MANGANESE(III)ACETATE-BASED FREE-RADICAL ADDITIONS OF β-DICARBONYL COMPOUNDS TO BICYCLIC SYSTEMS

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Approval of the Graduate School of Natural and Applied Sciences

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ABSTRACT

MANGANESE(III)ACETATE-BASED FREE-RADICAL ADDITIONS OF β-DICARBONYL COMPOUNDS TO BICYCLIC SYSTEMS

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Additions of carbon-centered radicals to alkenes are useful method for cyclic compounds formation. Manganese(III)-based oxidative free-radical cyclizations, where the radicals are generated and terminated oxidatively, are established as efficient methods for the construction of cyclic molecule.

Treatment of a mixture of dimedone, $Mn(OAc)_3$, and $Cu(OAc)_2$ in glacial acetic acid with homobenzonorbornadiene (**80**) (4h at 50 °C) gave furan derivative (**107**), dihydrofuran adduct (**108**), in addition to rearranged product (**109**) as a major product. The reaction run under the same reaction conditions without using Cu(II)acetate for 8h afforded dihydrofuran adduct (**108**) along with dihydrofuran (**110**), where no rearranged products could be formed. On the other hand, reflux of alkene **80** with a mixture of acetylacetone, $Mn(OAc)_3$, and $Cu(OAc)_2$ in glacial acetic acid (3h at 50 °C) gave oxidative product (**131**) and rearranged product (**132**) (major). The reaction run under the same reaction conditions without using

Cu(II)acetate for 7h produced, in addition to the oxidative product **131**, a dihydrofuran derivative (**133**).

In a second system, we examined the oxidation of benzobarrelene **82** with $Mn(OAc)_3$, and $Cu(OAc)_2$ in glacial acetic acid (1h at 50 °C) in presence of dimedone resulted in the formation of five different products rearranged products (**148**, **149**) and a dihydrofuran (**109**), besides, a mixture containing two major rearranged isomers (**150/151**). The same reaction was carried out under the same conditions in absence of Cu(II) for 9h and gave the isomeric mixture **150/151** exclusively, and the yield was reduced.

The oxidative cyclization of acetylacetone with alkene **82** for 3h at 50 °C, afforded in addition to the dihydrofuran (**132)**, two rearranged products (**169**, **170**) and a mixture consisting of two isomers (**171/ 172**). The isomeric mixture was converted to one product by treatment with methanolic ammonia providing hydroxyl derivative which was oxidized by MnO_2 to afford product **174** in a good yield.

Additionally, we investigated the behavior of nitrogen bridge in the bicyclic system on the course of the reaction. Oxidation of N-carbethoxy-7-aza-2,3-benzonorbornadiene **83** with dimedone in the presence of $Cu(OAc)_2$ as well as in its absence in glacial acetic acid (2h at 50 °C), rearranged product (**189**) was obtained as the sole product. Regarding the reaction of aza-derivative **83** with acetylacetone in the presence of $Cu(OAc)_2$ (18 h at 50 °C), rearranged product **195** was resulted as sole product. The reaction of **83** was also run with out $Cu(OAc)_2$ for 22h and gave the rearranged product **195**.

Keywords: Manganese(III)acetate; free-radicals; rearrangement; bicyclic olefins; 1,3-dicarbonyl compounds; aza-benzonorbornadiene.

ÖZ

BİSİKLİK SİSTEMLERE MANGAN(III)ASETAT EŞLİGİNDE β-DİKARBONİL BİLEŞİKLERİNİN SERBENT RADİKEL OLARAK KATİLRRAN

Fadelalla Ali, Mohammed
Doktora, Kimya Bölümü
Tez Yöneticisi: Prof. Dr. Metin Balcı

Ocak 2007, 179 sayfa

Alkenlere radikalik katılmalar siklik bileşiklerin oluşturulmasında kullanışlı metotdandır. **Mn(III)** eşliğinde yapılan serbest radikal halkalaşma reaksiyonları oksidatif olarak sonlandığı için, siklik bileşiklerin elde edilmesinde yaygın olarak kullanılmaktadır.

Homobenzonorbornadienir **(80)** dimedon ile **$Mn(OAc)_3$** ve **$Cu(OAc)_2$** eşliğinde asetik asit içerisinde yapılan reaksiyonunda furan **107,** dhidrofuran **108** ve düzenlenme ürünü **(109)** oluştu. Aynı reaksiyon **$Cu(OAc)_2$** kullanılmadan yapıldığında dididrofuran **108** ve dihidrofuran **110** oluştu. Diğer taraftan alken **80** asetiaseton ile **$Mn(OAc)_3$** ve **$Cu(OAc)_2$** eşliğinde asetik asit içerisinde geri soğutucu altında kaynatıldığında **131** ve düzenlenme ürünü **132** elde edildi.

Aynı reaksiyon **$Cu(OAc)_2$** kullanılmadan yapıldığında **131** ve dihidrofuran **133** oluştu. Benzobaralenin **(82)** dimedon ile **$Mn(OAc)_3$** ve **$Cu(OAc)_2$** eşliğinde asetik asit içerisinde yapılan reaksiyonunda düzenlenme ürünleri **148, 149** dihidrofuran **109**

ve **150/151** izomer karışımı elde edildi. Aynı reaksiyon **$Cu(OAc)_2$** kullanılmadan yapıldığında ise sadece **150/151** izomer karışımının oluştuğu gözlendi.

Benzobarelenin **(82)** asetiaseton ile reaksiyonunda ise dihidrofuran **132** iki düzenlenme ürünü **169/170** ve **171/172** izomer karışımı elde edildi. İzomer karışımı yüksek verimle **174**'e dönüştürüldü.
N-karboetoksi-7-aza-2.2-benzonorbornadienin **(83)** dimedon ile reaksiyonu yapıldığında hem **$Cu(OAc)_2$** kullanıldığında hem de **$Cu(OAc)_2$** kullanılmadığında düzenlenme ürünü **189** elde edildi. Reaksiyon asetilaseton ile yapıldığında ise benzer sonuç gözlendi.

Anahtar Kelimeler: Mangan (III) asetat. Serbest radikal, Düzenlenme, bisiklik alken; bikarbonil bileşikleri; aza-benzonorbornadien.

To My parents, my Wife Eman, and to my daughters, Enas, Nuha, Hanin, and Roba, and my son, Abdulrauof.

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LIST OF ABBREVIATIONS

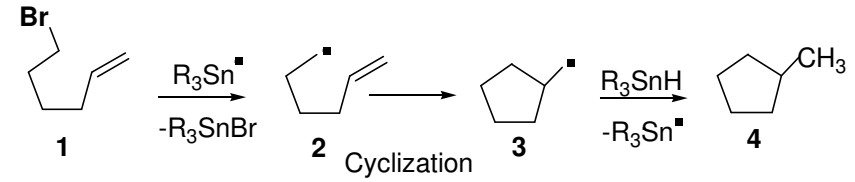
s	: singlet
t	: triplet
d	: doublet
dd	: doublet of doublet
ddd	:doublet of doublet of doublet
ddt	:doublet of doublet of triblet
Cosy	: Correlation spectroscopy
DEPT	: Distortionless enhancement by polarization transfer
HMQC	: Heteronuclear multiple quantum coherence
HMBC	: Heteronuclear multi-bond coherence
THF	: Tetrahydrofuran
OAc	: Acetate
Et	: Ethyl
Me	: Methyl
Ph	: Phenyl
IR	: Infrared
NMR	: Nuclear magnetic resonance
Hz	: Hertz
J	: Coupling constant
ppm	: parts per million

CHAPTER 1

INTRODUCTION

1.1. Oxidative Free-Radical Cyclization

Radical cyclization of alkenes has become a valuable method for the synthesis of cyclic compounds during the past 30 years [1-3] Reduction of halide or other functional group to a radical with R_3SnH, followed by cyclization and termination of the forming radical reductively by hydrogen abstraction from R_3SnH results in the production of hydrocarbons in high yields Scheme 1. However, this approach is limited, leading to unfunctionalized products, making manipulation of the molecule impossible.



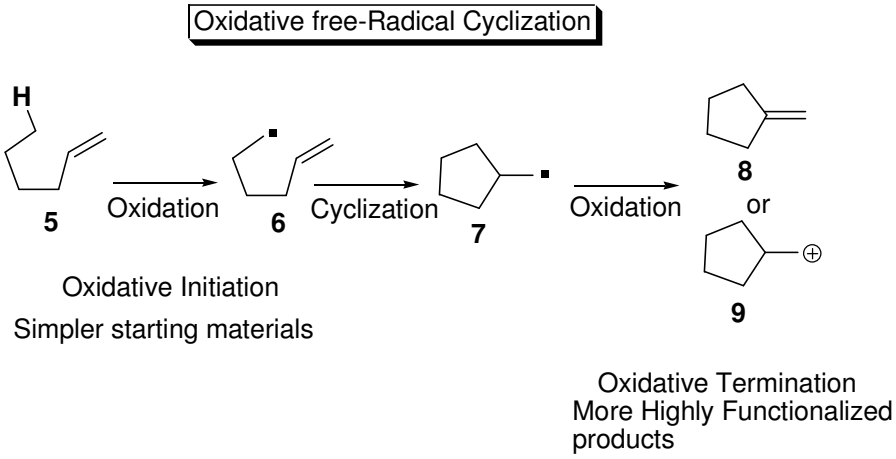
Reductive initiation

Reductive Termination

Less Highly Functionalized products

Scheme 1

Oxidative free-radical cyclizations where the initial radical is produced oxidatively and the cyclic radical is oxidized are more synthetically useful since highly functionalized products can be prepared from simple precursors (Scheme 2).

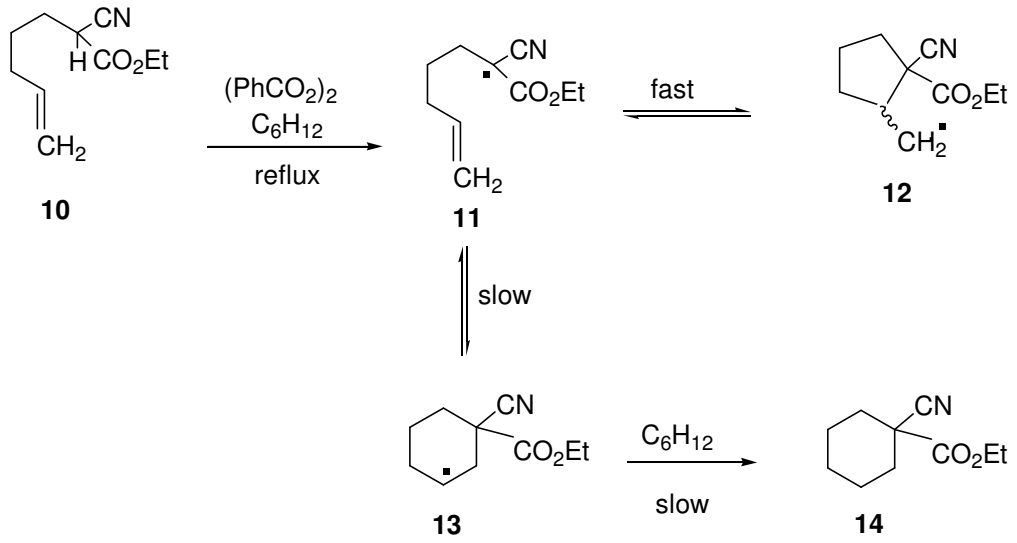


Scheme 2

An acyclic radical formed oxidatively is accomplished by loss of a proton and oxidation of the resulting anion with a one-electron oxidant to generate a radical, this radical can undergo cyclization to produce a new cyclic radical, which can be terminated oxidatively through many pathways including oxidation of a radical to a cation by one-electron oxidants, oxidation of the radical to an olefin with Cu(II) carboxylates, and reaction with heteroatom donors to give halides or sulfides are all oxidative terminations [1-3].

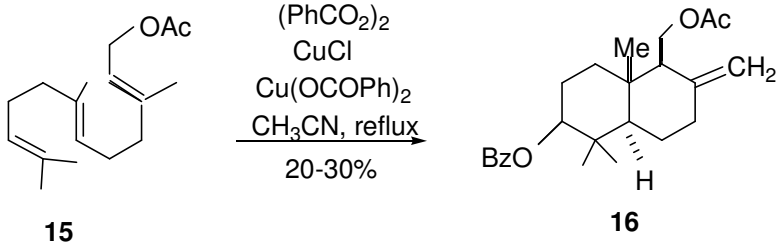
Mn(III), Ce(IV), V(V), Co(III), and Cu(II) are the most commonly used one-electron oxidants in such free-radical reactions [4,5,6]. Mn(III)acetate appears to be much more effective as a reagent than other metal oxidants, so that the vast majority of the work has used Mn(III) with and without Cu(II). Some early typical procedures for radical cyclizations were introduced by Julia in 1971 [7]. Refluxing of unsaturated cyanoacetate **10** with benzoyl peroxide in cyclohexane initiated

radical **11** oxidatively by removal of hydrogen atom, and this radical cyclized to give cyclopentylmethyl radical **12**, since the cyclization of **11** is reversible, the more stable radical **13** is formed and terminated by slow abstraction of hydrogen from cyclohexane to afford **14**.



These reactions proceed by oxidative initiation, but are terminated reductively.

Another example is the oxidative cyclization of farnesyl acetate **15** with benzoyl peroxide, cuprous chloride, and cupric benzoate in acetonitrile at reflux to give 20-30% of **16** (Breslow in 1968) [8].



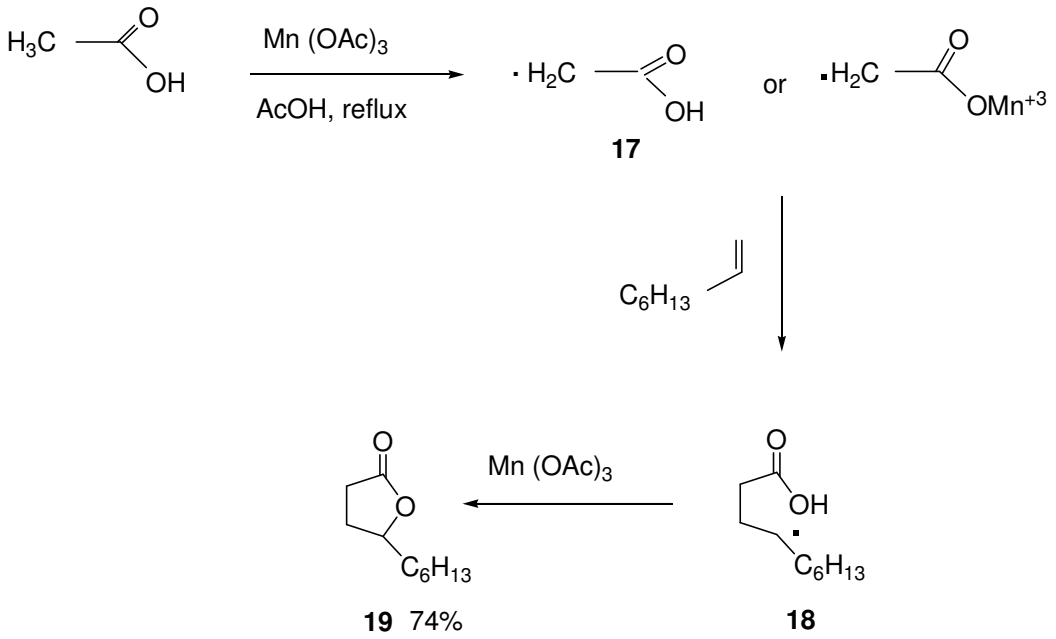
Scheme 3

1.2. Mn(III) acetate-Based oxidative Free-Radical Cyclizations.

Mn(III) oxidative cyclizations were initially investigated by Corey [9], Fristed [10], and Snider [11], and were successfully used in the synthesis of organic compounds.

Mn(III) acetate has been reported to produce a variety of olefins to γ-lactones.

In 1968 Heiba, and Dessau [12], and Bush and Finkbeiner [13] introduced a general approach to Mn(III)-based oxidative free-radical cyclization. Heating $Mn(OAc)_3$ in acetic acid at reflux (115 ^oC) produced the carboxymethyl radical **17,** this can add to olefin to give a secondary alkyl radical **18**, which is then oxidized by a second equivalent of $Mn(OAc)_3$ to afford a γ-lactone **19** Scheme 4.



Scheme 4

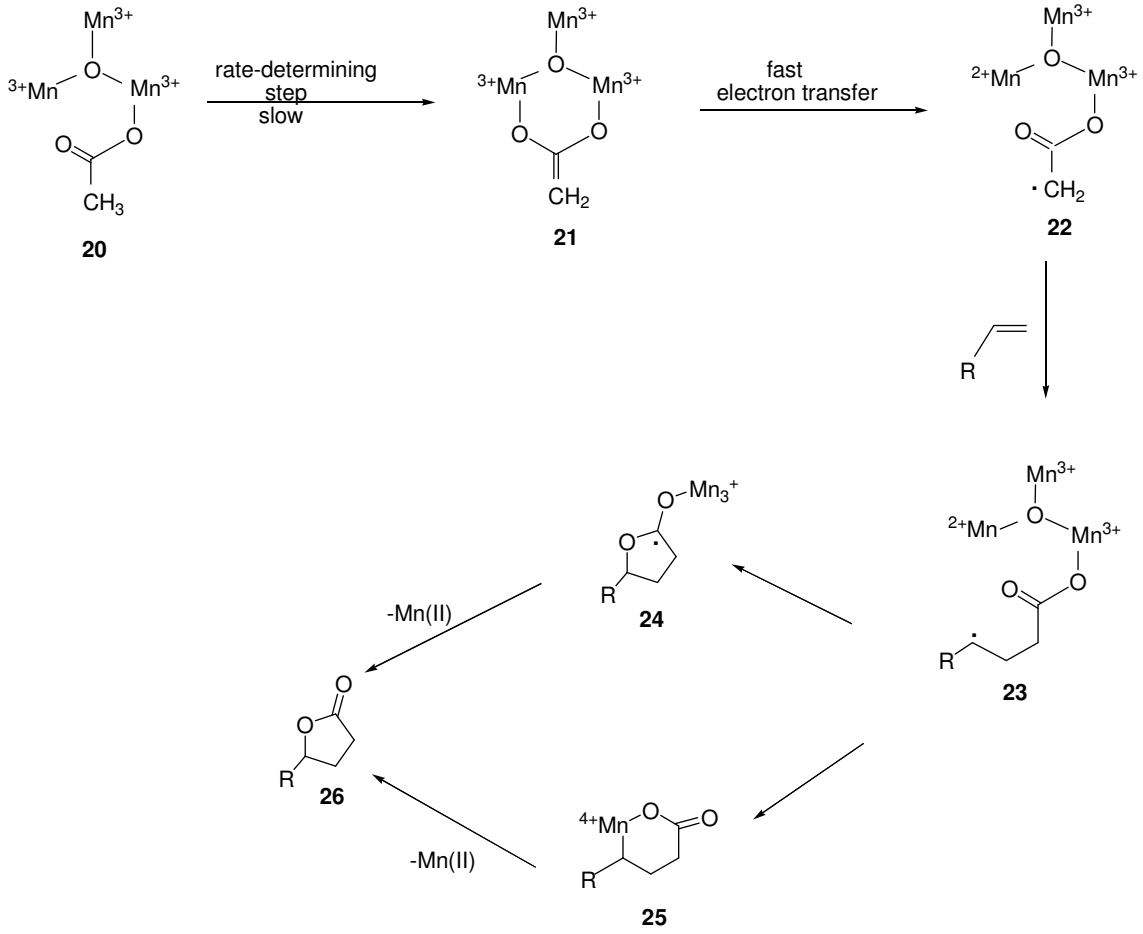
This reaction steps show the generation of a radical oxidatively from acetic acid, free-radical addition to alkenes efficiently forms a carbon-carbon bond, and

produces a synthetically useful γ-lactone by oxidation of the carbon-centered radical.

These oxidative additions have been extensively explored over the past 25 years and have been reviewed recently [4, 6, 14, 15]. Despite the widely used method, oxidative addition of acetic acid with Mn(III), the limitation of which is that oxidative cyclization of unsaturated acids have not been done since the optimal solvent for this oxidation, acetic acid, will be oxidized preferentially.

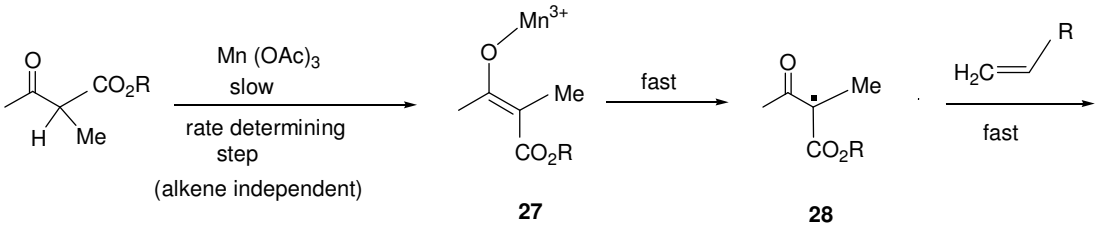
1.3. Initiation.

1.3.1. Mechanism of the Oxidative Free-Radical Addition of Acetic Acid to Alkenes by $Mn(OAc)_3.2H_2O$. The mechanism of the oxidative free-radical addition of acetic acid to alkene with $Mn(OAc)_3.2H_2O$ has been extensively studied by Fristad and Peterson [16], found that the rate determining step in the oxidation of acetic acid by Mn(III) is the lose of a proton from a complexed acetate such as **20** to give **21** which rapidly suffers electron transfer to the oxo-centered metal system to form radical **22** the resulting radical **22** then adds to the alkene to produce **23**. Formation of lacton **26** may occur through two possible pathways, cyclization to 6-membered ring intermediate **25** followed by reductive elimination, or cyclization of radical **23** to form cyclic radical **24**, followed by subsequent oxidation by Mn(III) will produce γ-butyrolactone **26** (Scheme 5).



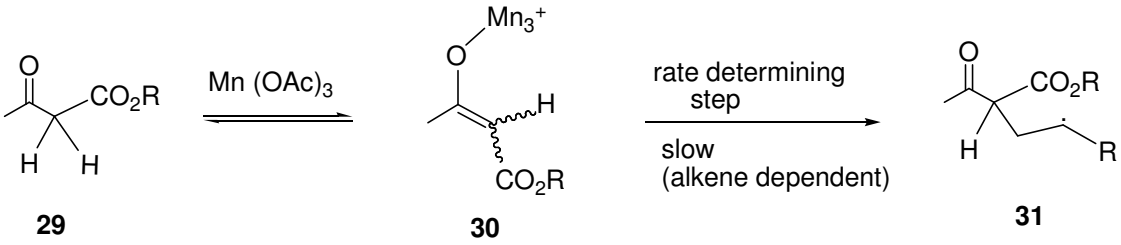
Scheme 5

The rate of the reaction is independent of alkene concentration, since the alkene is not involved in the rate determining step, and also it is concluded that the rate and the yield of lactone **26** formation is increased in the presence of potassium acetate, and the relative rate of oxidation of acetic acid with $Mn(OAc)_3.2H_2O$ increases with increasing acidity of the α-proton of the acid [17]. Snider and co-workers found a similar mechanism in the oxidation of α-alkyl β-keto esters [18].



The first step in this reaction is the enolization of α-substituted keto esters to give **27** which is slow, while the electron transfer and loss of Mn(II) to generate radical **28** is fast, so the rate of the reaction is independent of alkene concentration or the nature of the tether cyclizations. Since enolization is rate determining step, iodine or bromine atom-transfer cyclizations were studied indicated that the free-radical **28** is involved in the Mn(III)-mediated oxidation cyclizations [19].

On the other hand, the enolization of α-unsubstituted keto esters is fast and reversible, and electron transfer to generate radical is very slow .



The rate determining step depends on alkene concentration or the nature of the tether in intramolecular reaction and is the addition of Mn(III) enolate to the alkene to give radical **31** with loss of Mn(II). A radical analogous to **28** does not appear to be an intermediate in these reactions. The presence of the α-alkyl substituent was the reason of the difference in these two mechanisms. A methyl group slows down the formation of Mn(III) enolate **27** since it is electron donating and decreases the acidity of the α-proton. On the other hand, the methyl group should facilitate the oxidation of **27** to give radical **28** since it will stabilize the radical [20-21] the nature of the reaction depends on both; the rate of formation of the Mn(III) enolate,

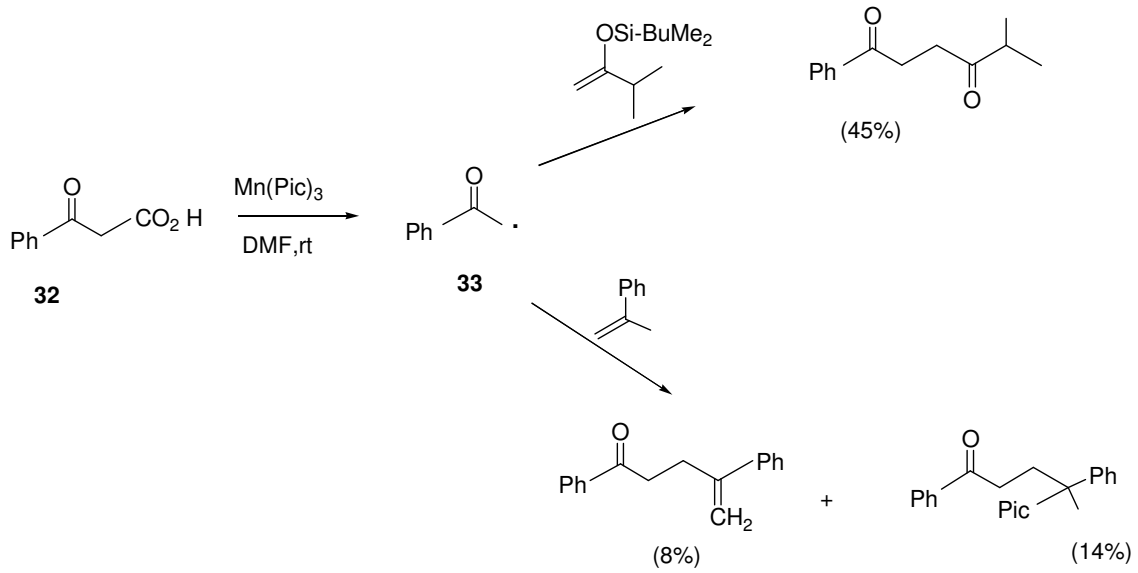
which corresponds to the pKa, and the ease of oxidation of the enolate to give a free radical. For most compounds enolization is the rate determining step. For very acidic compounds such as α-unsubstituted β-keto esters and β-diketones, enolization occurs readily and oxidation is slow [5].

1.3.2. Oxidants

I. Mn(III) Ion

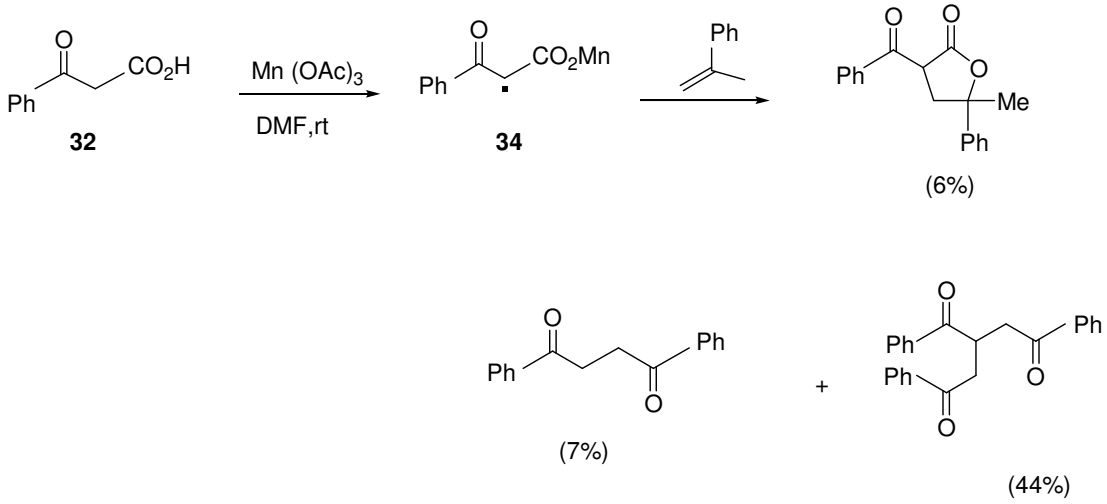
$Mn(OAc)_3.2H_2O$, one-electron oxidant, is a commercially available reagent which is widely used in oxidative cyclizations. It can also be prepared from potassium permanganate and manganous acetate in acetic acid [4]. Anhydrous $Mn(OAc)_3$ is more reactive than the dihydrate. With the anhydrous reagent, reaction times are slightly shorter, but the yields of the products are usually comparable. Potassium or sodium acetate can be used with $Mn(OAc)_3.2H_2O$. Acetate anion increases the rate of enolization and acts as a buffer.

Acetic acid is the typical solvent for $Mn(OAc)_3.2H_2O$ oxidative cyclizations, use of trifluoroacetic acid as a co-solvent increases the rate of the reaction, but often decreases the yield of products. DMSO, ethanol, methanol, dioxane, acetonitrile, and even benzene can be used, although the reactions require higher temperatures and lower yields of the products are sometimes obtained. Narasaka introduced manganese(III) picolinate [$Mn(pic)_3$] in DMF as a useful reagent for the oxidation of β-keto acids to radicals, the oxidative cleavage of cyclopropanols to give β-keto radicals, and the oxidation of nitroalkanes to cation radicals. Oxidation of the β-keto acid **32** with $Mn(OAc)_3.2H_2O$ gave very different results from that with $Mn(pic)_3$. Oxidation with $Mn(pic)_3$ in DMF results in decarboxylation to give the α-keto radical **33** (Scheme 6).



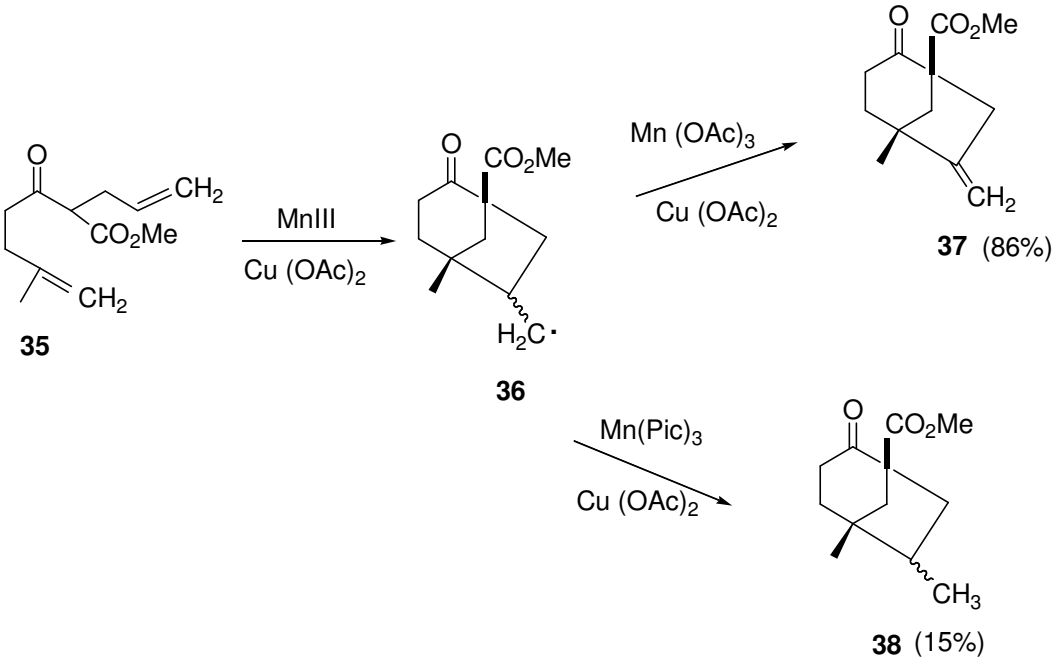
Scheme 6

Oxidation of **32** with $Mn(OAc)_3$ in DMF leads to dimers and trimers and β-keto acid radical **34** that adds to α-methylstyrene to give 6% of the lactone as shown in Scheme 7 [22-26].



Scheme 7

Snider et al [27] examined the tandem oxidative cyclization with different Mn(III) reagents and $Cu(OAc)_2$. Oxidative cyclization of **35** with $Mn(OAc)_3$ and $Cu(OAc)_2$ gave 86% of **37** and 0% of **38**, while use of $Mn(pic)_3$ and $Cu(OAc)_2$ afforded 0% of **37** and 15% of **38**, it is established that $Mn(pic)_3$, but not $Mn(OAc)_3$, reacts with the bicyclic radical **36** more rapidly than $Cu(OAc)_2$ does. A one-electron oxidant, such as Mn(III), Cu(II), Ce(IV), is needed for both the generation of the acyclic radical and oxidation of the cyclic radical (Scheme 8).

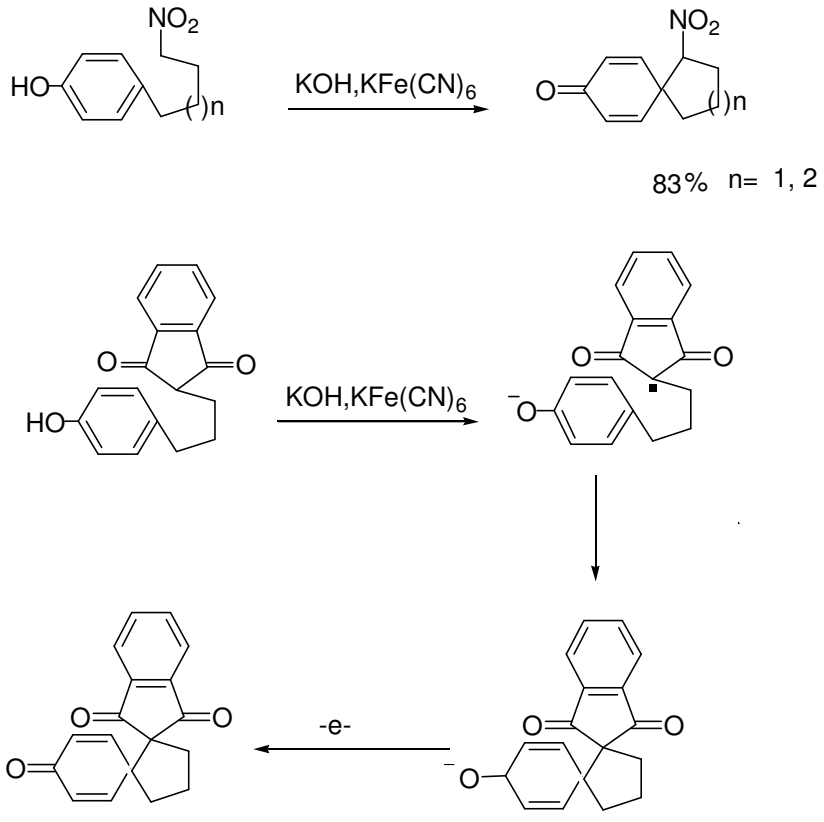


Scheme 8

$Mn(AcAc)_3$ and MnF_3 are other available Mn(III) reagents, $Mn(AcAc)_3$ has been used for oxidative coupling of phenols [28]. While both reagents are suitable for oxidative radical cyclizations, they have no advantages over $Mn(OAc)_3.2H_2O$.

