DEVELOPMENT OF SYNTHETIC METHODOLOGIES DIRECTED TOWARDS THE GENERATION OF FIVE MEMBERED RING ALLENES

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Approval of the Graduate School of Natural and Applied Sciences

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I certify that this thesis satisfies all the requirements as a thesis for the degree of Doctor of Philosophy.

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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 Doctor of Philosophy.

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ABSTRACT

DEVELOPMENT OF SYNTHETIC METHODOLOGIES
DIRECTED TOWARDS THE GENERATION OF
FIVE MEMBERED RING ALLENES:

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Chemists have always been fascinated by the cumulated diene system of allenes with its extraordinary properties such as the axial chirality of the elongated tetrahedron and a higher reactivity than non-cumulated C-C double bonds.

The equilibrium geometry for an allene is linear with orthogonal pairs of substituents. An allene incorporated into a carbocyclic ring of nine or more carbon atoms is relatively unstrained. However, if the ring size is decreased, the linear perpendicular allene will be twisted and bent until, at some point, the energy gained by π bonding in the two double bonds will be insufficient to offset the increased strain. Furthermore, ring constraints will exert torsion toward a planar arrangement of ligands. Therefore, one of the fundemantal questions is the influence of ring size on the barrier to π bond rotation.

Herein we wish to unveil a review of our research related to desperately seeking for five membered ring allenes such as, cyclopenta-1,2-diene (**1**) and some of its

derivatives, e.g. **2**, and **3**. Furthermore, we will address a simple, mild and efficient method for the reduction of 1,4-benzoquinones **4** to corresponding hydroquinones **5**.

Keywords: Allene, Cyclic Allene, Cyclopenta-1,2-diene, Carbene, Doering-Moore-Skattebol Method, 1,4-benzoquinone, phenol, reduction.

ÖZ

BEŞ ÜYELİ SİKLİK ALLENLERİN SENTEZİNE YÖNELİK SENTETİK ÇALIŞMALAR

Algı, Fatih
Doktora, Kimya Bölümü
Tez Yöneticisi: Prof. Dr. Metin Balcı

Haziran 2006, 194 sayfa

Allenler kümüle dien sisteminin oluşturduğu uzamış tetrahedronun kiral özellik göstermesi ve diğer C-C çift bağlarına göre daha reaktif olmaları nedeniyle kimyacıların her zaman ilgisini çekmektedir.

Allenler ideal olarak ortogonal substitient çiftleriyle doğrusal bir geometriye sahiptirler. Dokuz ve daha fazla karbon atomu içeren siklik allenler göreceli olarak gerilimsizdir. Bununla beraber halka küçüldükçe düzlemsel olan allen, iki çift bağdaki π bağı enerjisi artan gerilim enerjisini dengeleyemeyene dek bükülecektir. Ayrıca halka gerilimi, ortogonal ligandları düzlemsel yapıya doğru zorlayacaktır. Elektronik yapıları allenleri bir hayli kararsız ara ürünler haline getirir. Bu nedenle temel sorulardan bir tanesi halka büyüklüğünün π bağı rotasyon bariyerine etkisinin ne olduğudur.

Bu çalışmada beş üyeli gerilimli siklik allenlerden **1-3**'ün sentezini hedef alan sentetik metotlar geliştirilecek ve bunun yanı sıra sözkonusu metotlarla elde edilecek araştırma sonuçları derlenecektir. Ayrıca 1,4-benzokinonların (**4)** kolayca

hidrokinonlara (**5)** indirgenmesini sağlayan yeni ve etkin bir yöntem geliştirilecektir.

Anahtar Kelimeler: Allen, Siklik Allen, Siklopenta-1,2-dien, Karben, Doering-Moore-Skattebol metodu, 1,4-Benzokinon, Fenol, İndirgeme.

To all the people of Academy

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I would like to express my sincere thanks to my supervisor Prof. Dr. Metin Balcı for his continuous guidance, endless support, as well as patience and encouragement throught this work. His interpretation of NMR spectra is so much incredible so that it was a great pleasure to work with him as it always is.

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I would like to thank to Prof. Dr. Ayhan S. Demir who let us to get some of the GC/MS spectra and his skillful assistants, especially Ömer Reis and Asuman Aybey for taking these spectra.

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My special appreciation and gratitude is devoted to Duygu D. Günbaş for her unique friendship and making a design of Appendices.

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LIST OF ABBREVIATIONS

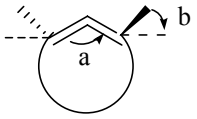
AM1	: Austin model 1
B3LYP	: Becke 3 parameter functional and Lee, Yang, Parr correlation functional
COSY	: Correlation spectroscopy
DEPT	: Distortionless enhancement by polarization transfer
DFT	: Density functional theory
DMSO	: Dimethylsulfoxide
DPIBF	: Diphenylisobenzofuran
GC/MS	: Gas chromatography and mass spectrum
HBr	: Hydrogen bromide
HF	Hartree Fock
HMBC	: Heteronuclear multi-bond coherence
HMQC	: Heteronuclear multiple quantum coherence
Hz	: Hertz
IR	: Infrared
IUPAC	: International union of pure and applied chemistry
J	: Coupling constant
k	: Rate constant
KOBu*t*	: Potassium *tert*-butoxide
MCSCF	: Multi-configuration self-consistent field
MeLi	: Methyllithium
MNDO	: Modified neglect of diatomic overlap
MPn	: Moller Plesset
n-BuLi	: *n*-Butyllithium
NMR	: Nuclear magnetic resonance

CHAPTER 1

INTRODUCTION

Dienes are mainly classified in three groups according to the order of the double bonds: isolated, conjugated, and cumulated dienes in which a carbon atom is attached to other two carbons by the means of two double bonds, in other words, the allenes.

The equilibrium geometry for allene is linear with orthogonal pairs of substituents. Linear allenes are inherently not "strained". Strain implies some deviation from an ideal bonding geometry; this is not true for compounds, which contain ordinary sp^2-hybridized carbons. The strain in cyclic allenes arises from the deformation of linear geometry, that is, the deformation of C=C=C angle. Ring constraints bend the allene and exert torsion toward a planar arrangement of ligands.



a = Bending angle
b = Torsional angle

Figure 1. Bending and torsional angles in cyclic allenes.

Model semi empirical and *ab initio* [1-2] molecular orbital calculations show that the bending potential is remarkably soft for the first 20°, resulting in only ca. 4 kcal/mol estimated strain, but rises steeply beyond this. Moreover, calculations show that bending and torsion are coupled motions; optimized structures for artificially bent allene show the hydrogens twisted toward planarity.

In bent allenes, the majority of strain derives from the weakened π bonds. Bending also destroys the degeneracy of π and π^* orbitals; correlation with orbitals of planar allene.

Molecular models readily demonstrate that rings of ten or more carbons will accommodate an allene without geometric deformation and its concomitant strain. In rings of nine or fewer, there should be increasing strain, as the allene bends. Eventually the allene may be forced to planarity, although it is not yet known for what ring size this occurs. Predicted bending angles and out of plane torsional angles with respect to ring size (MNDO calculations) are summarized below (Fig. 2).

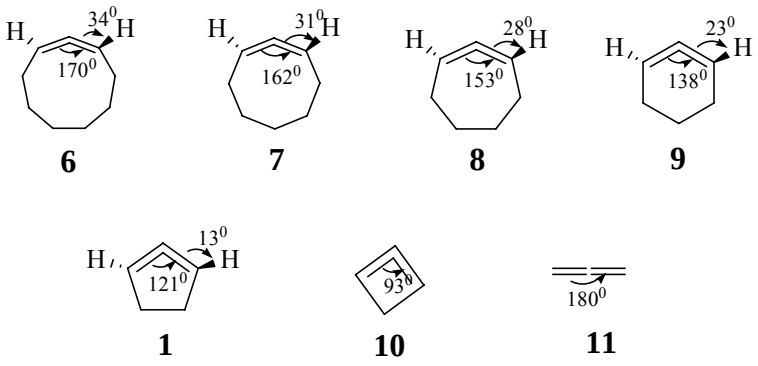


Figure 2. Predicted angles from MNDO calculations.

According to this picture, ring constraints must increase bending, torsion, and strain in smaller cyclic allenes. This is actually the case since crude strain estimates of 30, 20, 15, and 10 kcal/mol for five to eight membered ring allenes, respectively [1-2]. It is also noteworthy that bent, planar allene should be unstrained by ring constraints.

Chemists have always been fascinated by the cumulated diene system of allenes with its extraordinary properties such as the axial chirality of the elongated tetrahedron and a higher reactivity than non-cumulated C-C double bonds. Although the development of synthetic methodologies directed towards the synthesis of allenes has been confined to the last three decades with the few pioneering efforts being scattered across the first of these decades, the past sliver of this century provides enough evidence that allenes continious to entertain scientists in laboratories around the world in good numbers. Johnson [1] and Balci [2] comprehensively reviewed this field in two separate reports. Christl and colleagues have updated this survey in a companion to another account [3].

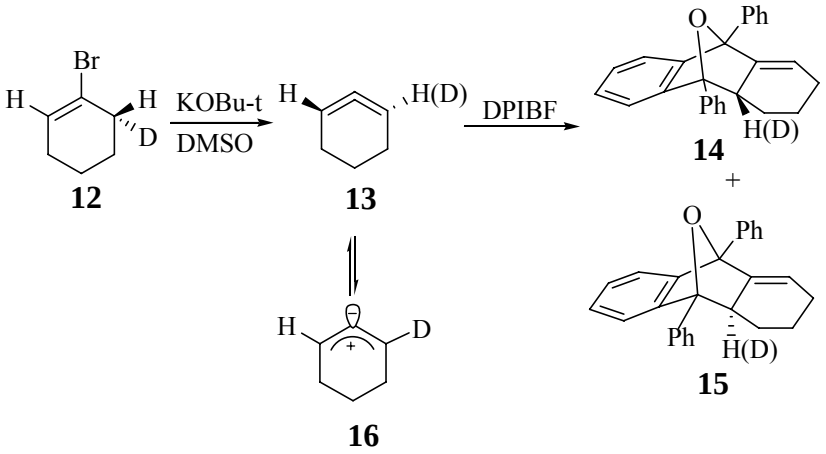
To keep this reminding contribution within reasonable bounds, we will only track the trends of past five years. Even then, we will only illustrate the trends with those discoveries that cought our eye. Older literature will be cited only in an effort to note the foundations of these fresher reports. Readers wishing more background have a string of older reports to consult.

1.1. CYCLIC ALLENES [†]

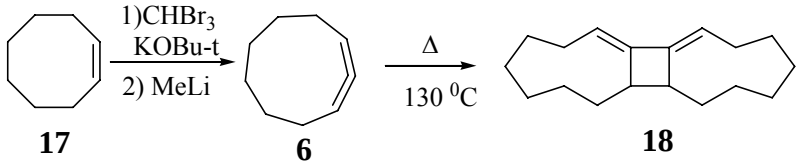
To begin the present survey, a valuable development from Balci and Jones will be considered. Balci and Jones have reported the dehydrohalogenation of optically active 1-bromo-6-deuteriocyclohexene (**12**) and trapped allene **13** with DPIBF. The resulting products, **14** and **15**, were optically active and having nonplanar structures [4]. Evidently, this pioneering case showed a principle which was

[†] For detailed discussions see refs. 1-3.

thereby established that allene **13** is chiral meaning that it has a single structure. It was further suggested that at around 80 ^{o}C, conversion of the nonplanar form of cyclohexa-1,2-diene to a symmetrical isomer (presumably **16**) competes with its reaction with the allene trap. The chirality of cyclohexa-1,2-diene (**9**) was also supported with MCSCF calculations [1-2].

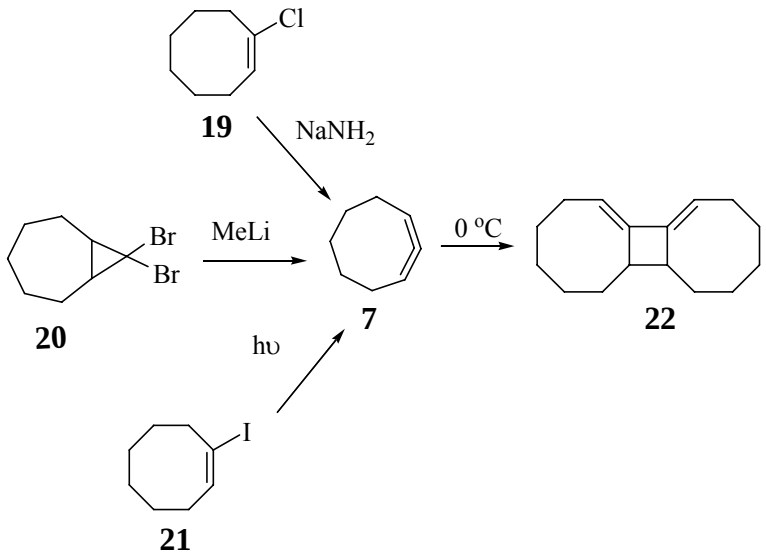


At room temperature, cyclonona-1,2-diene (**6**) is a distillable liquid, and can be stored virtually unlimited. Skattebøl was the first who synthesized this compound from **17** [5]. The dimerization of **6** takes place only at 130 ^{o}C.

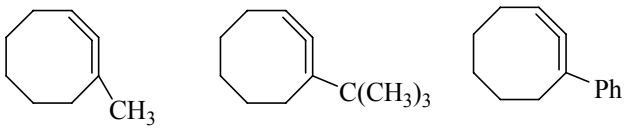


However, the stability of phenyl derived cyclonona-1,2-diene (**6**) is decreased dramatically. Christl *et al.* have reported that the dimerization of 1-phenyl-cyclonona-1,2-diene takes place even at 20 ^{o}C [6].

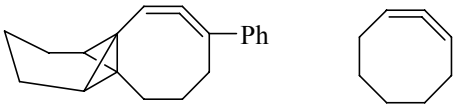
Cycloocta-1,2-diene (**7**) readily dimerizes, but cold, dilute solutions are suitable for rapid IR and NMR spectrum analysis [7]. The facile dimerization of allenes doubtless results from twofold strain release upon C_2- $C_{2'}$ bonding.



The eight-membered ring allenes **23-27** represent the range of compounds known. Allene **24** is the only eight membered cycloallene stable at 20 ^{o}C. In contrast to parent **7** and **23,** allene **24** does not dimerize, even on prolonged standing at ambient temperature.

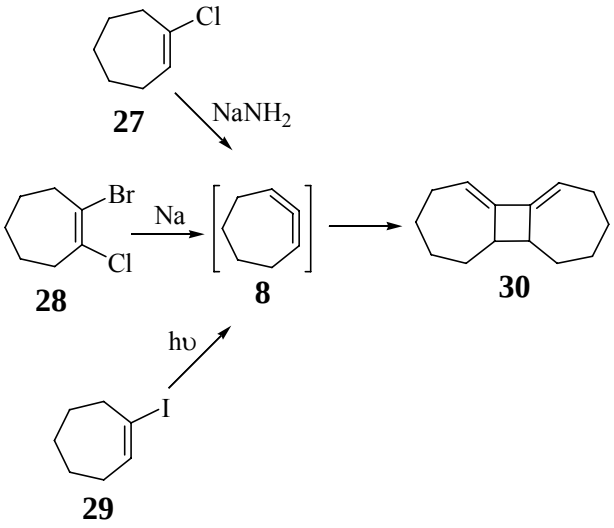


23 **24** **25**



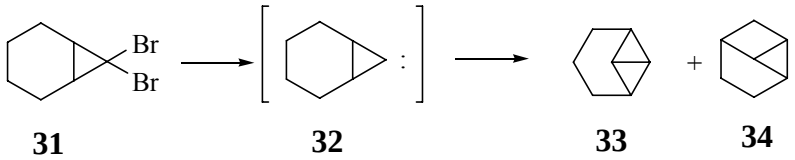
26 **7**

It was proved that cyclohepta-1,2-diene (**8**) is too reactive to be isolated, or even to be observed spectroscopically. It can easily be synthesized by elimination route, but paradoxically, Dooring-Moore- Skattebøl reactions are failed in the synthesis of **8**.



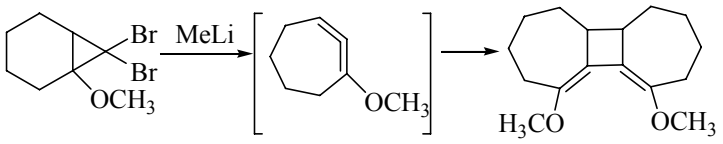
27 **28** **8** **30** **29**

It was suggested that a carbenoid structure or free carbene was assumed to be involved as the intermediate in the formation of **33** and **34**. Furthermore, DFT calculations by Schlleyer and colleagues have shown that the ring opening of **32** to **8** has unusually high activation energy barrier of 14.6 kcal/mol due to the unfavourable conformational changes in the cyclohexane moity of **32** during the reaction [8]. However, activation barriers for intramolecular CH-insertions were found to be 6.4 and 9.1 kcal/mol, respectively.



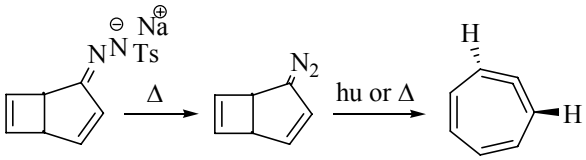
31 **32** **33** **34**

Interestingly, when the same method is applied for methoxy derivative **35**, dimer **37** can be isolated in 85% yield.



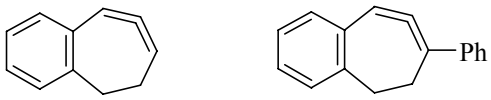
35 **36** **37**

Chapman and Abelt have used diazo precursor **38** to generate the parent cyclohepta-1,2,4,6-tetraene (**40**) [9].



38 **39** **40**

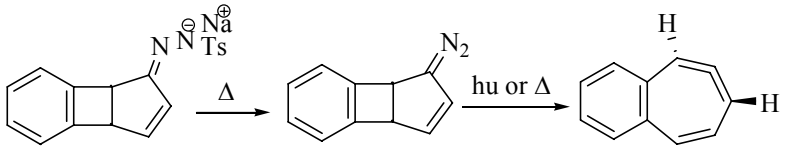
Benzannulated seven membered ring allenes such as **41** and **42** are also known.



42 **43**

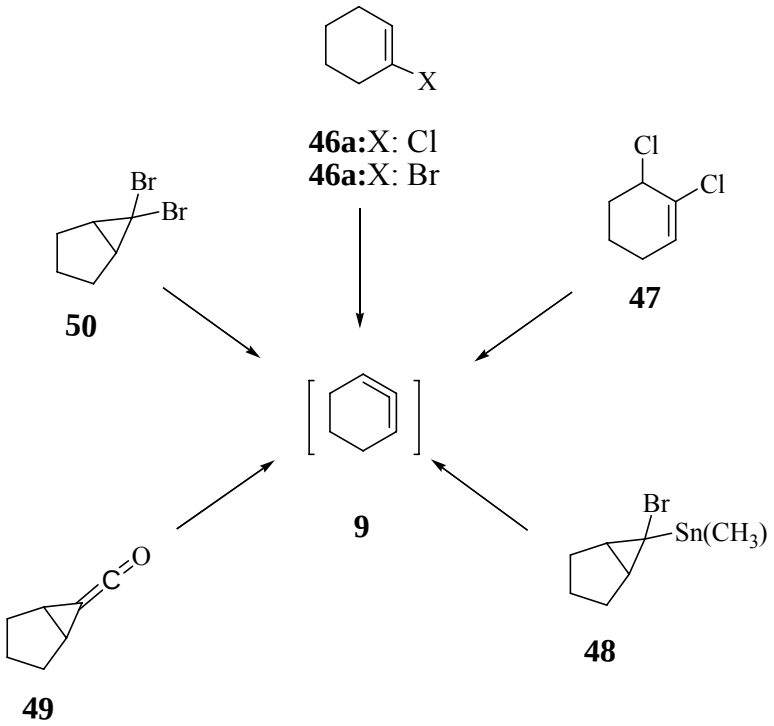
It is noteworthy that the annulation of benzene to seven membered ring changes the conformation of the ring in a manner that is suitable for the ring opening of cyclopropylidene to give allene. Moreover, the stability of the 1-halo-1-lithiocyclopropanes formed initially may increase enough to favour other reactions at the expense of allene formation [10].

In a recent matrix isolation study, McMahon and *co-workers* have reported the generation, spectroscopic characterization, photochemical and thermal reactivity of 4,5-benzocyclohepta-1,2,4,6-tetraene (**45** [11].

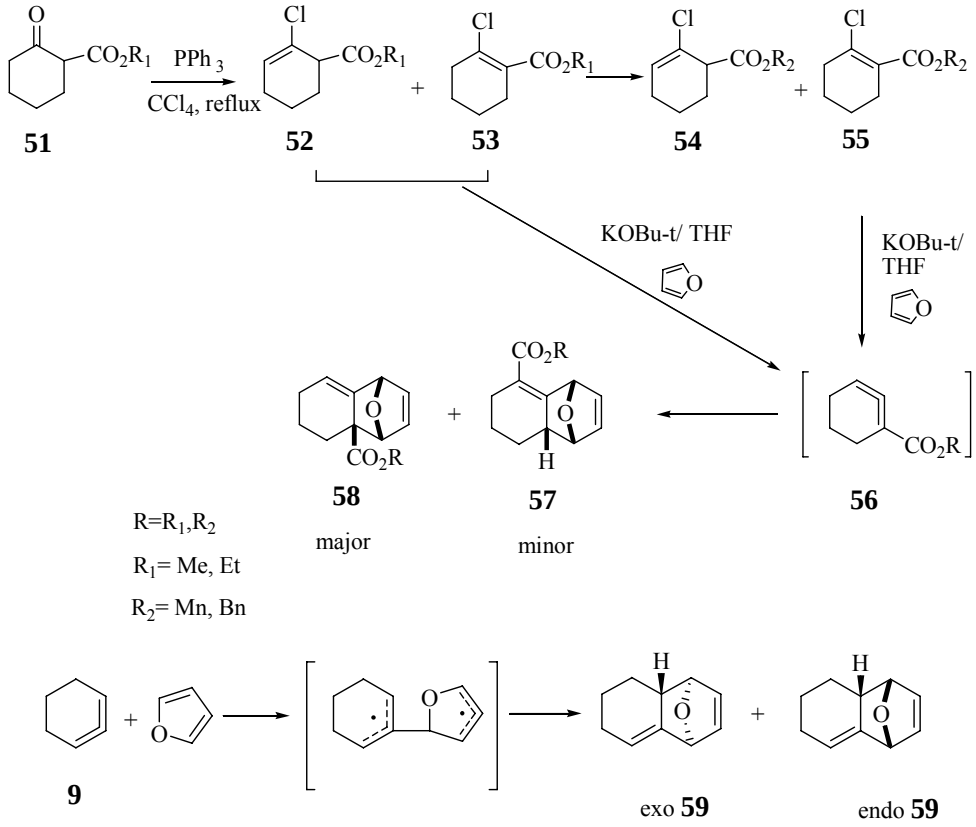


43 **44** **45**

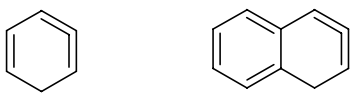
Among the cyclic allenes, cyclohexa-1,2-diene (**9**) is of much more recent vintage. Enormous efforts have been devoted towards the synthesis of cyclohexa-1,2-diene (**9**) [2].



Recently, Tolbert and *colleagues* presented convincing theoretical evidence that even [4+2] cycloadducts of cyclohexa-1,2-diene (**9**) with conjugated dienes such as furan proceed in two steps via a diradical intermediate [12].

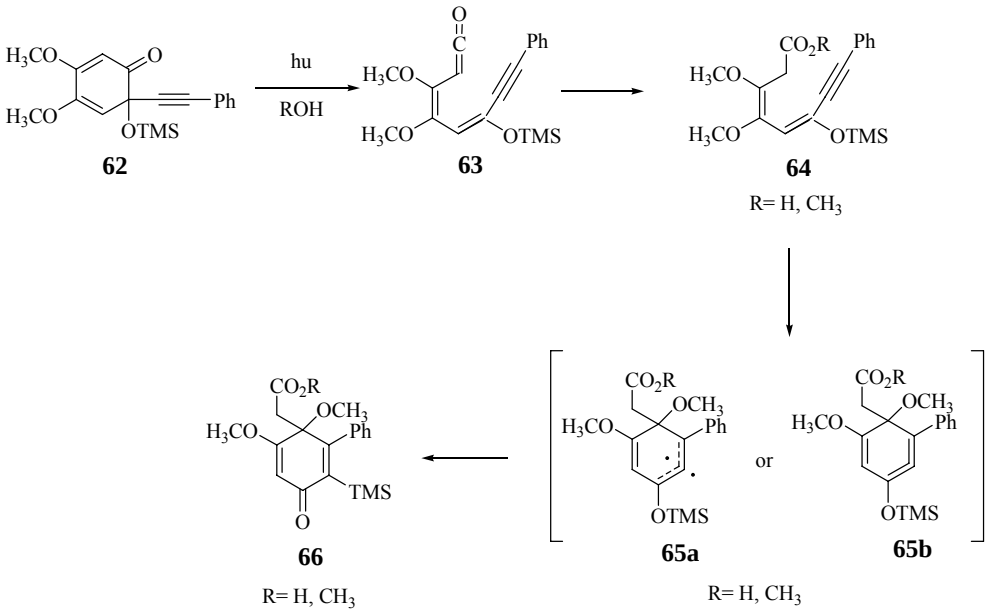


Furthermore, there are experimental evidence for the existence of cyclohexa-1,2,4-triene (**60**) and its benzannulated derivative **61** [13-15].

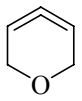


60 **61**

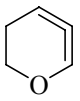
Zertuche and *co-workers* have reported the photolysis of **62** that involves the electrocyclic ring opening that generates ketene **63**, which is immediately captured by nucleophilic species present in the reaction media to give dienyne **64** [16]. They have demonstrated using HF and MP2 *ab initio* calculations that the electrocyclization of **64** can generate intermediates that can be best described as the cyclic allene **65**.



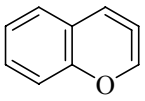
We bring this section to a close by turning the spotlight on heteroatom containing cyclic allenes **67-75** [2, 17-20]. The generation and chemical behaviour along with computational calculations about these heterocyclic allenes **67-75** are reported. The reader interested in the wider picture is referred to the corresponding materials.



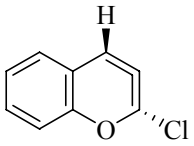
67[2]



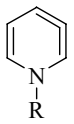
68[2]



69[2]

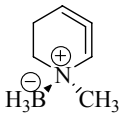


70[17]

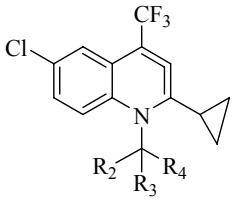


71[2] R=H
R=CH_3
R=Ph

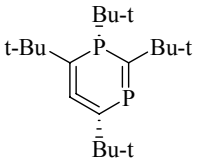
72[2]



73[18]



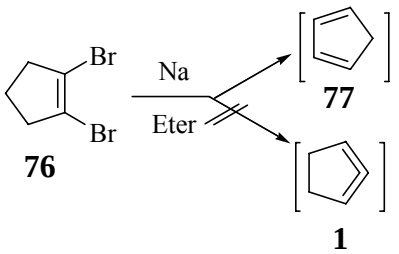
74[19]



75[20]

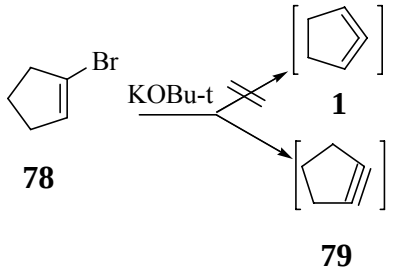
1.2. CYCLOPENTA-1,2-DIENE (1)

By far the larger numbers of reports target the cyclic allenes with rings of six- or more carbon atoms. While the examples are numerous and breadth is panoramic, it is comforting that only a relatively small number of designs concerning the five-membered ring allenes are reported. The pioneering work of Favorski over seventy years ago is our starting point. In an attempt to the synthesis of cyclopenta-1,2-diene (**1**) cyclopenta-1,3-diene (**77**) was isolated as the sole product [21].

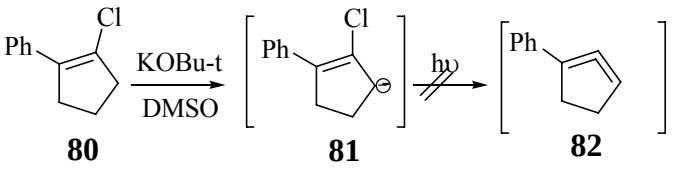


76 **77** **1**

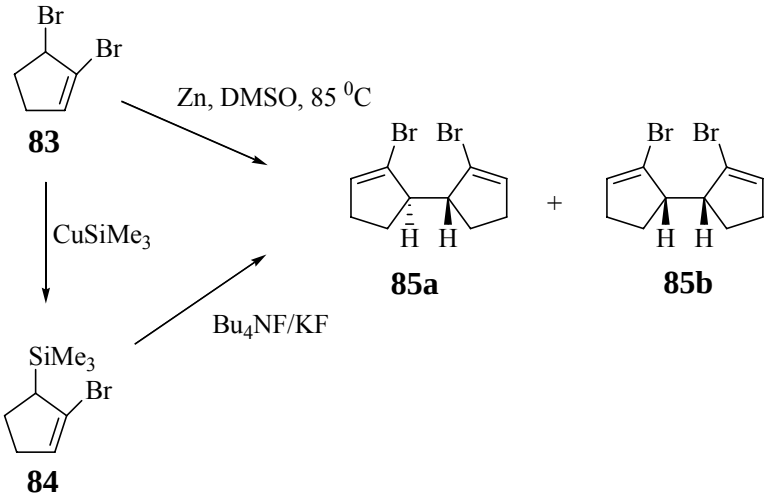
A closely related case is from Wittig's laboratory. Dehydrobromination of 1-bromocyclopentene (**78**) gave no more result except the formation of strained cyclic alkyne (**79**) [22].



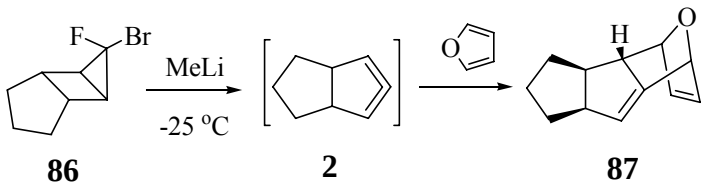
There also exist substituent-targeted versions of cyclopenta-1,2-diene (**1**). A literal extension can be found as allene **82** in the work of Johnson *et al.* where photodehalogenation of 1-chloro-2-phenylcyclopentene (**80**) was studied. All they met was a failure [23].



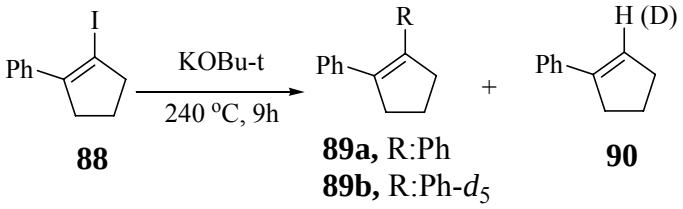
The early research of Balci and *co-workers* is also noteworthy, especially because it was found that two isomeric Wurtz-like condensation products **85a** and **85b** were formed rather than allene **1** [24-26].



It is a particular pleasure to note that a real advance on the chemistry of five-membered ring allenes, a previously intransigent target came in the year 2002. The report of allene **2** which was trapped by furan to give **87** from Balci's laboratory is therefore quite an event [27].

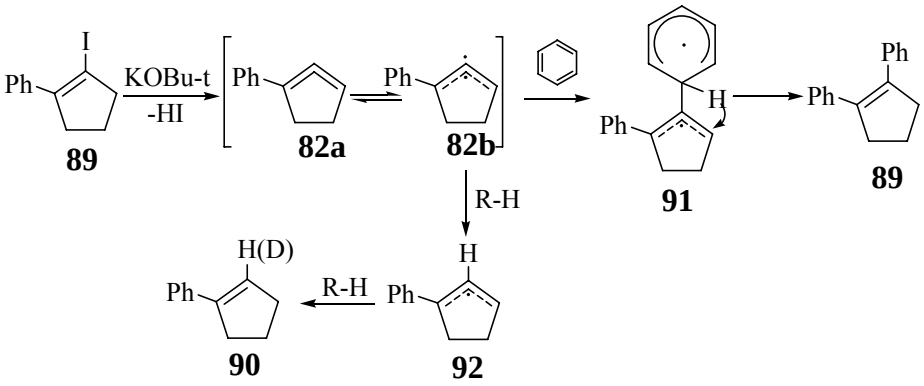


Soon after, an indirect but clever approach to allene **82** which employs the base-promoted elimination reaction of 1-(2-iodocyclopent-1-en-1yl)benzene (**88**) was presented by Balci *et al*. [28]. Repetition of the reaction under identical conditions in deuterated solvent resulted in deuterium scrambling.



88 **89a,** R:Ph **90**
89b, R:Ph-d_5

On the basis of these results, the authors assumed that the HI elimination gave the strained five-membered ring allene **82a**, in equilibrium with the diradical intermediate **82b**. This radicalic intermediate is intercepted by benzene ring (benzyl radical) followed by proton abstraction to provide the diphenyl alkenes **89**.

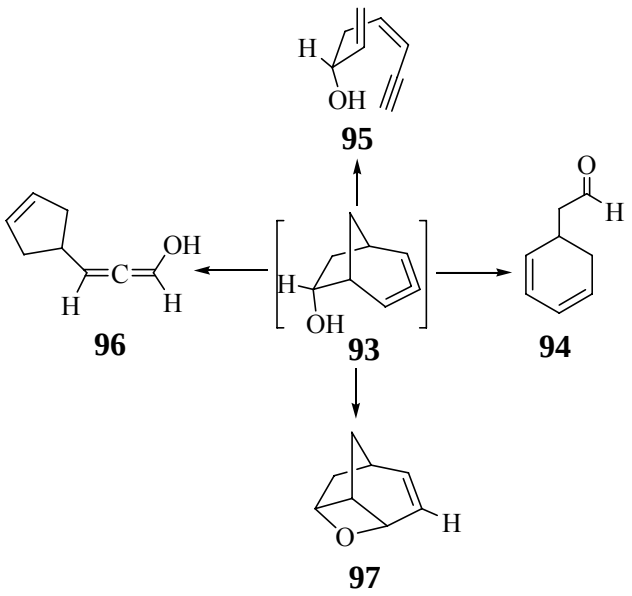


89 **82a** **82b** **91** **89**
90 **92**

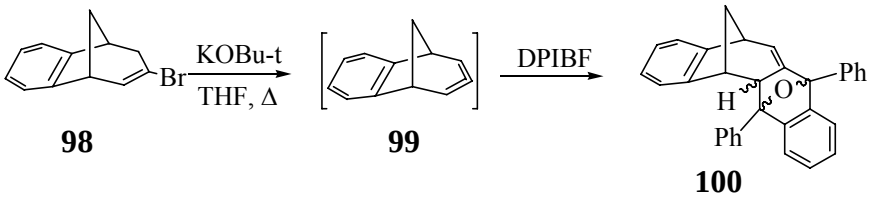
The foregoing pages have illustrated how synthetic chemists most of whom have an academic flavor have constructed cyclic diverse allenes. Our final concern in this section will be strained bicyclic allenes.

1.3. STRAINED BICYLIC ALLENES

As implied at the start of this chapter, we will only show the recent trends unless otherwise required. We launch this segment of the survey with a computational study of Sevin *et al.* Sevin and Dogan have focused on the possibilities of intramolecular trapping and fragmentation products of *endo*-bicyclo[3.2.1]octa-2,3-dien-6-ol (**93**) with the concerted reaction mechanism by using quantum chemical calculations [29]. The computational calculations show that the formations of cyclohexa-2,4-dien-1-ylacetaldehyde (**94**) and (5Z)-octa-1,5-dien-7-yn-3-ol (**95**) are competitive and appear more favour than the intramolecular trapping product 2-oxatricyclo[4.2.1.$0^{3,8}$]non-4-ene (**97**).

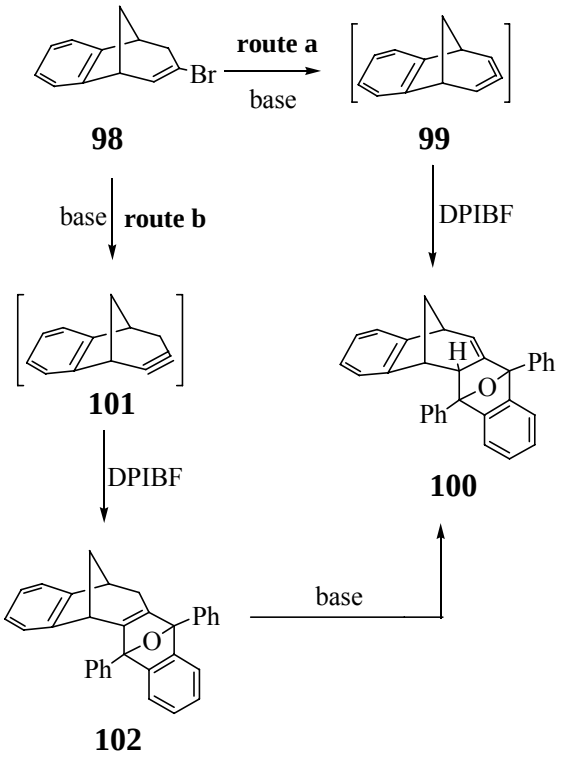


In a clutch of papers Balci *et al.* investigated the fate of bicyclic allene **99** [26, 30-35]. Compound **98** was treated with KOBu-t in the presence of DPIBF and compound **100** was isolated of which formation is most reasonably explained by the intermediacy of allene **99**.

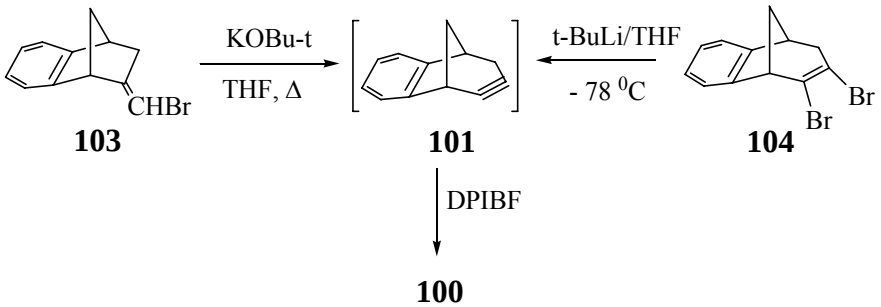


98 **99** **100**

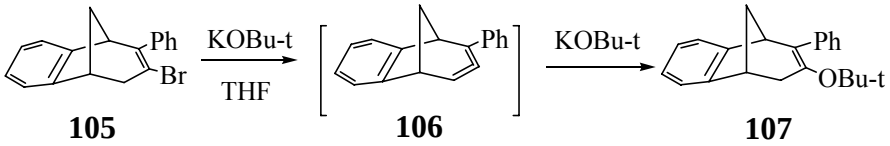
However, as they have noticed, an alternate mechanism for the formation of **100** may operate via the bicyclic alkyne **101** in which the base-promoted isomerization of the double bond would give the observed products.



In order to distinguish between these two possible mechanisms, Balci *et al.* have investigated the generation of the alkyne **101** on two independent ways and isolated the same cycloadducts **100**, which clearly indicates that the intermediate is the alkyne **101**.

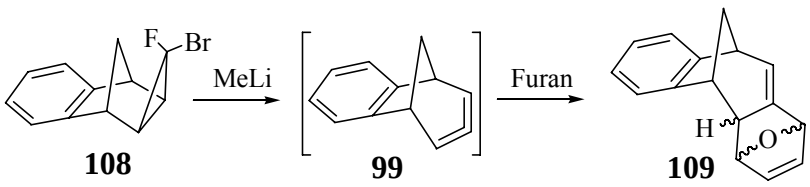


Since even with these results allene formation cannot be excluded in the base promoted reaction of **98**, they have repeated the reaction by using phenyl derivative **105**. The isolation of enol ether **107** indicated the formation of allene **106**, which was trapped by *tert*-butoxide ion.



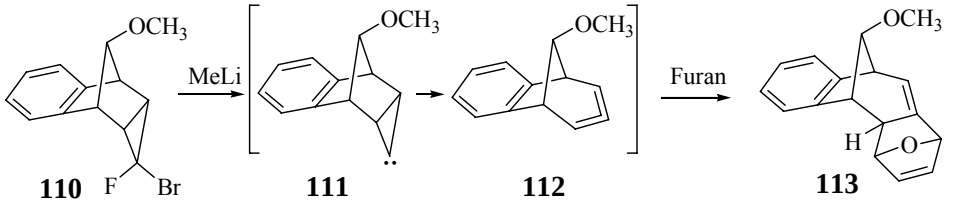
105 **106** **107**

Balci's laboratory continious its expertise in strained bicyclic allenes by developing a series of synthetic routes. The long story of allene **99** ends up with a certain entrapment by furan [36].

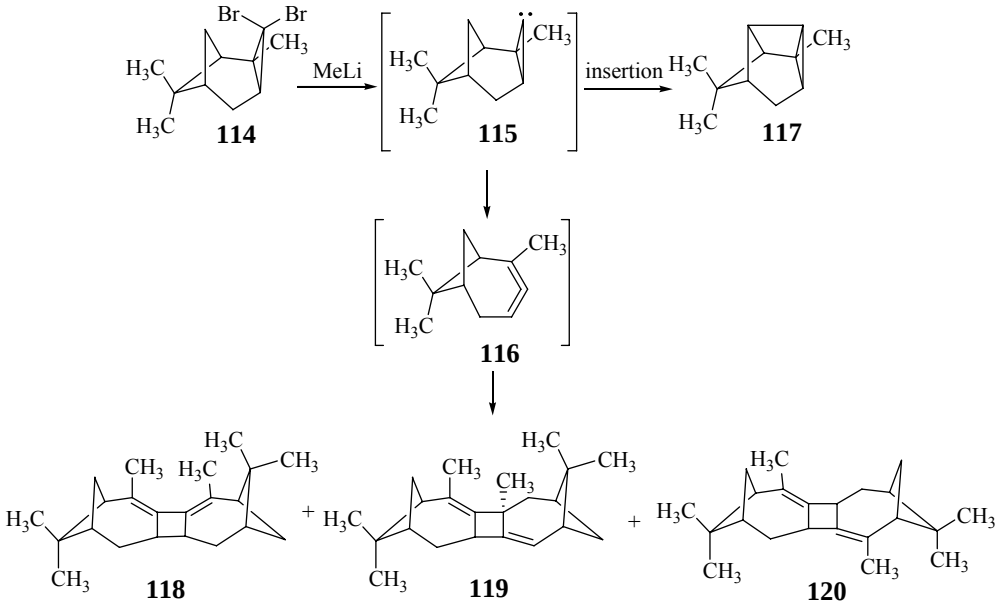


108 **99** **109**

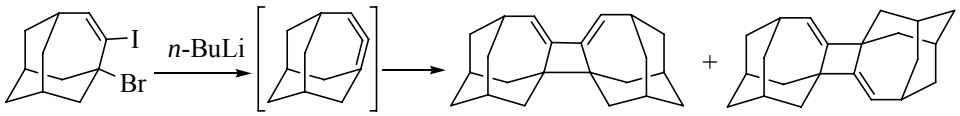
Furthermore, Balci *et al.* have synthesized **110** in order to test the behaviour of the *endo*-cyclopropylidene **111** [37]. When **110** was subjected to MeLi in the presence of furan, the reaction gave **113** via allene **112**.



On the other hand, the application of carbenoid method to α-pinene resulted in the formation of products **117**-**120** [38]. The formation of **117** clearly indicates the presence of free carbene **115** that undergoes CH-insertion whereas three dimeric products **118**-**120** confirms the existence of the allene **138** at the same time in the reaction mixture.



We conclude this section with the report of Okazaki *et al.* concerning a novel tricyclic allene **122**, which readily dimerizes or being trapped with DPIBF [39].

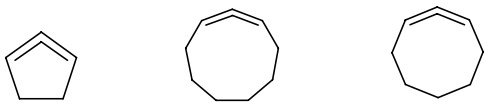


121 **122** **123** **124**

To close, even this curtailed survey serves to illustrate the wide scope of strained cyclic allenes in its most basic manifestation. Combining those streams of thought must surely cause a further flowering of this already fertile field which suggests there are many more to come.

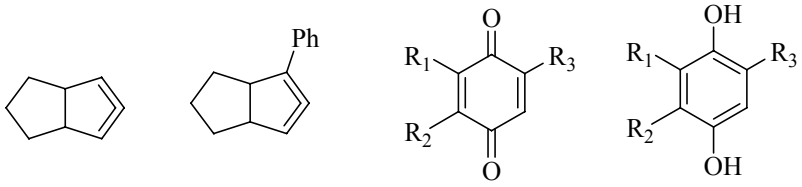
1.4. THE AIM OF THE STUDY

An allene incorporated into a carbocyclic ring of nine or more carbon atoms is relatively unstrained. Cyclonona-1,2-diene (**6**) is a distillable liquid while cycloocta-1,2-diene (**7**) rapidly dimerizes at room temperature and its ^{1}H-NMR spectrum has been measured at –60 ^{o}C. However, if the ring size is decreased, the linear perpendicular allene will be twisted and bent until, at some point, the energy gained by π bonding in the double bonds will be insufficient to offset the increased strain. Furthermore, ring constraints will exert torsion toward a planar arrangement of ligands. Therefore, one of the fundamental questions is the influence of ring size on the barrier to π bond rotation. Cyclopenta-1,2-diene (**1**) still remains elusive.



1 **6** **7**

Herein we wish to unveil a review of our research related to desperately seeking for five-membered ring allenes such as, cyclopenta-1,2-diene (**1**) and some of its derivatives, e.g. **2**, and **3**. Furthermore, we will address a simple, mild and efficient method for the reduction of 1,4-benzoquinones **4** to corresponding hydroquinones **5**.



2 **3** **4** **5**

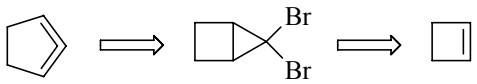
Figure 3. The targeted allenes **2-3**, 1,4-benzoquinones **4** and hydroquinones **5**.

CHAPTER 2

RESULTS AND DISCUSSION

In principle, one of the best ways to generate allenes directly is rearrangement of cyclopropylidenes to cyclic allenes [27]. This method has been successfully applied to the synthesis of six- and seven-membered ring allenes as described in the previous chapter. For the generation of a five-membered ring allene, the addition of a dihalocarbene to a cyclobutene unit is necessary.

Our initial exploratory efforts directed towards the generation of five-membered ring allenes involved the synthesis of key compounds as precursors. In the first episode, we focused on the generation of cyclopenta-1,2-diene (**1**). Retrosynthetic path which ends up with cyclobutene (**126**) was depicted below.



1 **125** **126**

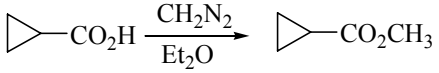
2.1. Cyclopenta-1,2-diene (1).[†]

2.1.1. The Synthesis of Cyclobutyl-4-methylbenzenesulfonate (131).

[†] A similar work was found as a dissertation presented in 1989 to the faculty of the Graduate School of Atatürk University by M. Ceylan in partial fulfillment of the requirements for the degree of Master of Science.

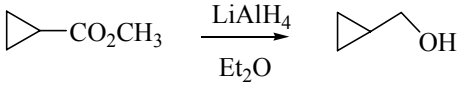
In a search of a convenient source of the required cyclobutene (**126**), we have found that the cyclobutyl tosylate **131** can provide, in good yields, cyclobutene (**126**) free of its isomeric impurities [40]. The precursor of the target alkene, cyclobutyltosylate **131** was prepared from cyclopropyl carboxylic acid (**127**) via a four-step synthesis.

First of all, commercial cyclopropyl carboxylic acid (**127**) was converted to its methyl ester by treatment with diazomethane in ether.



127 **128**

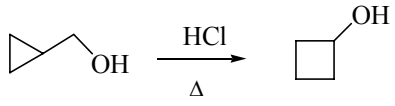
The hydride reduction of ester **128** [‡] in ethereal solution at room temperature resulted in the formation of alcohol **129**.



128 **129**

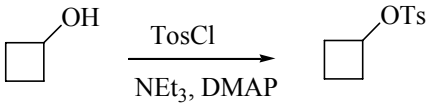
Acid catalyzed rearrangement of alcohol **129** furnished **130** in moderate yield.

[‡] See Appendix for spectral data. Spectral data is not discussed except for new compounds.



129 **130**

Subsequent treatment of **130** with tosylchloride gave ester **131** exclusively.

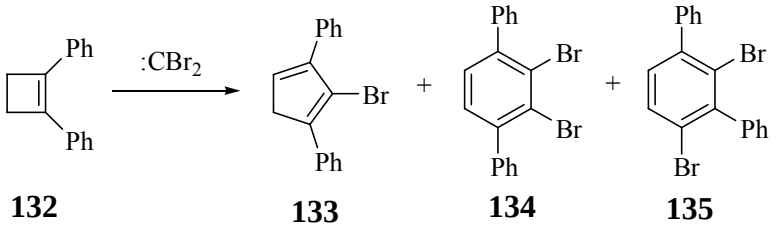


130 **131**

2.1.2. The synthesis of Cyclobutene (126) and Carbene Addition.

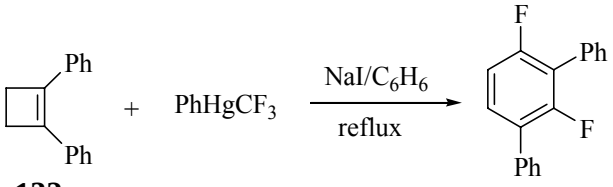
Carbenes are versatile intermediates that undergo insertion, rearrangement and facile addition reactions and their importance for synthetic chemists can hardly be overestimated. The most common and thoroughly investigated reaction of carbenes is their addition to carbon-carbon double bonds. Although much literature concerning dihalocarbene reactions with open chain and cyclic alkenes larger than four-membered rings exists, only a few studies with small-ring alkenes have been reported [27, 41-42].

Brinker and *colleagues* have reported that when 1,2-diphenylcyclobutene (**132)** was treated with dibromocarbene, the reaction gave derivatives of cyclopentadiene and of benzene **133-135** [42b].



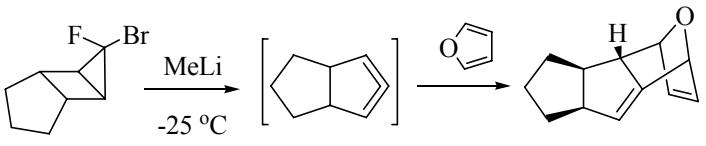
132 **133** **134** **135**

Very recently, Lewis and *co-workers* have reported that the reactions of difluorocarbene with 1,2-diphenylcyclobutene (**132**) gave 1,3-difluoro-2,4-diphenylbenzene (**136**) in one step by ring expansion [42b].



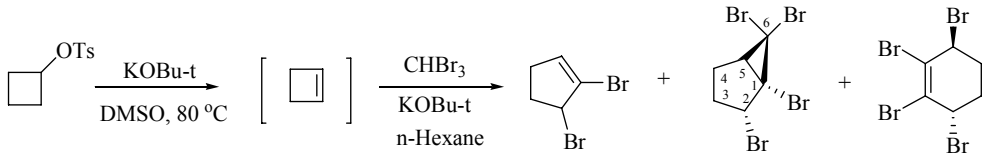
132 **136**

Moreover, we have reported the synthesis of *gem*-bromofluorocyclopropane **86** and its conversion to the corresponding strained cyclic allene **2** [27].



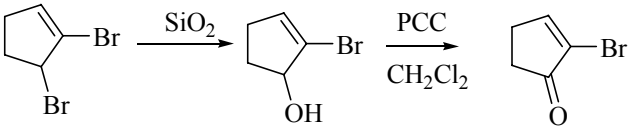
86 **2** **87**

In the light of these literature data, we have applied the carbene chemistry to cylobutene **126** in order to get the corresponding 5,5-dibromobicyclo[2.1.0]pentane (**125**). Upon treatment with potassium *t*-butoxide in dimethylsulfoxide at 80 ^{o}C the tosylate **131** underwent base induced elimination to give cyclobutene (**126**, bp. 2 ^{o}C), which was carried in nitrogen into a trap containing a solution of $CHBr_3$ in *n*-hexane cooled with solid CO_2 (-80 ^{o}C). This was followed by warming the solution to –30 ^{o}C and subsequent addition of base at this temperature. To our delight, the reaction gave adducts **83**, **137**, and **138** in a ratio of 1:4:8, respectively.



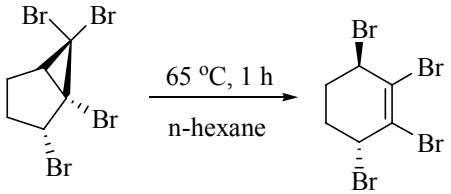
131 **126** **83** **137** **138**

The spectroscopic data for 1,5-dibromocyclopentene **83** was in good agreement with those previously reported [43]. The attempt to purify compound **83** indicated that it hydrolyses to a small extent to the corresponding alcohol **139** during the column chromatography. The structure of alcohol **139** was also proved chemically by oxidation to the known enone **140** [43].



83 **139** **140**

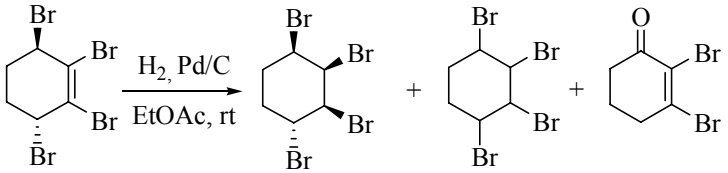
The structure of 1,2,6,6-tetrabromobicyclo[3.1.0]hexane (**137**) was elucidated on the basis of NMR and MS spectroscopic data. The GC-MS spectrum showed the presence of four bromine atoms with an M^+ signal corresponding to 396. The ^1H NMR spectrum of **137** revealed five sets of proton signals; a doublet of doublets centered at 4.66 ppm, a doublet of doublets of doublets at 2.03 ppm and three sets of multiplets at 2.39, 2.66 and 2.84 ppm. The exact configuration of the bromine atom at the C-2 carbon atom could not be determined. However, when the cyclopropane adduct **137** was heated in *n*-hexane at 65°C, it rearranged smoothly to the 1,2,3,6-tetrabromocyclohex-1-ene (**138**), thus clearly indicating an isomeric relationship between these two compounds. It was also noted that this rearrangement of **137** to **138** takes place upon standing at room temperature for a few days.



137 **138**

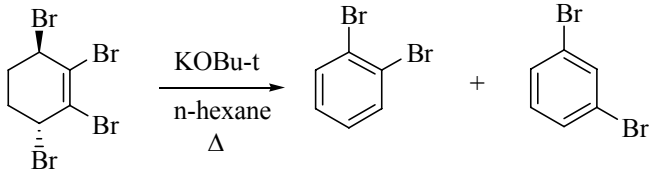
The isomeric tetrabromide **138** showed a broad doublet (J = 2.3 Hz) at 4.77 ppm and two quasi doublets (J = 10.7 Hz) centered at 2.52 and 2.07 ppm, respectively. The three-line ^{13}C-NMR spectrum clearly shows the symmetry in the molecule. However, on the basis of the NMR data alone we were not able to distinguish the two possible isomeric tetrabromides (*cis*-, and *trans*- configurations of the bromine atoms at the C-3 and C-6 carbon atoms). For that reason, we have done some chemistry with this compound to reveal the exact configuration of bromine atoms.

For example, catalytic hydrogenation of **138** in ethyl acetate followed by column chromatography on silica gel gave a mixture of two inseparable tetrabromides **141** and **142** (4:1), (the configuration of **142** is not known), along with 2,3-dibromocyclohex-2-en-1-one (**143**) whose formation mechanism will be investigated elsewhere.



138 **141** **142** **143**

On the other hand, the HBr elimination from **138** gave a 3:1 mixture of aromatic compounds of which spectral data were consistent with 1,2-dibromobenzene (**144**) and 1,3- dibromobenzene (**145**), respectively [44].



138 **144** **145**

Finally, the *trans*-configuration of the bromine atoms at the C-3 and C-6 carbon atoms was determined unambiguously by X-ray crystallographic analysis to be *trans*- (Fig. 4).

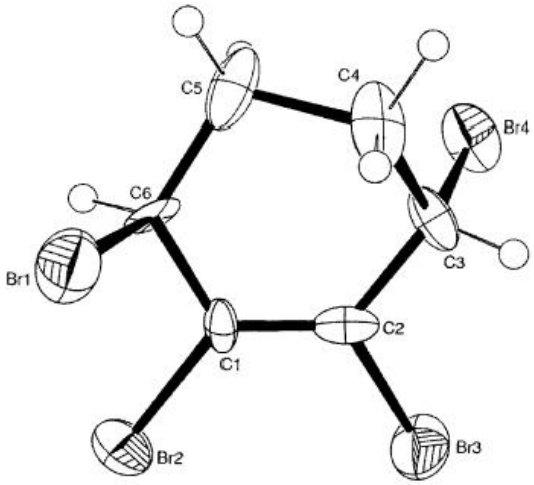
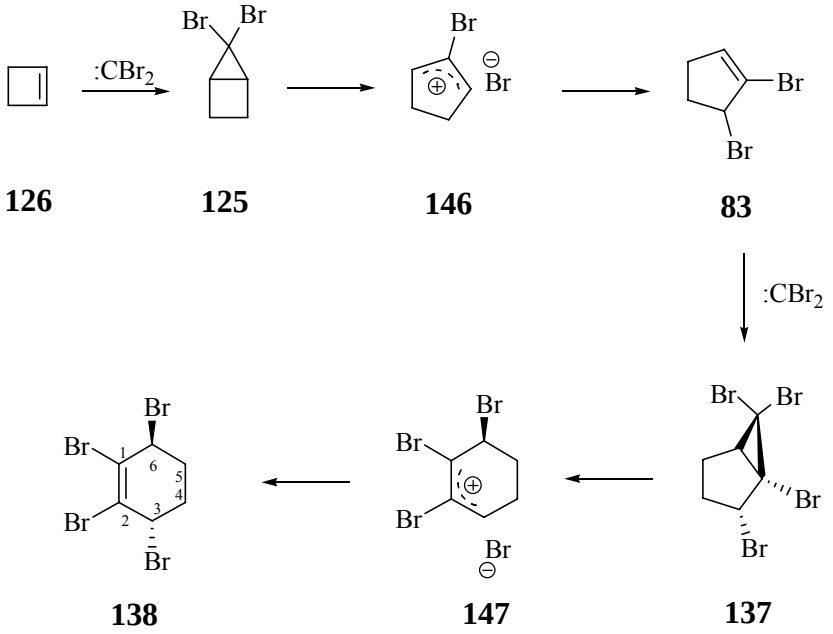


Figure 4. The X-ray crystal structure of **138**.

The mechanism for the formation of the products presumably involves the intermediacy of the strained 5,5-dibromobicyclo[2.1.0]pentane (**125**). Electrocyclic ring opening reaction of **125** produces first the cation **146**. The dissociation of the bromide ion and the opening of the three membered-rings take place at the same time. Capture of the bromide gives the dibromide **83**. Addition of a second mole of $:CBr_2$ to the double bond in **83** forms the bicyclic addition product **137**. The exclusive formation of the tetrabromide **138** upon heating of **137** indicates that the ring opening process is governed by the Woodward–Hoffman rules [45].

The *trans*-configuration of the bromine atoms at C-3 and C-6 carbon atoms in **138** proves furthermore the *trans*-configuration of the bromine atom at C-2 and the cyclopropane ring in **137**. It is noteworthy that the addition of the carbene to **83** is directed towards the sterically less-hindered face of the double bond, which is in agreement with the stereochemistry of the tetrabromide **137**.

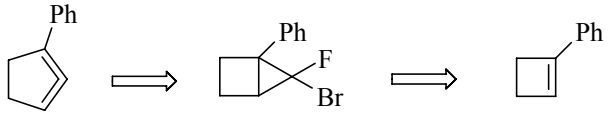


126 **125** **146** **83** **137** **147** **138**

These results clearly suggest that cyclopenta-1,2-diene (**1**) remains a though nut to crack due to the unavailability of a suitable precursor, i.e. 5,5-dibromobicyclo[2.1.0]pentane (**125**).

At this stage we turned our attention to phenyl derivative **82** where the presence of a benzene ring might be a mitigating factor for the availability of the corresponding carbene adducts, e.g. **148**. Furthermore, it would overwhelme the tedious and chancy reaction conditions involved in the case of naked cyclobutene

(**126**) which is a gas at room temperature. That is why cyclobutenylbenzene (**149**) was taken into account.



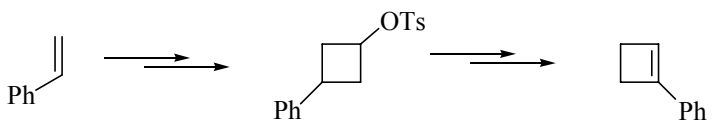
82 **148** **149**

2.2. 1-Phenyl-cyclopenta-1,2-diene (82).

Our studies commenced with a comprehensive screen of substrates as potential precursors.

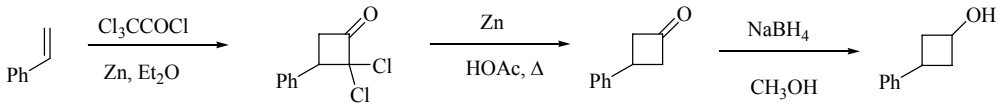
2.2.1. Attempted Synthesis of Cyclobutenylbenzene (149) Via Base Induced Elimination.

We first tried to synthesize phenylcyclobutene **149** by starting from styrene **150**. We anticipated that the base induced elimination of sulfonate from **154** might result in the formation of thermodynamically favored cyclobutene **149**.



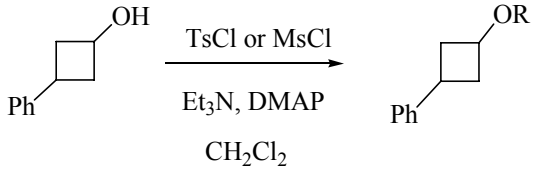
150 **154** **149**

The reported synthesis of **155** began with the dichloroketene addition to styrene (**150**) [46a]. Displacement of chlorines in **151** with hydrogen by treatment with Zn/ HOAc [46b], followed by $NaBH_4$ reduction provided alcohol **153** [47] in good yield.



150 **151** **152** **153**

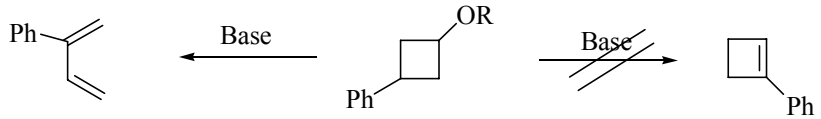
Conversion of alcohol **153** to sulfonic esters **154** was achieved by the treatment with *p*-toluenesulfonylchloride and methanesulfonylchloride in the presence of NEt_3 and catalytic amount of DMAP in CH_2Cl_2, respectively [48].



153

154a R:Ms
154b R:Ts

We were unpleased to find that attempted base induced eliminations of sulfonates furnished the open chain partner **155** instead of the desired cyclobutene **149**, unfortunately.

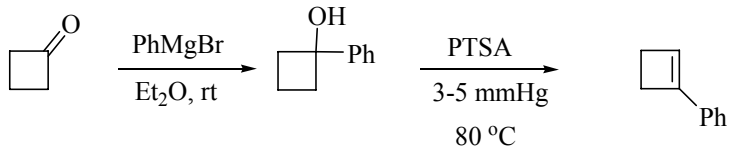


155 **154a** R:Ms **154b** R:Ts **149**

Hence, the acid catalyzed formation of alkene **149** was considered.

