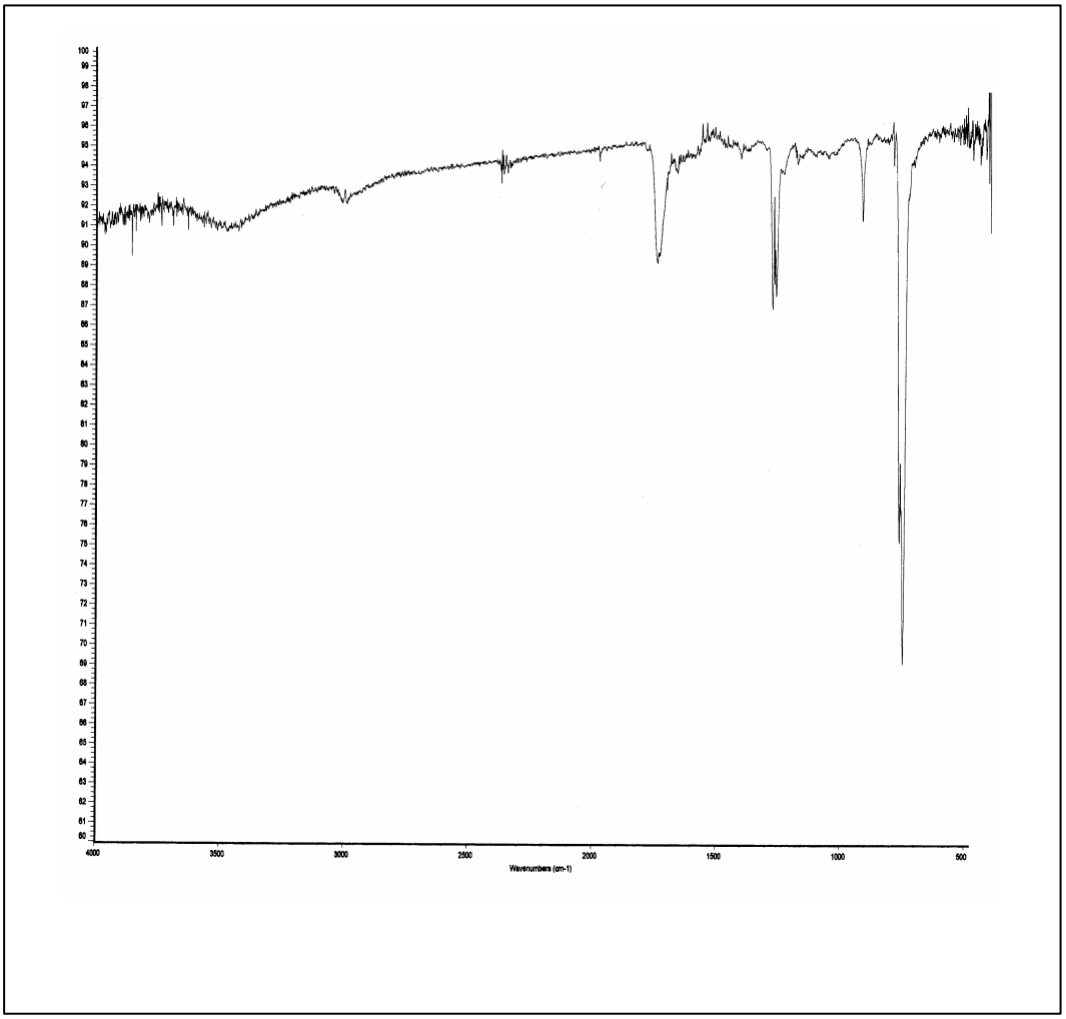


Figure 49: IR Spectrum of compound **95**



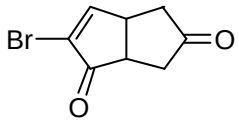
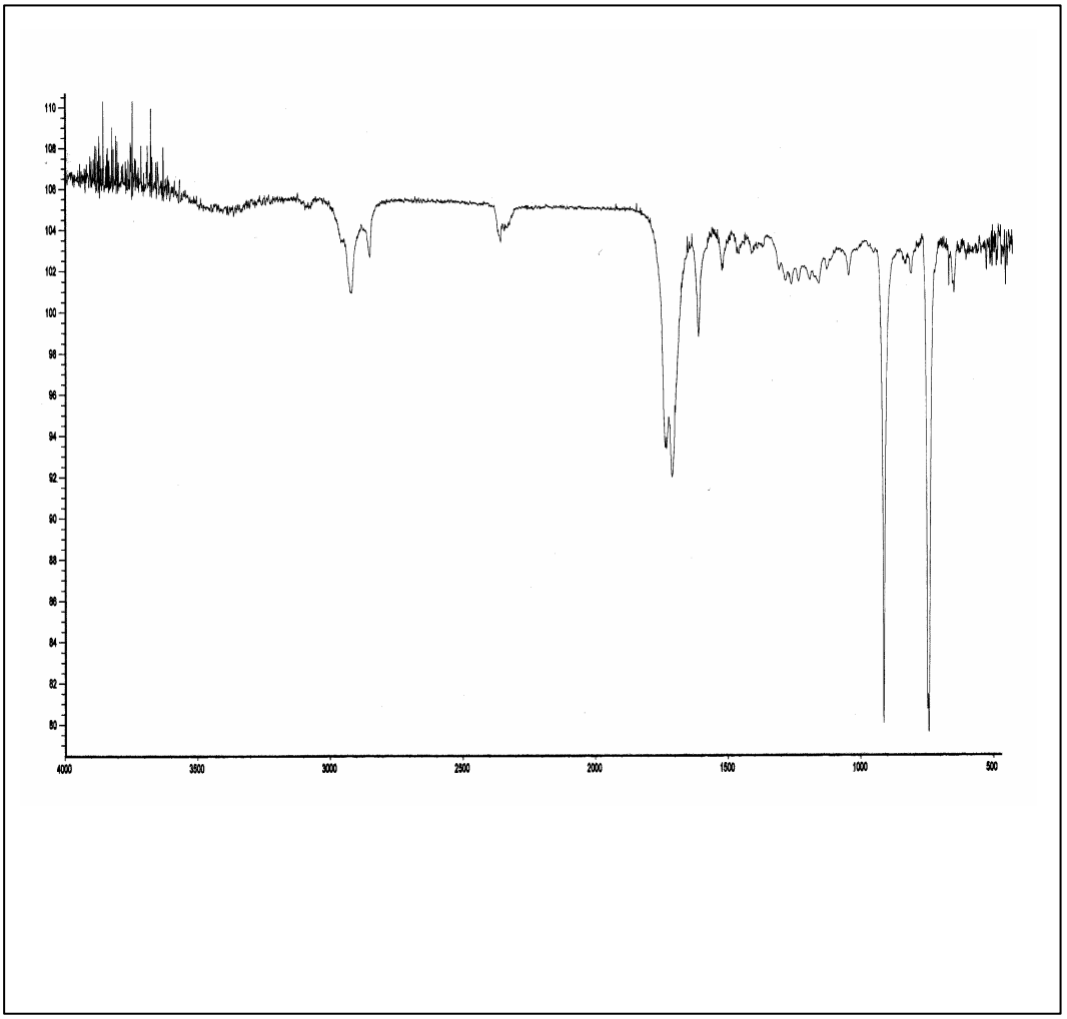


Figure 50: IR Spectrum of compound **98**



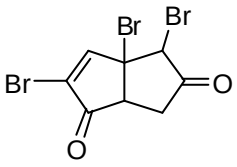


Figure 51: IR Spectrum of compound **141**