II. Ce(IV), Fe(III), V(V).

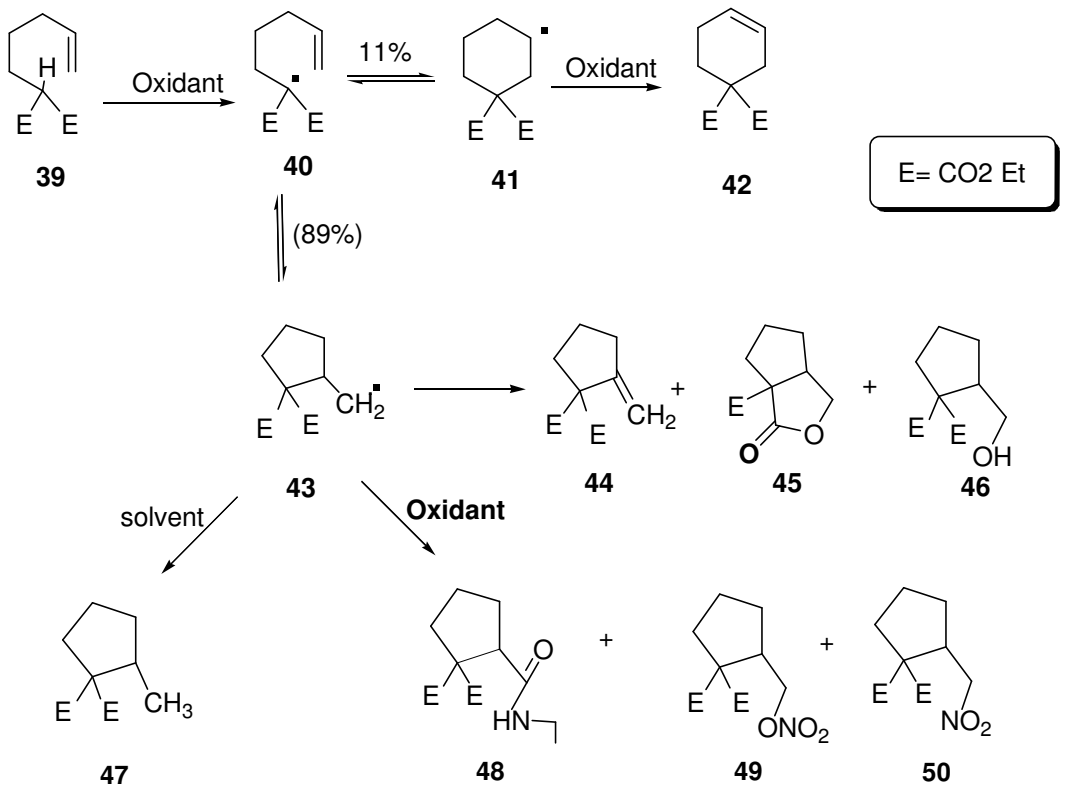
Many other one-electron oxidants have been used for generating radicals. Hirao et al. have used VO $(OEt)Cl_2$ to generate radicals from diketene in ethanol [29]. Kende has shown that alkaline potassium ferricyanide induces oxidative cyclization of phenols with aside chain bearing a nitro group or a readily enolizable carbonyl group (Scheme 9) [30-33].



Scheme 9

These reactions probably proceed by oxidation to the radical, cyclization to the radical anion, and further oxidation as illustrated in the Scheme 9.

In 1989 Citterio and co-workers have used ferric perchlorate in a cetonitrile for oxidative intermolecular additions of malonate esters to styrenes and oxidative cyclizations of unsaturated malonate esters and compared this reagent to $Mn(OAc)_3$ and ceric ammonium nitrate [34-40]. $Co(OAc)_2$ and molecular oxygen in acetic acid have been used for the oxidative addition of β-diketones and β-keto esters to alkenes [41-43]. Baciocchi and co-workers have also used ceric ammonium nitrate in alcohol solvents to oxidize malonate esters to radicals [44, 45]. The utility of ceric ammonium nitrate for oxidative cyclization malonate esters and β-keto esters to aromatic systems has been examined by Citterio and co-workers [36, 37, 38, 46, 47]. All of these oxidants are suitable for generating radicals from 1,3-dicarbonyl compounds. However, the oxidant is also necessary for termination of the radical reaction. The differences in termination are obviously seen in the oxidative cyclization of diethyl 4-pentylmalonate **39**, which has been studied with Ce(IV), Fe(III), and Mn(III), (Scheme 10).



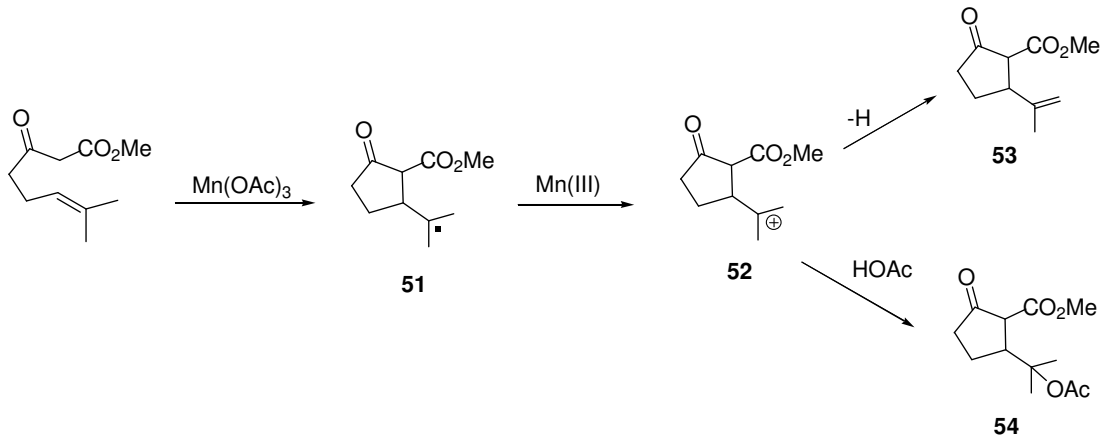
Scheme 10

Oxidative cyclization of **39** with 2 equiv of $Mn(OAc)_3.2H_2O$ and 1 equiv of $Cu(OAc)_2.2H_2O$ in acetic acid at 55 ^oC gives **45, 44**, and **42** in 48%, 20%, and 7% yields. Oxidation of **39** generates radical **40**, which then cyclizes to a 9: 1 mixture of cyclopentylmethyl radical **43** and cyclohexyl radical **41**. Oxidation of **41** with Mn(III) or Cu(II) forms **42**; oxidation of **43** with Cu(II) gives **44** and **45**, the ratio of which is solvent dependent; ranging from as high as (3.75 : 1) in acetonitrile to as low as (0.04: 1) in DMSO, with intermediate values in AcOH (2.4:1), (0.64:1) in EtOH, DMF (0.55 : 1), and MeOH (0.48 : 1). Oxidation of **39** with $Fe(ClO_4)_3.9H_2O$ in acetonitrile gives **42, 44**, and **45** in 7%, 4% in yields, and **47** (reductive product), **46,48** in 7%, 10%, 6% yields, the last three products were not observed with $Mn(OAc)_3$ and $Cu(OAc)_2$. Oxidation of **39** with ceric ammonium nitrate affords 20% of lactone **45** and 23% of **49**, whereas oxidative cyclization of

39 with both ceric ammonium nitrate and $Cu(BF_4)_2$ affords 86% of lactone **45** in AcOH and 81% of **49** in AcOH containing Ac_2O. The oxidation of **39** with different oxidants showed that the major differences are in the termination step. All oxidants give radical **40**, and the oxidative termination step is oxidant, ligand, and solvent dependent [48].

1.4. Termination

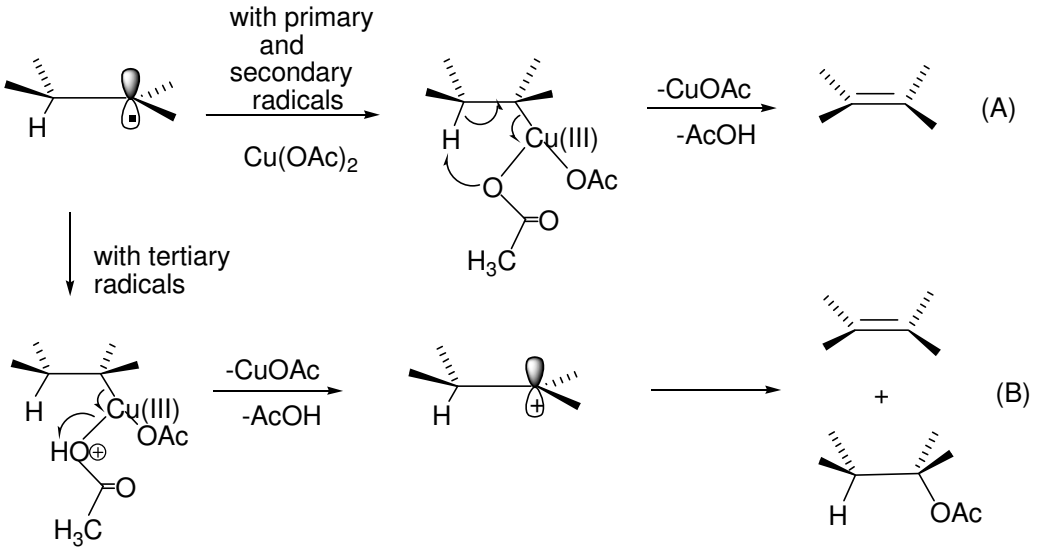
i. Oxidative termination with $Mn(OAc)_3.2H_2O$. $Mn(OAc)_3$ is involved in both initiation and termination steps of the radical process. It is known to oxidize tertiary and allylic radicals to cations that lose a proton to give an alkene or react with nucleophile, such as acetate. Tertiary radicals such as **51** are readily oxidized by Mn(III) to cations such as **52** which lose a proton to give **53** or react with solvent to give **54** (Scheme 11) [49].



Scheme 11

On the other hand, $Mn(OAc)_3$ oxidizes primary and secondary radicals slowly, which are common intermediates in oxidative free-radical reactions, so that hydrogen atom abstraction from the solvent or starting material becomes the predominate process, and alkene can be formed efficiently if $Cu(OAc)_2$ is used as cooxidant.

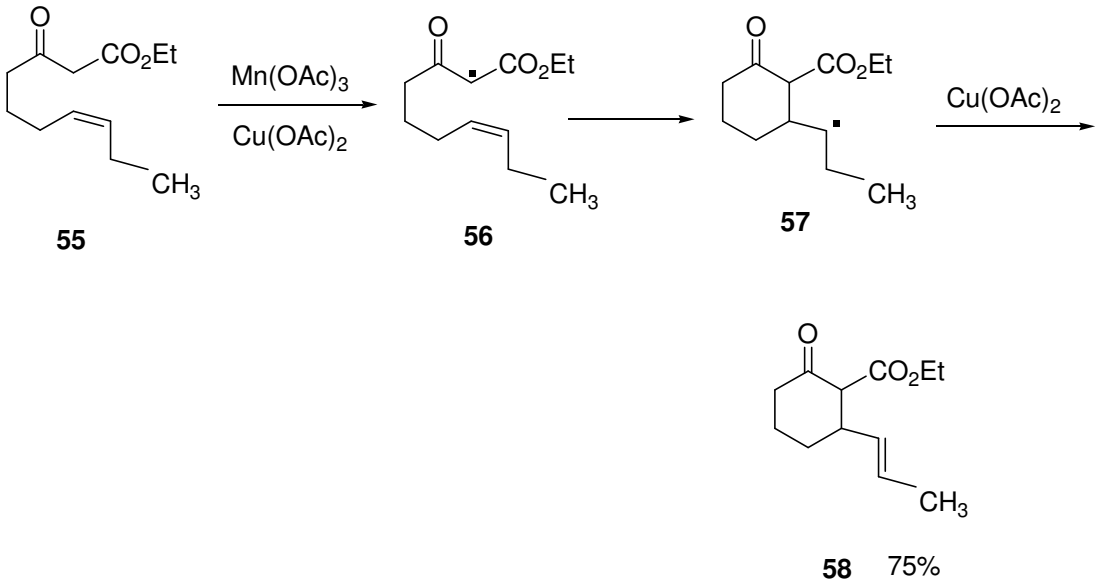
ii. Oxidative termination with $Cu(OAc)_2$. $Cu(II)_2$ acetate is thermodynamically weaker oxidant than Mn(III) acetate. However, Kochi and co-workers showed that Cu(II) reacts rapidly with primary and secondary radicals (~10^6 s^{-1} M^{-1}) to give an alkylcopper(III) intermediates (Scheme 12 A) [50, 51], which lose Cu(I) by oxidative elimination to form an alkene, and this is the preferred pathway from the reaction of $Cu(OAc)_2$ with primary and secondary radicals. Heiba and Dessau have used $Mn(OAc)_3.2H_2O$ and $Cu(OAc)_2$ together and they found that Cu(II) oxidizes secondary radicals to alkene 350 times faster than Mn(III) does [52]. Cu(II) carboxylate reacts with tertiary radicals to form the Cu(III) intermediate, which undergoes electron transfer to form a cation that can lose a proton to give an alkene or react with acetate (Scheme 12 B).



Scheme 12

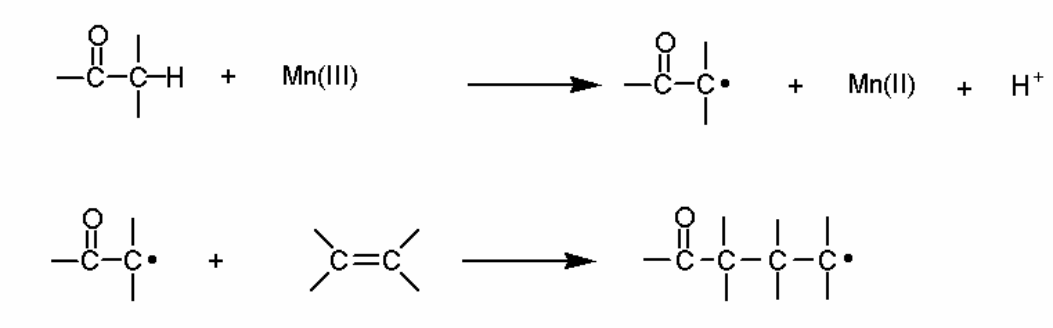
Cu(I), produced from the oxidative elimination is rapidly oxidized to Cu(II) by Mn(III), so only a catalytic amount of $Cu(OAc)_2$ is needed and 2 equiv of $Mn(OAc)_3.2H_2O$ are required, and at lower concentration of $Cu(OAc)_2$ hydrogen

atom abstraction can be competitive. The organocopper(III) intermediate formed from primary radicals can interact with adjacent functionality to give lactones as in the conversion of **43** to **45** (see Scheme 10). Another example has been developed by Snider and co-workers [18], the oxidative cyclization of unsaturated β-keto ester **55** to cyclohexanone **58** with 2 equiv of $Mn(OAc)_3$ and 1 equiv of $Cu(OAc)_2$ in 75% yield. Oxidation of **55** with Mn(III) gives resonance-stabilized radical **56** which undergoes 6-exo-cyclization to give secondary radical **57**. Oxidation by Cu(II) affords **58** (Scheme 13).



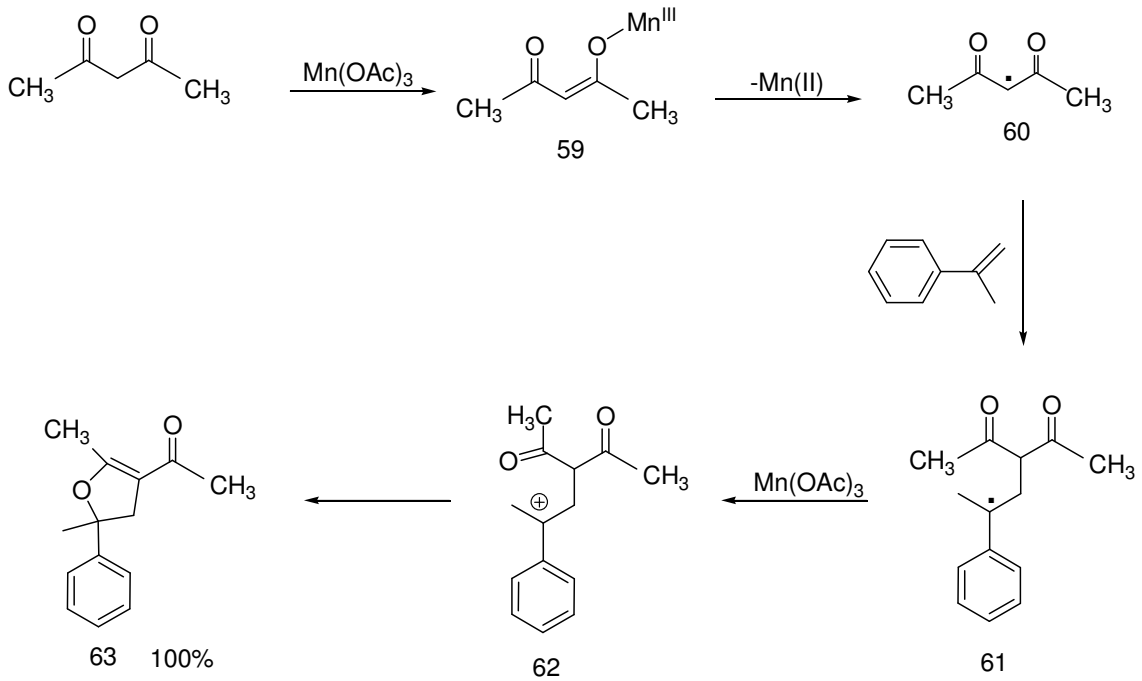
Scheme 13

1.5. Oxidative Free-Radical Addition of β-Dicarbonyl compounds to alkenes by $Mn(OAc)_3.2H_2O$. The one-electron oxidation by Mn(III) acetate of the carbonyl compounds bearing an α-C-H generates α-keto radicals, can add to olefinic systems. The sequence of such reactions is shown below:



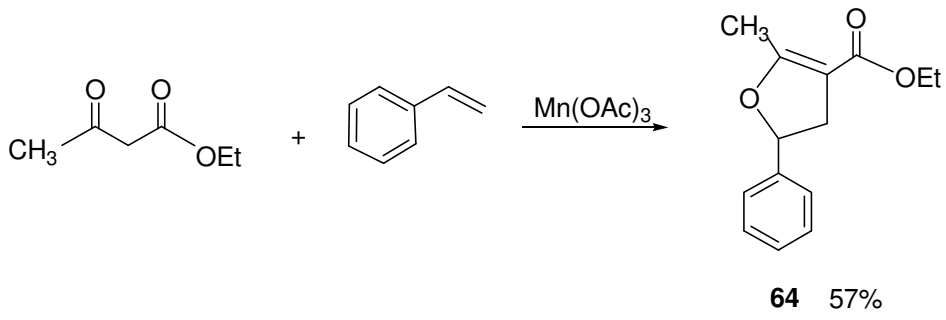
These substrates being more acidic than acetic acid (pKa of 9 while α-hydrogen of acetic acid has a pKa of ~ 25), so β-dicarbonyl compounds can be oxidized by $Mn(OAc)_3.2H_2O$ much faster than the oxidation of acetic acid, which is used as a solvent, and it carried out at 25 °C while that of acetic acid takes place at reflux. In 1974 Heiba and Dessau reported the synthesis of a series of dihydrofurans from 1,3-diketone and β-keto esters [53].

Oxidation of acetylacetone with Mn(III) in the presence of α-methylstyrene in acetic acid afforded dihydrofuran **63** in 100% yield, (acetylacetone is preferentially oxidized). This reaction proceeds with involving a resonance stabilized radical **60**, which then adds to the styrene to generate benzylic radical **61** that is first oxidized to a cation **62** by Mn(III) and then it cyclizes to the carbonyl group and is further oxidized to dihydrofuran **63** (Scheme 14).



Scheme 14

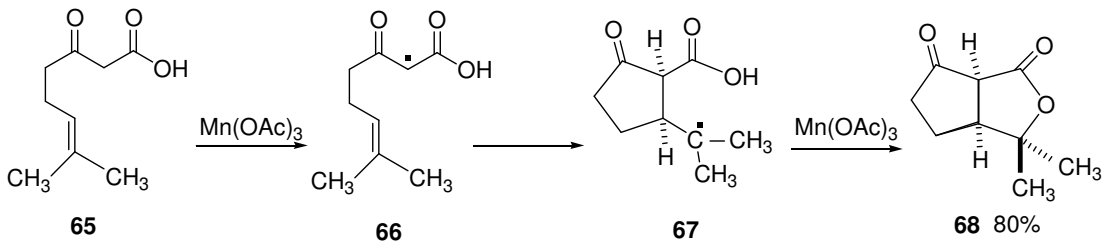
In a similar manner, ethyl acetoacetate is oxidized to dihydrofuran **64** in yield of 57% [53].



64 57%

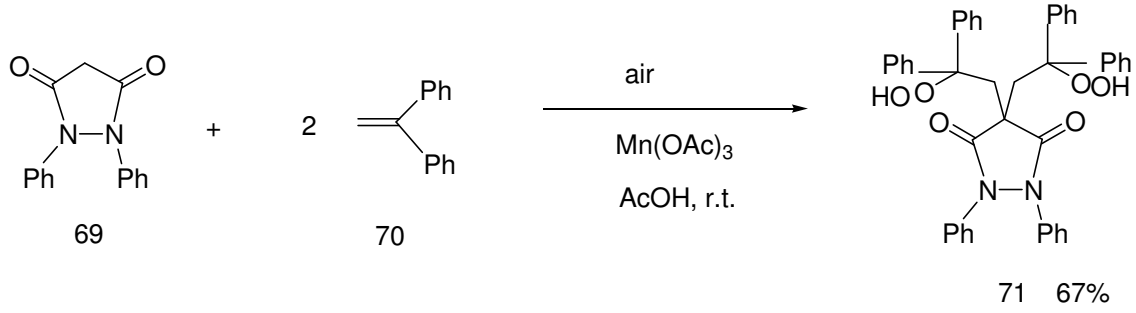
In 1984, Corey and Kang reported the first cyclization of β-dicarbonyl compounds with Mn(III) [9]. Oxidation of unsaturated β-keto acid **65** at 25 °C with Mn(III) generates resonance stabilized radical **66,** which cyclizes to give tertiary radical **67,** a second cyclization to the carbonyl group and oxidation affords lactone **68** in 80% yield (Scheme 15). In 1985, Snider reported the oxidative cyclization of

unsaturated β-keto esters; see Scheme 13, and Fristed surveyed the cyclization of unsaturated malonic and cynoacetic acids [10]



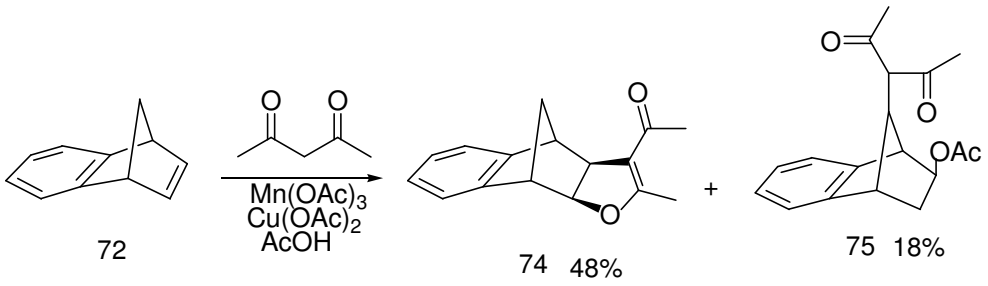
Scheme 15

In 2003 Nishino reported the catalyzed aerobic oxidation of 1,2-disubstituted pyrazolidine-3,5-diones **69** in the presence of alkene in acetic acid in air, afforded derivative **71** 67% in yield [54].

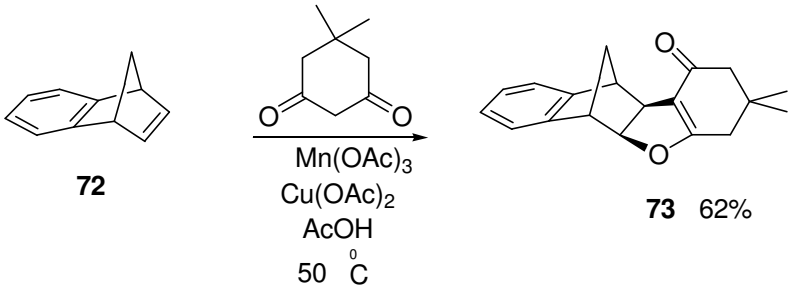


Scheme 16

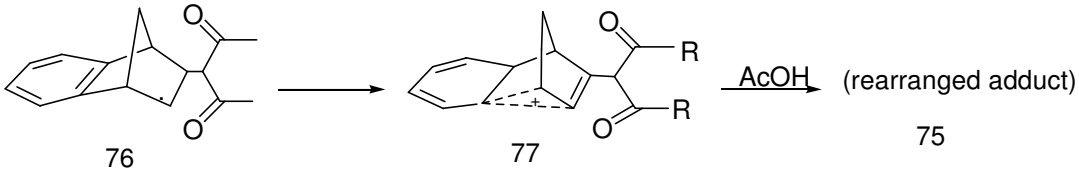
Balci and co-workers (in 2005) have reported the oxidative free-radical additions of 1,3-dicarbonyl compounds, such as dimedone and acetylacetone to unsaturated bicyclic systems (e.g; benzonorbornadiene (**72)** and oxabenzonorbornadiene **78**) [55] (Scheme, 17, 18).



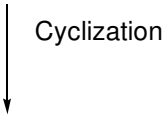
72 74 48% 75 18%



72 **73** 62%



76 77

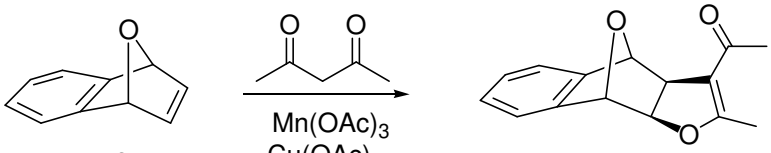


a; R = CH_3

b; R-R = $^{-}CH_2C(CH_3)_2CH_2^{-}$

73 / 76

Scheme 17

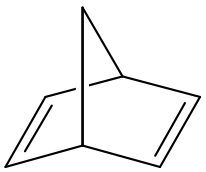


78 **79** 78%

Scheme 18

1.6. Bicyclic Alkenes

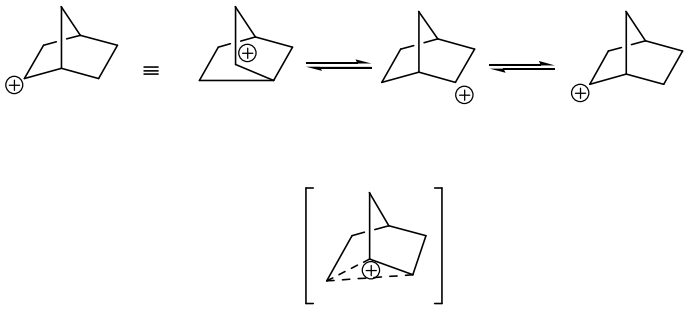
Owing to their strained structure and π-electron properties, unsaturated bicyclic systems are molecules of considerable potential mechanistic interest. For instance, molecules such as norbornadiene are the important examples of photo chemical di-π-methane rearrangement and Wagner-Meerwein rearrangement (Zimmerman 1969) [56].



Norbornadiene

1.6.1. Non-Classical Carbocations

Nonclassical or bridged structures are either readily attainable intermediates or transition states for many cations and are involved in rearrangement processes. For norbornyl cation, the bridged structure is the most stable structure as suggested by Winsten (1952) in the solvolysis of exo-2-norbornyl brosylate by σ participation of 1,6 bond, which assists in the departure of the leaving group with delocalization to a bridged nonclassical cation (more stable intermediate), and involving equilibrating classical cations (Scheme 19) [57].

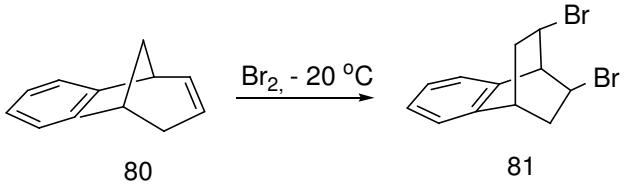


Nonclassical cation
(more stable intermediate)

Scheme 19

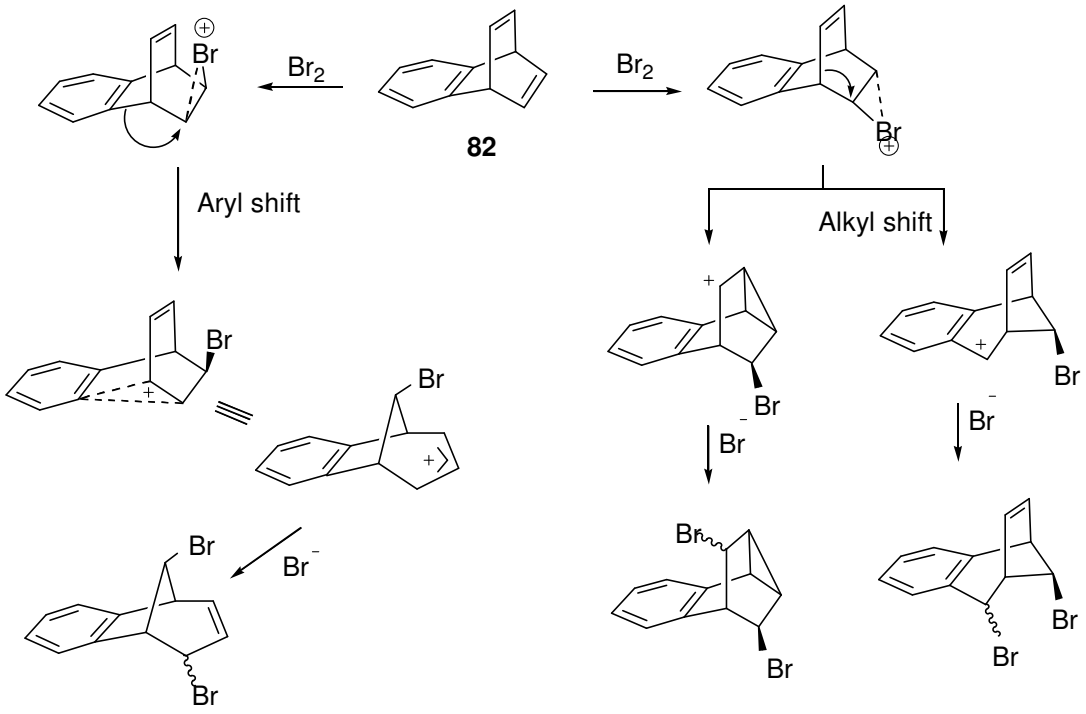
1.6.2. Bromination of bicyclic alkenes

The addition of bromine to the carbon-carbon double bond is formally one of the typical reactions of unsaturated compounds, yields trans 1,2-dibromo derivatives. However, bromination of bicyclic olefin at low temperatures leads to rearrangements of the molecular skeleton and results in the formation of rearranged products via Wagner-Meerwein rearrangement, with accompanying aryl and alkyl migration. Furthermore high temperature bromination prevents skeletal rearrangement, also in addition to a competition between radical and ionic mechanism as reported by Balci et al [58]. An example is the bromination of homobenzonorbornadiene **80** at -20 °C proceeded with rearrangement to give di-anti-bromo adduct **81**[59].



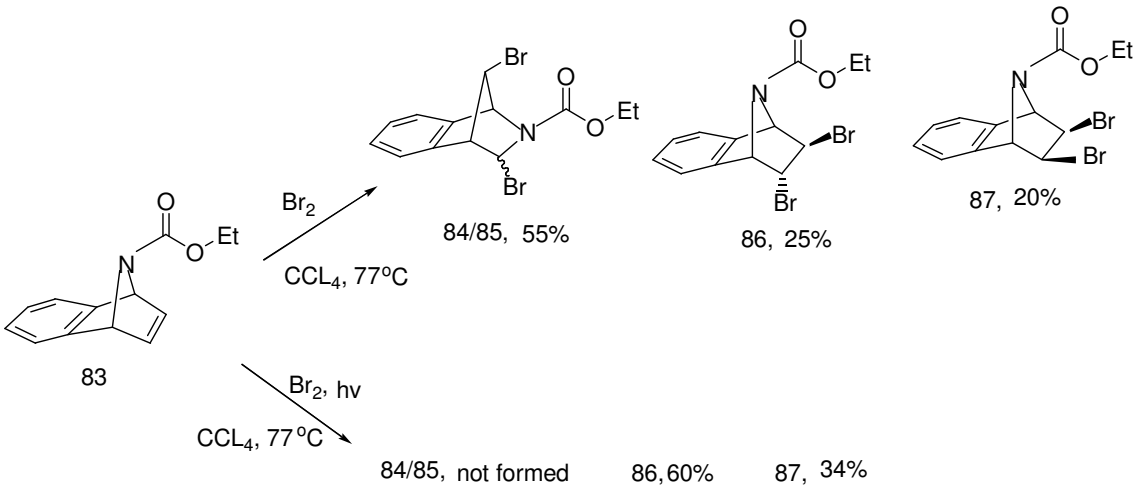
80 81

In 1994, Dastan and Balci [58], investigated the bromination of benzobarrelene **82** at 10 °C, and they expected the normal addition of one molecule of bromine. However, **82** reacted quantitatively with bromine, and the structural determination of the formed products revealed that the barrelene skeleton was rearranged completely. For the formation of the rearranged products the following mechanism was proposed:



On the other hand, high temperature bromination of **82** at 150 °C, afforded some products, among them were the non-rearranged products, which formed as major products.

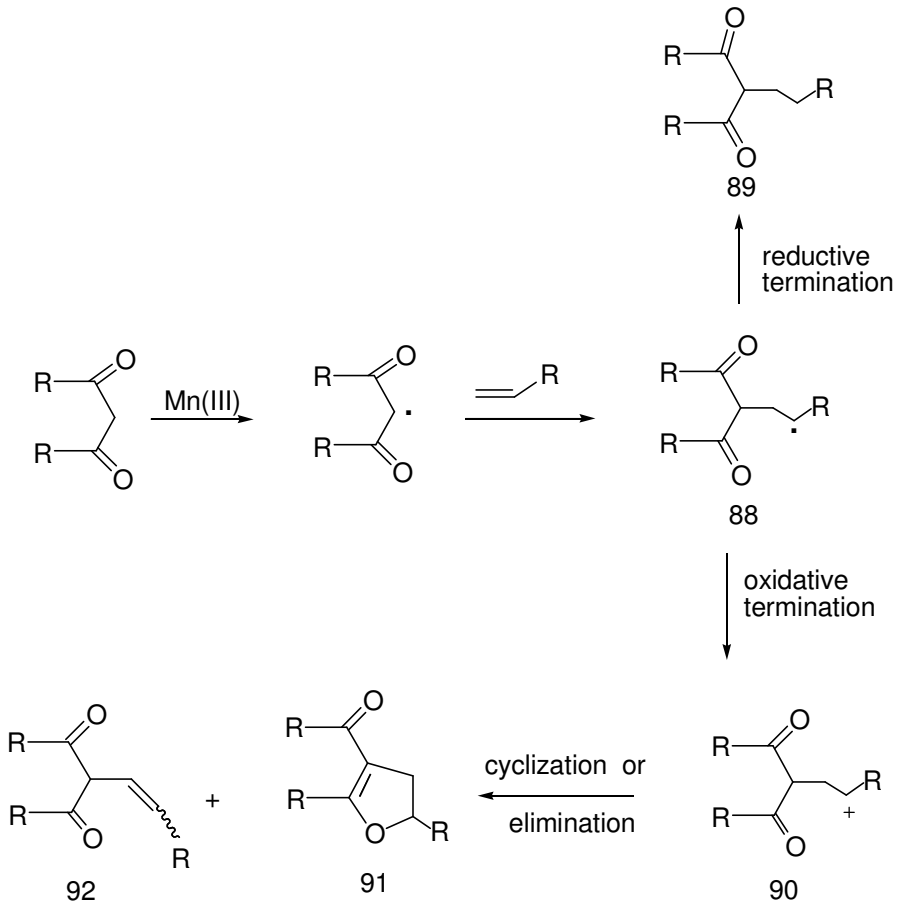
The high temperature bromination of N-carbethoxy-7-aza-2,3-benzonorbornadiene **83**, was also studied by Balci and co-workers in 2002 [60]. Bromination of **83** at 77 °C gave in addition to non-rearranged isomers **86** and **87**, isomeric rearranged products **84** and **85**. It was concluded that the formation of rearranged isomers **84**, **85** and non-rearranged products **86**, **87** there is a competition between radical and ionic reactions. However, the bromination at high temperature, with internal irradiation, completely suppressed the formation of rearranged products, (Scheme 20).