2.2.2. Synthesis of 1-Phenylcyclobutene (149) Via Acid Catalyzed Elimination.

Treatment of cyclobutanone (**156**)[‡] with Grignard reagent resulted in the formation of alcohol **157**, quantitavely [49-50]. To our delight, alcohol **157** underwent water elimination to give phenylcyclobutene **149** in the presence of PTSA as catalyst at some pressures, albeit in low yield.

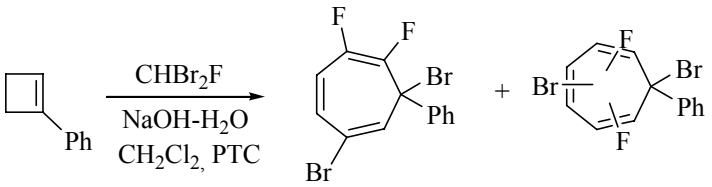


156 **157** **149**

[‡] Attempted synthesis of **156** gave very low yields unless otherwise not formed.

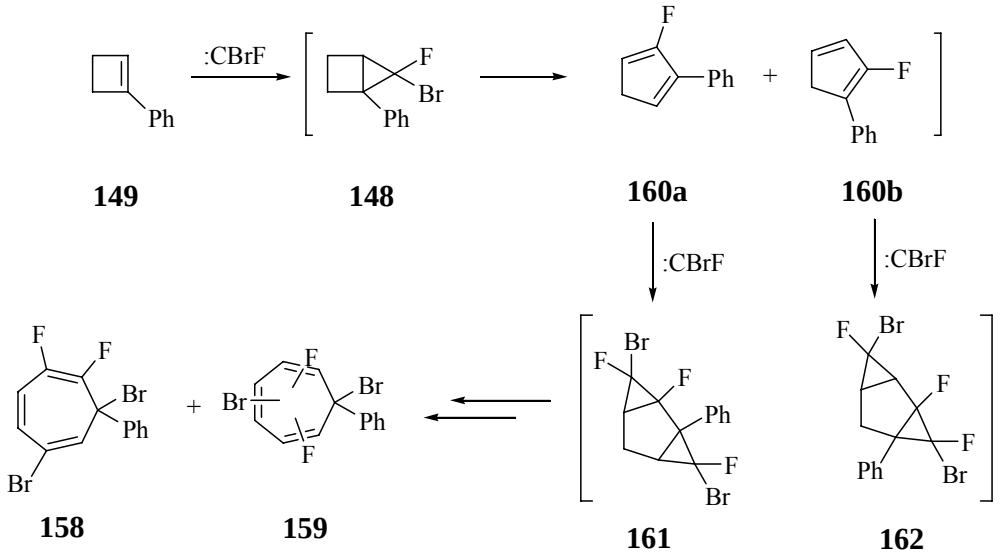
2.2.3. Carbene Addition to 1-Phenylcyclobutene (149).

The addition of bromofluorocarbene under phase transfer conditions led to the formation of a complex product mixture. Repeated column chromatography on fluorisil only gave adducts **158** and **159** which remained uncharacterized due to their inexpediency.

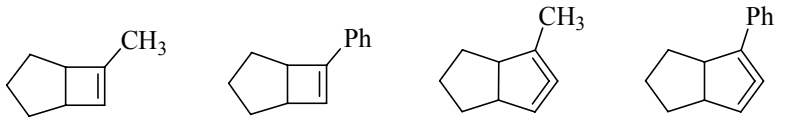


149 **158** **159**

The formation seven-membered ring product suggests that the initially formed intermediate *gem*-bromofluorocyclopropane **148** undergoes facile ring-opening reaction to give cyclopentadienes **160a** and **160b**. However, the next addition of carbene to cyclopentadienes **160a** and **160b** would probably afford bis-adducts **161** and **162** which would further rearrange to corresponding products **158** and **159** via ring opening reaction. These results bear the assumption that phenyl ring attached to cyclopropane ring plays an important role in the ring opening reaction.



In order to get further insights into the affects of substituents as -CH_3; and -C_6H_5, we decided to do the same chemistry with the bicyclic appendages: namely 6-methylbicyclo[3.2.0]hept-6-ene (**163**) and 6-phenylbicyclo[3.2.0]hept-6-ene (**164**). Furthermore, there is no escaping the fact that isolation of the corresponding *gem*-bromofluorocyclopropanes, if possible, have ample opportunity for the generation of corresponding allenes **165** and **3**.

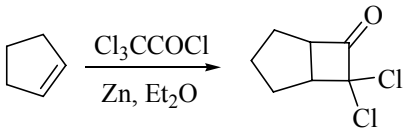


In the following episode, we will first try to synthesize the cyclobutenes **163** and **164** as the precursors for the target allenes **165** and **3**, respectively. We envisaged

that both of the bicyclic skeletons can be accessed by starting from cyclopentene **166**.

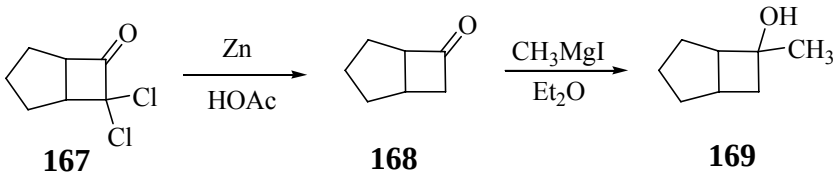
2.3. Attempted Synthesis of 6-Methylbicyclo[3.2.0]hept-6-ene (163).

Here, cyclopentene **166** undergoes cycloaddition with *in situ* generated dichloroketene to give dichlorocyclobutanone **167** [51].



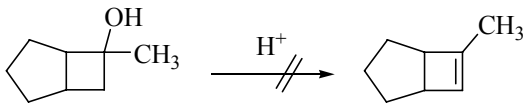
166 **167**

As compound **167** was synthesized, the next step was to remove the chlorines in order to obtain the ketone **168**. The adduct **167** was dissolved in acetic acid and given drop wise at room temperature to a mixture of zinc dust and acetic acid to give cyclobutanone **168** in good yield. Then the addition of Grignard reagent prepared from CH_3I and Mg resulted in the formation of alcohol **169** almost quantitavely, of which spectral data was consistent with the literature [52].



167 **168** **169**

Nonetheless, attempted acid catalyzed dehydration of **169** resulted only in the recovered starting material, thus impeding the generation of allene **165**.

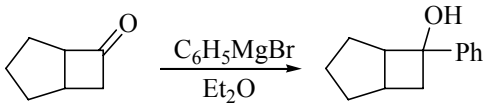


169 **163**

Eventually, the phenyl-derived cyclobutene **165** was taken into account.

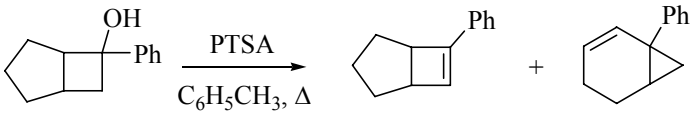
2.4.1. Synthesis of 6-Phenylbicyclo[3.2.0]hept-6-ene (164).

Bicyclic ketone **168** was treated with phenyl magnesium bromide (generated from bromobenzene and magnesium) to give alcohol **170** almost quantitatively [53].



168 **170**

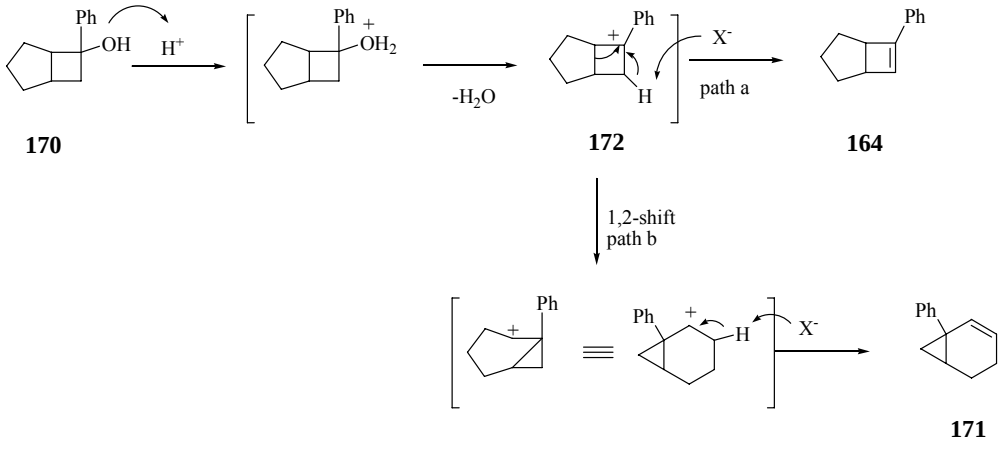
Gratifyingly, the acid catalyzed dehydration of alcohol **170** resulted in the formation of cyclobutene **164** [54a] along with norcaren **171** in a ratio of 3:1, respectively [54b].



170 **164** **171**

The presence of cyclopropane ring on **171** was proven on the basis of the coupling constants between proton and carbon nuclei (J_{CH}) of which size strongly depends on the s character of the hybridization on the carbon [J_{CH}= 500. (s ratio)] . From the proton coupled ^{13}C-NMR spectrum of the compound **171**, the coupling constants between the cylopropane carbons and protons ($^1J_{CH}$) were found to be 158.4 and 160.4 Hz, which are characteristic of the cyclopropane carbons [55].

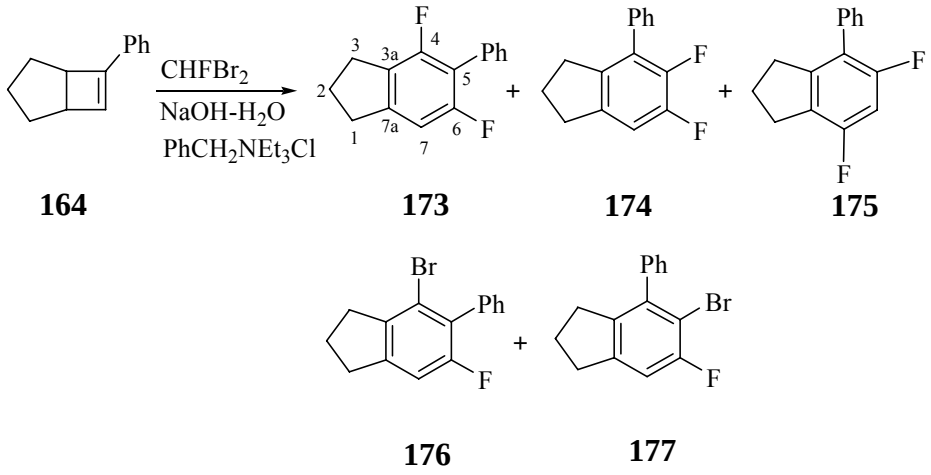
The formation of the products can be rationalized on the basis of the intermediacy of carbocation **172**, which in turn eliminate a hydrogen to give **164** (path a), or 1,2-alkyl shift before elimination to give **171** (path b).



170 **172** **164** **171**

2.4.2. Carbene Addition to 6-Phenylbicyclo[3.2.0]hept-6-ene (164).

To our surprise, the addition of bromofluorocarbene to **164** under phase transfer conditions led to the formation of a complex mixture of products. GC-MS analysis indicated the formation of five different compounds with two different M^+ signals at 229 and 288/290. We obtained compounds **173-177** after repeated column chromatographic separations on 1% $AgNO_3$ in silica gel.



164 **173** **174** **175**

176 **177**

The ^{1}H-NMR spectrum of **173** shows four sets of signals: a multiplet for the protons of the phenyl ring at 7.35-7.22 ppm, a doublet at 6.81 ppm (J= 9.0 Hz, 1H, H_7) along with a triplet at 2.86 ppm (J= 7.4 Hz, 4H) and a quintet at 2.05 ppm (J= 7.7 Hz, 2H), which indicates the presence of three adjacent methylenic protons in the structure. A notable feature of the proton spectrum was the absence of a similar coupling constant of H_7 (9.0 Hz) to any other proton: the magnitude of the coupling constant suggested this splitting arises from the interaction of the proton with a fluorine atom which is ortho to this proton ($^2J_{HF}$ = 8-12 Hz) [56]. Furthermore, ^{19}F-NMR spectrum has shown the presence of two fluorine atoms at -118.8 and -117.6 ppm, which are in the range of the chemical shifts of fluorine

atoms attached to the aromatic ring, giving rise to doublets with a coupling constant of 5.6 Hz of which magnitude clearly suggests that the two fluorine atoms are meta ($^4J_{FF}$) to one another [56].

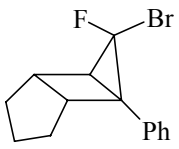
Table 1. ^{19}F-NMR chemical shifts (in ppm) and coupling constants (in Hz) with spin multiplities for fluoro-indane derivatives in $CDCl_3$.

Compound	**F_a**	**F_b**	**J_{FF}**
173	-117.6 (d)	-118.8 (dd)	$^4J = 5.6$
174	-140.6 (dd)	-146.2 (dd)	$^3J = 20.3$
175	-115.6 (t)	-117.4 (t)	$^4J = 7.0$
176	-113.3 (d)	--	--
177	-119.3 (d)	--	--

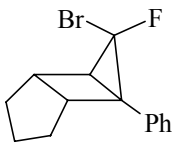
The comprehensive evidence for the structure **173** comes from the proton-decoupled ^{13}C-NMR spectrum in conjunction with 2D-NMR (DEPT-135, HMQC and HMBC) experiments. The aromatic carbon with an attached proton (δ 107.8), as shown by the DEPT experiment, is split into doublets of doublets (J_{CF} = 23.5 and 3.6 Hz). The magnitude of these coupling constants indicates that this carbon is ortho to one fluorine and para to the other [56]. The carbon holding the phenyl ring resonates at 116.3 ppm as triplets with a coupling constant (J_{CF}) of 19.0 Hz which strongly indicates the presence of two fluorine atoms in the ortho position of this carbon. Similar C-F coupling constant arguments can be made for the doublets of doublets at δ 126.0 (C_{3a}, J_{CF} = 19.6 and 2.8 Hz, ortho to one fluorine and para to the other) and 146.8 (C_{7a}, J_{CF} = 9.5 and 7.8 Hz, meta to both fluorines). The carbon atoms bonded to the fluorines appear as doublet of doublets centered at δ 159.5 (J_{CF} = 245.1 and 5.7 Hz), and δ 156.3 (J_{CF} = 247.4 and 7.8 Hz). The magnitude of the smaller C-F coupling constant in these carbon resonances unambiguously indicates that the two fluorine atoms are meta to one another [56].

When taken together, these data firmly establish the structure of the previously unknown compound **173**.

The observation of such products as **173-177** led us to propose a complex mechanistic scenario for the addition of bromofluorocarbene to cyclobutene **164**, which presumably involves the formation of *gem*-bromofluorocyclopropane **178**. The bromofluoro carbene can approach the double bond in **164** in two different ways, which in turn leads to the formation of **178a** (*endo*-fluoro, *exo*-bromo) and **178b** (*endo*-bromo-*exo*-fluoro). The formation of **178b** where the bulky bromine atom is in the *endo*-position cannot be excluded due to the steric reasons. As **178** is formed, it undergoes electrocyclic ring-expansion in order to decrease the accommodated strain arising from the fusion of three small rings (*three-*, *four-*, and *five*-membered rings, respectively).



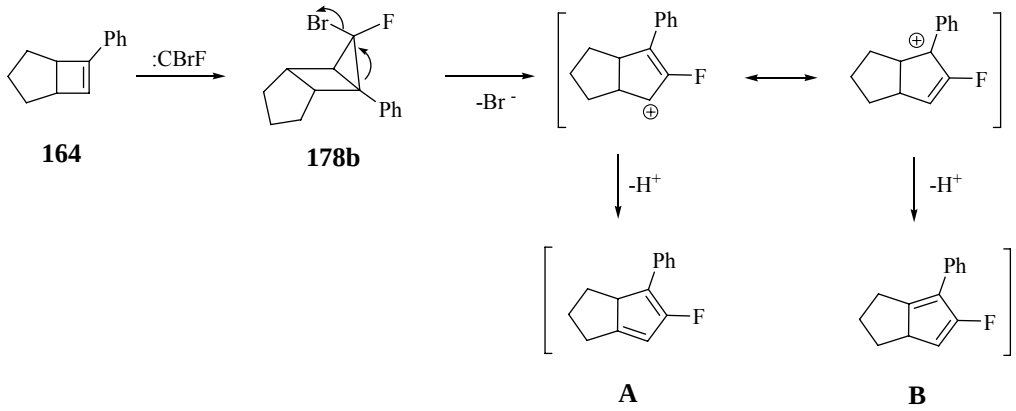
178a



178b

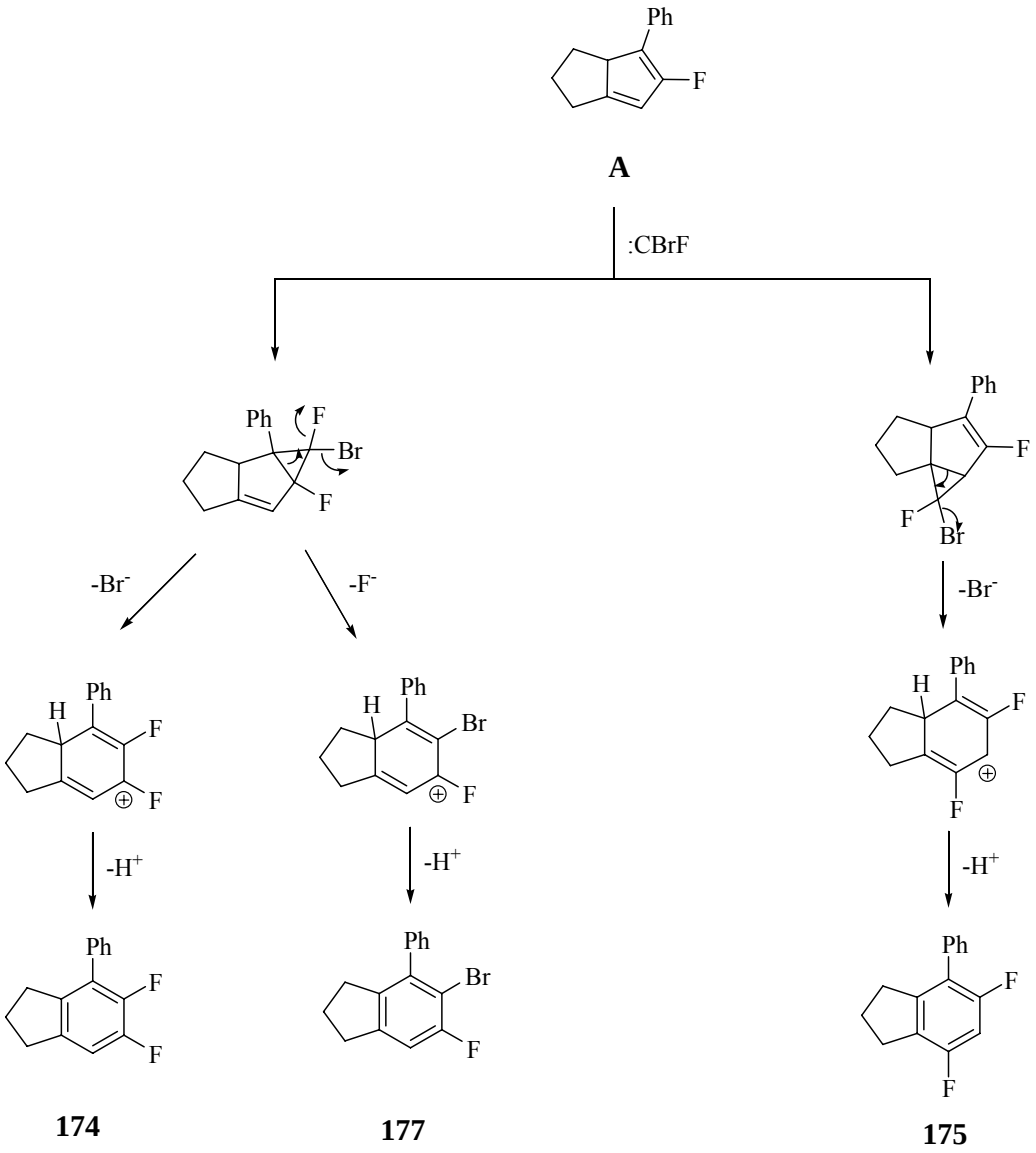
The ring opening reaction has been rationalized in terms of orbital symmetry conservation. It has been well established that the departing halide is the one that is in the *endo* position. According to the Woodward-Hoffmann rules [45], the isomer **178b** should easily undergo a ring opening reaction, whereas the isomer **178a**, where the bromine atom is in the *exo* position, should be stable. However, careful examination of the reaction mixture did not reveal the presence of the isomer **178a**. Therefore, we assume that the isomer **178a** also easily undergoes ring-opening reaction. Recently, Lewis *et al.* [42b] have demonstrated that the

product obtained by the addition of difluorocarbene to 1,2-diphenylcyclobutene (**132**) can easily undergo a ring opening reaction in spite of the fact that the departing halogen is a fluorine atom.

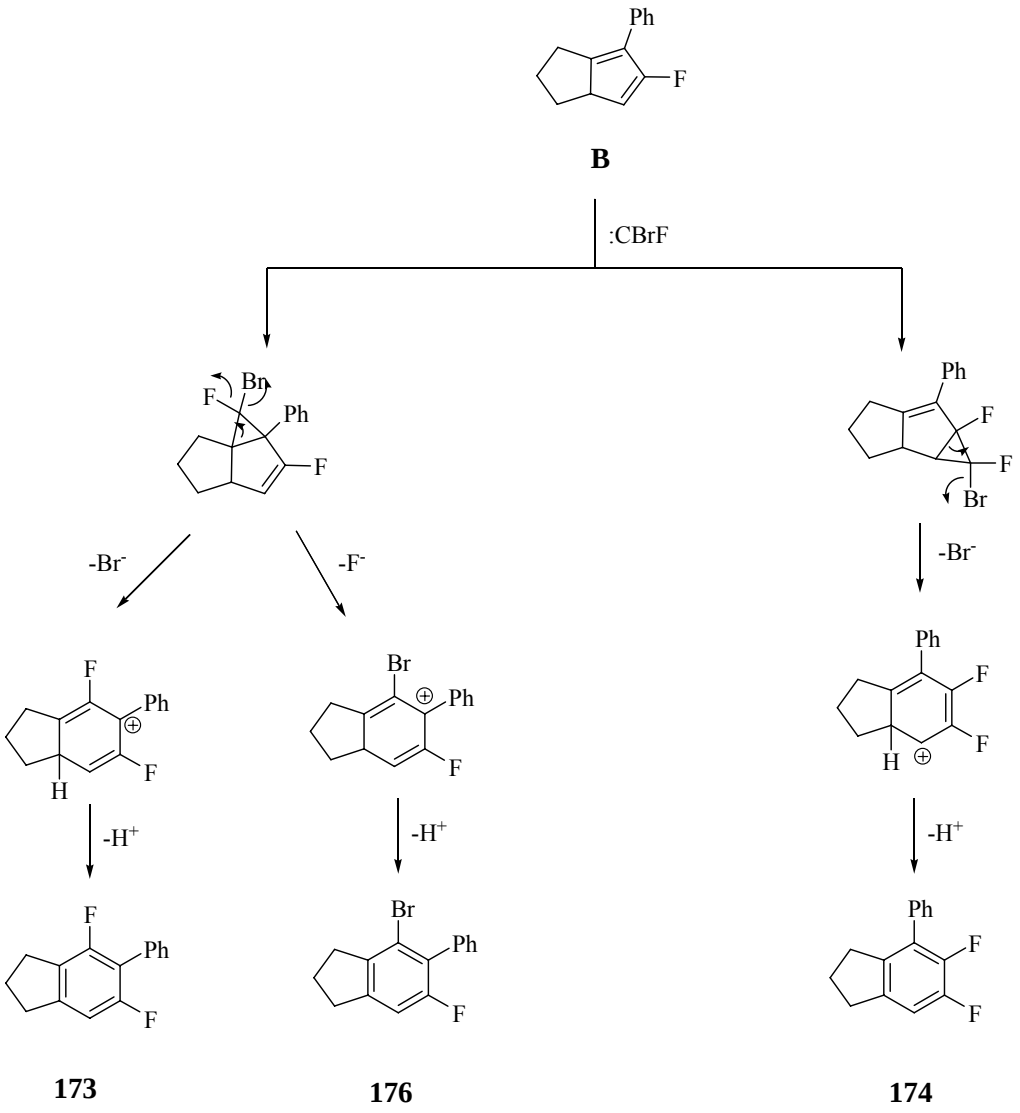


164 **178b** **A** **B**

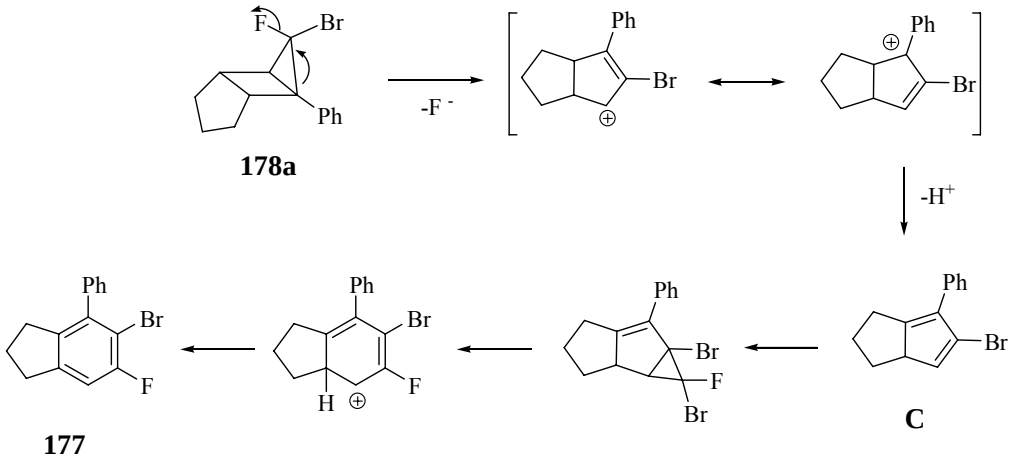
Once the ring-expansion of **178b** occurred, the two cationic intermediates formed could provide the cyclopentadienes **A** and **B** by the direct elimination of a proton. After the formation of **A** and **B**, the second addition of bromofluorocarbene might take place with two alternate paths for each, due to the presence of two unequal double bonds. The proposed mechanism with alternate paths is depicted for each case. Furthermore, it is reasonable that cyclopentadienes such as **A** and **B** under reaction conditions are prone to undergo fast intramolecular 1,5-H-shifts before bromofluorocarbene attack takes place as it would further complicate the reaction mechanism.



It is obvious that the presence of the cyclopentadiene **A** alone in the reaction can explain the formation of **174**, **175** and **177** but not **173** and **176**. In analogy, the formation of **173**, **174**, and **176** can be explained by the addition of bromofluoro carbene to the cyclopentadiene derivative **B** as shown below.

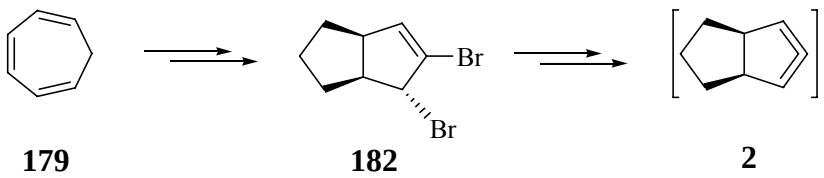


The *endo*-fluoro-*exo*-bromo isomer **178a** can also easily undergo a ring-opening reaction where the departing halide is a fluorine atom. We assume that the phenyl substituent aids in fluoride ion loss. The second addition of bromofluorocarbene to the formed cyclopentadiene derivative **C** will result in the formation of **177**.



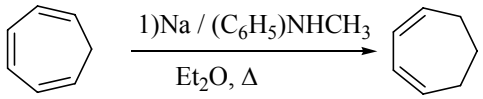
These results clearly proves the assumption that phenyl ring attached to cyclopropane ring plays a crucial role in the ring opening reaction in a way that it aids halide ion loss. Perhaps, in special case of **178**, the fusion of five-membered ring to cyclobutene unit as in the case of **164** cannot be underrated. It might probably rise the strain energy of the adduct **178**, which undergoes rearrangement in order to diminish the accommodated strain. Nonetheless, this provides a route to the fluorinated phenyl-indanes which are highly difficult to synthesize starting from indane.

All the cases discussed so far in this part have exploited the carbene chemistry in one way or another. Another avenue of accessing cyclic allenes is the elimination route. In what follows, the attempted generation of the known allene **2** via the β-elimination route will be discussed. The synthetic route was depicted below.



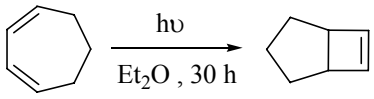
2.5. Attempted Synthesis of 2-Dehydro-3a,4,5,6,6a-pentahydropentalene (2). [27]

There exist some numerous routes leading to the synthesis of cyclohepta-1,3-diene **180** in the literature [27]. Among these, the most efficient one was the treatment of cycloheptatriene **179** with metallic sodium in the presence of N-methyl aniline at the reflux temperature of diethyl ether.



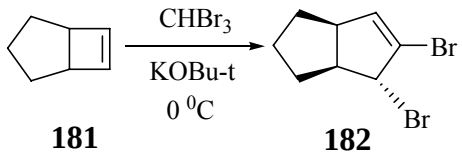
179 **180**

Direct irradiation at 254 nm of cyclohepta-1,3-diene (**180**), in ethereal solution with a mercury arc for 30 hours at room temperature furnished photo isomer **181**.



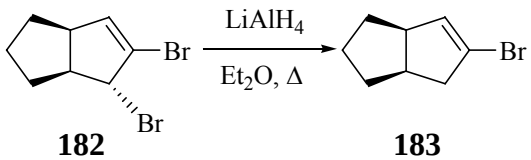
180 **181**

The reaction of bicyclo[3.2.0]hept-6-ene (**181**) with dibromocarbene, initiated at 0 ^{o}C then stirred for 6 hours at room temperature, gave compound **182**.



181 **182**

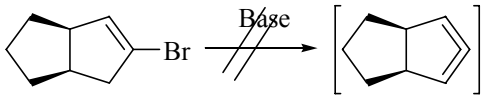
Fortunately, the treatment of dibromo compound **182** with $LiAlH_4$ at the reflux temperature of diethylether under a stream of nitrogen, provided vinylbromide **183** exclusively, after a usual work-up, and distillation.



182 **183**

The structure of **183** has been elucidated on the basis of ^{1}H-, ^{13}C-, GC-MS and IR spectroscopy. The ^{1}H-NMR spectrum indicated that the olefinic proton (H_6) gave broad singlet at 5.58 ppm whereas the protons of the ring junction (H_{3a} and H_{6a}) gave rise to multiplets at 3.06 and 2.71-2.57 ppm. However, the allylic methylene protons set an AB system at 2.83 ppm (dd, A-part of AB system, J=16.4- 9.4 Hz, H_4), and 2.21 ppm (d, B-part of AB system, J=16.4 Hz, $H_{4'}$). Other methylenic protons resonated as multiplets between 1.74-1.35 ppm. The eight-line ^{13}C-NMR spectrum with two olefinic carbons was consistent with the structure.

With **183** in hand, we first tried the hydrogen bromide elimination with KOBu-*t* in THF at different temperatures (rt, reflux); these conditions only resulted in the recovery of the starting material.

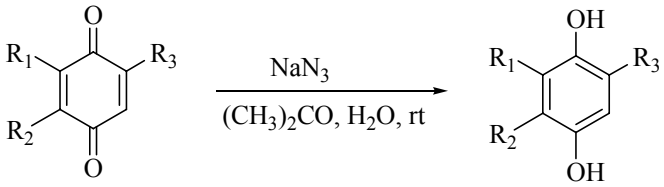


183 **2**

To our disappointment, however, when we carried out the reaction with spectacular increase of the strength of base (i.e. KOBu-*t*, $NaN(Si(CH_3)_3)_2$, LDA, *t*-BuLi, *n*-BuLi *etc*.) at various conditions; the reaction did not proceed, and the starting material **183** remained essentially unaltered. To this end, all reaction results suggested that the elimination of bromine in **183** was in fact not possible to generate the allene **2** under the given conditions.

It is clear even from the preceding pages that much of the failure of generation and interception of five-membered ring allenes has arison from the unavailability of suitable precursors under the given conditions.

Our final foray in the present manuscript addresses a simple, mild and efficient method for the reduction of 1,4-benzoquinones **4** to corresponding hydroquinones **5**.



4 **5**

2.6. Reduction of 1,4-Benzoquinones 4 to Hydroquinones 5.

It is well known that the anions of nonmetals act as reducing agents in redox reactions. In particular, azide ion that is the only three-atom dipole usually make fleeting appereances in organic synthesis: it serves as one of the most reliable means to introduce a nitrogen substituent [57]. A traditional source of this ion is sodium azide which is widely used in both pure and applied fields: as preservative for proteins, for growth inhibition of bacteria, as well as in perfusion of cells to block the mitochondrial electron transport chain.

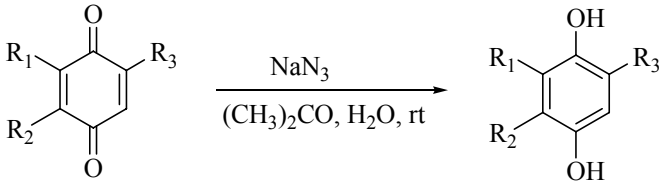
On the other hand, benzoquinones, which are ubiquitous to living systems and represent important cofactors for electron transfer in photosynthesis and respiration [58], find widespread use in medicine as antitumor, antifungal, and antiparasitic drugs, as well as antibiotics [59]. Their cytotoxic and/or therapeutic activity is frequently related to their reduction by flavoenzymes [59g]. Enormous effort has been devoted either to reveal structure-biological activity relationship [61] or to understand the formation of active metabolites via bioreductive [60] activation of quinone-containing drugs, and the effects of the reduced forms of the drug on cellular function, since hydroquinones have been shown to be able to alkylate essential proteins and inactivate enzymes, either directly or following reduction [59-61]. For that reason, reduction of benzoquinones to hydroquinones and the reverse reaction is an important process [62].

Apart from the aforementioned considerations, benzoquinones and hydroquinones are important class of compounds due to their frequently encountered structural motifs in and their usefullness as intermediates for the synthesis of a variety of compounds including natural, as well as nonnatural and/or biologically active compounds, dyes, and dye chromophores etc., respectively [63-64].

During the course of a program aimed at opening new libraries of benzoquinone containing heterocycles, we became interested in selective reduction of the quinone moiety into hydroquinone for some steps by a convenient method.

Although a number of methods [64] for the conversion of benzoquinones to hydroquinones are presently available, the new and simple ones devoid of side reactions, if possible, are welcome. Furthermore, as a quick glance to the following cited reports will demonstrate, almost all the existing methods suffer from some drawbacks: low yields, high cost of the catalyst [65] used, difficulties on controlling the reaction when starting quinones contain other reducible and/or labile groups since very active metal hydrides [66] strong Lewis acids/bases [67) complex organometalic reagents [68] multicomponent reagents [69] are used as reductants which have limited functional group tolerance.

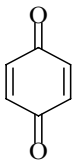
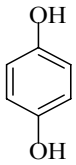
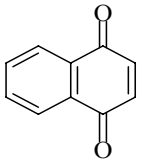
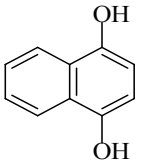
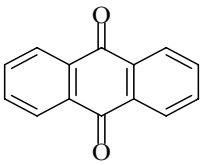
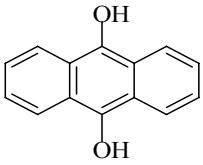
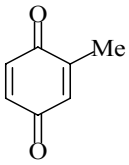
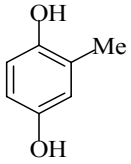
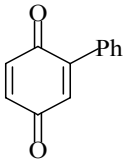
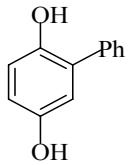
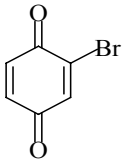
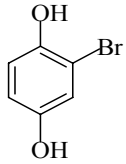
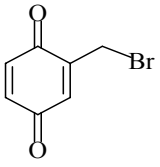
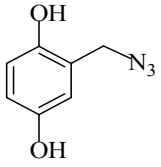
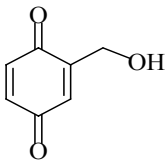
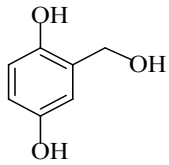
In order to rationalize the phenomena, benzoquinone was choosen as a model substrate. In an initial attempt it was treated with NaN_3 in acetone, at room temperature. The reaction provided the corresponding hydroquinone albeit in low yield (ca. 20%, NMR). Dimetoxyethane gave similar results as the solvent. In order to increase the yield, it was necessary to load excess NaN_3 (5 equiv). Moreover, it was found that addition of water as a co-solvent caused a slight increase in the rate of the reaction. Thus a mixture of acetone-water (9:1) was taken as the solvent system which resulted in an increased yield up to 75%. Finally, these optimizations were chosen as the standart conditions.



4 **5**

To test the scope and the limitations of this method, a variety of quinones including benzannulated ones (Entries 2-3), alkyl (Entries 4, 7-8), aryl (Entry 5) and halogen (Entry 6) as substituent were subjected to the reaction under the standart set of conditions to afford hydroquinones which were characterized on the basis of physical and spectral (^{1}H-, and ^{13}C-NMR, IR, elemental analysis) data. The results are summarized in Table 2.

Table 2. Reduction of 1,4-benzoquinones **4** to hydroquinones **5** by NaN_3

Entry	Quinones (**4**)	Hydroquinones (**5**)	Yield(%)	Mp (^oC) Found	Mp (^oC) Reported
1			75	173	171[68a]
2			70	175	176[70b]
3			NR[d]	--	--
4			85	125	125[68a]
5			85	97	98[68a]
6			95	114	111[70]
7			65	[e]	--
8			78	97	96[71]

In most cases, moderate to good yields were achieved with one exception. Interestingly, the reaction of anthraquinone (Entry 3) did not proceed even on heating at the reflux temperature for a prolonged period of time, and the starting material remained essentially unaltered. This peculiar behaviour was attributed to relatively higher redox potential (ΔV=0.57 V) of anthraquinone when compared to that of benzoquinone [72].

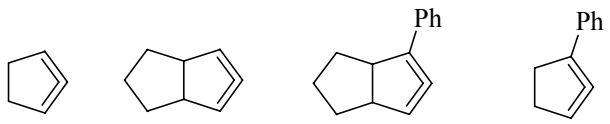
It is noteworthy to mention that bromomethyl quinone [73] (Entry 7) was converted to azidomethyl hydroquinone in one step under these conditions. To the best of our knowledge, this is one of the most rare examples that show the unique behaviour of such anion as the azide where it acts as both a reductant and nucleophile in a reaction at the same time.

In summary, a simple, mild and efficient method was presented for the conversion of 1,4-benzoquinones (**4**) to the corresponding hydroquinones (**5**) by the action of NaN_3 under neutral conditions in the presence of water. As the foregoing pages illustrated this novel method offers functional group compatibility and puts away all the drawbacks involved in the previously existing methods. We believe that it will find applications in synthetic chemistry wherein selective reduction of quinones is needed.

CHAPTER 3

CONCLUSSION

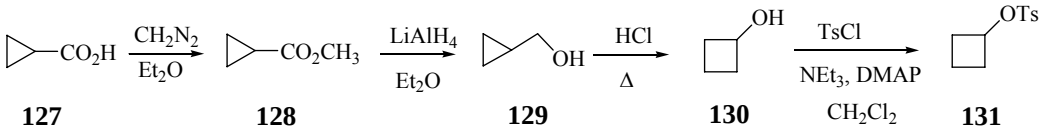
Chemists have always been fascinated by the cumulated diene system of allenes with its extraordinary properties such as the axial chirality of the elongated tetrahedron and a higher reactivity than non-cumulated C-C double bonds. Over the last three decades, the generation and interception of strained cyclic cumulenes represent a fundamental research field of interest in synthetic organic chemistry. In this area, we have examined the possibility of generating the five-membered ring allenes herein, a particularly daunting challenge given their prominent feature of being insusceptible to survive, unless otherwise not formed. To put it bluntly, five-membered ring allenes are sticky. Nonetheless, our success with this class of strained organic compounds exemplified with the first generation and trapping of a five-membered ring allene [45] encoureged us to investigate the fate of these compounds, and search for the limits of the existence of cyclopenta-1,2-diene (**1**) and a number of its derivatives, e.g. **2**, **3**, and **82**.



1 **2** **3** **82**

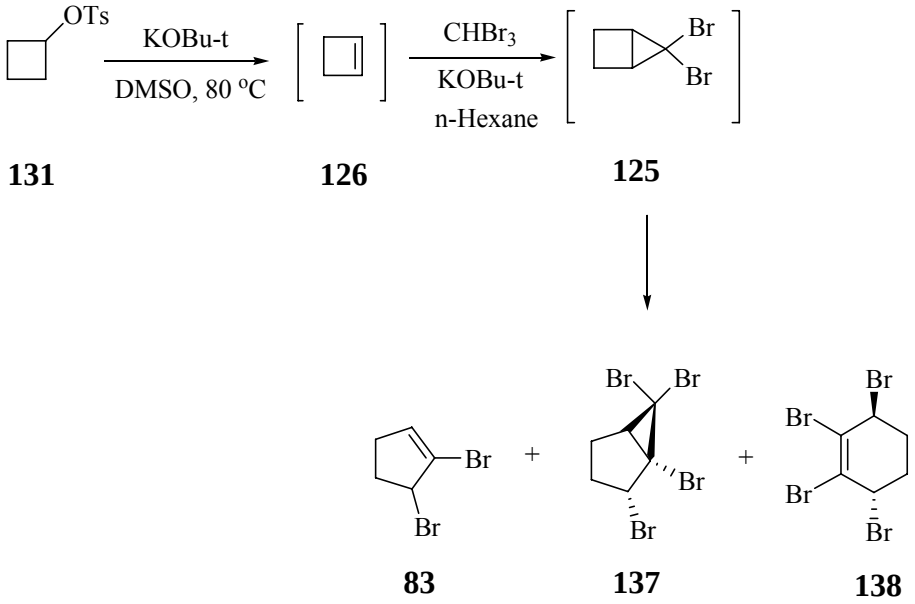
Our studies commenced with a comprehensive screen of substrates as potential precursors en route to the targeted cyclic allenes. Initial explaratory efforts

directed toward the generation of cyclopenta-1,2-diene (**1**) involved the preparation of cyclobutyltosylate **131**. Cyclobutyltosylate **131** was prepared from cyclopropylcarboxylic acid (**127**) or its methyl ester **128** via a three-step synthesis: the reaction of **128** with hydride converted to **129**, whose acid catalyzed ring enlargement resulted in cyclobutanol (**130**) in moderate yield, subsequent treatment of **130** with tosylchloride gave ester **131**, quantitatively. Base induced elimination of sulfonate from **131** furnished cyclobutene (**126**), which was trapped at low temperatures.

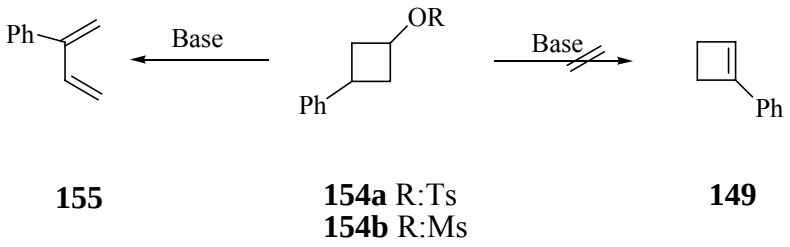


127 **128** **129** **130** **131**

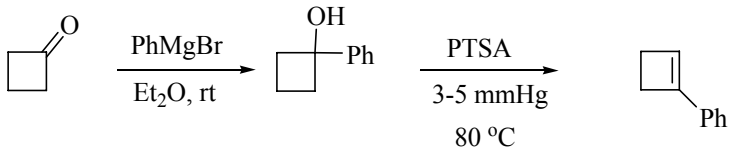
To our delight, addition of carbene to **126** gave adducts 1,5-dibromocyclopentene (**83**); 1,2,6,6-tetrabromo-bicyclo[3.1.0]hexane (**137**); and (3R(S),6R(S))-1,2,3,6-tetrabromo-cyclohex-1-ene (**138**) in a ratio of 1:4:8, respectively. The structures of adducts **137** and **138** were fully characterized by both chemical and spectroscopic methods, including the single crystal structure analysis for **138**. Since, the isolation of *gem*-dibromocyclopropane **125** was not possible due to the facile ring opening reaction, the generation of cyclopenta-1,2-diene (**1**) was impeded.



In an attempt to synthesize 1-phenylcyclobutene (**149**) via base induced elimination of sulfonates from esters **154a** and **154b**, we found that the reactions only provided the open chain partner 2-phenyl-1,3-butadiene (**155**), instead of the desired **149**.

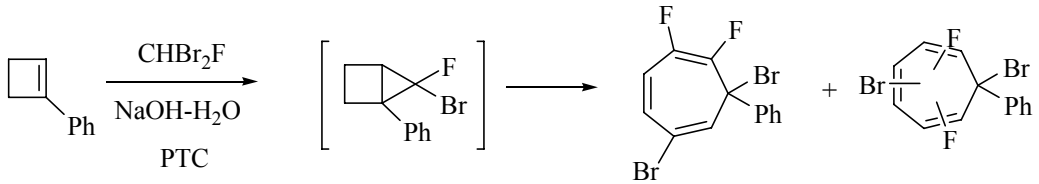


On the other hand, it became possible to obtain **149** via acid catalyzed dehydration of 1-phenyl-cyclobutanol (**157**) after the treatment of cyclobutanone (**156**) with PhMgBr.



156 **157** **149**

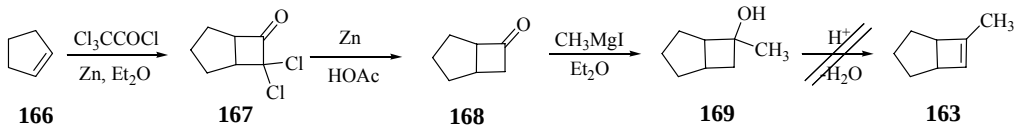
Interestingly, the addition of bromofluorocarbene to alkene **149** furnished compounds **158** and **159** which stimulated us to get further insights into the affect of substituents; i.e. methyl and phenyl, on the facile ring opening reaction of such cyclopropanes as **148**.



149 **148** **158** **159**

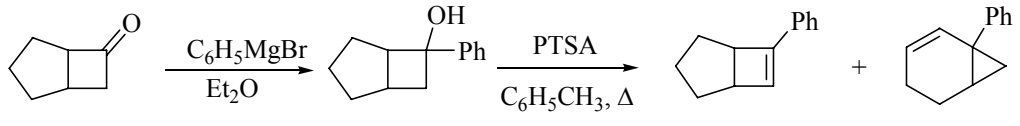
In this respect, we first examined the synthesis of 6-methyl-bicyclo[3.2.0]heptan-6-ol (**163**). Dichloroketene addition to cyclopent-1-ene (**166**) followed by dechlorination provided bicyclo[3.2.0]heptan-6-one (**168**).

The reaction of ketone **168** with CH_3MgI gave 6-methyl-bicyclo[3.2.0]heptan-6-ol (**169**). Nonetheless, attempted acid catalyzed dehydration resulted only in the recovered starting material.



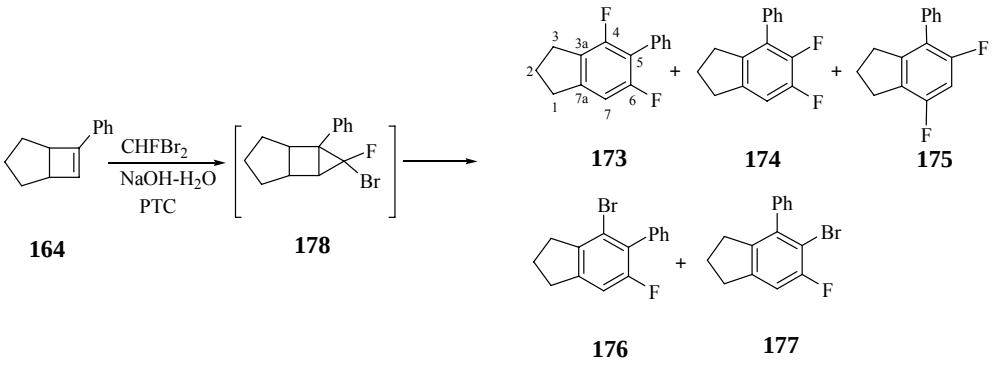
166 **167** **168** **169** **163**

At this stage, 6-phenyl-bicyclo[3.2.0]hept-6-ene (**164**) was taken into account. The reaction of ketone **168** with PhMgBr gave 6-phenyl-bicyclo[3.2.0]heptan-6-ol (**170**) quantitavely, which underwent acid catalyzed dehydration to furnish 6-phenyl-bicyclo[3.2.0]hept-6-ene (**164**) and 1-phenyl-bicyclo[4.1.0]hept-2-ene (**171**) in a ratio of 3:1, respectively.



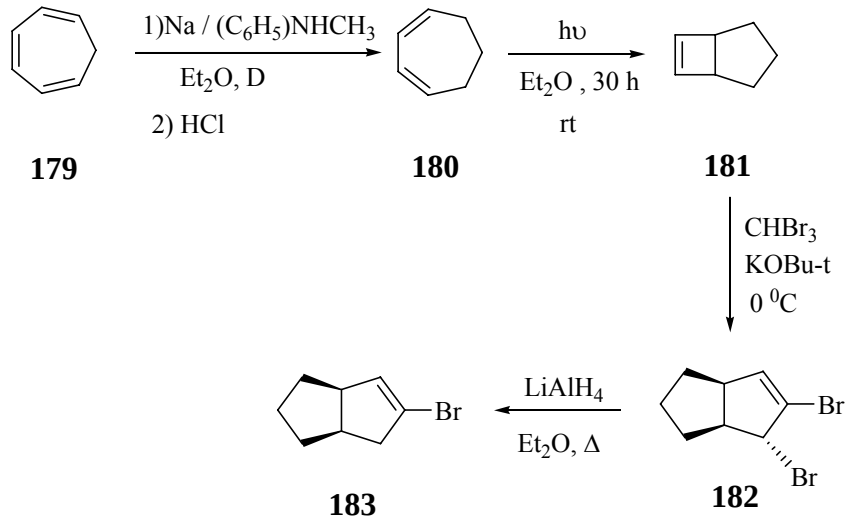
168 **170** **164** **171**

Surprisingly, the addition of bromofluorocarbene to alkene **164** provided compounds **173-177** of which structures were unequivocally supported by spectroscopic (^{1}H-, ^{13}C-, ^{19}F-, DEPT, COSY, HMBC, HMQC NMR experiments, IR, Mass spectrometry) data, and combustion analysis. The formation mechanism of the products was discussed.



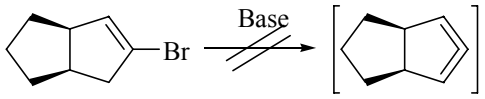
The sheer number of examples discussed so far, i.e. **148** and **178**, underscores the powerful effect of phenyl substituent aiding the halide ion loss within the cyclopropane framework. In the special case of **178**, this provided a route to the fluorinated phenyl-indenes such as **173-177** by ring expansion in one step, which are highly difficult to synthesize starting from indane, and paved the way for synthesis of other structurally diverse indenes.

Finally, the generation of the known allene **2** via elimination route was investigated which involved the four-step synthesis of 5-bromo-1,2,3,3a,4,6a-hexahydro-pentalene (**183**). Synthetic route, starting from cyclohepta-1,3,5-triene (**179**), led to the formation of bicyclo[3.2.0]hept-6-ene (**181**) via photolysis of cyclohepta-1,3-diene (**180**). Dibromocarbene addition to alkene **181** and subsequent hydride reduction of 4,5-dibromo-1,2,3,3a,4,6a-hexahydro-pentalene (**182**) furnished 5-bromo-1,2,3,3a,4,6a-hexahydro-pentalene (**183**) of which structure was elucidated on the basis of ^{1}H- and ^{13}C-NMR, GC-MS, IR spectroscopy and elemental analysis.



179 **180** **181** **182** **183**

To our disappointment, however, attempts to eliminate HBr from **183** with various bases at different conditions to generate allene **2** all met with failure; **183** remaining essentially unaltered. This peculiar behavior of **183**, which might be attributed to the high activation barrier proved the inability of β-elimination route to generate allene **2**.

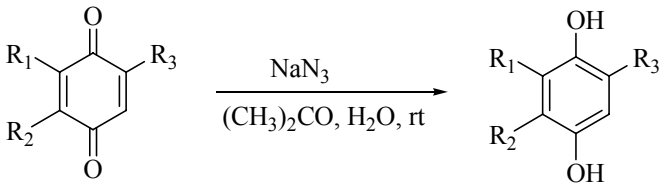


183 **2**

Overall, the smallest member of strained cyclic allenes, cyclopenta-1,2-diene (**1**) and a number of its derivatives (**2**, **3** and **82**) were investigated by the development of some synthetic routes.

However, in no case could the corresponding allene precursor and/or allene adduct be observed or their structures proven spectroscopically under the given reaction conditions. In spite of these penalties, the five-membered ring allenes represent a field in its infancy. To conclude, we are left with the feeling that the basic ideas concerning the generation of five-membered ring allenes are yet to be exploited widely. Nonetheless, it is to be hoped that pathfinding examples and rich mine of information collected here will be a spur toward that wider exploitation.

Finally, a simple, mild and efficient method was presented for the conversion of 1,4-benzoquinones **4** to the corresponding hydroquinones **5** by the action of NaN_3 under neutral conditions in the presence of water. As the foregoing pages illustrated this novel method offers functional group compatibility and puts away all the drawbacks involved in the previously existing methods. We believe that it will find applications in synthetic chemistry wherein selective reduction of quinones is needed.



4 **5**

Some parts of the research described herein were published in the following journals;

1. *Addition of dibromocarbene to cyclobutene: characterization and mechanism of formation of the products,* Algi, F.; Hökelek, T.; Balci, M. *J. Chem. Res. (S),* **2004**, 10, 658.
2. *Bromofluorocarbene addition to 6-phenylbicyclol[3.2.0]hept-6-ene: characterization and formation mechanism of the products,* Algi, F.; Balci, M. *ARKIVOC*, **2006**, 10, 173.
3. *A simple, mild and efficient method for the reduction of 1,4-benzoquinones to hydroquinones by the action of* NaN_3*,* Algi, F.; Balci, M. *Synthetic Commun.*, in press.

CHAPTER 4

EXPERIMENTAL

4.1. General Consideration.

Nuclear Magnetic Resonance (^{1}H-, ^{13}C- ^{19}F- and 2D-) spectra were recorded on a Bruker Instruments Avance Series-Spectrospin DPX-400, Ultra Shield (400, 100 and 376.3 MHz for ^{1}H-, ^{13}C- and ^{19}F- nuclei), High Performance digital FT-NMR spectrometer with TMS and TFA ($\delta_{CFCl3} = \delta_{TFA} - 76.8$ ppm) as the internal and external standards respectively, and the upfield as negative. Coupling constants (J values) are reported in Hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet).

Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer. Band positions are reported in reciprocal centimeters (cm^{-1}).

GC was performed by Thermo Quest Trace 2000 Series GC instrument using 30m x 0.25mm i.d. x 0.25um ft Phenomenex Zebron ZB-5 5% Phenyl Polysiloxane column. Mass data obtained by Thermo Quest Finnigan Automass Multi instrument were reported for M^{+} and high mass fragments derived from M^{+} in electron impact (EI) mode.

Column chromatographic separations were performed by using Fluka Silicagel 60 (particle size 0.060-0.200 mm). The relative proportions of solvents refer to volume: volume ratio. Routine thin layer chromotography (TLC) was effected by using precoated 0.25 mm silica gel plates purchased from Fluka.
All the solvent purifications were done as stated in the literature [73].

4.2.1. The synthesis of Cyclopropylcarbinol (129).

11.6 g (0.10 mol) of cyclopropyl carboxylic acid **127** or equivalent amount of its methyl ester **128** produced by the reaction of diazomethane and acid, was dropwise added to a stirred suspension of 5 g (0.21 mol) $LiAlH_4$ in 350 mL of anhydrous ether. The mixture was further stirred 2 h at room temperature and then cooled with an ice bath before the destruction of the excess hydride with water carefully. After the evolution of hydrogen was completed, the mixture was extracted with ether (3x100 mL), combined organic layers were dried over $MgSO_4$, to give after removal of the solvent and distillation of the residue 9 g (93%) of alcohol **129**.

129: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.20 (dd, J=6.8-1.0 Hz, 1H), 3.07 (bs, 1H), 0.86 (m, 1H), 0.30 (bd, J=8.0 Hz, 2H), 0.01 (bd, J=8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 67.3, 13.6, 3.0; IR ($CHCl_3$, cm^{-1}): 3349, 3081, 3007, 2921, 2873, 2046, 1927, 1467, 1431, 1317, 1255, 1155, 1096, 1029, 924, 900, 830, 771, 481.

4.2.2. The synthesis of Cyclobutanol (130).

To a stirred solution of 165 mL distilled water and 16 mL (0.17 mol) conc. HCl was added 14 g (0.20 mol) of cyclopropylcarbinol **129**. The mixture was heated up to reflux for 3-3.5 h. After cooling the mixture was neutralized with NaOH (6 g, 0.15 mol), and the neutralization was completed with $NaHCO_3$. The aqueous layer was saturated with NaCl, and extracted several times with ether; the organic layers were combined, dried over $MgSO_4$, to give after removal of the solvent and distillation of the residue 12.6 g (90%) of **130** (b.p. 123 ^{o}C).

130: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.15 (bs, 1H), 3.97 (m, 1H), 2.04 (m, 2H), 1.70 (m, 2H), 1.43 (m, 1H), 1.21 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ

66.8, 33.5, 12.3; IR ($CHCl_3$, cm^{-1}): 3303, 2974, 2937, 2895, 2873, 2742, 2665, 2523, 2436, 2353, 2214, 2124, 2053, 1465, 1338, 1238, 1200, 1131, 1090, 1031, 960, 930, 902, 752, 609, 467.

4.2.3. The synthesis of Toluene-4-sulfonic acid cyclobutyl ester (131).

Compound **131** was obtained by the reaction of the cyclobutanol (**130**) with 1.1 equivalent of tosylchloride in pyridine at 0 ^oC for 48 h. After usual work up, the yellow pale residue treated under high vacuum (3.10^{-2} mm Hg) at room temperature for 3 h, to give **131** in 90% yield, without impurities.

131 [40] **:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.70 (d, A-part of AB-system, J=8.0 Hz, 2H), 7.27 (d, B-part of AB-system, J=8.0 Hz, 2H), 4.69 (p, J=7.5 Hz, 1H), 2.40 (s, 3H), 2.11 (m, 4H), 1.72 (m, 1H), 1.46 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 144.5, 134.9, 129.9, 128.2, 74.0, 31.2, 21.9, 13.4; IR ($CHCl_3$, cm^{-1}): 2991, 2950, 2877, 2736, 2696, 2589, 2532, 2362, 2287, 2192, 1926, 1808, 1770, 1598, 1494, 1446, 1365, 1245, 1177, 1097, 1047, 927, 852, 815, 752, 671, 555, 505.

4.2.4. Cyclobutene (126) and Dibromocarbene Addition.

A solution of 6.78 g (30 mmol) of tosyloxycyclobutane **131** in 10 mL of dry, DMSO was added dropwise over 10 min to a stirred mixture of 8.4 g (75 mmol) of KOBu-t in 120 mL of dry DMSO at 80^0C under the stream of nitrogen. After stirring and heating for 100 min the evolved cyclobutene **126** (bp. 2 ^oC) was carried in nitrogen into a trap containing a solution of 3.9 g (15 mmol) of $CHBr_3$ in 100 mL n-hexane cooled with solid CO_2 (-80^0). Then the mixture was allowed to warm to -30^0 and 1.7 g (17 mmol) KOBu-t was added. After 1 h, the mixture was allowed to warm to room temperature during 8 h, washed with ice cold water and extracted with hexane (3x100 mL), dried over $MgSO_4$, the solvent was removed under reduced pressure to give 0.7 g (8%) of crude product. The residue was chromotographed on silica gel with hexane as eluent until no more fractions

were collected to give **83**, **137**, and **138** in a ratio of 1:4:8, respectively. Finally, elution of the column material with 9:1 hexane-EtOAc gave the alcohol **139** (80 mg).

1,5-Dibromo-cyclopentene (83) [43] : colorless liquid, 95 mg (1.4%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.02 (bs, 1H), 4.81 (m, 1H), 2.49 (m, 2H), 2.38 (m, 1H), 2.24 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 137.0, 124.0, 60.5, 35.8, 31.6; IR ($CHCl_3$, cm^{-1}): 2974, 2929, 2850, 2358, 1602, 1429, 1338, 1261, 1184, 1085, 1060, 1014, 947, 912, 826, 800, 694, 592, 437.

1,2,6,6-tetrabromo-bicyclo[3.1.0]hexane (137): colorless liquid, 670 mg (5.7%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.66 (dd, J=7.1-2.0 Hz, 1H), 2.84 (m, 1H), 2.66 (m, 1H), 2.39 (m, 2H), 2.03 (ddd, J=13.6-8.9-2.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 56.8, 48.1, 38.4, 33.4, 28.6, 27.6; IR ($CHCl_3$, cm^{-1}); 2919, 2360, 2329, 1688, 1549, 1424, 1260, 1219, 1133, 1101, 1027, 913, 847, 775, 743, 691, 651, 607, 477. MS: 392/394/396/398/400 (M^+, 8), 313/315/317/319 (M^+-HBr, 38), 234/236/238 (M^+-2HBr, 82), 155/157 (M^+-2HBr-Br, 66), 148 (23), 133 (100), 115 (37), 105 (100), 91 (100), 77 (100). Anal. Calcd. for $C_6H_6Br_4$: C, 18.12; H, 1.52. Found: C, 18.08; H, 1.48.

(3R(S),6R(S))-1,2,3,6-tetrabromocyclohex-1-ene (138): White solid, m.p. 126-128 ^{o}C, 1.43 g (12%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.77 (bd, J=2.3 Hz, 2H), 2.07 (quasi d, J=10.7 Hz, 1H), 2.51 (quasi d, J=10.7 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 129.4, 52.9, 29.3; IR ($CHCl_3$, cm^{-1}): 2956, 2921, 2851, 2353, 1594, 1462, 1431, 1378, 1303, 1202, 1152, 1111, 1046, 998, 952, 867, 785, 706, 647, 581, 510, 442. Anal. Calcd. for $C_6H_6Br_4$: C, 18.12; H, 1.52. Found: C, 18.16; H, 1.46.

2-Bromocyclopent-2-enol (139) [43] : 180 mg (3.8%); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.81 (bs, 1H), 4.46 (m, 1H), 3.13 (bs, OH), 2.16 (m, 3H), 1.67 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 134.1, 125.6, 79.3, 32.3 30.6; IR ($CHCl_3$,

cm^{-1}): 3343, 3079, 2934, 2853, 2694, 1618, 1434, 1325, 1238, 1153, 1050, 986, 922, 901, 814, 772, 583, 432.

4.2.5. The synthesis of 2-Bromo-cyclopent-2-enone (140).

A solution of 300 mg (2 mmol) alcohol **139** in 5 mL CH_2Cl_2 was dropwise added to a stirring solution of 450 mg (2.1 mmol) PCC in 10 mL CH_2Cl_2 at 0 ^oC. The mixture was stirred 3 h at room temperature and filtered. The filtrate was washed with water and the organic layer was dried over $MgSO_4$. After the removal of the solvent the residue was filtered through a short column with CH_2Cl_2 as eluent to give 250 mg (1.5 mmol, 84%) of enone **140**.

140 [43] **:** ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.70 (t, J=2.9 Hz, 1H), 2.60 (m, 2H), 2.41 (m, 2H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 202.2, 162.7, 126.3, 32.6, 28.5; IR ($CHCl_3$, cm^{-1}): 2960, 2850, 1720, 1440, 1420, 1310, 1180, 980, 930.