Scheme 20

1.6.3 Aim of the work

During the past decade Mn(III)-based oxidative free-radical cyclization have been developed as a general procedure for producing highly functionalized products from simple precursors. These cyclizations have been initiated by the reaction of relatively acidic compounds, such as 1,3-diketones, acetoacetates, malonates, and α-sulfinyl or α-nitro ketones, with $Mn(OAc)_3$ to form a Mn(III)enolate, which undergoes electron transfer to give Mn(II) and a radical. Generally, addition of an oxidatively or reductively generated radical to the double bonds occurs in two pathways; inter- and intramolecularly generating new radicals (**88**). This cyclization can be terminated reductively by hydrogen atom abstraction. If this formed radical is terminated oxidatively, the radical center in **88** can be oxidized to carbocation **90** that react with a nucleophile to give dihydrofuran **91** [9], and a proton loss would end up with the formation of an alkene **92** [12, 13] (Scheme 21).

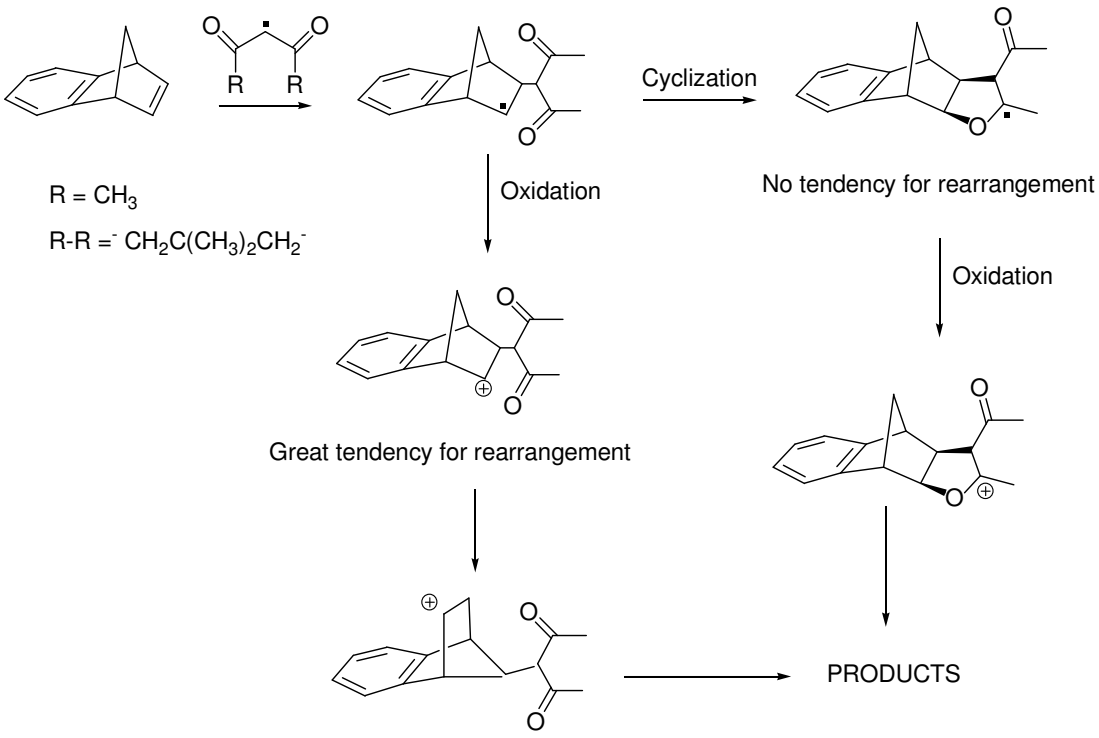


Scheme 21

Furthermore, the primary and secondary radicals can be oxidized by both $Mn(OAc)_3$ and $Cu(OAc)_2$ with relative reactivity order 1: 350 [52].

This study is aimed not only at the preparation of some new bicyclic compounds using the methods of oxidative free-radical additions of 1,3-dicarbonyl substrates to bicyclic olefins in presence of $Mn(OAc)_3$ with and without $Cu(OAc)_2$, but also to follow the mode of the $Mn(OAc)_3$ oxidation and to see whether the second oxidation takes place before or after the cyclization reaction, so that we generated the secondary radicals of type **88** in bicyclic systems. If the oxidation takes place before cyclization, then it is likely that the non-classical carbocation formed would

undergo rearrangement [61] (Scheme 22). On the other hand, it is well known that the 2-norbornyl radical does not undergo rapid rearrangement [62].



Scheme 22

To elucidate this mechanism, Dimedone **93** and acetylacetone **94** were chosen as model compounds to explore the reaction. Homobenzonorbornadiene **80**, benzobarrelene **82** and aza-benzonorbornadiene **83** were chosen as radical acceptor alkenes (Fig. 1).

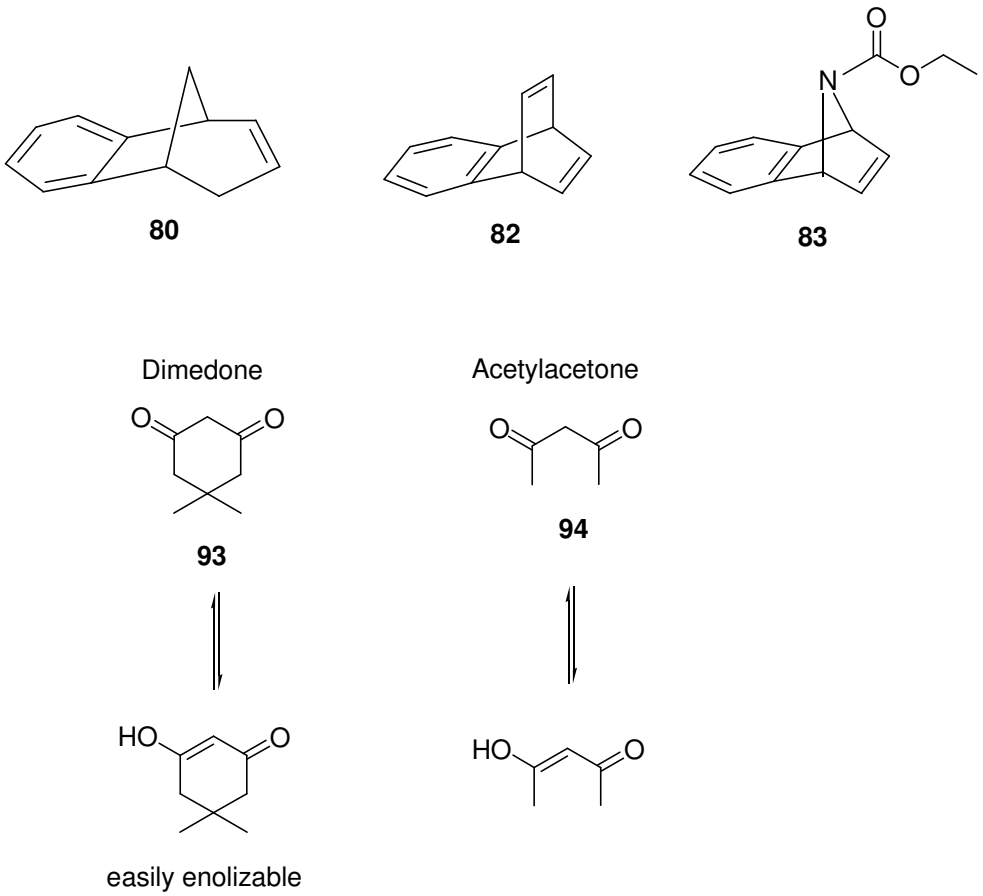


Figure 1 Radical acceptor alkenes, and 1,3-dicarbonyl compounds.

CHAPTER 2

RESULTS AND DISCUSSION

The methodology adopted has been based on an oxidative method using Mn(III) acetate to generate radicals. A common feature of Mn(III) is the oxidation of β-dicarbonyl compounds to generate electrophilic radical intermediates which can add to nucleophilic alkenes.

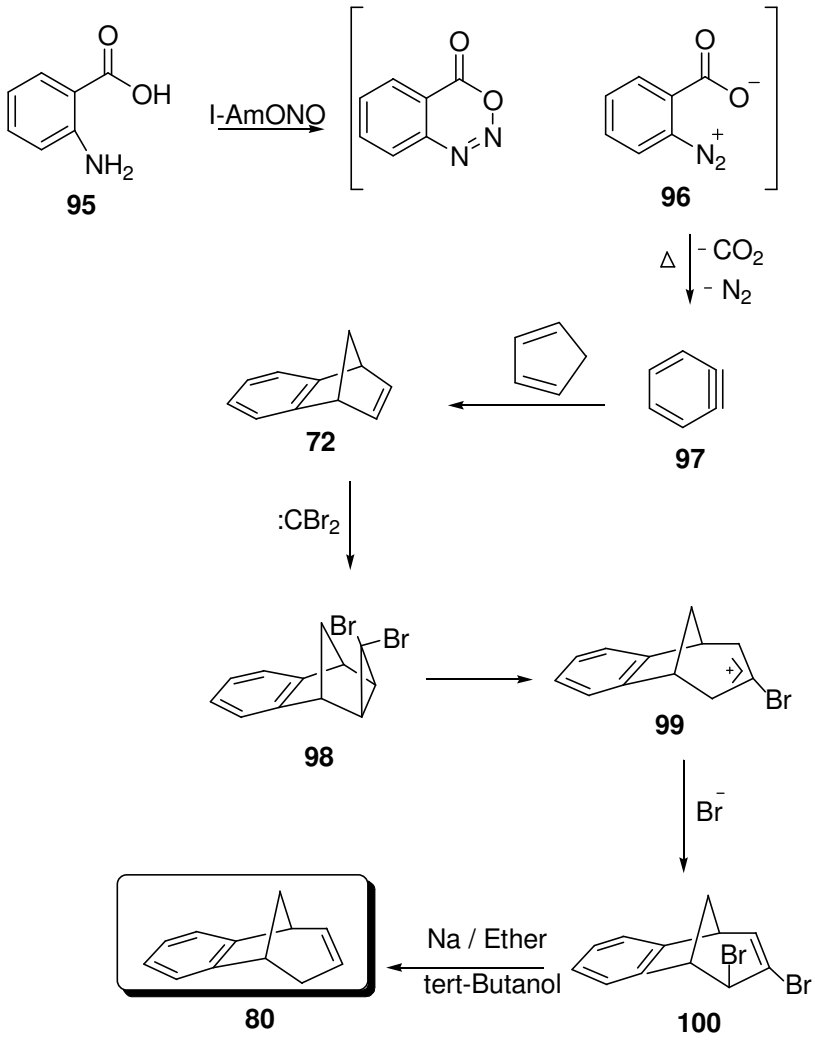
The manganese acetate reaction was studied in the presence and absence of added cupric acetate since cupric acetate has a dramatic effect on both the rate and the yield of reaction.

In this work, we investigated the free-radical addition reactions of enolizable β-dicarbonyl substrates such as dimedone **93** and acetylacetone **94** to unsaturated bicyclic [3.2.1] and [2.2.2] systems that exhibit a great tendency to undergo Wagner-Meerwein rearrangement.

Our work was initiated with a bicyclic [3.2.1] system, homobenzonorbornadiene **80** was chosen as a radical acceptor alkene. The oxidative free-radical addition reactions were performed in 1 : 1 : 2 molar ratio {β-dicarbonyl : olefin : $Mn(OAc)_3$} under N_2 atmosphere, at 50°C in acetic acid, products were purified by column chromatography and preparative TLC. Yields represent isolated products after chromatography, crystallization, and are based on reacted starting alkene.

2.1 Preparation of starting material

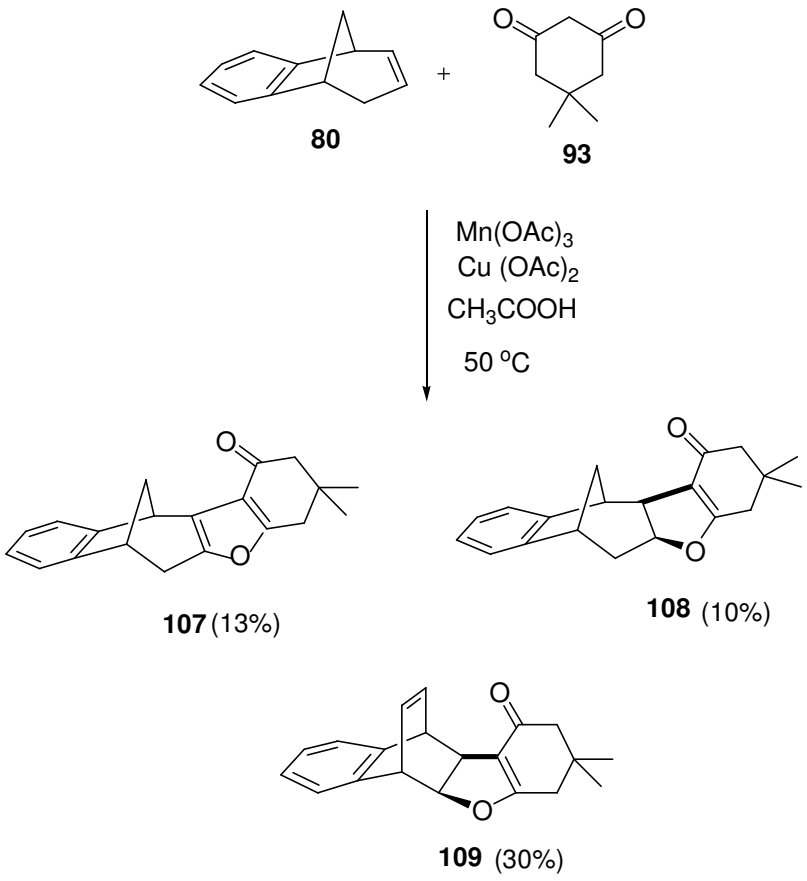
The key compound was benzonorbornadiene **72**, which is synthesized according to the literature [63], and for the synthesis of a target compound **80,** dibromocarbene was added to benzonorbornadiene **72** at -10°C. The carbene addition product **98** rearranged to allylic bromide **100**, where the ring opening is controlled by Woodward-Hoffmann rules. Reductive debromination of **100** affords benzo[6,7] bicyclo [3.2.1]octa-2,6-diene **80** [60] as shown below (Scheme 2.1).



Scheme 2.1

2.1.1. Reaction of homobenzonorbornadiene (80) and dimedone (93) with $Mn(OAc)_3$ in the presence of $Cu(OAc)_2$.

First of all we initiated the study by the oxidation of homobenzonorbornadiene **80** with a mixture of dimedone **93**, 2 equivalent of $Mn(OAc)_3$, and 1 equivalent of $Cu(OAc)_2$ in acetic acid (4h at 50 °C), and the analysis of the crude ^{1}H-NMR spectrum indicated that the reaction mixture consisted mainly of three products in the ratios of 1.25:1:1.8 respectively, with recovery of the starting material **80** (23%), these products were separated chromatographically and characterized as furan derivative **107**, dihydrofuran adduct **108,** and rearranged product **109** (major) (Scheme 2.2).

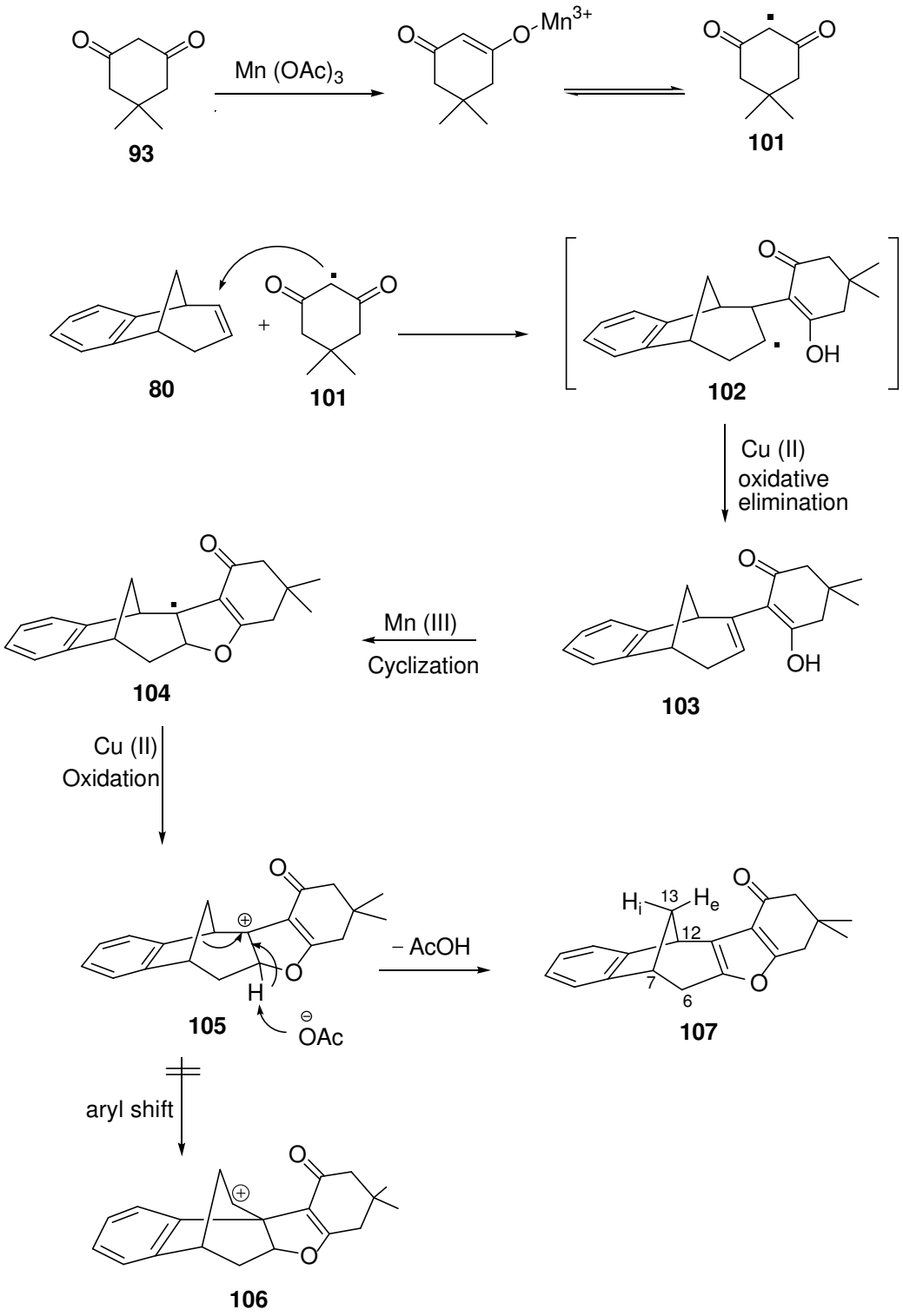


Scheme 2.2

2.1.2. The formation mechanism of Furan derivative (107).

Formation of the first isolated fraction, the unique furan derivative **107**, can be best explained by the proposed mechanism given in Scheme 2.3.

The initial step involves the oxidation of dimedone **93** by $Mn(OAc)_3.2H_2O$ affords resonance stabilized radical **101**, which rapidly adds to the double bond in homobenzonorbornadiene **80** to generate secondary radical **102**, this radical can undergo either further oxidation by the second equivalent of $Mn(OAc)_3.2H_2O$ or by $Cu(OAc)_3.2H_2O$ to a cation (which is less likely to occur in presence of copper acetate) or rapid oxidative β-hydride elimination on the reaction with copper acetate and converted to more substituted double bond **103** (Zatisev product) without the intermediacy of cation (since this is the preferred route from the reaction of Cu(II) with secondary radicals, and it is well known that the oxidation of secondary radicals to alkenes by cupric acetate is faster than Mn(III) does [55-57]. Enolization occurs to give Mn(III) enolate, which is the key of the catalytic reaction, electron-transfer with loss of Mn(II) followed by intramolecular oxidative cyclization provides tertiary carbon radical **104**, that undergoes further oxidation by Cu(II) carboxylate to give the organocopper(III) intermediate (consult Scheme 12), and then electron transfer to give a cation **105**, proton loss woud result in the formation of the furan derivative **107** (tandem product formed by double oxidation).


Mn (OAc)3
Mn3+
93
101
80
101
102
OH
Cu (II)
oxidative
elimination
103
OH
Mn (III)
Cyclization
104
Cu (II)
Oxidation
105
OAc
H
– AcOH
107
Hi
He
13
12
7
6
aryl shift
106

Scheme 2.3

According to the proposed mechanism it is important to note that the cyclization took place before second oxidation, and in view of our assumption the rearrangement of molecular skeleton can occur if the second oxidation takes place before cyclization not after. Moreover, in this reaction the rearrangement process can not take place in spite of formation of non-classical carbocation **105** which would lead to the skeleton rearrangement with accompanying aryl shift producing compound **106**. Nevertheless, it could be that the stereo electronical effects play the most influential role, and thus the aryl-shift rearrangement is prevented because of the possible formation of a highly strained structure which means that the reaction possesses a high activation energy barrier, and that is kinetically disfavored.

The molecular structure of furan product **107** was determined on the basis of the ^{1}H; ^{13}C-NMR spectral data, besides the X-ray crystallographic analyses (Fig. 2).

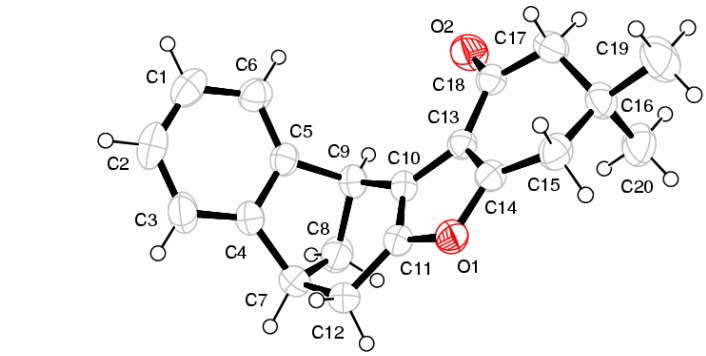
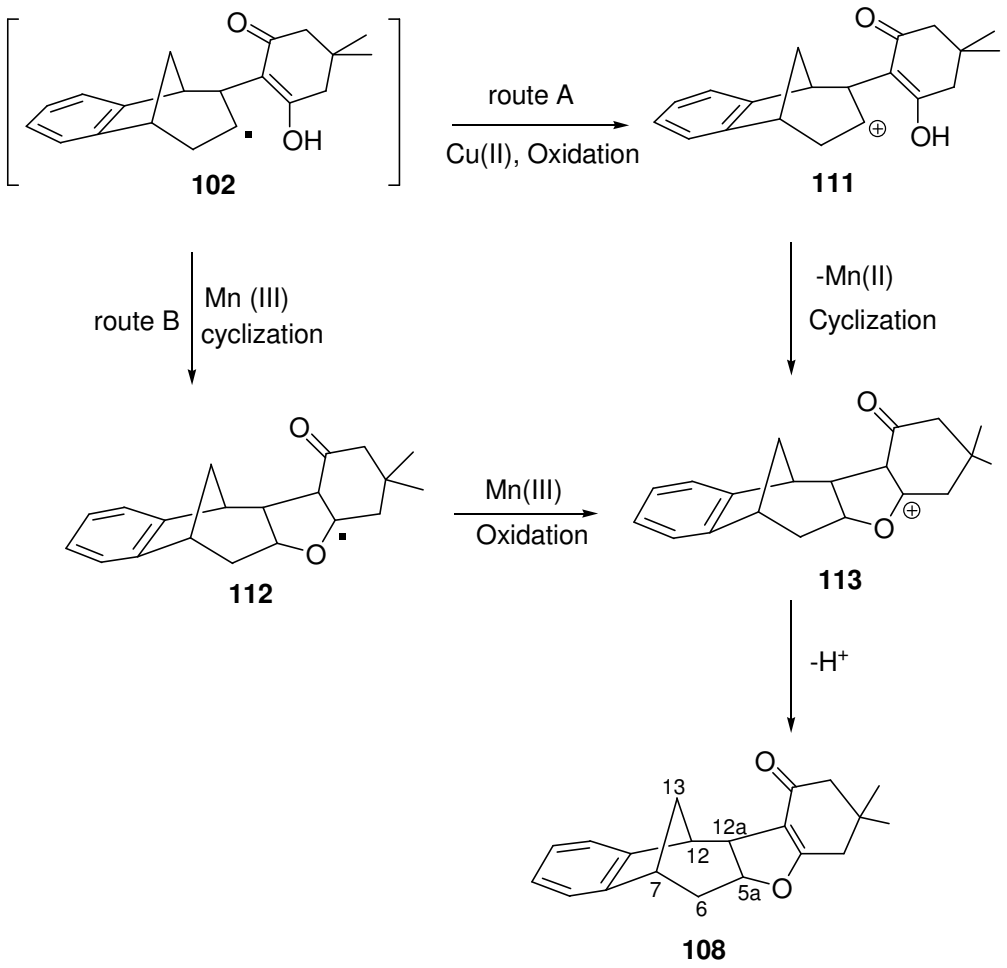


Figure 2. The X-ray crystal structure of **107**.

The ^{1}H-NMR spectrum of **107** indicated that the aromatic protons gave multiplet in the range 6.91-7.2 ppm. The protons on the bridging methylene group (C-13) possess an AB-system whose A-part, the high field resonance internal proton H_{13i} is further coupled with the adjacent bridgehead protons H_7 and H_{12} shows triplet of doublet at 2.32 ppm, doublet splitting originates from the coupling with the geminal proton H_{13e} (J= 10.4 Hz) and triplet splitting from the bridgehead protons H_7 and H_{12} ($J_{13i,7}$=$J_{13i,12}$= 4.7 Hz). However, the B-part of the system (external proton H_{13e}) shows a doublet (J= 10.4 Hz) at 1.95 ppm and does not show any coupling with the adjacent bridgehead protons H_7 and H_{12}. Inspection of Dreidings models indicates that the dihedral angle between H_{13e} and bridgehead protons H_7 and H_{12} is near 90° and that between H_{13i} and H_7 and H_{12} is near 20-30°. The bridgehead protons H_7 and H_{12} appear at 4.26 ppm as a doublet (J= 4.7 Hz, H_{12}), the splitting originates from the coupling with bridge proton H_{13i}, and at 3.5 ppm as triplet, the splittings (J= 4.7 Hz; J=5.0 Hz, H_7), arised from the coupling with bridge proton H_{13i} and from coupling with one of the adjacent methylenic protons (C-6-H_{endo}). The protons of the methylene group (C-6) resonate as an AB-system, the A-part H_{6endo} is split into a doublet of doublets at 3.0 ppm by the geminal proton H_{6exo}, further doublet splitting of doublet lines arised from the coupling with the bridgehead proton H_7 (J=15.3 Hz, J= 4.7 Hz); while the B-part of the system (H_{6exo}) is split into a doublet at 2.48 ppm (J= 15.3 Hz). The two singlet peaks at 1.10 and 1.05 ppm are arised from the two methyl groups of the dimedone ring (6H, 2 CH_3), and also the four protons of the two isolated methylene groups of the same ring show broad singlet at 2.2 and 2.5 ppm which differ from the appearance of AB-system due to the long distance between them and the unsymmetrical structure of the bridge protons that probably affects the shape of AB-system. Finally, the X-ray structure analyses of **107** confirm the structural findings. On the other hand, a twenty-line ^{13}C-NMR spectrum is in good agreement with the structure.

2.1.3. The formation mechanism of dihydrofuran adduct (108).

For formation of the second isolated minor product **108**, it can be explained by a similar mechanism proposed [60]. Thus reaction proceeds by formation of the primarily formed radical **101** (generated from 1,3-dicarbonyl compound) followed by addition to the double bond in homobenzonorbornadiene forming a new secondary radical **102**. The resulting radical **102** can undergo two pathways. Either readily oxidized by $Cu(OAc)_2.H_2O$ to the cation **111** (path a), or rapid intramolecular cyclization with the enol form to give the intermediate **112** (path b). Although the two pathways lead to the same cation intermediate **113**, under these reaction conditions oxidation of radical **102** prior to cyclization is the quite possible pathway to give tertiary cyclic cation **113**, since the oxidation will compete with the cyclization if Cu(II) is present and also it would be much faster. Finally, the acetate anion abstracts hydrogen to form the dihydrofuran adduct **108** (Scheme 2.4).



Scheme 2.4

In the light of this mechanism, if the formation of dihydrofuran occurred through path a, so the second oxidation rate will be much faster than cyclization due to the presence of copper acetate.

The formation of dihydrofuran **108** can be rationalized on the basis of the more rapid cyclization of cation **111** due to the greater enol content of dimedone, as well as the stability of the resulting carbonyl stabilized dihydrofuran product toward acid-catalyzed ring opening under reaction and work up conditions, Tarbell et al. [64].

The ^{1}H-NMR spectrum of compound **108**, exhibits multiplet in the range 6.95-7.25 ppm arising from aromatic protons (4H); the proton of the ring junction appears as doublet of doublet at 4.36 ppm (J= 8.65 Hz, 1H, H_{5a}). The first doublet splitting arises by the proton $H_{12a,}$ and further doublet splitting originated from the coupling with the endo proton of the methylene group (C-6) and there is no coupling with the exo proton of the same group due to the large dihedral angle. With respect to the other ring junction proton H_{12a} while it splits into a doublet at 3.27 ppm, which arise from the coupling with H_{5a} (J= 8.65 Hz), it does not show any measurable coupling neither with bridgehead proton H_{12} nor with the bridge protons $H_{13,}$ so this result confirms the exo-configuration of the dihydrofuran ring owing to the absence of any coupling between H_{12} and H_{12a}, and between H_{5a} and H_{6exo} on the methylene group (which assign the endo-orientation of these protons). AB-system appears at 1.72 ppm for the bridge methylene group protons $H_{13syn,}$ and H_{13anti} as doublet (J= 11.9 Hz), and the two bridgehead protons H_{12} and H_7 resonate as broad singlets at 3.7 ppm (1H, H_{12}), and at 3.0 ppm (1H, H_7), respectively. The methylene protons (C-6) resonate at 2.1 ppm as multiplet and overlapped with the AB-system arised from the two isolated methylene groups of dimedone ring at 2.2 ppm as multiplet. Lastly, the signals at 1.04 and at 1.11 ppm are arised from the two methyl protons on dimedone ring.

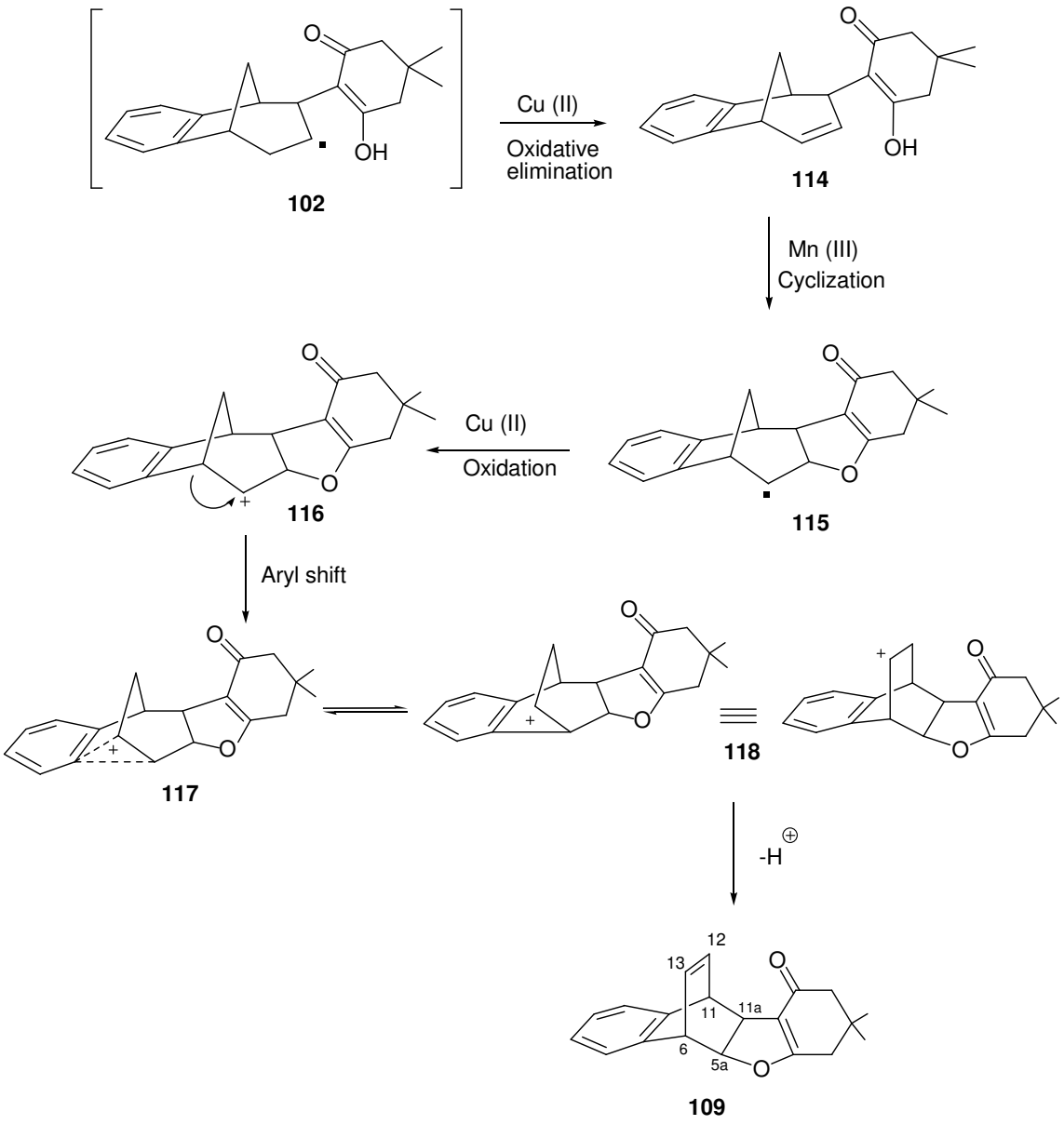
Furthermore, the ^{13}C-NMR spectral data confirmed the molecular structure of the dihydrofuran adduct **108**.

2.1.4 The formation mechanism of rearranged product (dihydrofuran) 109.

The major product (tandem product) was formed as a result of Wagner-Meerwein rearrangement. A proposed mechanism of which is given in Scheme 2.5.

The process begins with the a cyclic secondary primarily formed radical **102,** which reacts rapidly with $Cu(OAc)_3$.$2H_2O$ to give the intermediate **114** (less substituted double bond, Hoffman product), which then proceeds via oxidative cyclization by the second equivalent of $Mn(OAc)_3.2H_2O$ to afford a secondary

cyclic radical **115,** again fast oxidation by cupric acetate to the cation **116** with a high degree of nonclassical carbocation character, indicating by the extensive rearrangement to bicyclic [2.2.2] cation **117** via Wagner-Meerwein rearrangement with accompanying aryl migration that brings about the transformation of the [3.2.1] ring system into the [2.2.2] ring system. Deprotonation by acetate anion provides the rearranged product **109**.



Scheme 2.5

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The structural assignment for product **109** was based on its ^{1}H; ^{13}C-NMR spectral data in conjunction with 2D-NMR (DEPT-135 ; COSY ; HMQC ; and HMBC) experiments.

^{1}H-NMR spectrum of **109** exhibits multiplets for the aromatic protons in the range 7.05-7.24 ppm. The olefinic protons H_{12} , H_{13} split into two quasi triplets centered

at 6.44 and 6.36 ppm, respectively (J= 7.15 Hz, 2H), and the proton of the ring junction H_{5a} resonates as doublet of doublets at 4.92 ppm (J= 8.9 Hz, 1H), doublet splitting arised from the coupling with the other ring junction proton H_{11a} and further doublet originated from the coupling with bridgehead proton H_6 (J=3.7 Hz), whereas the other proton junction H_{11a} resonates at 3.34 ppm as broad doublet due to its coupling with H_{5a} (J= 8.9 Hz, 1H). The bridgehead proton H_6 gave rise to quasi triplet at 4.35 ppm originated by coupling with H_{5a} and also further coupling with olefinic proton H_{13} (J= 3.7 Hz), while the other bridgehead proton H_{11} gave broad doublet at 4.45 ppm (J= 3.9 Hz). Moreover, the four methylenic protons of dimedone ring show the presence of two AB-systems overlapped, while two of them appear at 2.13 ppm due to the neighboring carbonyl group (J=18 Hz), the other two appear at 2.1 ppm due to allylic conjunction (J=16 Hz). The two singlets at 1.12 and 1.08 ppm are due to the two methyl groups protons on the dimedone ring. Furthermore, the ^{13}C-NMR spectrum also supports the proposed structure by giving nine signals in sp^3 region and eleven signals in sp^2 region.

2.1.5. Reaction of homobenzonorbornadiene (80) and dimedone (93) with $Mn(OAc)_3$ alone.

Because of our interest, as a second goal we intended to see the effect of copper acetate on the reaction products, so we performed the oxidation of dimedone with Mn(III) acetate under the similar reaction conditions in presence of alkene **80** without the use of Cu(II) acetate, and it proceeds via a much slower reaction rate with a decrease in the yields of products (8h. at 50 °C), the dihydrofuran derivative **108** was obtained in 4% yield along with an other dihydrofuran adduct **110** (3%) with recovery of the starting material (30%) (Fig. 3).

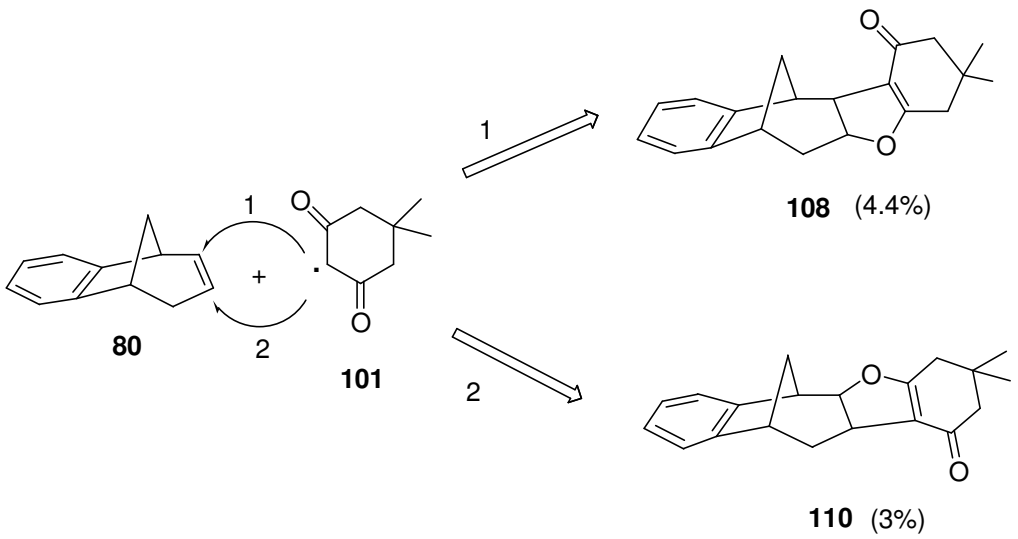
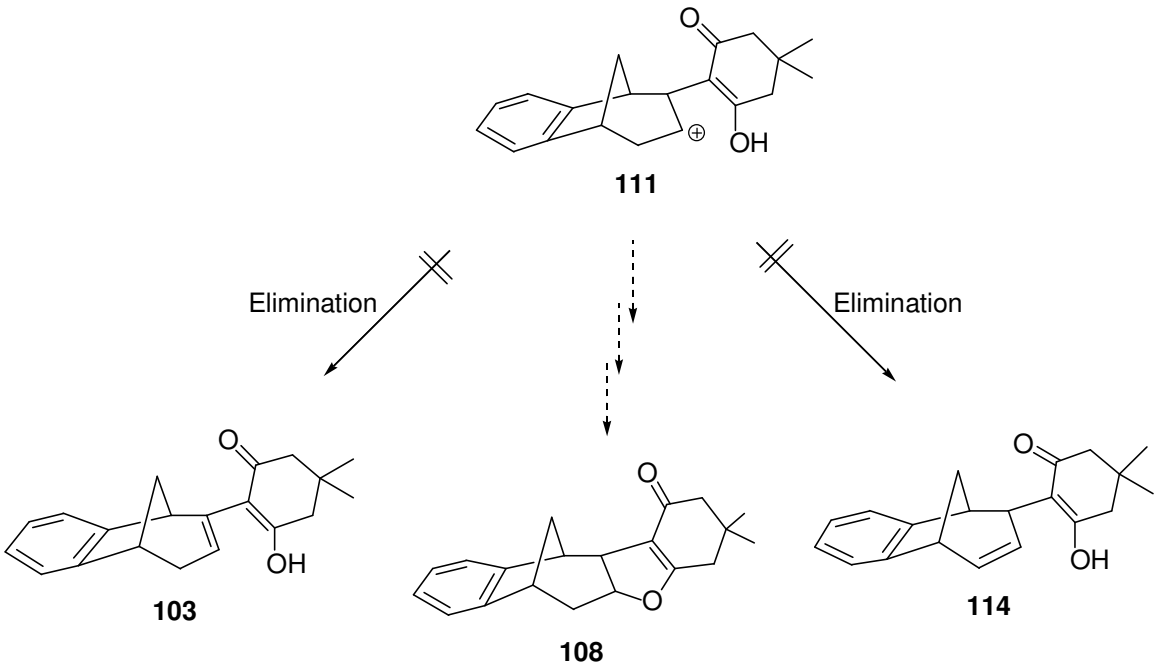


Figure 3. The dihydrofuran derivatives **108**, and **110**

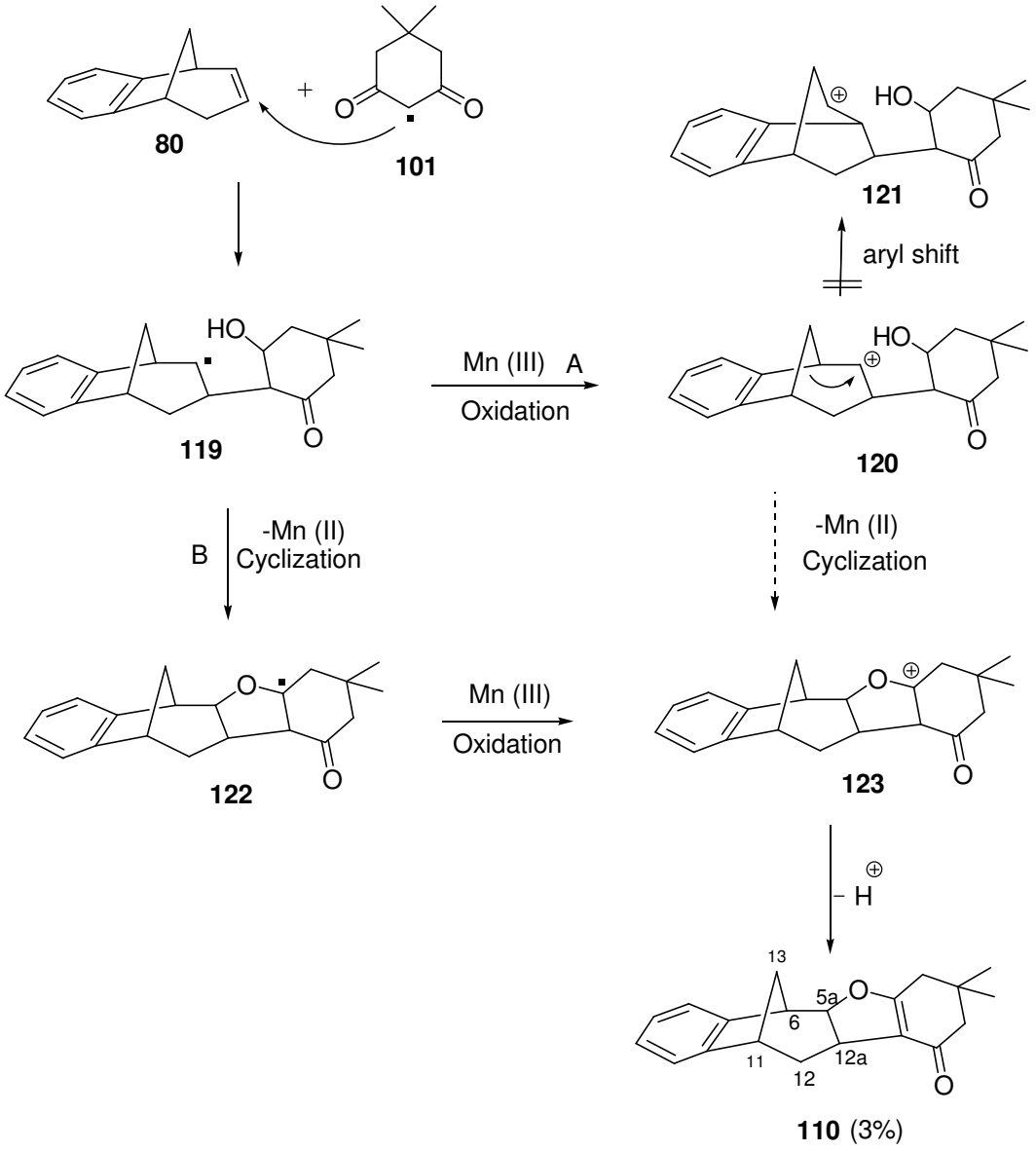
Careful examination of the reaction mixture did not reveal the formation of neither furan derivative **107** nor rearranged product **109**, since the intermediates **103** and **114** (from which products **107** and **109** are derived) (Schemes 2.3 and 2.5) resulting either from oxidative elimination of the secondary radical **102** which required the presence of copper acetate or from deprotonation of the same radical, are not formed (Scheme 2.6). Therefore, we believe that the presence of $Cu(OAc)_2$ is essential for the oxidative elimination of radical **102**, as well as for the effecting the cyclization of cationic intermediate **111** in course of rate (that lasted a much longer period), and the yields of products as well.



Scheme 2.6

2.1.6. The formation mechanism of dihydrofuran adduct (110).

We assume that the reaction mechanism of the formation of dihydrofuran product **110**, started with the primarily formed radical **101** which then adds to the double bond in homobenzonorbornadiene from a different side forming a new radical **119**, which undergoes two possible pathways: (a) oxidation by the second equivalent of $Mn(OAc)_3$ to the cation **120**. This cation would undergo aryl migration leading to rearranged product **121**. Since, on the basis of the fact that no rearranged products were observed excludes the formation of **120** as an intermediate indicating that the formation of this product might be through pathway b). (b) Undergoing intramolecular cyclization with the electron transfer of Mn(III) enolate forming tertiary radical **122**. Further oxidation by Mn(III) acetate would afford cation **123**, a proton loss would also provide product **110** (Scheme 2.7).



Scheme 2.7

The molecular structure of **110** was determined by its ^{1}H; ^{13}C-NMR spectral data in conjunction with 2D-NMR (DEPT-135; COSY; HMQC; and HMBC) experiments.

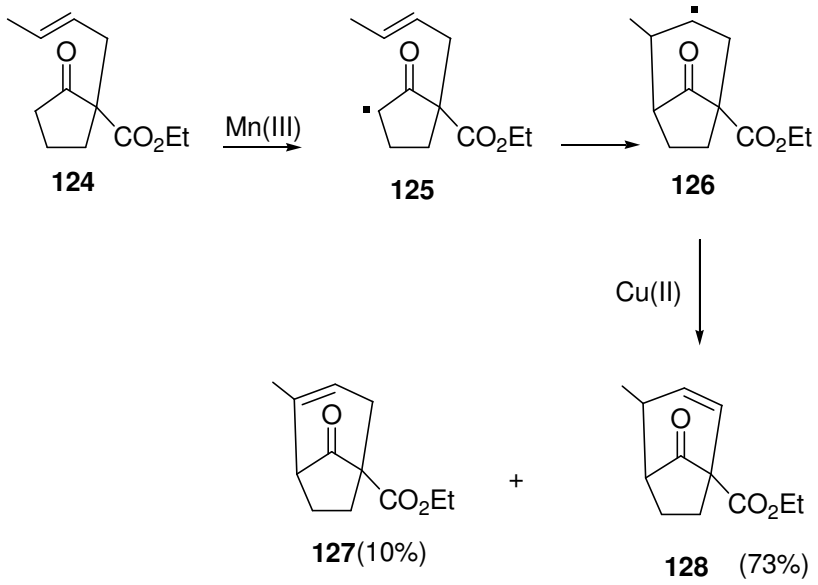
The ^{1}H-NMR spectrum of **110** shows that the phenyl protons resonate as multiplet at 7.15-7.25 ppm, and the bridging methylene protons set an AB-system, where the

B-part (H_{13e}) resonates as a doublet at 1.9 ppm (J=11.2 Hz), whereas the A-part of the system (H_{13i}) is overlapped with the AB-system of the methylene protons (C-2, C-4) of the dimedone ring.

The bridgehead proton H_{11} appears as doublet of triplet at 3.1 ppm, doublet lines arise from the coupling with the adjacent methylene proton (C-12 H_{12exo}) (J=3.3 Hz). The other bridgehead proton H_6 appears at 3.4 ppm as triplet originating from the coupling with bridge proton H_{13i} (this coupling was established on the basis of the correlations in COSY spectrum (Fig.) (J=4.0 Hz), and further coupling with the ring junction proton H_{5a} (J=3.2 Hz). The proton H-12 resonates at 1.39-1.47 ppm as doublet of doublets of doublets (H_{12exo}) doublet arising by the geminal proton (J =12.4 Hz), and other adjacent protons ($J_{12exo,H12a}$ =3.9 Hz, $J_{Hexo,H11}$=3.3 Hz). The proton (H_{12endo}) is split into a doublet by the geminal proton, H_{12exo}, (COSY spectrum shows correlation with H_{12exo}). The quasi quartet at 2.6 ppm belongs to the proton of the ring junction H_{12a} , whereas the other proton of the ring junction H_{5a} appears at 4.49 ppm as a doublet of doublets. Doublet splitting originate from the coupling with the other proton of ring junction H_{12a} (J=8.0 Hz), while the other doublet splitting originate from the coupling with the bridgehead proton H_6 (J=3.2 Hz). Finally, the four methylenic protons of dimedone ring show the presence of two AB-systems overlapped with the signals of H_{13i} and H_{12endo} at 2.13 ppm. The one singlet at 1.10 ppm belongs to the protons of the two methyl groups on the dimedone ring. Furthermore, the ^{13}C-NMR spectrum also confirms the proposed structure by giving eleven carbon signals in sp^3 region and eight carbon signals in sp^2 region, in addition to one signal of carbonyl carbon at 194.5 ppm.

Finally, on the light of these findings, we might demonstrate that first of all the unique furan derivative **107** was obtained where the cyclization occurred before the second oxidation. Secondly, the reaction carried out with the presence of Cu $(OAc)_2$ led to the formation of less substituted double bond, intermediate **114** by rapid oxidative β-hydride elimination of radical **102**, and brought about the formation of rearranged product. Furthermore copper acetate is necessary since the

secondary radicals are oxidized faster by copper acetate than by $Mn(OAc)_3$, so that reaction carried out without copper acetate shows a decrease in the rate and in the yield of reaction as well. What is more, the rearranged product **109** was indeed formed in the higher yield among the counter product **107** suggests that oxidative elimination by copper acetate is a regiospecific reaction [65]. Snider et al [66] have found that the oxidative elimination of radical **126** takes place on the less hindered side of this radical **126**, giving the less substituted double bond **128** (Hoffmann product) in high yield (Scheme 2.8).

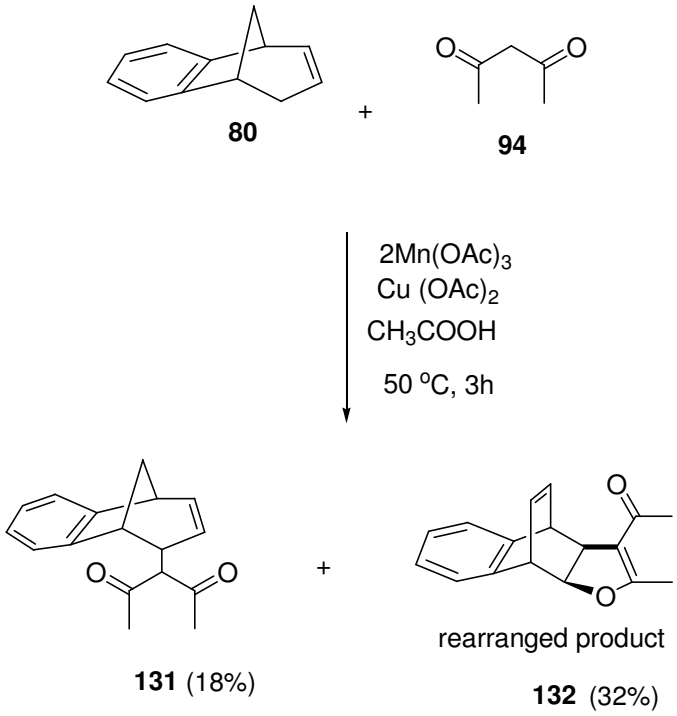


Scheme 2.8

Similarly our results gave the rearranged product **109** which derived from the less substituted double bond intermediate in higher yield comparatively with the yield of product **107** that derived from the more substituted alkene **103** (Scheme 2.3).

2.2. Reaction of homobenzonorbornadiene (80) and acetylacetone (94) with $Mn(OAc)_3$ in the presence of $Cu(OAc)_2$.

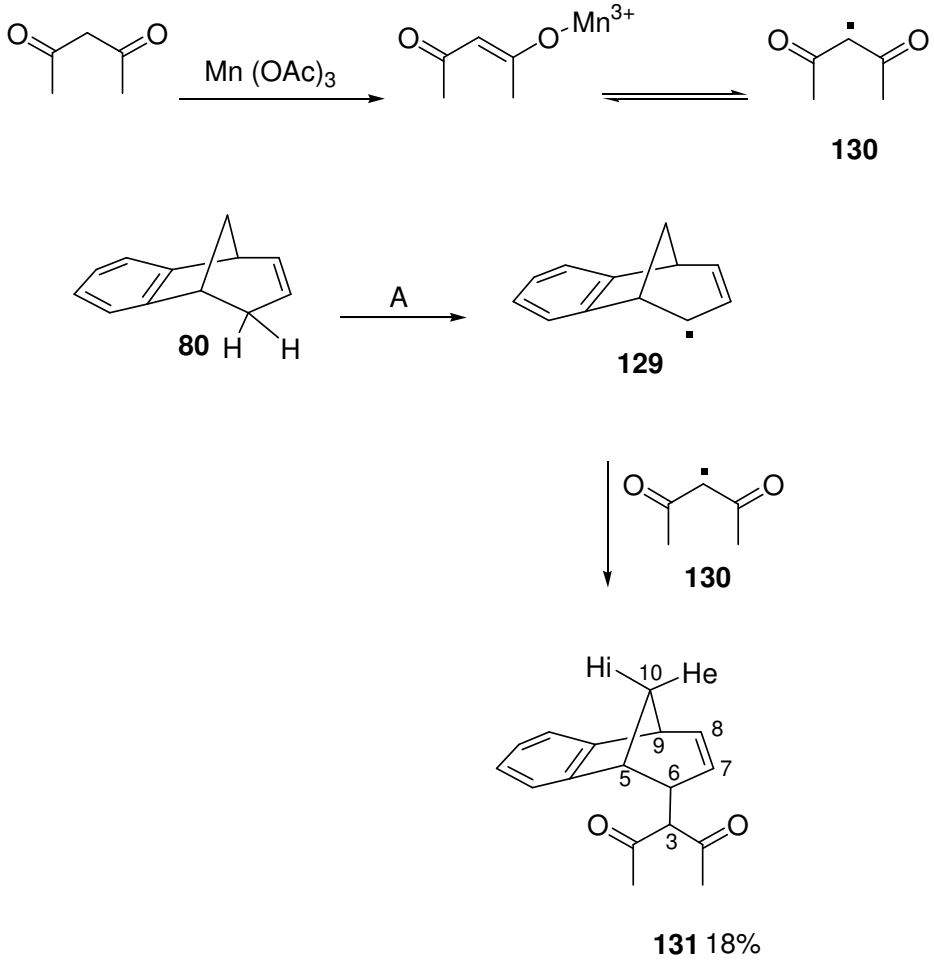
In the next step of this study acetylacetone compound **94** was chosen as a model compound to explore the reaction. The corresponding reaction of alkene **80** with acetylacetone, 2 equivalent $Mn(OAc)_3.2H_2O$ and 1 equivalent $Cu(OAc)_2$ in acetic acid for 3h gave two major separable products, oxidative product **131** and rearranged product **132** in ratio of 2 : 2.5 respectively, (Scheme 2.9), and unreacted alkene was recovered in (20%).



Scheme 2.9

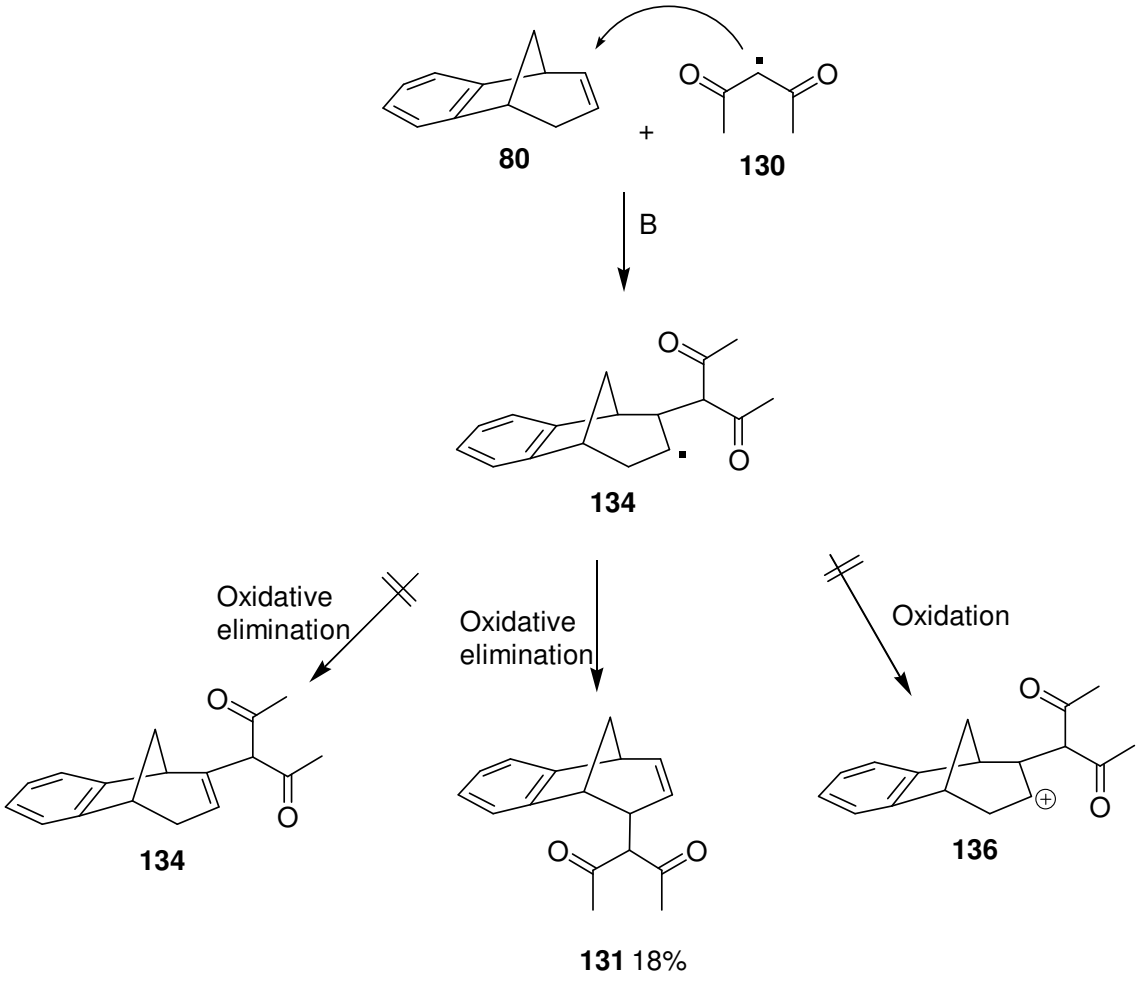
2.2.1. The formation mechanism of oxidative product (131).

Formation of product **131** occurs in the presence and absence of cupric acetate, as illustrated in the following mechanism through two possible routes (Scheme 2.10 A and Scheme 2.11 B). The process (a) was thought to involve the allylic radical **129**, which formed by removing of allylic-H from homobenzonorbornadiene **80** under the reaction conditions, followed by reaction of allylic radical **129** with the primarily formed radical **130** (generated from the acetylacetone) providing a new carbon-carbon bond, product **131** (Scheme 2.10).



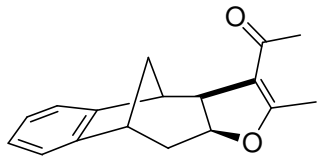
Scheme 2.10

The process (b) may proceed through the initial reaction of electrophilic Mn(III) acetate with the nucleophilic enol form of acetylacetone **94** to provide stabilized radical **130**, which reacts smoothly with electron rich alkene **80** giving a cyclic secondary radical **134**, which also leads to the formation of product **131** either through facile β-hydride elimination by $Cu(OAc)_3.2H_2O$ (Scheme 2.11), or through Mn(III) oxidation giving cation **136** followed by deprotonation.



Scheme 2.11

It is important to note that a remarkable difference between the mechanisms shown in Scheme 2.10 and 2.11 which led to the formation of the oxidative product **131** is in the first oxidation step. In the former process, the alkene **80** was oxidized preferentially that led to the allylic alkylation reaction of homobenzonorbornadiene, whereas in the latter process the reaction proceeded typically. Furthermore, in the reaction run with the copper acetate, we did not observe any trace amount of dihydrofuran product **133** {formed upon the reaction with acetylacetone in absence of Cu(II)}, which strongly means that the formation of oxidative product **131** did not proceed through the cationic intermediate (**136**) which leads to dihydrofuran product **133** in the reaction run in the absence of copper acetate (Scheme 2.15).



133

This observation suggests that the oxidative addition product **131** is quiet probably formed through route A (Scheme 2.10). Moreover, the absence of more substituted alkene (**135**) which would result from the oxidative elimination of radical **134** on the reaction with Cu(II) acetate {having structure similar to that of **103** resulted from the reaction using dimedone (see Scheme 2.3)}, unlike dimedone which undergoes complete enolization that can be in conjugation with the new formed double bond. Acetylacetone is not extensively enolized, so that it could be the prior reason for absence of such intermediate indicating that the oxidative elimination steps in these two reactions are different. The structure of product **131** was characterized according to ^{1}H; ^{13}C-NMR spectrum in conjunction with 2D-NMR (DEPT-135; COSY; HMQC and HMBC) experiments. The ^{1}H-NMR spectrum revealed the presence of ten sets of signals: multiplet at 7.33 ppm for one aromatic proton, and the other three appear also as multiplet in the range 7.04-7.16 ppm. The bridging methylene protons (C-10), one appears at 2.22 ppm as a doublet of

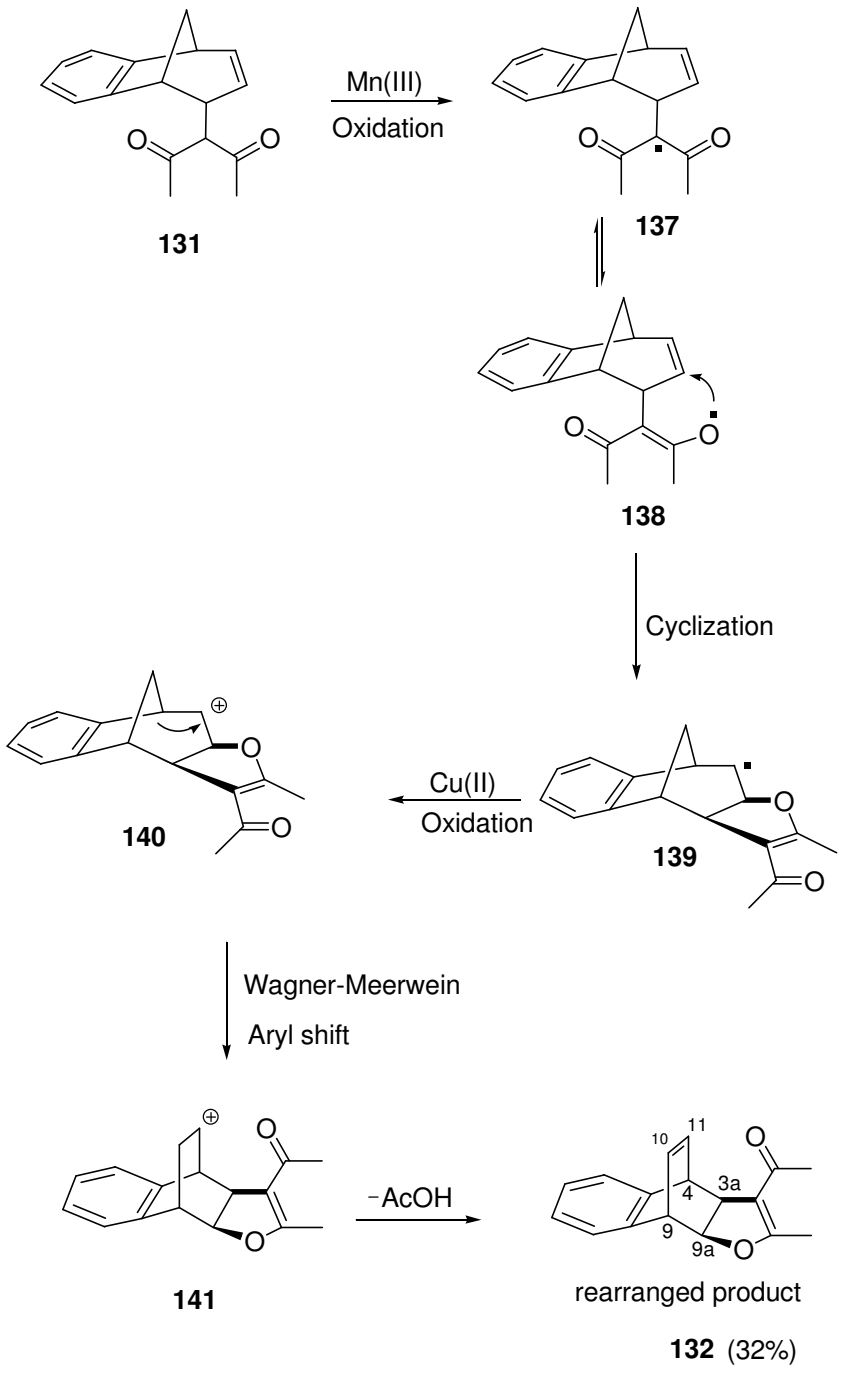
doublet (J=10.4 Hz, J=4.6 Hz, H_{10i}), doublet splitting due to coupling with the geminal proton (J=10.4 Hz) and further doublet arised by the bridgehead proton H_5 (J= 4.6 Hz), whereas the external proton H_{10e} does not show any coupling with the bridgehead protons due to the large dihedral angle, so it appears as a doublet at 1.98 ppm split by the geminal proton H_{10i} (J=10.4 Hz). The bridgehead proton H_9 resonates at 3.4 ppm as doublet of doublets coupled by one of the olefinic protons H_8 (J=7.2 Hz) and by H_{10i} (J= 4.6 Hz), and the other bridgehead proton H_5 appears as doublet at 2.85 ppm split by bridge proton H_{10i} (J= 4.6 Hz). Additionally, the resonance signal of the olefinic proton H_7 gives multiplet at 4.95 ppm while the other olefinic proton H_8 resonates at 6.24 ppm as quasi triplet (J=16.2 Hz, J=7.2 Hz). The methine proton on C-3 appears at 3.91 ppm as a doublet due to coupling with the methine proton on C-6 (J=11.0 Hz), and the signals at 2.99 ppm belong to H_6 resonating as doublet of doublets. Doublet splitting originates by coupling with adjacent methine proton H_3 (J=11.0 Hz) and further doublet splitting by the double bond proton H_7 (J=1.45 Hz). The two singlets at 2.4 and 2.2 ppm belong to the two methyl groups. The ^{13}C-NMR spectrum of this molecule consists as expected of seven lines in the sp^3 region and nine lines in the sp^2 region confirm the structure of the molecule.

2.2.2. The formation mechanism of rearranged product (dihydrofuran, 132).

This rearranged product is produced via a Wagner-Meerwein rearrangement.

For formation of the rearranged product **132**, we assume that **131** was formed first which was then transferred into the rearranged product. The reaction mechanism presumably proceeds via the formation of Mn(III) enolate (formed upon the oxidation of product **131** with Mn $(OAc)_3$), which then loses Mn(II) by one-electron transfer (OET) to give the tertiary radical **137**, which isomerizes into electrophilic oxy radical **138**, and then this oxy radical undergoes intramolecular oxidation of the double bond to afford a cyclic secondary radical **139**. Further rapid oxidation by $Cu(OAc)_3.2H_2O$ forms a carbocation **140**, which is prone to rearrangement accompanying aryl shift leading to the formation of bicyclic [2.2.2]

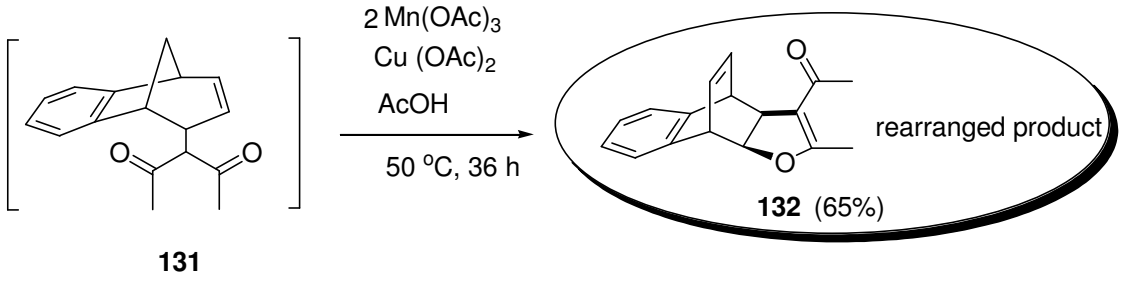
ring system carbocation **141**, deprotonation of the resulting carbocation **141** can afford product **132** (Scheme 2.12).



Scheme 2.12

To the best of our knowledge, the formation of this type of radical (oxy radical **138**), that would oxidize the double bond, in the manganese(III) acetate-mediated reaction with alkenes has never been reported before, and it could be considered as a new approach in the modified Mn(III) acetate-mediated reactions.

In order to prove our proposed mechanism and to make clear evidence which supports that the rearranged product **132** is indeed derived from the former product **131**, we next examined the mode of reaction of compound **131**. We found that treatment of product **131** with $Mn(OAc)_3.2H_2O$ and $Cu(OAc)_2$ in acetic acid for (36h at 50°C), gave the rearranged product **132** (Scheme 2.13), and this experiment proves that compound **131** might be an intermediate for the formation of rearranged compound **132**, although the reaction of **131** giving **132** required a longer period of heating than that (3h) for the direct formation of **132** from homobenzonorbornadiene **80**. Now we conclude that the two rearranged products **109** and **132**, resulting from the reaction of alkene **80** with dimedone and acetylacetone, are obviously derived from the similar intermediates (less substituted double bond).