4.2.6. The thermal rearrangement of 1,2,6,6-tetrabromo-bicyclo[3.1.0]hexane (137) to 1,2,3,6-Tetrabromocyclohex-1-ene (138).

A solution of 100 mg **137** in hexane was heated up to reflux for 1 h. After cooling to room temperature, the solvent was removed under pressure to give 76 mg of residue whose spectral data was consistent with **138**.

4.2.7. The synthesis of 1,2,3,4-tetrabromo-cyclohexanes (141-142) and 2,3-dibromo-cyclohex-2-ene-1-one (143).

Into a 50 ml, two-necked, round-bottomed flask were placed Pd/C (10%) (10 mg) catalyst and of the tetrabromide **138** 100 mg (0.25 mmol) in AcOEt (20 ml). One of the necks was attached to hydrogen gas with a three-way stopcock; the other neck was capped with a rubber septum. The reactants were degassed and flushed with hydrogen gas, while stirring magnetically. After 4 h the solution was decanted from the catalyst, the solvent rotoevaporated and the residue

chromatographed on silica gel with hexane-EtOAc (19:1) as eluent. The first fraction consisted of a mixture of **141** and **142** (50 mg, 49%, in a ratio of 4:1).

***(1R(S),2R(S),3S(R),4R(S))-1,2,3,4-tetrabromocyclohexan*e (141):** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.78 (bs, 1H), 4.34 (bs, 1H), 2.17 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 71.3, 53.6, 26.6; IR ($CHCl_3$, cm^{-1}): 2958, 2955, 2854, 2088, 1639, 1461, 1434, 1378, 1305, 1278, 1203, 1116, 1051, 970, 914, 852, 773, 728, 686, 628, 530, 476.

142: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.72 (bs, 1H), 4.25 (bs, 1H), 2.15 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 72.0, 51.5, 28.7; IR ($CHCl_3$, cm^{-1}): 2955, 2850, 2095, 1650, 1451, 1443, 1370, 1296, 1260, 12001, 1126, 1043, 980, 912, 851, 776, 725, 680, 622, 538, 496. The exact configuration of **142** was not determined).

As the second fraction, the enone **143** was isolated 24 mg (40%).

2,3-Dibromocyclohex-2-en-1-one (143): ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.83 (t, J=6.1 Hz, 2H), 2.48 (t, J=6.5 Hz, 2H), 1.98 (qui., J=6.3 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 187.6, 149.1, 128.0, 38.9, 37.2, 22.8; IR ($CHCl_3$, cm^{-1}): 1680, 1652, 1575, 1255, 1219, 1183, 1135, 991, 913, 842, 794, 687, 659, 607, 535. MS: 252/254/256 (M^+, 100), 224/226/228 (M^+-CO, 49), 173/175 (M^+-Br, 62), 145/147 (M^+-CO –HBr, 70), 117/119 (36). Anal. Calcd for $C_6H_6Br_2O$: C, 28.38; H, 2.38. Found: C, 28.23; H, 2.32.

4.2.8. The syntheses of 1,2-dibromobenzene (144) and 1,3-dibromobenzene (145)

A solution of 100 mg (0.25 mmol) **138** and 120 mg (1.07 mmol) KOt-Bu in 30 mL THF was refluxed 1 h. After dilution with water, the mixture was extracted

with hexane (3x50 mL), and combined organic layers were dried over $MgSO_4$ and the solvent was removed to give a mixture (51 mg, 86%) of **144** and **145** in a ratio of 4:1, whose spectral data was consistent with the literature [44].

4.3.1. The synthesis of 2,2-Dichloro-3-phenyl-cyclobutanone (151).

A 1000-mL three-neck flask was equipped with a nitrogen inlet, a condenser, and pressure-regulated dropping funnel. Under a blanket of nitrogen gas, 15.6 g (0.15 mole) of styrene **150** and 10.5 g (0.16 mole) ordinary zinc dust was put in the presence of 300 mL dry ether as the solvent. A solution of 29.1 g (0.16 mole) trichloroacetylchloride in 200 mL dry ether was given dropwise within 2 h at 0 ^oC. After the addition was completed a vigorous reaction started and the colour was turned into brown. As the reaction was completed, the zinc salts were filtered through celite 545. The product was extracted with ether (3x150 mL), then the organic phase was washed with saturated sodium bicarbonate solution, and finally with brine. The solution was dried over $MgSO_4$ and the product was concentrated. Finally, the product was further purified by vacuum distillation to give 12.9 g (0.06 mole) of **151** (bp. 110 ^oC/5 mmHg) in a yield of 40%.

151 [46a] **:** ^{1}H-NMR (400 MHz) δ 7.49-7.40 (m, 3H), 7.35 (d, J=7.1 Hz, 2H), 4.28 (t, J=10.2 Hz, 1H), 3.76 (dd, A- part of AB system, J=10.3-10.2 Hz, 1H), 3.60 (dd, B- part of AB system, J=10.3-10.2 Hz, 1H); ^{13}C-NMR (100 MHz) δ 190.8, 134.9, 129.0, 128.6, 128.4, 51.0, 46.0.

4.3.2. The synthesis of 3-Phenyl-cyclobutanone (152).

To a 500-mL two-neck flask, 8 g (0.122 mole) zinc dust and 150 mL glacial acetic acid was put while stirring magnetically. A condenser was connected. To the other neck a pressure regulated dropping funnel, containing 12.9 g (0.060 mole) **151** in 100 mL of glacial acetic acid was plugged. This solution was given dropwise at room temperature to the zinc dust-acetic acid solution. After the dropping was ceased, the temperature was raised to 70 ^oC and kept constant at this temperature while stirring 15 h magnetically. Here the system was diluted with distilled water

to dissolve the formed zinc salt. The mixture was then filtered through ordinary filter paper, and extracted with ether (3x150 mL), washed with first water, saturated $NaHCO_3$ solution, and finally with brine. The solution was dried over $MgSO_4$, and concentrated under vacuo. Vacuum distillation gave 5.84 g (0.040 mole) of pure **152** as a colourless liquid (bp. 90 ^oC/5 mmHg) in a yield of 66%.

152 [46b] **:** ^{1}H-NMR (400 MHz) δ 7.11-7.01 (m, 5H), 3.45-3.41 (m, 1H), 3.27-3.21 (m, 2H), 3.03-2.96 (m, 2H); ^{13}C-NMR (100 MHz) δ 205.5, 143.9, 129.0, 126.9, 126.8, 55.0, 28.9.

4.3.3. The synthesis of 3-Phenyl-cyclobutanol (153).

1.4 g (40 mmol) of $NaBH_4$ was added portionwise to a magnetically stirring solution of 5.84 g (40 mmol) ketone **152** in 100 mL methanol. After the addition was completed the reaction was further stirred for 30 min. The mixture was diluted with water and extracted with ether (3x150 mL). Combined organic layers were dried over $MgSO_4$, filtered, and the solvent was removed by rotary evaporator to give 5.5 g (37 mmol) of alcohol **153** in 93% yield.

153 [47] **:** ^{1}H-NMR (400 MHz) δ 7.28-6.99 (m, 5H), 4.12 (p, J=7.5 Hz, 1H), 3.44 (s, 1H), 2.86-2.77 (m, 1H), 2.66-2.60 (m, 2H), 1.97-1.90 (m, 2H); ^{13}C-NMR (100 MHz) δ 144.9, 128.7, 127.0, 126.3, 63.4, 41.2, 30.5.

4.3.4. The synthesis of Methanesulfonicacid 3-Phenyl-cyclobutyl ester (154a).

4.1 g (41.1 mmol) NEt_3 was dropwise added to a solution of 5.5 g (37 mmol) alcohol **153** in 100 mL CH_2Cl_2 that was cooled with an ice bath. Then 4.7 g (41 mmol) of mesitylchloride in 50 mL CH_2Cl_2 was dropwise added to the mixture at 0 ^oC. The reaction was monitored by TLC, and after 4 h the mixture was diluted with water, washed with $NaHCO_3$, and dried over $MgSO_4$. The solvent was removed under pressure to give 7.9 g (35 mmol) of **154a** in a yield of 94%.

154a: ^{1}H-NMR (400 MHz) δ 7.33-7.20 (m, 2H), 7.15 (d, J=6.8 Hz, 3H), 4.94 (p, J=7.5 Hz, 1H), 3.08-3.01 (m, 1H), 2.92 (s, 3H), 2.88-2.80 (m, 2H), 2.41-2.32 (m, 2H); ^{13}C-NMR (100 MHz) δ 143.2, 128.8, 126.9, 126.7, 70.0, 38.8, 38.6, 31.4.

4.3.5. The synthesis of Toluene-4-sulfonic acid 3-Phenyl-cyclobutyl ester (154b).

4.1 g (41.1 mmol) NEt_3 was dropwise added to a solution of 5.5 g (37 mmol) alcohol **153** in 100 mL CH_2Cl_2 which was cooled with an ice bath. Then 7.8 g (41 mmol) of tosylchloride in 50 mL CH_2Cl_2 was dropwise added to the mixture at 0 ^{o}C. The reaction was monitored by TLC, and after 5 h the mixture was diluted with water, washed with $NaHCO_3$, and dried over $MgSO_4$. The solvent was removed under pressure to give 10.6 g (35 mmol) of **154b** in a yield of 94%.

154b [48] : ^{1}H-NMR (400 MHz) δ 7.82 (d, A- part of AB system, J=8.0 Hz, 2H), 7.35 (d, B- part of AB system, J=8.0 Hz, 2H), 7.30-7.25 (m, 2H), 7.21-7.13 (m, 3H), 4.82 (p, J=7.5 Hz, 1H), 3.03-2.96 (m, 1H), 2.73-2.67 (m, 2H), 2.48 (s, 3H), 2.33-2.25 (m, 2H); ^{13}C-NMR (100 MHz) δ 144.4, 143.2, 135.0, 130.0, 128.7, 128.2, 126.8, 126.7, 70.4, 38.7, 31.5, 22.0.

4.4.1. The synthesis of 1-Phenyl-cyclobutanol (157).

To a 250-mL two-neck flask, 1.2 g (0.049 mole) magnesium and a piece of iodine crystal in 50 mL dry ether was put and let to stir magnetically in a water bath. A condenser was connected. To the other neck a pressure regulated dropping funnel, containing 7.8 g (0.049 mole) C_6H_5Br in 50 mL of dry ether was plugged. This solution was given dropwise at room temperature to the magnesium suspension. An exothermic reaction was started (if the reaction was not observed the flask was gently heated until it begins). After the dropping was ceased, it was allowed to cool to room temperature. Then the contents of the flask were taken into the

dropping funnel and were added dropwise to a solution of 3.15 g (0.045 mole) cyclobutanone (**156**) in 50 mL dry ether. After the addition was completed, the reaction was further stirred 1 h at room temperature. A saturated solution of NH_4Cl was added. The mixture was extracted with ether (3x100 mL), dried over $MgSO_4$, and the solvent was removed by rotary evaporator to give 5.52 g (0.040 mole) **157** as a white solid (mp. 45 ^oC) in 90% yield.

157 [49] **:** ^{1}H-NMR (400 MHz) δ 7.50 (d, J=7.4 Hz, 2H), 7.37 (t, J=7.6 Hz, 2H), 7.29-7.25 (t, J=7.2 Hz, 1H), 2.61-2.55 (m, 2H), 2.42-2.35 (m, 2H), 2.10-1.98 (m, 2H), 1.77-1.66 (m, 1H); ^{13}C-NMR (100 MHz) δ 146.7, 128.7, 127.5, 125.2, 77.3, 37.2, 13.4.

4.4.2. The synthesis of 1-Phenyl-Cyclobutene (149).

A mixture of 4.93 g (30 mmol) 1-phenyl-cyclobutanol **157** and 5 mg of PTSA was heated under reduced pressure (3-5 mmHg) in an oil bath at 80 ^oC and the product was allowed to distill (bp. 37 ^oC/0.01 mmHg) from the reaction flask through a short column. The yield of pale yellow oil was 0.23 g (2 mmol, 5.4%).

149 [50] **:** ^{1}H-NMR (400 MHz) δ 7.30-7.22 (m, 4H), 7.17-7.14 (m, 1H), 6.23 (bdd, J=1.9-1.2 Hz, 1H), 2.82-2.75 (m, 2H), 2.50 (bd, J=2.4 Hz, 2H); ^{13}C-NMR (100 MHz) δ 146.1, 134.6, 127.8, 126.9, 126.3, 123.8, 28.3, 25.8.

4.4.3. Carbene Addition to 1-Phenyl-Cyclobutene (149).

To a magnetically stirring solution of 0.7 g (5 mmol) olefin **149**, 1.45 g (7.5 mmol) $CHBr_2F$ [45] and 0.25 g (1 mmol) $PhCH_2NEt_3Cl$ in 100 ml CH_2Cl_2, a solution of 1.25 g (30 mmol) NaOH dissolved in 1.5 mL water was drop wise

added at -5 ^{o}C over a period of 2 h. After stirring for an additional 8 h at room temperature, the reaction mixture was diluted with water to 250 mL and extracted with CH_2Cl_2 (3x 100 mL), dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (Fluorisil, 80 g) with hexane as eluent to give compounds **158** (0.3 g, 0.8 mmol, 16%, colourless liquid) and **159 (**0.3 g, 0.8 mmol, 16%, colourless liquid).

4.5.1. The synthesis of 7,7-Dichlorobicyclo [3.2.0]heptan-6-one (167).

A 1000-mL three-necked flask was equipped with a nitrogen inlet, a condenser, and pressure-regulated dropping funnel. Under a blanket of nitrogen gas, 10 g (0.15 mole) of cyclopentene **166** and 10.5 g (0.16 mole) ordinary zinc dust was put in the presence of 300 mL dry ether as the solvent. A solution of 29.1 g (0.16 mole) trichloroacetylchloride in 200 mL dry ether was given dropwise within 2 h at 0 ^{o}C. After the addition was completed a vigorous reaction started and the colour was turned into brown. As the reaction was completed, the zinc salts were filtered through celite 545. The product was extracted with ether (3x150 mL), then the organic phase was washed with saturated sodium bicarbonate solution, and finally with brine. The solution was dried over $MgSO_4$ and the product was concentrated. Finally, the product was further purified by vacuum distillation to give 10.8 g (0.06 mole) of **167** as a yellowish liquid (bp. 70 ^{o}C/5 mmHg) in a yield of 40%.

167 [51] **:** ^{1}H-NMR (400 MHz) δ 3.81 (t, J=7.8 Hz, 1H), 3.15 (t, J=7.8 Hz, 1H), 2.10-2.04 (m, 1H), 1.99-1.93 (m, 1H), 1.66-1.55 (m, 2H), 1.48-1.31 (m, 2H); ^{13}C-NMR (100 MHz) δ 198.5, 88.9, 62.4, 52.8, 30.8, 30.3, 26.1.

4.5.2. The synthesis of Bicyclo [3.2.0]heptan-6-one (168).

A 500-mL two-neck flask containing 8 g (0.122 mole) zinc dust and 150 mL glacial acetic acid was let to stir magnetically. A condenser was connected. To the other neck a pressure regulated dropping funnel, containing 10.8 g (0.060 mole)

167 in 100 mL of glacial acetic acid was plugged. This solution was given dropwise at room temperature to the zinc dust-acetic acid solution. After the dropping was ceased, the temperature was raised to 70 ^{o}C and kept constant at this temperature while stirring 15 h magnetically. Here the system was diluted with distilled water to dissolve the formed zinc salt. The mixture was then filtered through ordinary filter paper, and extracted with ether (3x150 mL), washed with first water, then saturated $NaHCO_3$, solution and, finally with brine. The solution was dried over $MgSO_4$, and was concentrated under vacuo. Vacuum distillation gave 5 g (0.045 mole) of pure **168** as a colourless liquid (bp. 30-35 ^{o}C/5 mmHg) in a yield of 75%.

168 : ^{1}H-NMR (400 MHz) δ 3.28 (bs, 1H), 2.96-2.89 (m, 1H), 2.66-2.59 (m, 1H), 2.20 (d, J=7.6 Hz, 1H), 1.78 (d, J=7.6 Hz, 1H), 1.60-1.56 (m, 2H), 1.54-1.46 (m, 1H), 1.39-1.26 (m, 2H); ^{13}C-NMR (100 MHz) δ 213.0, 65.1, 51.8, 32.9, 30.0, 29.2, 24.0.

4.5.3. The synthesis of 6-Methyl-bicyclo[3.2.0]heptan-6-ol (169).

A 250-mL two-neck flask containing 1.2 g (0.049 mole) magnesium and a piece of iodine crystal in 50 mL dry ether was let to stir magnetically in a water bath. A condenser was connected. To the other neck a pressure regulated dropping funnel, containing 7.0 g (0.049 mole) CH_3I in 50 mL of dry ether was plugged. This solution was given dropwise at room temperature to the magnesium suspension. An exothermic reaction was started (if the reaction was not observed the flask was gently heated until it begins). After the dropping was ceased, it was allowed to cool to room temperature. After cooling, the contents of the flask was taken into the dropping funnel and was added dropwise to a solution of 5 g (0.045 mole) ketone **168** in 50 mL dry ether. After the addition was completed, the reaction was further stirred 2 h at room temperature. A saturated solution of NH_4Cl was added. The mixture was extracted with ether (3x100 mL), dried over $MgSO_4$, and the solvent was removed by rotary evaporator. Vacuum distillation gave 5 g (0.039 mole) **169** as a colourless liquid (bp. 40-42 ^{o}C/ 5 mmHg) in 86% yield.

169 [52] **:** ^{1}H-NMR (400 MHz) δ 2.38-2.35 (m, 1H), 2.25 (p, J=6.5 Hz, 1H), 2.02-1.96 (m, 1H), 1.80-1.75 (m, 1H), 1.68-1.62 (m, 2H), 1.43-1.30 (m, 4H), 1.22 (s, 3H); ^{13}C-NMR (100 MHz) δ 69.4, 50.9, 41.2, 32.7, 31.0, 30.9, 26.3, 26.0.

4.6.1. The synthesis of 6-Phenyl-bicyclo[3.2.0]heptan-6-ol (170).

A 250-mL two-neck flask that was put 1.2 g (0.049 mole) magnesium and a piece of iodine crystal in 50 mL dry ether was let to stir magnetically in a water bath. A condenser was connected. To the other neck a pressure regulated dropping funnel, containing 7.8 g (0.049 mole) C_6H_5Br in 50 mL of dry ether was plugged. This solution was given dropwise at room temperature to the magnesium suspension. An exothermic reaction was started (if the reaction was not observed the flask was gently heated until it begins). After the dropping was ceased, it was allowed to cool to room temperature. After cooling, the contents of the flask was taken into the dropping funnel and was added dropwise to a solution of 5 g (0.045 mole) ketone **168** in 50 mL dry ether. After the addition was completed, the reaction was further stirred 2 h at room temperature. A saturated solution of NH_4Cl was added. The mixture was extracted with ether (3x100 mL), dried over $MgSO_4$ and the solvent was removed by rotary evaporator. Vacuum distillation gave 7.5 g (0.040 mole) **170**, which crystallized upon standing (white needle crystals, mp. 56-60 ^{o}C) in 88% yield.

170 [53] **:** ^{1}H-NMR (400 MHz) δ 7.30 (d, J=7.4 Hz, 2H), 7.13 (t, J=7.1 Hz, 2H), 7.01 (t, J=7.0 Hz, 1H), 2.76-2.73 (m, 1H), 2.48-2.38 (m, 2H), 1.91 (dd, J= 6.7-6.4 Hz, 1H), 1.79-1.75 (m, 1H), 1.71-1.58 (m, 2H), 1.43 (dd, J= 6.2-6.1 Hz, 1H), 1.36-1.24 (m, 3H); ^{13}C-NMR (100 MHz) δ 149.4, 129.0, 127.2, 124.6, 72.9, 51.3, 42.0, 33.2, 31.6, 27.0, 26.3.

4.6.2. The syntheses of 6-Phenyl-bicyclo[3.2.0]hept-6-ene (164) and 1-Phenyl-bicyclo[4.1.0]hept-2-ene (171).

A solution of 7.5 g (0.040 mole) alcohol **170** and 0.7 g (0.004 mole) PTSA in 100 mL toluene was heated up to reflux in a Dean-Stark trap, which was attached to a condenser. After 16 h the flask was allowed to cool to room temperature. The solution was washed first with $NaHCO_3$ solution, and then with brine, dried over $CaCl_2$. Rotary evaporator removed the solvent, and the residue was filtered on a silica gel (50 g) column eluting with hexane to give 4.1 g (24 mmol, yellowish liquid) of **164** and 1 g (6 mmol, colourless liquid) of **171** in a total yield of 75%.

164 [54a] **:** ^{1}H-NMR (400 MHz) δ 7.17-6.99 (m, 5H), 5.95 (bs, 1H), 3.31 (bdd, J=7.1-3.6 Hz, 1H), 2.98 (bdd, J=7.1-3.6 Hz, 1H), 1.63-1.09 (m, 6H); ^{13}C-NMR (100 MHz) δ 146.2, 134.1, 128.4, 128.0, 127.4, 124.8, 46.2, 44.0, 26.9, 26.3, 23.8.

171 [54b] **:** ^{1}H-NMR (400 MHz) δ 7.21-7.17 (m, 4H), 7.10-7.04 (m, 1H), 6.08 (dd, A- part of AB system, J=10.0-2.2 Hz, 1H), 5.48 (ddd, B- part of AB system, J=10.0-6.4-2.2 Hz, 1H), 2.02-1.92 (m, 2H), 1.79-1.67 (m, 2H), 1.44-1.42 (m, 1H), 1.27 (dd, J=8.5-4.9 Hz, 1H), 1.04 (bt, J=5.4 Hz, 1H); ^{13}C-NMR (100 MHz) δ 146.5, 133.0, 128.7, 127.5, 126.0, 123.2, 25.6, 24.3, 20.8, 19.0, 18.4; MS (m/z, relative intensity): 169 (M^{+}, 65), 153 (100), 141 (90), 127 (65), 114 (45), 101 (15), 90 (30), 76 (45), 50 (35). Anal. Calcd for $C_{13}H_{14}$: C, 91.71; H, 8.29. Found: C, 91.70; H, 8.29.

4.6.3. Carbene Addition to 6-Phenyl-Bicyclo[3.2.0]hept-6-ene (164).

To a magnetically stirring solution of 1 g (6 mmol) olefin **164**, 2.8 g (14.8 mmol) $CHBr_2F$ [45] and 0.25 g (1 mmol) $PhCH_2NEt_3Cl$ in 100 ml CH_2Cl_2, a solution of 2.2 g (54 mmol) NaOH dissolved in 2.5 mL water was drop wise added at -5 ^{o}C

over a period of 2 h. After stirring for an additional 8 h at room temperature, the reaction mixture was diluted with water to 250 mL and extracted with CH_2Cl_2 (3x 100 mL), dried over $MgSO_4$, and the solvent was removed under reduced pressure. Repeated column chromatography (1% $AgNO_3$-silica gel, 100 g) with hexane as eluent gave compounds **173** (0.20 g, 13%, colourless liquid), **174** (0.40 g, 27%, colourless liquid), **175** (0.30 g, 20%, colourless liquid), **176** (0.10 g, 7%, colourless liquid), and **177** (0.20 g, 13%, colourless liquid).

4,6-difluoro-5-phenyl-indane (**173**): colorless liquid, ^{1}H-NMR (400 MHz) δ 7.35-7.22 (m, 5H), 6.81 (d, $^{2}J_{HF}$ = 9.0 Hz, 1H, H_7), 2.85 (t, J=7.4 Hz, 4H), 2.06 (p, J=7.4 Hz, 2H); ^{13}C-NMR (100 MHz) δ 159.5 (dd, $^{1,3}J_{CF}$ = 245.1-5.7 Hz, C_4), 156.3 (dd, $^{1,3}J_{CF}$ = 247.4-7.8 Hz, C_6), 146.8 (dd, $^{3,3}J_{CF}$ = 9.5-7.8 Hz, C_{7a}), 130.8 (C_{orto}), 130.4 (C_{ipso}), 128.5 (C_{meta}), 128.1 (C_{para}), 126.0 (dd, $^{2,4}J_{CF}$ = 19.6-2.8 Hz, C_{3a}), 116.3 (t, $^{2}J_{CF}$ =19.0 Hz, C_5), 107.8 (dd, $^{2,4}J_{CF}$ =23.5-3.6 Hz, C_7), 33.8 (C_1), 29.0 (C_3), 25.8 (C_2); ^{19}F-NMR (376.3 MHz, $CDCl_3$) δ -117.6 (d, $^{4}J_{FF}$ = 5.6 Hz, F-C_6), -118.8 (d, $^{4}J_{FF}$ = 5.6 Hz, F-C_4); MS (m/z, relative intensity): 230 (M^+, 70), 152 (25), 132 (10), 100 (10), 76 (10), 50 (7). IR ($CHCl_3$, cm^{-1}): 3084, 3056, 3021, 2951, 2944, 2909, 2853, 2832, 1644, 1567, 1462, 1420, 1329, 1266, 1106, 1022, 847, 763, 686, 560. Anal. Calcd. for $C_{15}H_{12}F_2$: C, 78.24; H, 5.25. Found: C, 78.20; H, 5.26.

5,6-difluoro-4-phenyl-indane (**174**): colorless liquid, ^{1}H-NMR (400 MHz) δ 7.46-7.35 (m, 5H), 6.88 (dd, $^{2}J_{HF}$ = 9.4-7.1 Hz, 1H, H_7), 2.95 (t, J=7.3 Hz, 2H), 2.80 (t, J=7.3 Hz, 2H), 2.08 (p, J=7.3 Hz, 2H); ^{13}C-NMR (100 MHz) δ 150.1 (dd, $^{1,2}J_{CF}$ = 245.0-14.5 Hz, C_5), 146.9 (dd, $^{1,2}J_{CF}$ =243.7-13.7 Hz, C_6), 139.4 (dd, $^{3,4}J_{CF}$ = 6.0-3.5 Hz, C_{3a}), 138.7 (bs, C_{7a}), 134.4 (C_{ipso}), 130.0, 128.6, 127.8, 127.7 (bd, $^{2}J_{CF}$ = 10.4 Hz, C_4), 111.9 (dd, $^{2,3}J_{CF}$ =17.5-0.0 Hz, C_7), 33.4 (C_1), 32.8 (C_3), 26.3 (C_2); ^{19}F-NMR (376.3 MHz, $CDCl_3$) δ -140.6 (d, $^{3}J_{FF}$ = 20.3 Hz, F-C_6), -146.2 (d, $^{3}J_{FF}$ = 20.3 Hz, F-C_5); MS (m/z, relative intensity): 230 (M^+, 95), 152 (50), 132 (12), 100 (15), 76 (8), 62 (5), 50 (10). IR ($CHCl_3$, cm^{-1}): 3056, 2958, 2951, 2846, 1700, 1616, 1476, 1441,1343, 1203, 1238, 1126, 1071, 1029, 868,

770, 700, 644, 574. Anal. Calcd. for $C_{15}H_{12}F_2$: C, 78.24; H, 5.25. Found: C, 78.20; H, 5.26.

5,7-difluoro-4-phenyl-indane (**175**): colorless liquid, ^{1}H-NMR (400 MHz) δ 7.36-7.22 (m, 5H), 6.62 (t, $^2J_{HF}$ = 9.2 Hz, 1H, H_6), 2.87 (t, J=7.4 Hz, 2H), 2.75 (t, J=7.4 Hz, 2H), 2.01 (p, J=7.4 Hz, 2H); ^{13}C-NMR (100 MHz) δ 159.1 (dd, $^{1,3}J_{CF}$ = 244.9-9.5 Hz, C_5), 158.1 (dd, $^{1,3}J_{CF}$ =246.7-12.6 Hz, C_7), 147.7 (t, $^3J_{CF}$ = 5.2 Hz, C_{3a}), 134.6 (C_{ipso}),129.8, 128.5, 128.1, 125.7 (dd, $^{2,4}J_{CF}$ = 14.9-3.3 Hz, C_{7a}), 122.4 (dd, $^{2,4}J_{CF}$ = 16.2-3.1 Hz, C_4), 102.1 (dd, $^2J_{CF}$ = 27.5-24.7 Hz, C_6), 33.6 (C_3), 29.8 (C_1), 26.0 (C_2); ^{19}F-NMR (376.3 MHz, $CDCl_3$) δ -115.6 (d, $^4J_{FF}$ = 6.9 Hz), -117.4 (d, $^4J_{FF}$ = 6.9 Hz); MS (m/z, relative intensity): 230 (M^+, 80), 152 (25), 132 (8), 100 (10), 76 (5), 62 (3), 50 (7). IR ($CHCl_3$, cm^{-1}): 2944, 2923, 2846, 1721, 1658, 1609, 1455, 1371, 1287, 1217, 1113, 1085, 973, 882, 763, 707, 679, 637, 567. Anal. Calcd. for $C_{15}H_{12}F_2$: C, 78.24; H, 5.25. Found: C, 78.20; H, 5.26.

4-bromo-6-fluoro-5-phenyl-indane (**176**): colorless liquid, ^{1}H-NMR (400 MHz) δ 7.36-7.27 (m, 3H), 7.19 (bd, J=7.9 Hz, 2H), 6.87 (d, $^2J_{HF}$ = 8.7 Hz, 1H, H_7), 2.99 (t, J=7.5 Hz, 2H), 2.90 (t, J=7.5 Hz, 2H), 2.08 (p, J=7.5 Hz, 2H); ^{13}C-NMR (100 MHz) δ 159.2 (d, $^1J_{CF}$ = 245.4 Hz,C_6), 145.5 (d, $^3J_{CF}$ = 8.5 Hz, C_{7a}), 140.8 (d, $^4J_{CF}$ = 2.8 Hz, C_{3a}), 135.4 (C_{ipso}), 130.6 (C_o), 128.5 (d, $^2J_{CF}$ = 26.9 Hz, C_5), 128.3 (C_m), 128.2 (C_p), 121.6 (d, $^3J_{CF}$ = 3.9 Hz, C_4), 110.9 (d, $^2J_{CF}$ = 24.0 Hz, C_7), 35.1 (C_1), 34.6 (C_3), 24.8 (C_2); ^{19}F-NMR (376.3 MHz, $CDCl_3$) δ -113.3 (s, F-C_6); MS (m/z, relative intensity): 290/288 (M^+, 95), 210 (30), 195 (70), 182 (55), 168 (10), 132 (30), 103 (25), 91 (25), 50 (10). IR ($CHCl_3$, cm^{-1}): 2958, 2951, 2916, 2846,1658, 1609, 1588, 1490, 1399, 1357, 1217, 1113, 1092, 1043, 903, 819, 777, 651, 588. Anal. Calcd. for $C_{15}H_{12}BrF$: C, 61.88; H, 4.15. Found: C, 61.86; H, 4.17.

5-bromo-6-fluoro-4-phenyl-indane (**177**): colorless liquid, ^{1}H-NMR (400 MHz) δ 7.32 (t, J= 7.3 Hz, 2H), 7.27-7.21 (m, 3H), 7.07 (d, $^2J_{HF}$ = 9.2 Hz, 1H, H_7), 2.89 (t, J=7.4 Hz, 2H), 2.85 (t, J=7.5 Hz, 2H), 1.98 (p, J=7.4 Hz, 2H); ^{13}C-

NMR (100 MHz) δ 158.8 (d, $^{1}J_{CF}$ = 247.0 Hz, C_6), 146.0 (d, $^{4}J_{CF}$ = 0, C_{3a}), 140.3 (d, $^{3}J_{CF}$ = 0, C_{7a}), 134.4 (C_{ipso}), 129.7 (C_{meta}), 128.5 (C_{orto}), 127.9 (C_{para}), 125.6 (d, $^{2}J_{CF}$ = 16.3 Hz, C_5), 118.3 (d, $^{3}J_{CF}$ = 10.7 Hz, C_4), 117.4 (d, $^{2}J_{CF}$ = 26.9 Hz, C_7), 34.5 (C_3), 34.4 (d, $^{4}J_{CF}$ = 2.9 Hz, C_1), 25.2 (C_2); ^{19}F-NMR (376.3 MHz, $CDCl_3$) δ -119.3 (s, F-C_6); MS (m/z, relative intensity): 290/288 (M^+, 85), 210 (45), 195 (65), 182 (55), 132 (40), 103 (30), 91 (35), 76 (20), 50 (15), 43 (50). IR ($CHCl_3$, cm^{-1}): 2959, 2944, 2916, 2853, 1679,1623, 1455, 1406, 1371, 1217, 1126, 1092, 868, 770, 707, 644, 602, 546. Anal. Calcd. for $C_{15}H_{12}BrF$: C, 61.88; H, 4.15. Found: C, 61.86; H, 4.17.

4.7. The synthesis of 5-Bromo-1,2,3,3a,4,6a-hexahydro-pentalene (183).

To a magnetically stirring suspension of 0.72 g (19 mmol) $LiAlH_4$ in 40 mL dry ether, a solution of 5.0 g (19 mmol) dibromo **182**[27] in 30 mL dry ether was dropwise added in 30 min under the stream of nitrogen. The reaction mixture was heated up to reflux for 21 h. After cooling, excess hydride was decomposed by the carefull addition of water. The mixture was further diluted with water and the aqueous layer was extracted with diethyl ether (3x100 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give 3.5 g of crude product which was distilled to give pure **183** (3.0 g, colorless liquid, bp. 46 ^{o}C/ 5 mmHg) in a yield of 85%.

183: ^{1}H-NMR (400 MHz) δ 5.58 (bs, 1H), 3.06 (m, 1H), 2.83 (dd, J=16.4-9.4 Hz, 1H), 2.71-2.57 (m, 1H), 2.21 (d, J=16.4 Hz, 1H), 1.74-1.68 (m, 1H), 1.64-1.58 (m, 1H), 1.54-1.35 (m, 4H); ^{13}C-NMR (100 MHz) δ 134.8, 119.6, 50.6, 48.1, 41.2, 35.8, 32.3, 25.6; IR ($CHCl_3$, cm^{-1}): 2938, 2862, 1625, 1446, 1377, 1246, 1213, 1173, 1092, 1049, 1012, 957, 907, 843, 788, 766, 686; MS (m/z, relative intensity): 187 (M^+, 25), 156 (60), 143 (20), 118 (25), 106 (35), 94 (30), 90 (50), 78 (100), 66 (55), 56 (60), 41 (70). Anal. Calcd. for $C_8H_{11}Br$: C, 51.36; H, 5.93. Found: C, 51.30; H, 5.90.

4.8. Represantative procedure for the reduction of quinones 4 to hydroquinones 5 with NaN_3.

25 mmol of NaN_3 was added in one protion to a solution of 5 mmol of benzoquinone in 70 mL acetone-water (9:1) mixture at room temperature. After completion (5-12 h, TLC), the reaction mixture was concentrated in vacuo and saturated NH_4Cl was added. The mixture was extracted with ether (3x100 mL). Combined organic layers washed with brine, dried over $MgSO_4$, and solvent was removed to give analytically pure products which were crystallized from hexane-ether, or further purified by flash column chromatography (SiO_2, ethylacetate/hexane, 15:85) to remove coloured impurities.

2-(azidomethyl)benzene-1,4-diol (Table 2, Entry 7): Dark red oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.78-6.67 (m, 3H), 5.39 (bs, OH, 1H), 5.12 (bs, OH, 1H), 4.34 (s, -CH_2, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 149.3, 148.0, 122.8, 117.0, 116.7, 116.4, 50.7 ; IR ($CHCl_3$, cm^{-1}): 3377, 2923, 2839, 2098, 1651, 1504, 1448, 1329, 1259, 1182, 1099, 861, 805. Anal. Calcd for $C_7H_7N_3O_2$: C, 50.91; H, 4.27; N, 25.44. Found: C, 50.80; H, 4.18; N, 25.23.

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APPENDIX A

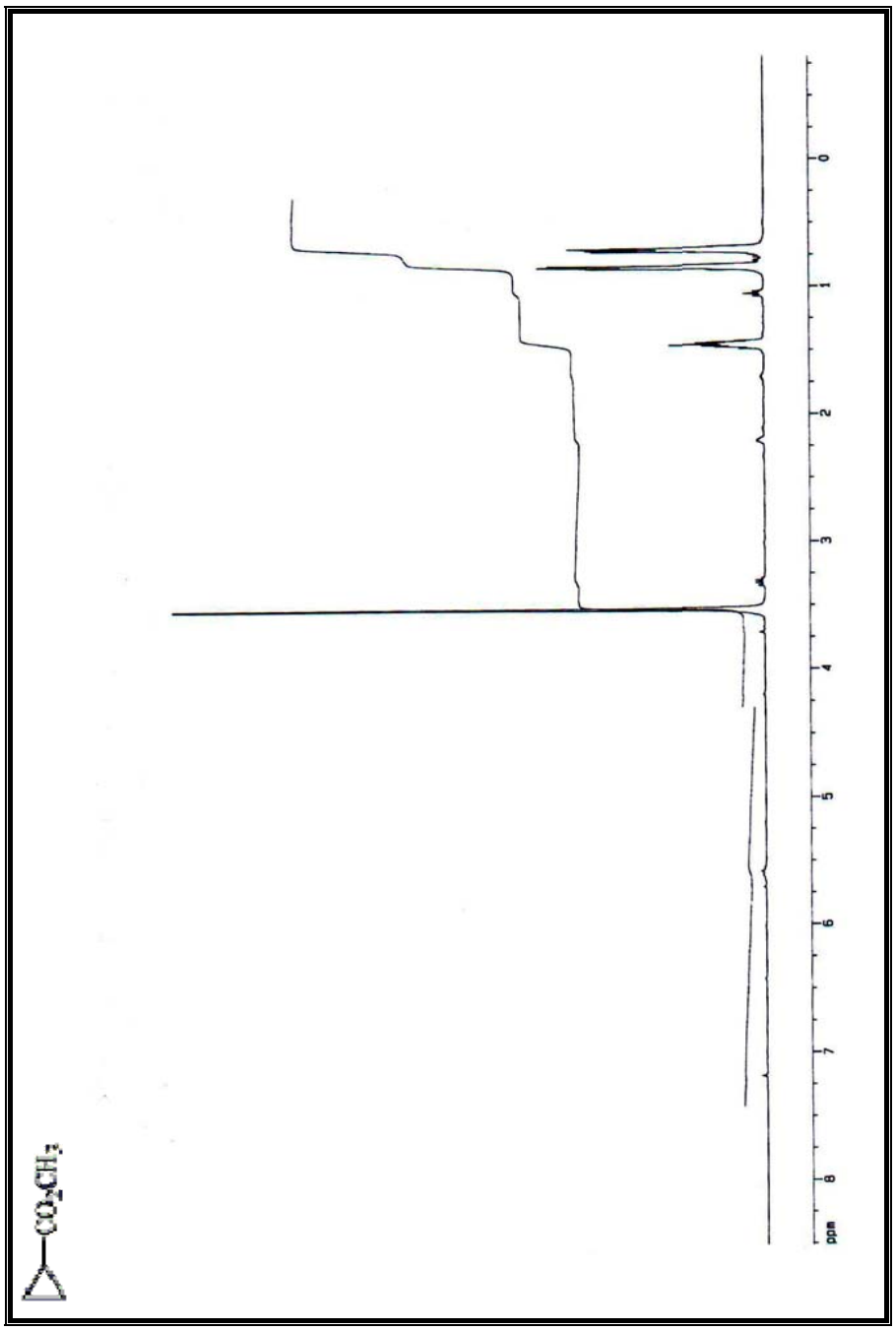

Figure A1 ^{1}H-NMR Spectrum of Compound **128**.

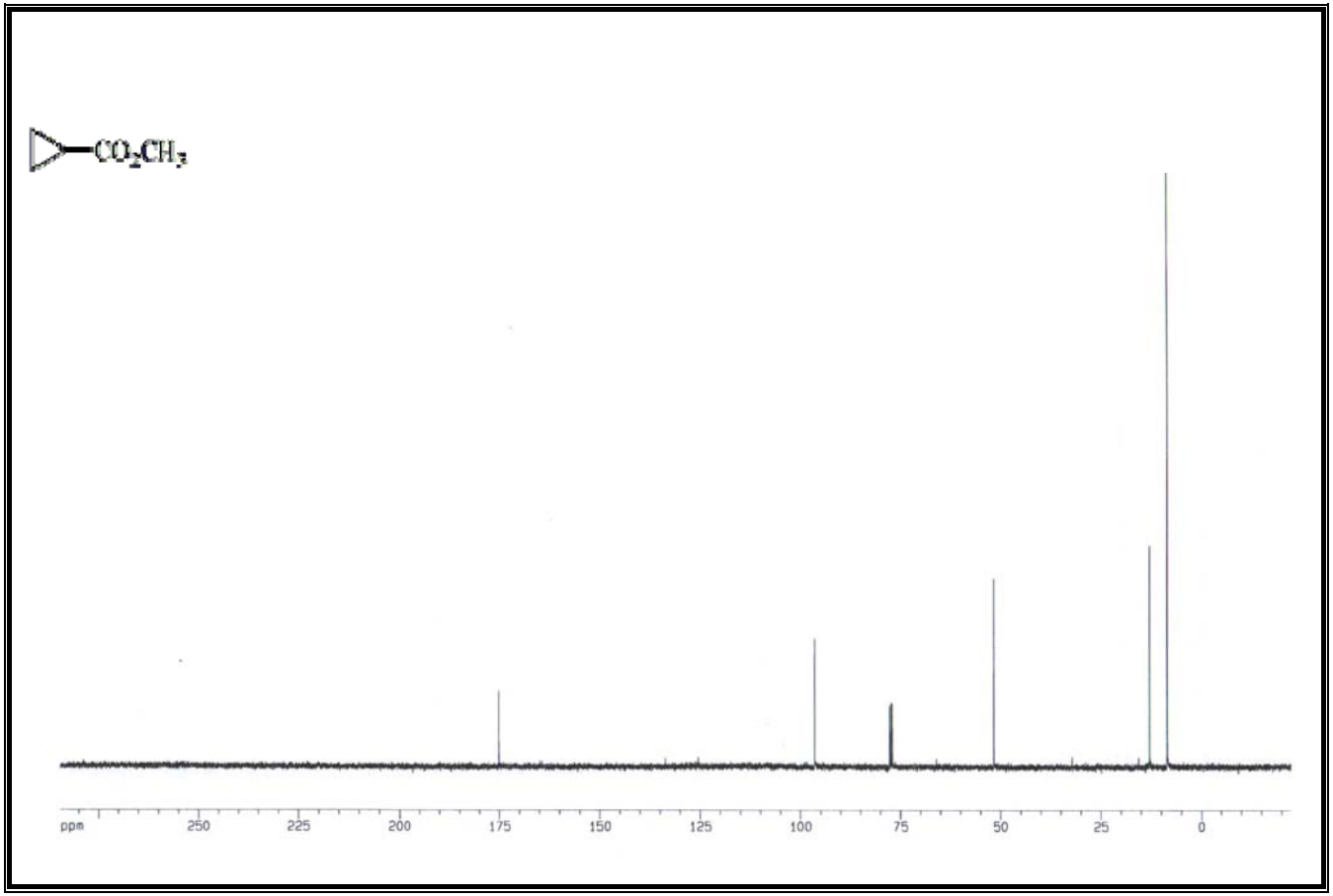

Figure A2 ^{13}C-NMR Spectrum of Compound **128**.

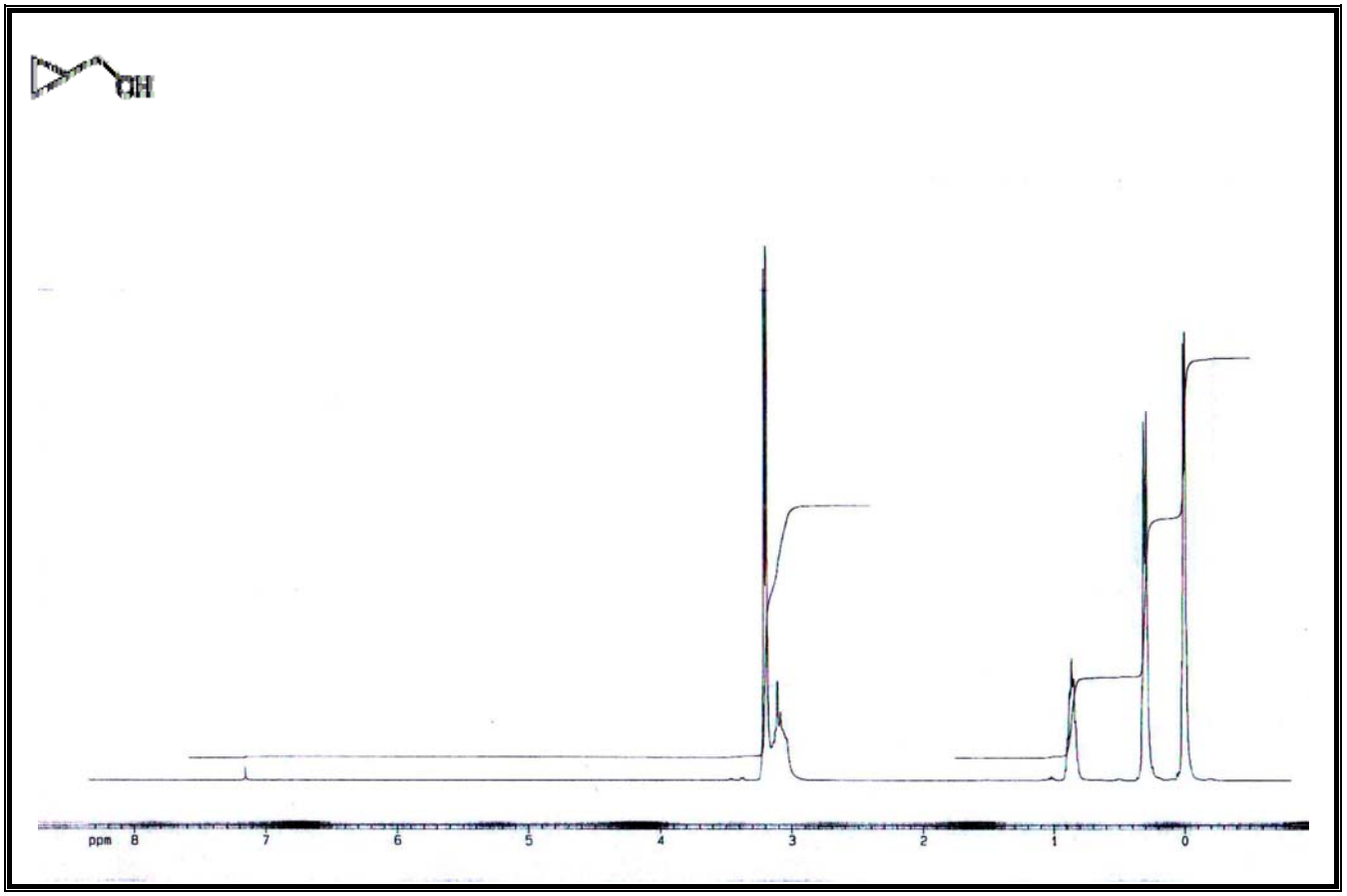

Figure A3 ^{1}H-NMR Spectrum of Compound **129**.

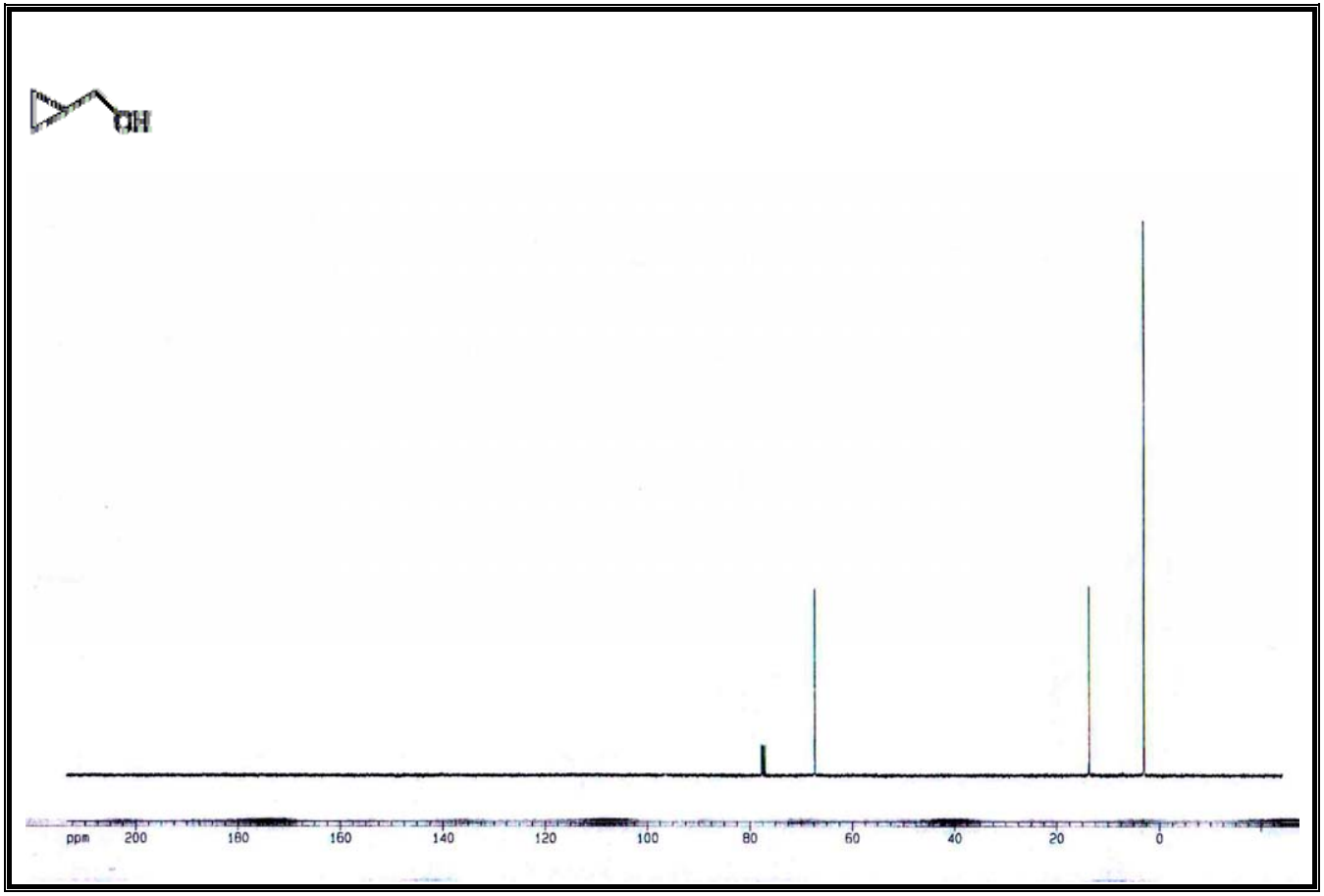

Figure A4 ^{13}C-NMR Spectrum of Compound **129**.

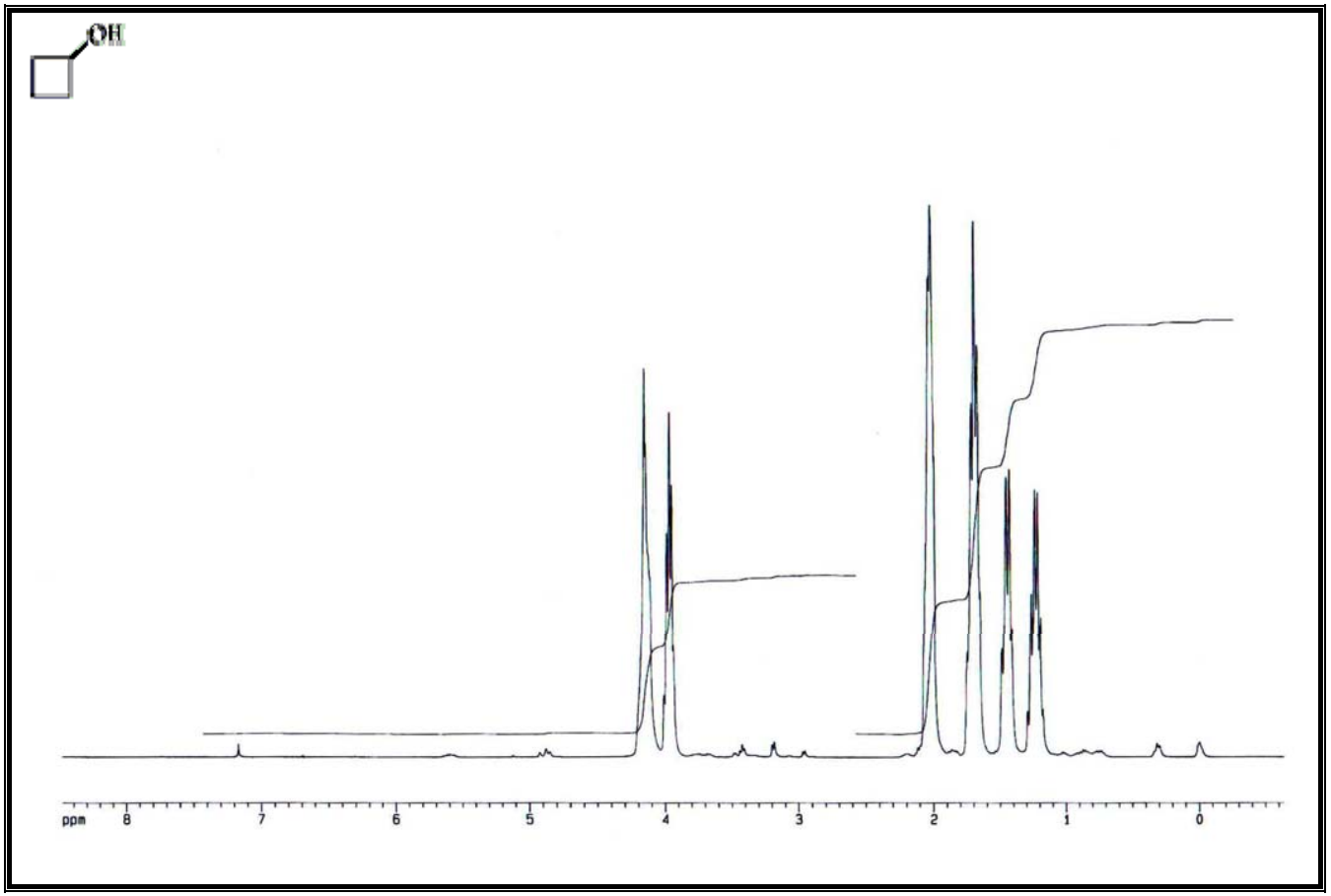

Figure A5 ^{1}H-NMR Spectrum of Compound **130**.

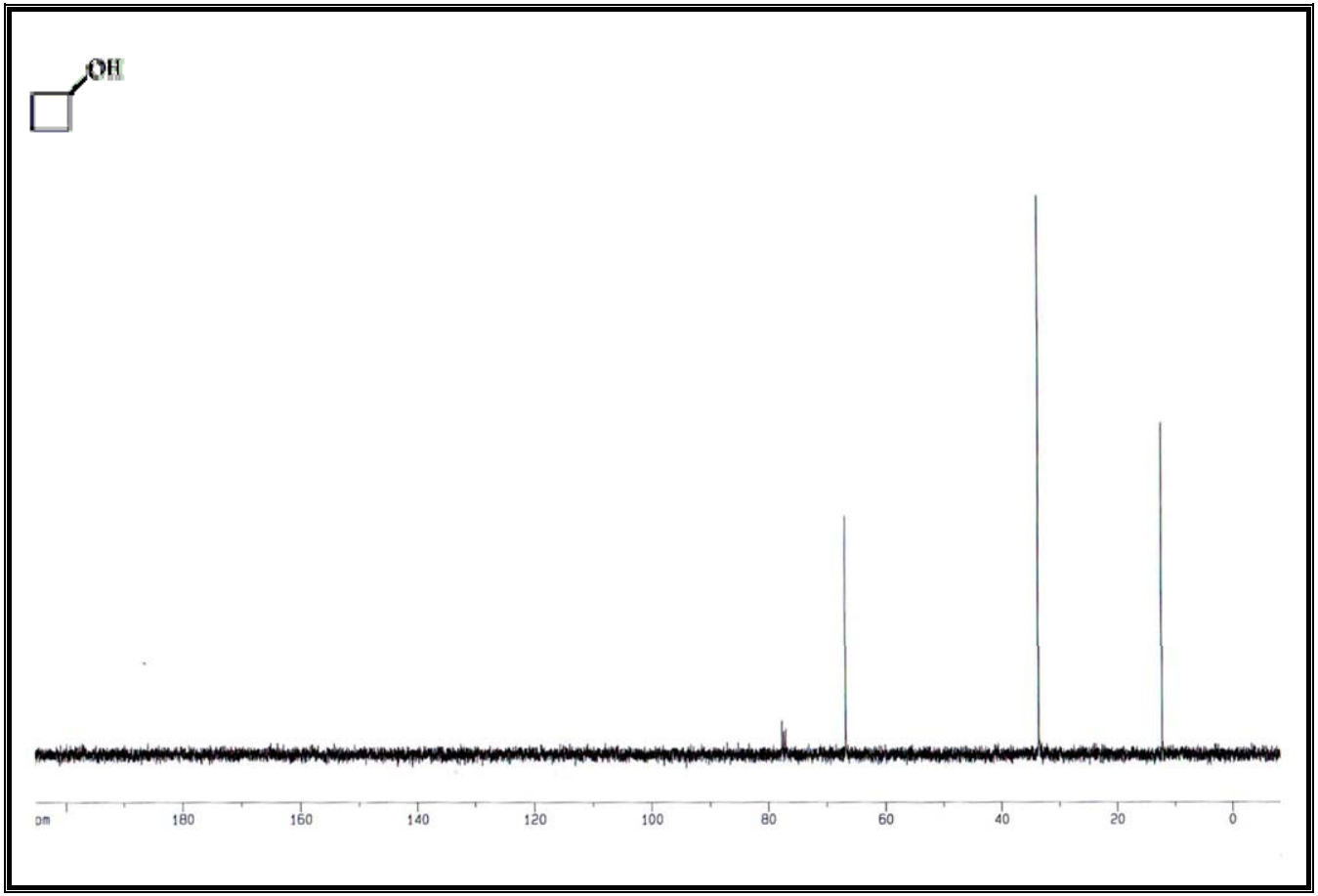

Figure A6 ^{1}H-NMR Spectrum of Compound **130**.

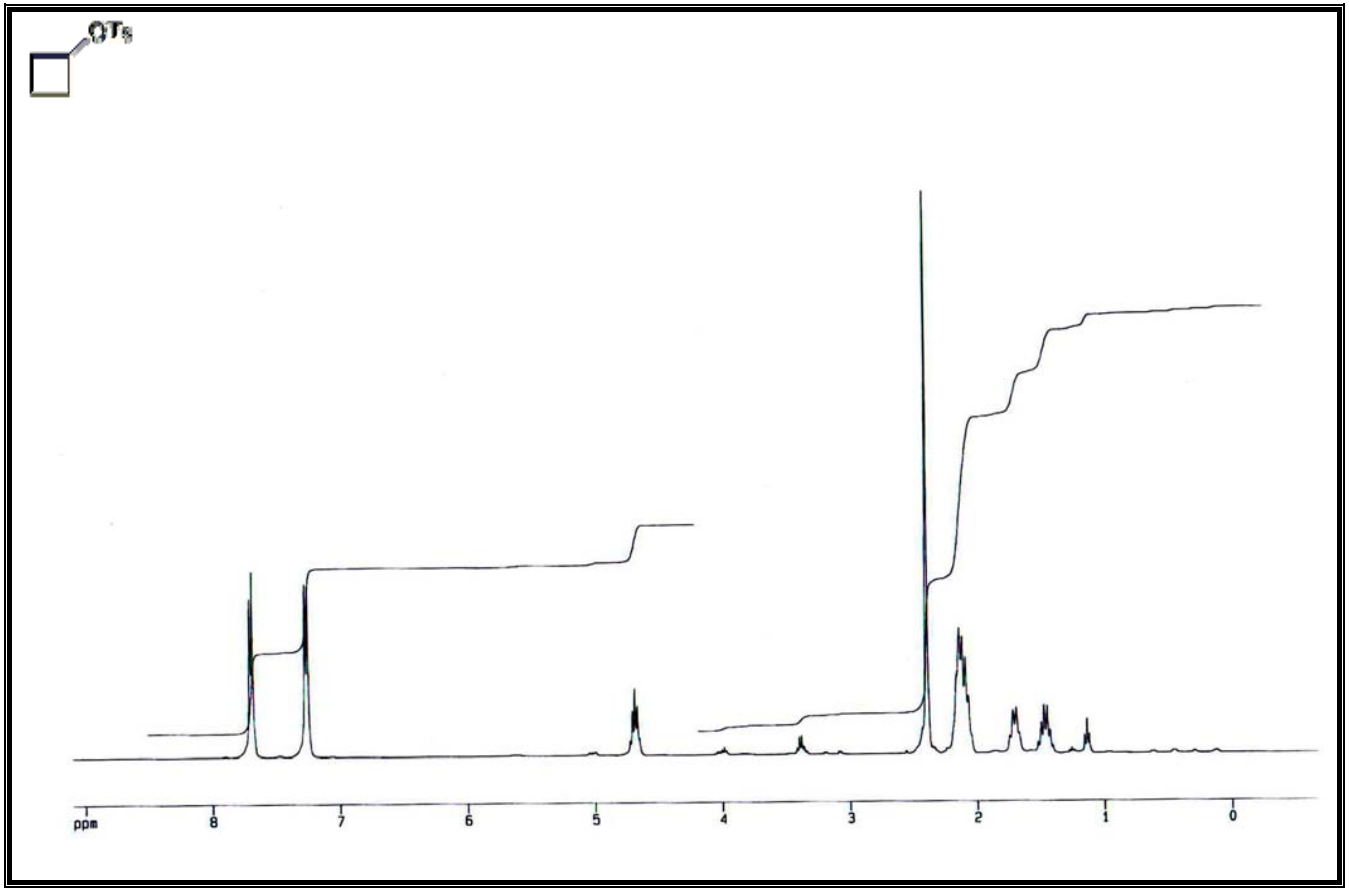

Figure A7 ^{1}H-NMR Spectrum of Compound **131**.

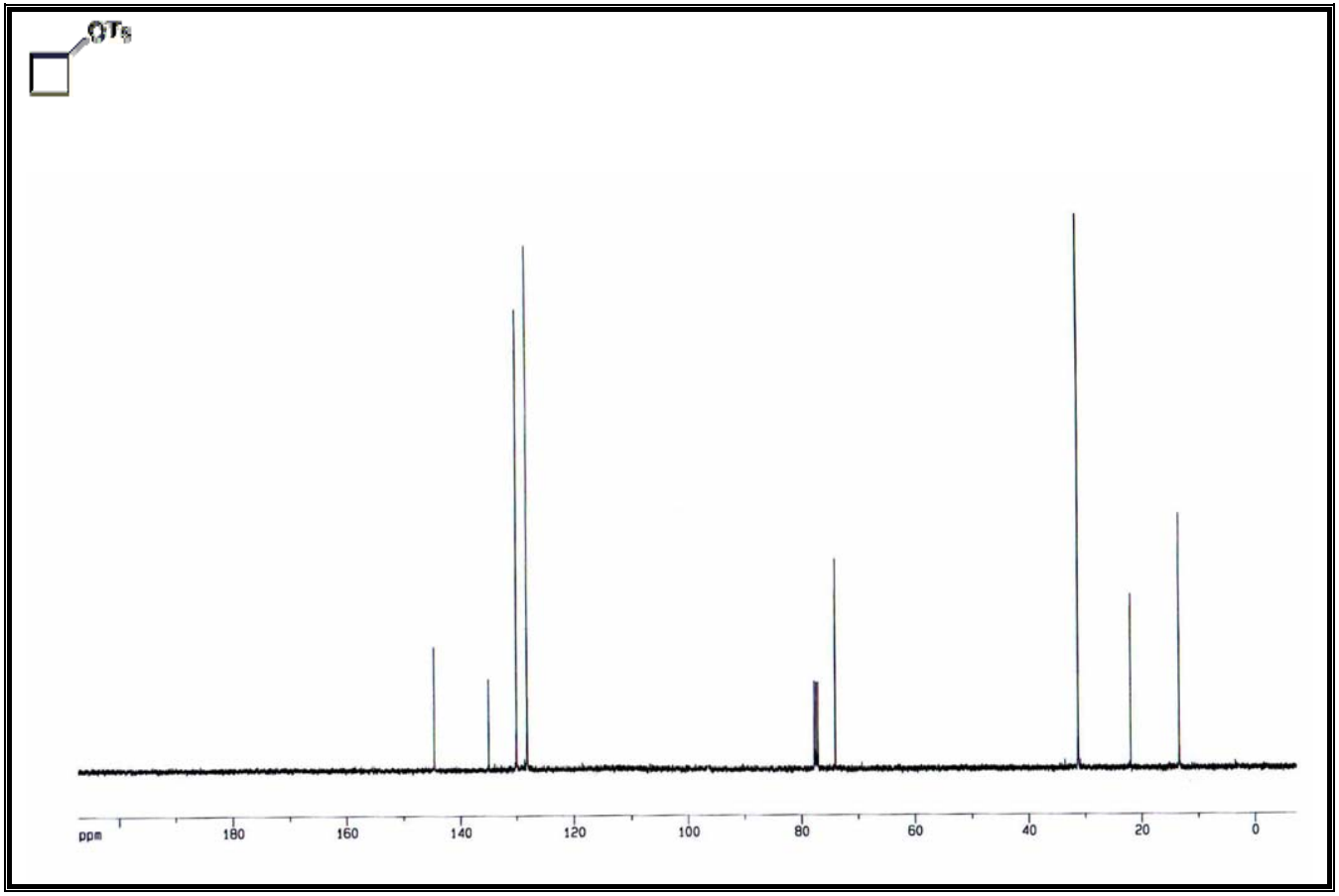

Figure A8 ^{13}C-NMR Spectrum of Compound **131**.