Scheme 2.13

The structure of **132** was determined on the basis of its ^1H; ^{13}C-NMR spectral data. Further supporting by the X-ray crystallographic analyses (Fig. 4).

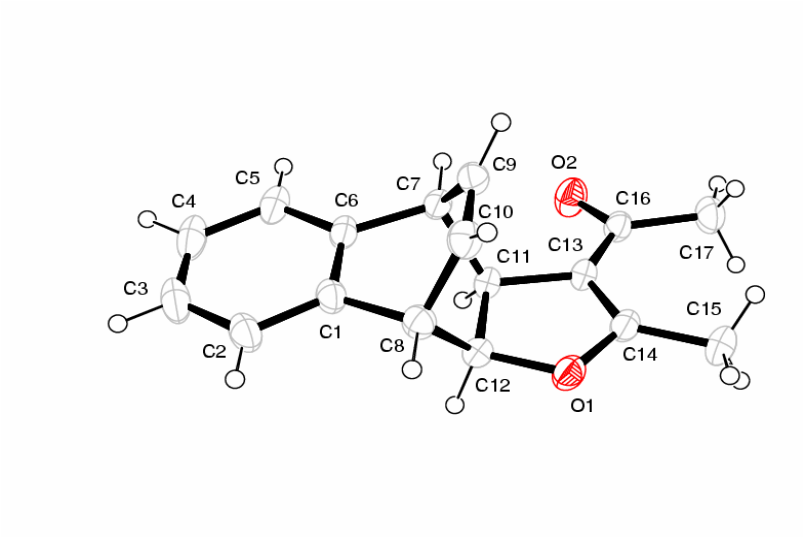
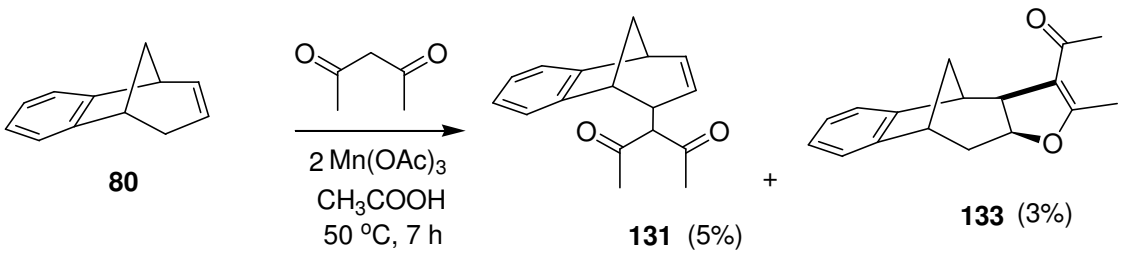


Figure 4. The X-ray crystal structure of **132**.

^{1}H-NMR spectrum of **132** exhibits multiplet system arising from the aromatic protons in the range 7.02-7.24 ppm. The olefinic protons H_{10} ; H_{11} split into two quasi triplets centered at 6.43 and 6.34 ppm respectively, (J=6.85 Hz, 2H), and the proton of the ring junction H_{9a} resonates as doublet of doublets at 4.74 ppm (J=9.3 Hz, 1H), doublet splitting arised from the coupling with the other ring junction proton H_{3a} and further doublet originated from the coupling with bridgehead proton H_9 (J=8.3 Hz), whereas the proton H_{3a} resonates at 3.36 ppm as broad doublet due to its coupling with H_{9a} (J=9.3 Hz, 1H). The bridgehead proton H_9 gave rise to triplet at 4.3 ppm originated from coupling with H_{9a} (J=8.3 Hz) and also further coupling with olefinic proton H_{10} (J=5.5 Hz), and the other bridgehead proton H_4 gave broad doublet at 4.34 ppm (J=3.9 Hz). Moreover, The two singlets at 2.12 and 2.25 ppm are arised from the two methyl groups protons. Furthermore, the ^{13}C-NMR spectrum also supports the proposed structure by giving six signals in sp^3 region and eleven signals in sp^2 region.

2.2.3. Reaction of homobenzonorbornadiene (80) and acetylacetone with $Mn(OAc)_3$ in absence of $Cu(OAc)_2$.

We also performed the reaction of homobenzonorbornadiene **80** with acetylacetone **94** under similar reaction conditions in absence of $Cu(OAc)_2$ and it lasted 7h, oxidative product **131** and a dihydrofuran product **133** were obtained in ratio of (1.5:1) respectively, with recovery of alkene **80** (35%) (Scheme 2.14) and no rearranged product could be found.



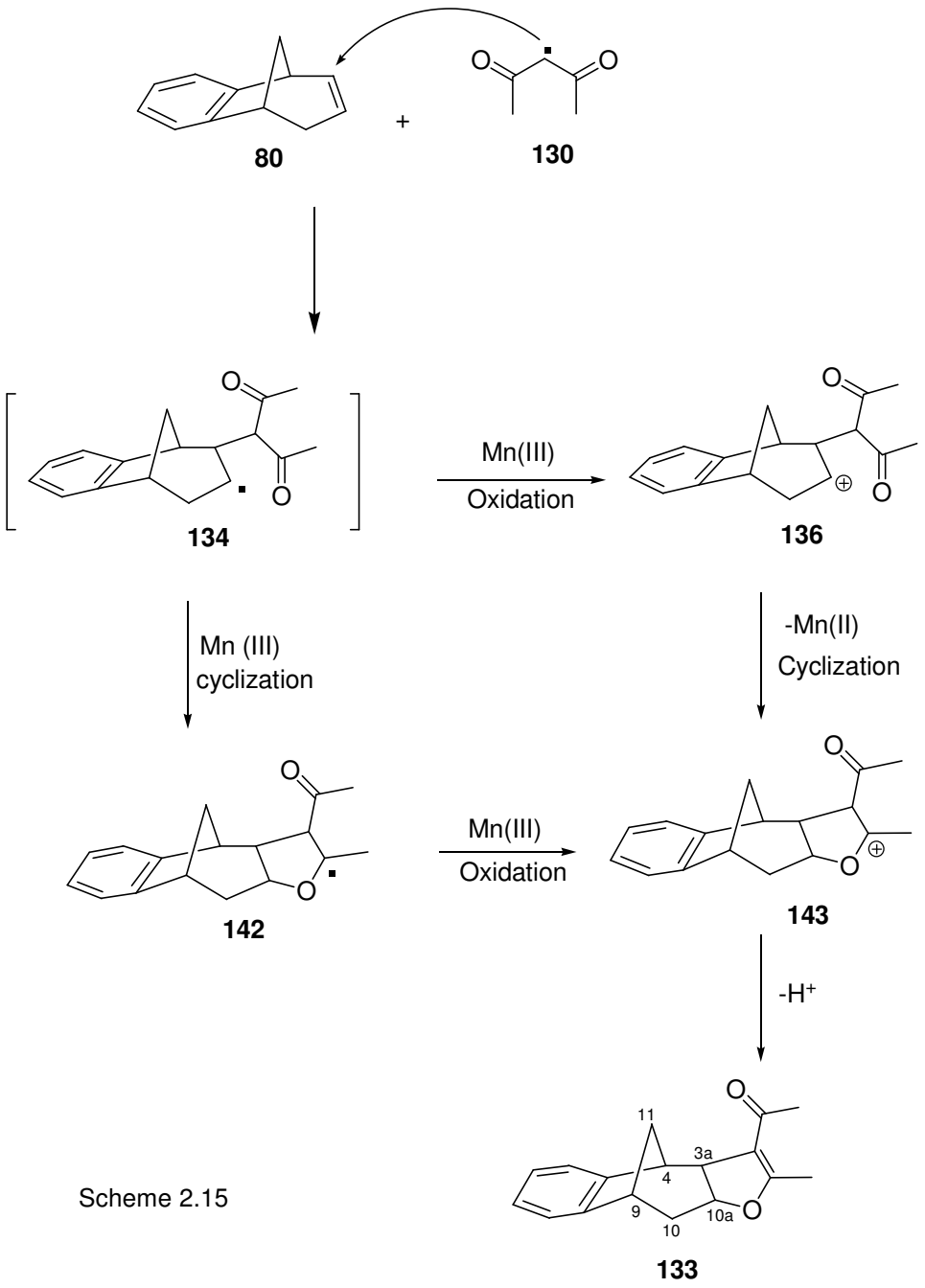
Scheme 2.14

2.2.4. The formation mechanism of dihydrofuran derivative 133.

The proposed mechanism of the formation of dihydrofuran derivative **133** is shown in Scheme 2.15.

The process started with the initially formed a secondary radical **130** (generated from the acetylacetone) that adds to the double bond in homobenzonorbornadiene producing a new radical **134**, which undergoes two possible routes: either by slow oxidation with the high valent metal ion providing cation **136**, which then was attacked by the oxygen lone pair to form a cyclic product **143** followed by deprotonation by acetate anion yielded the dihydrofuran derivative **133**, or by radical oxidative cyclization to the carbonyl group afforded tertiary radical **142** that

is first oxidized to a cation **143** by Mn(III) and then hydrogen elimination to give product **133** (Scheme 2.15). The structure of dihydrofuran adduct **133** was established by its ^{1}H; and ^{13}C-NMR spectral data which confirmed the proposed structure.

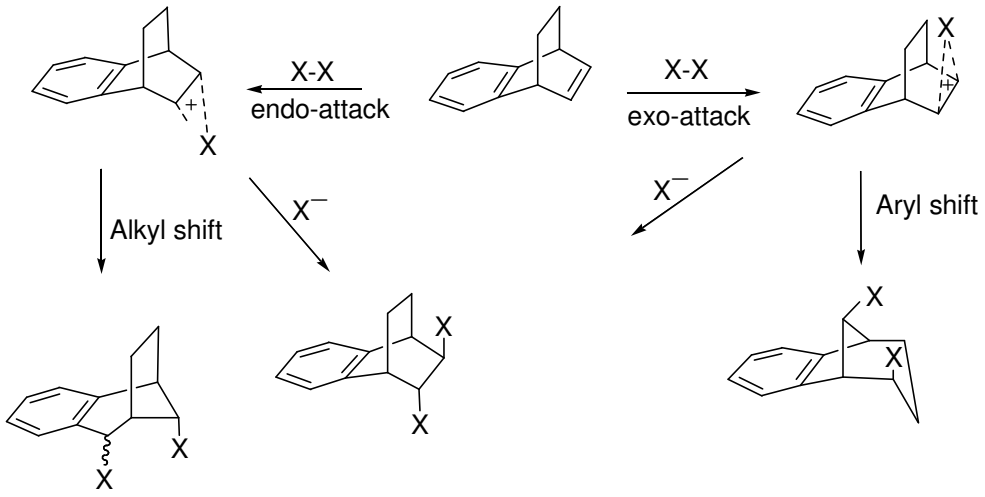


Scheme 2.15

These results were interpreted to mean that copper acetate is necessary to success the reaction so as to form aryl shift products **109** and **132**, since these products were not observed in the outcome reaction carried out without $Cu(OAc)_2$, besides, acceleration the rate of reactions. Moreover, it was expected the formation of oxidative product **131** by hydrogen elimination of cation **136** (Scheme 2.15). Yet, this cation proceeds via slow intramolecular cyclization to produce dihydrofuran **133**, so product **131** might not be resulted from this intermediate. Also the formation of dihydrofuran **133**, which was not found in the reaction done in presence of copper acetate, is strongly confirms that the formation of oxidative product **131** was by the oxidative elimination of radical **134** with out preceding of cation intermediate. Furthermore, the absence of more substituted alkene product **135** which would result from the oxidative elimination of radical **134** on the reaction with Cu(II) acetate {having structure similar to that of **103** (Scheme 2.3)}, unlike dimedone which undergoes complete enolization that can be in conjugation with the new formed double bond, acetylacetone is not extensively enolized so that it could be the prior reason of absence of a such intermediate indicating that the oxidative elimination steps in these two reactions are different. Additionally, our results obtained from the all reactions carried out without the use of copper acetate are differ from that reported in other studies [58] which revealed that the secondary radicals may either terminated by manganic acetate reductively or be oxidized to cations which upon deprotonation gave alkenes, whereas in our study the secondary radicals formed in the reaction carried out in absence of Cu(II) acetate were converted to cations on the reaction with Mn(III) acetate and then cyclized oxidatively giving different dihydrofuran products, while the alkenes resulting from the oxidative elimination steps were not formed.

Finally, we assume that all cyclic radicals were converted to the final products with equal efficiency and these products were stable to the reaction and work up conditions as well as during the separation on the silica gel chromatography.

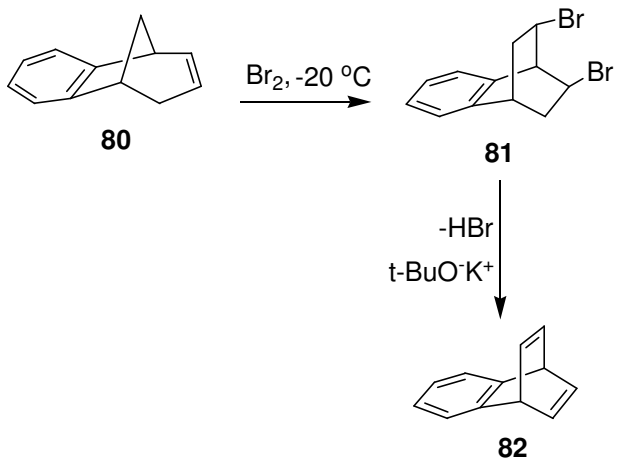
In a second bicyclic system, we examined the oxidation of benzobarrelene **82** with manganese acetate in presence and in absence of cupric acetate. Benzobarrelene **82** is a molecule of considerable potential mechanistic interest. It has been shown that electrophilic addition to bicyclic systems such as **82** can lead to a multiplicity of products [67]. Attack on the double bond may be endo or exo, and the intermediate may react with nucleophile to give non-rearranged products or undergo Wagner-Meerwein rearrangement involving either aryl group or alkyl bridge before reacting to give rearranged products (Scheme 2.16) [68].



Scheme 2.16

Balci et al. [58] have reported that bromination of benzobarrelene **82** at low and high temperatures, while bromination at low temperature benzobarrelene gave 100% rearranged products arising from alkyl and aryl shifts via Wagner-Meerwein rearrangement, bromination at high temperature gave rearranged and non-rearranged products in a ratio of 1:1

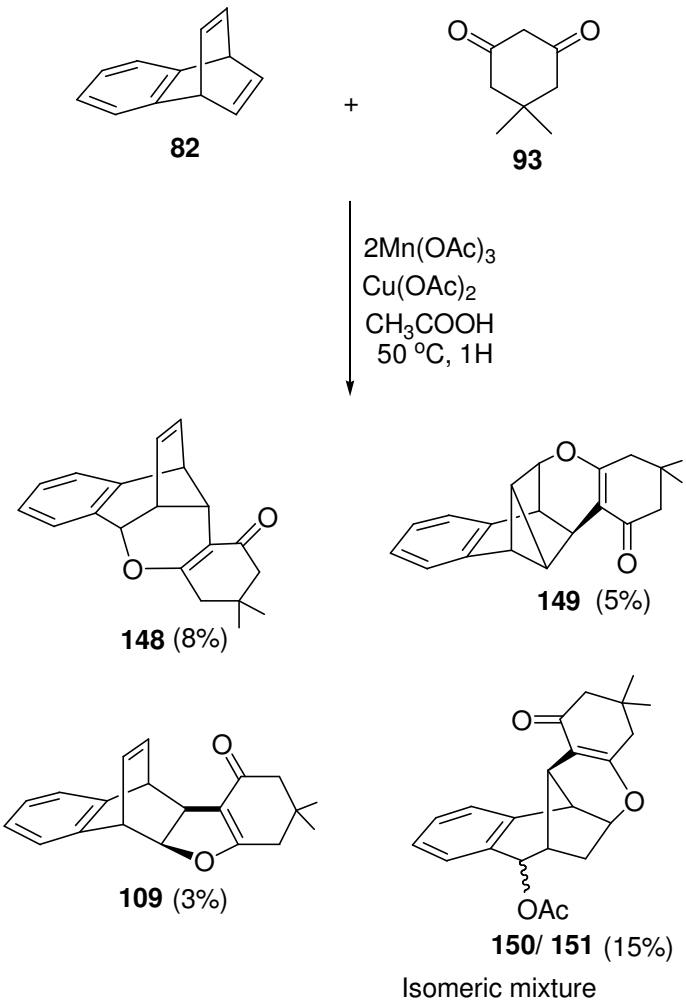
The starting material, benzobarrelene **82**, was prepared according to the published methode [60] as shown in Scheme 2.17.



Scheme 2.17

2.3. Reaction of benzobarrelene (82) and dimedone (93) with $Mn(OAc)_3$ in the presence of $Cu(OAc)_2$.

The oxidative free-radical addition of a mixture of 2 equivalent of $Mn(OAc)_3.2H_2O$, 1 equivalent of $Cu(OAc)_2.2H_2O$, and dimedone in acetic acid (1h at 50°C) to benzobarrelene **82** resulted in formation of five different products in a ratio of 1.5 : 2 : 1: 2 : 4 (Scheme 2.18) along with unreacted alkene was recovered in 4% yield. Column chromatography allowed us to isolate two separable rearranged products (**148**, **149**) and a dihydrofuran derivative (**109**), besides, a mixture containing two major rearranged isomers (**150/151**) in a ratio of 1 : 2, which were separated by fractional crystallization.



Scheme 2.18

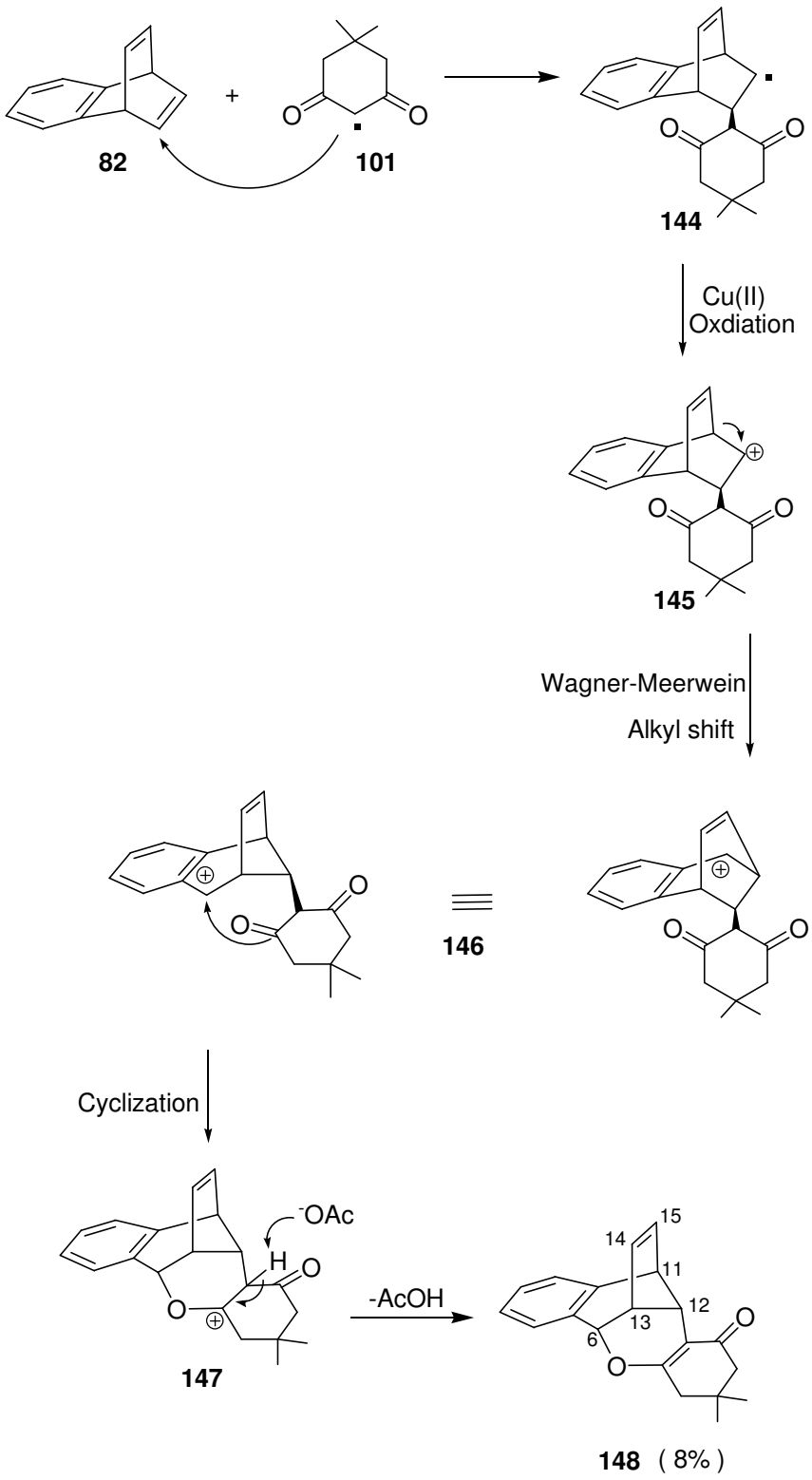
Structural determination of these products (**148**, **149**, and **150**, **151**) revealed that the barrelene skeleton was rearranged completely via Wegner-Meerwein rearrangement with alkyl shift process under action of Mn(III)-initiated oxidative free-radical reactions. However, with careful examination of the isolated fractions we could not found any trace amount of rearranged products resulting from aryl migration process, and as a result we assumed that the free-radical additions to the double bond in the hydrocarbon **82** was from the endo-face.

2.3.1. The formation mechanism of product 148.

Generally a positive charge when placed on the double bond of benzobarrelene **82** induces a Wagner-Meerwein rearrangement and transforms the [2.2.2] ring system into the [3.2.1] ring system that can react with a nucleophile to give the products.

This compound **148** is formed as a result of Wagner-Meerwein rearrangement accompanying alkyl migration. The formation mechanism is outlined in Scheme 2.19. We propose that the process begins with the radical **101** which formed from dimedone **93** by action with $Mn(OAc)_3.2H_2O$ and $Cu(OAc)_2.2H_2O$ through a single electron transfer (SET) reaction. This radical then undergoes endo-electrophilic addition to the double bond in benzobarrelene **82** producing a new cyclic radical **144** (radical intermediates are much less likely to rearrange) [69], the next step is the oxidation by Cu(II) acetate provides intermediate **145** with a high degree of nonclassical carbocation character, that proceeds via Wagner-Meerwein rearrangement to alkyl shift cation **146**. At this stage we assume that addition of radical **101** has occurred from the endo-face of the double bond, and the driving force of this mode of addition is probably the secondary orbitals interactions between the aromatic ring and the carbonyl groups.

The formation of product **148** was thought to occur by a nucleophilic attack of oxygen lone pair on the precursor cation **146** leading to a cyclic product **147**, and then the acetate anion abstracts acidic hydrogen from **147** to give the first rearranged compound **148**.


82
101
144
Cu(II)
Oxdiation
145
Wagner-Meerwein
Alkyl shift
146
Cyclization
-OAc
147
-AcOH
148 (8%)

Scheme 2.19

The structure assignment of compound **148** follow mainly from ^{1}H and ^{13}C-NMR data, and further elucidation was accomplished by 2D-NMR (DEPT-135; COSY; HMQC and HMBC) experiments.

Analysis of the ^{1}H-NMR spectrum of the molecule **148** shows that protons of the phenyl group give multiplets, one proton appears at 6.8 and the other three in the range 6.96-7.11 ppm. The olefinic protons $H_{15,}$ shows resonance at 5.83 ppm as a doublet of doublets, doublet splitting arised by coupling with a vicinal proton H_{14} (J=5.7 Hz) and further coupling to the bridgehead proton H_{11} (J= 3.2 Hz). The olefinic proton H_{14} also appears as a doublet of doublets at 6.58 ppm by coupling with the vicinal proton H_{15} (J= 5.7 Hz) further coupling with the bridgehead proton H_{13} (J=3.1 Hz). The signal of the bridgehead proton H_{13} at 2.68 ppm is seen to be simplified to doublet of triplets, it is split into doublet by ring junction proton H_{12} (J= 4.5 Hz), besides being coupled to olefinic proton H_{14} and methine proton H_6 this generated its doublet of triplet patterns ($J_{13,14}$=3.1 Hz, $J_{13,6}$=2.3 Hz). The resonance signal of methine group proton H_6 at 5.06 ppm is split into doublet by the adjacent bridgehead proton H_{13} (J=2.3 Hz), and the ring junction proton H_{12} gives rise to triplet at 3.24 ppm by coupling with two bridgehead protons H_{13} and H_{11} ($J_{12,13}$= 4.5 Hz, $J_{12,11}$= 4.3 Hz). The other bridgehead proton H_{11} gives triplet at 3.52 ppm due to coupling with olefinic proton H_{15} (J= 3.2 Hz) and by coupling with the proton H_{12} (J= 4.3 Hz). Moreover, the two methylenic groups of dimedone ring appear as a pair of AB-systems overlapped, while two of them appear at 2.13 ppm (low field) due to the neighboring carbonyl group (J= 18 Hz), the others appear at 2.1 ppm (high field) due to allylic conjunction (J= 16 Hz). The two singlets at 0.94 and 0.61 ppm are due to the protons of two methyl groups on the dimedone ring.

Furthermore, the ^{13}C-NMR spectrum also supports the proposed structure by giving nine carbon signals in sp^3 region and ten carbon signals in sp^2 region, in addition to one signal of carbonyl carbon at 196.4 ppm.

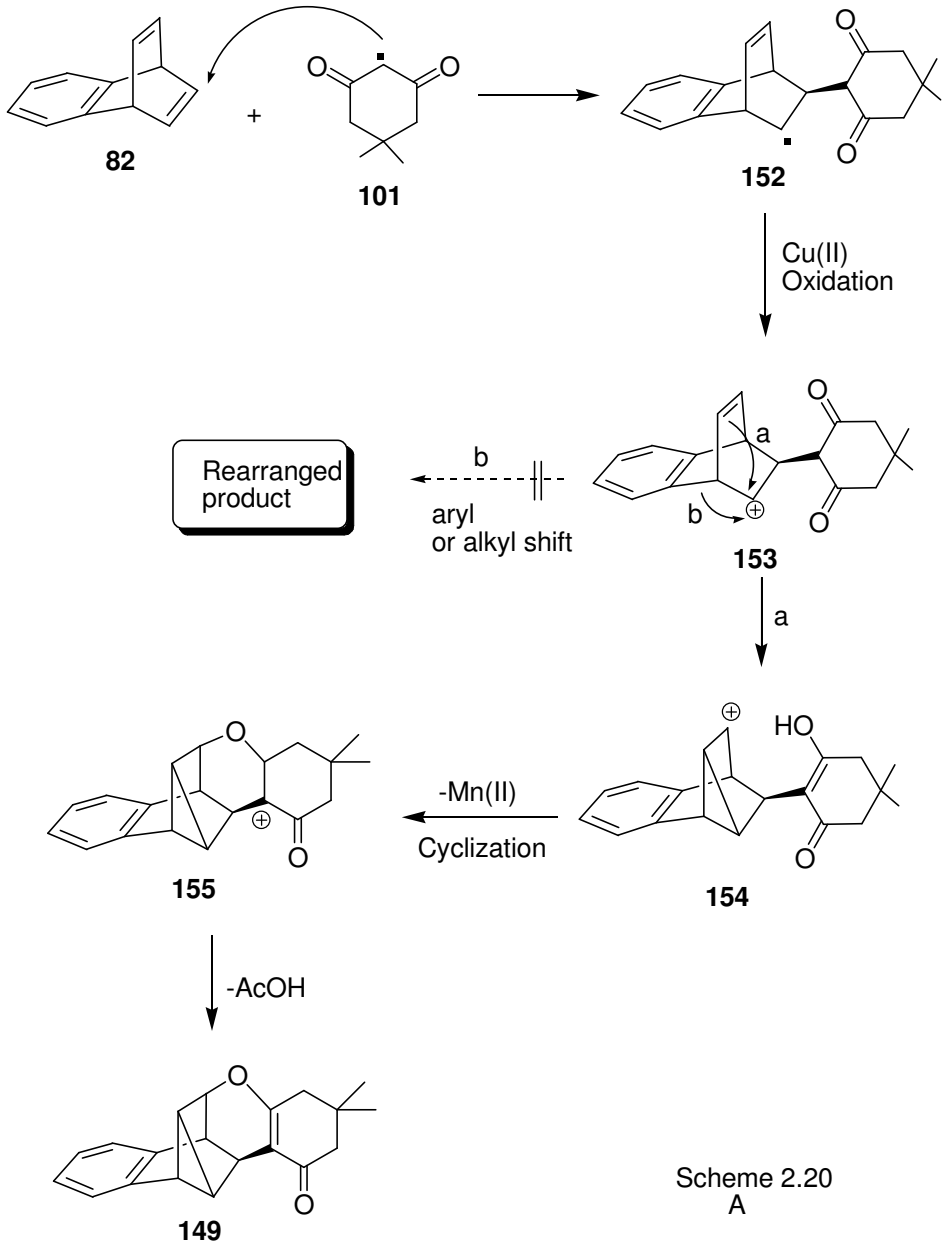
2.3.3. The formation mechanism of rearranged product 149.

The proposed mechanism for formation of product **149** is fully understood, and may occur through two possible pathways for a rearrangement. The two pathways are depicted in Scheme 2.21 A and B.

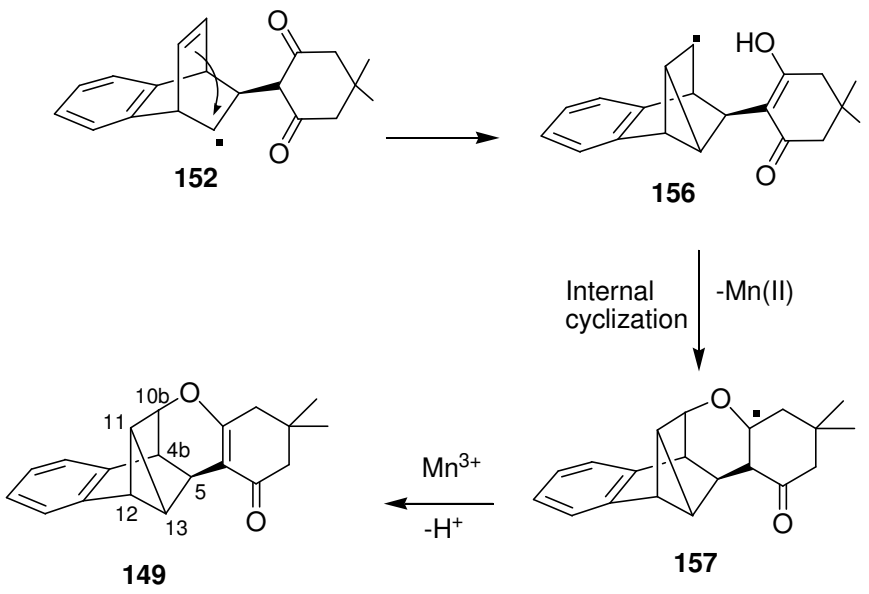
We propose that the initially formed radical **101** can add to the double bond in benzobarrelene **82** from the exo-face to form a cyclic radical **152** that undergoes two competing reactions. (1) Oxidation by $Cu(OAc)_2$ led to nonclassical carbocation **153**. At this stage cation **153** is expected to rearrange accompanying alkyl or aryl migration (since the second oxidation took place before cyclization) as we have previously observed. In contrast to that, in this reaction cationic intermediate **153** was attacked by the electron rich center (double bond participation) introducing cyclopropane ring within a new cationic intermediate **154** which could cyclized on to the enol form of dimedone to give the product **155** followed by deprotonation to yield the product **149** in 5% yield as shown in Scheme 2.20 A. (2) Radical **152** undergoes rapid double bond participation (before second oxidation to take place) to form cyclic propane within a new radical **156**, and the next step could involve cyclization leading to β-keto radical **157** followed by oxidation, and deprotonation which would also give product **149** as demonstrated in Scheme 2.20 B.

Since the formation of highly strained cyclopropane ring would be accompanied with a high energy barrier, and so that the system kinetically discourages the formation of the rather strained ring and tends to escape from a such process, thus cation **153** should have to proceed via Wagner-Meerwein rearrangement (instead of double bond participation) which brings about the formation of alkyl or aryl shift product where cyclopropane ring would not be found, but a such rearranged product was not observed, it is therefore the formation of product **149** was formed according to the mechanism described in the pathway (b) (this is the operative pathway).

By the analysis of the NMR spectra (including COSY spectrum Fig. A.41) it is confirmed that compound **149** does not contain a double bond, since the addition of primarily formed radical **101** to benzobarrelene was accompanied by the disappearance of two double bonds, we should supposed that, in comparison with other products, another ring is formed (cyclopropane ring).



Scheme 2.20
A



Scheme 2.20
B

The proposed structure of compound **149** was determined on the basis of the ^{1}H and ^{13}C-NMR spectra, and was accomplished by 2D-NMR (DEPT-135; COSY; HMQC and HMBC) experiments.

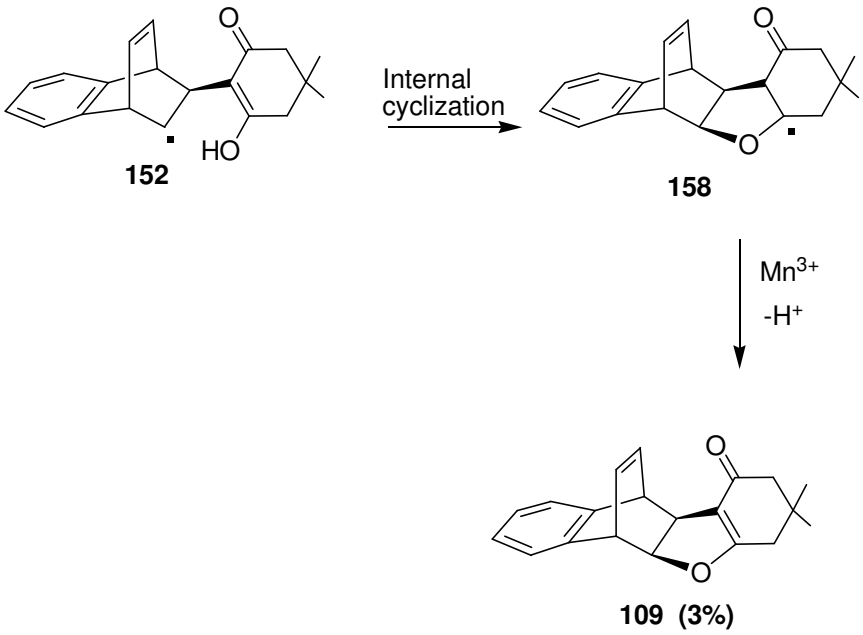
The ^{1}H-NMR spectrum of **149** exhibits multiplet in the range 7.04-7.26 ppm arised from the aromatic protons. For the three methine groups protons of the cyclopropane ring, one appears at 1.77 ppm as quasi doublet of doublets (J= 7.2 Hz, J= 5.5 Hz, H_{11}), and by referring to COSY spectrum (Fig. A.41) we found that proton H-11 has correlation with both proton H-10b and H-4b, where the other two protons show resonance at 2.06 ppm as triplet ($J_{12,11} = J_{12,13} = 7.2$ Hz, H_{12}) and at 1.99 ppm as quasi doublet of doublets due to proton H-13 (J= 5.5 Hz). Noteworthy is that COSY experiment revealed that there is very strong correlations between the three protons of the cyclopropane ring (H-11, H-12, and H-13) each proton correlates with the two other protons (Fig. A.42) and a such pattern is specific only in the case of cyclopropane, and besides the presence of remarkable shifts in the resonance of the three methylene carbons of cyclopropane, quite up field under 20

ppm which is evident in ^{13}C-NMR spectrum and this also confirms the formation of cyclopropane. The methine groups protons (H-10b, H-4b, and H-5) are resonances appear as broad singlet at 4.34, 3.0, and 2.73 ppm, respectively. The isolated methylene groups show two broading AB-systems in the range 2.18-2.30 ppm. Finally, the singlets at 1.10 and 1.08 ppm belong to the two methylenic protons on the dimedone ring. Furthermore, the ^{13}C-NMR spectrum confirms the proposed structure of **149** by giving eleven carbon signals in sp^3 region and eight carbon signals in sp^2 region, in addition to one signal of carbonyl carbon at 195.2 ppm.

2.3.4. The formation mechanism of dihydrofuran adduct 109.

It is a normal addition product arised from exo-addition of radical **101** to the double bond in benzobarrelene **82.** For formation of dihydrofuran derivative found to proceed without rearrangement as shown in the following proposed mechanism (Scheme 2.21).

At first manganese(III)-enolate should be formed, and then rapid electron transfer with the loss of manganese(II) followed by subsequent addition to the double bond in alkene **82** gave radical intermediate **152**, which is attacked by the hydroxyl oxygen of the enol form providing the tertiary carbon radical **158**. And at this stage we assume that the cyclization occurred before the second oxidation and as a result no rearrangement could take place. In the last step in this reaction radical **158** undergoes deprotonation to afford the dihydrofuran adduct **109**.



Scheme 2.21

The fact that the non-rearranged product **109** was obtained suggested that the intramolecular oxidative cyclization is faster than the second oxidation.

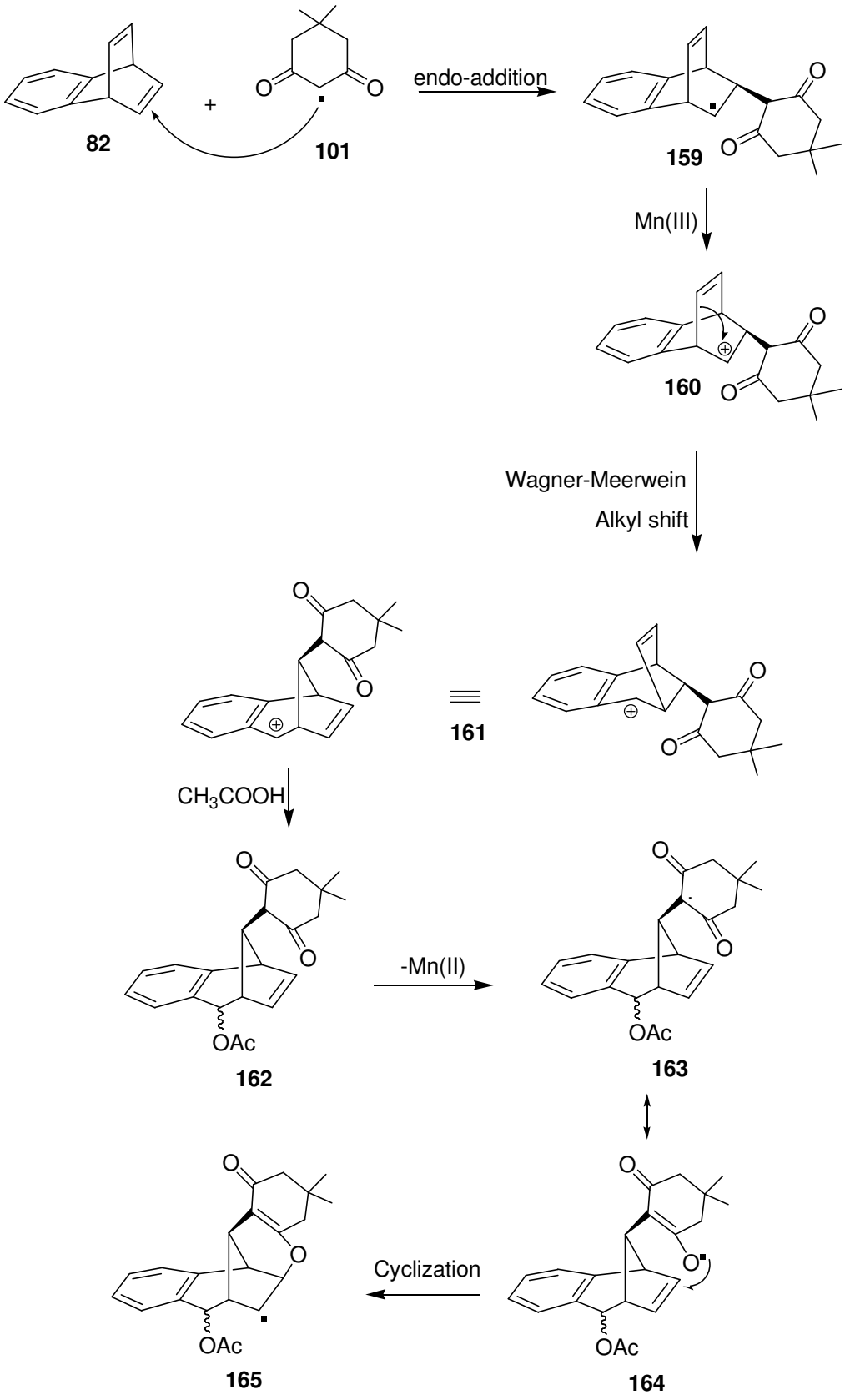
The structure determination of dihydrofuran was easily established by comparison of the spectral data with those of that obtained by the reaction of homobenzonorbornadiene with dimedone (Scheme 2.5).

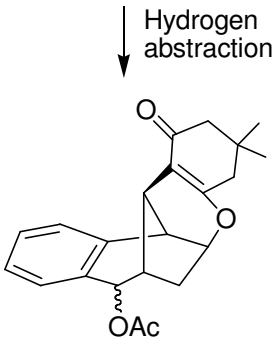
2.3.5. The formation mechanism of the two major isomers 150 and 151.

The fourth fraction isolated was a mixture containing two isomers **150** and **151** in a ratio of 1 : 2 respectively. Structural determination of these isomers revealed that barrelene skeleton was rearranged via Wagner-Meerwein rearrangement with accompanying alkyl migration. These two isomers were obtained via a similar mechanism that can be accounted for according to the mechanism outlined in Scheme 2.22.

The reaction proceeds by the formation of the enolate complex, which is the key to the catalytic reaction, and easily oxidized the alkene **82** generating a secondary cyclic radical **159** that undergoes rapid oxidation by additional $Mn(OAc)_3$ or by $Cu(OAc)_2$ to nonclassical carbocation **160**. Now this carbocation intermediate is expected to proceed via alkyl or aryl migration. However, only alkyl shift can take place to form the intermediate **161**. The formation of the aryl shift intermediate is completely hindered by steric repulsion that would be imposed between the aromatic moiety and the enolizable dimedone due to its endo-orientation. The rearranged intermediate **161** is then captured by the acetate anion to give product **162**, probably as a mixture of isomers that still have one α-hydrogen and can undergoes further oxidation by the Mn(III) acetate much faster than the starting material to furnish electrophilic oxy radical **164**. Attacking of the susceptible double bond by the electrophilic oxy radical shown to afford the radical intermediate **165**, which then terminated reductively by abstraction a hydrogen atom from the environment (solvent or another molecule of dimedone) producing the isomeric mixture **150/ 151** in 15% combined yield.

The fractional crystallization of this isomeric mixture allowed us to isolate two purified isomers **150** and **151** in 6.5% and 8.5% yields respectively.


endo-addition
Mn(III)
Wagner-Meerwein
Alkyl shift
CH3COOH
-Mn(II)
Cyclization
OAc
82
101
159
160
161
162
163
164
165



150/ **151** (15%)

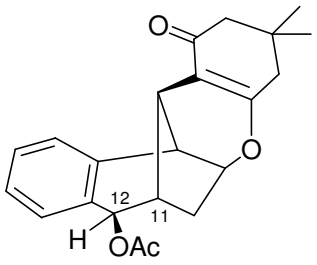
Scheme 2.22

The structural assignment for products **150** and **151** was based on their ^{1}H; ^{13}C-NMR spectral data in conjunction with 2D-NMR (DEPT-135; COSY; HMQC; and HMBC) experiments. Furthermore, the ^{1}H, and ^{13}C-NMR spectrum pattern of **150** was very similar to that of **151** which indicates that they are stereoisomers.

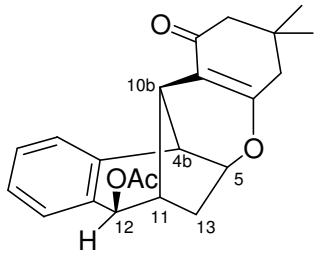
2.3.6. Reaction of benzobarrelene (82) and dimedone (93) with $Mn(OAc)_3$ in absence of $Cu(OAc)_2$.

On the other hand, conducting the oxidation of benzobarrelene **82** with only $Mn(OAc)_3$ under the same reaction conditions with dimedone at 50 °C (9h.) gave the isomeric mixture **150/151** exclusively, and the yield was reduced to 9% combined yield with recovered alkene yield of about 6%

The formation of the two major isomers (distereoisomers) were evident in the ^{1}H-NMR spectrum of the crude reaction mixture in a ratio corresponding to that obtained in the reaction carried out in the presence of copper acetate.



150 (4%)
endo-isomer



151 (5%)
exo-isomer

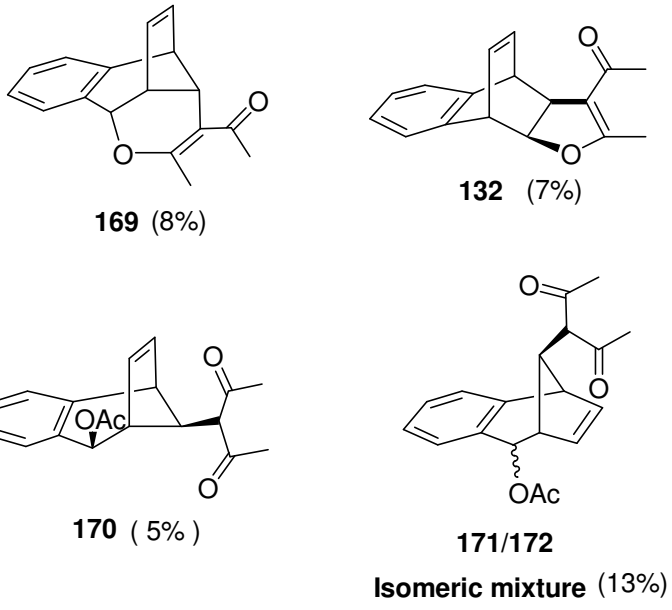
These isomers have been characterized properly, especially by 2D-NMR (DEPT-135; COSY; HMQC) spectra data. The exact structural assignments were made by measuring the coupling constants between the bridgehead protons (H-11) and alkoxy protons (H-12), which was found for the endo-isomer (J=5.3 Hz), whereas for the exo-isomer (J=3.1). Furthermore, the analysis of COSY spectra enabled us to assign the stereochemistry of these two isomers. While the COSY spectrum of isomer **150** (Fig A.50) clearly shows that the methine group proton (H_{12}) has a very strong correlation with the bridgehead proton (H_{11}) indicating the exo-orientation of H_{12} and endo-configuration of the acetate group (endo-isomer), the COSY spectrum of isomer **151** (Fig A.57) shows a weak correlation between the same two protons (H_{12} and H_{11}) indicates the endo-orientation of methine proton H_{12} and exo-configuration of the acetate group (exo-isomer). Additionally, the methine group proton H_{12} in the exo isomer **151** is shielded by the phenyl group and resonates at 5.58 ppm as compared with 6.15 ppm in the endo-isomer.

In summary, we demonstrated that the regioselectivities of the above reactions suggest that the oxidative free-radical additions occur at endo side of the double bond in benzobarrelene and the driving force is the secondary orbital interactions between the carbonyl group on the introduced dimedone ring and the π-moiety on the aromatic ring which is supplied by the formation of alkyl shift intermediates. Moreover, the second oxidation process took place before the cyclization, it therefore led to the Wegner-Meerwein rearrangement of the endo-intermediates

(**144**, **159**). Alkyl shift products were exclusively formed as major products and this can be explained in terms of the formation of endo-addition of radical **101** to the π-system, whereas the aryl shift products were not involved due to the geometrical conformations of endo intermediates. Additionally, the formation of two isomers **150** and **151** which terminated reductively in the reaction carried out with and with out copper acetate suggested that the metal oxidant reacts sufficiently slowly with the secondary radical **165** to allow reductive termination to compete.

2.4. Reaction of benzobarrelene (82) and acetylacetone (94) with $Mn(OAc)_3$ in the presence of $Cu(OAc)_2$.

The oxidation of benzobarrelene **82** with acetylacetone **94** in the presence of 2 equivalent of $Mn(OAc)_3$ and 1 equivalent of $Cu(OAc)_2$ in acetic acid for 3 h at 50°C afforded in addition to the dihydrofuran derivative (**132)**, two rearranged products (**169**, **170**) and a mixture consisting of two isomers (**171/ 172**) in a ratios of 1 : 1.2 : 1 : 10, respectively as shown in Scheme 2.24 with unreacted alkene has also recovered in 3% yield. These compounds were separated by column chromatography and were characterized by means of spectral data.



169 (8%)

132 (7%)

170 (5%)

171/172

Isomeric mixture (13%)

Scheme 2.23

All of the rearranged products (**169**,**171**, **and 171/172**) are formed as a result of Wagner-Meerwein rearrangement accompanying alkyl migration and can be explained in terms of the formation of the endo-intermediates formed by endo-free radical additions to the double bond in alkene **82**.

2.4.1. The formation mechanism of the rearranged product 169.

It is the first rearranged fraction isolated in yield of 8%, and it was formed by the mechanism shown in Scheme 2.24 similar to that described for the formation of the corresponding product **148** (Scheme 2.19), and the structure determination of which was based on ^{1}H; ^{13}C-NMR spectral data that is completely in agreement with the proposed structure. Since it′s spectral data correspond closely to that interpreted for the analogous product **148** and there is no considerable difference between two spectra, so we don't need to analyze it here.

2.4.2. The formation mechanism of the dihydrofuran adduct 132.

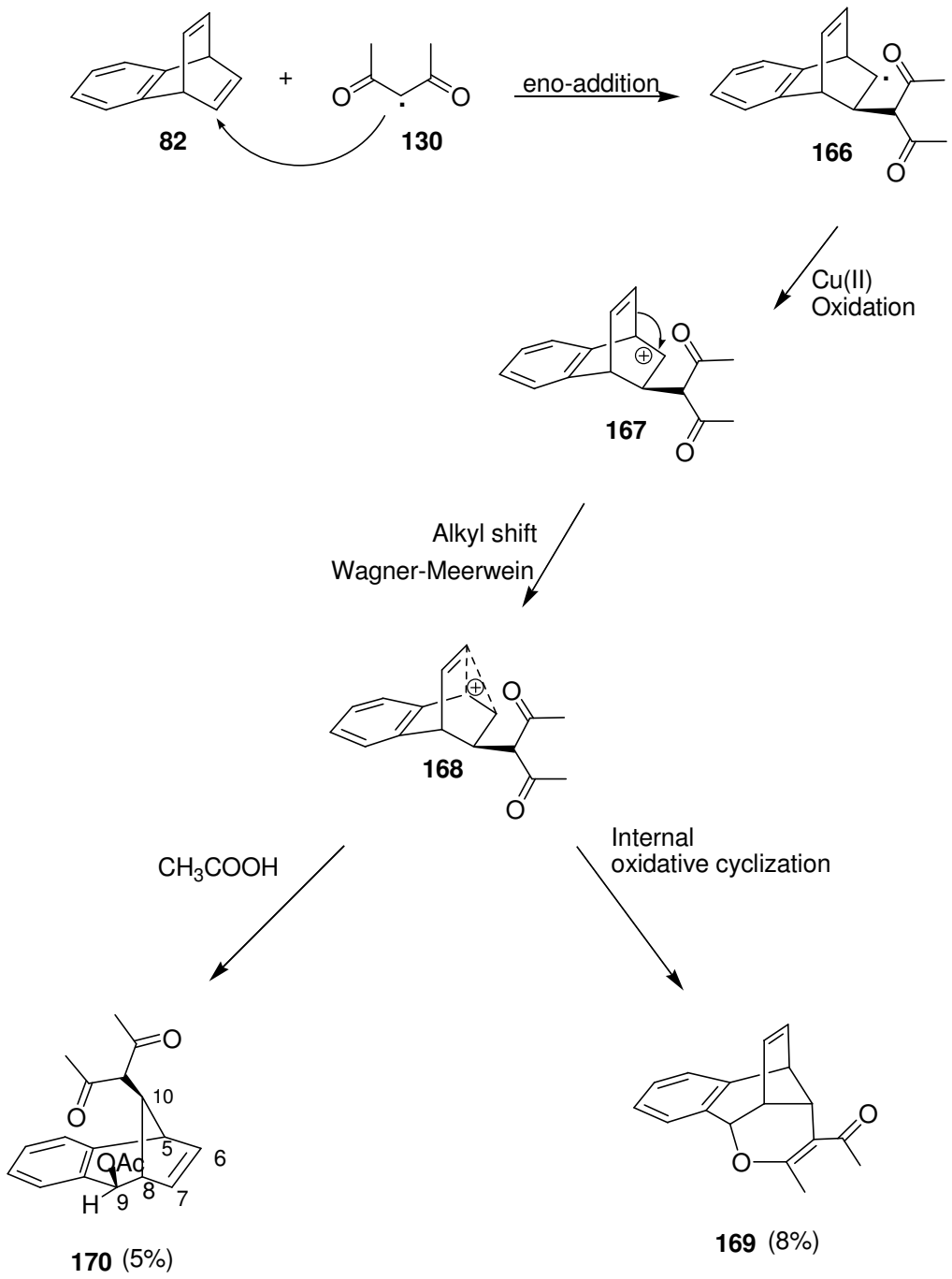
The formation of the second fraction isolated in 7% yield, the normal addition product, was straightforward. We assume that it was produced via formation of exo-intermediate resulted from exo-addition of radical **130** (generated from the acetylacetone) to the double bond in alkene **82** and it proceeds in the sequence steps similar to that described in the formation mechanism of dihydrofuran product **109** (Scheme 2.21).

The structure determination of dihydrofuran was easily established by comparison of the spectral data with those of the dihydrofuran product **132** obtained by the reaction of homobenzonorbornadiene with acetylacetone.

2.4.3. The formation mechanism of the product 170.

For the formation of the rearranged product **170**, we proposed the following mechanism given in Scheme 2.24.

We propose that the reaction initiated with the intermediate radical **166** (generated from endo-addition of radical **130**), which would be oxidized by $Cu(OAc)_2$ to non-classical carbocation **167**. This carbocation intermediate proceeded via alkyl migration leads to rearrangement of the molecular skeleton of barrelene producing intermediate **168**, at this stage intermediate **168** is expected to undergoes either (1) cyclization at the carbonyl oxygen to provide product **169** via deprotonation, or (2) the acetate group would be introduced from the exo-face of cationic product **168** (from the same side of the bulky acetylacetone moiety) before cyclization to give the rearranged exo-product **170** in 5% yield.



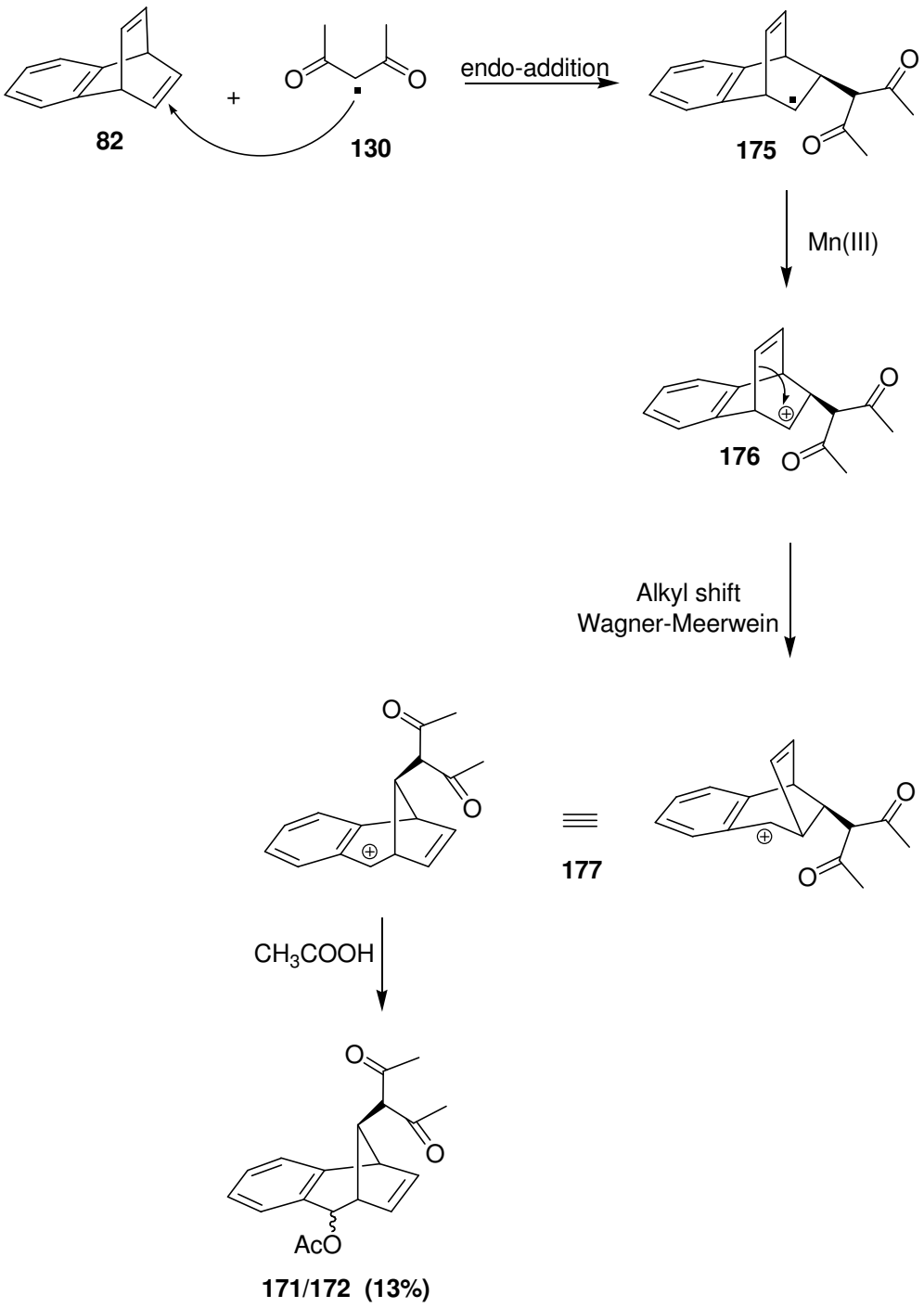
Scheme 2.24

The stereochemistry of **170** can be determined by measuring the coupling between the methine proton on C-9 and the bridgehead proton H-8, which was 3.2 Hz

indicating endo-orientation of H-9, and hence the stereochemistry of the acetate group should be arranged exo.

2.4.4. The formation mechanism of the isomeric mixture 171/172.

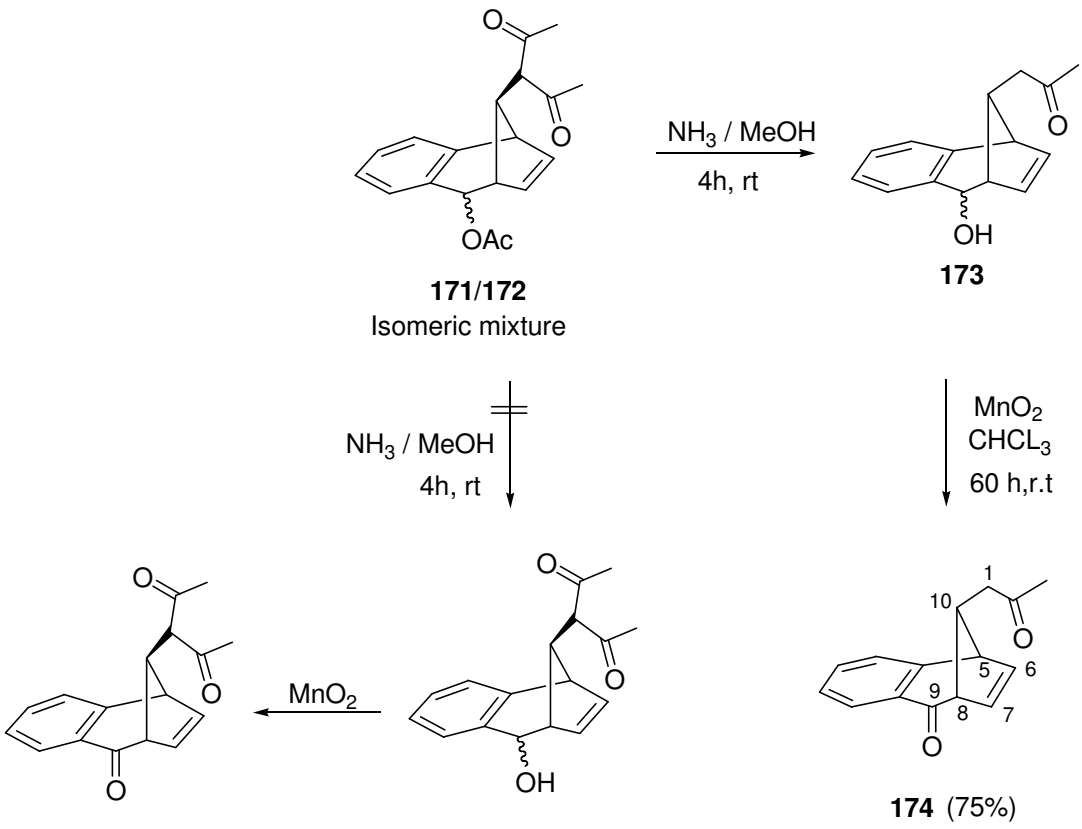
For the formation of the isomeric mixture **171/172**, we propose that the carbon radical **130** firstly adds to the double bond of benzobarrelene **82** gave a secondary cyclic radical **175**, subsequent oxidation provided non-classical carbocation **176**, then this carbocation intermediate is proceeded via Wagner-Meerwein rearrangement to alkyl shift rearranged intermediate **177**, while to the aryl shift intermediate was not observed. The rearranged intermediate **177** is then captured by the acetate anion gave product **171/172** as a mixture of isomers (major product) in 13% combined yield (Scheme 2.25).



Scheme 2.25

The ^{1}H-NMR spectrum of the isomeric mixture confirms the presence of one double bond and this mixture still have one α-hydrogen and can undergo further

oxidation by the Mn(III) acetate (similar to that in the case of the reaction using dimedone). However, a such reaction was not occurred which probably due to the week enolization of acetylacetone that is present as the keto form, and as a result, the Mn(III)-enolate complex might be inhibited or not stable, since the enolate complex is easily formed using hydroxyl moiety such as in the reaction using dimedone (see Scheme 2.22). The structural assignment of these isomers was based on the ^{1}H; ^{13}C-NMR spectra, and further support was achieved chemically. We did determine the correct structure by converted the isomeric mixture into one product, firstly the acetate group in product **171/172** was readily converted into hydroxyl group through an aminolysis reaction in presence of methanolic ammonia, affording the alcoholic derivative **173** whose assigned structure was confirmed by oxidation over MnO_2 to the ketone derivative **174**. Surprisingly, treatment of the isomeric mixture **171/172** with methanolic ammonia at ambient temperature led to removing of one of acetyl groups of the acetylacetone moiety as shown in Scheme 2.26.



Scheme 2.26

The structure of alcohol′s derivative **173** was characterized by its ^{1}H, and ^{13}C-NMR spectral data.

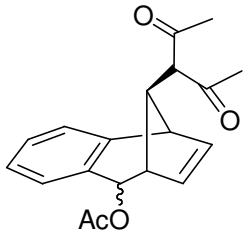
The ^{1}H-NMR spectrum of compound **174** would be expected to have remarkable shift to lower field for one of the aromatic protons since this proton is in the deshielding zone of the carbonyl carbon. One aromatic proton resonates at 7.89 ppm, the other three protons appear in the range 7.1-7.38 ppm as multiplet. The methylenic protons (C-1) appeared as a pair of AB-quartet in the range 2.59-2.78 ppm, a geminal AB-system (J=17.3 Hz) has further coupling with the bridge proton H-10 (J=7.2 Hz, and J=5.8 Hz). Yet, unsymmetrical coupling, which can be seen obviously in the different sizes of coupling between these protons and bridging methine proton, that is probably due to the dihedral relationship. The methine

proton (C-10) gives broad doublet of doublets at 3.29 ppm (J=7.2 Hz, and J=5.8 Hz). The bridgehead protons H-5 and H-8 resonated at 3.24 and at 3.46 ppm respectively, where H-8 shows a doublet due to coupling with olefinic proton H-7 (J= 2.7 Hz), the other (H-5) shows also a doublet due to coupling with olefinic proton H-6 (J= 3.1 Hz), the olefinic protons occur as doublet of doublets at 5.96 and at 6.55 ppm, doublet splitting originated from vicinal coupling with the olefinic proton (J= 5.1 Hz) besides being coupled to bridgehead protons and this gives their doublet of doublets patterns ($J_{7,8}$= 2.7 Hz, $J_{6,5}$= 3.1 Hz). Finally, the singlet at 2.1 ppm belongs to methyl protons of acetyl group.

The ^{13}C-NMR spectrum of compound **174** also confirmed the expected structure by giving five carbon signals in sp^3 region and eight carbon signals in sp^2 region, in addition to two signals of carbonyl carbons at 194.39 and 206.55 ppm.

2.4.5. Reaction of benzobarrelene (82) and acetylacetone (94) with $Mn(OAc)_3$ in absence of $Cu(OAc)_2$.

We next investigated the corresponding reaction of benzobarrelene **82** with acetylacetone under similar reaction conditions with out Cu(II) acetate with a longer reaction time (10h), and examination of the ^{1}H-NMR spectrum of the crude reaction mixture indicated the presence of isomeric mixture **171/ 172** in a ratio of 1 : 2 respectively, and in 8% combined yield.

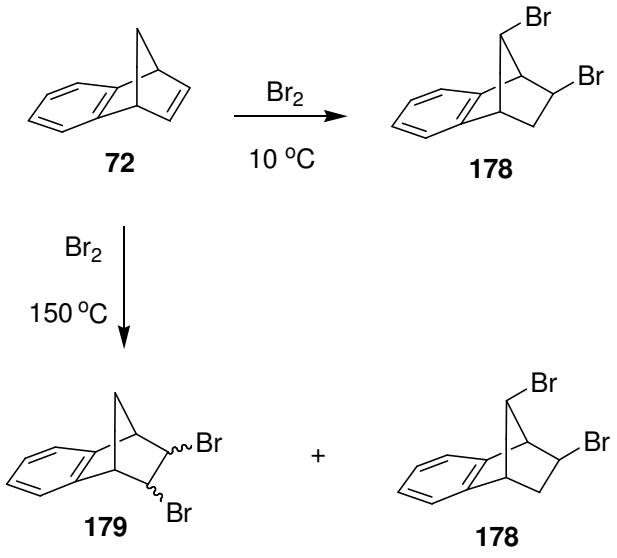


171/172 (8%)

2.5. Oxidative free radical additions of 1,3-dicarbonyl compounds to 7-aza-benzonorbornadiene (83).

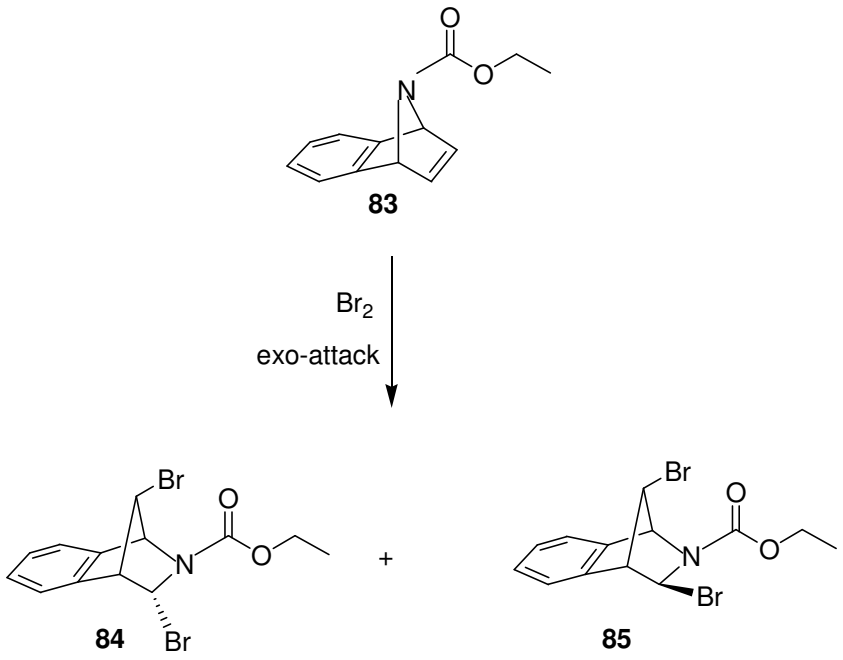
As an additional investigation of Mn(III) acetate-mediated free-radical additions, we use N-carbethoxy-7-aza-2,3-benzonorbornadiene **83** as a radical acceptor alkene in order to test the behavior of nitrogen bridge in the bicyclic system on the course of the reaction since it is expected that the electronic factors would play role in the mode of benzonorbornadiene′s reaction.

The N-carbethoxy-7-aza-2, 3-benzonorbornadiene **83** was synthesized by the addition of benzyne to the N-carbethoxy pyrrole as described in the literature [70]. It is reported [71] that the electrophilic addition of bromine to benzonorbornadiene **72** gave a rearranged dibromide **178**, whereas high temperature bromination of **72** at 150°C resulted in the formation of non-rearranged products **179** and rearranged product **178** as well (Scheme 2.27).



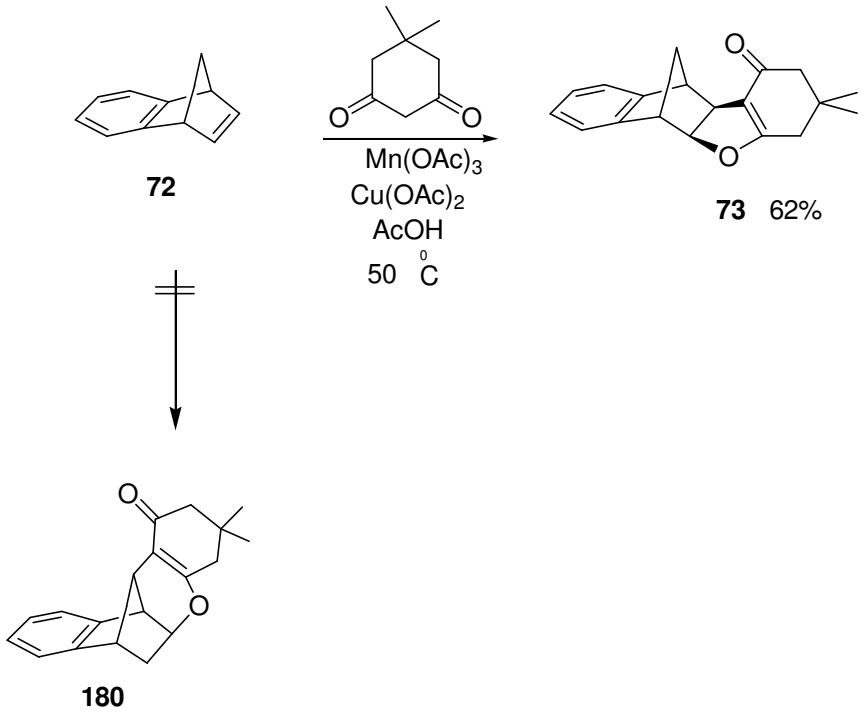
Scheme 2.27

In the case of bromination of N-carbethoxy-aza-benzonorbornadiene **83** [60] two rearranged products (**84/85**) were formed which were not stable at room temperature (also consult Scheme 20).