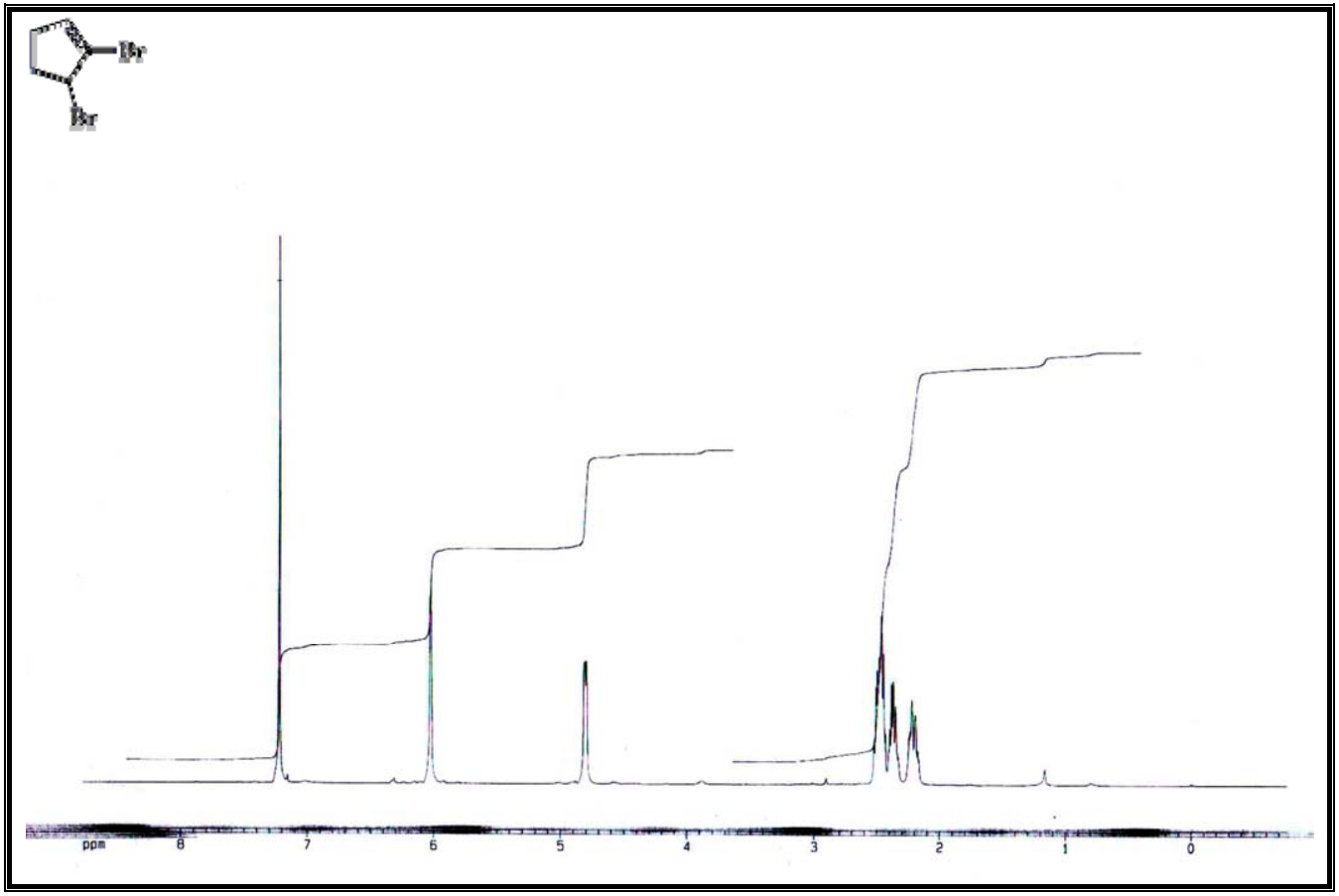

Figure A9 ^{1}H-NMR Spectrum of Compound **83**.

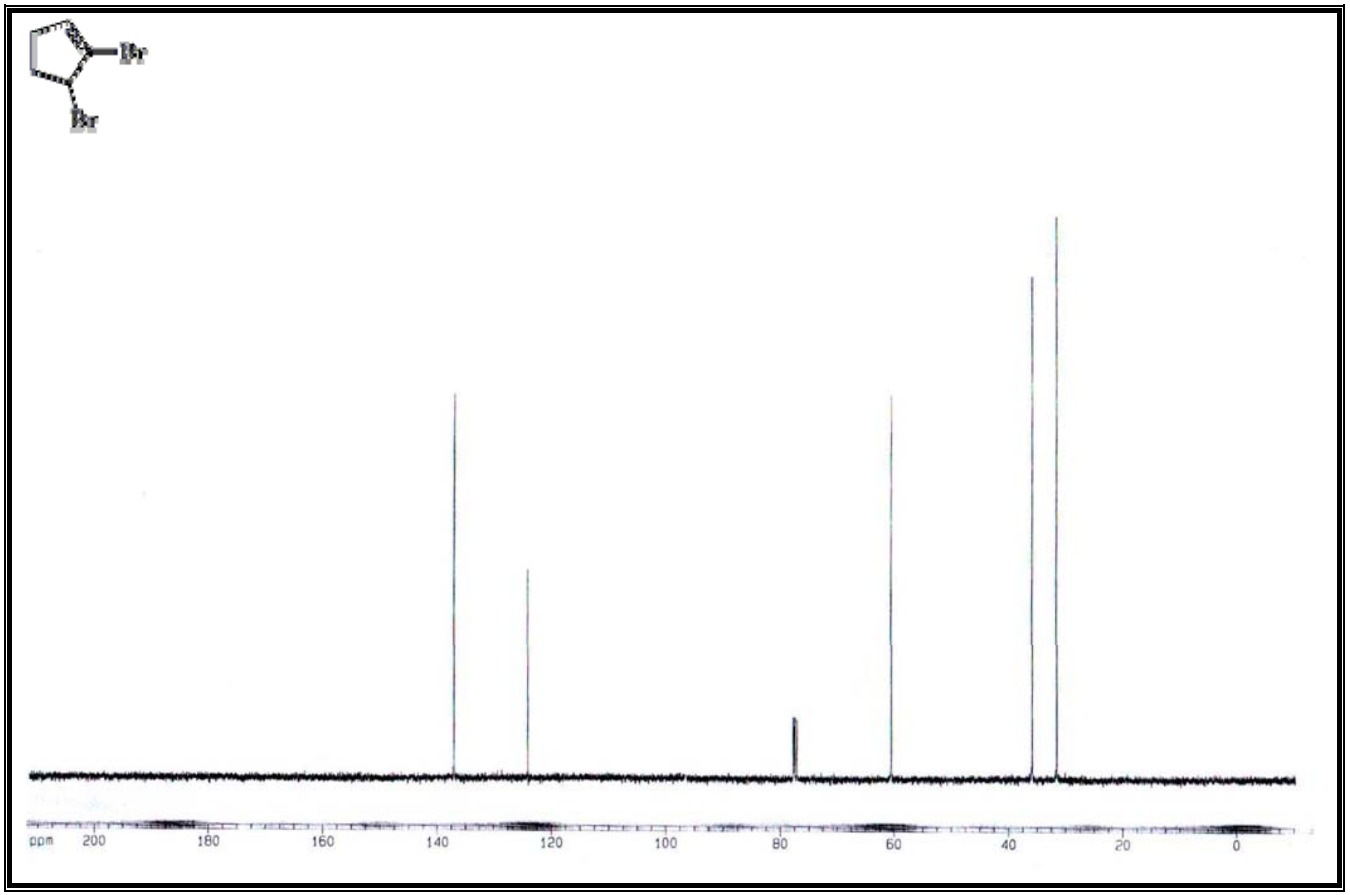

Figure A10 ^{13}C-NMR Spectrum of Compound **83**.

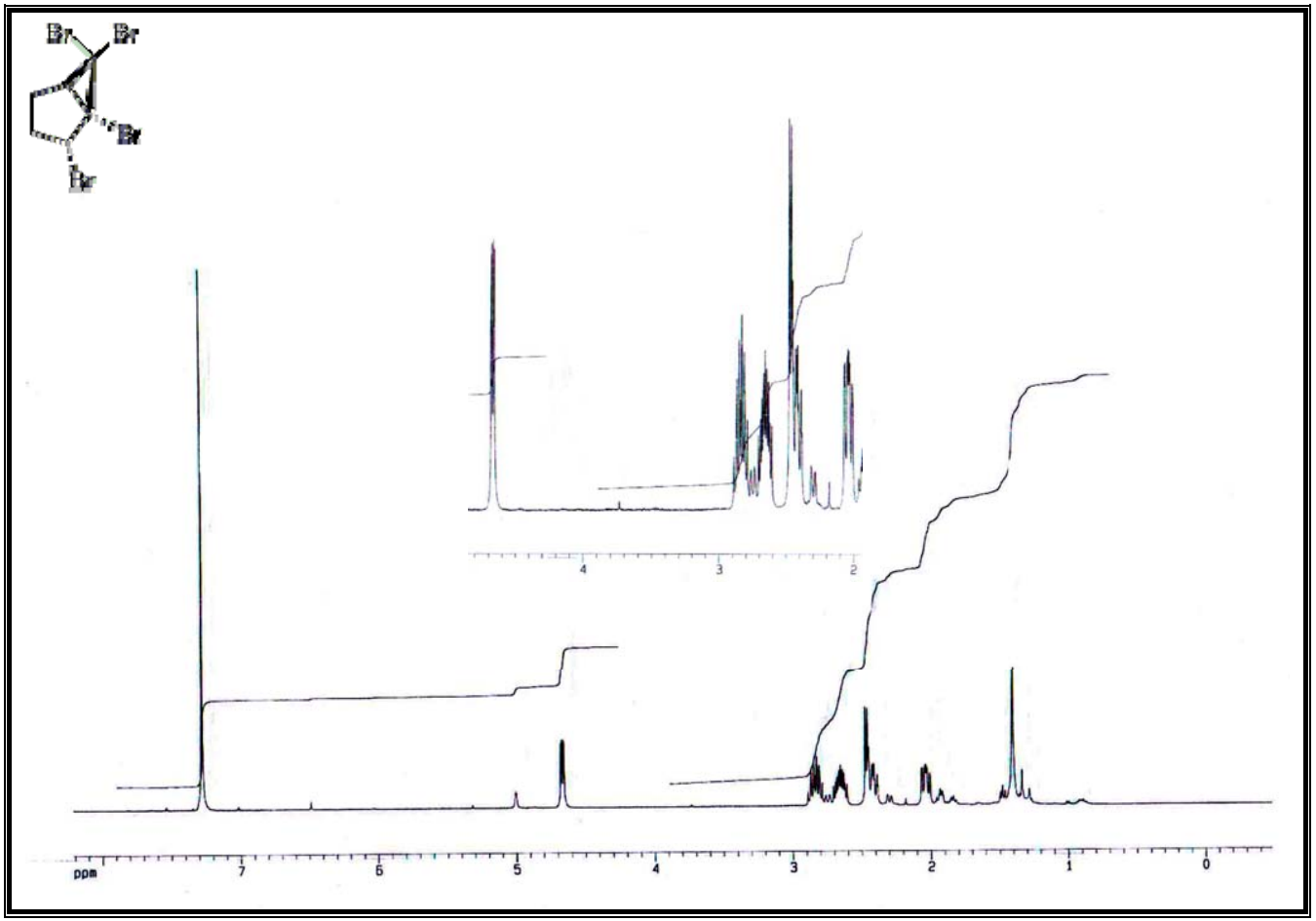

Figure A11 ^{1}H-NMR Spectrum of Compound **137**.

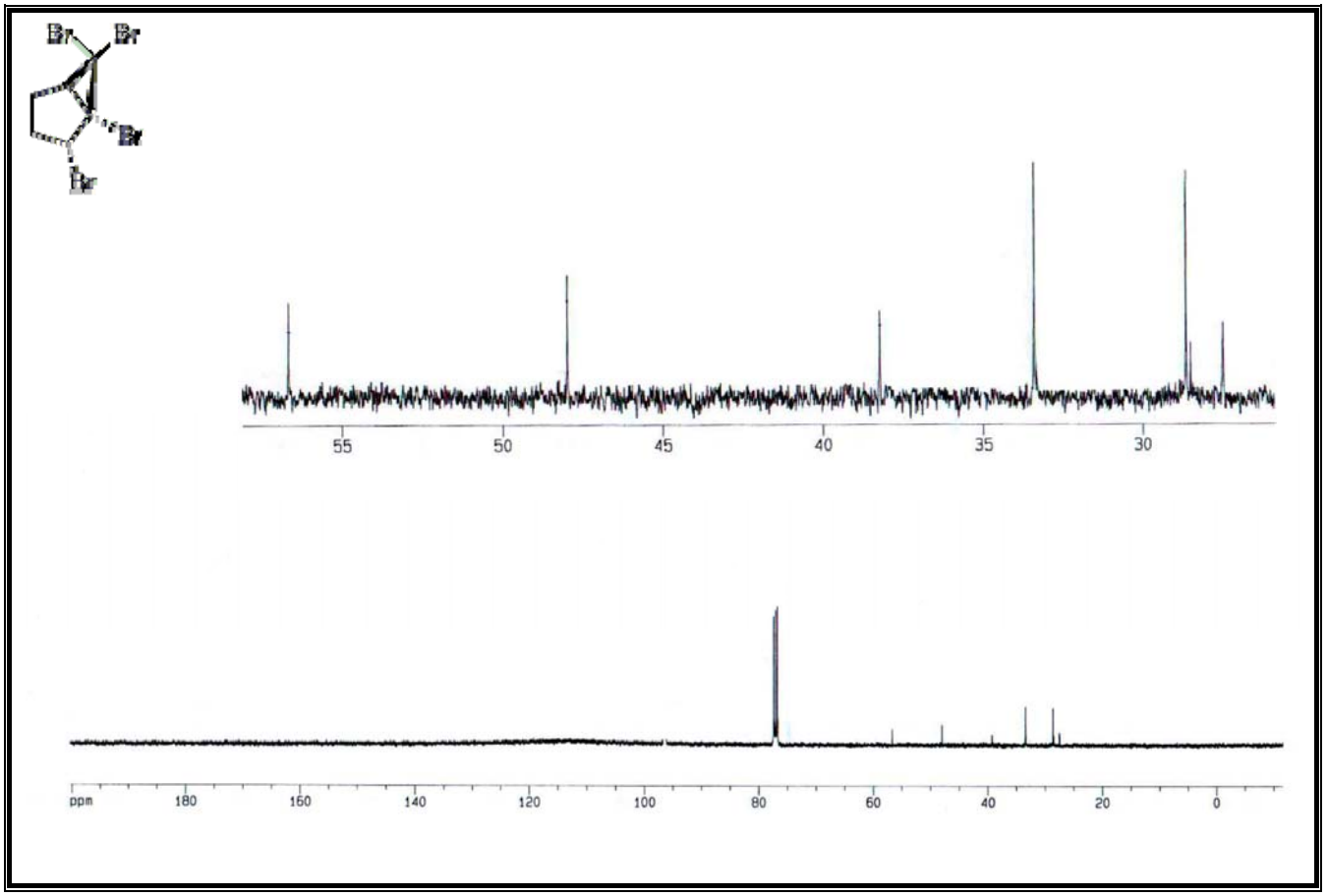

Figure A12 ^{13}C-NMR Spectrum of Compound **137**.

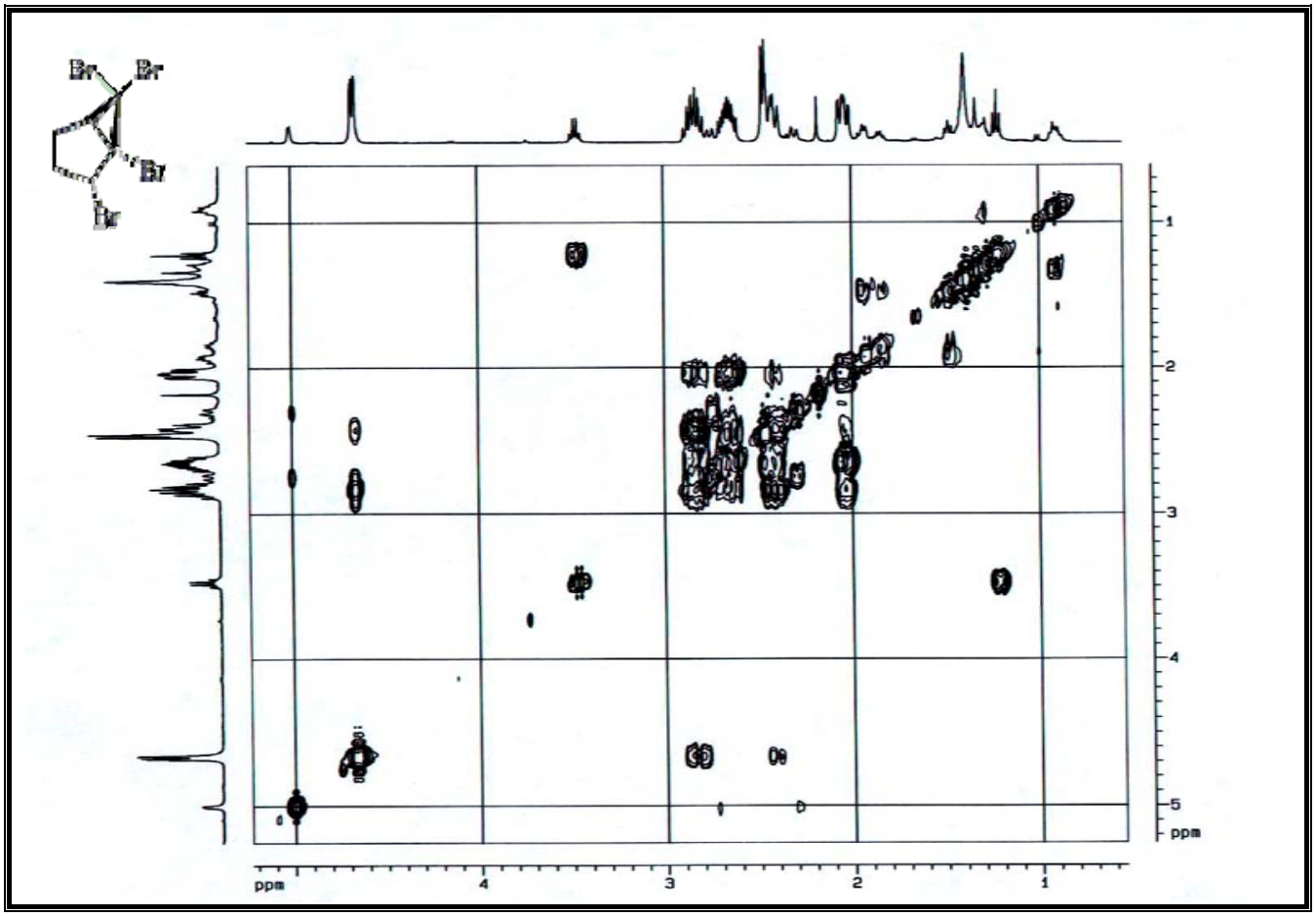

Figure A13 COSY Spectrum of Compound **137**.

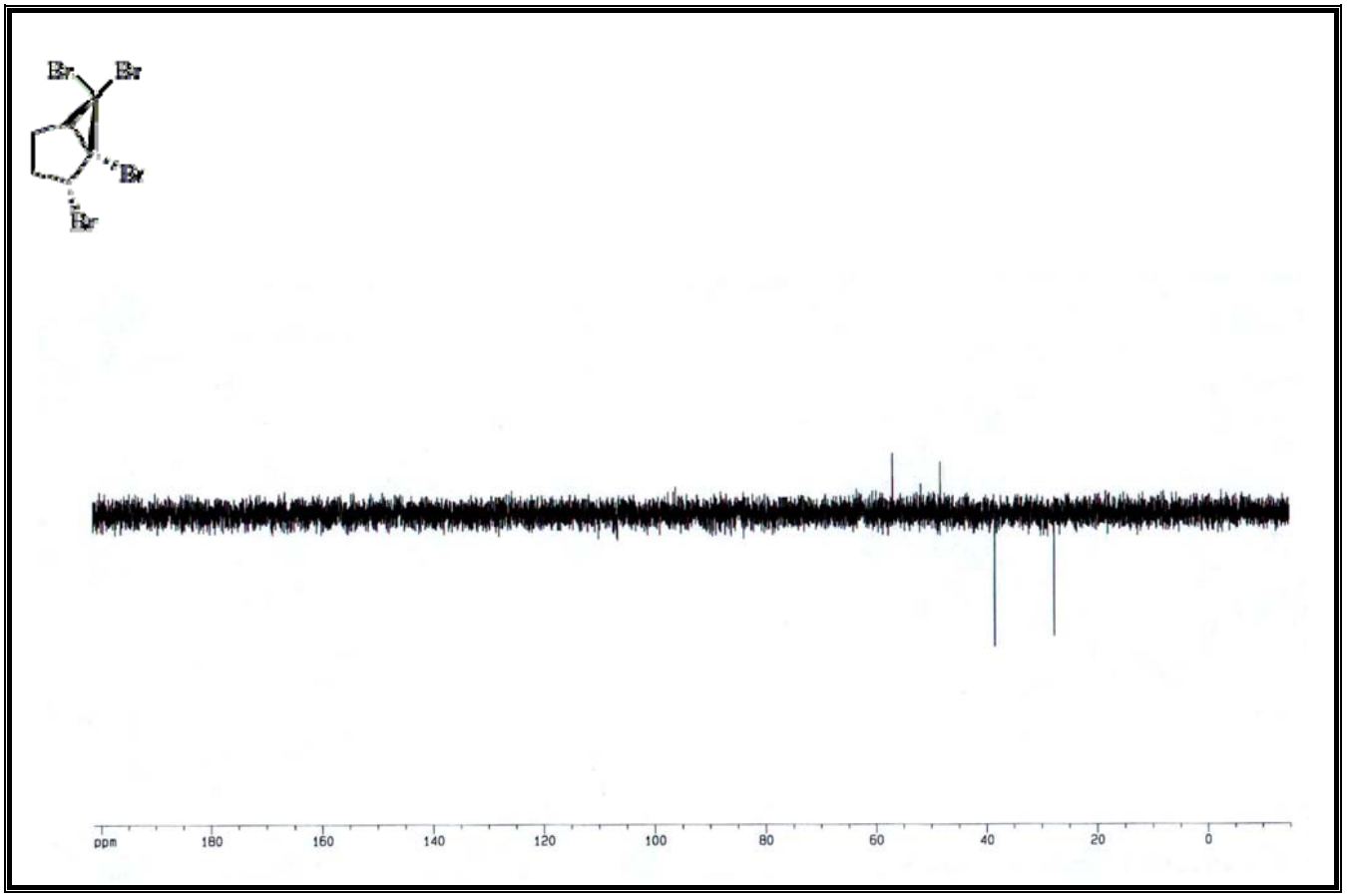

Figure A14 DEPT-135 Spectrum of Compound **137**.

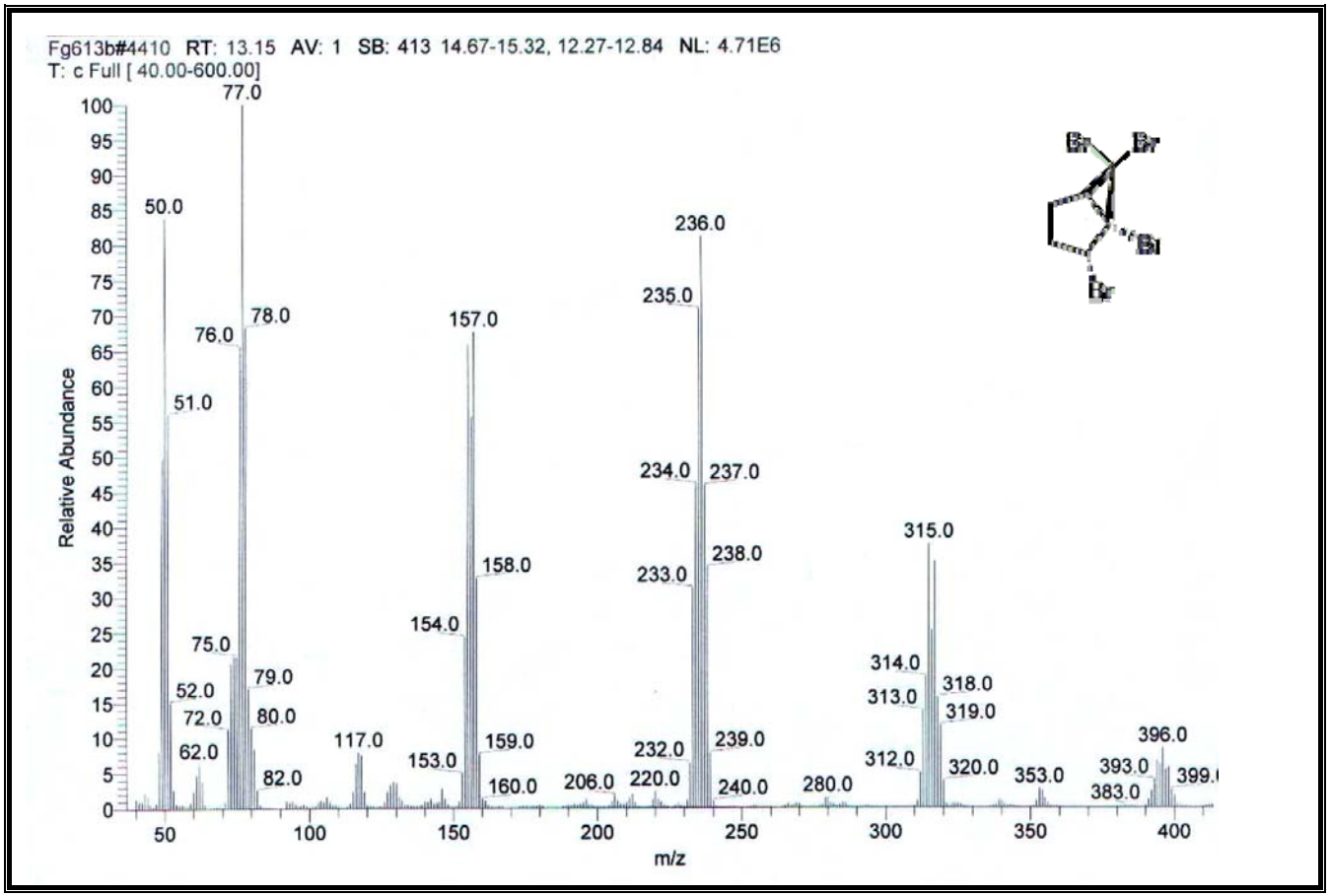

Figure A15 GC-MS Spectrum of Compound **137**.

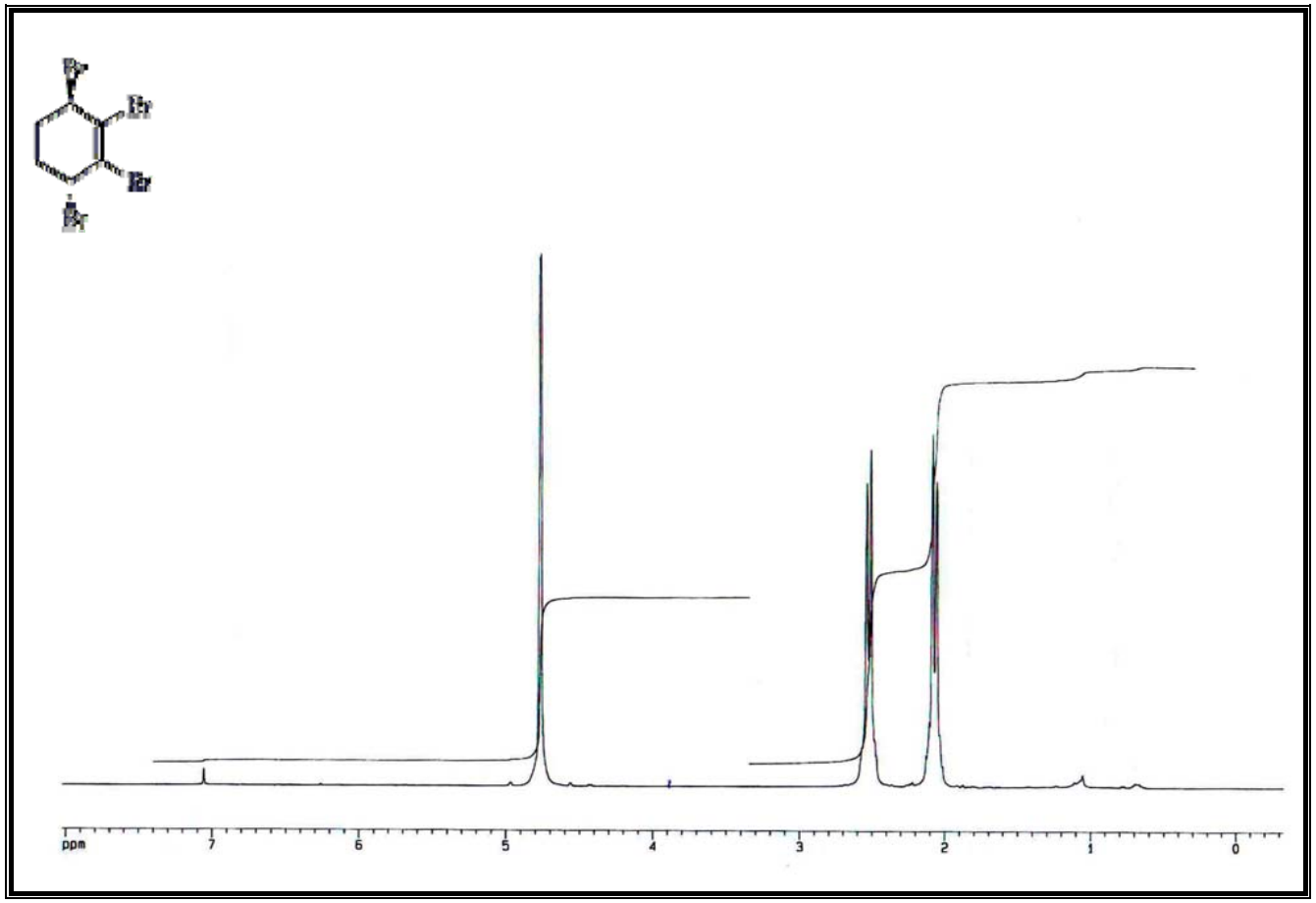

Figure A16 ^{1}H-NMR Spectrum of Compound **138**.

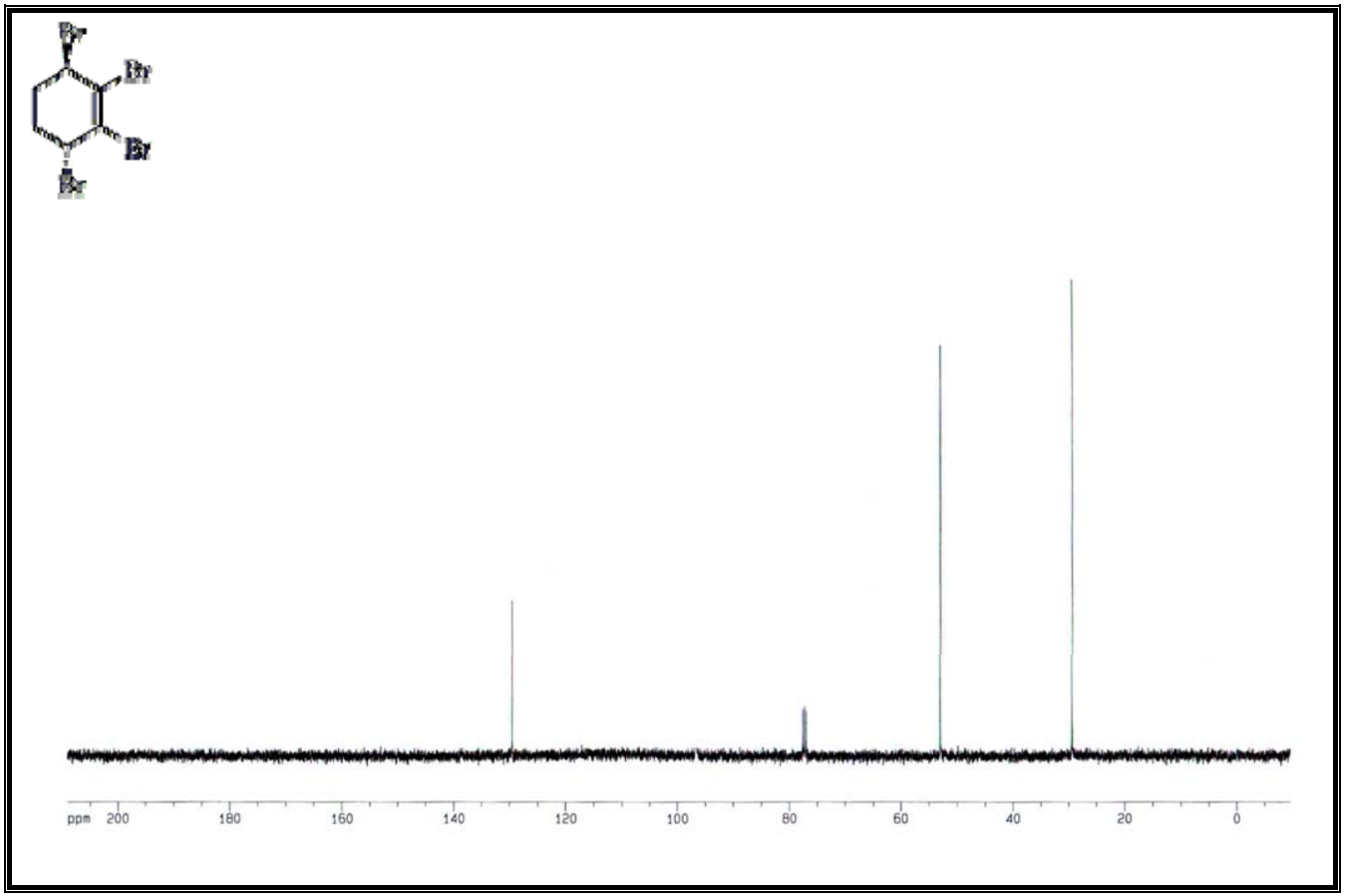

Figure A17 ^{13}C- Spectrum of Compound **138**.

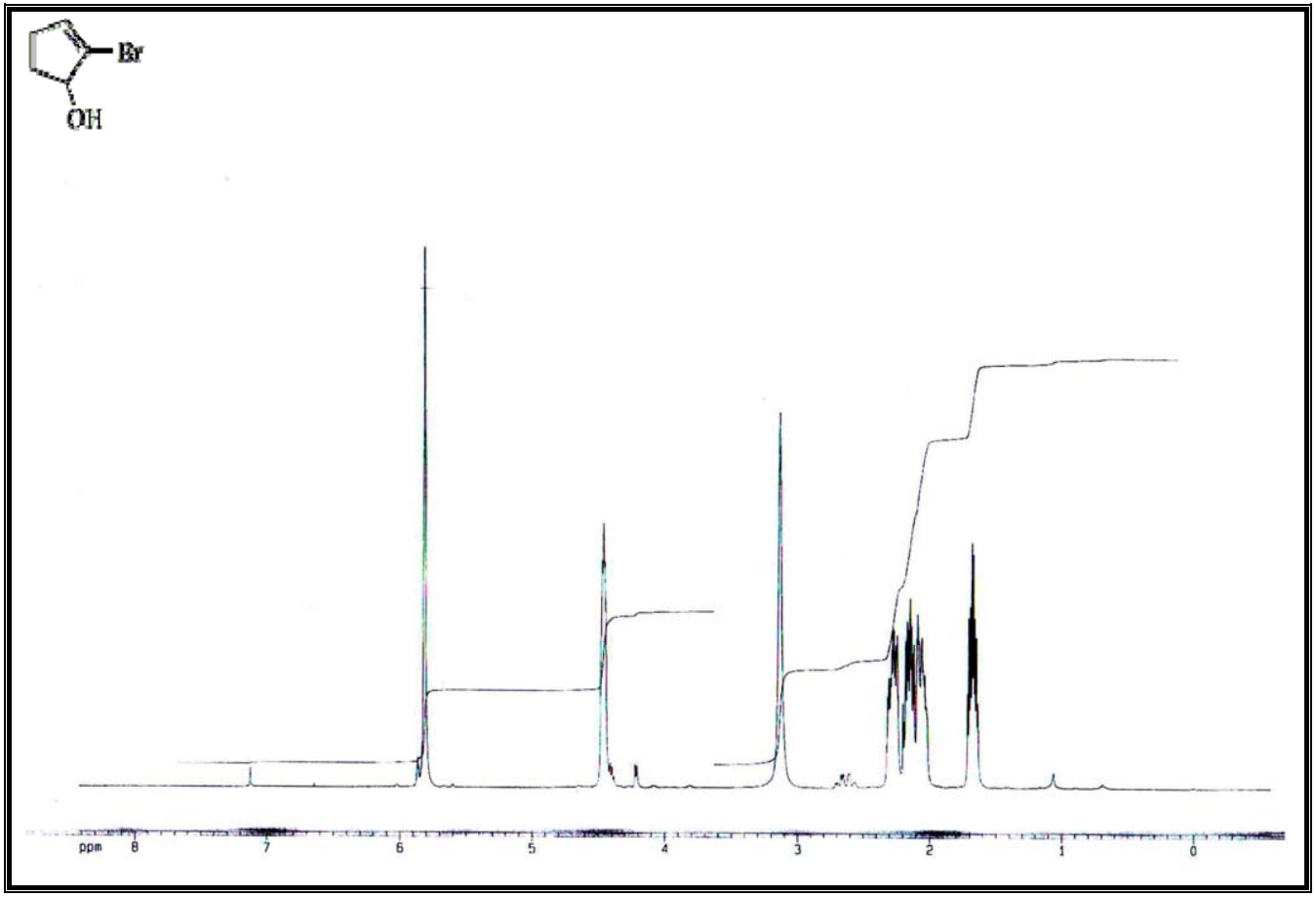

Figure A18 ^{1}H-NMR Spectrum of Compound **139**.

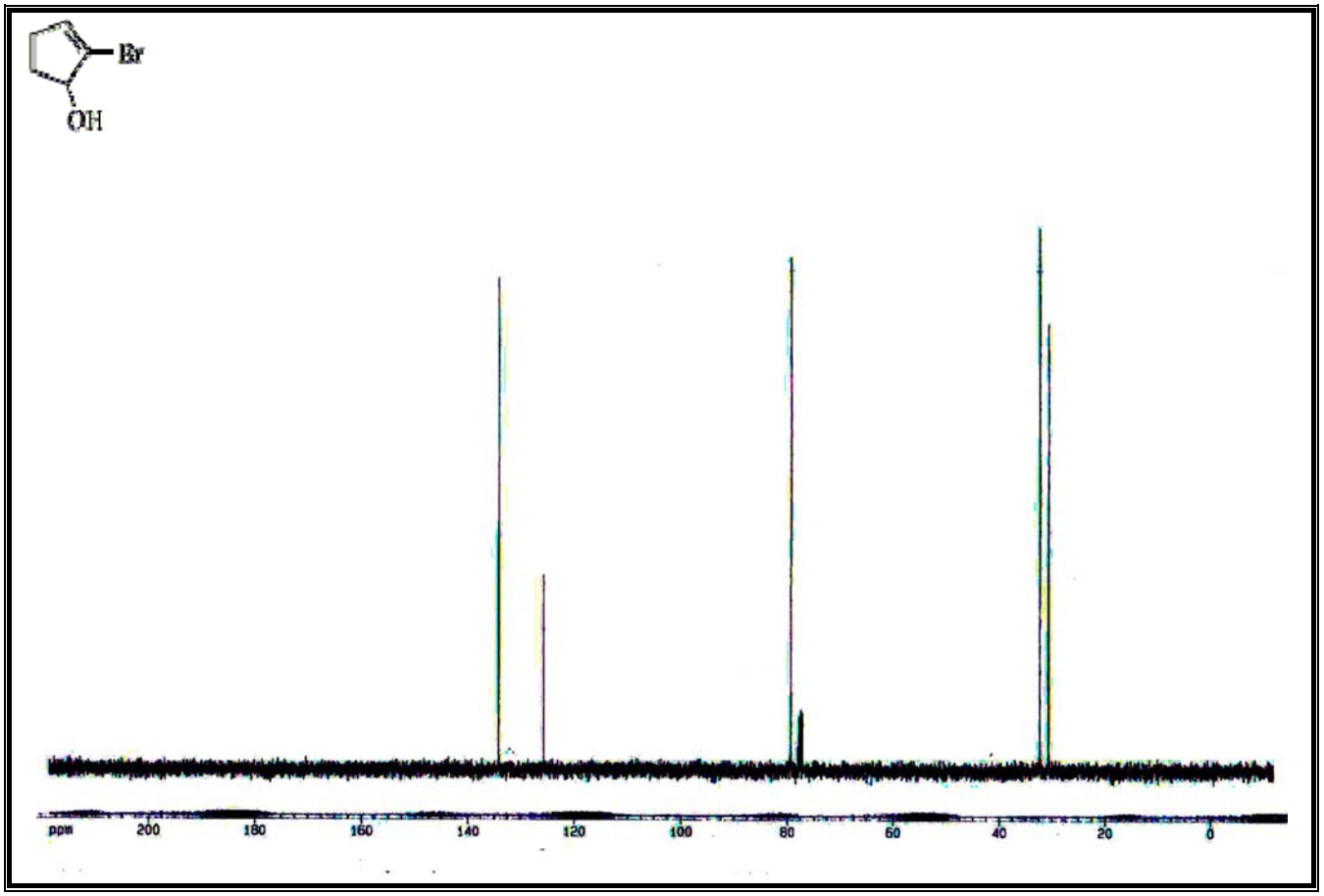

Figure A19 ^{13}C-NMR Spectrum of Compound **139**.

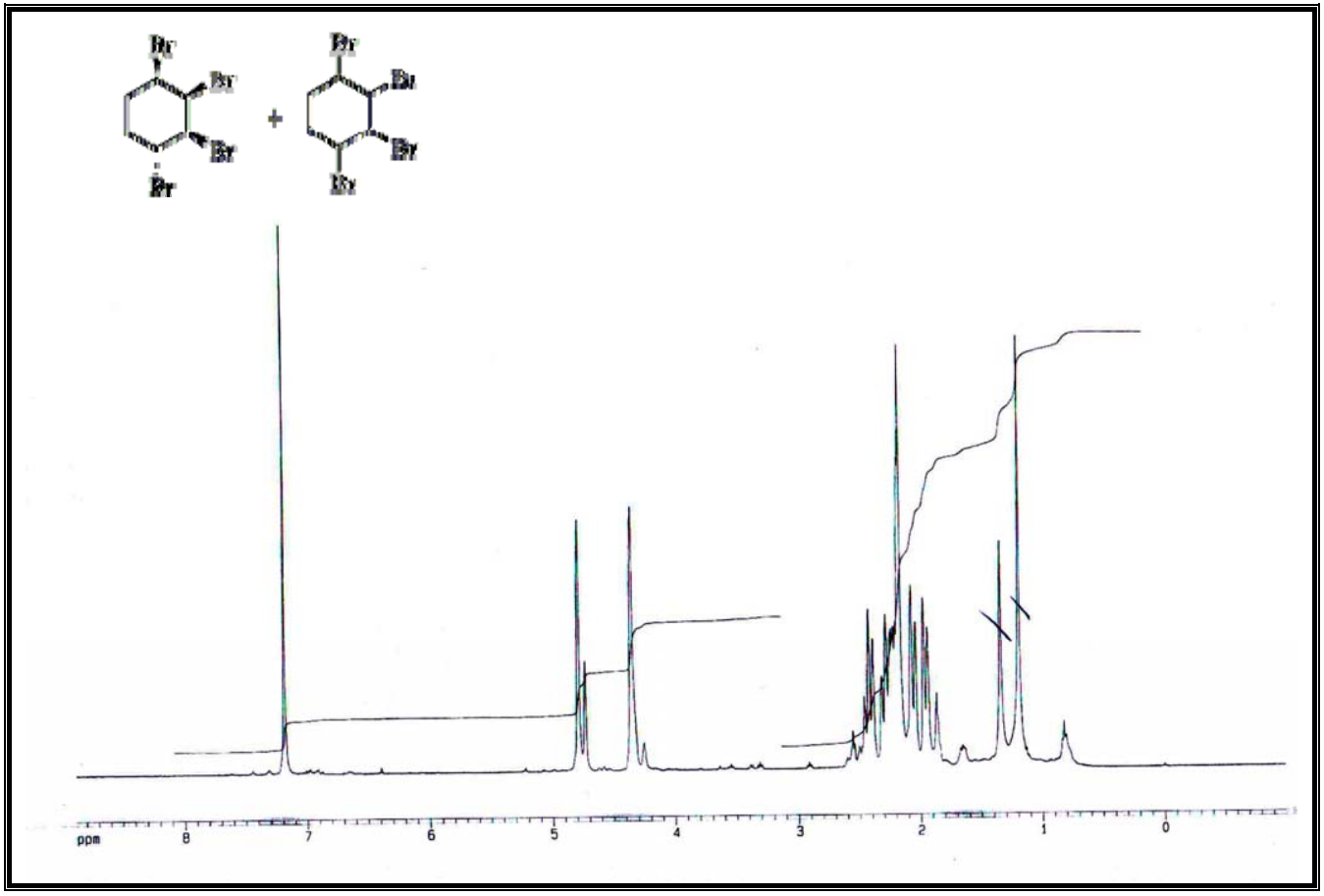

Figure A20 ^{1}H-NMR Spectrum of Compounds **141+142**.

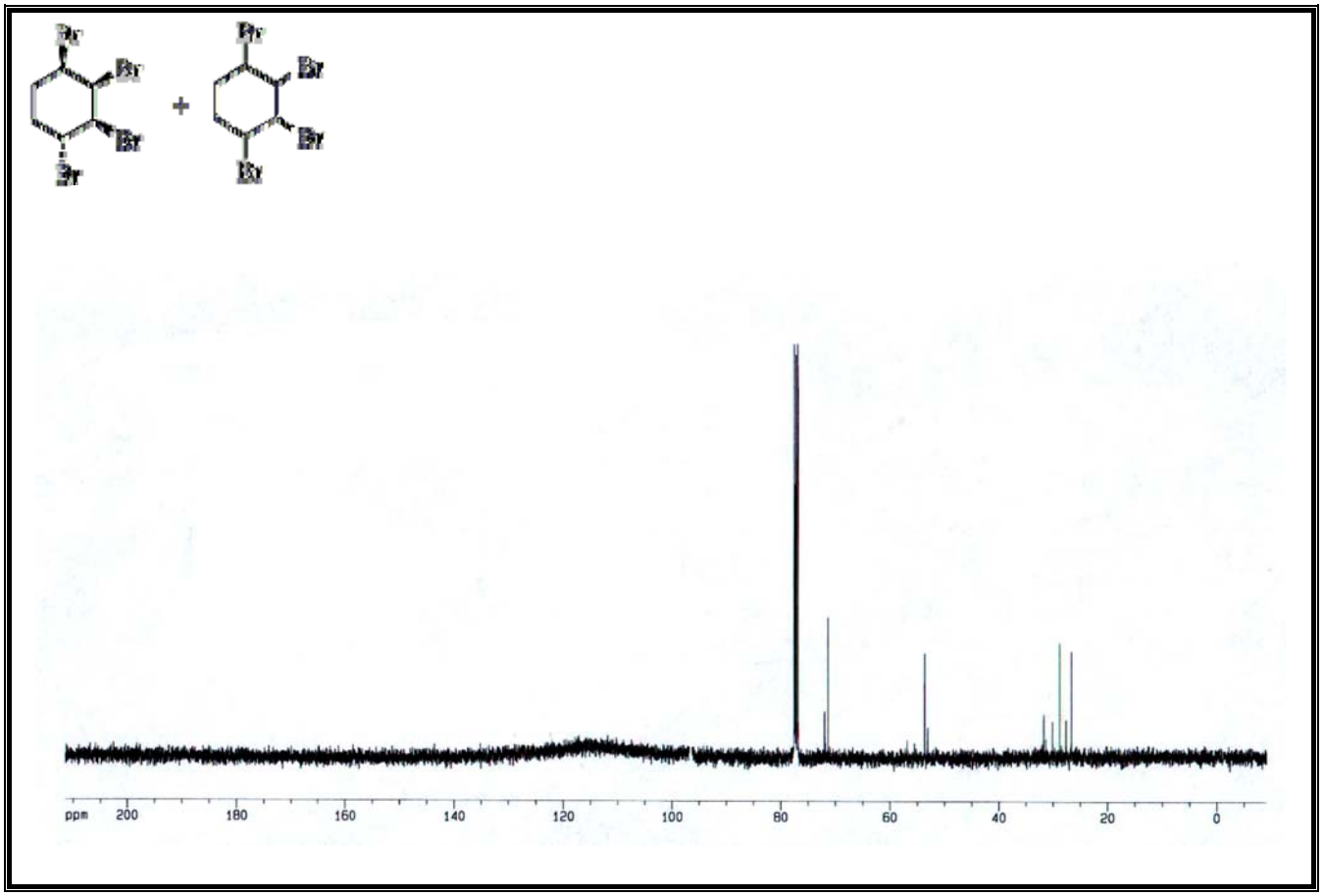

Figure A21 ^{13}C-NMR Spectrum of Compounds **141+142**.

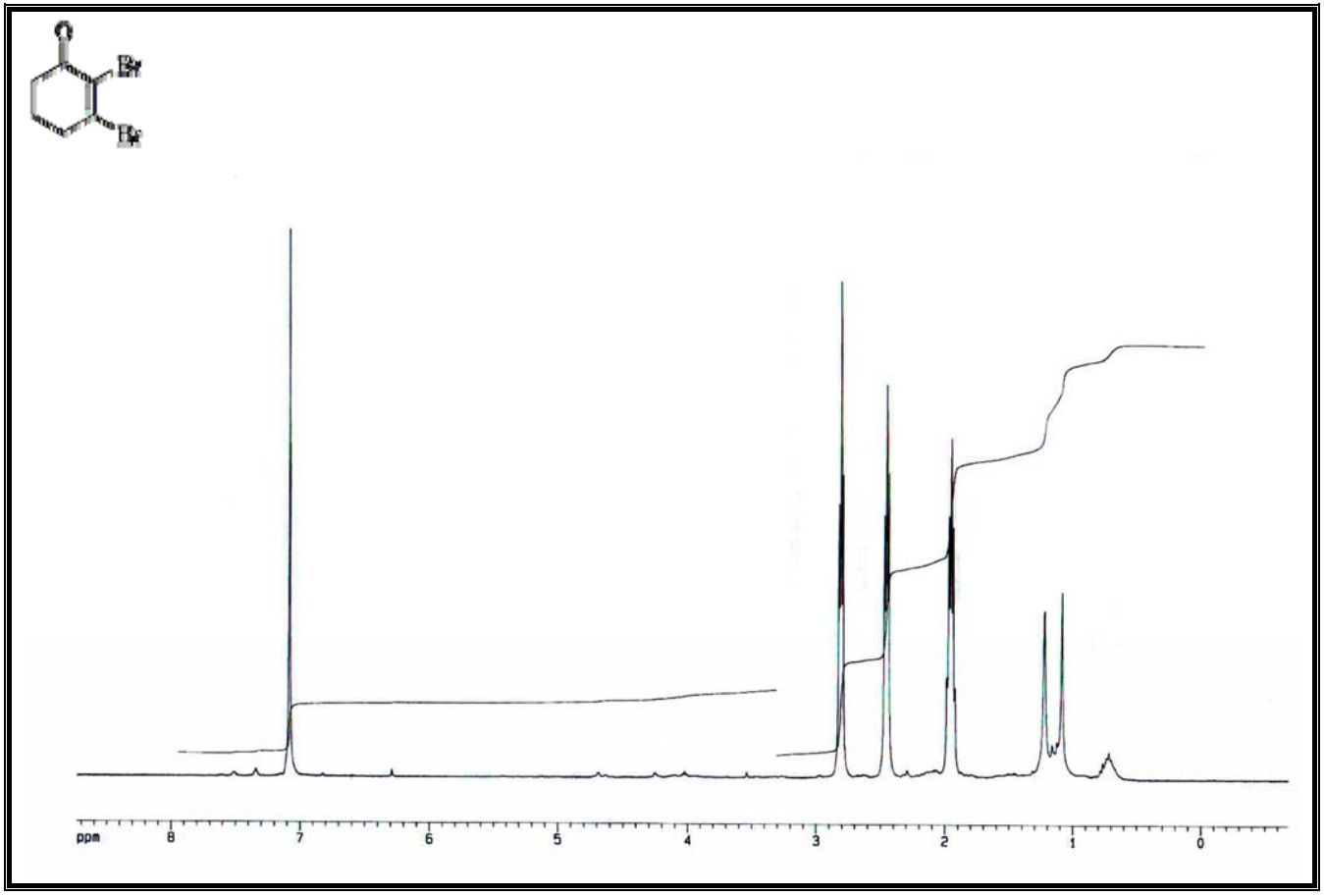

Figure A22 ^{1}H-NMR Spectrum of Compound **143**.

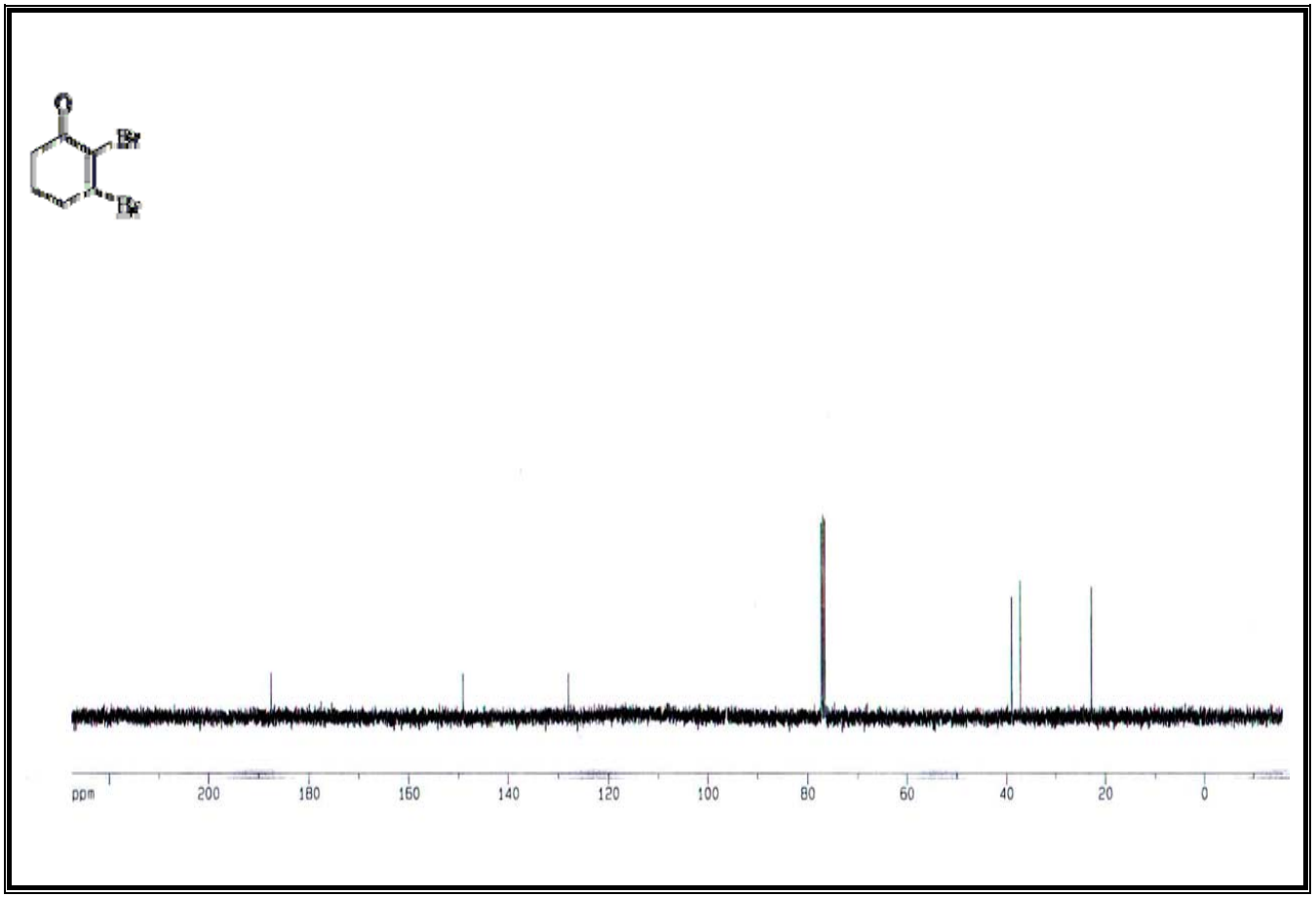

Figure A23 ^{13}C-NMR Spectrum of Compound **143**.

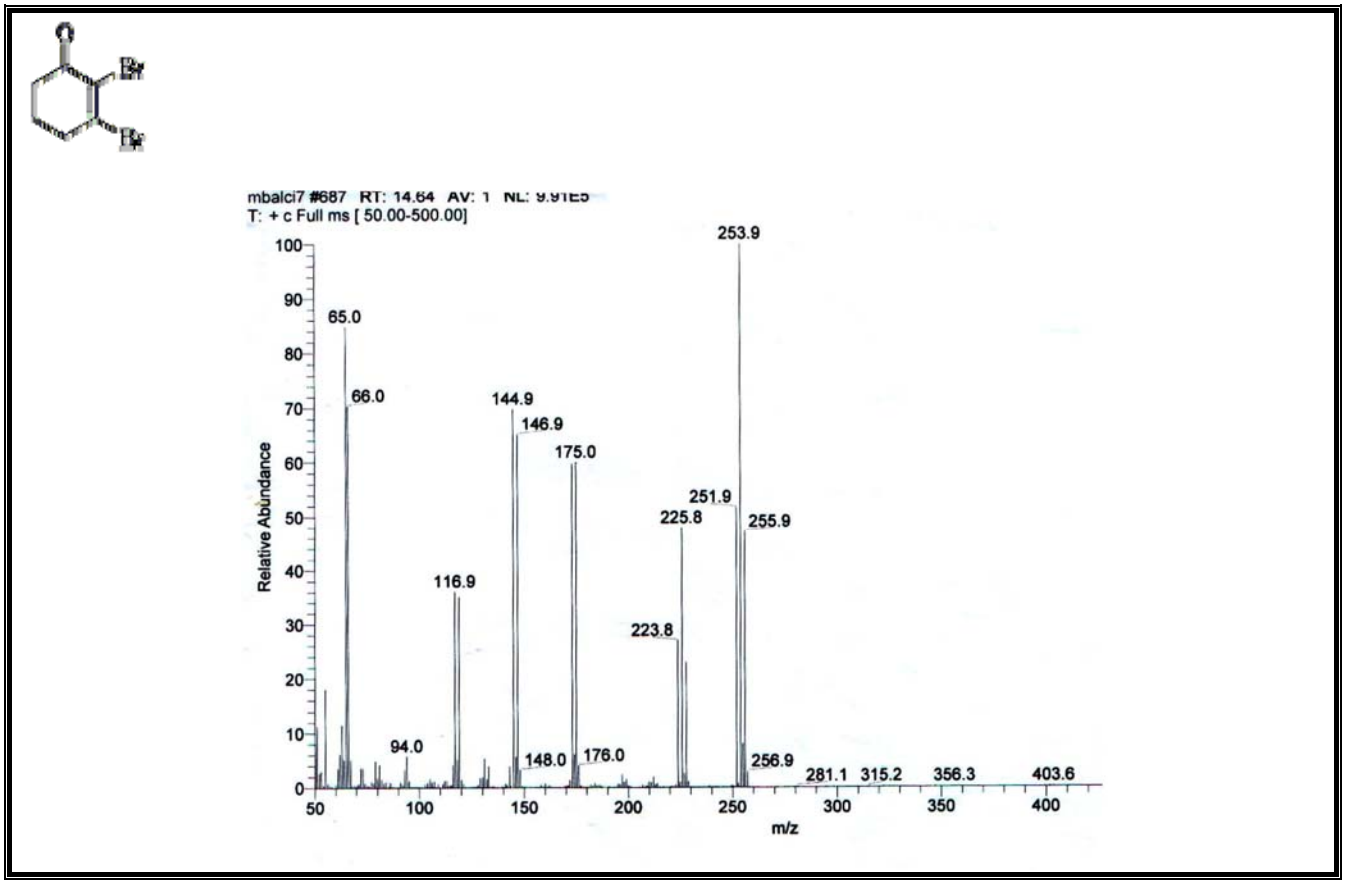

Figure A24 GC-MS Spectrum of Compound **143**.