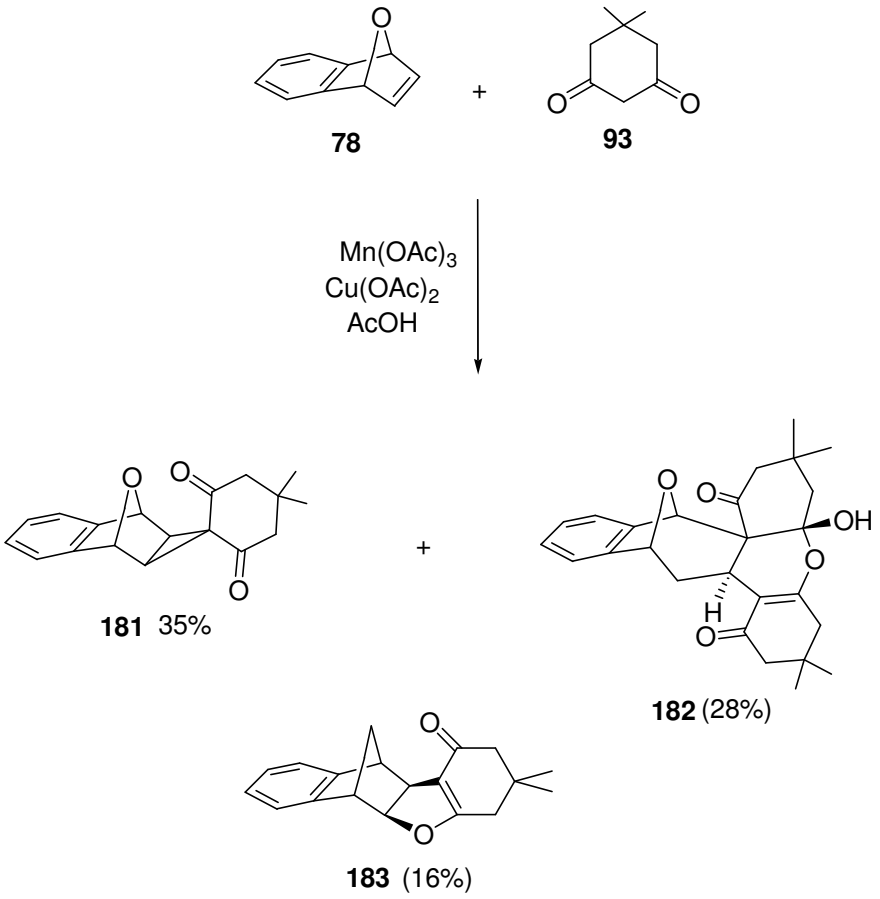
Furthermore, the Mn(III) acetate oxidative cyclization of benzonorbornadiene **72** and oxabenzonorbornadiene **78** have been studied by Caliskan and Balci [55].

The oxidation of **72** led to dihydrofuran adduct **73** while the rearranged product **180** was not formed as shown in Scheme 2.28.



Scheme 2.28

The oxidation of oxabenzonorbornadiene **78** under the same reaction conditions with dimedone yielded three different products (**181**, **182**, and **183**), respectively (Scheme 2.29), and no rearranged product could be found.



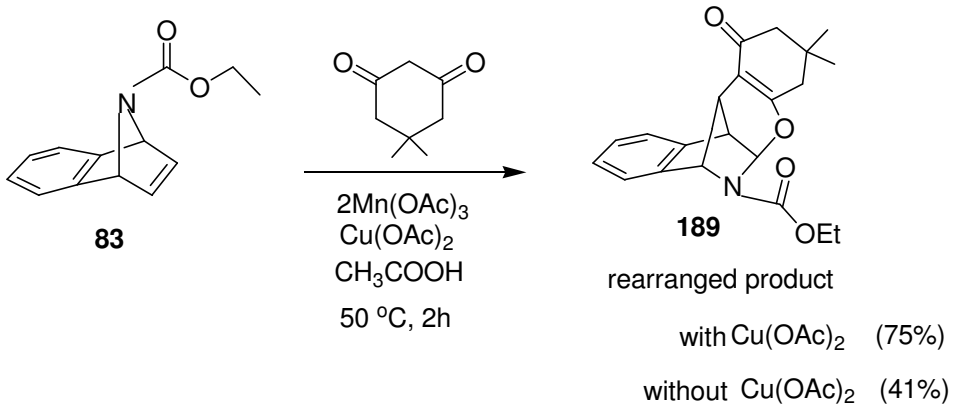
Scheme 2.29

On the other hand, reaction of **78** with acetylacetone gave **79** as the sole product in 78% yield (see Scheme 18). The behavior of oxabenzonorbornadiene **78** can be attributed to the oxygen atom located at the bridge. The addition of dimedone to oxabenzonorbornadiene gives cyclopropane compound **181**, since dimedone is an easily enolizable compound, the enol functionality can interact with the bridge oxygen atom resulting in hydrogen bonding. On the other hand, acetylacetone is not a good enolizable compound, so it cannot form hydrogen bonding with the bridge oxygen. It undergoes a normal addition product. Careful examination of the reaction mixture did not reveal the formation of any trace of the rearranged products.

2.5.1. Reaction of N-carbethoxy-7-aza-2,3-benzonorbornadiene (83) and dimedone with $Mn(OAc)_3$ in the presence and in the absence of $Cu(OAc)_2$.

Contrary to our prediction, oxidation of N-carbethoxy-7-aza-2,3-benzonorbornadiene **83** led to only one fraction.

First aza derivative **83** was treated with a mixture of 2 equivalent of $Mn(OAc)_3$ and 1 equivalent of $Cu(OAc)_2$ in acetic acid at 50 °C (2h), after chromatographic separation by TLC while eluting with hexane-ethylacetate (7/1), one rearranged product was obtained (**189**) as the sole product and the best yield (75%) was achieved with unrecovered alkene **83**, and also this product was produced as sole product when the reaction was run without copper acetate with the same reaction rate (2h) while the yield was reduced to 41% (Scheme 2.30).

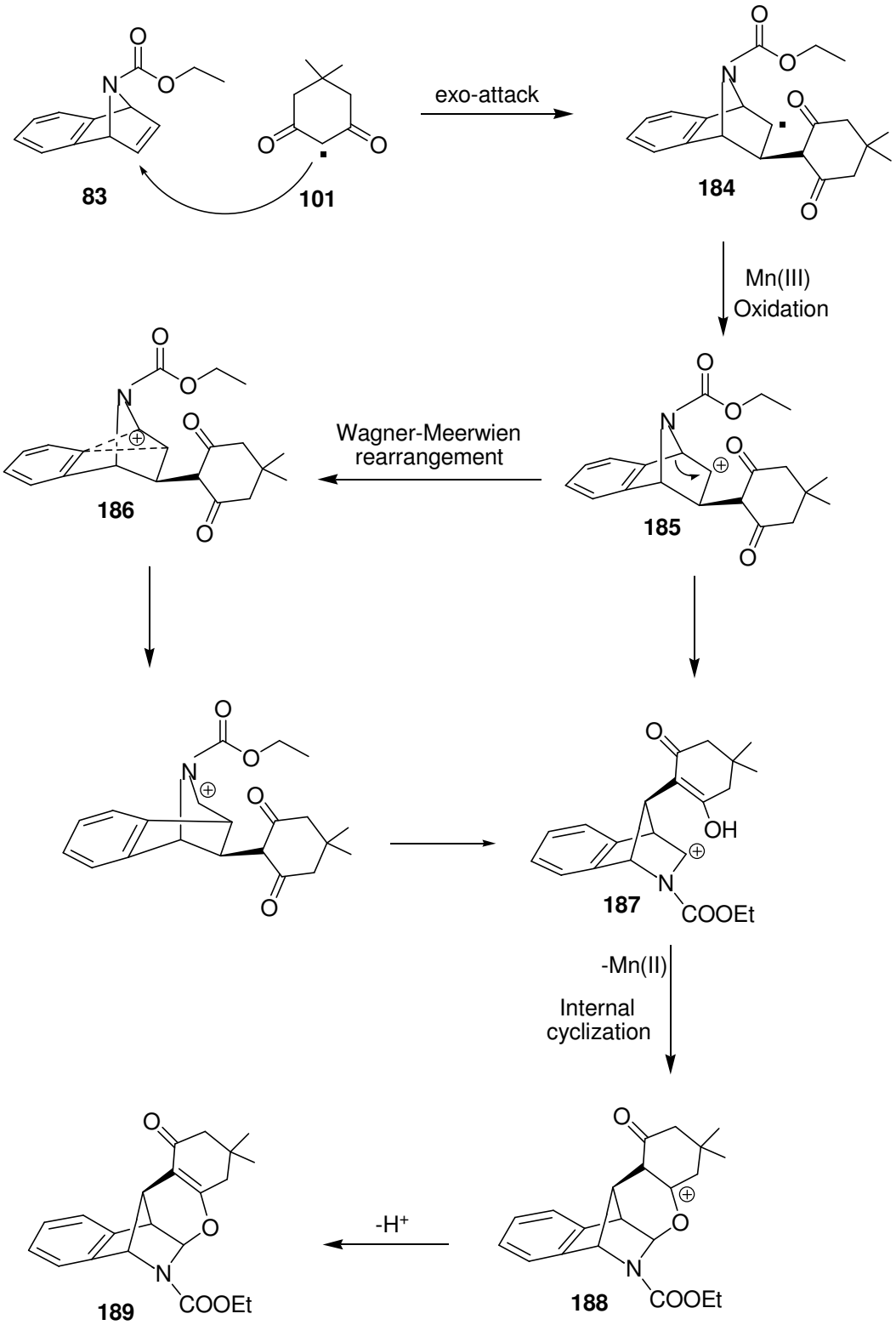


Scheme 2.30

2.5.2. The formation mechanism of rearranged product 189.

A proposal mechanism for the formation of the Wagner-Meerwein aryl shift product is demonstrated in Scheme 2.31.

A pathway for the formation of rearranged product **189** involves exo-addition of the initially formed radical **101** to the double bond in aza derivative alkene **83** producing exo-intermediate **184**. Cu(II) or Mn(III) oxidation furnishes a non-classical carbocation **185** with a high tendency to rearrange via Wagner-Meerwein aryl shift migration providing the cation **187**, which can easily undergoe intramolecular oxidative cyclization initiated by loss of Mn(II) with subsequent attack at cationic center by oxygen lone pair and then followed by simple deprotonation of product **188** leads to the rearranged product **189** in 75% yield.


exo-attack
83
101
184
Mn(III)
Oxidation
185
Wagner-Meerwien
rearrangement
186
187
OH
COOEt
-Mn(II)
Internal
cyclization
188
COOEt
-H+
189
COOEt

Scheme 2.31

The rearranged product **189** was characterized by spectroscopic methods and elemental analysis as well as the X-ray crystallographic analyses (Fig. 5).

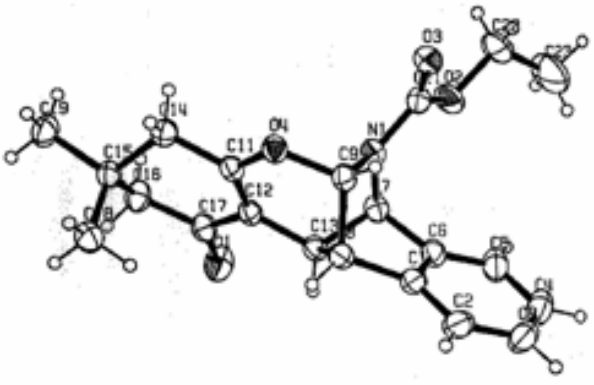


Figure 5. The X-ray crystal structure of **189**

According to the ^{1}H-NMR spectrum of product **189** it is indicated that **189** exists in equilibrium (Fig. 6).

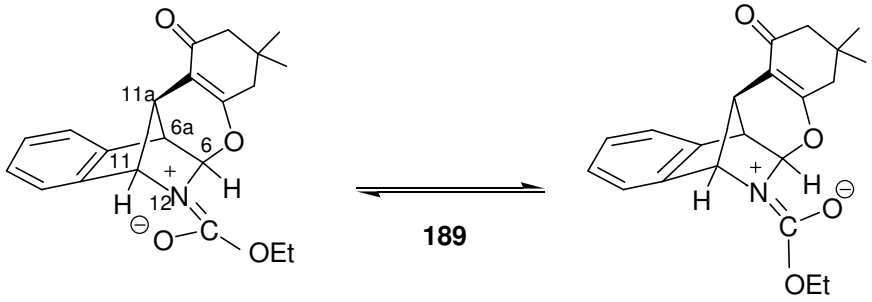


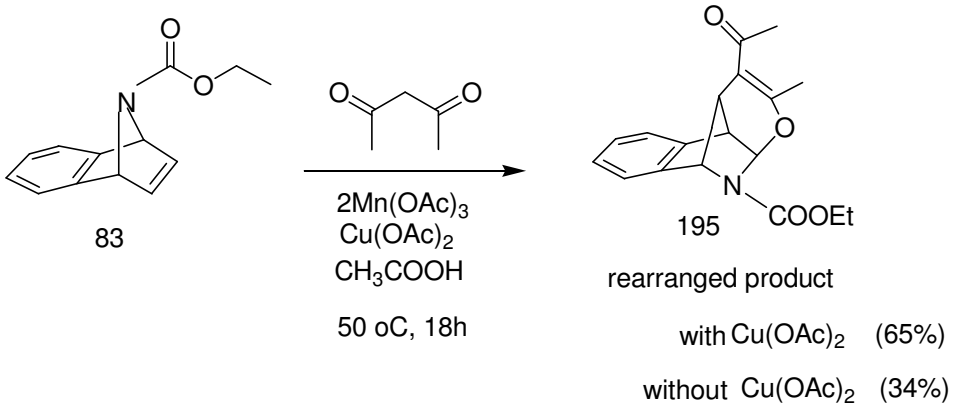
Figure 6. Isomerization of compound **189**

The bridgehead proton H-11 and methine proton H-6, each shows two separate signals at 5.0 and 5.56 ppm respectively indicating the presence of a rapidly equilibrium due to the bond rotation (C=N) that restricted at room temperature. Furthermore, this was confirmed by raising the temperature to 60°C which caused the two signals of each proton (H-11, H-6) and also for the other protons, to broaden, and then coalesce due to the fast exchange of the equilibrating system as obviously shown in ^{1}H-NMR spectrum (Fig. A.66).

2.6. Reaction of N-carbethoxy-7-aza-2,3-benzonorbornadiene (83) and acetylacetone with $Mn(OAc)_3$ in the presence and in the absence of $Cu(OAc)_2$.

A similar reaction of aza derivative **83** with acetylacetone in the presence of 2 equivalent $Mn(OAc)_3$, 1 equivalent of $Cu(OAc)_2$ in acetic acid was investigated.

To our surprising, after the purification of the crude product by preparative TLC, the corresponding rearranged product was also resulted as sole product in a good yield (65%), although it needed longer reaction times (18h) in comparison with the reaction using dimedone (2h) (Scheme 2.32). The oxidation of alkene **83** was also run with out $Cu(OAc)_2$ under the same reaction conditions and the same rearranged product was obtained in 34% yield where the reaction lasted 22h



83

195

rearranged product

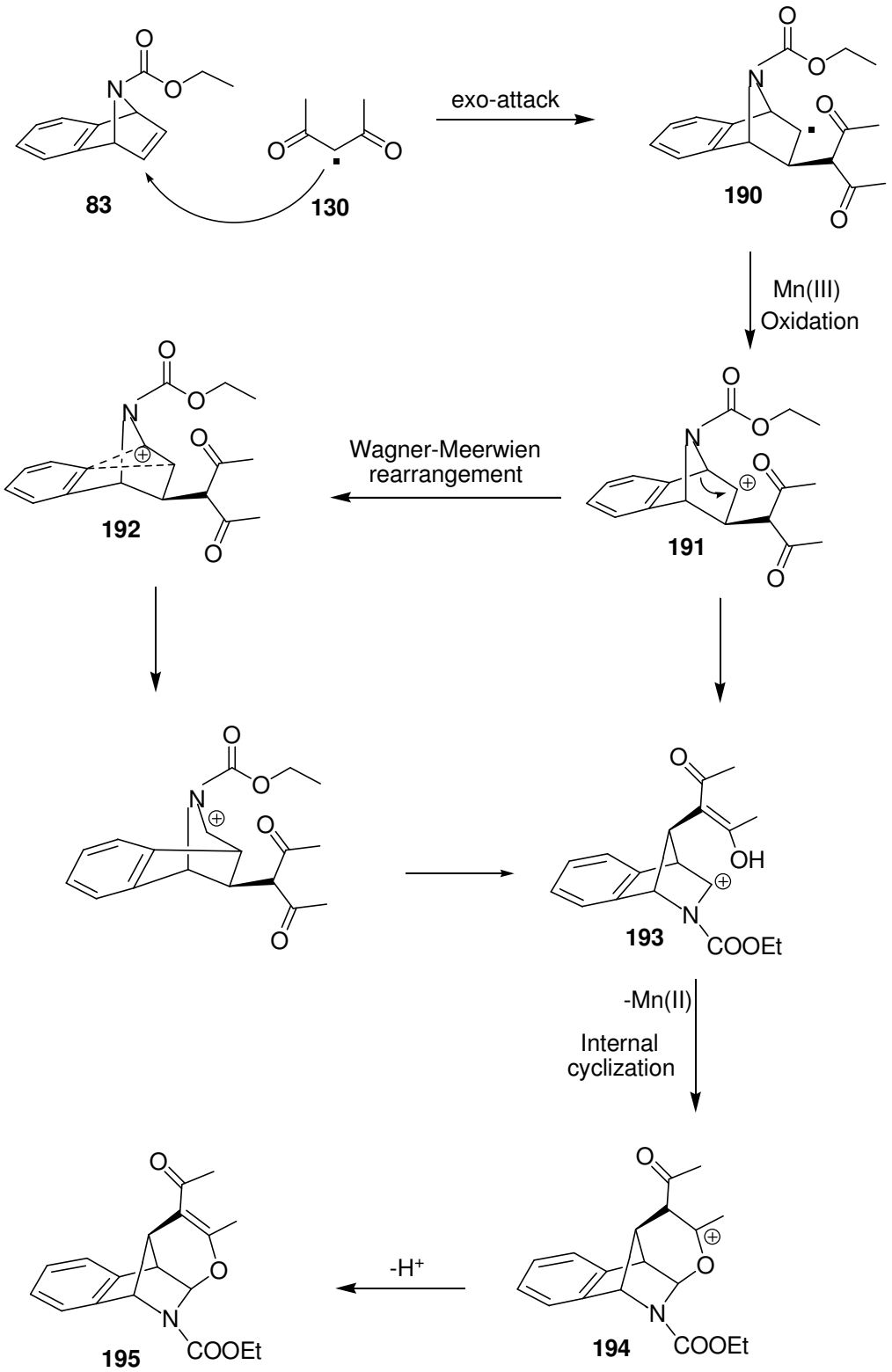
with $Cu(OAc)_2$ (65%)

without $Cu(OAc)_2$ (34%)

Scheme 2.32

2.6.2 The formation mechanism of rearranged product 195.

The formation mechanism of rearranged product is similar to that applied for the formation of corresponding product resulted from the reaction using dimedone and as shown in Scheme 2.33.


exo-attack
83
130
190
Mn(III)
Oxidation
191
Wagner-Meerwien
rearrangement
192
193
OH
COOEt
-Mn(II)
Internal
cyclization
194
COOEt
-H+
195
COOEt

Scheme 2.33

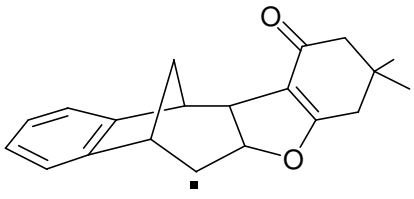
The isolated rearranged product was characterized by ^{1}H and ^{13}C-NMR spectral data. Now, we may conclude that the electronic feature of the bridging nitrogen played a role in the mode of reaction outcome since it might be the nucleophilicity of nitrogen provided some complexation for the incoming electrophilic radicals, that brought about the addition of the free-radicals **101** and **130** from the exo-face of the double bond in aza-benzonorbornadiene **83**, could lead to the preferential formation of the exo addition intermediates.

CHAPTER 3

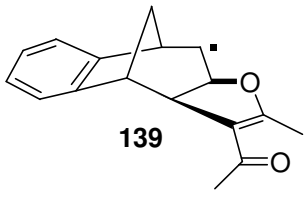
CONCLUSION

The primary goal of this work was to establish whether the second oxidation in the reaction of $Mn(OAc)_3$ with bicyclic olefins (which have great tendency to undergo Wagner-Meerwein rearrangement), takes place before cyclization or after.

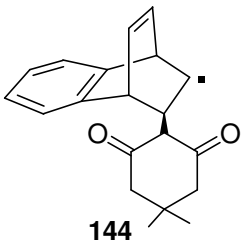
The resulting nonclassical carbocation intermediate can then undergo molecular skeleton rearrangement in the manganese(III)acetate oxidations of bicyclic system. We can now conclude that free-radicals such as **115**, **139**, and **144** (Shemes: 2.5, 2.12, and 2.19), are oxidized before cyclizations occur, and then non-classical Carbocations are produced which induced Wagner-Meerwein rearrangement in the bicyclic systems leading to formation of the rearranged products.



115

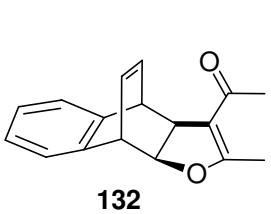


139

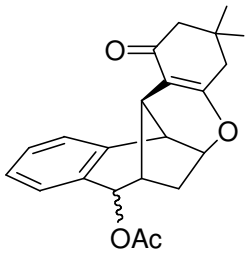


144

An unexpected observation in this work was the formation of unique tandem product, furan derivative (**107**), which was formed as a result of tandem oxidation reaction. Additionally, the unusual electrophilic oxo-radical (which has not been reported in the developed Mn(III)acetate-based oxidative cyclizations), was the attacking species in the reactions of formation of rearranged products **132** (Scheme 2.12) and **150/151**, isomeric mixture (Scheme 2.22). Thus, this new radical can be generated from dicarbonyl compounds and manganese(III)acetate, and it undergoes efficient addition to carbon-carbon double bond, which provides novel approaches to organic synthesis.

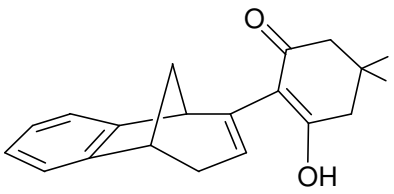


132

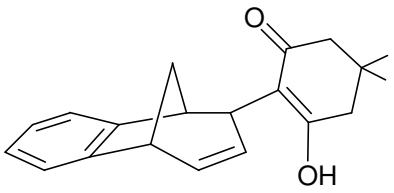


150/ 151

This work has further demonstrated that homobenzonorbornadiene system undergoes first allylic alkylation followed by addition of dicarbonyl compound. What is more, this work showed that the reactions carried out in the presence of copper acetate, the free-radical additions of 1,3-dicarbonyl compounds to bicyclic systems, mainly rearranged products are formed, and also the absence of cupric acetate has dramatic effect on the reactions rate as well as on the yields of the formed products.

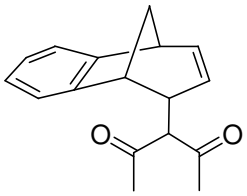


103



114

We also noted that the intermediates such as **103** and **114**, resulted from the reaction of homobenzonorbornadiene **80** with dimedone (Schemes: 2.3 and 2.5), which can enolize further were not isolated. On the other hand, intermediate product **131** (having a structure similar to that of **114**) in the case of the reaction with acetylacetone, which cannot enolize further, was isolated.

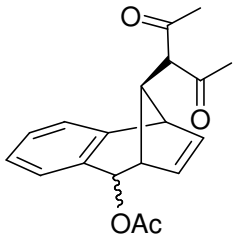


131

Our results of formation of rearranged product **109**, derived from the oxidative intermediate **114** (Hoffmann product), in high yield comparatively with the yield of furan product **107** (derived from the oxidative intermediate **103**, Zatisev product), suggested oxidative elimination by copper acetate is a regiospecific reaction [65].

In the case of [2.2.2] system, benzobarrelene **82**, 1,3-dicarbonyl free-radical additions from the endo-face of the double bond led to the formation of alkyl shift products exclusively while the aryl shift products were not formed, it might be due to geometrical conformation reasons which suppressed the aryl migration. Furthermore, it could be the secondary orbital interactions that supplied the formation of alkyl shift intermediates.

The formation of a 2:1 isomeric mixture **150/151** corresponds to the 2:1 ratio of isomeric mixture **171/172**, obtained from the reaction of benzobarrelene with 1,3-dicarbonyl compounds in presence and in absence of copper acetate, suggesting that the oxidative cyclization reactions in both cases are similar.



171/172

Our results in case of aza-homobenzonorbornadiene **83** showed that 1,3-dicarbonyl free-radical additions gave one rearranged product as sole product in high yields in presence and in absence of copper acetate.

CHAPTER 4

EXPERIMENTAL

4.1. General Consideration.

All reactions were carried out in flame-dried glassware with magnetic stirring.

Manganese triacetate dihydrate ($Mn(OAc)_3 .2H_2O$) and 1,3-dicarbonyl compounds were purchased from Merck chemical Co. and used without further purification. All the solvents purifications were done according to standard procedures stated in the literature [72]. All oxidative free-radical additions were carried out under nitrogen atmosphere and monitored by TLC for disappearance of starting material.

Melting points were determined by using a capillary melting point apparatus (Thomas-Hoover) and were uncorrected.

Column chromatographic separations were performed by using Merck Silica gel 60 (particle size 0.06-0.200 mm). The relative proportions of solvents refer to volume: volume ratio. Routine thin layer chromatography (TLC) was effected by using precoated 0.25 mm silica gel plates purchased from Fluka.

All Nuclear Magnetic Resonance (^1H; ^{13}C-NMR), ultra shield(400, and 100 MHz, spectra were recorded on a Bruker instruments Avance series-Spectrospin DPX-400 spectrometer with tetramethyl silane as an internal reference. Chemical shifts are reported in parts per million downfield from $(CH_3)_4 Si$ (δ). Coupling constants

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 377 IR recording spectrophotometer and are reported in cm^{-1}

4.1.1 General procedure

A solution of manganese(III) acetate dihydrate (10 mmol) and copper(II) acetate (1 mmol) in a glacial acetic (20 ml) in a flame-dried flask was heated under nitrogen atmosphere in a thermostated oil bath to 50 °C. A solution of 1,3-diketone (5 mmol) and olefin (5 mmol) in 5 ml a glacial acetic acid was then added to the mixture. Reaction is considered complete when the dark brown reaction mixture turned colorless to light bluish-green and contained variable amounts of white precipitate.

4.1.2. The preparation of benzonorbornadiene (72) [63].

Isoamylnitrile (64.35 g, 0.55 mol) in CH_2Cl_2 (800 ml) was magnetically stirred at the reflux temperature of dichloromethane for 1 minute. Anthranilic acid (68.5 g, 0.5 mol) and cyclopentadiene cracked freshly (33 g, 0.5 mol) in acetone (300 ml) were added dropwise for 2h at room temperature. The reaction mixture was stirred for an additional six hours at reflux temperature. The solvent was removed and organic layer washed with 750 ml saturated $NaHCO_3$ and one liter hexane, dried over $CaCl_2$. The solvent was removed and oily residue was obtained (21 g, 0.142 mol) at 72-81 °C under 10 mmHg with 28.8% yield.

4.1.3. Synthesis of exo-2,3-dibromo-6,7-benzobicyclo [3.2.1] octa-3,6-diene (100) [63].

A solution of $CHBr_3$ (67g) in hexane (100 ml) was dropwise added with stirring at -10 °C under stream of N_2 gas to a mixture of benzonorbornadiene (**97**) (20 g, 0.15

mol) and potassium tert-butoxide (30 g, 0.26 mol) in hexane (100 ml), over a period of 4h. Stirring was continued for 30 min. The organic layer was washed with water, dried with $CaCl_2$ and distilled to remove potassium tert-butoxide, $CHBr_3$ and excess benzonorbornadiene. Further distillation under reduced pressure gave dibromo product (**100**) (12.3 g, 0.04 mol 28%), b.p. 150-153 °C (0.4 mmHg) that was recrystallized from hexane affording rods of pure sample, m.p. 83 °C.

4.1.4. Preparation of homobenzonorbornadiene (80) [60].

Metallic sodium (28.5 g, 1.24 mol) was cut into small pieces and combined with 300 ml of anhydrous ether. This was mechanically stirred at gentle reflux under a nitrogen atmosphere while a mixture of dibromide **100** (29.02 g, 0.129 mol), tert-butyl alcohol (74.0g, i.o mol), and ether (50 ml) was added dropwise during 3h. After stirring at reflux overnight, heating was discontinued and methanol (50 ml) and then water (200 l) were added dropwise. The mixture was poured into water (200 ml), the organic layer was separated, and the water layer was extracted with ether (3× 100 ml). Combined organic layers were washed with water and brine, dried ($MgSO_4$), and concentrated. Distillation afforded alkene **80** (16.42 g, 83.5%) as a colorless oil: bp 45°C (0.1 mm); the spectral data for **80** as reported in the literature.

4.2. The oxidative addition of dimedone (93) to homobenzonorbornadiene (80) with $Mn(OAc)_3.2H_2O$ and $Cu(OAc)_2.2H_2O$.

Into a 100 ml three-necked round-bottomed flask were placed $Mn(OAc)_3.2H_2O$ (2.7 g, 10 mmol) and $Cu(OAc)_2.2H_2O$ (0.18 g, 1 mmol) in a 20 ml a glacial acetic acid and then a mixture of dimedone (0.7 g, 5 mmol) and alkene **80** (0.78 g, 5 mmol) in 5 ml acetic acid was added. The reaction mixture was stirred at 50 °C under N_2 for 4h, and the color of the solution was carefully monitored. The dark brown solution became lighter as the Mn(III) was reduced. When the reaction was complete, the solution was colorless to light blue with variable amounts of white

precipitate present. The reaction mixture was poured into 200 ml water to dissolve the precipitate, extracted with 200 ml methylene chloride, the organic phase was separated and the an aqueous phase was further extracted with methylene chloride (100 ml). The combined organic extracts were washed sequentially with a saturated aqueous solution of $NaHCO_3$, two portions of water, dried over $MgSO_4$, and then filtered. The solvent was removed by rotary evaporator giving 1.7 g of crude product, subsequent silica gel (160 g) chromatography while eluting with 4:1 hexane/AcOEt affording unreacted alkene as a first fraction (0.18 g, 23%), followed by product **107** (0.195 g, 13.3%), followed by **108** (0.146 g, 10%), followed by rearranged product **109** (0.44 g, 30%) in yields.

The spectral data for 3,3-dimethyl-2,3,4,6,7,12-hexahydro-1H-7,12-methanobenzo[b]benzo[5,6]cyclohepta[1,2-d]furan-1-one (107) : colorless solid, m.p:129-131°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 6.91-7.20 (m, 4H, aromatic.), 4.26 (d, J=4.7 Hz, 1H,), 3.5 (t, J=4.7 Hz, 1H) 3.0 (dd, A-part of AB system, J=15.3-4.7 Hz, 1H), 2.48 (d, B-part of AB system, J=15.3 Hz, 1H) 2.32 (dt, A-part of AB system, J=10.2-4.7 Hz, 1H), 1.95 (d, B-part of AB system, J=10.2 Hz, 1H), 2.2 (bs, 2H, -CH_2) 2.45 (bs, 2H, -CH_2), 2.5 (AB-system, J=18 Hz, 2H, -CH_2), 2.2 (AB-system, J=16 Hz, 2H, -CH_2), 1.01 (s, 3H, -CH_3) 1.05 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 193.7, 163.8, 151.8, 147, 144.1, 126.6, 126.1, 123.5, 123, 121.2, 117.5, 52.4, 42.3, 40, (bs, 37.6), 35.1, 30.7, 29.1, 28.5; IR (KBr, cm^{-1}): 3063.3, 3020.9, 2963, 2941, 2830, 1668, 1565, 1461.88, 1348.18, 1280, 1230, 1041, 976, 762. Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.16; H, 6.89. Found: C, 82.56; H, 7.07.

The spectral data for 3,3-dimethyl-2,3,4,5a,6,7,12,12a-octahydro-1H-7,12-methanobenzo[b]benzo[5,6]cyclohepta[1,2-d]furan-1-one (108): colorless solid, mp: 132.7-133.9°C; ^{1}H-NMR (400 MHz, C_6D_6) δ (ppm): 6.95-7.25 (m, 4H, aromatic), 4.36 (dd, J=8.6 Hz, 1H, H_{5a}), 3.7 (bs, 1H, H_{12}), 3.27 (d, J=8.6 Hz, 1H, H_{12a}), 3.0 (bs, 1H, H_7), 1.72 (d, J=11.9 Hz, 2H, H_{13}), 2.1 (m, 2H, H_6, -CH_2), 2.20 (m, 4H, -CH_2), 0.95 (s, 3H, -CH_3), 1.1 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$)

δ (ppm): 189.9, 172.0, 142.6, 141.7, 122.6, 122.6, 118.6, 118.3, 109.5, 78.3, 47.1, 40.6, 36.7, 34.0, 33.9, 33.2, 31.9, 29.9, (bs, 24.46); IR (KBr, cm^{-1}): 3381.6, 3281, 3065, 30195, 2957, 28685, 1720.5, 1621, 1467, 1400, 1278, 122.9, 1043, 968, 756, 565, 552. Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.6; H, 7.04. Found: C, 82.12; H, 6.40.

The spectral data for 3,3-dimethyl-3,4,5a,6,11,11a-hexahydro-6,11-ethenobenzo[b]naphto[2,3-d]furan-1(2H)-one 109: colorless solid, mp:132.7-133.9°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm):7.05-7.14 (m, 4H, aromatic), 6.36 (quasi t, J=7.1 Hz, 1H, H_{12}), 6.44 (quasi t, J=7.1 Hz, 1H, H_{13}), 4.92 (dd, J=8.9-3.7 Hz, 1H, H_{5a}), 3.34 (bd, J=8.9 Hz, 1H, H_{11a}), 4.35 (quasi t, J=3.7 Hz, 1H, H_6), 4.45 (bd, J=3.9 Hz, 1H, H_{11}), 2.13 (AB-system, J=18 Hz, 2H, -CH_2), 2.1 (AB-system, J=16 Hz, 2H, -CH_2) 1.12 (s, 3H, -CH_3), 1.08 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 193.2, 178.1, 143.8, 138.4, 135.7, 130.3, 126.4, 125.5, 124.4, 123.8, 113.6, 88.1, 50.9, 47.0, 45.1, 42.2, 37.8, 34.1, 29.6, 27.9; IR (KBr, cm^{-1}): 3431, 3286, 3051, 2961, 2924, 1633 (C=O), 1461, 1402, 1365, 1215 (C-O-C), 1140, 1047, 966, 712, 586. Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.09; H, 6.90. Found: C, 81.23; H, 7.09.