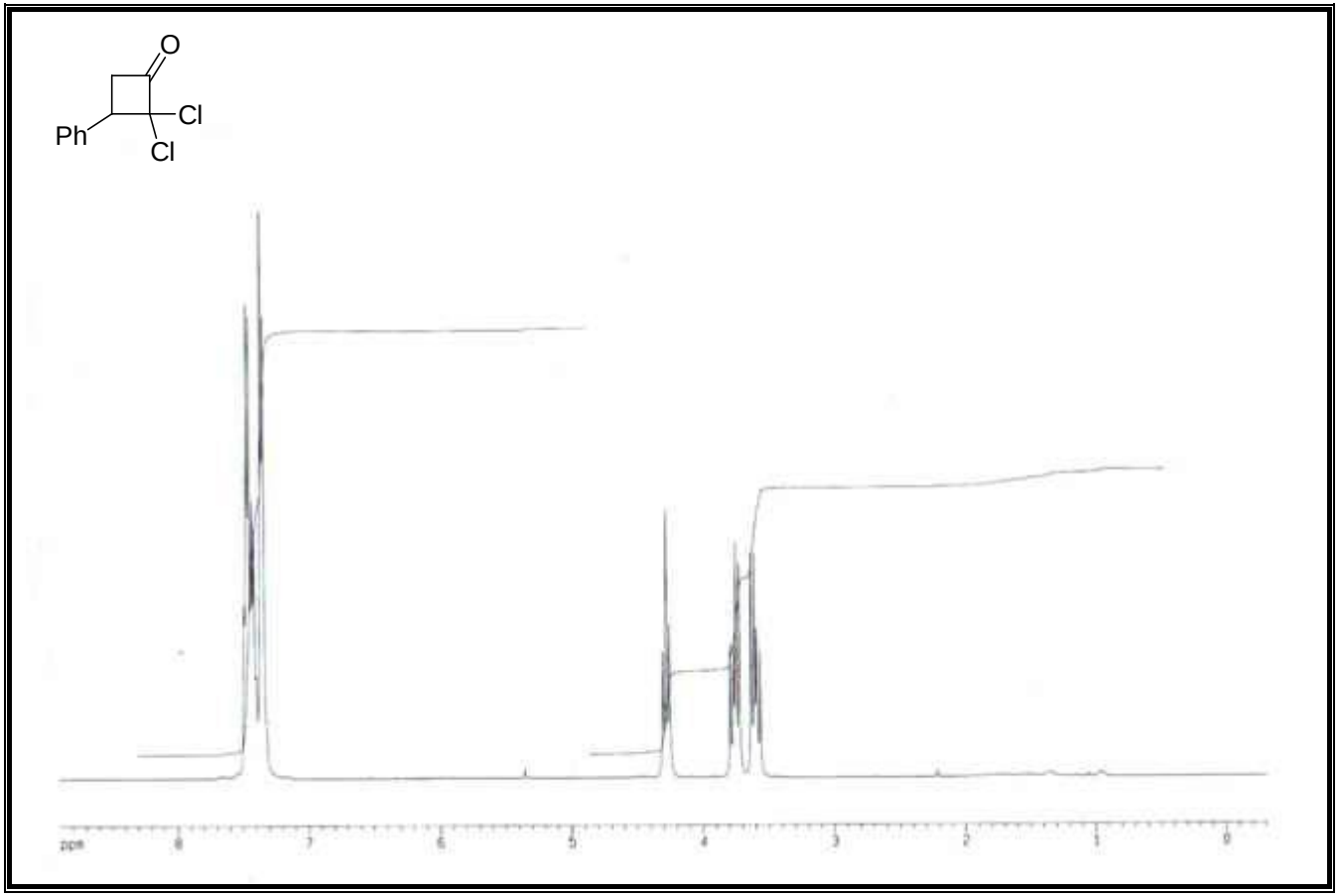

Figure A25 ^{1}H-NMR Spectrum of Compound **151**.

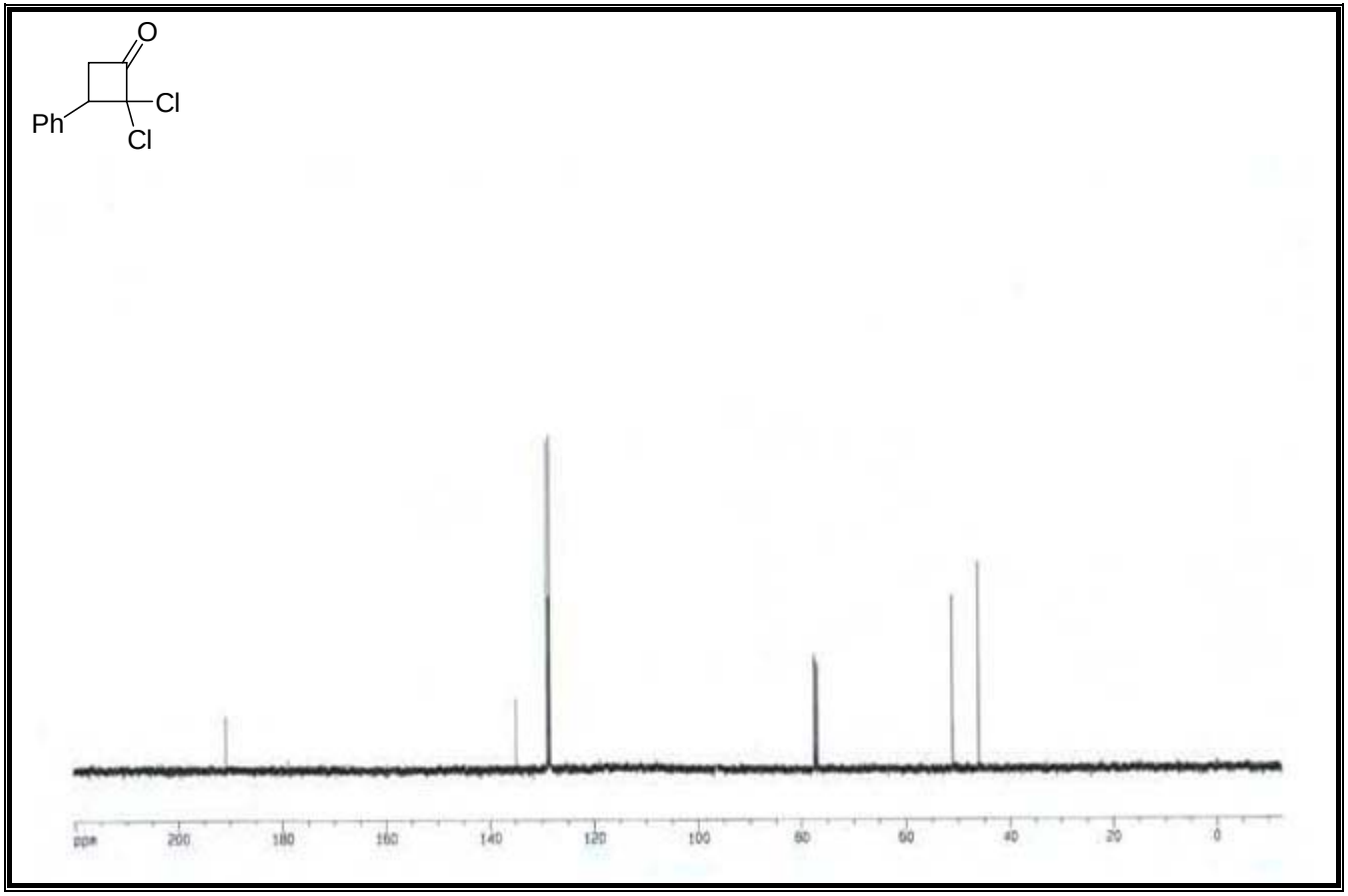

Figure A26 ^{13}C-NMR Spectrum of Compound **151**.

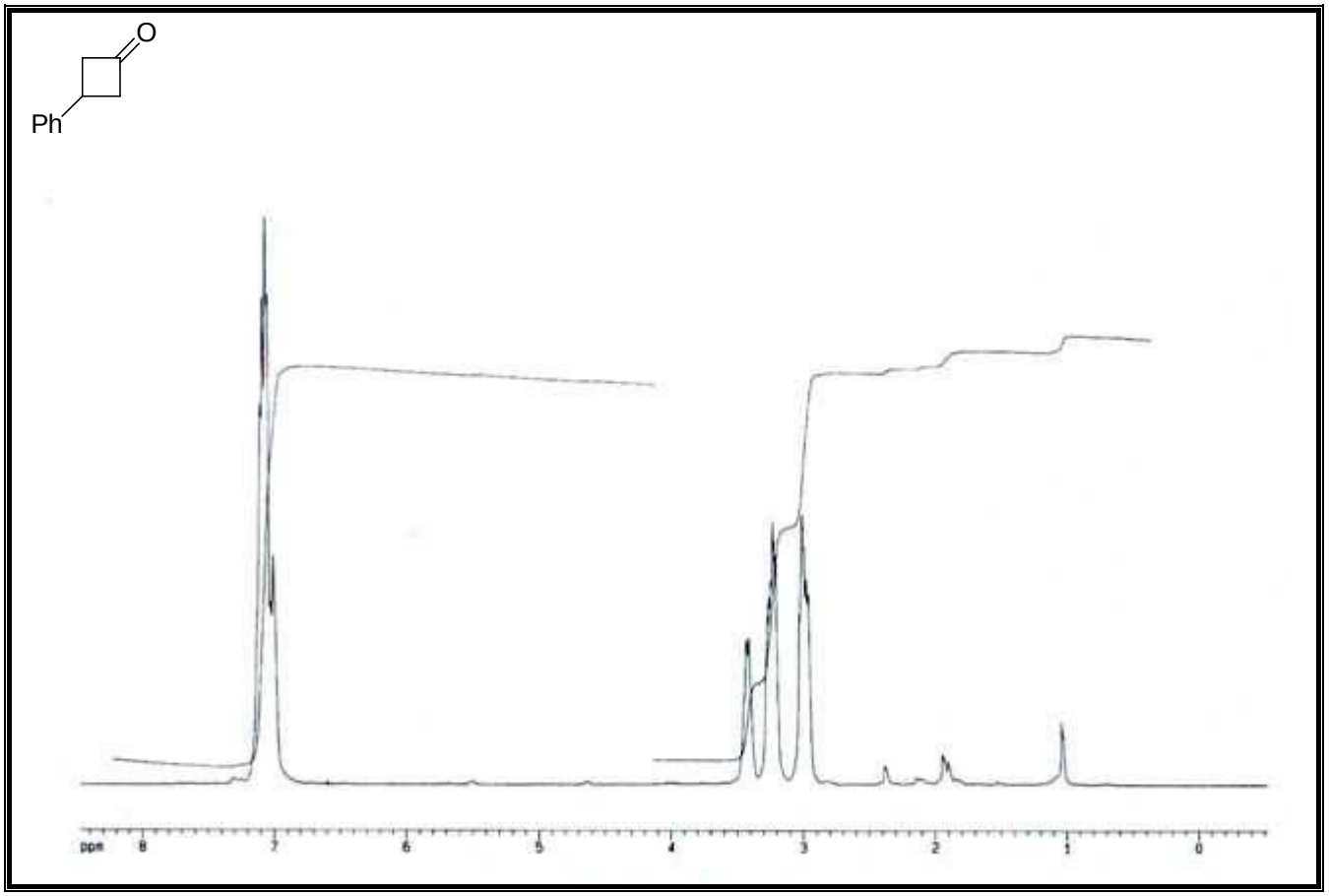

Figure A27 ^{1}H-NMR Spectrum of Compound **152**.

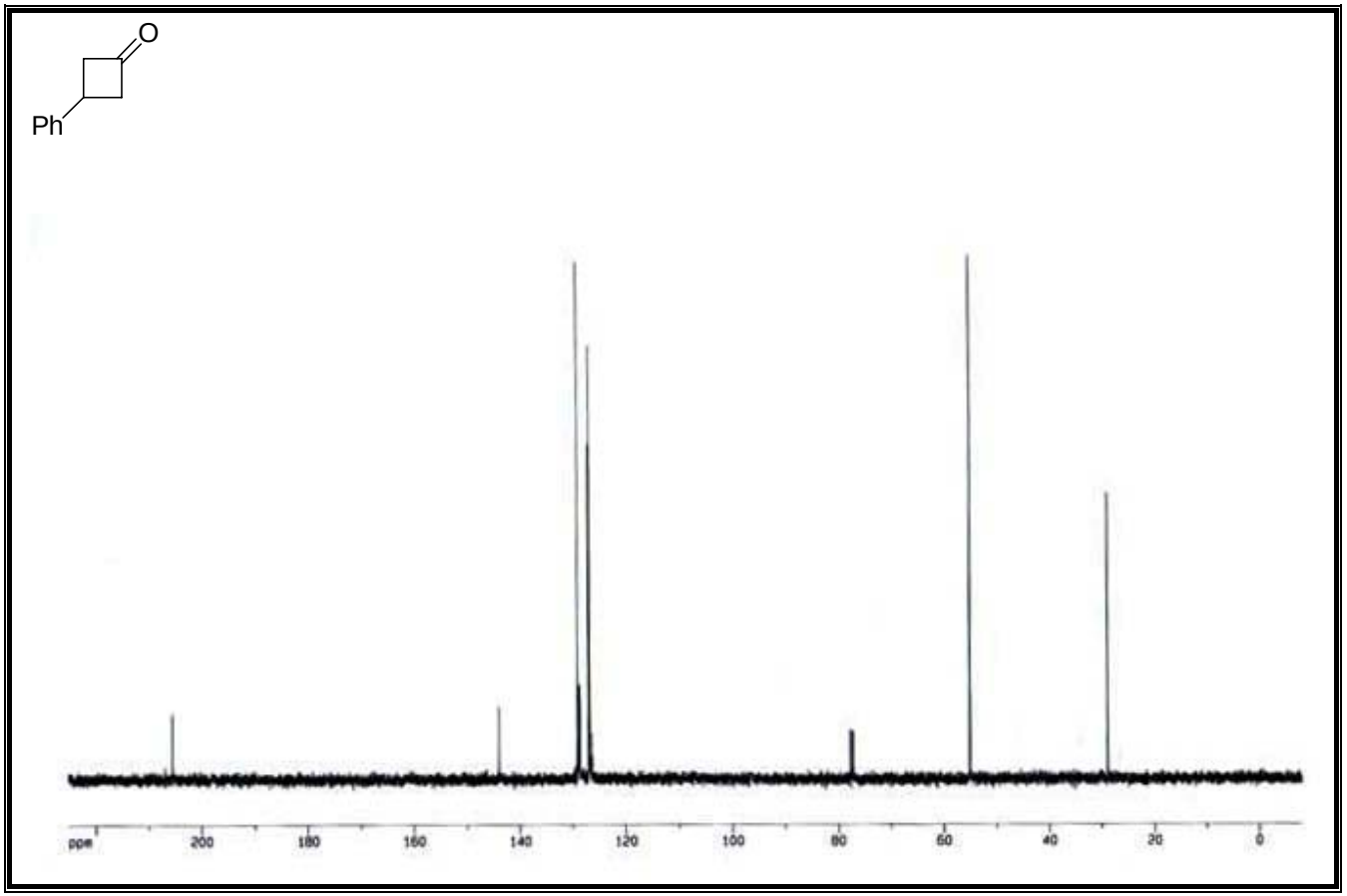

Figure A28 ^{13}C-NMR Spectrum of Compound **152**.

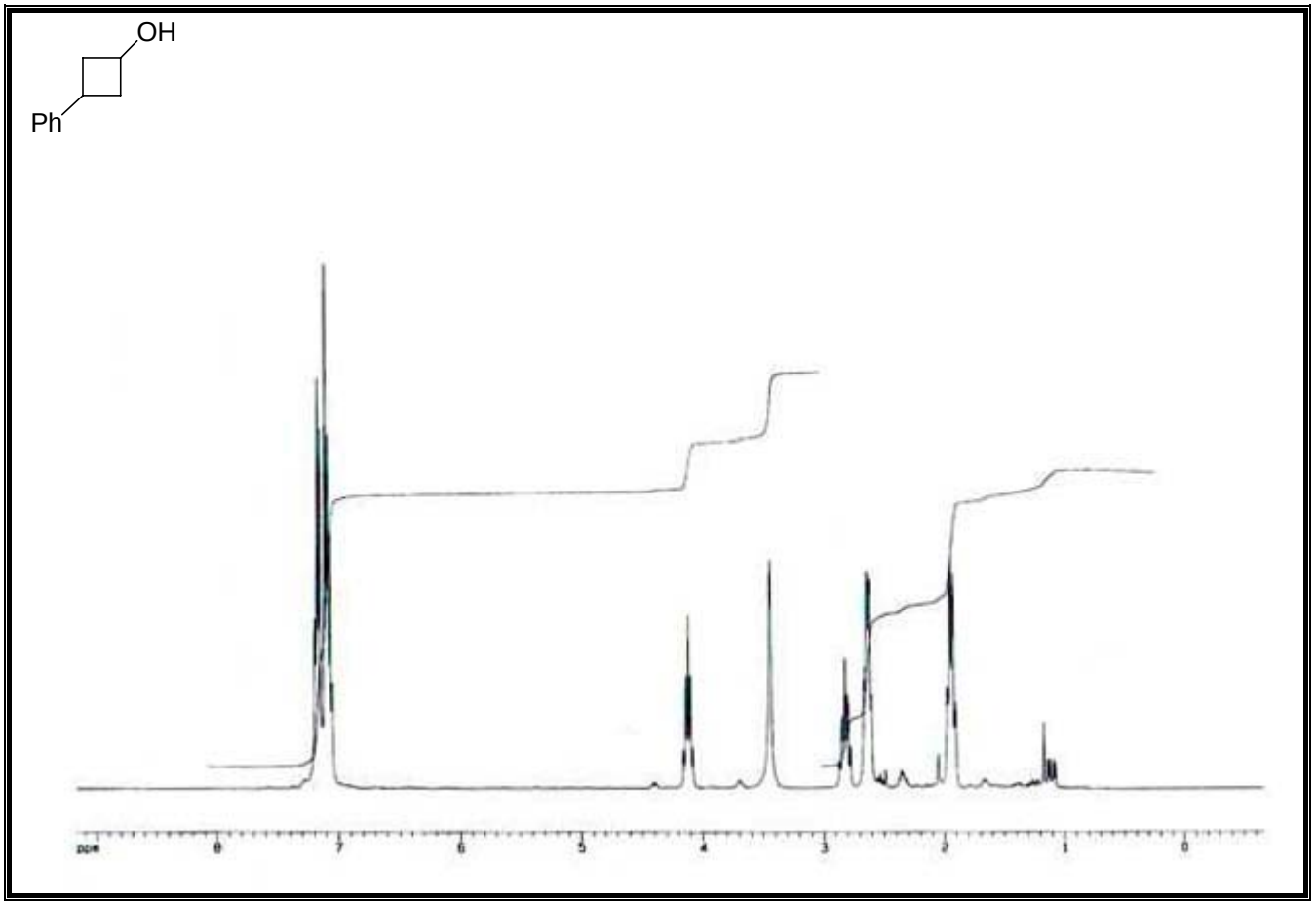

Figure A29 ^{1}H-NMR Spectrum of Compound **153**.

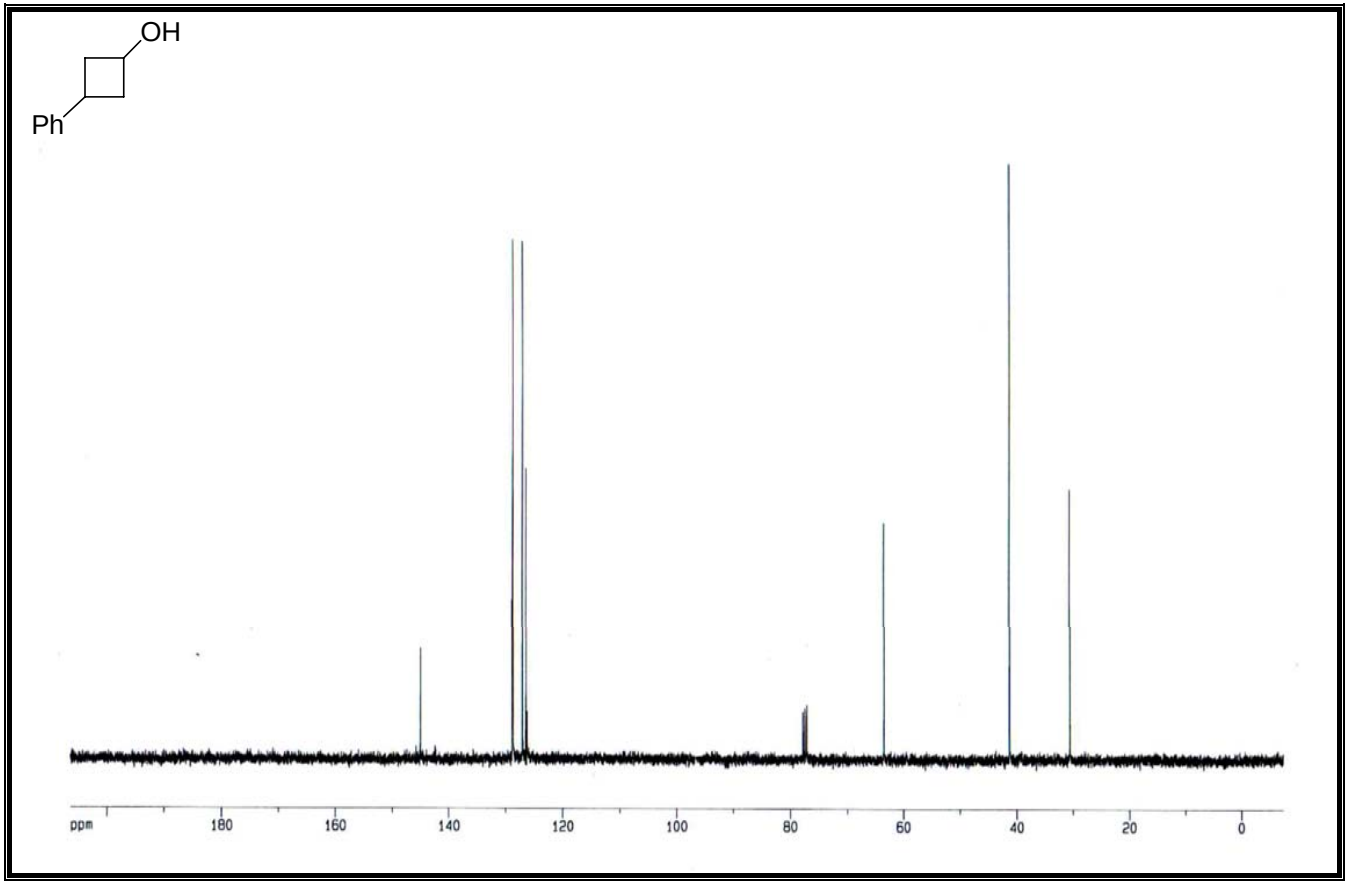

Figure A30 ^{13}C-NMR Spectrum of Compound **153**.

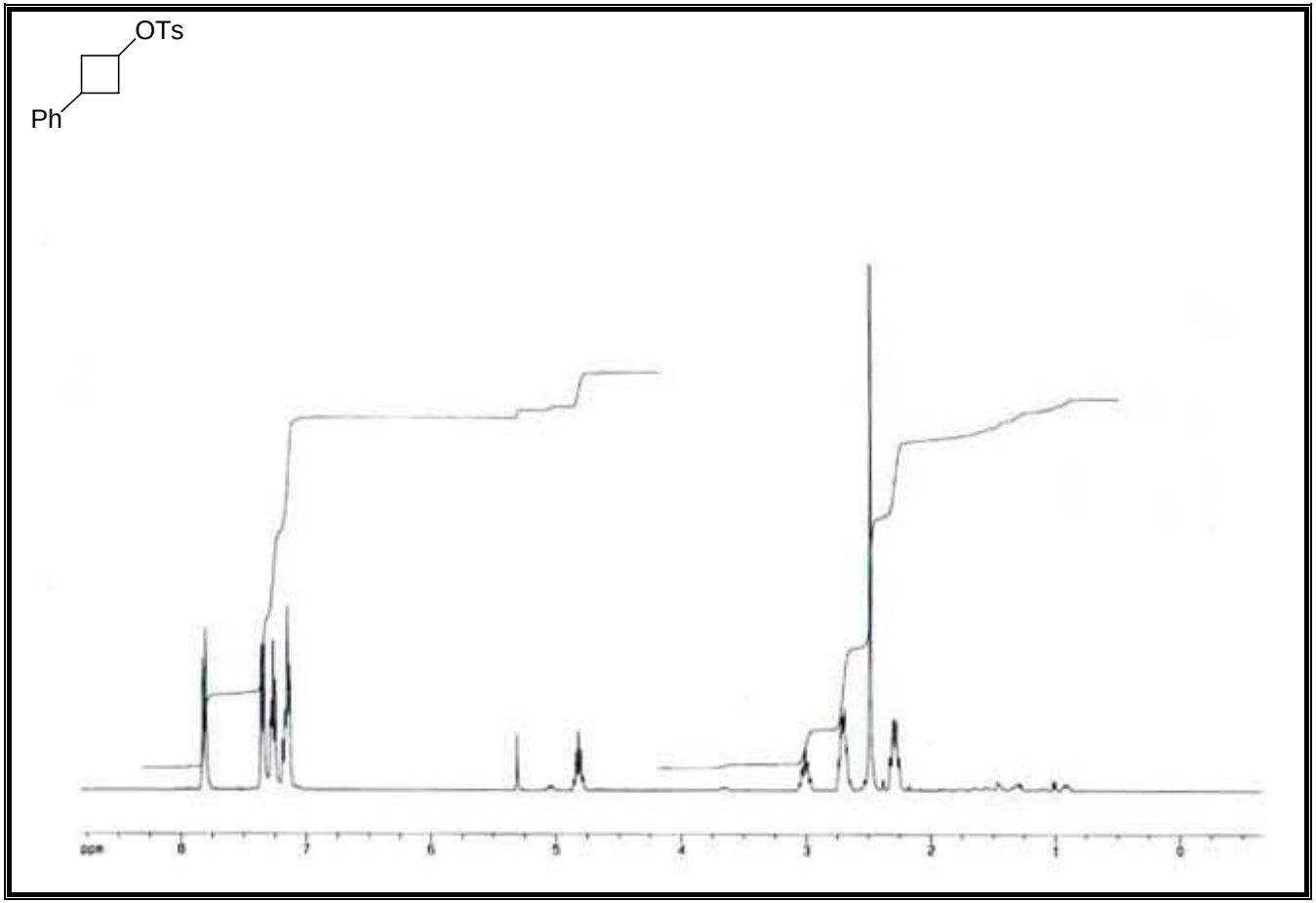

Figure A31 ^{1}H-NMR Spectrum of Compound **154a**.

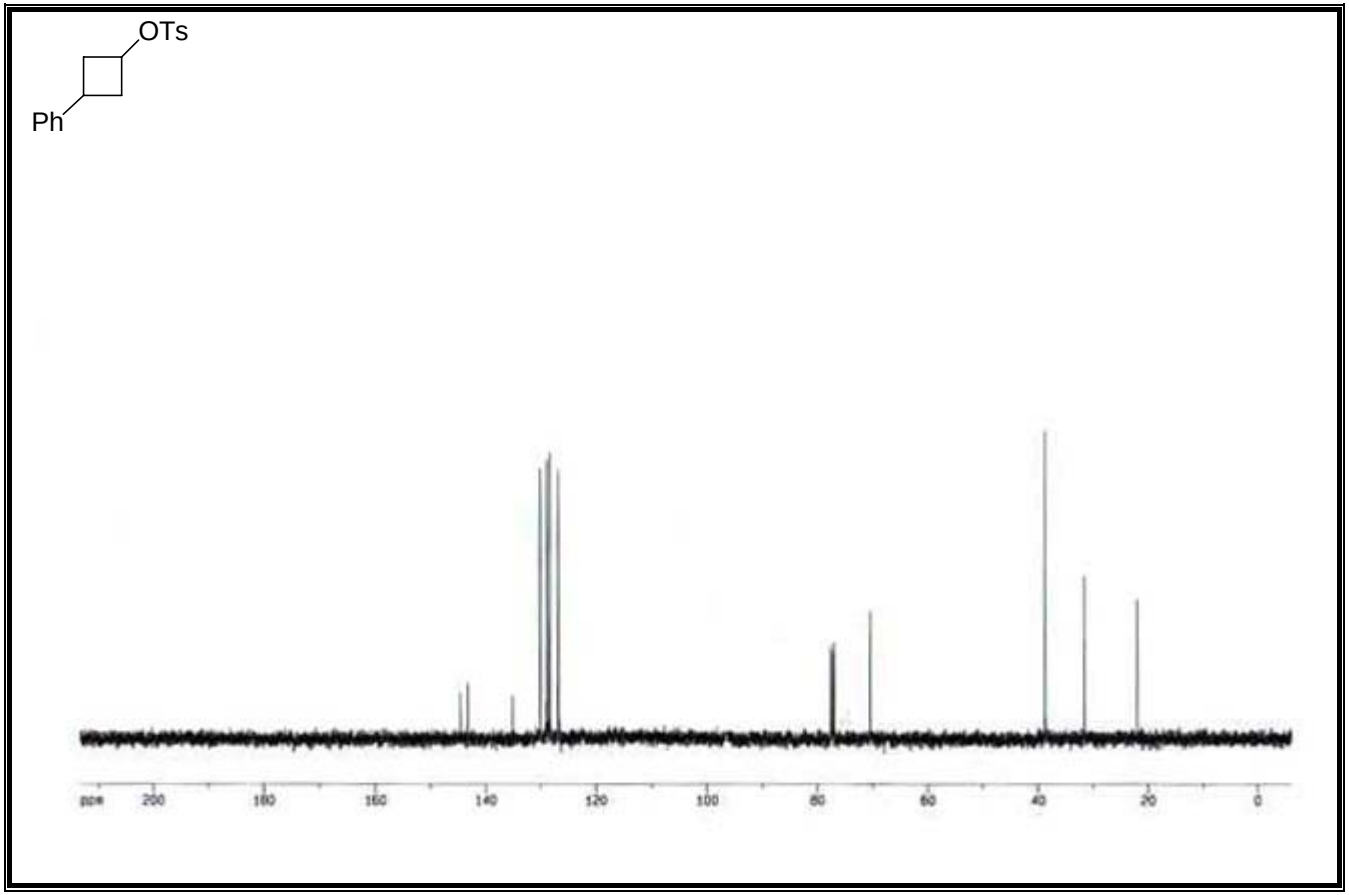

Figure A32 ^{13}C-NMR Spectrum of Compound **154a**.

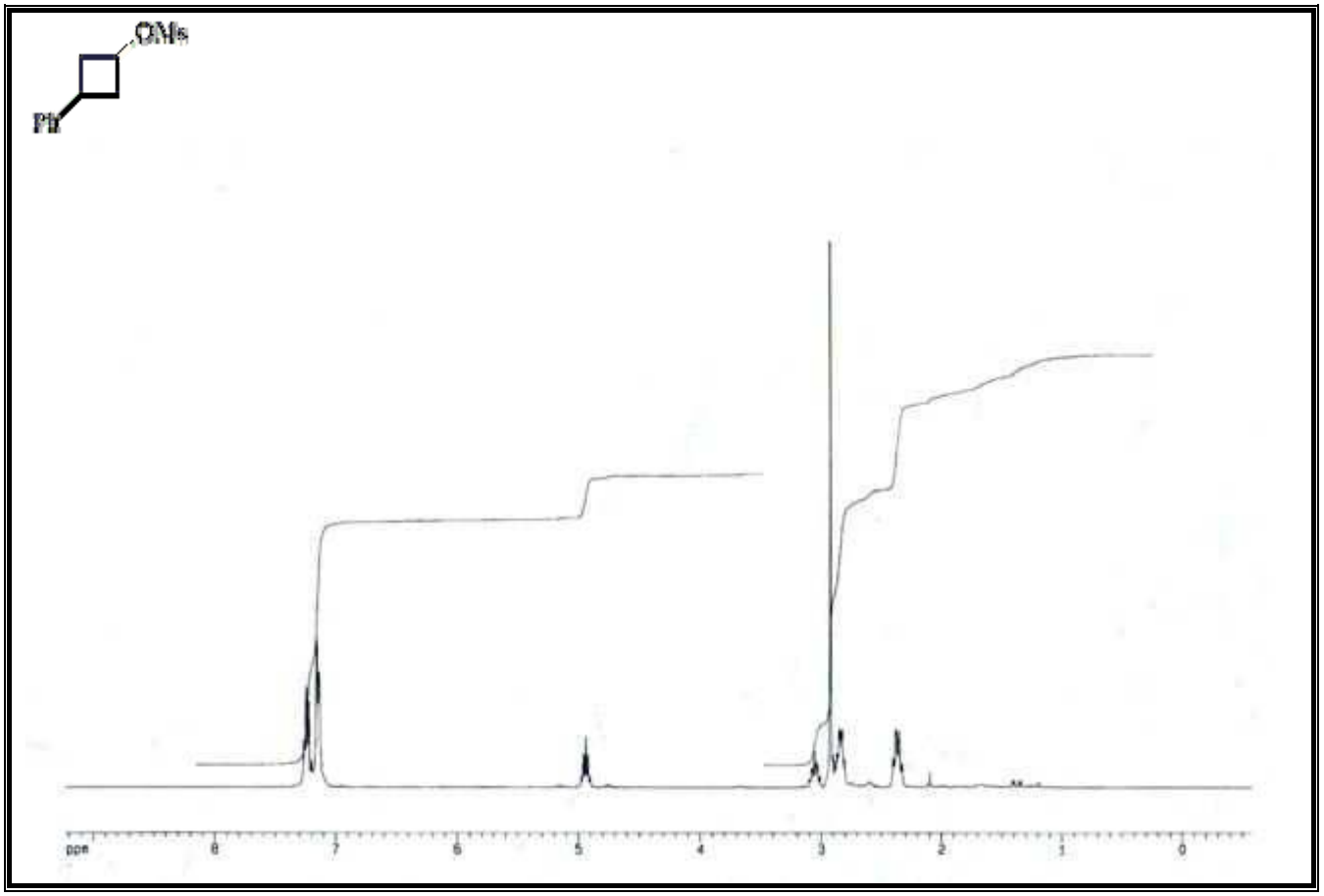

Figure A33 ^{1}H-NMR Spectrum of Compound **154b**.

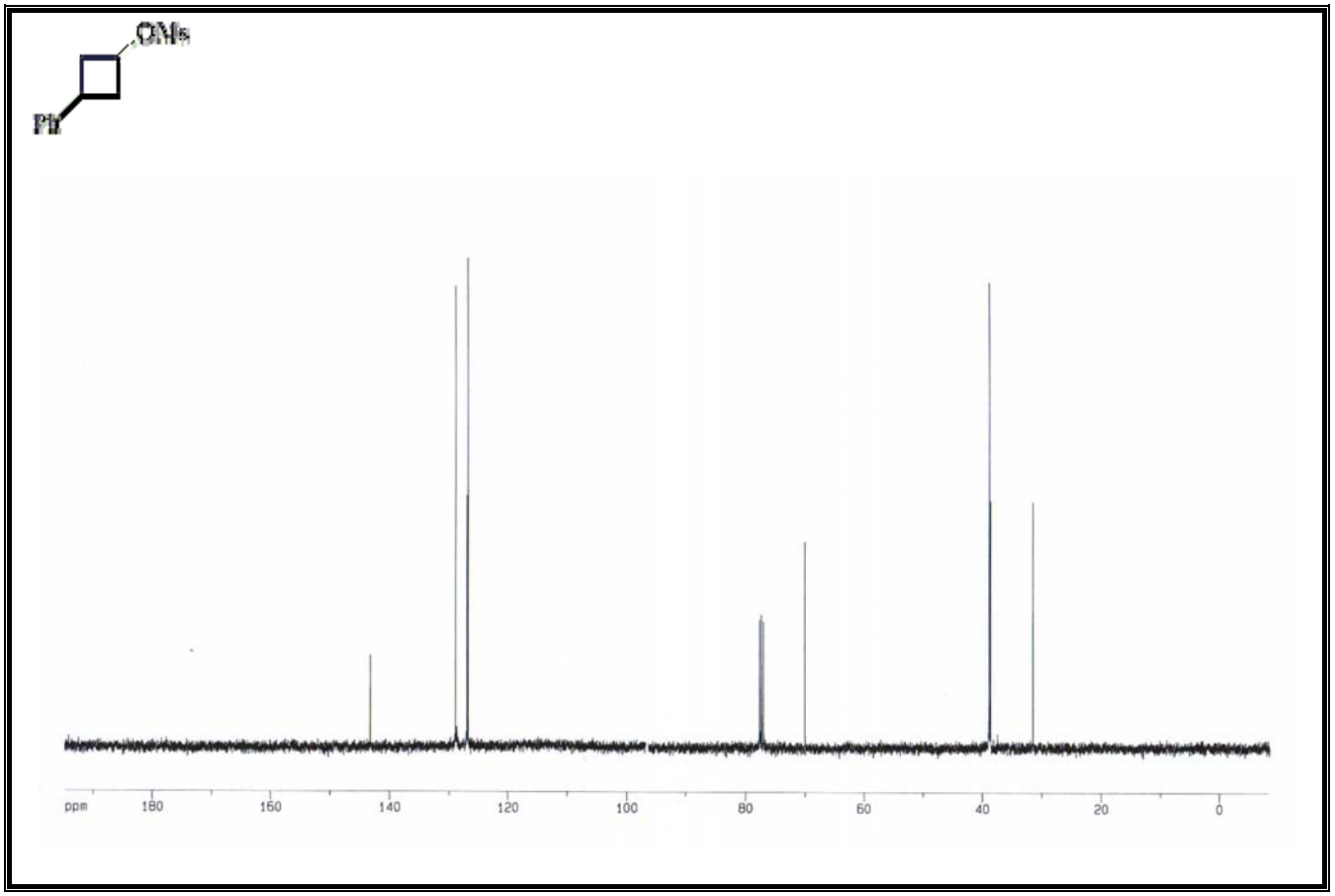

Figure A34 ^{13}C-NMR spectrum of Compound **154b**.

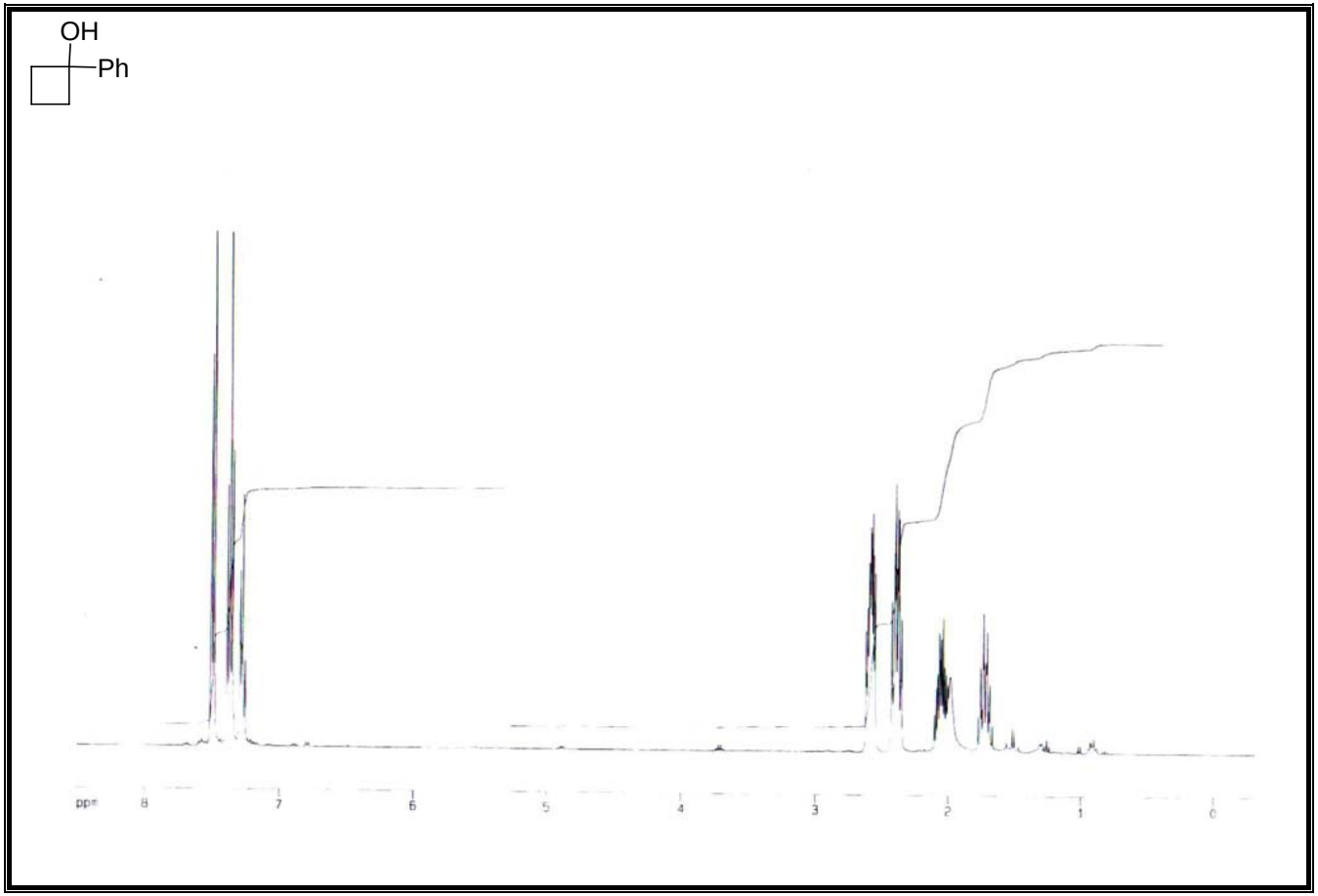

Figure A35 ^{1}H-NMR Spectrum of Compound **156**.

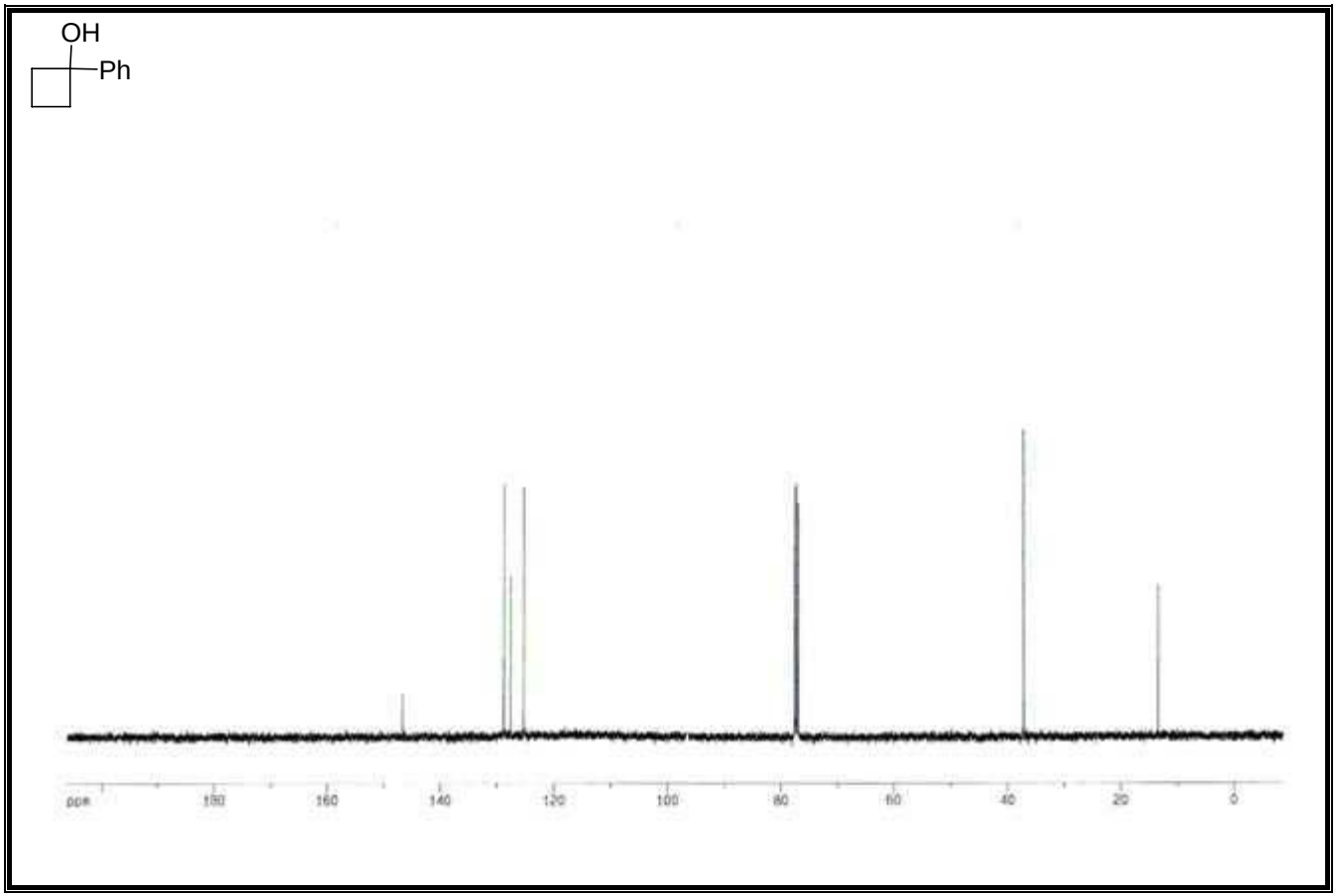

Figure A36 ^{13}C-NMR Spectrum of Compound **156**.

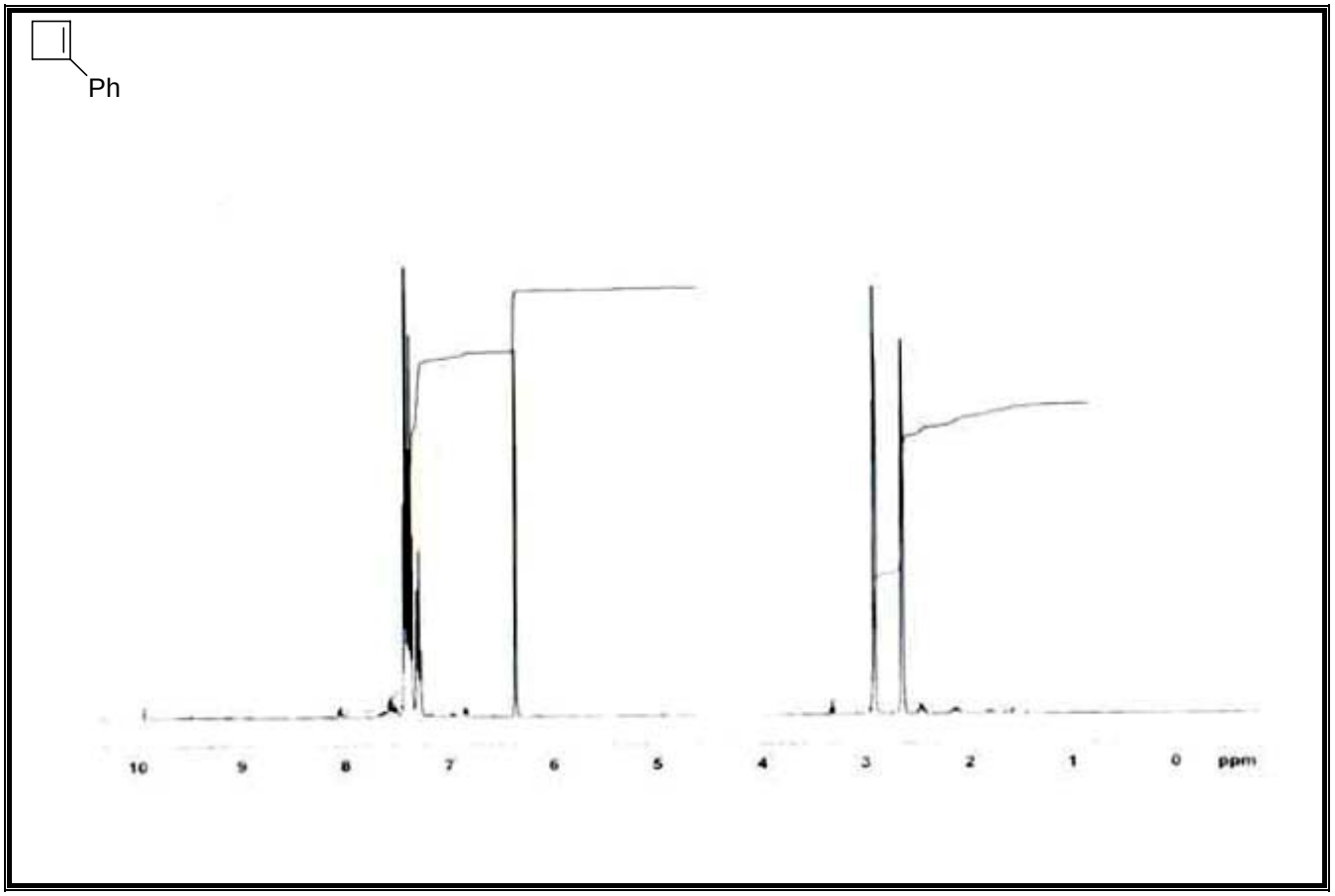

Figure A37 ^{1}H-NMR Spectrum of Compound **149**.

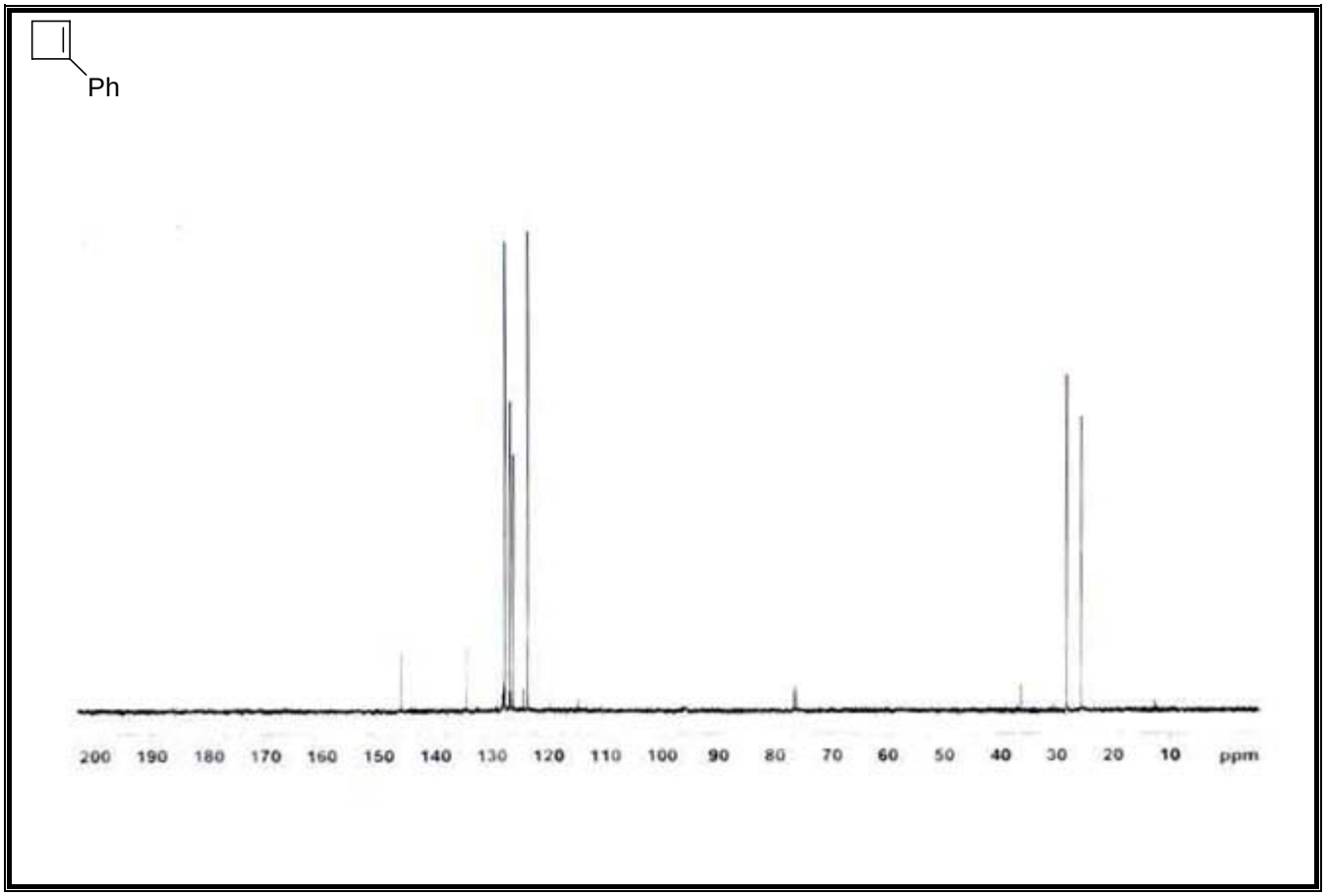

Figure A38 ^{13}C-NMR Spectrum of Compound **149**.

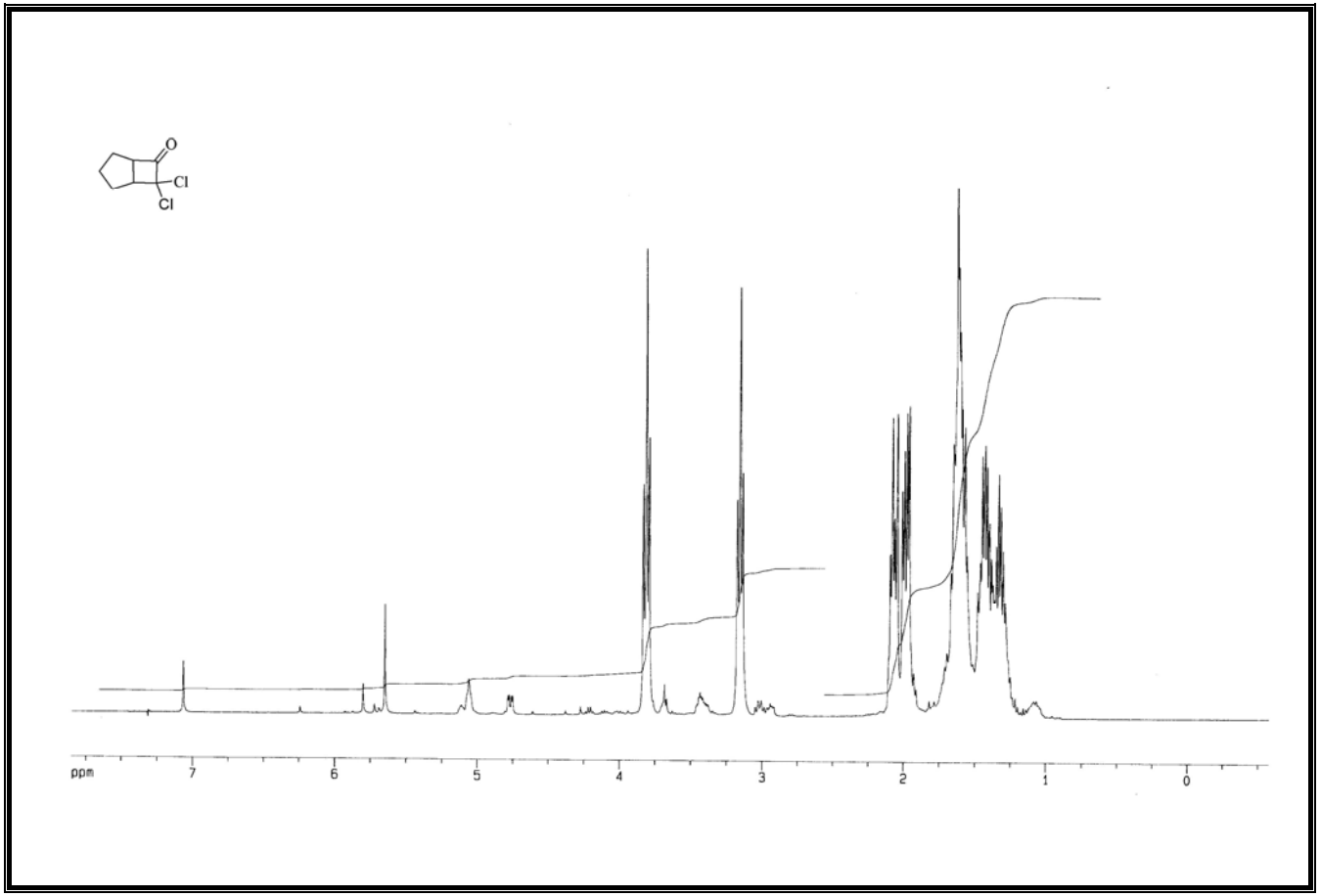

Figure A39 ^{1}H-NMR Spectrum of Compound **167**.

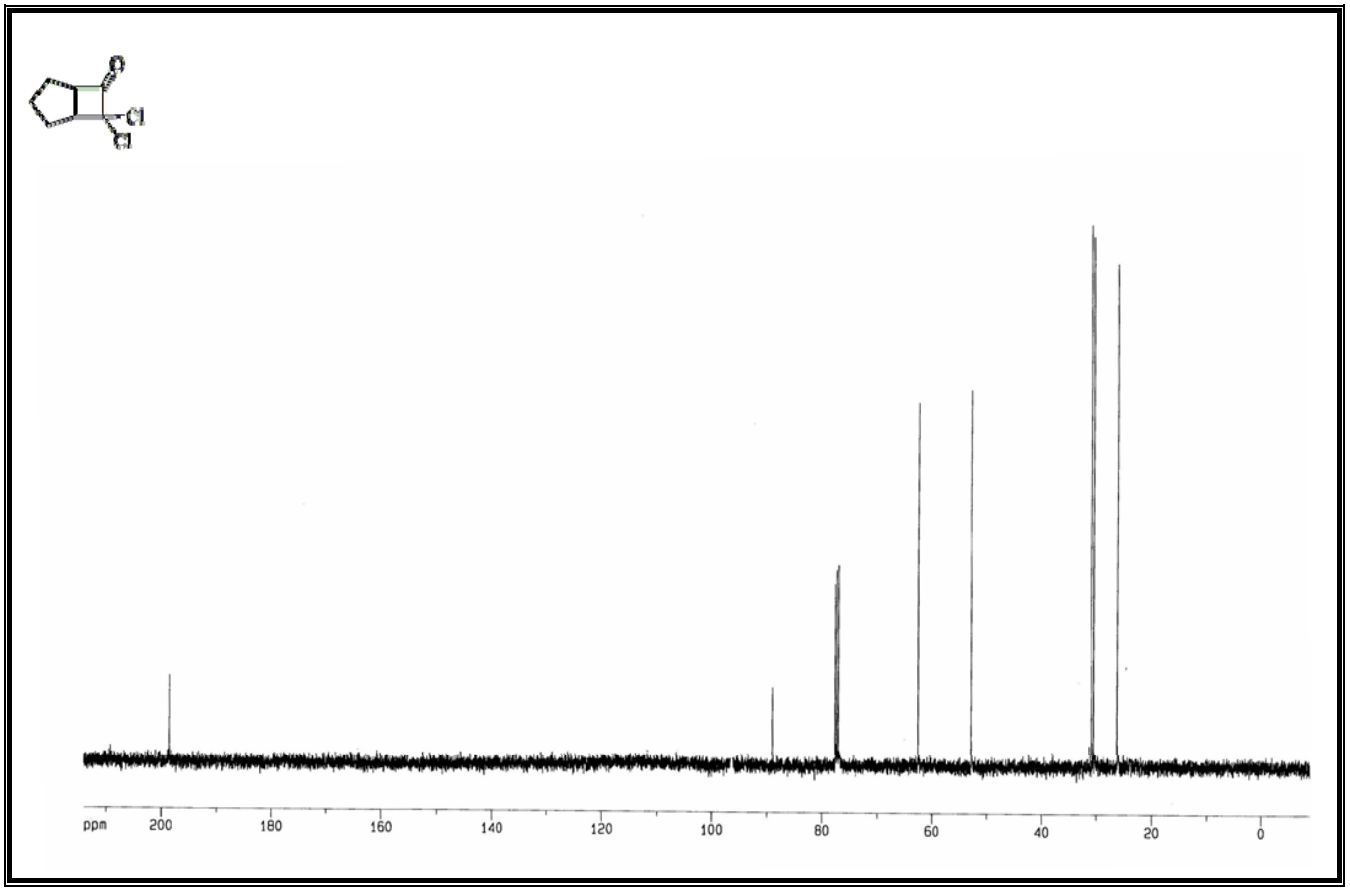

Figure A40 ^{13}C-NMR Spectrum of Compound **167**.

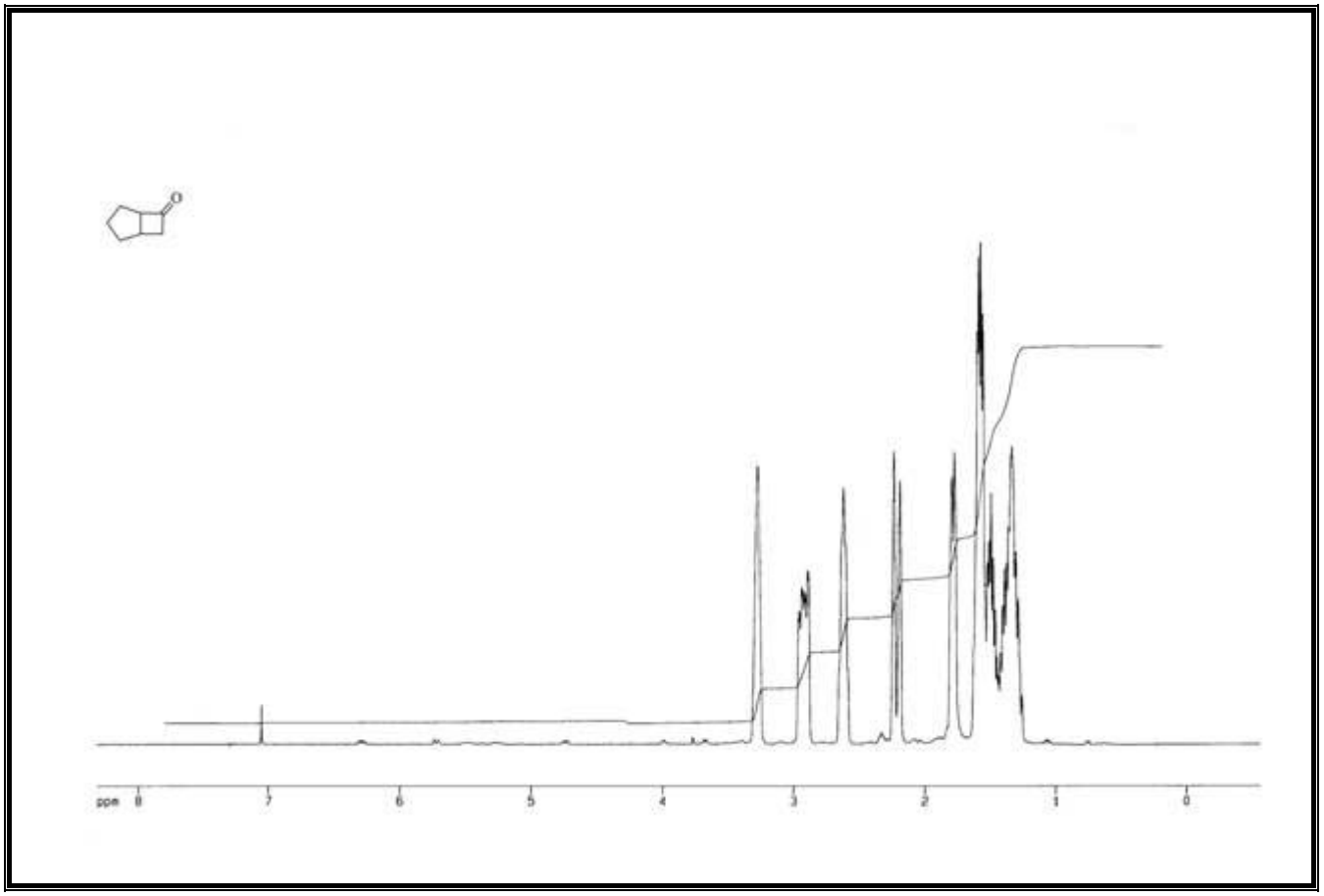

Figure A41 ^{1}H-NMR Spectrum of Compound **168**.

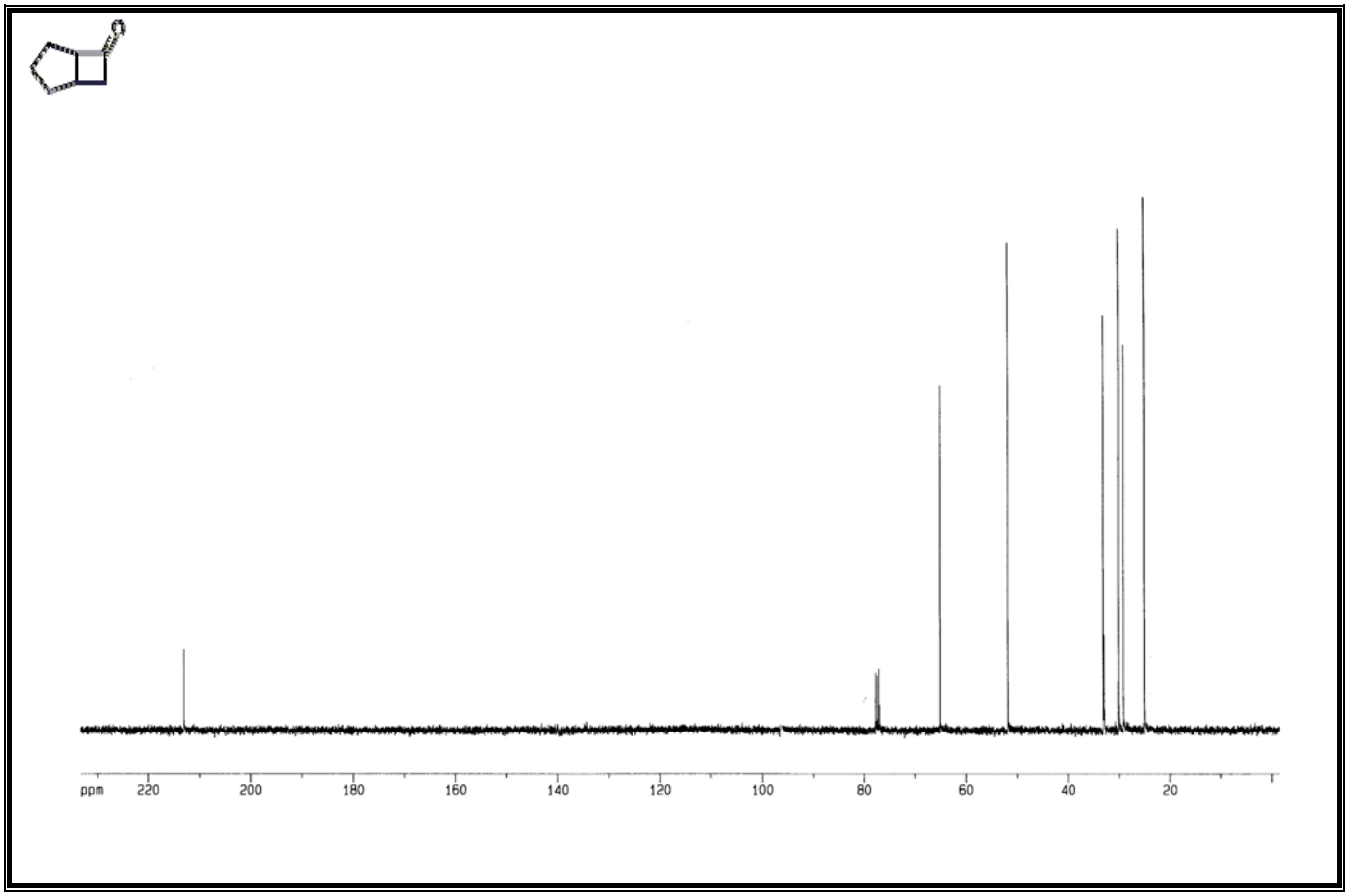

Figure A42 ^{13}C-NMR Spectrum of Compound **168**.

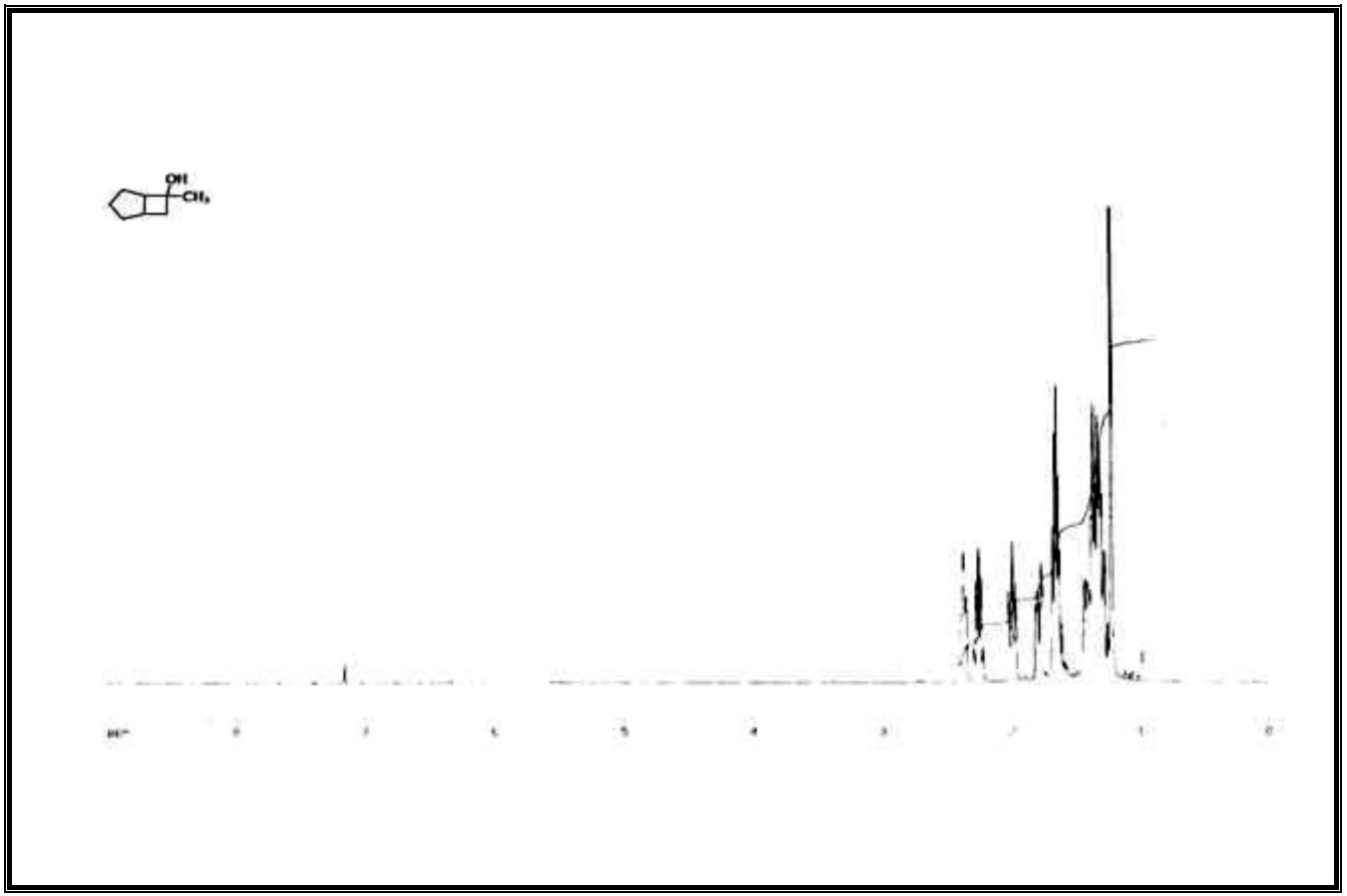

Figure A43 ^{1}H-NMR Spectrum of Compound **169**.

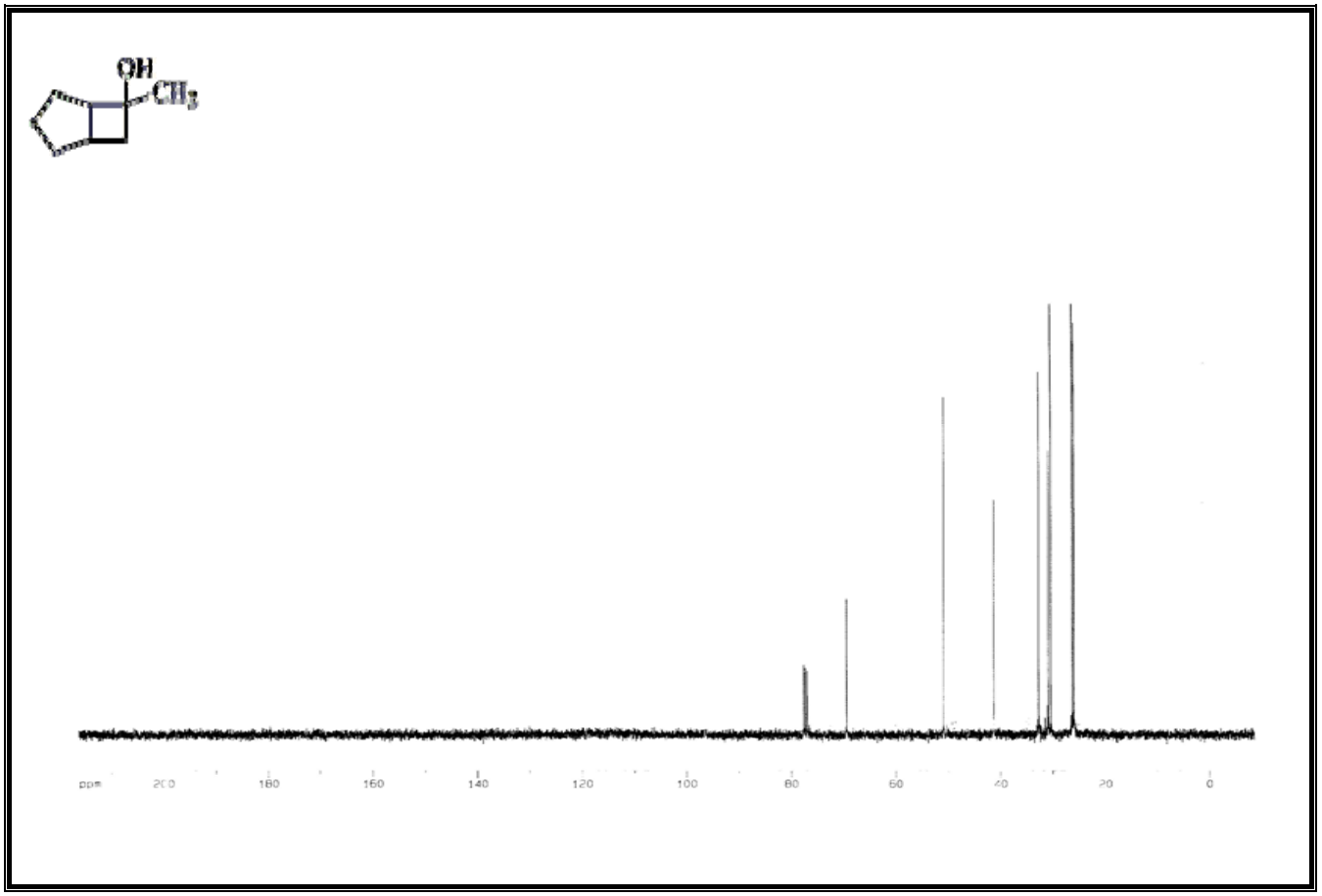

Figure A44 ^{13}C-NMR pectrum of Compound **169**.

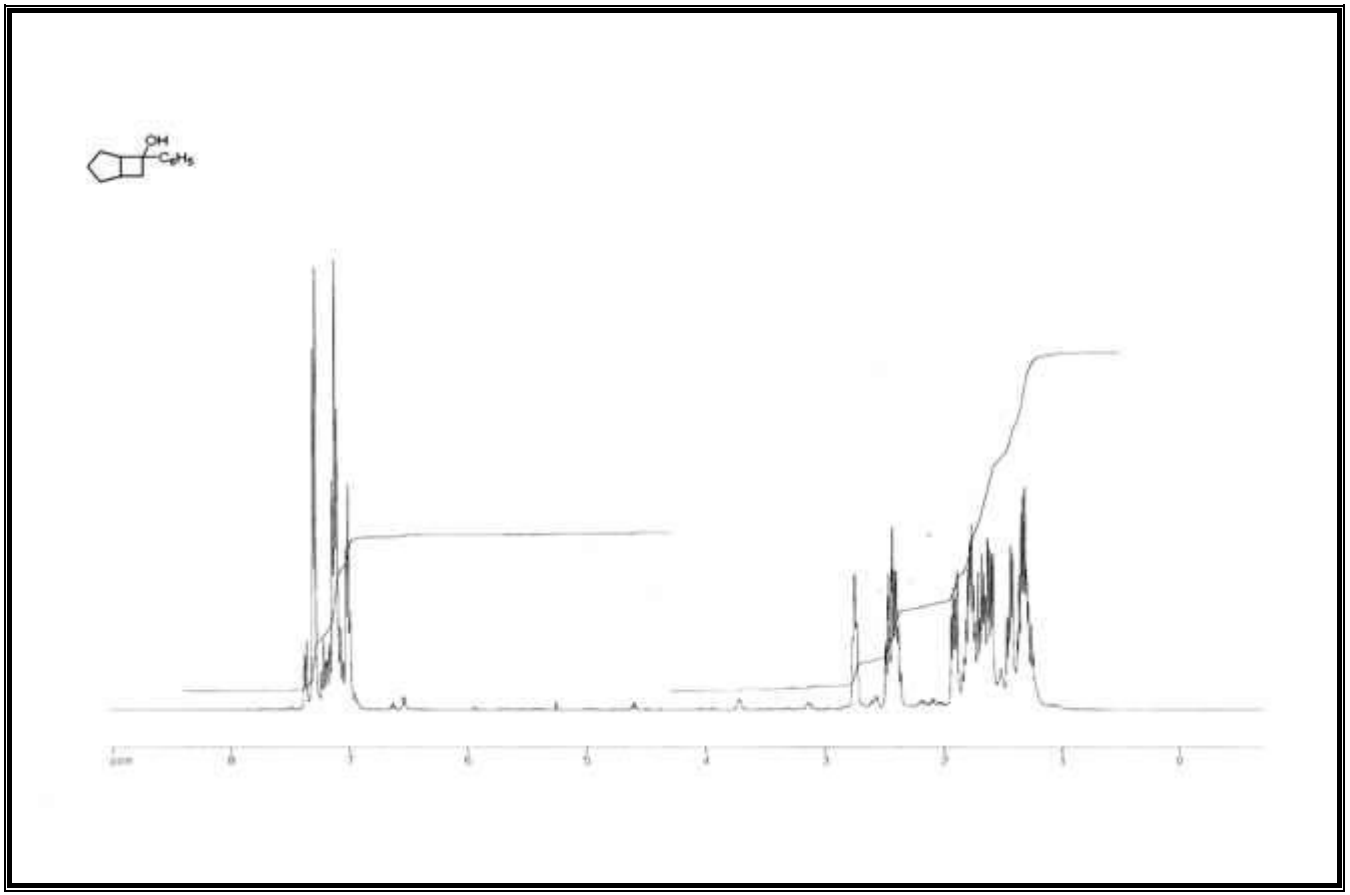

Figure A45 ^{1}H-NMR Spectrum of Compound **170**.

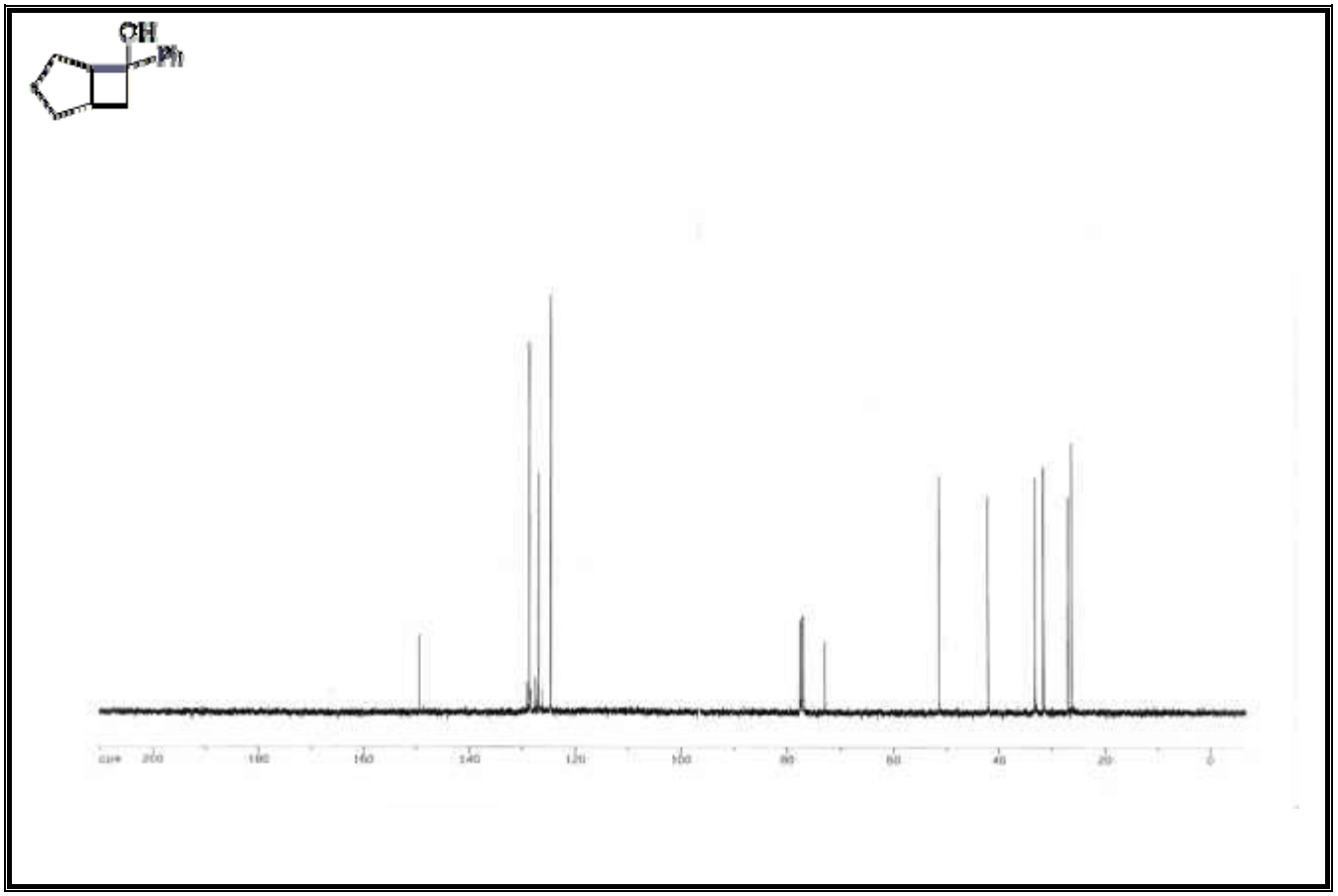

Figure A46 ^{13}C-NMR Spectrum of Compound **170**.

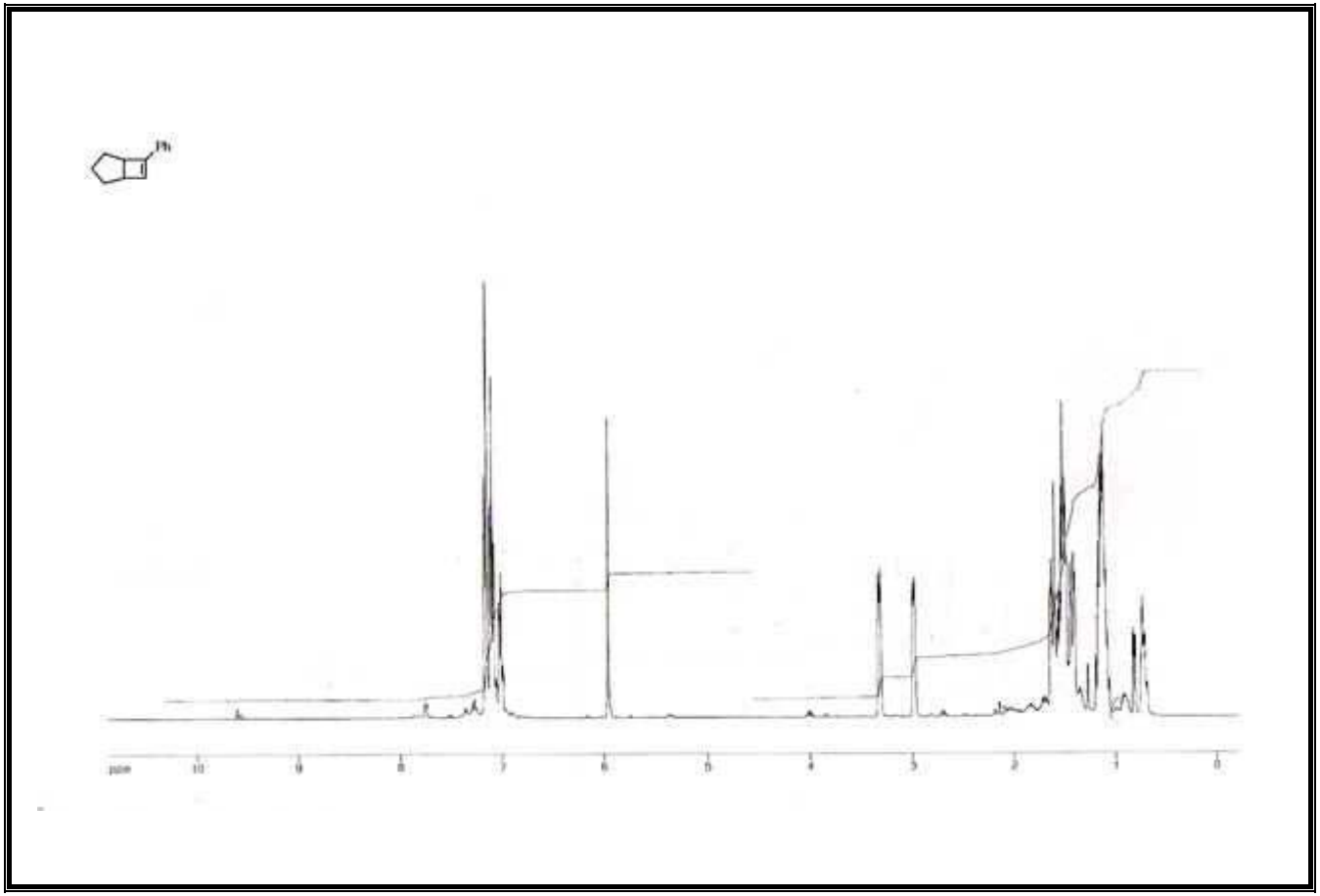

Figure A47 ^{1}H-NMR Spectrum of Compound **164**.

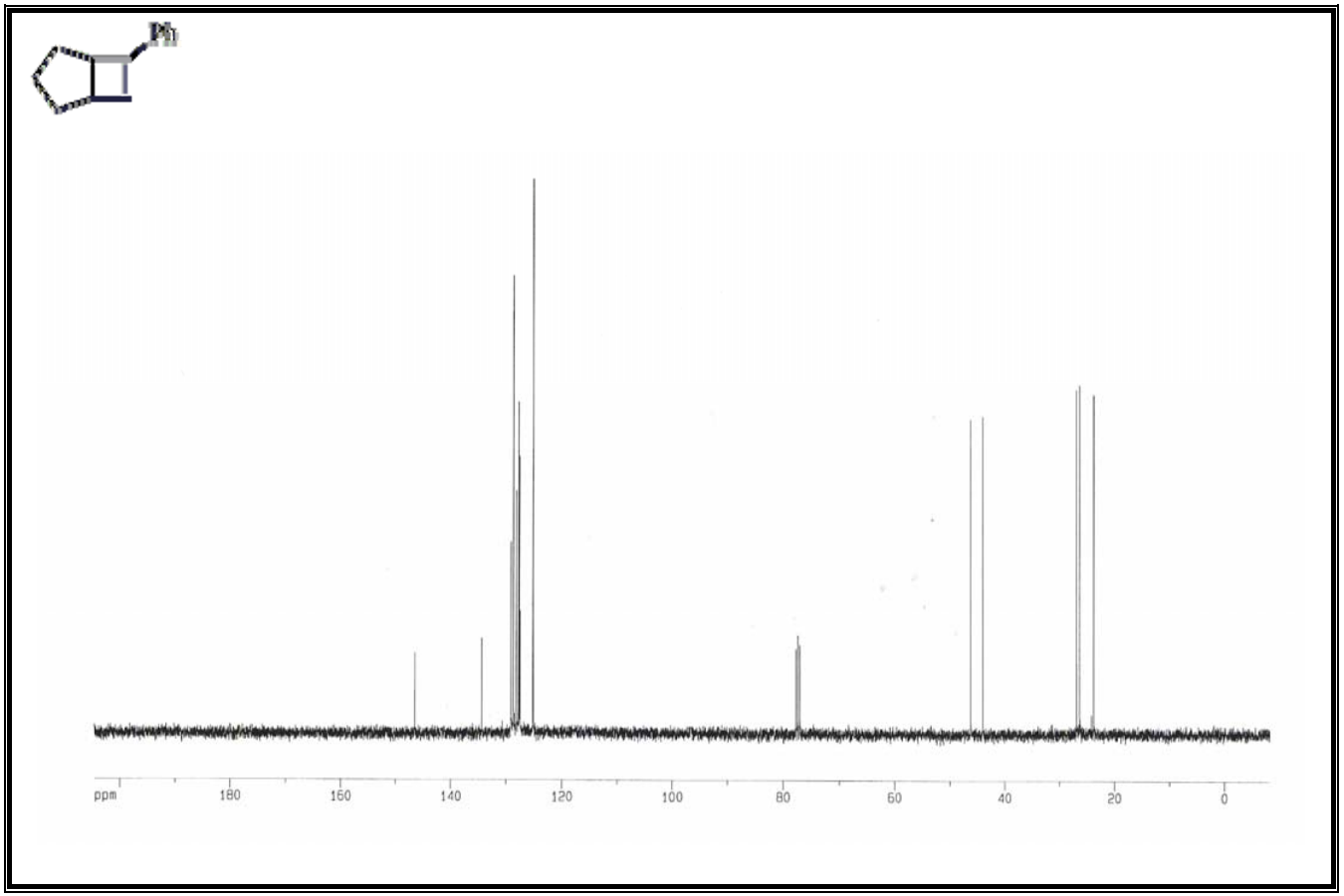

Figure A48 ^{13}C-NMR Spectrum of Compound **164**.

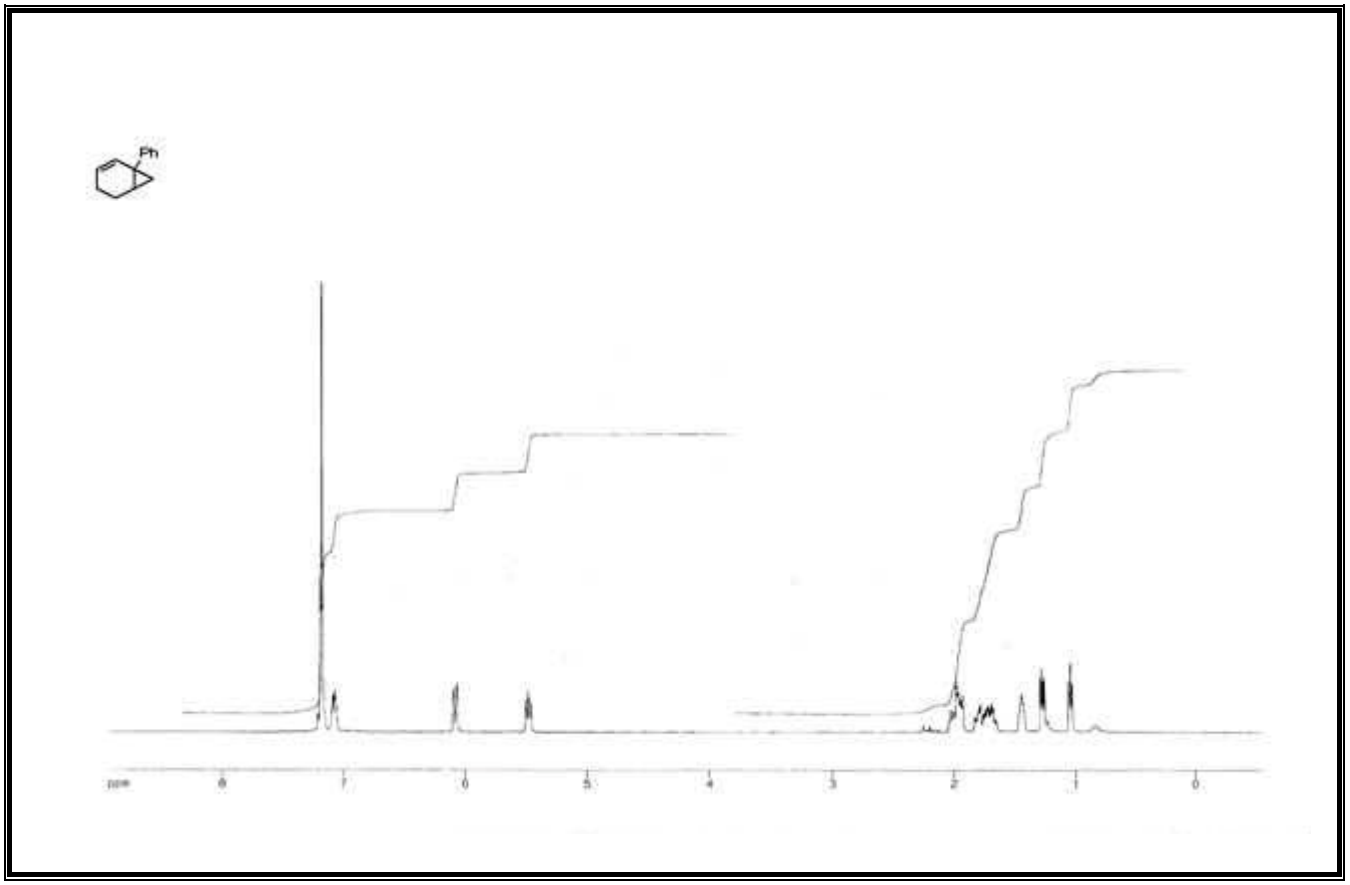

Figure A49 ^{1}H-NMR Spectrum of Compound **171**.

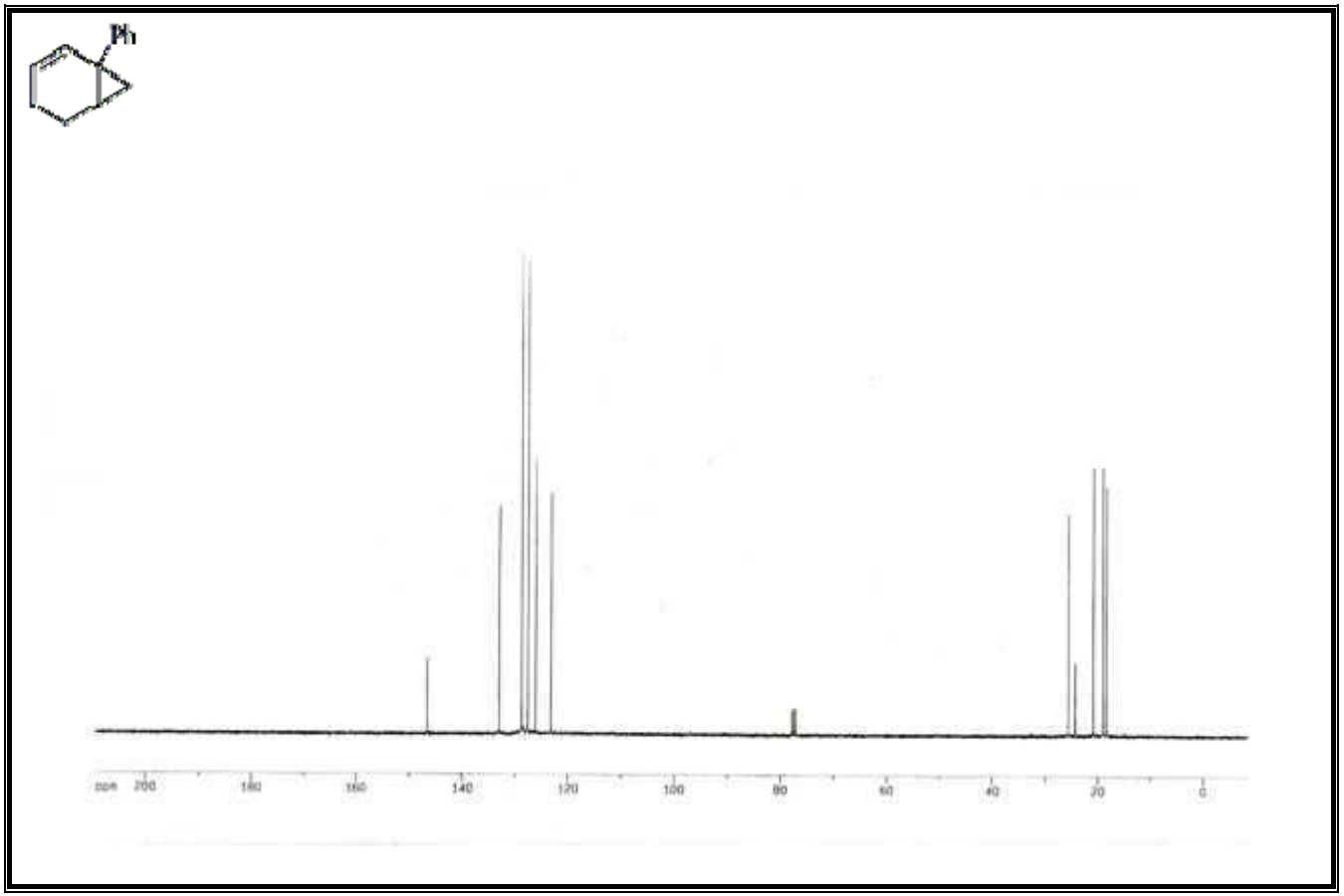

Figure A50 ^{13}C-NMR Spectrum of Compound **171**.

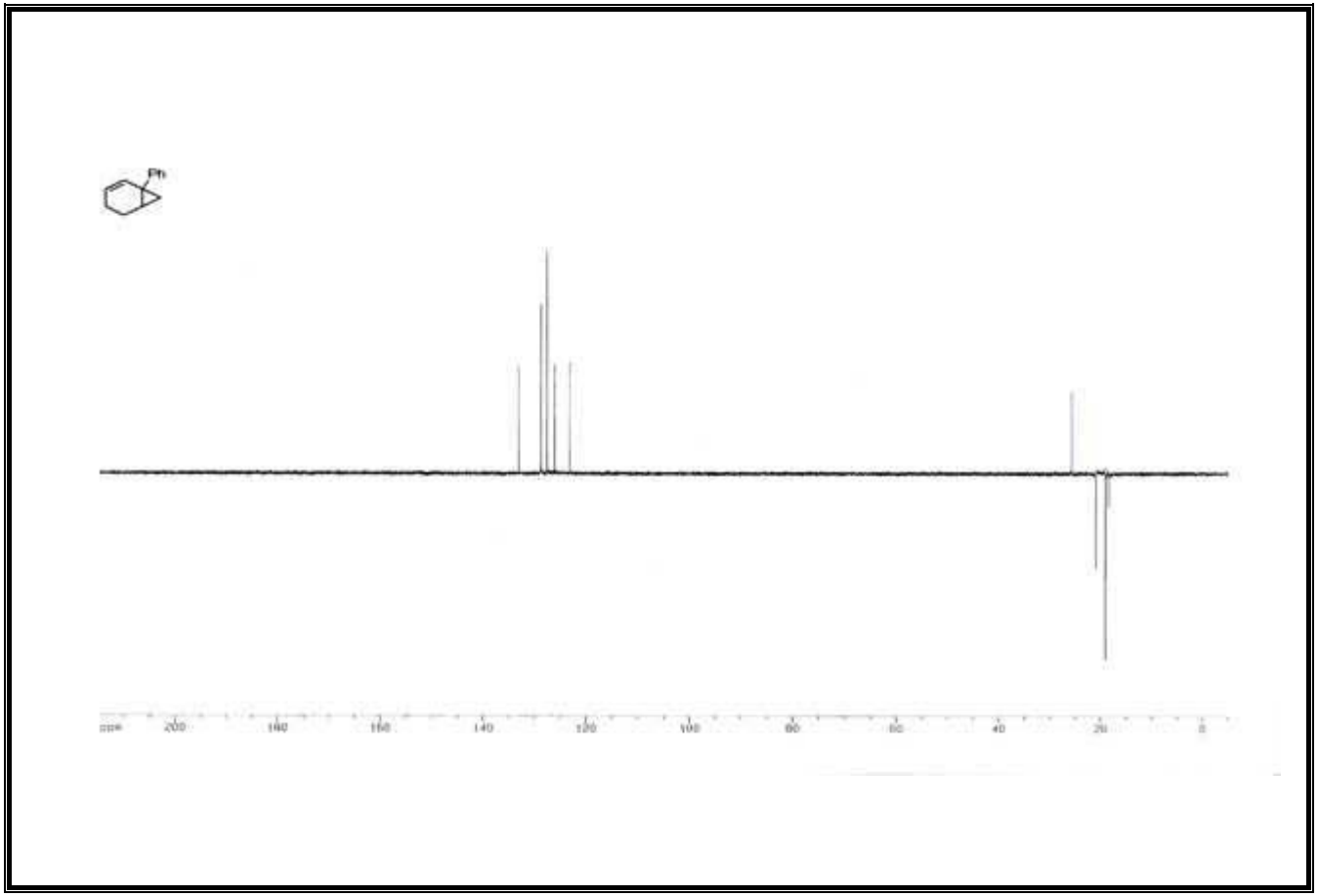

Figure A51 DEPT-135 Spectrum of Compound **171**.

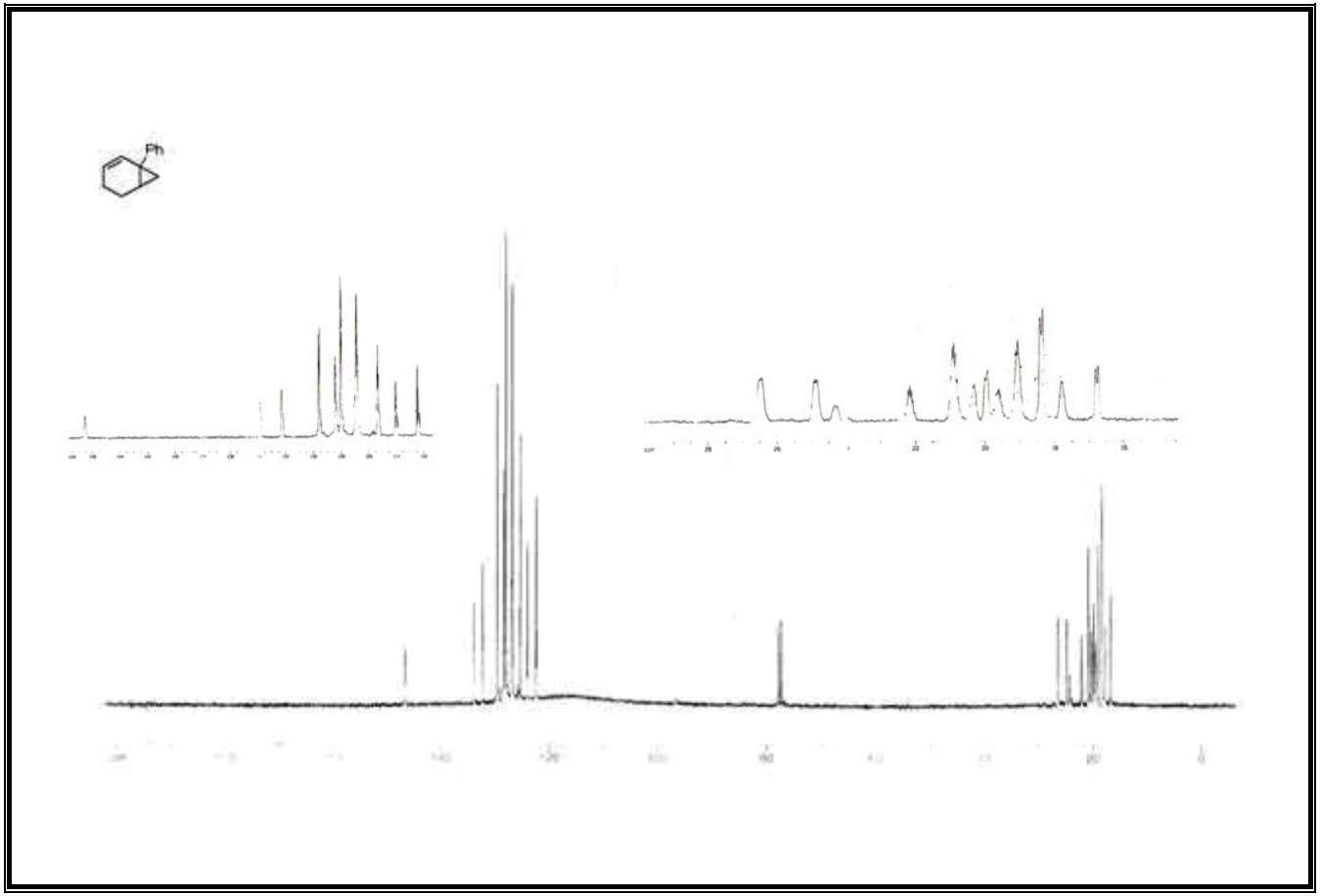

Figure A52 Proton coupled ^{13}C-NMR Srectrum of Compound **171**.

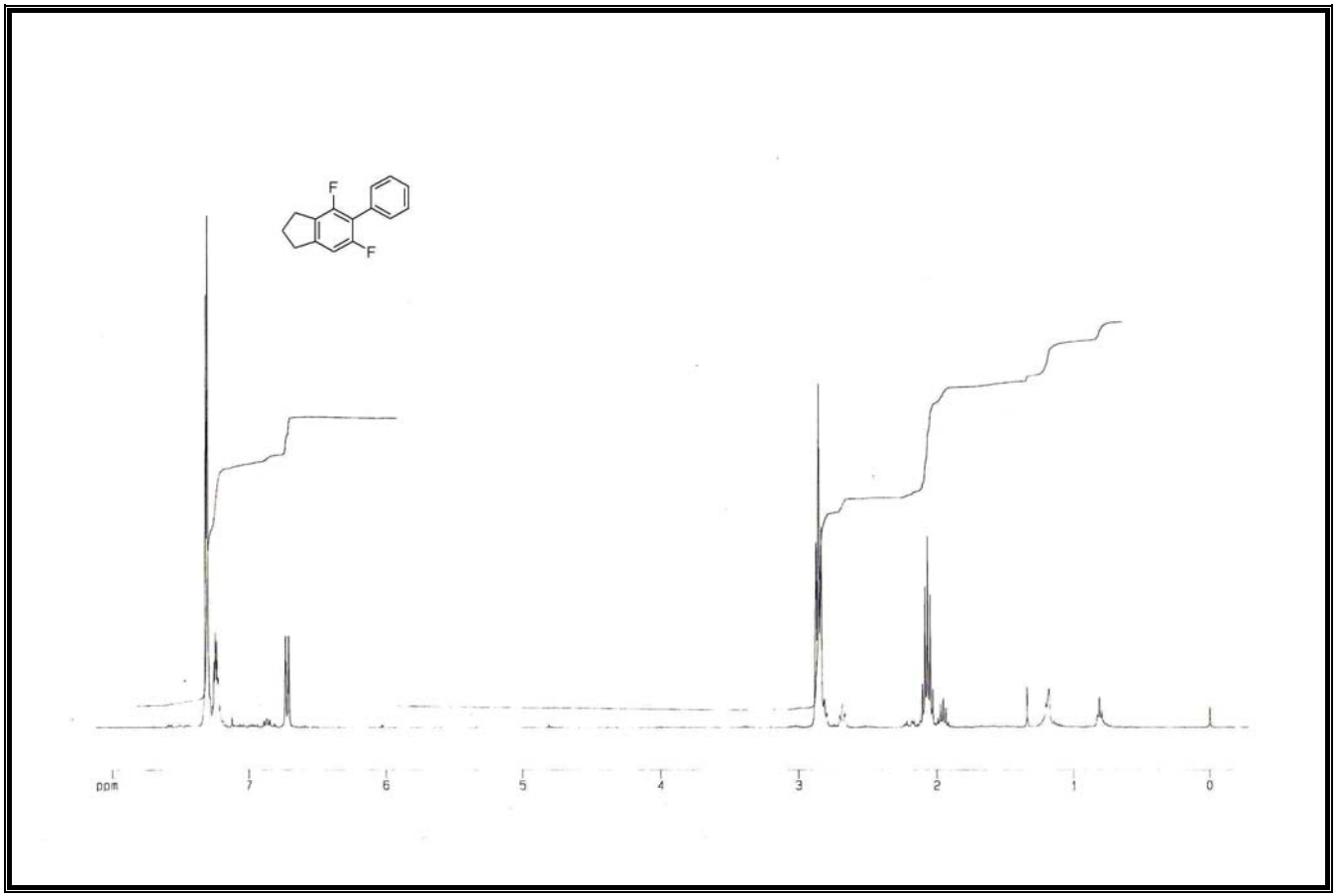

Figure A53 ^{1}H-NMR Srectrum of Compound **173**.

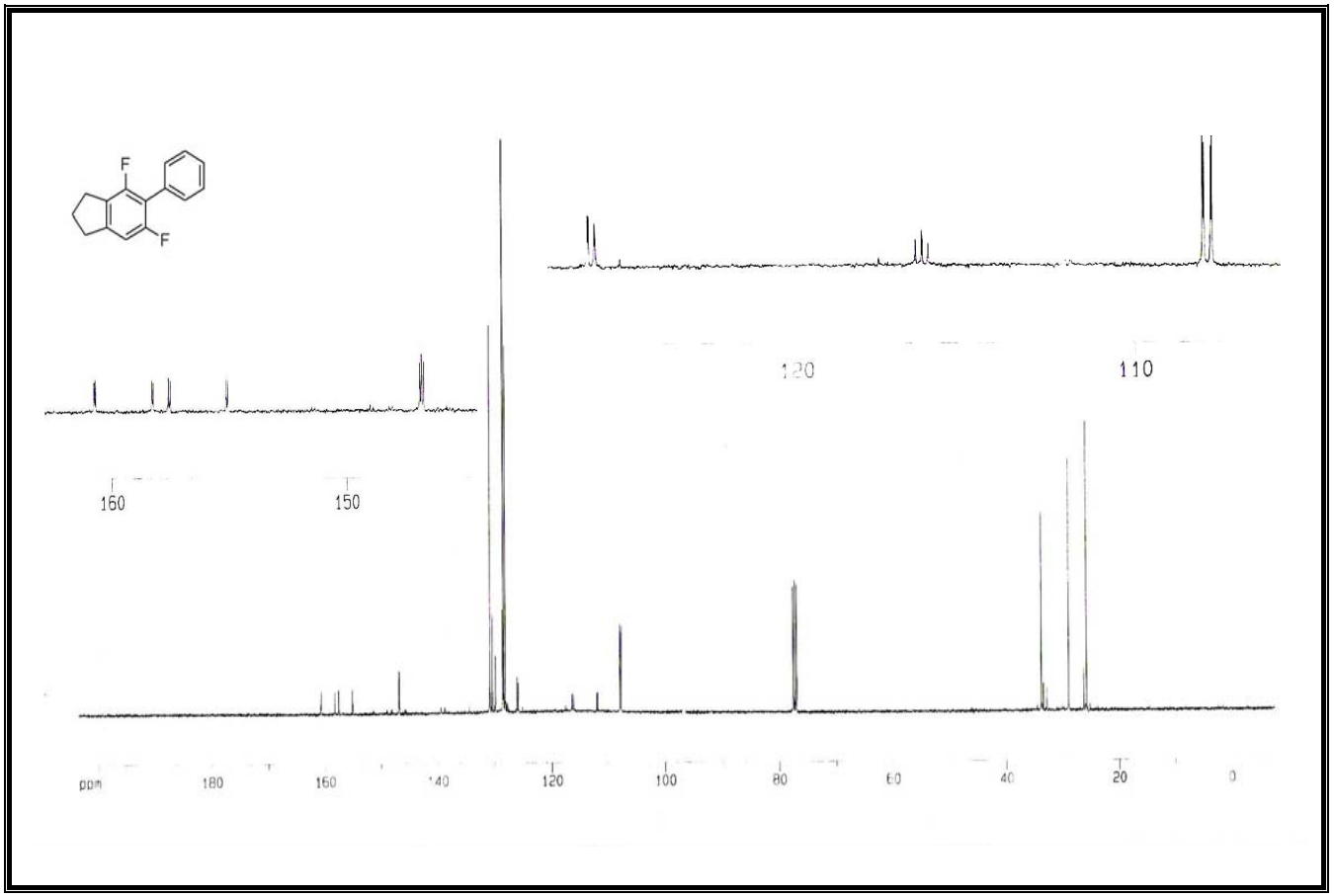

Figure A54 ^{13}C-NMR Srectrum of Compound **173**.

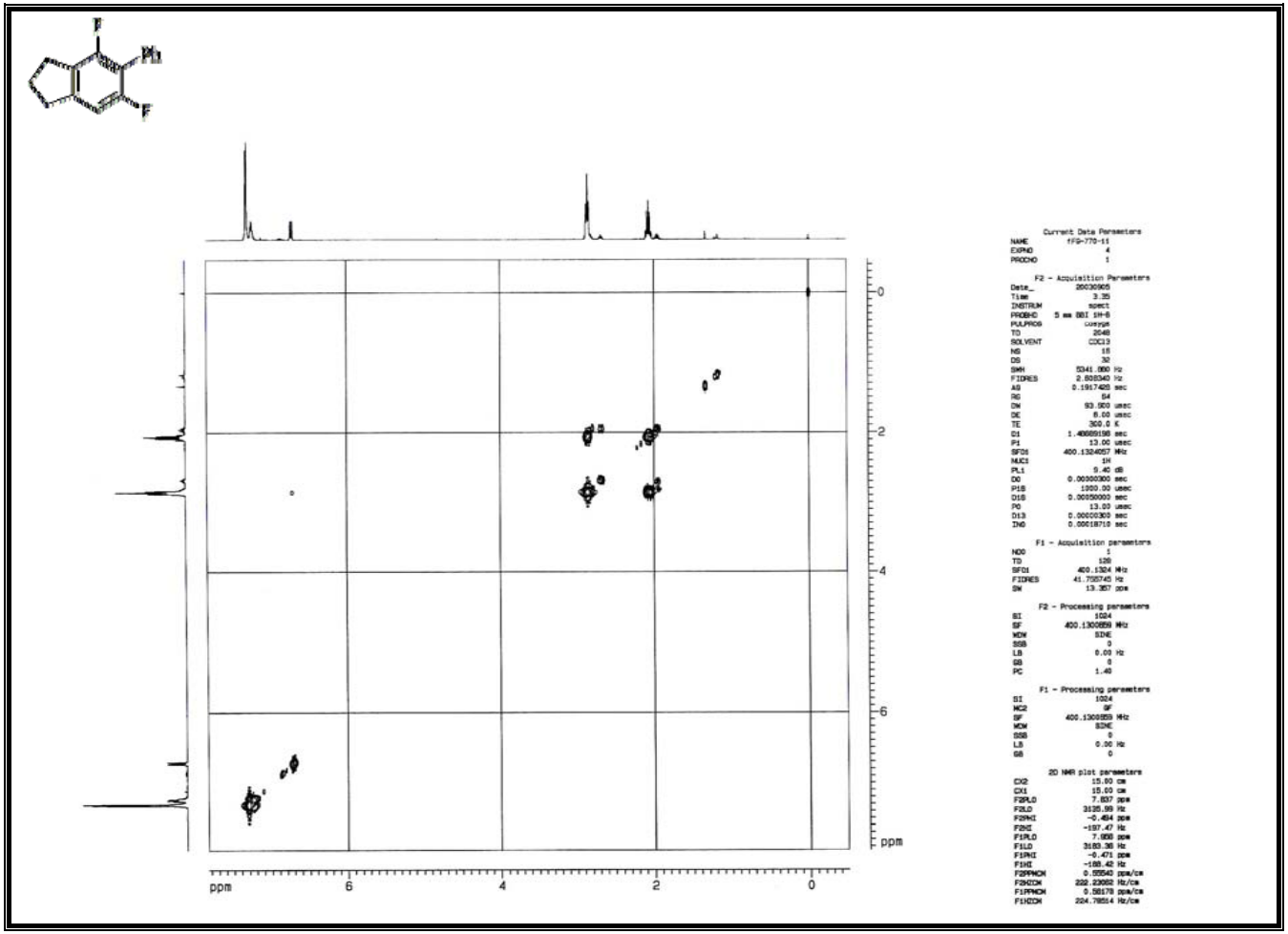

Figure A55 COSY Spectrum of Compound **173**.

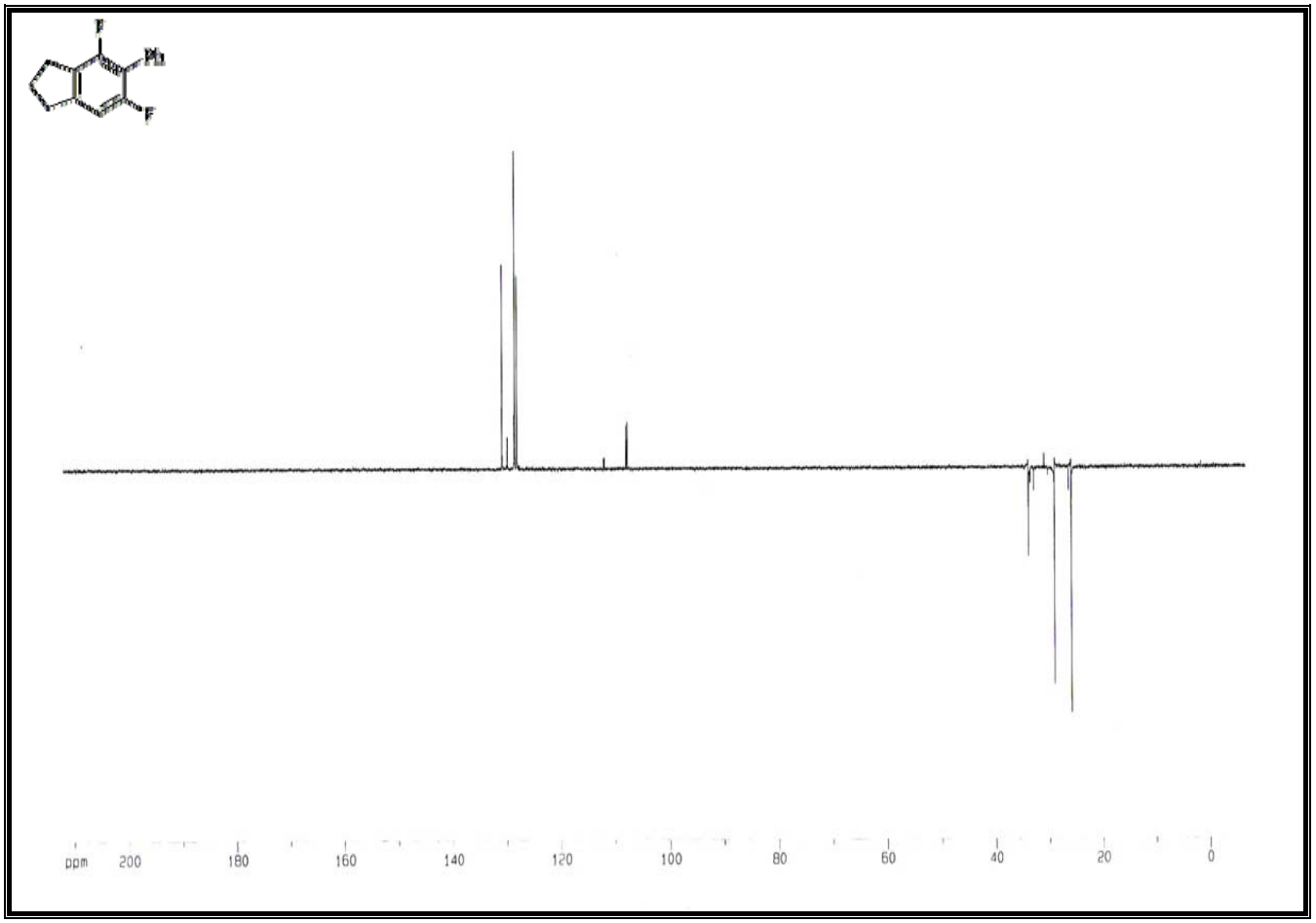

Figure A56 DEPT-135 Spectrum of Compound **173**.

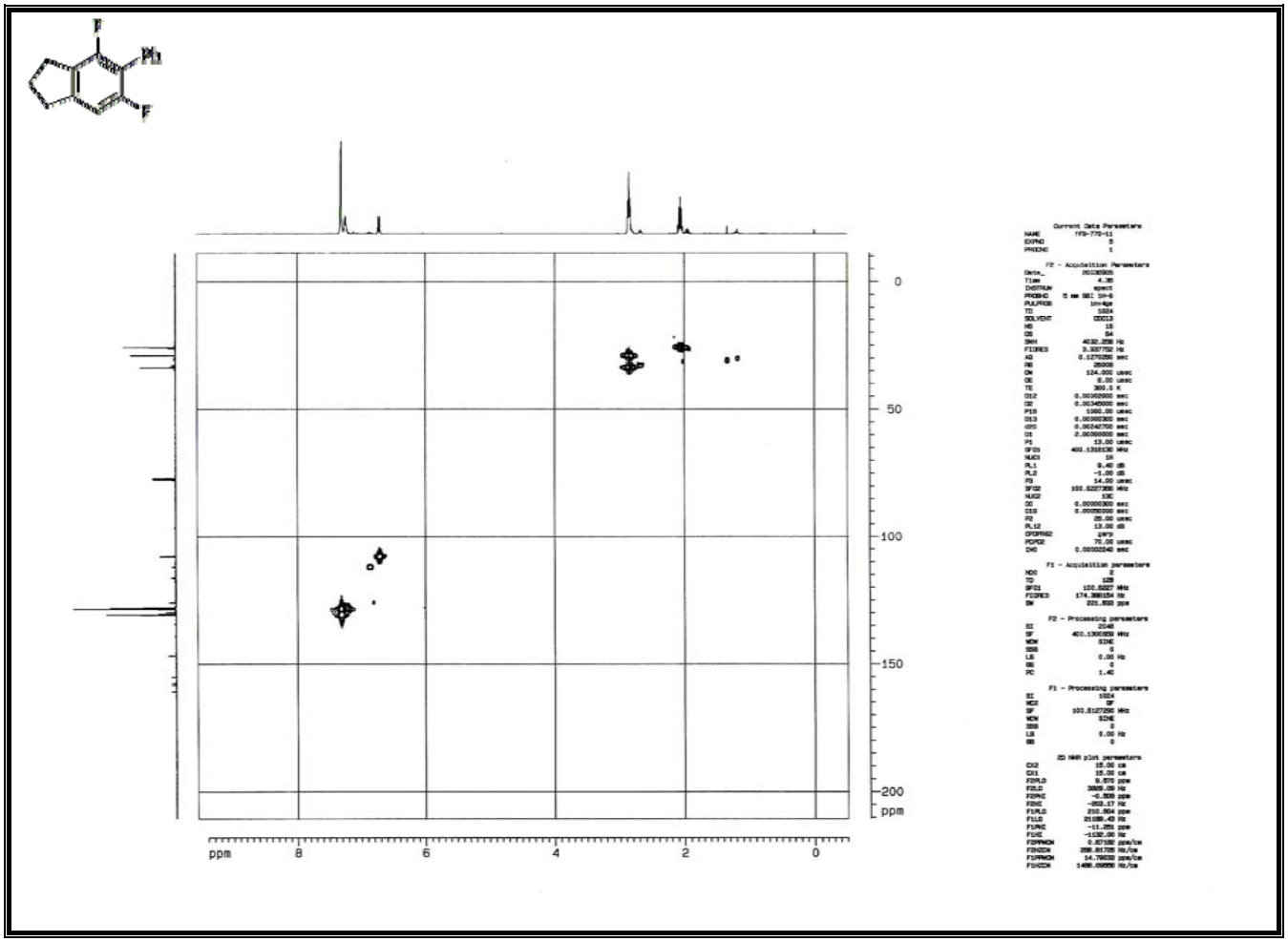

Figure A57 HMQC Spectrum of Compound **173**.

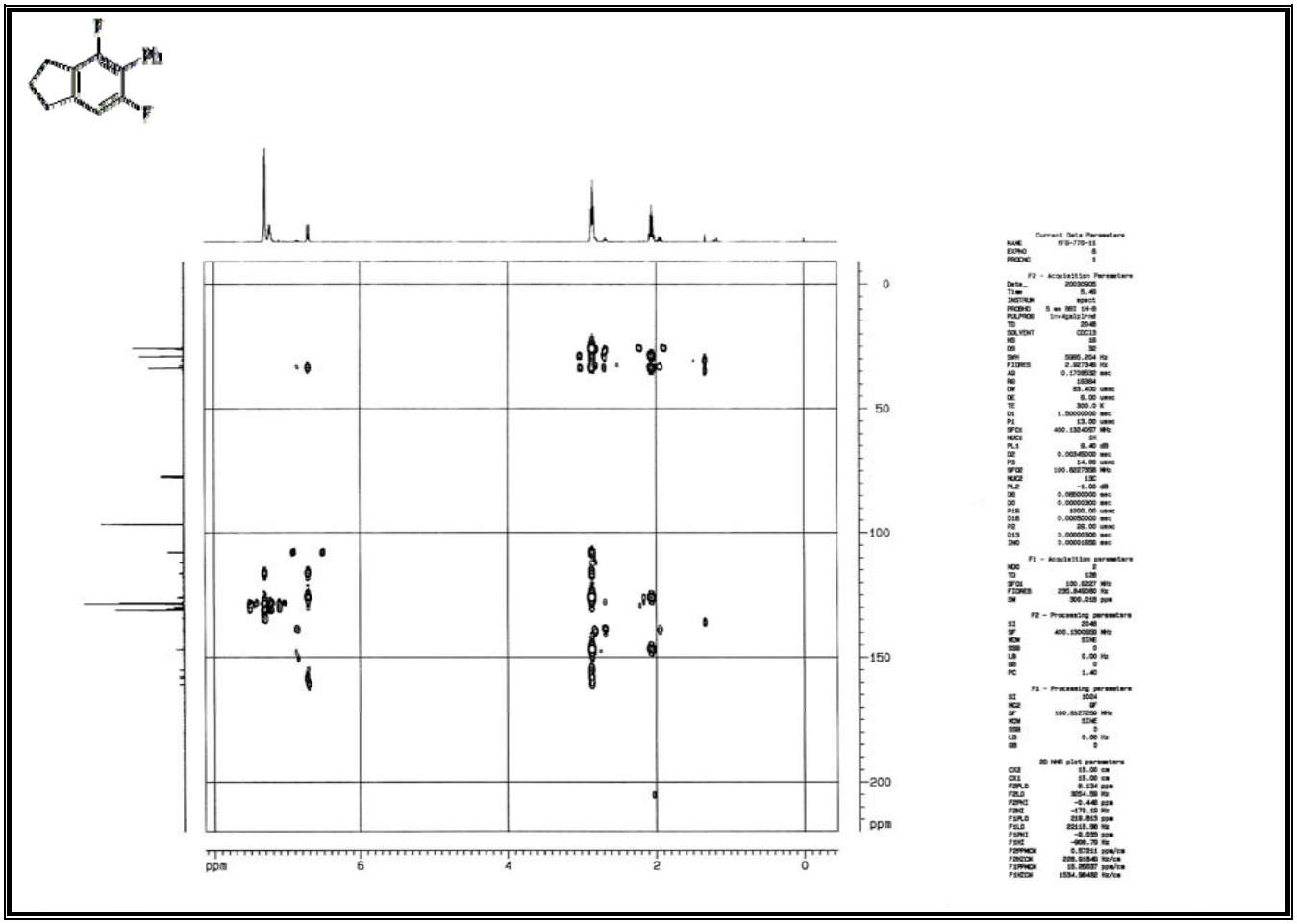

Figure A58 HMBC Spectrum of Compound **173**.

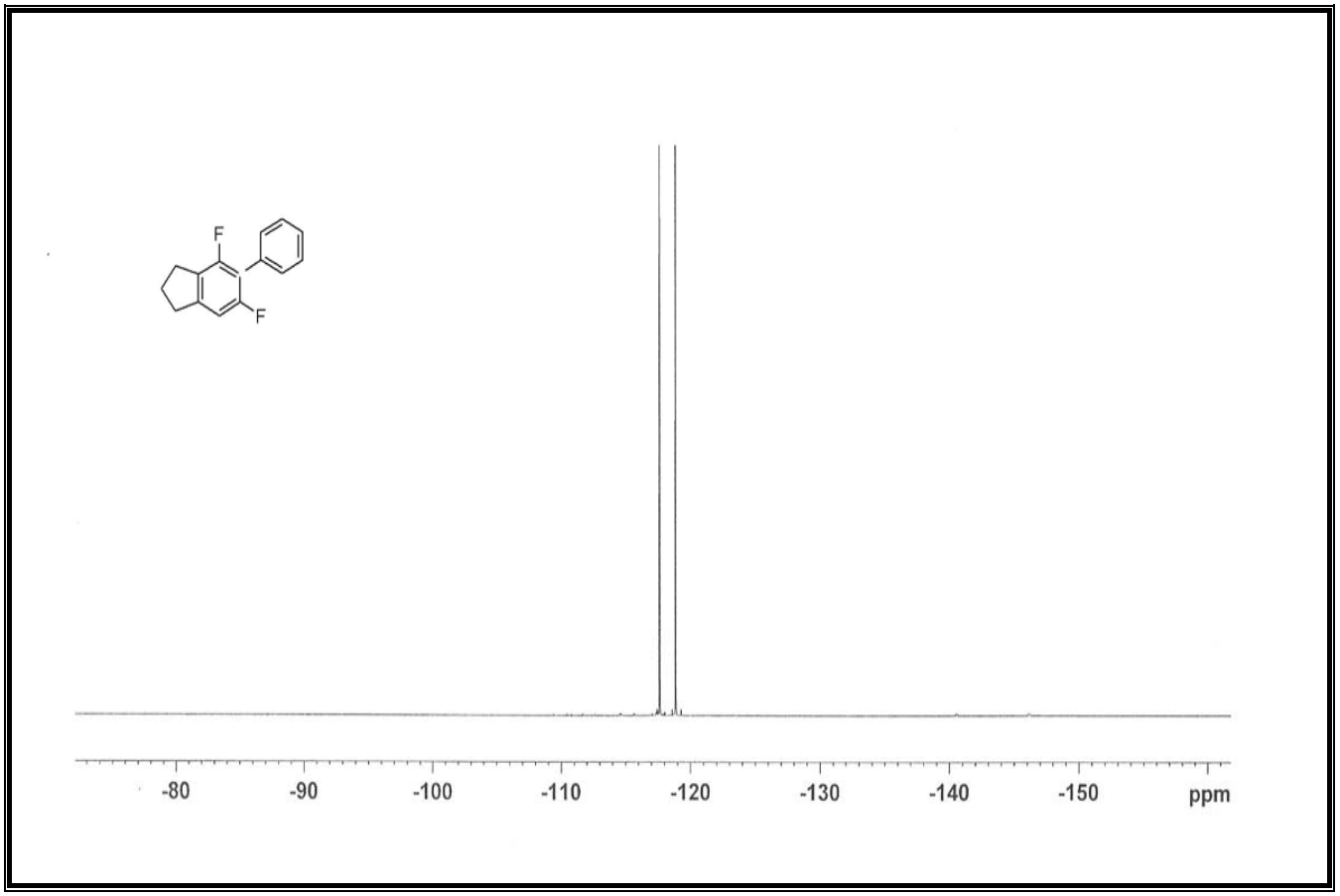

Figure A59 ^{19}F-NMR Spectrum of Compound **173**.

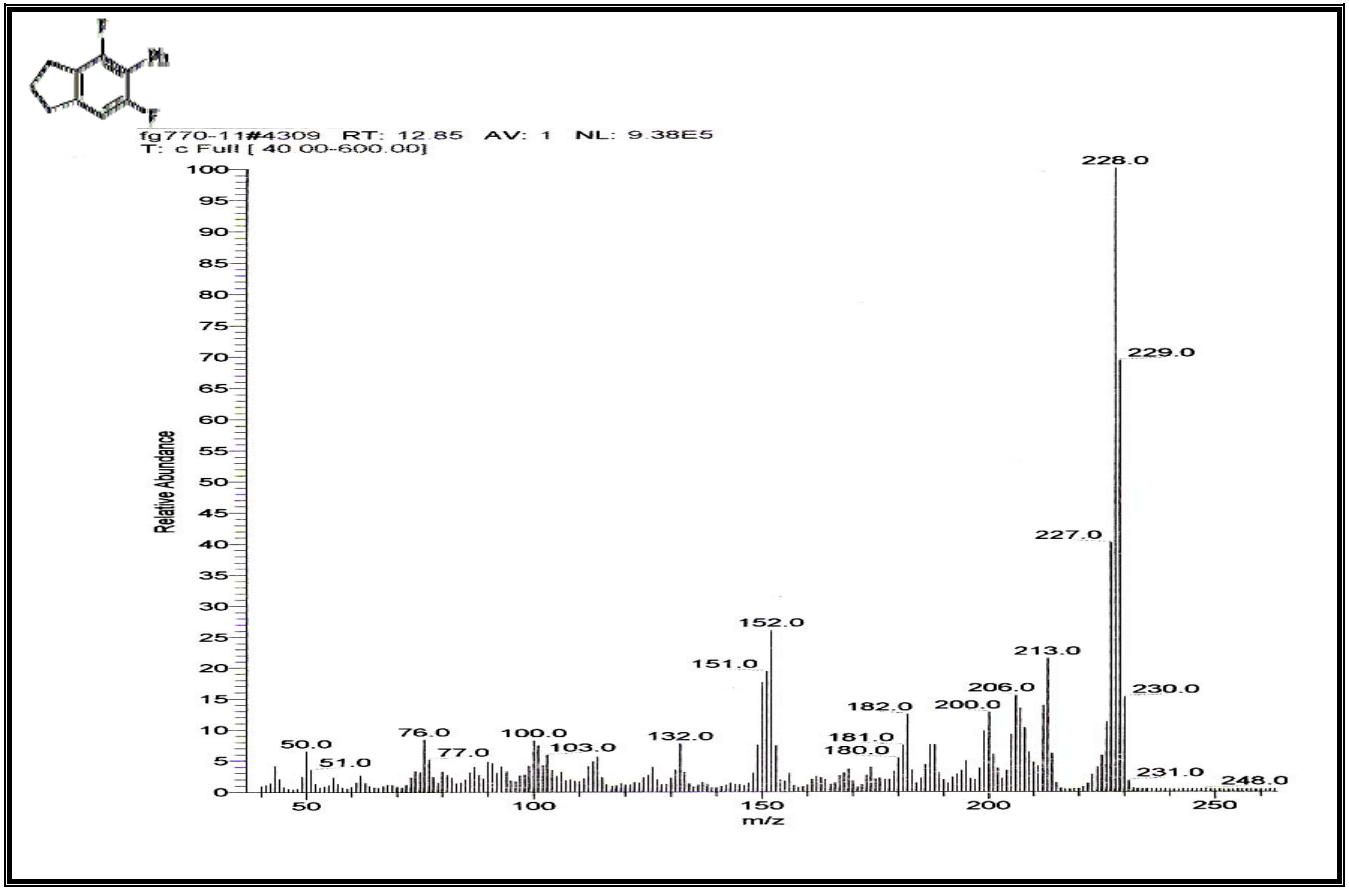

Figure A60 GC-MS Spectrum of Compound **173**.

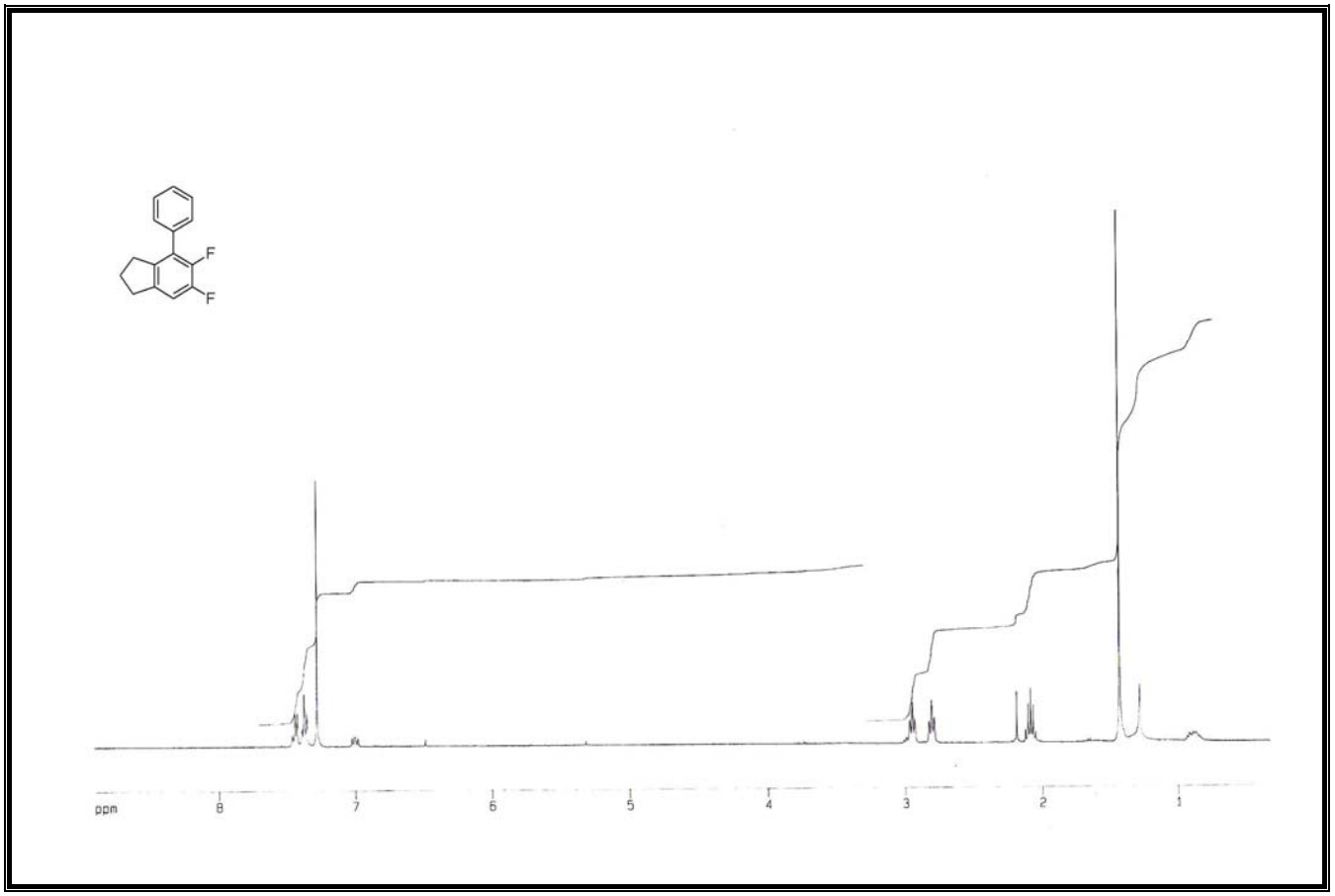

Figure A61 ^{1}H-NMR Spectrum of Compound **174**.

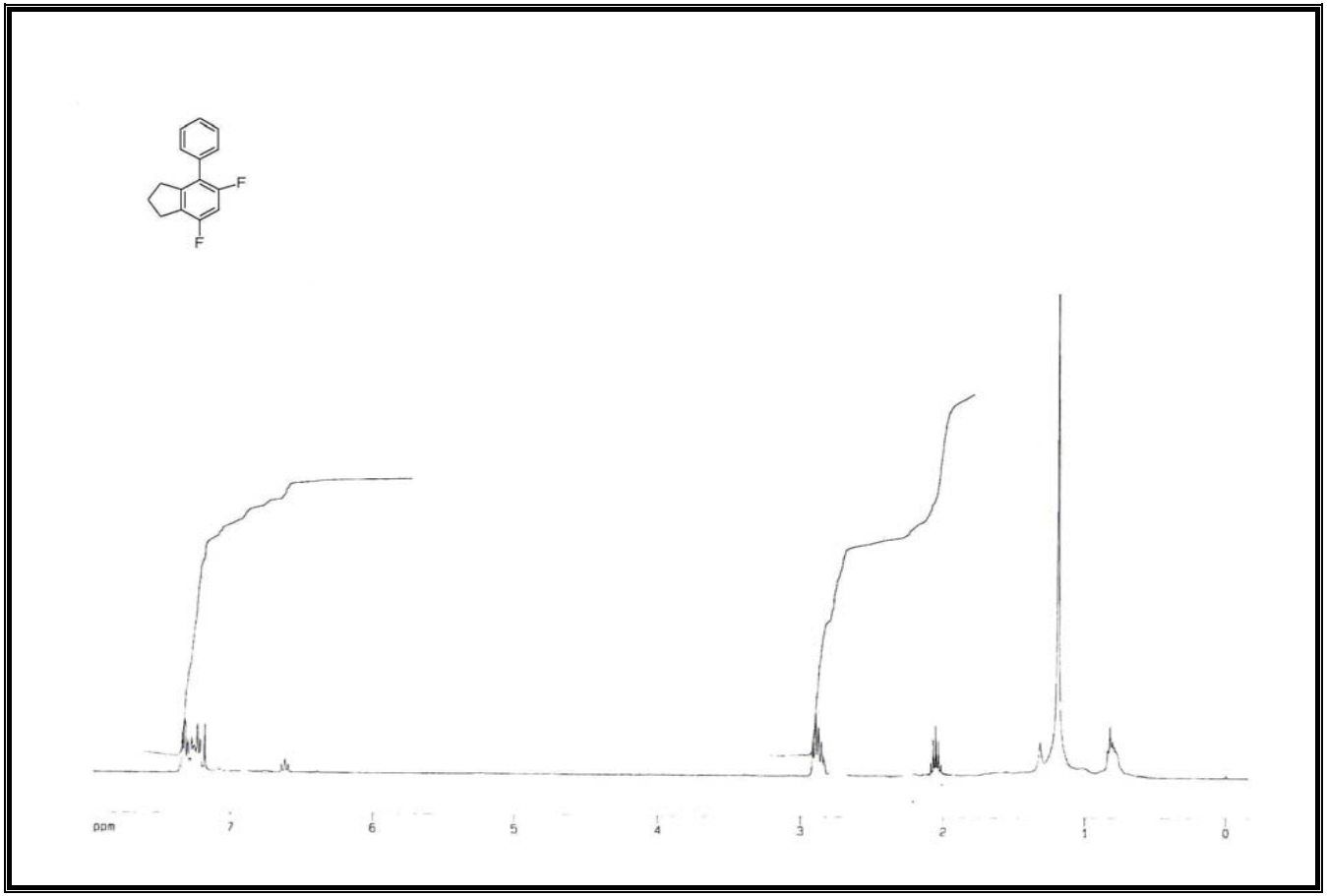

Figure A62 ^{1}H-NMR Spectrum of Compound **175**.

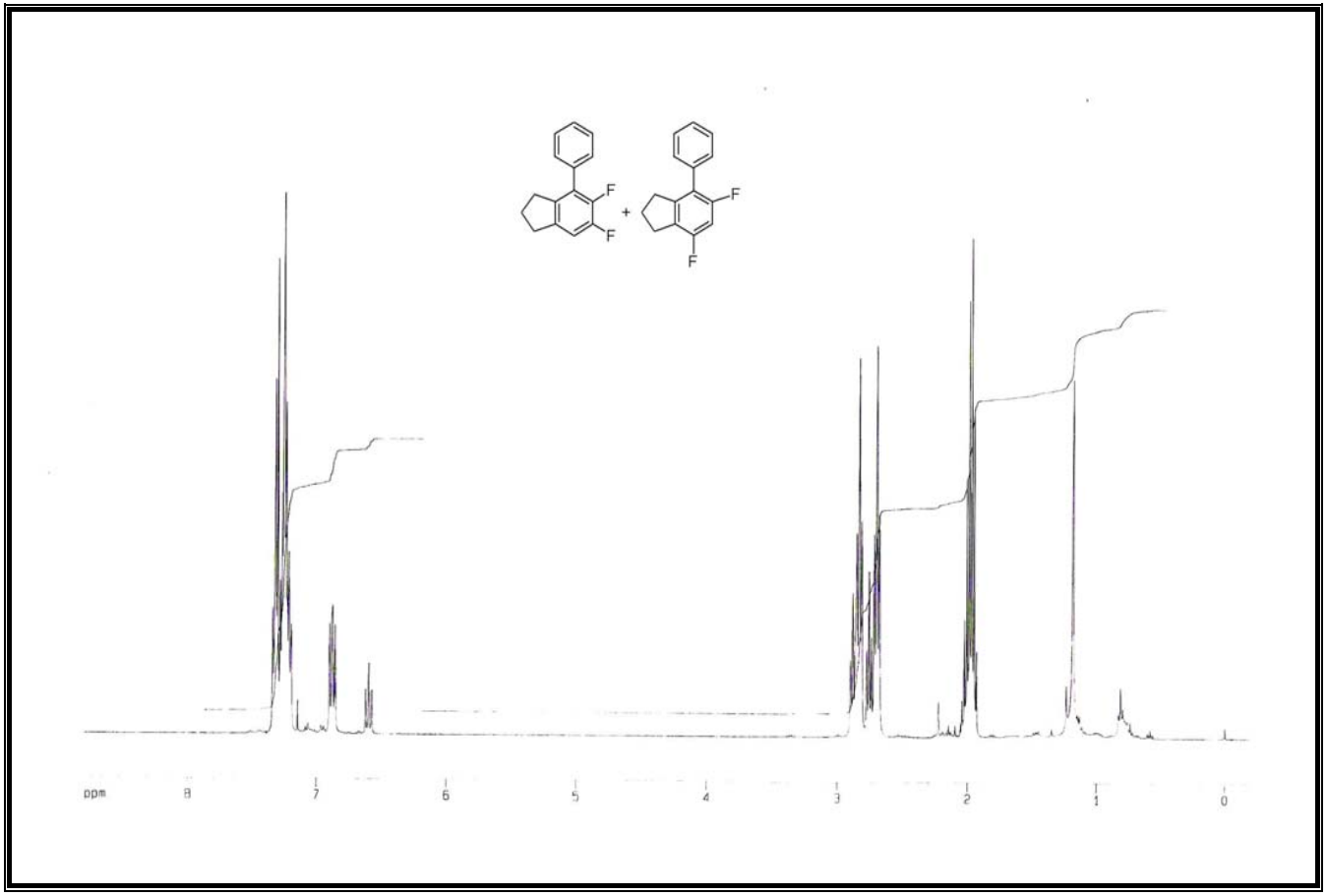

Figure A63 ^{1}H-NMR Spectrum of Compounds **174**+**175**..

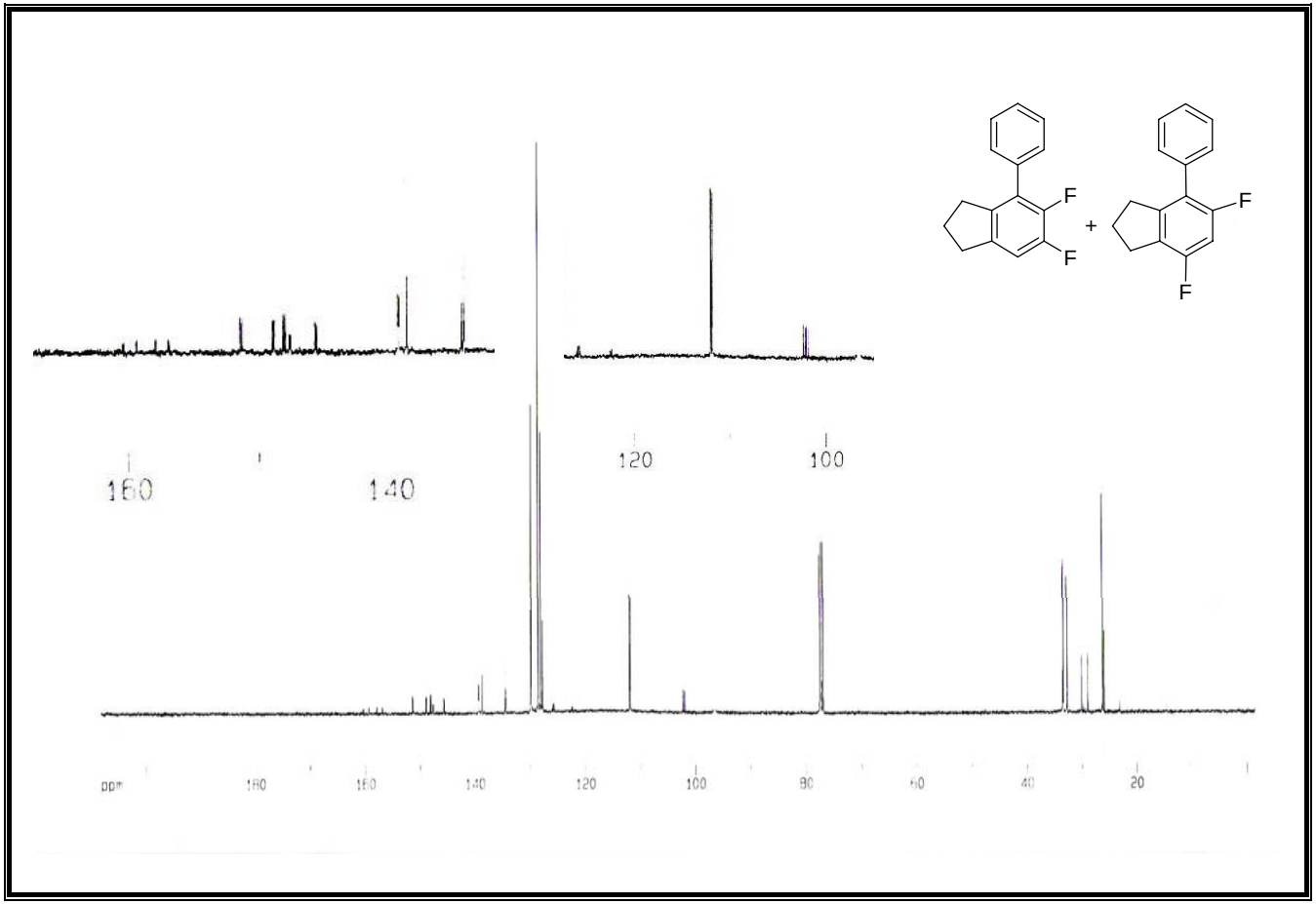

Figure A64 ^{13}C-NMR Spectrum of Compounds **174**+**175**.

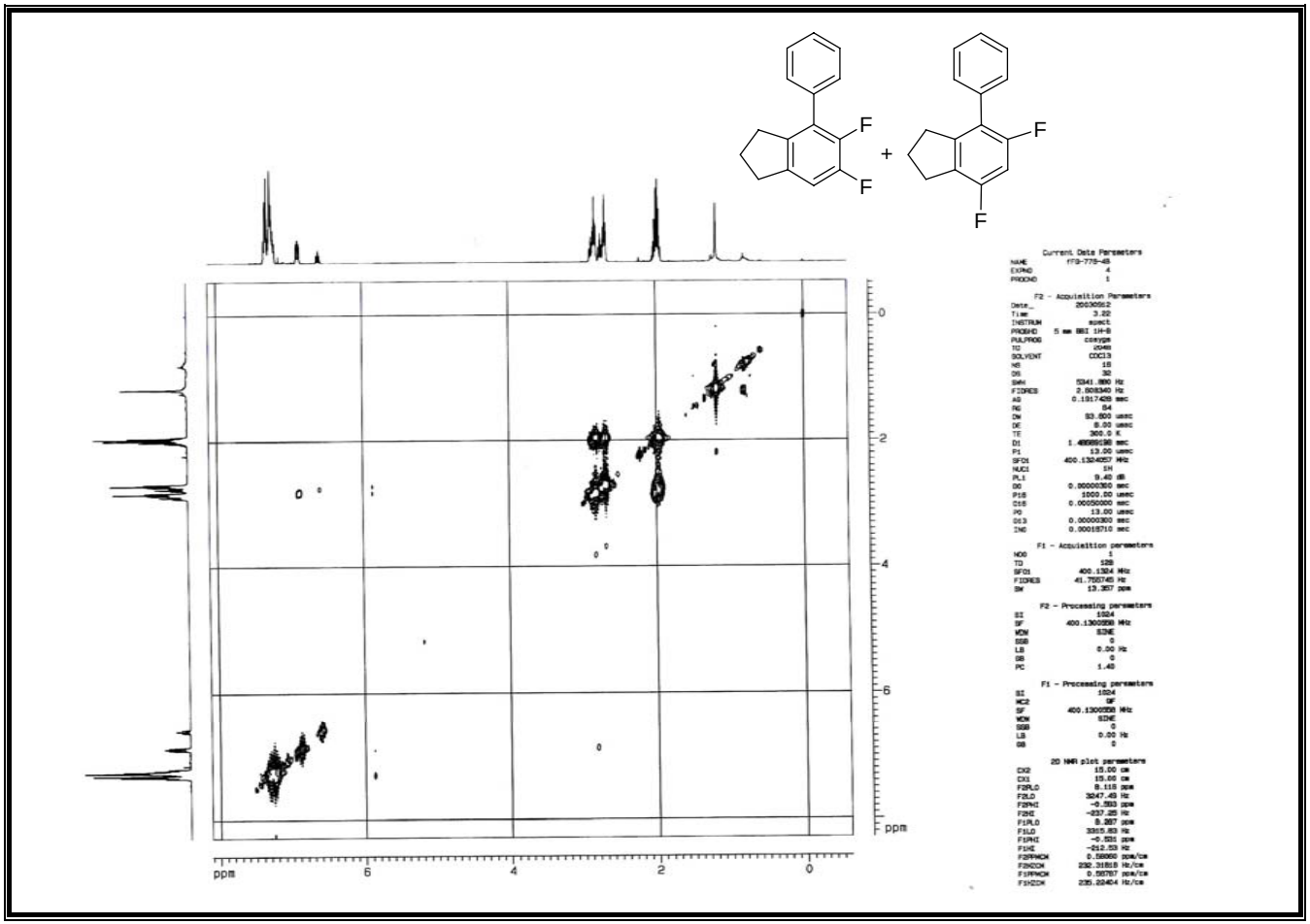

Figure A65 COSY Spectrum of Compounds **174**+**175**.

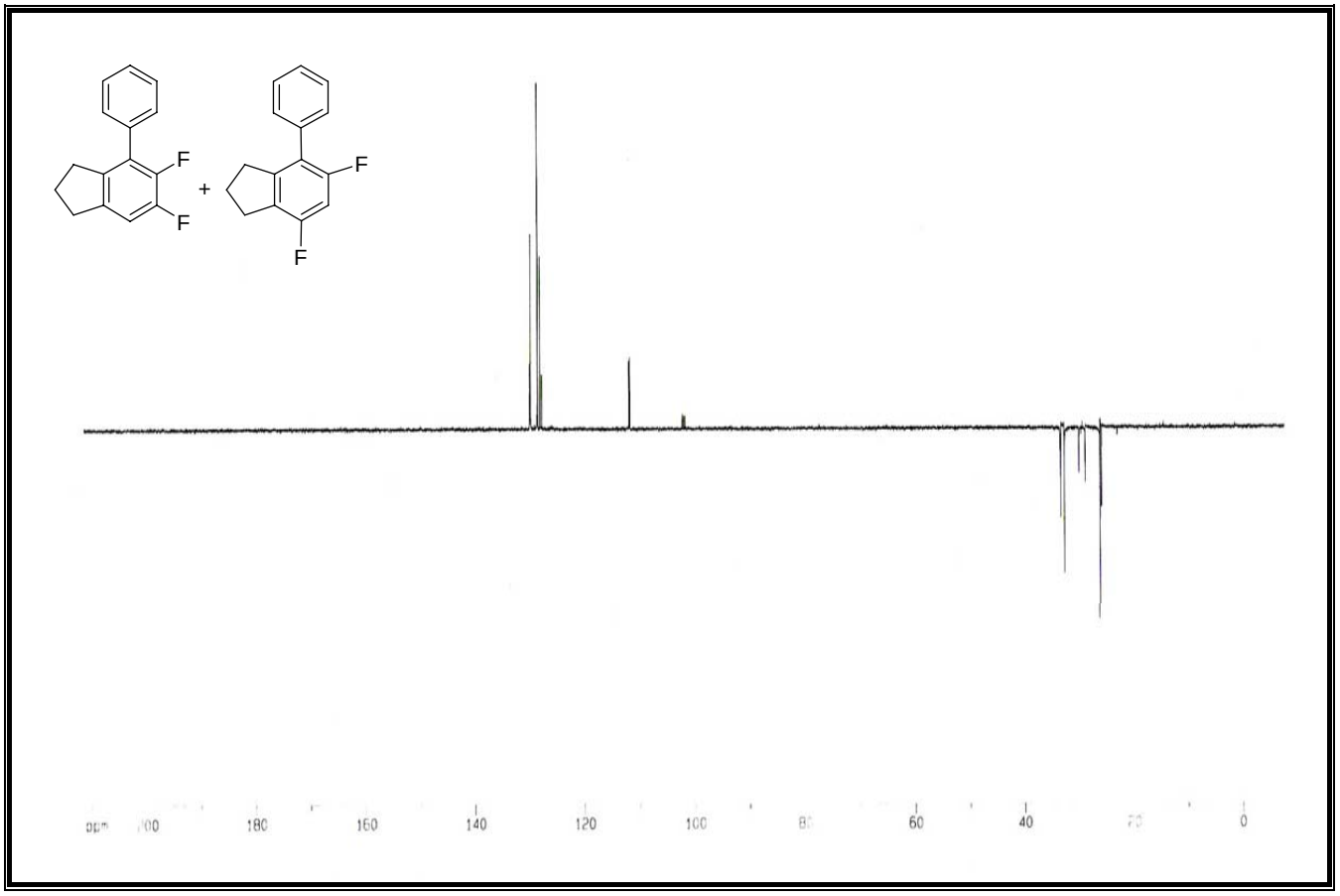

Figure A66 DEPT-135 Spectrum of Compounds **174**+**175**.

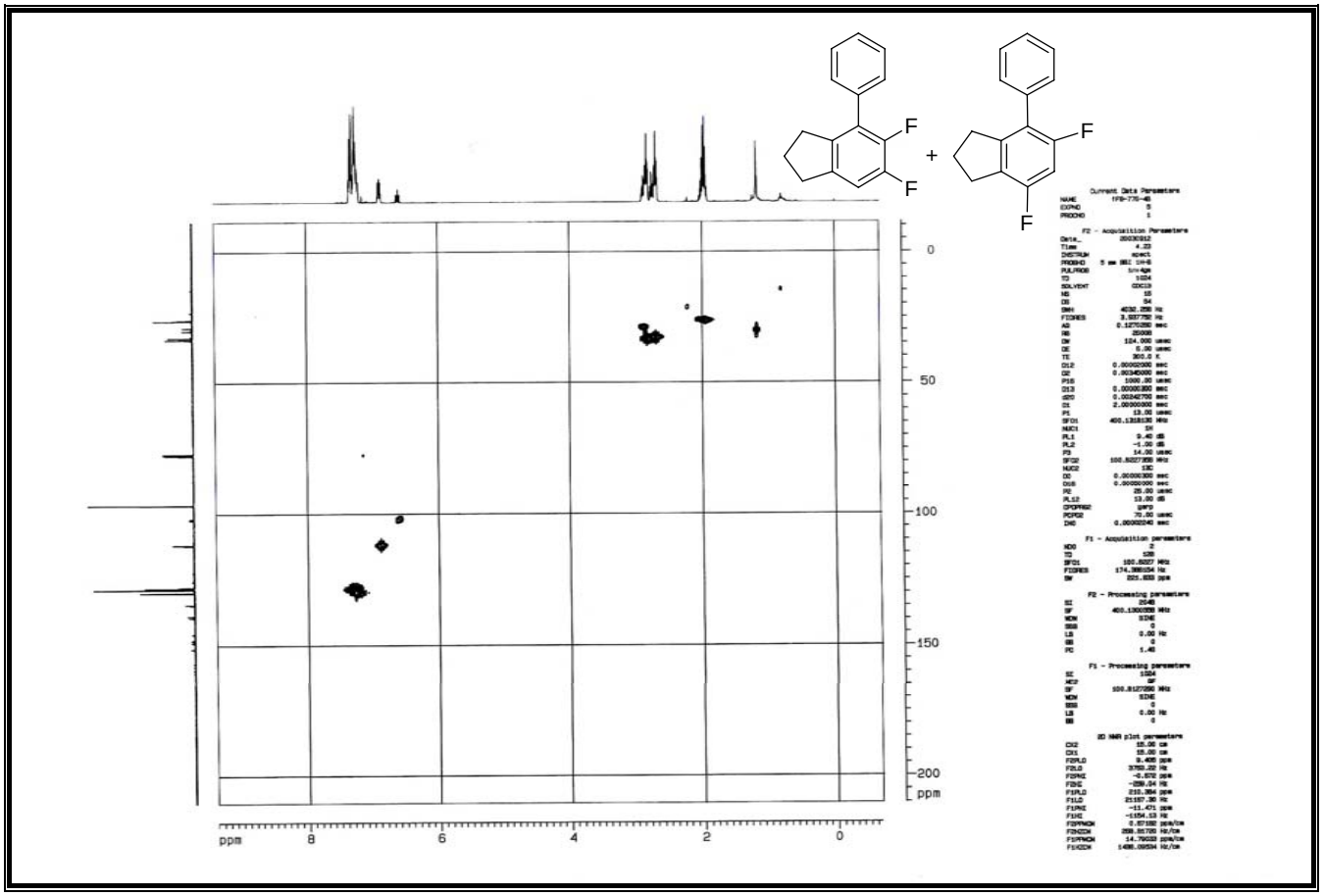

Figure A67 HMQC Spectrum of Compounds **174**+**175**.

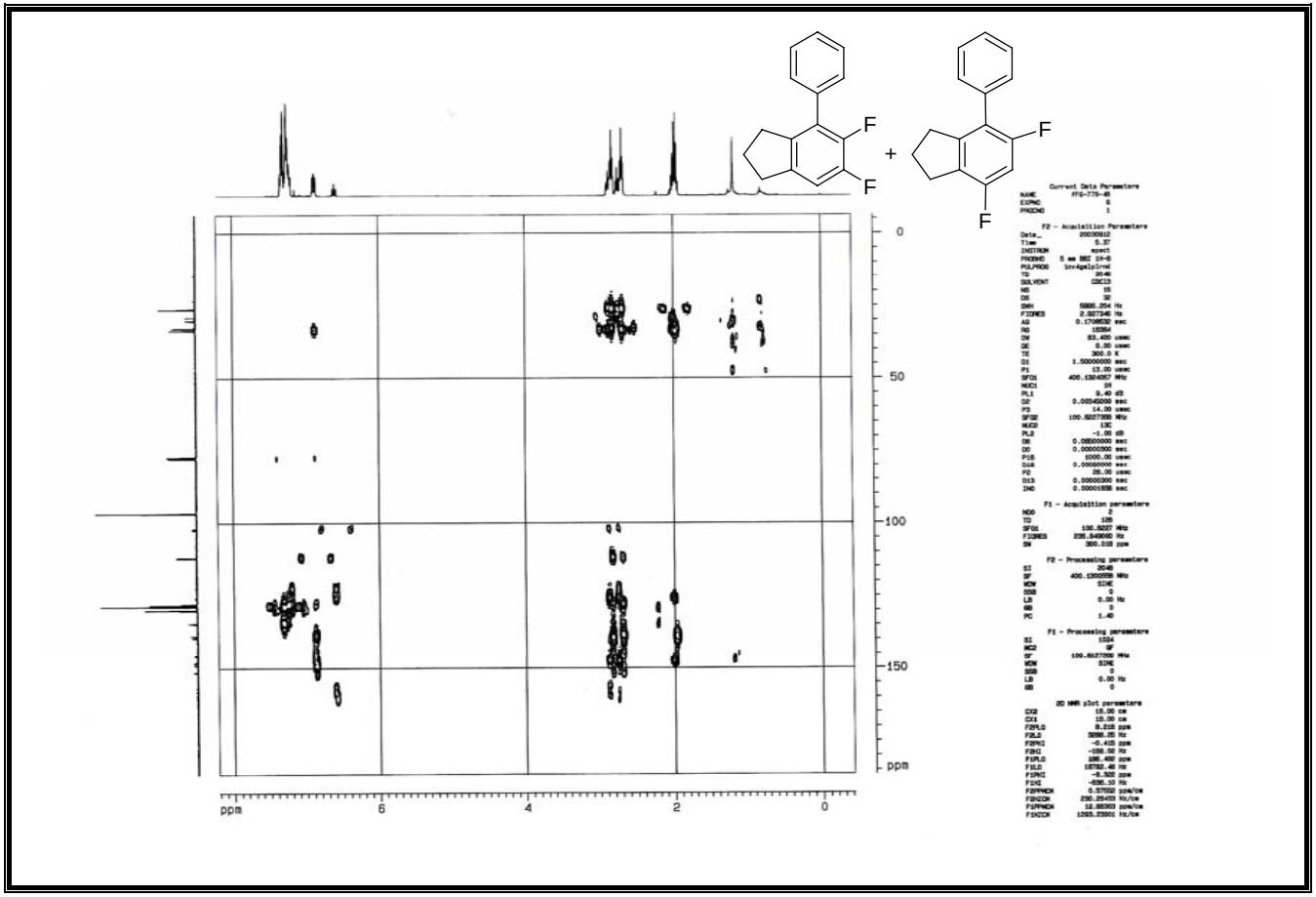

Figure A68 HMBC Spectrum of Compound **174**+**175**.

Figure A69 GC-MS Spectra of Compounds **174** (left) and **175** (right).

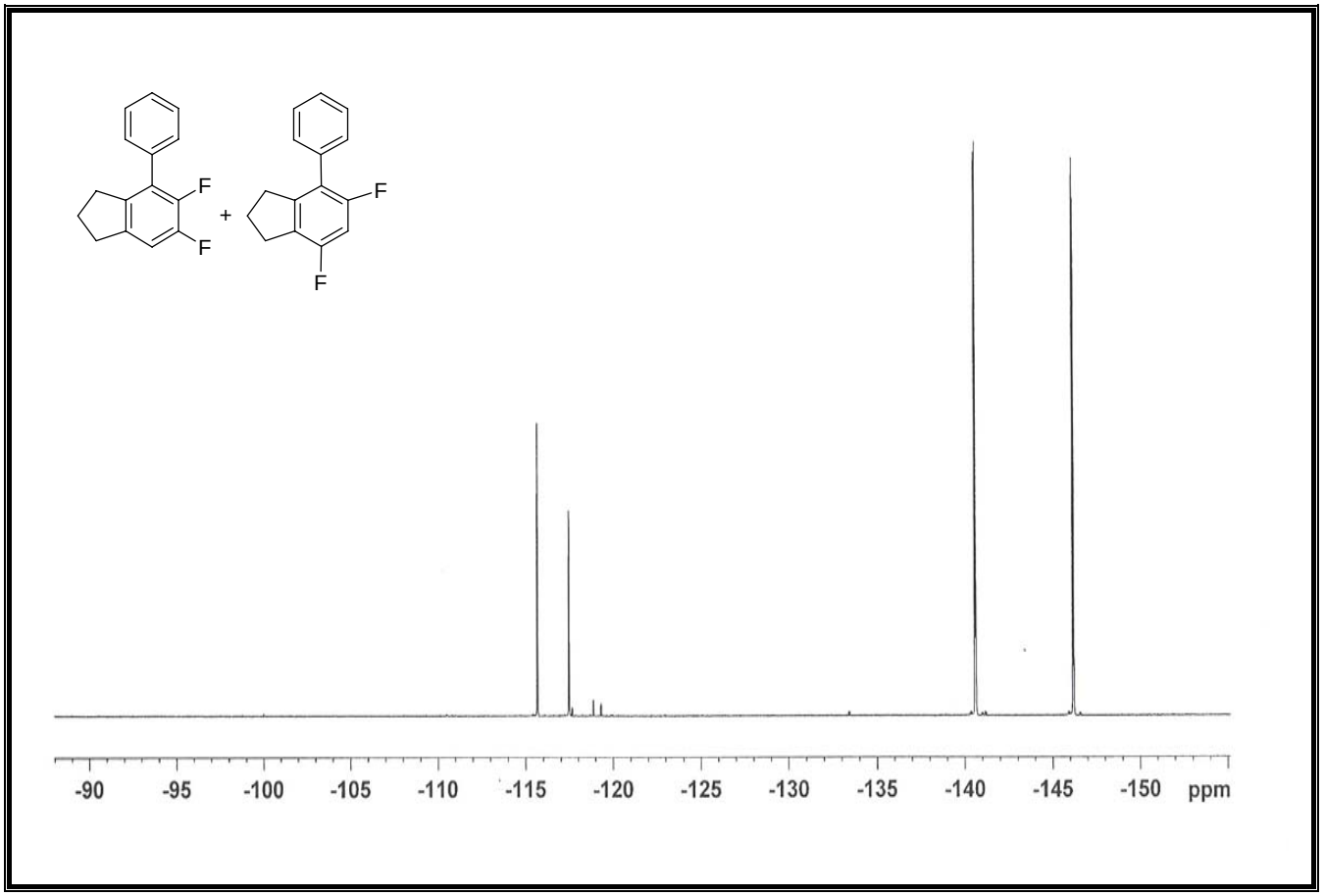

Figure A70 ^{19}F-NMR Spectrum of Compounds **174**+**175**.

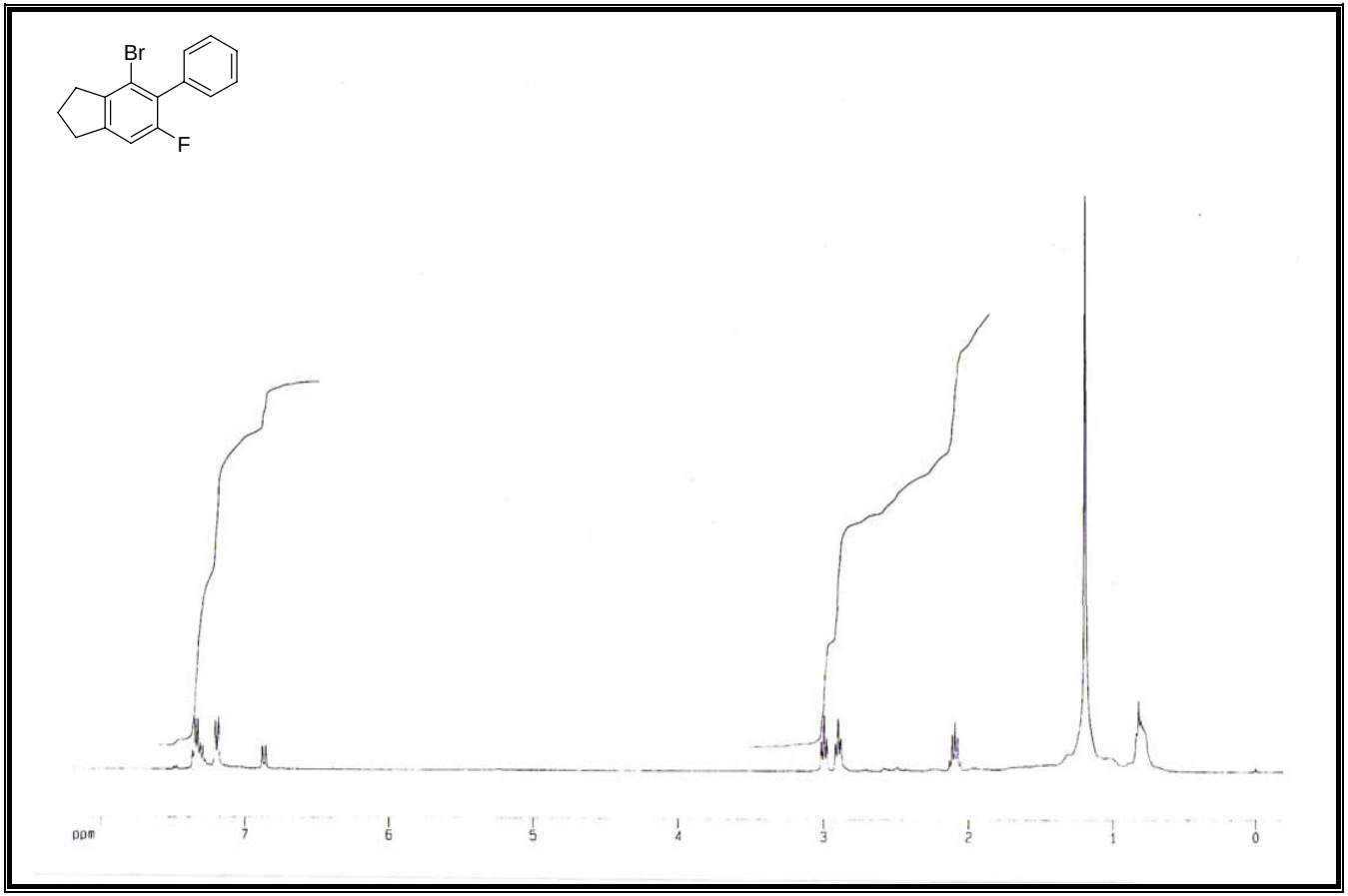

Figure A71 ^{1}H-NMR Spectrum of Compound **176**.

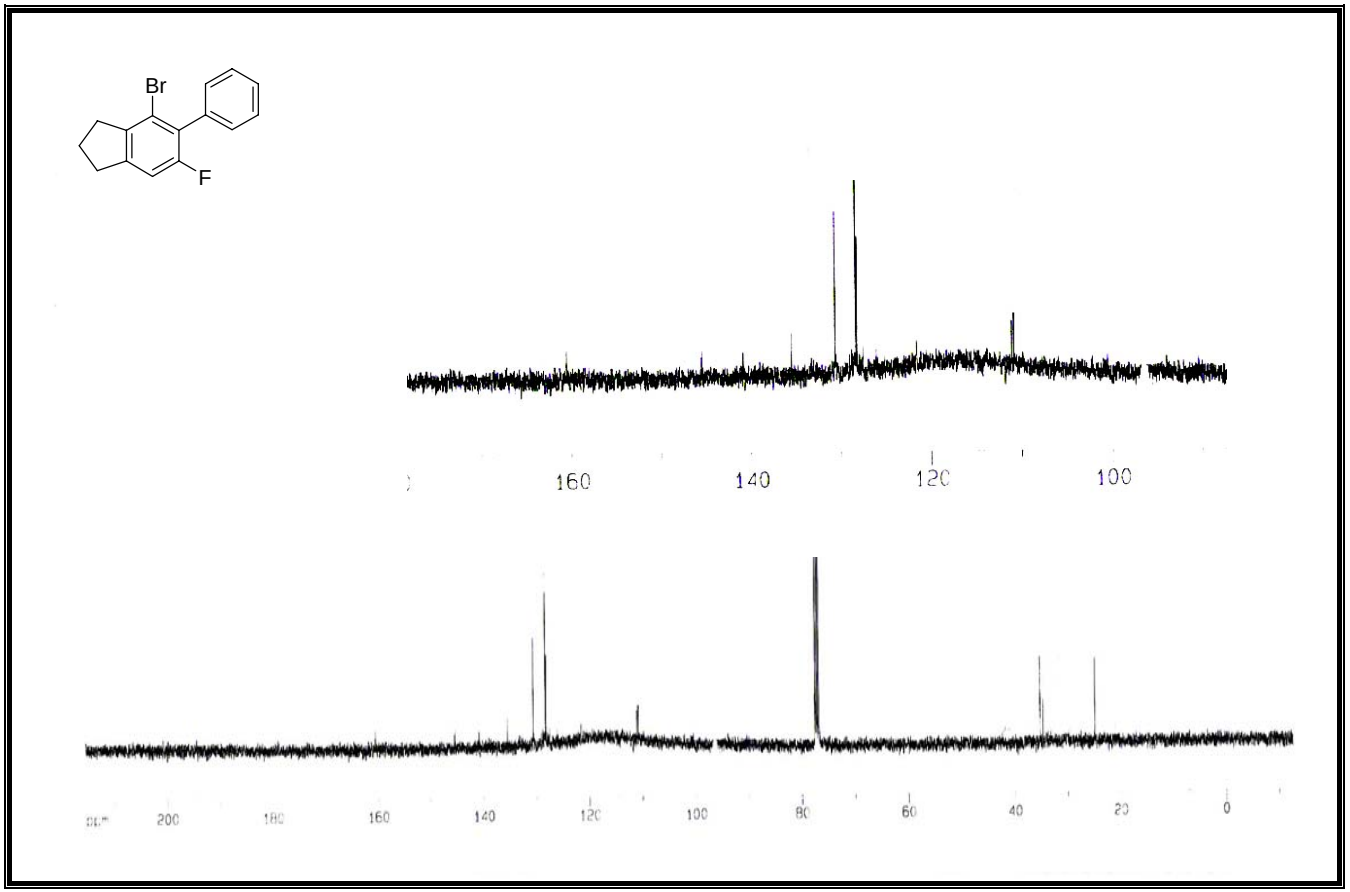

Figure A72 ^{13}C-NMR Spectrum of Compound **176**.

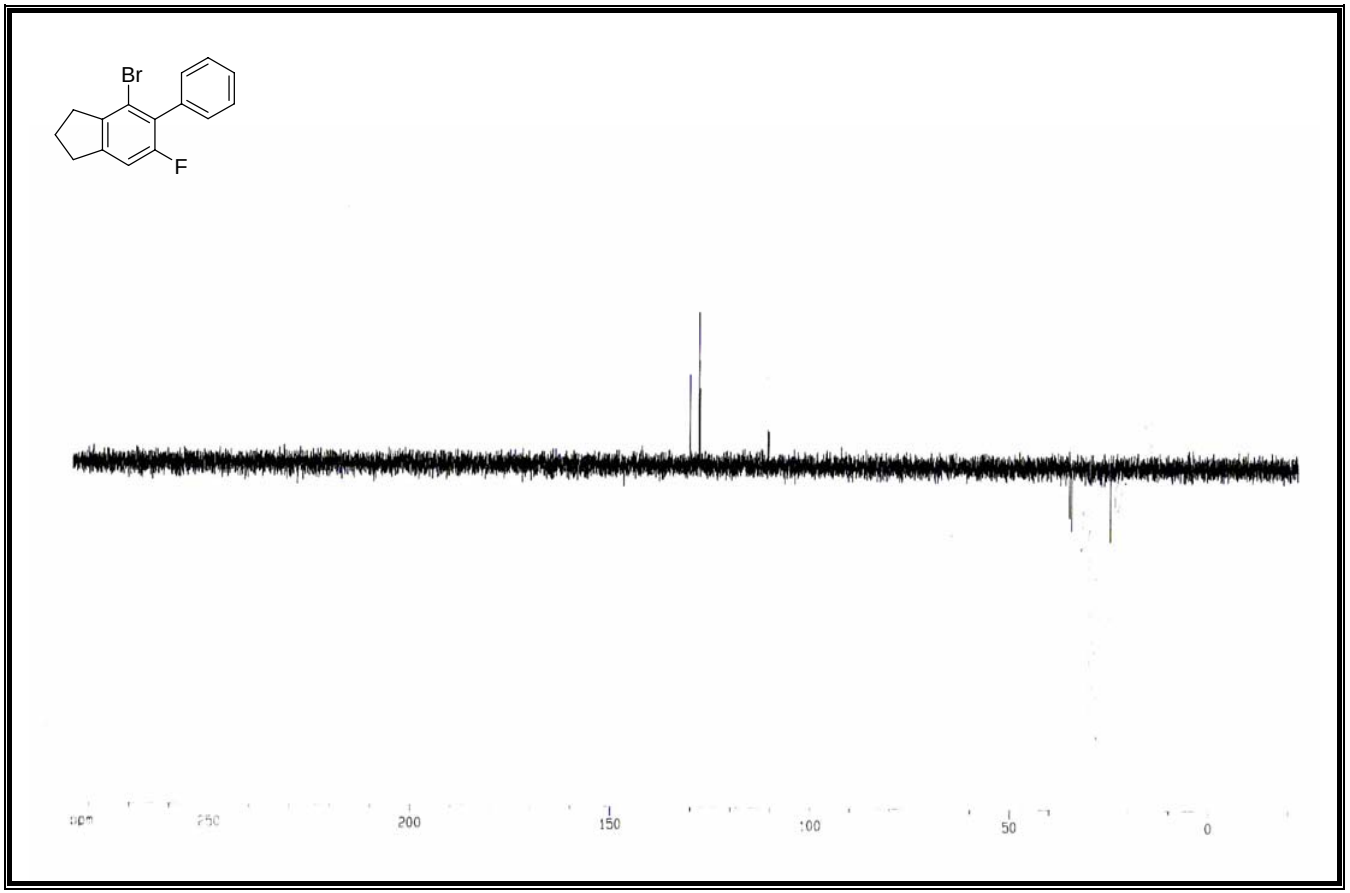

Figure A73 DEPT-135 Spectrum of Compound **176**.

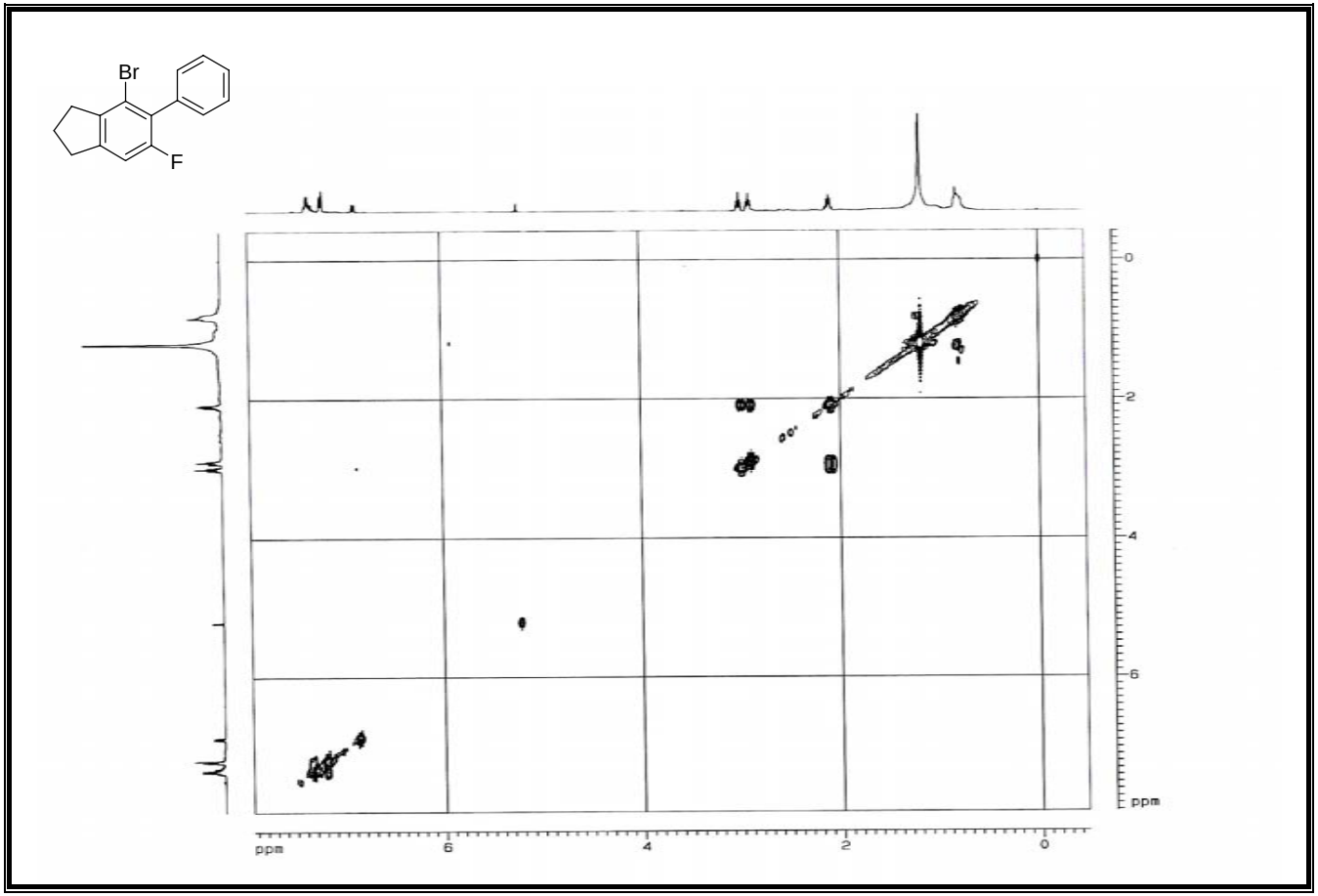

Figure A74 COSY Spectrum of Compound **176**.

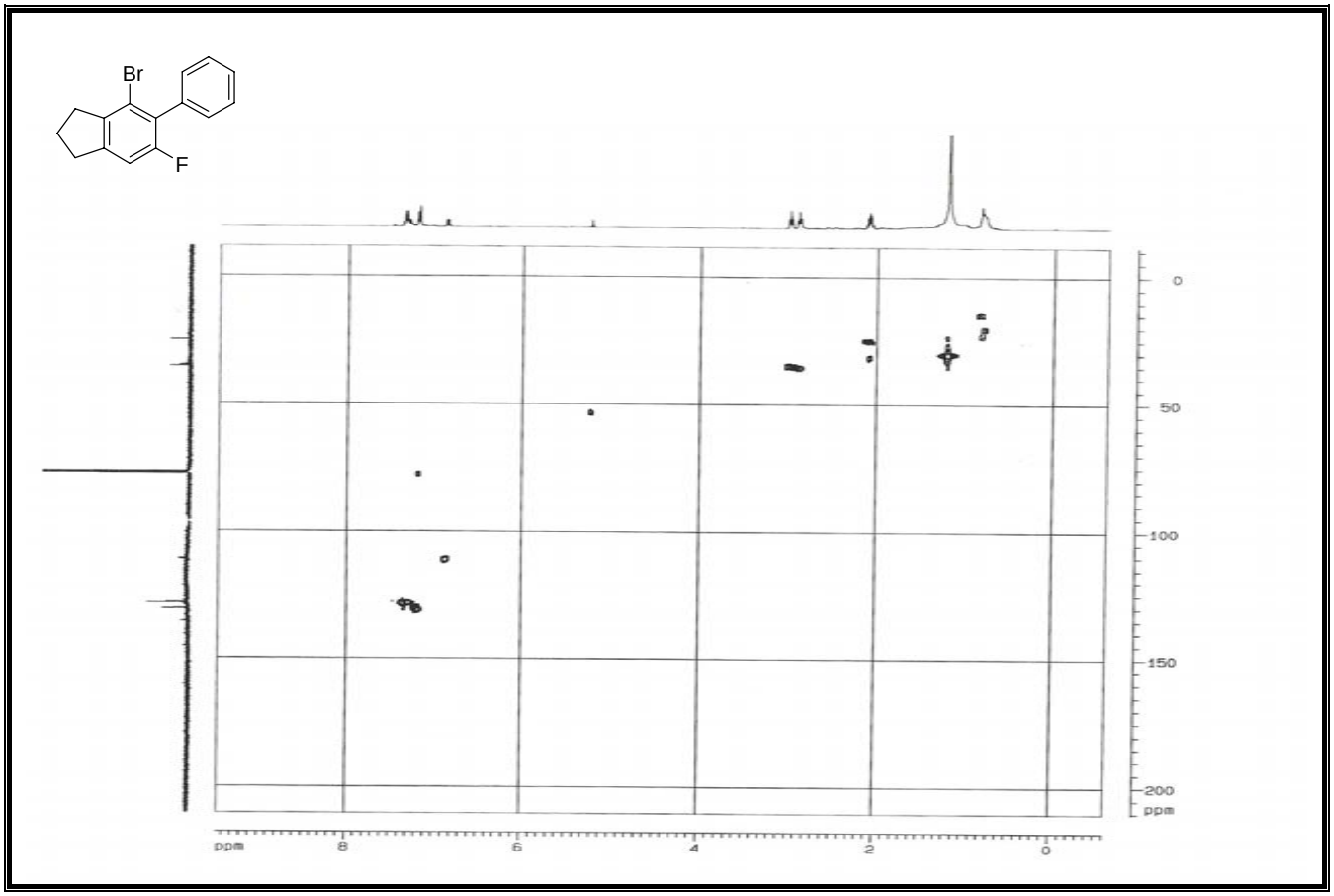

Figure A75 HMQC Spectrum of Compound **176**.

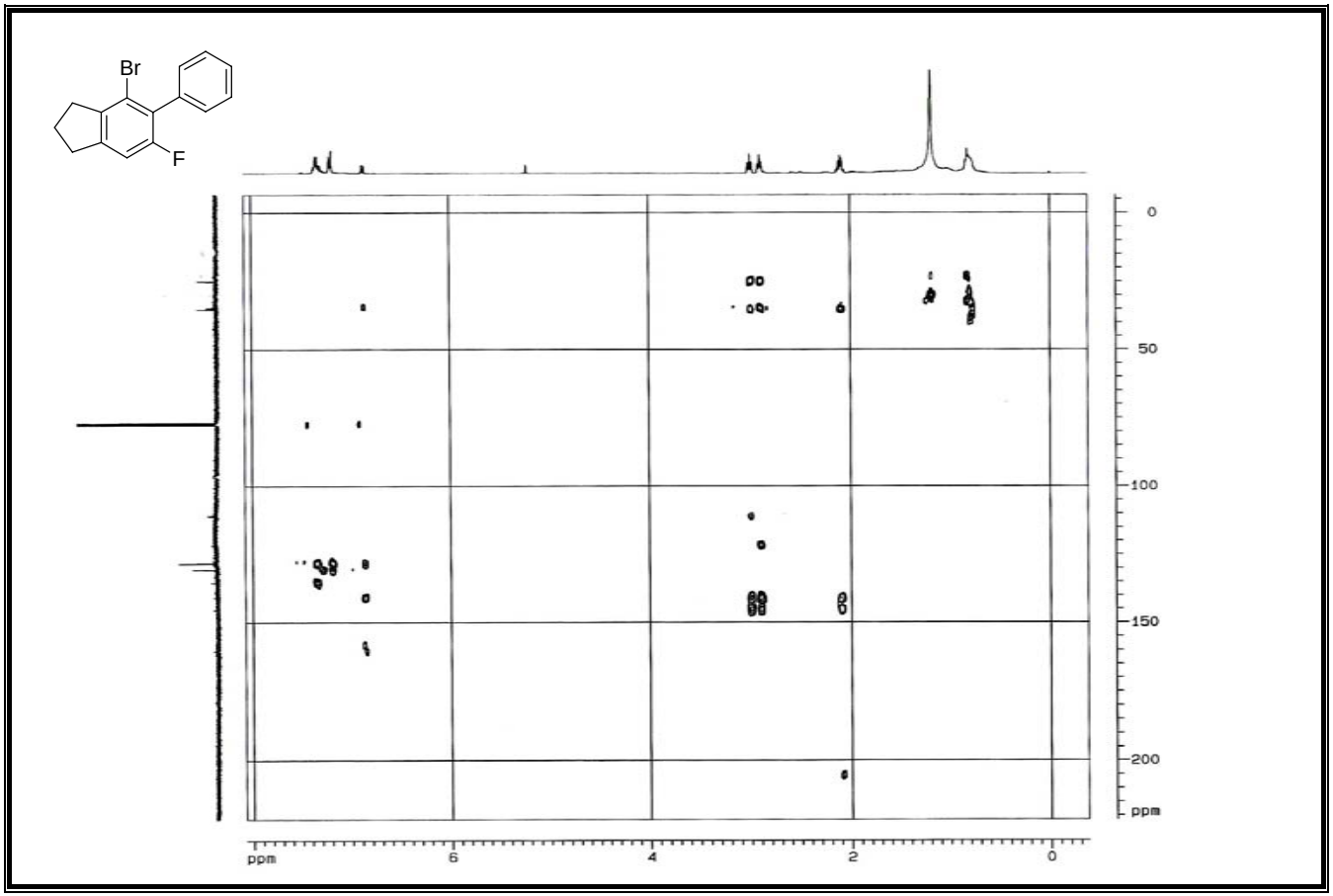

Figure A76 HMBC Spectrum of Compound **176**.

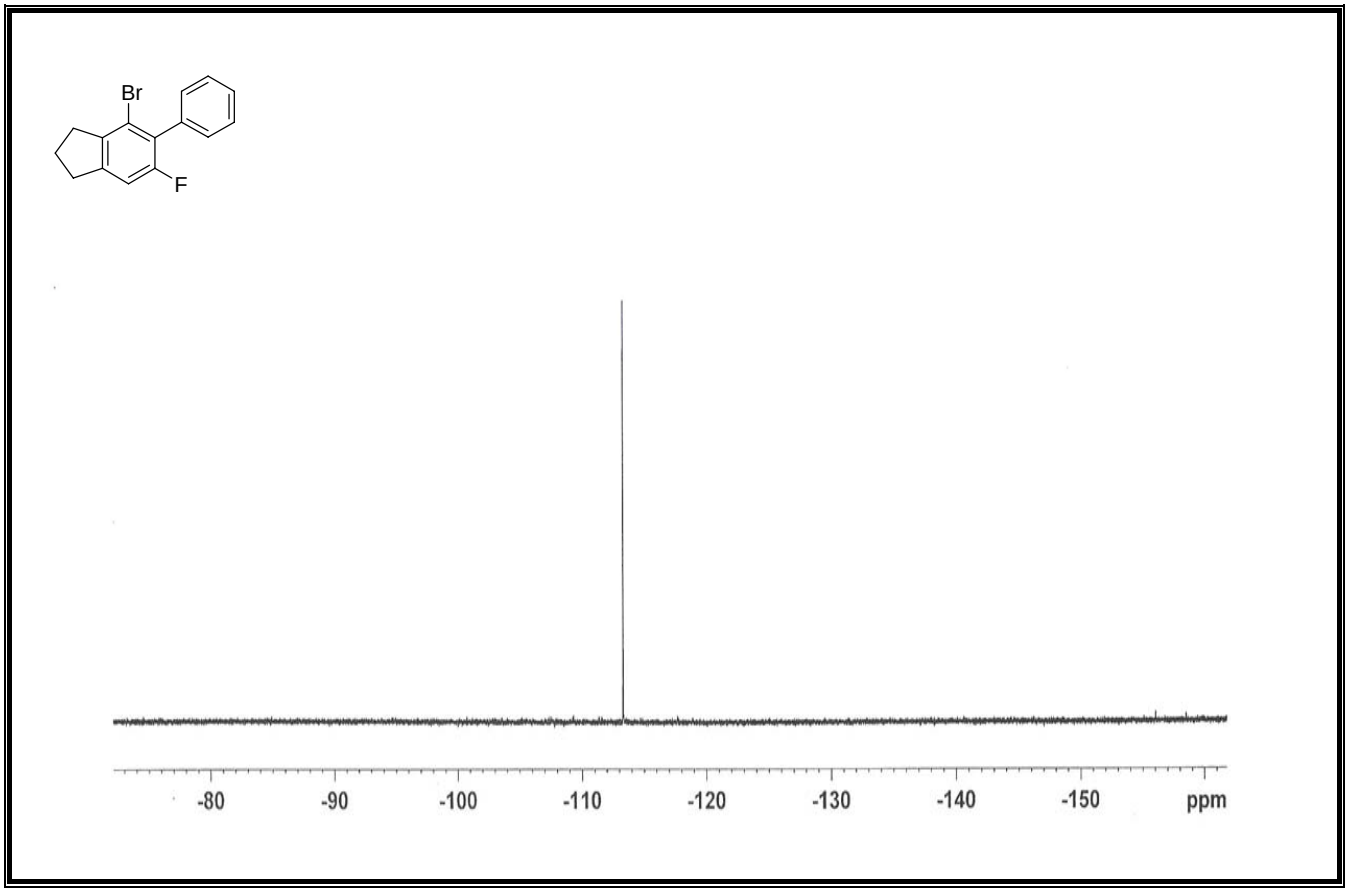

Figure A77 ^{19}F-NMR Spectrum of Compound **176**.

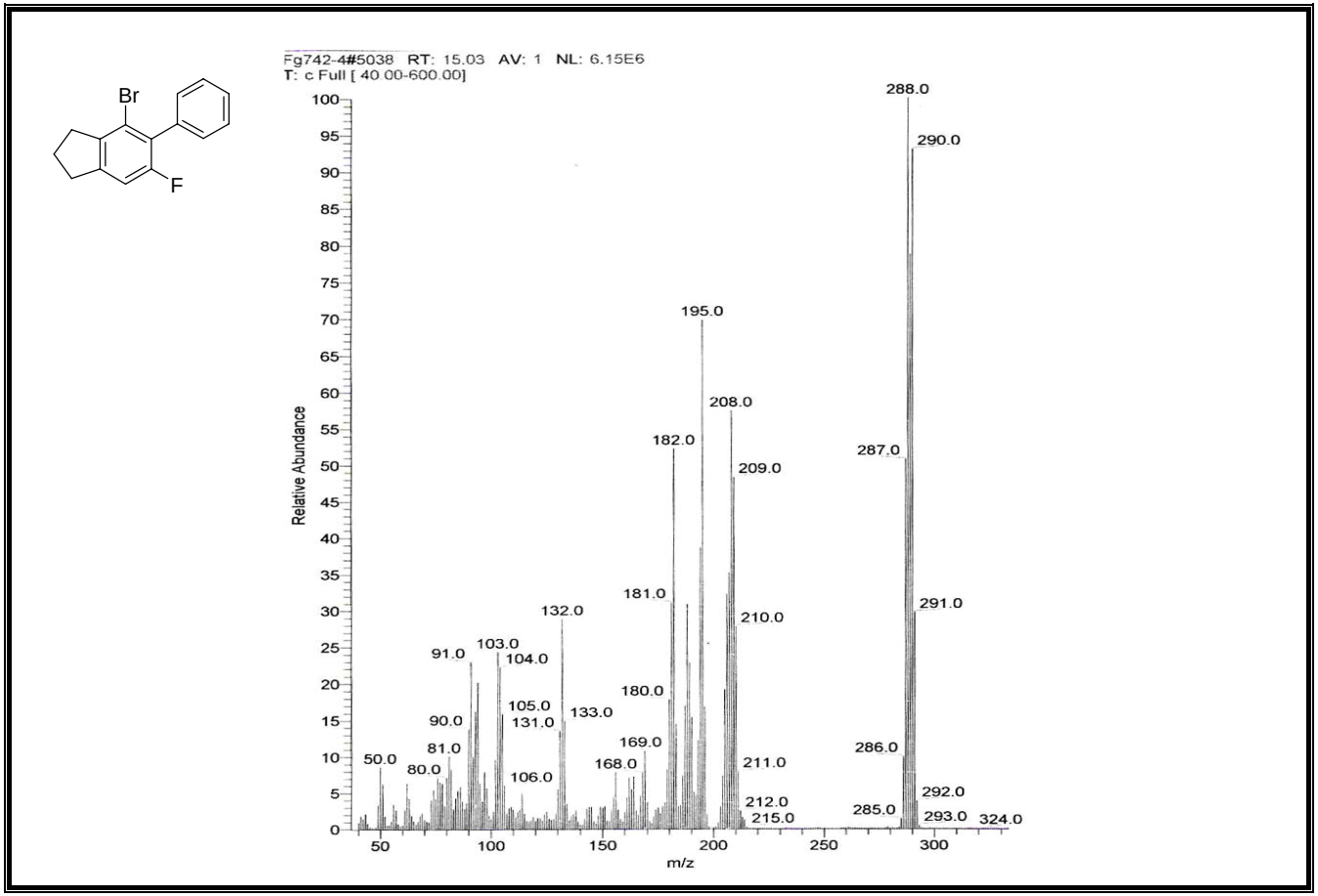

Figure A78 GC-MS Spectrum of Compound **176**.

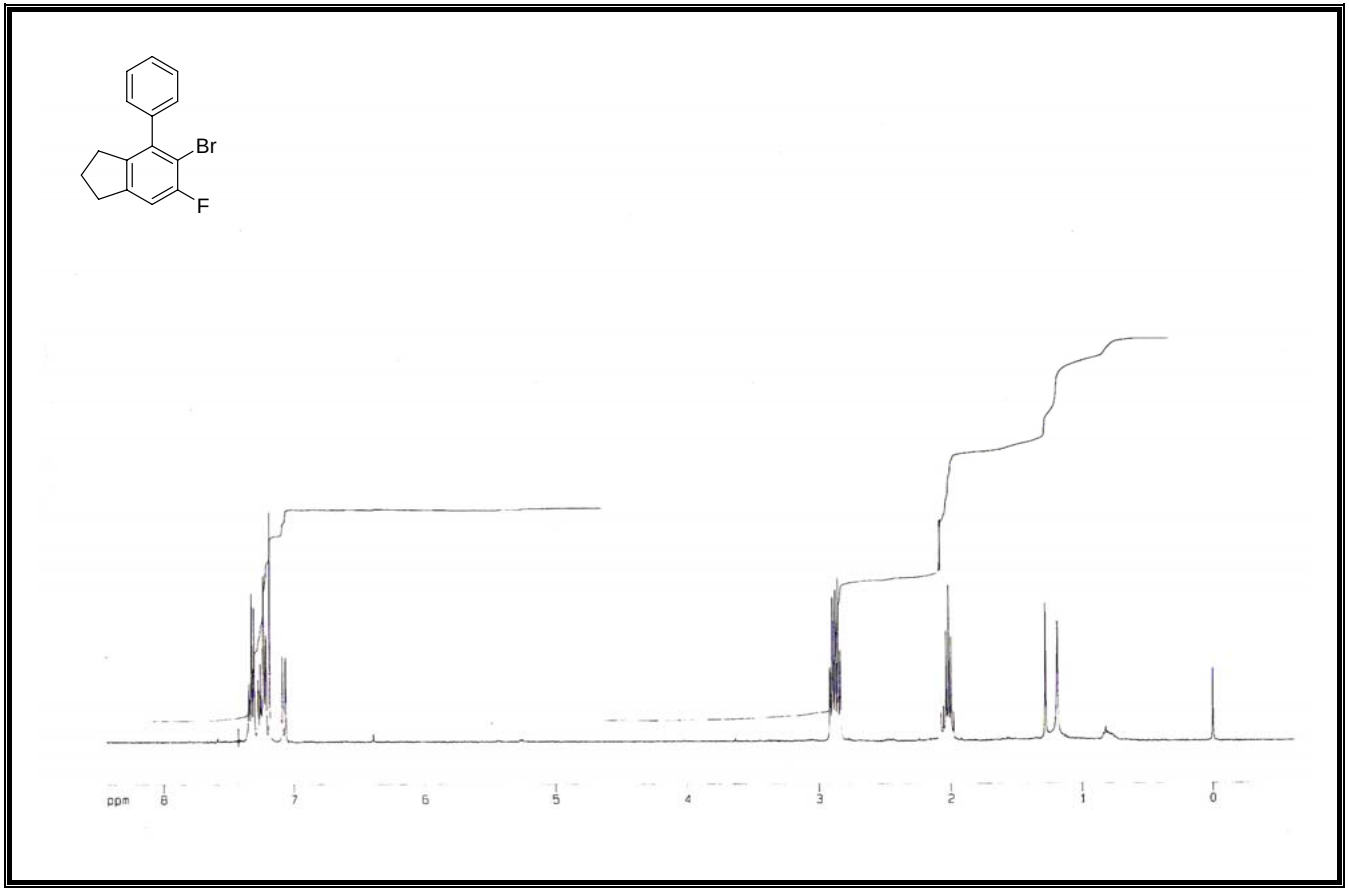

Figure A79 ^{1}H-NMR Spectrum of Compound **177**.

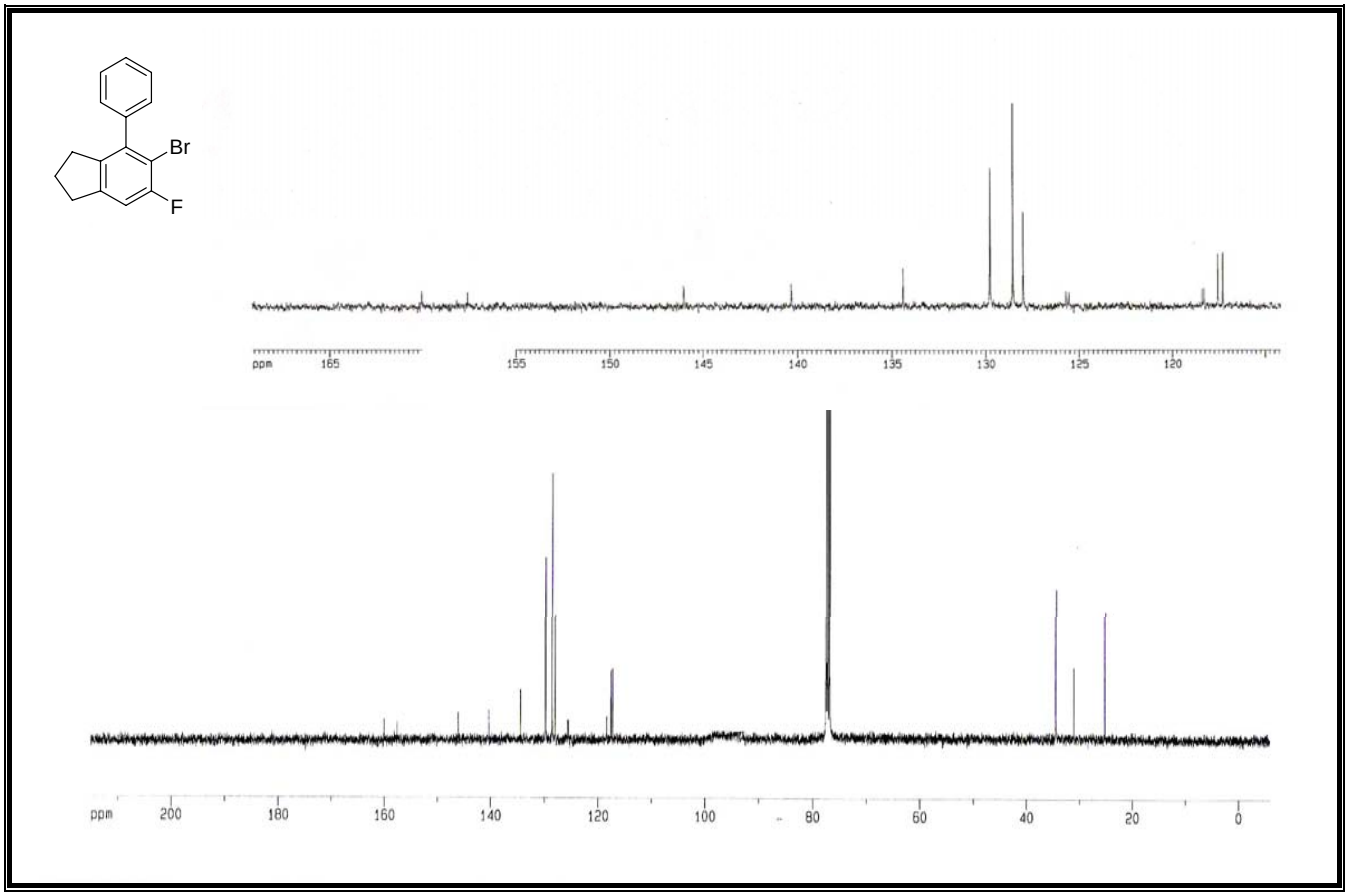

Figure A80 ^{13}C-NMR Spectrum of Compound **177**.

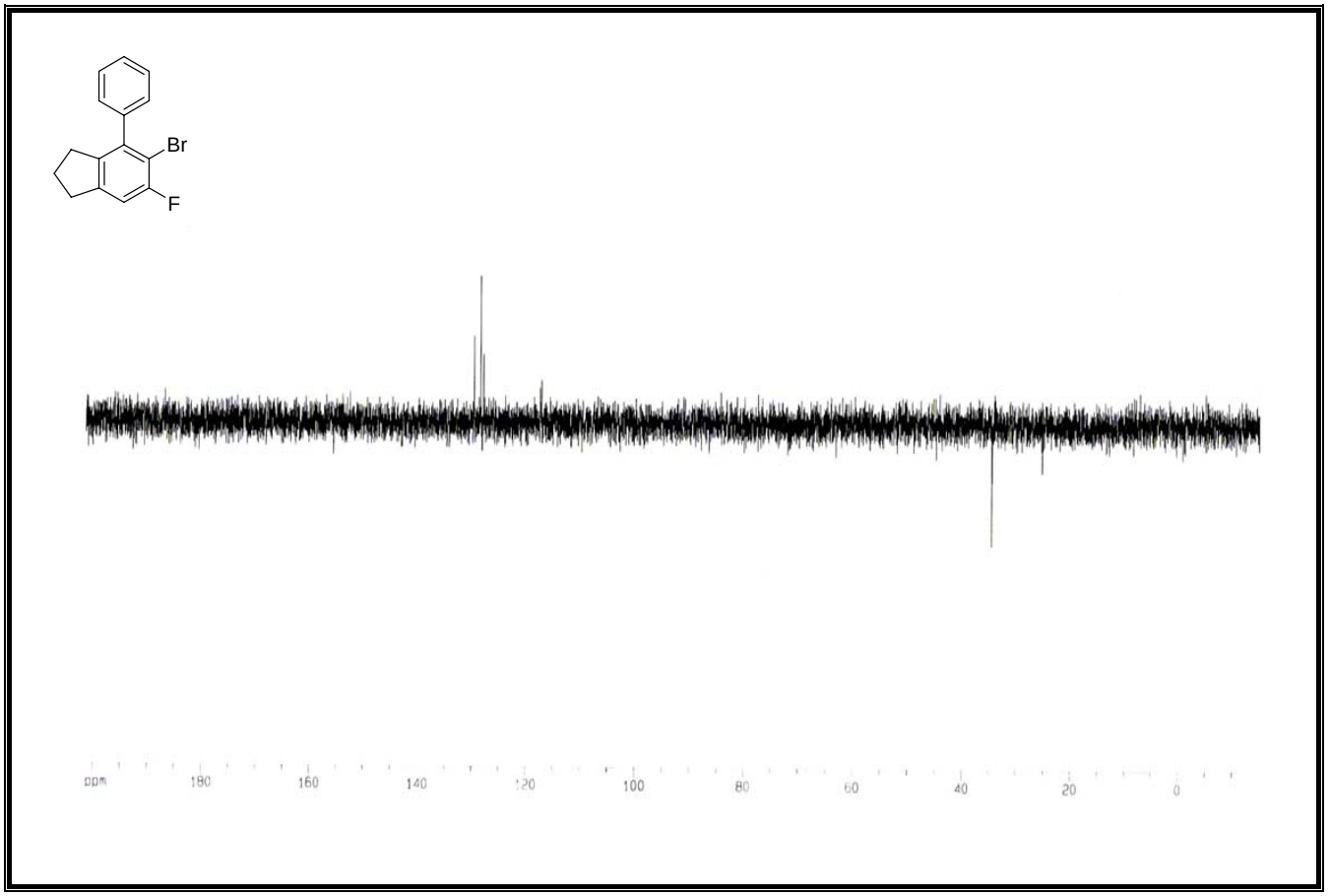

Figure A81 DEPT-135 Spectrum of Compound **177**.

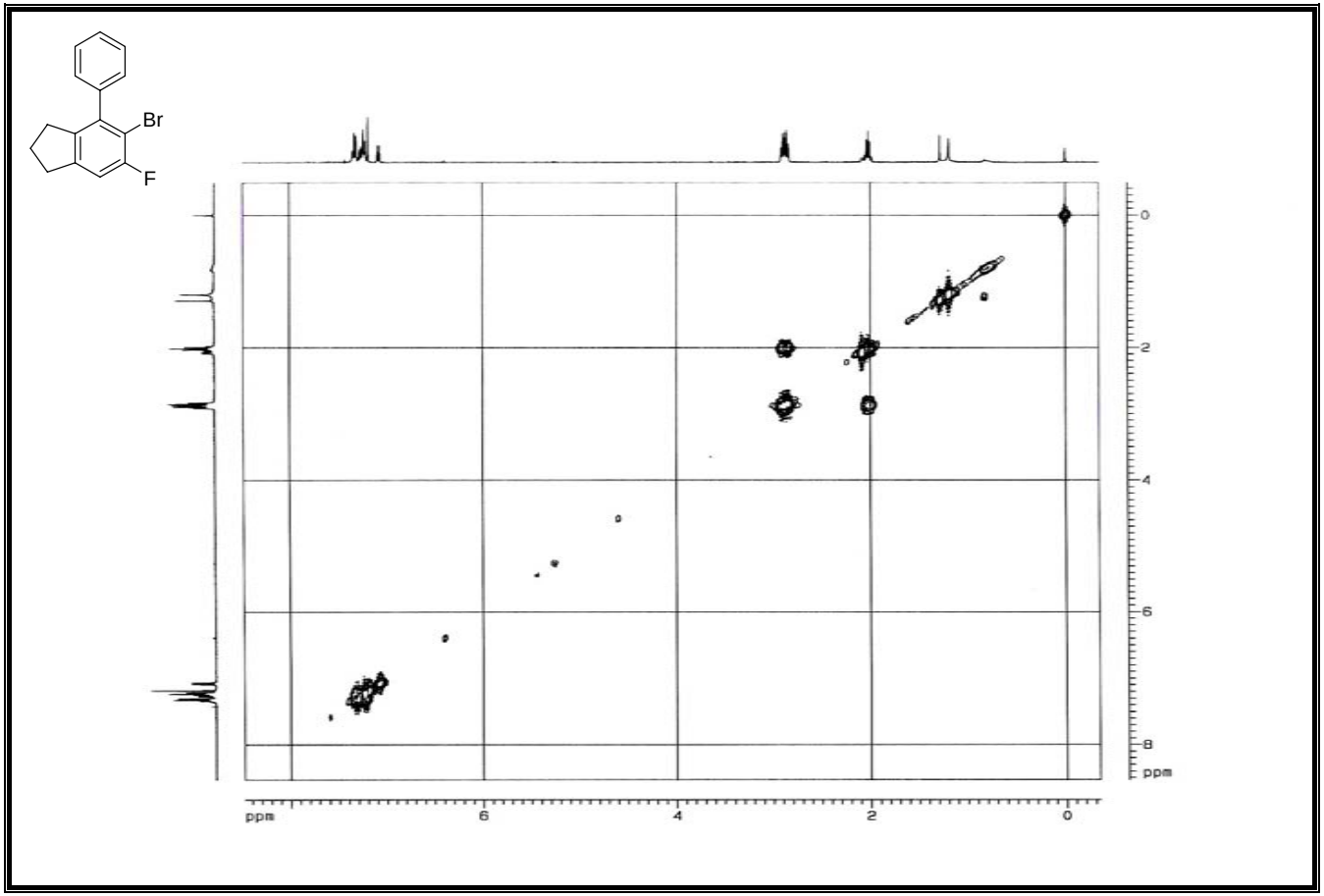

Figure A82 COSY Spectrum of Compound **177**.

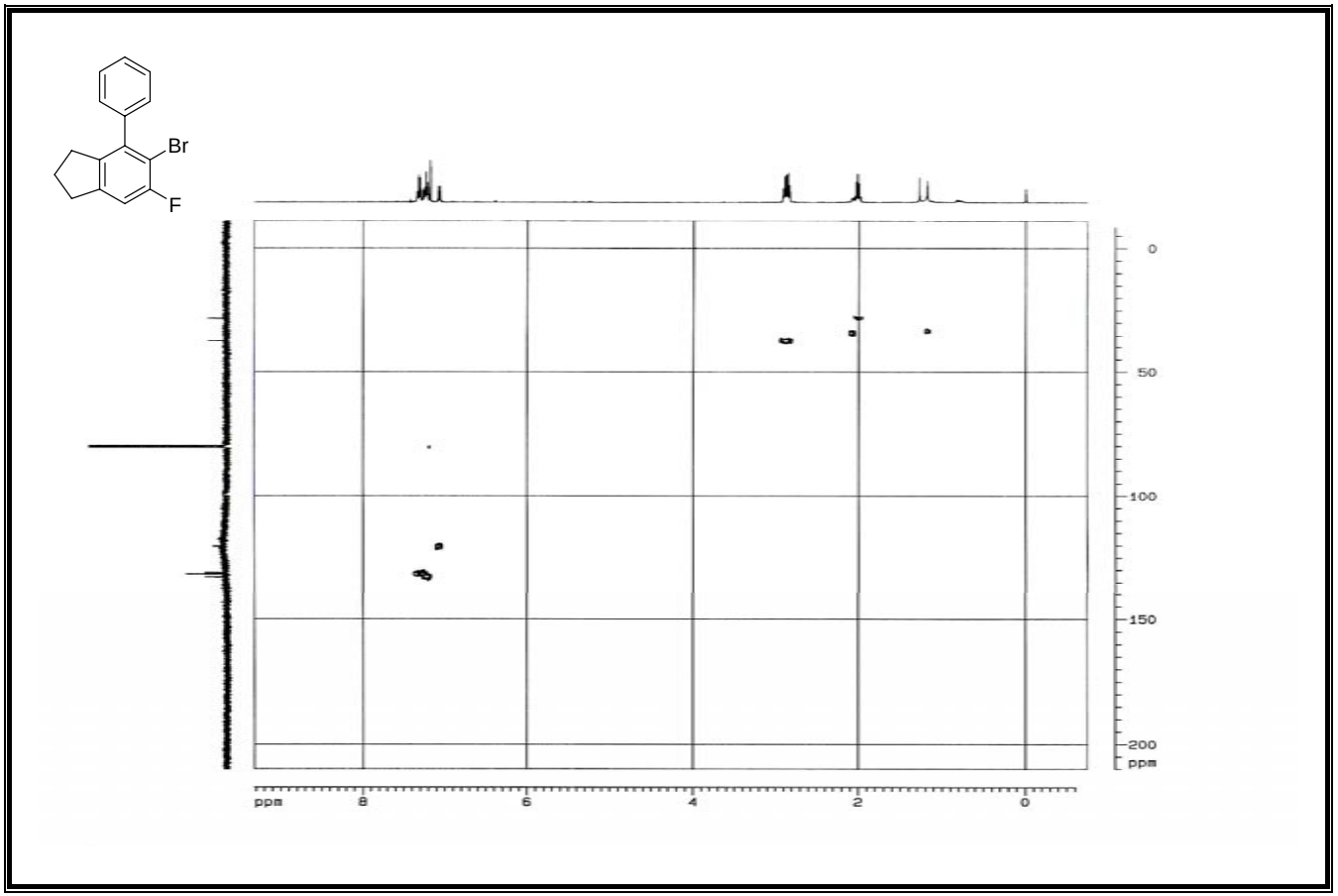

Figure A83 HMQC Spectrum of Compound **177**.

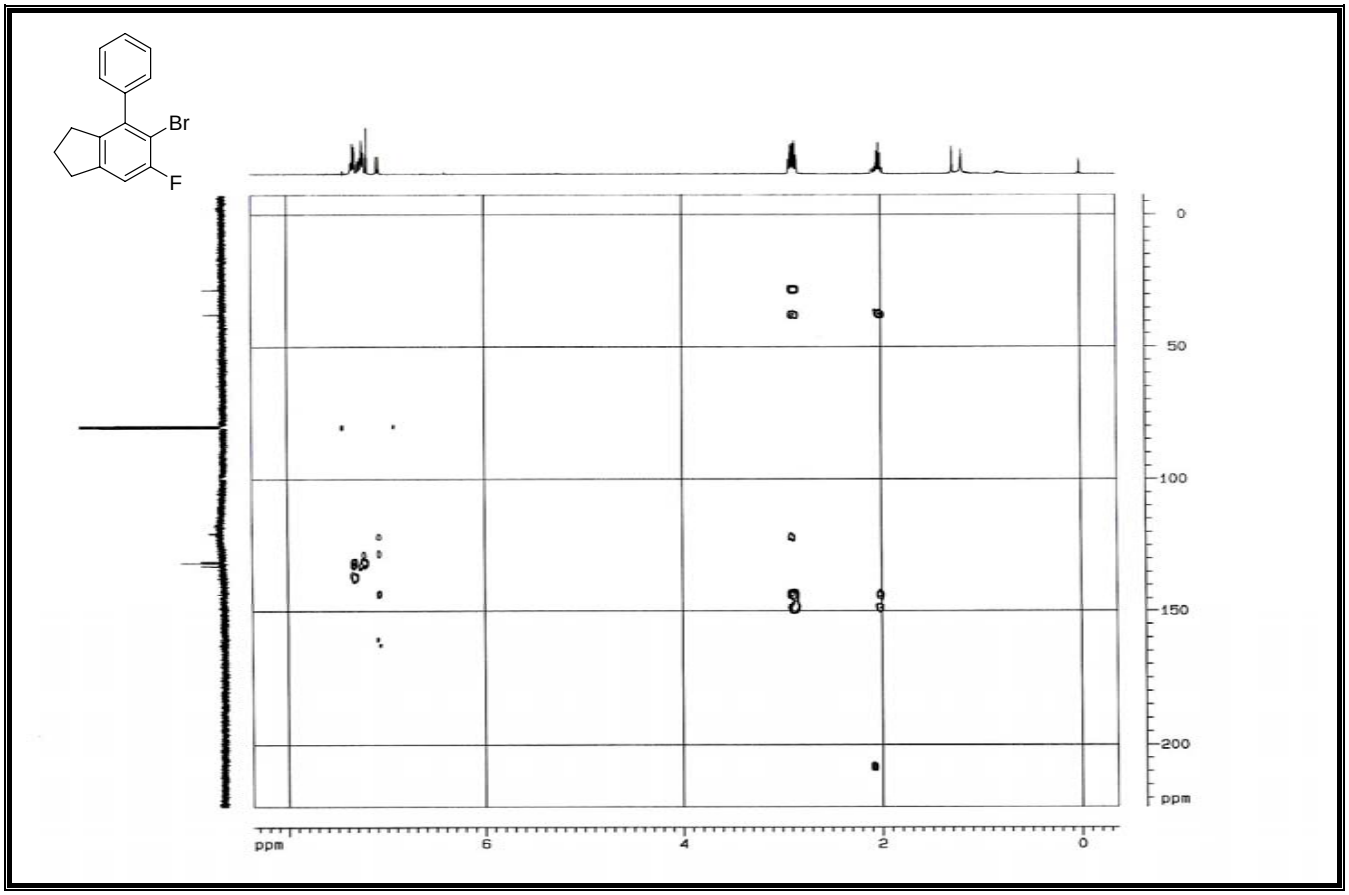

Figure A84 HMBC Spectrum of Compound **177**.

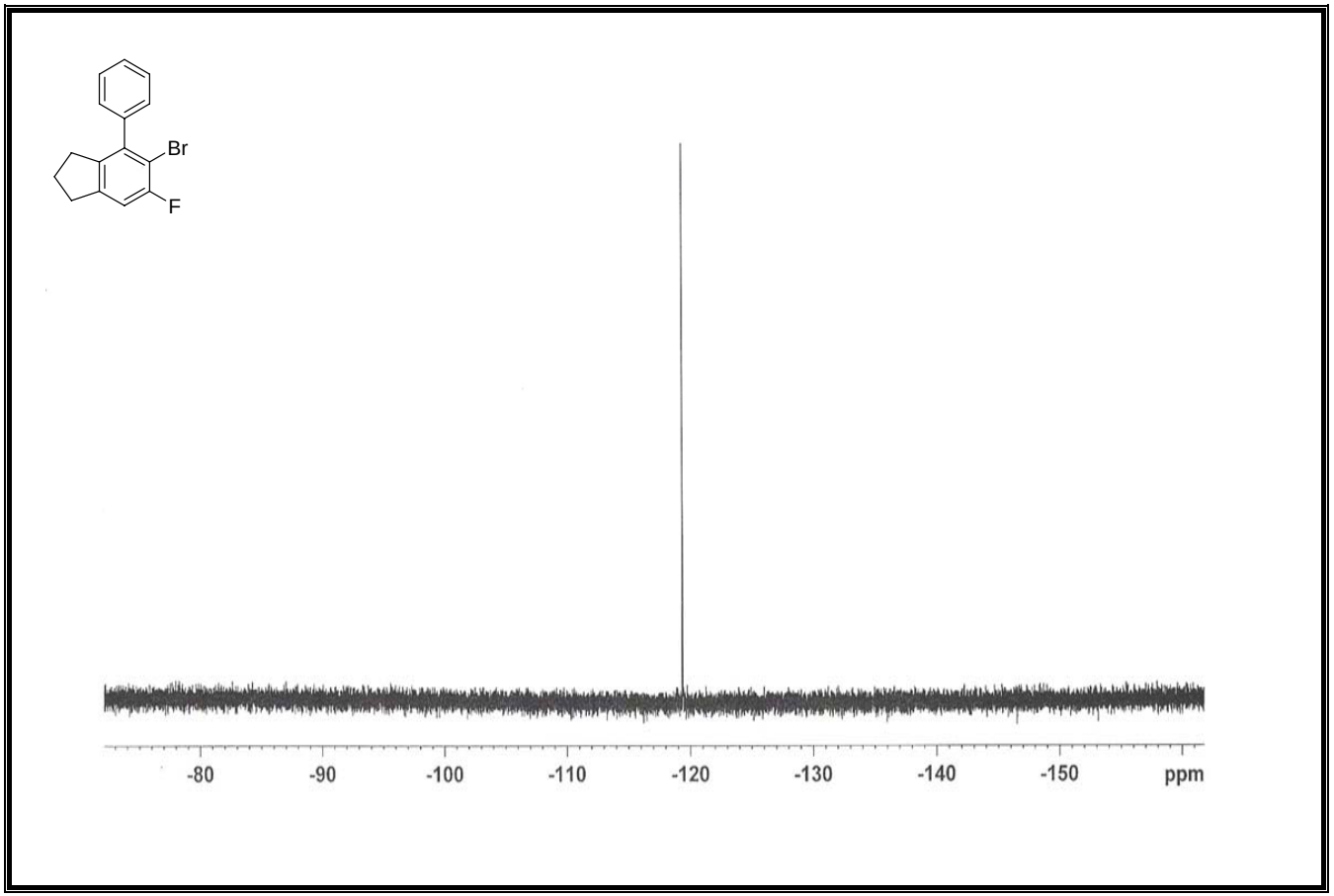

Figure A85 ^{19}F-NMR Spectrum of Compound **177**.

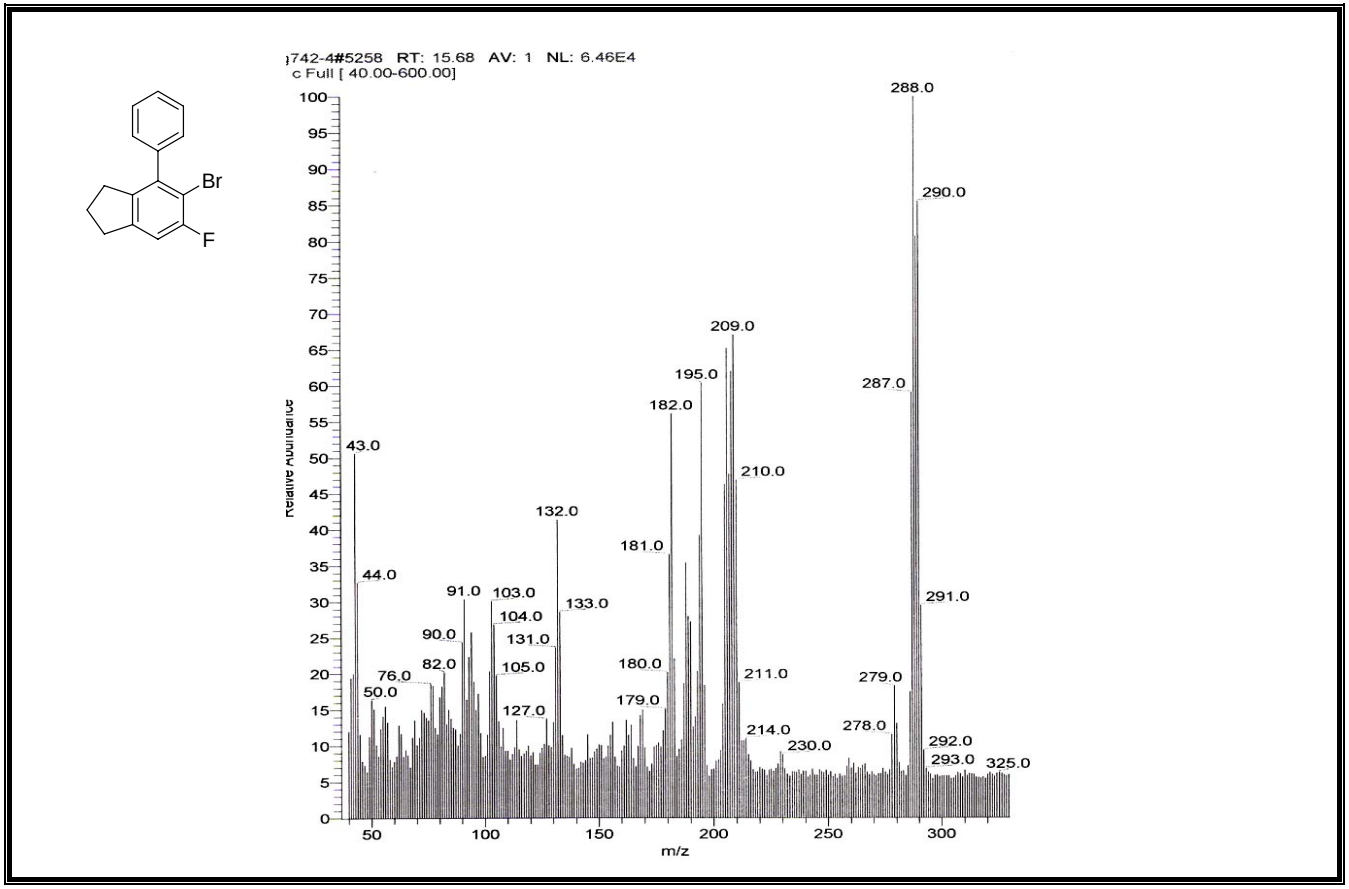

Figure A86 GC-MS Spectrum of Compound **177**.

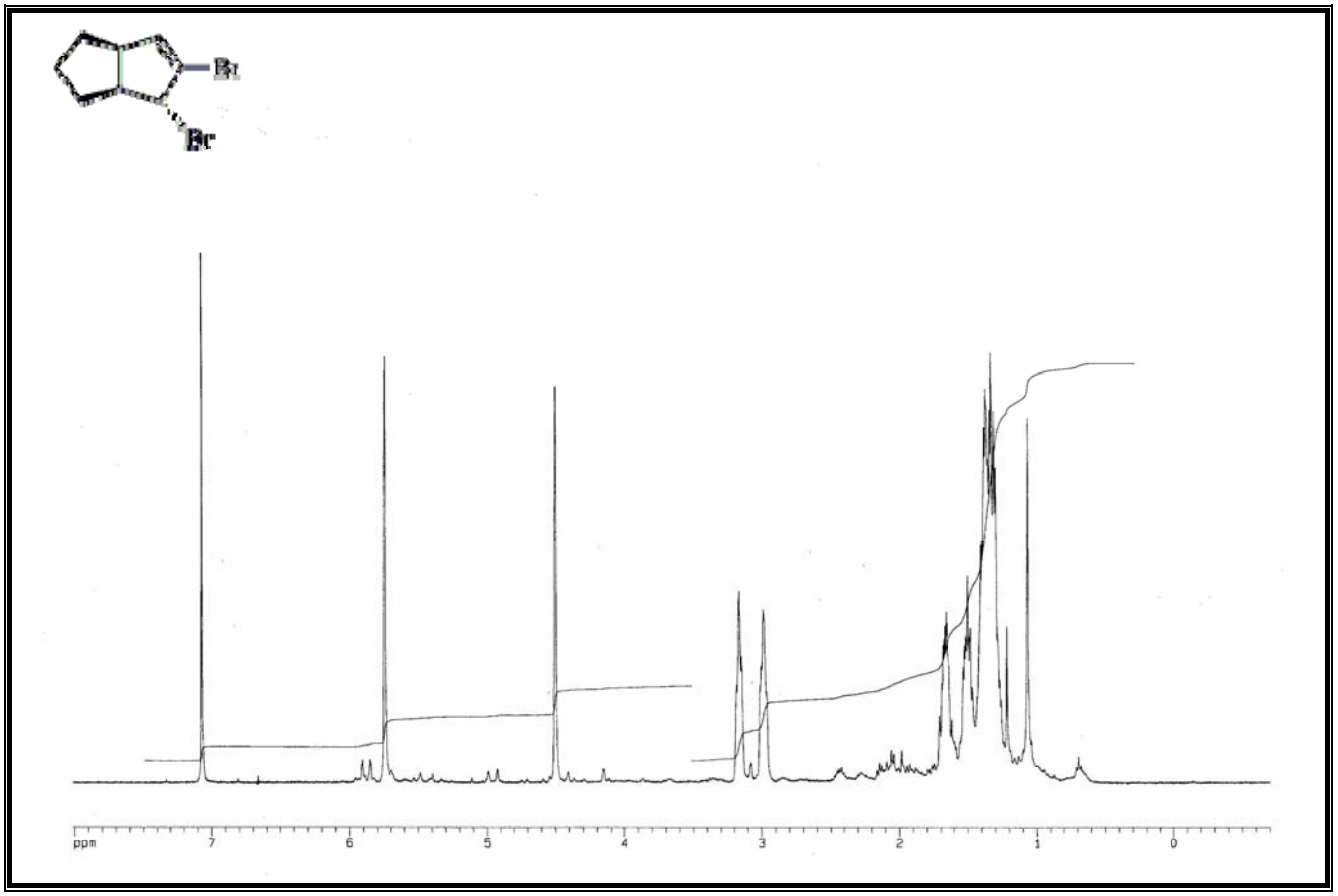

Figure A87 ^{1}H-NMR Spectrum of Compound **182**.

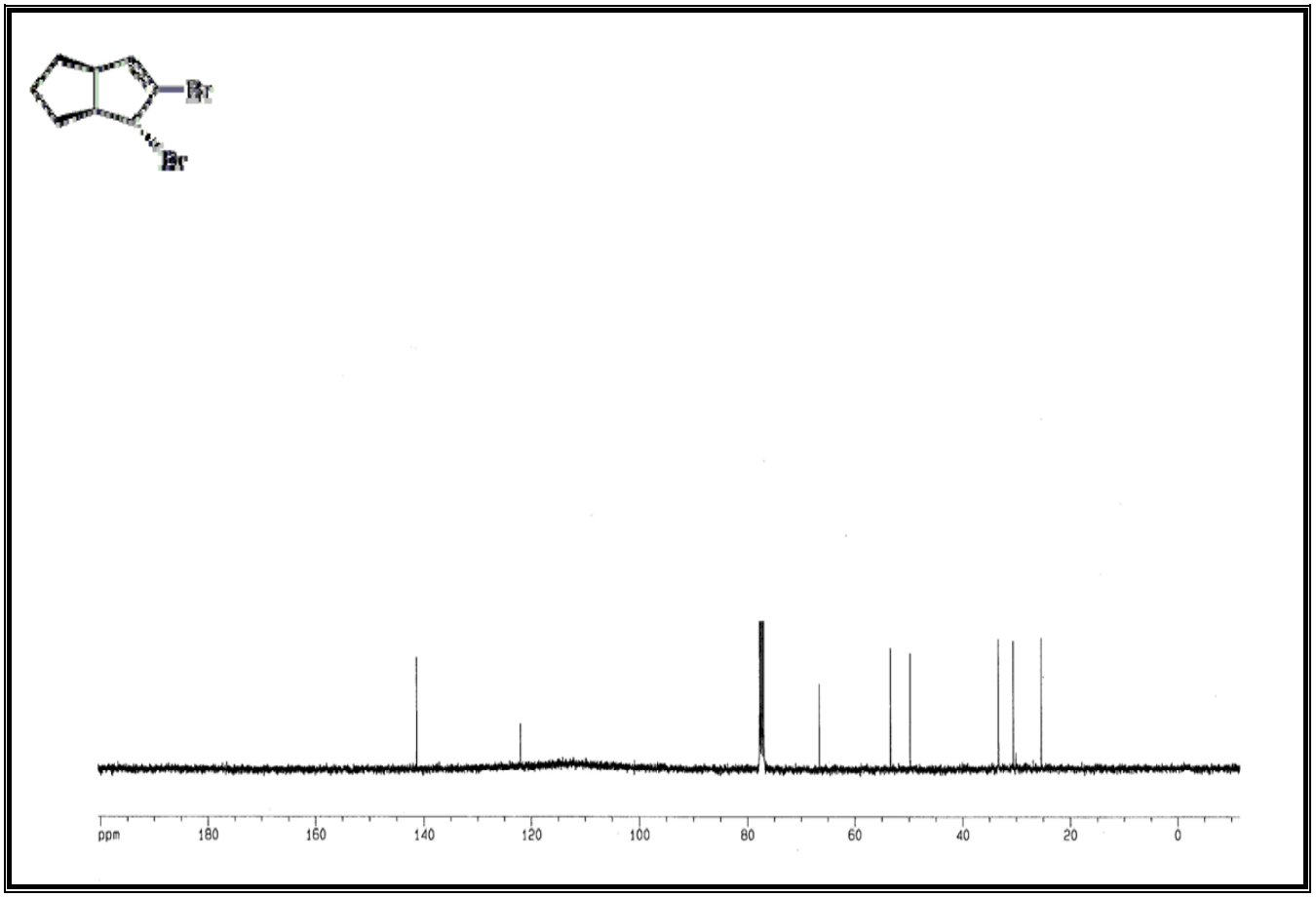

Figure A88 ^{13}C-NMR Spectrum of Compound **182**.

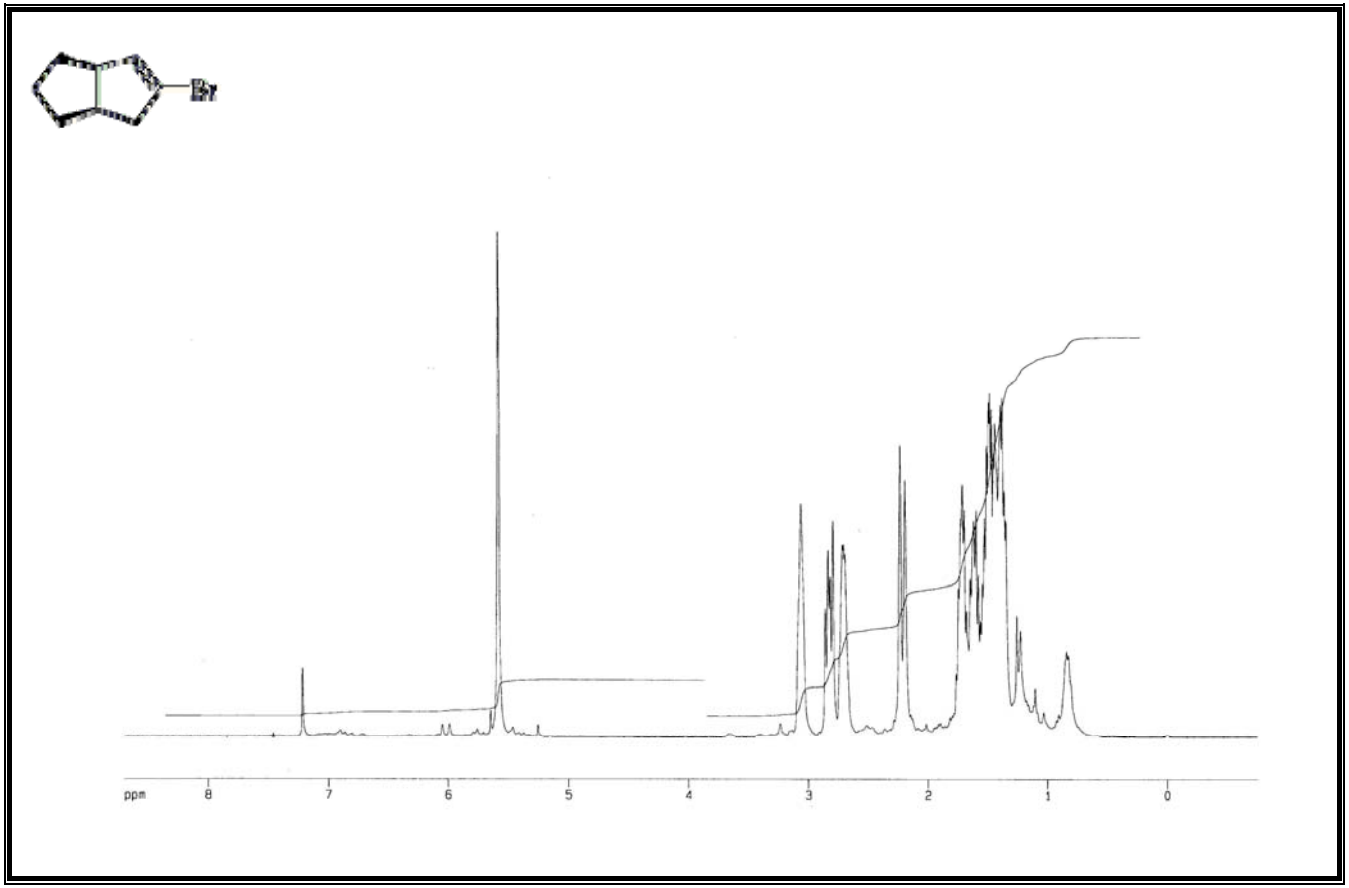

Figure A89 ^{1}H-NMR Spectrum of Compound **183**.

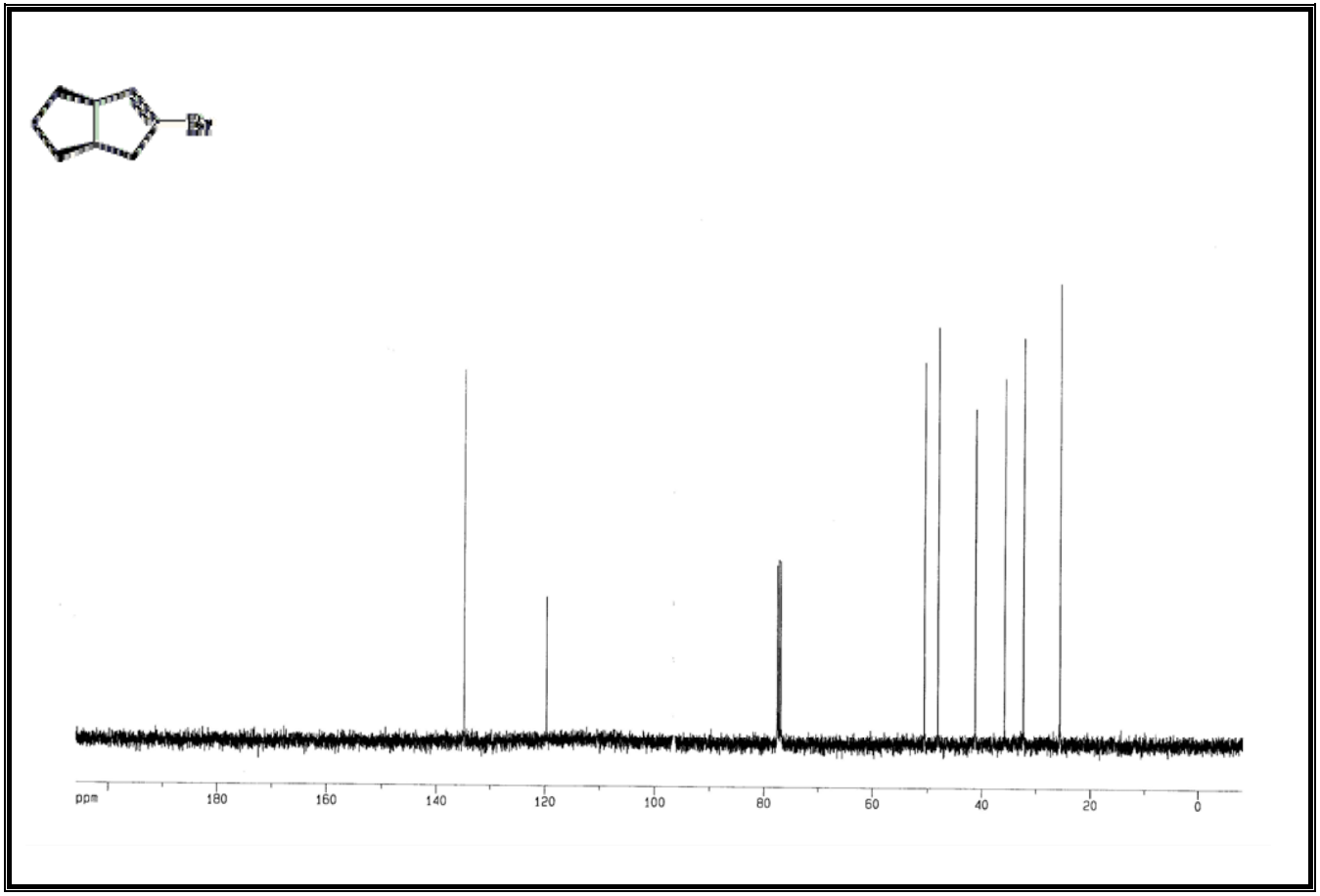

Figure A90 ^{13}C-NMR Spectrum of Compound **183**.

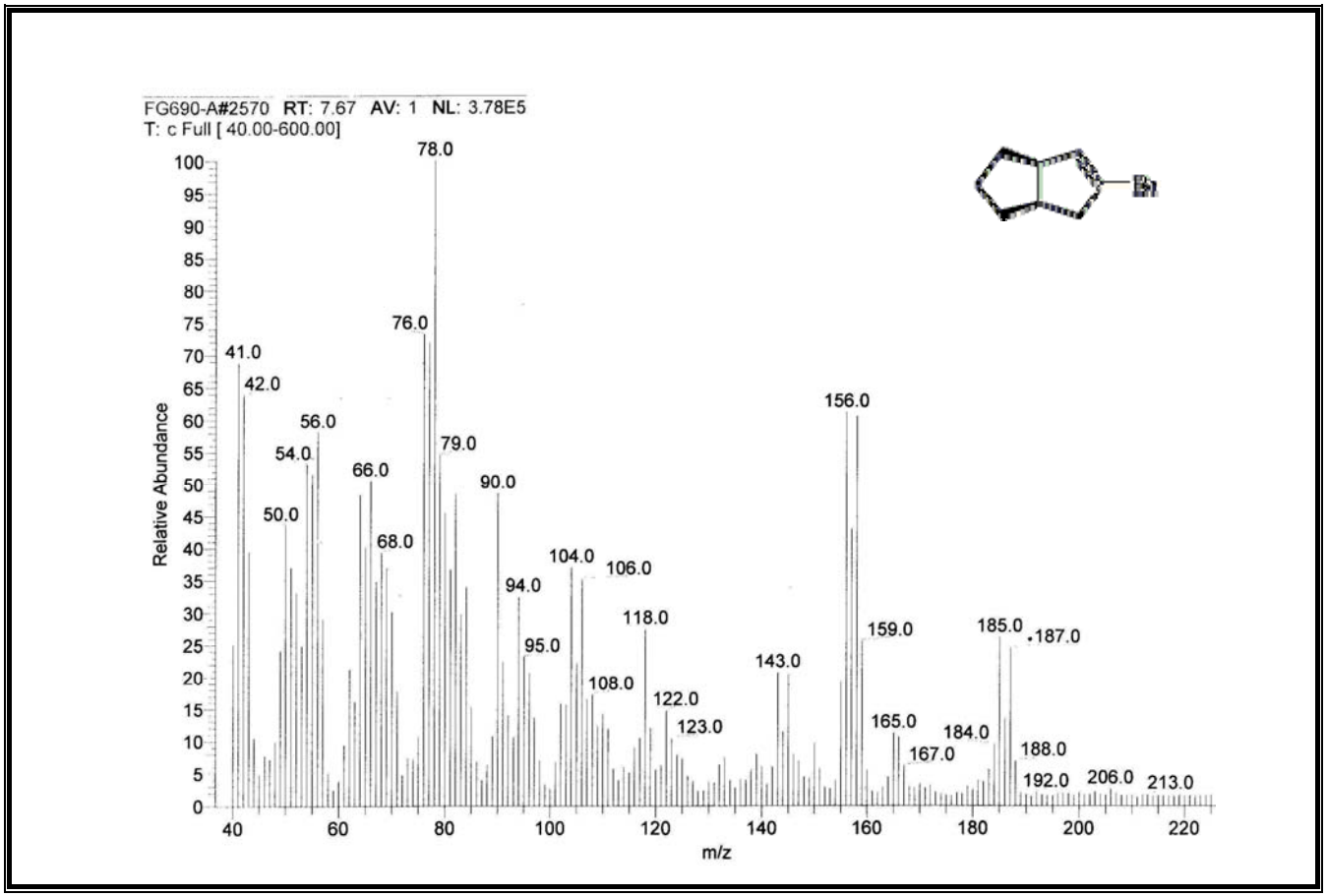

Figure A91 GC-MS Spectrum of Compound **183**.

APPENDIX B

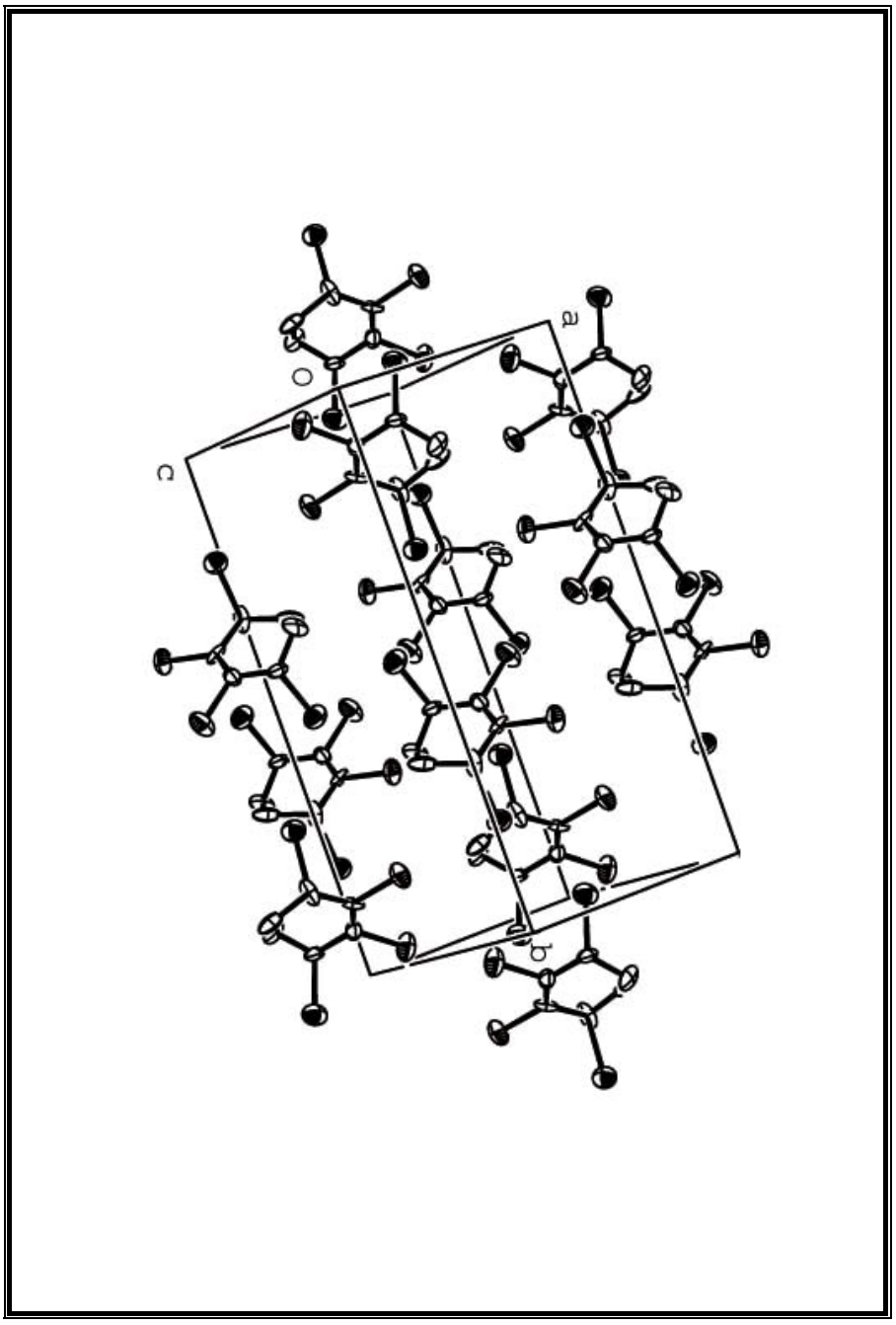

Figure A92 Crystal lattice of Compound **138**.

X-RAY Data of Compound 138

Table A1. Crystal Data and Details of the Structure Determination

Formula	$C_6H_6Br_4$
Formula Weight	397.71
Crystal System	monoclinic
Space Group	P 2_1/n
a, b, c [Å]	7.2905(12), 17.3912(13), 8.0259(17)
α, β, γ [°]	90, 109.80(12), 90
V[Å^3]	957.5(8)
Z	4
D_x [g.cm^{-3}]	2.759
μ(Mo K_α) [mm^{-1}]	16.741
F(000)	728
Crystal Size [mm]	0.10 X 0.20 X 0.40
Radiation [Å]	Mo K_α (0.71073)
Theta Min-Max [°]	3.78 – 25.21
Total and Unique Data, R(int)	1848, 1731, 0.0395
Observed Data [I > 2.0 σ(I)]	718
Nref, Npar	1731, 92
R, wR, S	0.0714, 0.1562, 0.852
(Δ/σ_{max}) and (Δ/σ_{av})	0.000, 0.000
$(\Delta\rho_{max})$ and $(\Delta\rho_{min})$ [e. Å^{-3}]	1.168, -1.113

Table A2. Bond Distances [Å] and angles [˚].

Br1 - C4	2.019(19)	C1 - C6	1.52(2)
Br2 - C1	1.969(16)	C2 - C3	1.61(2)
Br3 - C6	1.881(16)	C3 - C4	1.55(3)
Br4 - C5	1.830(15)	C4 - C5	1.50(2)
C1 - C2	1.50(3)	C5 - C6	1.33(2)
Br1 – C4 – C3	109.3(11)	Br4 – C5 – C6	124.8(12)
Br1 – C4 – C5	108.8(10)	C2 – C1 – C6	112.0(13)
Br2 – C1 – C2	112.2(15)	C1 – C2 – C3	109.3(14)
Br2 – C1 – C6	109.7(10)	C2 – C3 – C4	106.2(16)
Br3 – C6 – C1	114.4(11)	C3 – C4 – C5	116.3(14)
Br3 – C6 – C5	120.8(12)	C4 – C5 – C6	120.5(14)
Br4 – C5 – C4	114.8(10)	C1 – C6 – C5	124.5(15)

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about twice as large as those based on F, and R-factors based on ALL data will be even larger.

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C3 0.065(13) 0.027(10) 0.033(10) -0.005(8) 0.004(9) -0.022(9)
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All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

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C3 C4 H4 107.4 . . ?

Br1 C4 H4 107.4 . . ?

C2 C1 C6 111.9(14) . . ?

C2 C1 Br2 112.2(14) . . ?

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C4 C3 C2 106.1(16) . . ?

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C4 C5 Br4 114.7(10) . . ?

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Br3 C6 C5 C4 -175.8(11) . . . . ?
C1 C6 C5 Br4 179.4(12) . . . . ?
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Br1 C4 C5 C6 -108.6(15) . . . . ?
C3 C4 C5 Br4 -165.8(12) . . . . ?
Br1 C4 C5 Br4 70.3(12) . . . . ?
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VITA

Fatih Algı was born in Konya on June 9, 1976. He was graduated in 1994 from Göl Anatolian Teachers High School in Kastamonu. After receiving his B.S. degree from Gazi University Gazi Education Faculty, Department of Chemistry Education in June 1998, he has been as a teacher for a short time in Uzunbey Elementary School of National Ministry of Education in Ankara. Then he became a research assistant at Chemistry Department of Canakkale Onsekiz Mart University in 1999. He began his carreer with an M.S. study under the supervision of Prof. Dr. Metin Balci at the Chemistry Department of Middle East Technical University, where he went on his Ph.D. study with Prof. Balci's team.