4.2.1. The oxidative addition of dimedone (93) to homobenzonorbornadiene (80) with $Mn(OAc)_3.2H_2O$ alone.

Into a 100 ml three-necked round-bottomed flask were placed $Mn(OAc)_3.2H_2O$ (2.7 g, 10 mmol) in 20 ml a glacial acetic acid and then a mixture of dimedone (0.7 g, 5 mmol) and alkene **80** (0.78 g, 5 mmol) in 5 ml acetic acid was added. The reaction mixture was stirred at 50 °C for 8h under N_2 and the progress of the reaction was monitored by TLC. After completion of reaction the mixture (buffy colour) was poured into 200 ml water, extracted with 200 ml methylene chloride, the organic phase was separated and an aqueous phase was further extracted with methylene chloride (100 ml). The combined organic extracts were washed sequentially with a saturated aqueous solution of $NaHCO_3$, two portions of water, dried over $MgSO_4$, and the filtered. The solvent was removed by rotary evaporator

giving 0.91 g of crude product, subsequent silica gel (160 g) chromatography while eluting with 4:1 hexane/AcOEt affording product **108** (0.07 g, 4.4%), followed by **110** (0.04g, 3%) in yields, with recovery of alkene **80** as a first fraction in (30%) of yield.

The data for 3,3-dimethyl-2,3,4,6,11,12-hexahydro-1H-6,11-methanobenzo[b]benzo[4,5]cyclohepta[1,2-d]furan-1-one (110): bright yellow solid, mp: 134.2-136.9°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.15-7.25 (m, 4H, aromatic), 1.9 (AB-system, J=11.2 Hz, 1H, H_{13e}), 3.1 (dt, J=3.3 Hz, 1H, H_{11}), 3.4 (t, J=4.0-3.2 Hz, 1H, H_6), 1.39-1.47 (ddd, J=12.4-3.4-3.3 Hz, 1H, H_{12}), 2.6 (quasi q, 1H, H_{12a}), 4.49 (dd, J=8.0-3.2 Hz, 1H, H_{5a}), 2.13 (AB-system, 4H,2-CH_2), 1.10 (s, 6H, 2-CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 194.5, 176.0, 146.5, 142.8, 127.8, 126.6, 123.2, 123.1, 119.3, 86.8, 51.0, 43.4, 38.3, 37.9, 36.5, 36.4, 34.0, 32.8, 29.3, 27.8; IR (KBr, cm^{-1}): 3416, 3065, 3046, 3020, 2953, 2868, 1772, 1722, 1646, 1629, 1511, 1469, 1402, 1367, 1278, 1222, 1194, 1138, 1055, 945, 928, 735, 704, 673, 563. Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.6; H, 7.48. Found: C, 82.28; H, 6.78.

4.2.2. The oxidative addition of acetylacetone (94) to homobenzonorbornadiene (80) with $Mn(OAc)_3.2H_2O$ and $Cu((OAc)_2.2H_2O$.

To a stirred solution of $Mn(OAc)_3.2H_2O$ (2.7 g, 10 mmol) and $Cu(OAc)_2.2H_2O$ (0.18 g,1 mmol) in a 25 ml a glacial acetic acid at 50 °C was added homobenzonorbornadiene **80** (0.78 g, 5 mmol) and acetylacetone **94** (.5 g, 5 mmol) under N_2 and the solution was stirred for 3h, at which time the reaction was blue and contained white precipitate. After completion of reaction, work up as above, the solvent was removed by rotary evaporator to afford 1.13 g of crud. Flash chromatography on silica gel (163 g) {eluted with 4:1 hexane-EtOAc} gave two products, **131** in (18%) and **132** in (32%) yields.
As the first fraction isolated was the starting material (30 mg).

The second fraction was the oxidative product **131**, (0.22 g), followed by the rearranged product **132** (0.40 g).

4.2.3. Transformation of 131 to 132.

Following the general procedure, compound **131** (0.5 g, 2 mmol) was treated with $Mn(OAc)_3.2H_2O$ (1.35 g, 5 mmol) and $Cu(OAc)_2.2H_2O$ (0.09 g, 0.5 mmol) in a glacial acetic acid (20 ml), the reaction mixture was stirred at 50 °C under N_2 for 3 h, work up as above, the solvent was removed affording product **132** in yield of (0.32 g, 65%).

The data for 3-(6,9-dihydro-5H-5,9-methanobenzo [a] [7] annulen-6-yl) pentane-2,4-dione (131): further purification by TLC afforded pale yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm):7.0-7.33 (m, 4H, aromatic), 2.22 (dd, J=10.4-4.6 Hz, 1H, H_{10i}), 1.98 (d, J=10.4 Hz, 1H, H_{10e}), 3.4 (dd, J=7.2-4.6 Hz, 1H, H_9), 2.85 (d, J=4.6 Hz, 1H, H_5), 4.95 (m, 1H, H_7), 6.24 (quasi t, J=16.2-7.2 Hz, 1H, H_8), 3.91 (d, J=11.0 Hz, 1H, H_3), 2.99 (dd, J=11.0-1.45 Hz, 1H, H_6), 2.4 (s, 3H, -CH_3), 2.2 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 202.5, 202.2, 151.2, 144.8, 137.0, 126.3, 123.7, 123.2, 120.6 (bs) 72.2, 42.7, 41.1, 40.9, 37.1, 29.5, 29.1; IR (KBr, cm^{-1}): 3431, 3286, 3051, 2961, 2924, 1633, 1461, 1402, 1215, 1140, 1047, 966, 712, 586. Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.31; H, 7.08; O, 12.61 Found: C, 81.82; H, 6.78

The spectral data for 1-(2-methyl-3a,4,9,9a-tetrahydro-4,9-ethenonaphtho[2,3-b]furan-3-yl)ethanone (132): yellow needless; mp: 143.3-144.1°C; H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.0-7.20 (m, 4H, aromatic), 6.34 (quasi t, J=6.8 Hz, 1H, H_{10}), 6.43 (quasi t, J=6.8 Hz, 1H, H_{11}), 4.74 (dd, J=9.3-8.3 Hz, 1H, H_{9a}), 4.34 (bd, J=3.9 Hz, 1H, H_4), 4.3 (t, J=8.3-5.5 Hz, 1H, H_9) 3.36 (bd, J=3.9 Hz, 1H, H_{3a}), 2.12 (s, 3H, -CH_3), 2.25 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 192.3, 169.8, 143.7, 138.8, 135.2, 130.7, 126.3, 125.5, 124.3, 123.6, 115.7, 84.8, 51.0, 45.2, 43.0, 29.1, 15.4; IR (KBr, cm^{-1}): 3456, 3217, 3059, 2974, 2926, 1627, 1610,

1386, 1220, 1147, 989, 943, 760, 704, 602. Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.9; H, 6.35; O, 12.75 Found : C, 80.2; H, 6.68

4.2.4. The oxidative addition of acetylacetone (94) to homobenzonorbornadiene (80) with $Mn(OAc)_3.2H_2O$ alone.

Using a procedure similar to that described above. A solution of acetylacetone **94** (0.25 g, 2.5 mmol) and homobenzonorbornadiene **80** (0.39 g, 2.5 mmol) in a glacial acetic acid (25 ml) with $Mn(OAc)_3.2H_2O$ (1.35 g, 5 mmol), was stirred at 50 °C under N_2 for 7h. Work up as above and the reaction mixture was washed with a saturated aqueous solution of $NaHCO_3$, two portions of water, dried $MgSO_4$, evaporation of the solvent gave 0.3g as crude product which was chromatographed on silica gel (eluted with 4:1 hexane-EtOAc), as a first fraction was alkene **80** (35%), followed by **131** (0.03 g, 5%), followed by **133** (0.02g, 3.3%).

The data for 2-methyl-1-(4,9,10,10a-tetrahydro-3aH-4,9-methanobenzo[4,5]cyclohepta[1,2-b]furan-3-yl)ethanone (133): yellow solid from hexane- AcOEt (3:1); H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.05-7.38 (m, 4H, aromatic), 4.32 (m, 1H, H_{10a}), 3.52 (d, J=3.8 Hz, 1H, H_4), 3.35 (bd, J=9.2 Hz, 1H, H_{3a}), 3.10 (bs, 1H, H_9), 1.85 (d, J=11.2 Hz, 2H, H_{11}), 2.44 (dd, J=11.4-7.5 Hz, 1H, H_{10endo}), 2.31 (d, J=11.4 Hz, 1H, H_{10exo}), 2.15 (s, 3H, -CH_3), 2.35 (s, 3H, -CH_3); Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.3; H, 6.35; Found : C, 80.52; H, 6.7

4.3. The oxidative addition of dimedone (93) to benzobarrelene (82) with $Mn(OAc)_3.2H_2O$ and $Cu(OAc)_2.2H_2O$.

In a 100 ml three-necked round-bottomed flask were placed $Mn(OAc)_3.2H_2O$ (2.7 g, 10 mmol) and $Cu(OAc)_2.2H_2O$ (0.18 g, 1 mmol) in 20 ml a glacial acetic acid and then a solution of dimedone (0.7 g, 5 mmol) and alkene **82** (0.77 g, 5 mmol) in 5 ml acetic acid was added. The reaction mixture was stirred at 50 °C under N_2 for

1h, and the color of the solution was carefully monitored. The dark brown solution became lighter as the Mn(III) was reduced. When the reaction was complete, the solution was colorless to light blue with variable amounts of whit precipitate present. The reaction mixture was poured into 200 ml water to dissolve the precipitate, extracted with 200 ml methylene chloride, the organic phase was separated and the aqueous phase was further extracted with methylene chloride (100 ml). The combined organic extracts were washed successively with a saturated aqueous $NaHCO_3$ then by water (40 ml × 2), dried $MgSO_4$ and concentrated. The residue (1.35 g) was chromatographed on silica gel (160 g) column by eluting with hexane/EtOAc (4:1) to give unreacted starting alkene **82** in (0.032 g, 4%) yield, followed by products: **148** (0.1 g, 8%), **149** (0.068 g, 5%), and then **109** (0.04 g, 3%) respectively, followed by the fourth fraction which consisted of a mixture of **150/151** in a ratio of 1 : 2 with a total yield (0.25 g, 15%), this mixture was submitted to fractional crystallization. Firstly, the endo-derivative **150** was crystallized from hexane-AcOEt (4:1) in refrigerator during one day (0.12 g, 6.5%). After filtration of **150** the solvent was evaporated and the oily residue was crystallized from hexane-AcOEt (3:1) to give **151** (0.15 g, 8.5%).

The data for 3,3-dimethyl-2,3,4,6,11,12-hexahydro-1H-11,6,12-prop[1]ene[1,3,3]triyldibenzo[b,f]oxocin-1-one (148): colorless solid from hexane-AcOEt (3;1), mp:135-138°C ; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 6.96-7.11 (m, 3H, aromatic), 6.8 (m, 1H, aromatic) 6.58 (dd, J=5.7-7.1 Hz, 1H, H_{14}) 5.83 (dd, J=5.7-3.2 Hz, 1H, H_{15}) 5.06 (d, J=2.3 Hz, 1H, H_6) 3.52 (t, J=4.3-3.2 Hz, 1H, H_{11}) 3.24 (t, J=4.5-4.3 Hz, 1H, H_{12}) 2.68 (dt, J=4.5-3.2-3.1 Hz, 1H, H_{13}) 2.2 (AB-system, J=18 Hz, 2H, -CH_2) 1.38 (AB-system, J=16 Hz, 2H, -CH_2) 0.94 (s, 3H, -CH_3) 0.61 (s, 3H, -CH_3) ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 196.4, 168.7, 147.3, 143.6, 131.6, 130.9, 128.7, 128.0, 127.0, 125.4, 113.9, 74.1, 50.4, 49.8, 42.0, 41.9, 41.0, 32.2, 28.1, 28.0; IR (KBr, cm^{-1}): 3281, 3057, 2957, 2953, 2924, 2866, 1652, 1621, 1456, 1386, 1342, 1244, 1207, 1170, 1118, 939, 901, 797, 766, 733, 650, 480 Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.1; H, 6.85; O, 11.05 Found: C, 81.51; H, 7.25

The data for 8,8-dimethyl-4b,5,7,8,9,10b,11,12-octahydro-10H-5,11,12-methanetriylnaphtho[1,2-c]chromen-10-one (149): white solid, mp: 143-145°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.04-7.26 (m, 4H, aromatic), 1.77 (quasi dd, J=7.2-5.5 Hz, 1H, H_{11}), 1.99 (quasi dd, J=5.5 Hz, 1H, H_{13}), 2.06 (t, J=7.2 Hz, 1H, H_{12}) 2.73 (bs, 1H, H_5) 3.0 (bs, 1H, H_{4b}), 4.34 (bs, 1H, H_{10b}) 1.08 (s, 3H, -CH_3) 1.1 (s, 3H, -CH_3);
^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 195.2, 168.7, 134.4, 134.1, 127.0, 125.4, 125.2, 125.1, 116.4, 82.0, 50.4, 41.8, 41.7, 32.5, 29.6, 28.6, 28.2, 25.7, 20.9, 17.9; IR (KBr, cm^{-1}): 3414, 3069, 3028, 2951, 2916, 2849, 1646, 1614, 1490, 1465, 1380, 1303, 1202, 1120, 1037, 980, 760, 721, 506. Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.19; H, 6.85; O, 11.05 Found: C, 82.19; H, 7.87

The data for 8,8-dimethyl-10-oxo-4b,7,8,9,10,10b,11,12-octahydro-5H-5,11-methanonaphtho[1,2-c]chromen-12-yl acetate (endo-isomer) (150): white solid, mp: 154.2-155.4°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.07-7.20 (m, 4H, aromatic), 6.15 (d, J=4.3 Hz, 1H, H_{12}), 4.60 (d, J=5.4 Hz, 1H, H_5), 3.27 (bs, 1H, H_{10b}) 2.91 (bs, 1H, H_{4b}) 2.87 (quasi dd, 4.3, 1H, H_{11}) 2.20 (d, J=5.4, 1H, H_{13exo}) 1.77 (dd, J=15.7-7.4 Hz, 1H, H_{13endo}) 2.17 (AB-system, J=18 Hz, 2H, -CH_2) 2.04 (AB-system, J=16 Hz, 2H, -CH_2) 0.99 (s, 3H, -CH_3) 1.01 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 194.0, 169.6, 167.0, 136.8, 132.7, 127.1, 127.1, 126.9, 126.7, 115.2, 83.2, 72.6, 49.3, 46.3, 44.0, 40.5, 35.7, 31.4, 30.4, 27.7, 26.9, 20.2; IR (KBr, cm^{-1}): 3439, 3283, 3067, 3032, 2963, 2886, 2864, 1729, 1648, 1623, 1390, 1253, 1234, 1051, 1030, 989, 929, 754, 606, 559. Anal. Calcd. for $C_{22}H_{24}O_4$: C, 75.07; H, 6.82; O, 18.11 Found: C, 76.07; H, 7.25

The data for 8,8-dimethyl-10-oxo-4b,7,8,9,10,10b,11,12-octahydro-5H-5,11-methanonaphtho[1,2-c]chromen-12-yl acetate (exo-isomer) (151): colorless powder, mp: 160.9-161.4°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.18-7.30 (m, 4H, aromatic), 2.07 (dd, A-part of AB-system, J=15.7-5.3 Hz, 1H, H_{13exo}), 1.60 (dd, B-part of AB-system, J=15.7-7.0 Hz, 1H, H_{13endo}), 4.63 (d, J=5.3 Hz, 1H, H_5) 2.8

(bd, J=7.0 Hz, 1H, H_{11}) 5.58 (d, J=3.1, 1H, H_{12}) 3.10 (bs, 1H, H_{4b}) 3.41 (bs, 1H,H_{10b}) 2.17 (AB-system, J=18 Hz, 2H, -CH_2) 2.04 (AB-system, J=16 Hz, 2H, -CH_2) 1.07 (s, 3H, -CH_3) 1.08 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 195.2, 170.8, 167.8, 138.5, 132.0, 130.9, 128.7, 128.4, 127.9, 116.1, 83.1, 73.3, 50.4, 47.2, 44.8, 41.4, 33.3, 32.5, 31.9, 28.7, 27.9, 21.4; IR (KBr, cm^{-1}): 3429, 3273, 3069, 3022, 2953, 2936, 2886, 2866, 1725, 1646, 1616, 1390, 1238, 1122, 1020, 985, 926, 756, 606, 546.

4.3.1. The oxidative addition of dimedone (93) to benzobarrelene (82) with $Mn(OAc)_3 .2H_2O$ alone.

Using a procedure similar to that described above. In a 100 ml three-necked round-bottomed flask were placed $Mn(OAc)_3 .2H_2O$ (2.7 g, 10 mmol) in 20 ml a glacial acetic acid and then a solution of dimedone (0.7 g, 5 mmol) and alkene **82** (0.77 g, 5 mmol) in 5 ml acetic acid was added. The reaction mixture was stirred at 50 °C under N_2 for 8h. The dark brown solution became lighter as the Mn(III) was reduced. When the reaction was complete with variable amounts of whit precipitate present. The reaction mixture was poured into 200 ml water to dissolve the precipitate, extracted with 200 ml methylene chloride, the organic phase was separated and the aqueous phase was further extracted with methylene chloride (100 ml). The combined organic extracts were washed successively with a saturated aqueous $NaHCO_3$ then by water (40 ml × 2), dried $MgSO_4$ and concentrated. The residue (0.97 g) consists of the isomeric mixture of **150/151** in a ratio of 1 : 2 with a total yield (0.12 g, 9%) was formed as sole product with recovered alkene yield of about 6%

4.3.2. The oxidative addition of acetylacetone (94) to benzobarrelene (82) with $Mn(OAc)_3 . 2H_2O$ and $Cu(OAc)_2 . 2H_2O$.

To a stirred solution of $Mn(OAc)_3 .2H_2O$ (2.7 g, 10 mmol) and $Cu(OAc)_2.2H_2O$ (0.18 g, 1 mmol) in 20 ml a glacial acetic acid at 50 °C under N_2 atmosphere was

added a solution of benzobarrelene **82** (0.77 g, 5 mmol) and acetylacetone **94** (0.5 g, 5 mmol) in 5 ml acetic acid, and the reaction mixture was stirred for 3h, at which time the reaction was blue and contained white precipitate. After completion of reaction, work up as above, the solvent was removed by rotary evaporator to afford 1.13 g of crude. Flash chromatography on silica gel (eluted with 4:1 hexane-EtOAc) gave as a first fraction isolated, the starting material (0.030 g, 3%), followed by products: **169** (0.1 g, 8%), **132** (0.088 g, 7%), and then **170** (0.078 g, 5%) respectively, followed by the fourth fraction which consisted of a mixture of **171/172** in a ratio of 1 : 2 with a total yield (0.23 g, 13%).

The data for 1-(3-methyl-5,6-dihydro-1H-6,1,5-prop[1]ene[1,3,3]triyl-2-benzoxocin-4-yl)ethanone 169: white crystals from hexane-AcOEt (3:1); mp: 118-120°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.07-7.18 (m, 3H, aromatic), 6.63 (dd, J=5.6-3.1 Hz, 1H, aromatic) 5.96 (dd, J=5.6-3.2 Hz, 1H, H_{14}), 5.09 (d, J=3.0 Hz, 1H, H_6) 3.53 (t, J=4.2-3.2 Hz, 1H, H_{11}) 3.34 (t, J=4.4-4.2 Hz, 1H, H_{12}) 2.76 (dt, J=4.4-3.0 Hz, 1H, H_{13}) 2.1 (s, 3H, -CH_3) 2.27 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 196.6, 164.1, 146.3, 142.7, 131.3, 131.1, 129.1, 128.0, 127.4, 125.2, 114.1, 72.7, 50.9, 46.2, 41.0, 29.6, 20.6; IR (KBr, cm^{-1}): Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.9; H, 6.35. Found: C, 80.28; H, 6.54

The data for 10-(1-acetyl-2-oxopropyl)-8,9-dihydro-5H-5,8-methanobenzo[a][7]annulen-9-yl acetate (170): white needles, mp: 95-97°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.16-7.28 (m, 4H, aromatic), 6.52 (dd, J=8.9-3.2 Hz, 1H, H_7) 6.05 (dd, J=8.9-3.2 Hz, 1H, H_6), 5.67 (s, 1H, H_9) 3.95 (d, J=12.0 Hz, 1H, H_{11}) 3.2 (dt, J=12.0-3.9 Hz, 1H, H_{10}) 3.16 (t, J=6.9-3.2 Hz, 1H, H_5) 2.9 (bs, 1H, H_8) 2.15 (s, 3H, -CH_3) 2.09 (s, 3H, -CH_3 of acetyl group) 2.05 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 202.6, 201.1, 169.9, 144.4, 139.4, 133.1, 130.7, 130.5, 127.9, 127.7, 126.4, 68.4, 67.5, 46.5, 46.0, 44.4, 30.0, 28.7, 21.1; IR (KBr, cm^{-1}): 3448, 3389, 3061, 2995, 2970, 2938, 1737, 1698, 1419, 1359, 1290, 1224, 1145, 960, 889, 771, 731, 583. Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.01; H, 6.41. Found: C, 72.24; H, 6.67

4.4. The synthesis of 1-(9-hydroxy-8,9-dihydro-5H-5,8-methanobenzo[a][7]annulen-10-yl)acetone (181) (Hydrolysis of 171/172).

The isomeric mixture **171/172** (50 mg) was dissolved in 50 ml absolute methanol and was put in a 50 ml two-necked flask. While being passed dry NH_3 through the solution, the mixture was stirred for 4h at room temperature. On evaporation of the solvent (40 mg, 0.2 mmol) of crude product **173** was obtained.

4.4.1. The synthesis of 10-(2-oxopropyl)-5,8-dihydro-9H-5,8-methanobenzo[a][7]annulen-9-one (174).

The crude **173** was dissolved in 50 ml chloroform and placed in a round-bottomed flask fitted with a magnetic stirrer. The oxidant, finely grounded MnO_2 reagent, was added. The solution was stirred at room temperature for 60 h, After filtration and evaporation of the solvent, the residue was recrystallized from hexane-EtOAc (3:1) to give **174** (35 mg, 75%).

The data for 174: white solid, mp: 112-114.2°C ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.89 (m, 1H, aromatic), 7.1-7.38 (m, 3H, aromatic), 2.59-2.78 (dq of AB-system, J=17.2-7.2 Hz, 1H, H_1, J=17.2-5.8 Hz, 1H, H_1) 6.55 (dd, J=5.1-2.7 Hz, 1H, H_7), 5.96 (dd, J=5.1-3.1 Hz, 1H, H_6) 3.46 (d, J=2.7 Hz, 1H, H_8) 3.24 (d, J=3.1 Hz, 1H, H_5) 3.29 (bdd, J=7.2-5.8 Hz, 1H, H_{10}) 2.1 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 206.5, 194.3, 147.5, 143, 132.6, 128.8, 128.4, 127.4, 127.3, 124.9, 60.9, 54.4, 51.8, 45.4, 30.9. Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.65; H, 6.19; O, 17.15 Found: C, 79.86; H, 6.35

4.4.2. The oxidative addition of acetylacetone (94) to benzobarrelene (82) with $Mn(OAc)_3$. $2H_2O$ alone.

To a stirred solution of $Mn(OAc)_3$.$2H_2O$ (2.7 g, 10 mmol) in 20 ml a glacial acetic acid at 50 °C under N_2 atmosphere was added a solution of benzobarrelene **82** (0.77

g, 5 mmol) and acetylacetone **94** (0.5 g, 5 mmol) in 5 ml acetic acid, and the reaction mixture was stirred for 10h, at which time the reaction was contained white precipitate. After completion of reaction, work up as above, the solvent was removed by rotary evaporator to afford 0.8 g of crude, which consisted of a mixture of **171/172** in a ratio of 1 : 2 with a total yield (0.95g, 8%).

4. 5. The oxidative addition of dimedone (93) to 7-aza-benzonorbornadiene (83), the synthesis of 3,3-dimethyl-ethyl 1-oxo-1,2,3,4,6,6a,11,11a-octahydro-6,11-epiminoindeno[1,2-c]chromene-12-carboxylate(189).

(A) With Mn(III) acetate and Cu(II) acetate. A solution of 7-aza-benzonorbornadiene **(83)** (0.535 g, 2.5 mmol), dimedone **(93)** (0.35 g, 2.5 mmol), and $Mn(OAc)_3 .2H_2O$ (1.35 g, 5 mmol) and $Cu(OAc)_2.2H_2O$ (0.12 g,1 mmol) in 25 ml a glacial acetic acid were placed in a 100 ml three-necked flask. The reaction mixture was stirred at 50 °C under N_2 atmosphere for 2h and was monitored carefully by thin layer chromatography until the alkene (**83**) was completely consumed. At that time, the dark brown solution became lighter with very small amount of white precipitate. The reaction mixture was poured into 200 ml water, extracted with 200 ml methylene chloride, the organic phase was separated and the aqueous phase was further extracted with methylene chloride (100 ml). The combined organic extracts were washed successively with a saturated aqueous $NaHCO_3$ then by water (40 ml × 2), dried $MgSO_4$ and concentrated. The residue (0.89 g) crystallized on standing at room temperature and was separated by TLC using hexane-AcOEt (4:1) and was further purified by recrystallization from hexane- AcOEt (3:1) giving (0.55 g, 65 %) of **189**. **(B) With Mn(III) acetate alone.** Using similar procedure described above with $Mn(OAc)_3 .2H_2O$ alone. The reaction was monitored by TLC, and after completion of reaction (2h) the dark brown solution changed to a dark red color. Work up, dried $MgSO_4$. After the removal of the solvent, the residue (1.45 g) was recrystallized to give **189** (0.35 g, 41%).

The data for (189): colorless solid, mp: 175.5-177.5 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.1-7.37 (m, 4H, aryl), 5.5 (bs, 1H, H_6), 5.0 (bs, 1H, H_{11}), 3.98 (q, J=7.1 Hz, 2H, -CH_2) 1.2 (t, J=7.1 Hz, 3H, -CH_3) 3.32 (bs, 1H, H_{6a}) 3.35 (bs, 1H, H_{11a}) 2.16 (AB-system, J=18 Hz, 2H, -CH_2), 2.44 (AB-system, J=16 Hz, 2H, -CH_2), 1.06 (s, 3H, -CH_3) 1.1 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 195.1, 168.3, 155.2, 146,5, 141.8, 127.2, 127.1, 123.6, 123.2, 113.5, 86.3, 70.6, 61.5, 51.0, 50.2, 45.6, 40.9, 32.4, 29.7, 27.2, 14.6; IR (KBr, cm^{-1}): 2967, 2922, 1714, 1646, 1617, 858, 775, 677. Anal. Calcd. for $C_{21}H_{24}O_4N$: C, 71.37; H, 6.56; N, 3.96 Found: C, 71.35; H, 6.53; N, 4.24

4.5.1 The oxidative addition of acetylacetone (94) to 7-aza-benzonorbornadiene (83), the synthesis of ethyl 4-acetyl-3-methyl-1,4a,5,9b-tetrahydro-1,5-epiminoindeno[1,2-c]pyran-10-carboxylate (195).

(A) With Mn(III) acetate and Cu(II) acetate. A solution of an alkene **(83)** (0.535 g, 2.5 mmol), acetylacetone **(94)** (0.25 g, 2.5 mmol), and $Mn(OAc)_3 .2H_2O$ (1.35 g, 5 mmol) and $Cu(OAc)_2.2H_2O$ (0.12 g, 1 mmol) in 25 ml a glacial acetic acid were placed in a 100 ml three-necked flask. The reaction mixture was stirred at 50 °C under N_2 atmosphere for 18h and was monitored carefully by thin layer chromatography until the alkene (**83**) was completely consumed. At that time, the dark brown solution became brownish-green with very small amount of white precipitate. The reaction mixture was poured into 200 ml water, extracted with 200 ml methylene chloride, the organic phase was separated and the aqueous phase was further extracted with methylene chloride (100 ml). The combined organic extracts were washed successively with a saturated aqueous $NaHCO_3$ then by water (40 ml $\times$ 2), dried $MgSO_4$ and concentrated. The residue (0.8 g) crystallized on standing at room temperature and was separated by TLC using hexane-AcOEt (4:1) and was further purified by recrystallization from hexane- AcOEt (3:1) giving (0.45g, 61%) of **195**. **(B) With Mn(III) acetate alone.** Using similar procedure described above with $Mn(OAc)_3 .2H_2O$ alone. The reaction was monitored by TLC, and after completion of reaction (2h) the dark brown solution changed to the buff colour.

Work up, dried $MgSO_4$. After the removal of the solvent, the residue (0.54 g) was recrystallized to give **195** (0.25 g, 34 %).

The data for 195: colorless solid, mp: 165-167.5 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm): 7.0-7.4 (m, 4H, aryl), 5.5 (bs, 1H, H_6), 5.0 (bs, 1H, H_{11}), 3.98 (q, J=6.9 Hz, 2H, -CH_2) 1.15 (t, J=6.9 Hz, 3H, -CH_3) 3.37 (bs, 1H, H_{11a}) 3.1 (bd, 1H, H_{6a}) 2.32 (s, 3H, -CH_3) 2.28 (s, 3H, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 196.1, 155.4, 146.1, 141.9, 127.3, 126.5, 123.8, 121.2, 114.5, 85.2, 70.8, 61.6, 55.9, 45.9, 45.2, 29.6, 20.0, 14.5; IR (KBr, cm^{-1}): 3391, 3328, 3046, 2980, 1710, 1670 (C-N), 1710, 1579, 1340, 872. Anal. Calcd. for $C_{18}H_{19}O_4N$: C, 69.0; H, 6.07; N, 4.47 Found: C, 68.96; H, 6.04; N, 4.71

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APPENDIX A

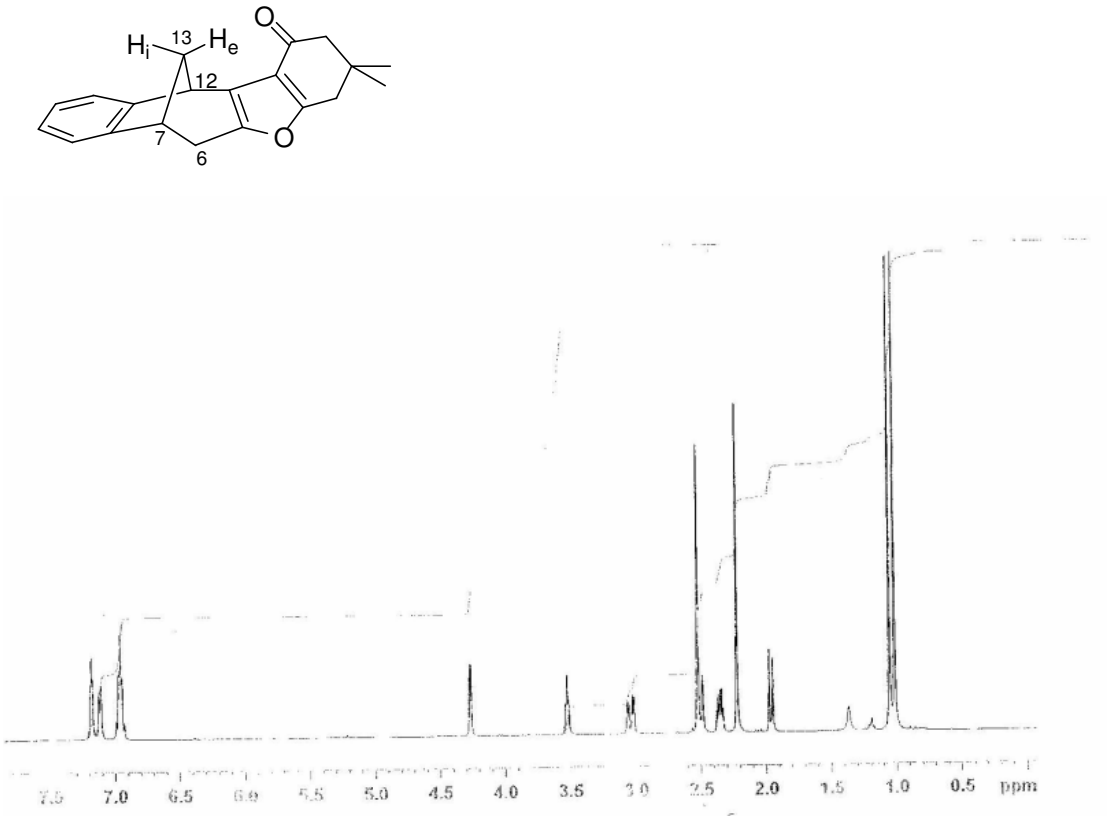


Figure A1 ^{1}H-NMR Spectrum of Compound **107**.

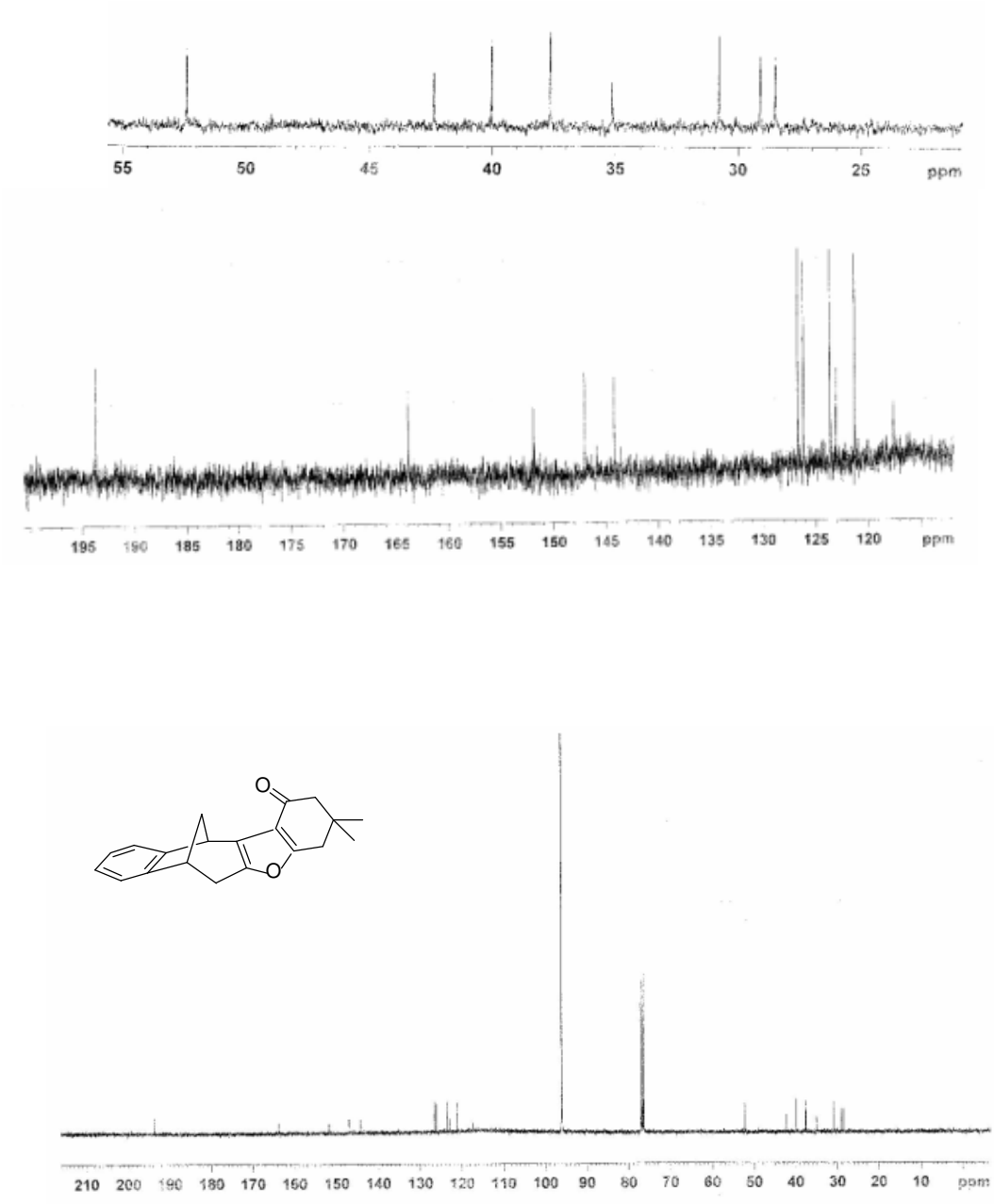


Figure A2 ^{13}C-NMR Spectrum **of 107**.

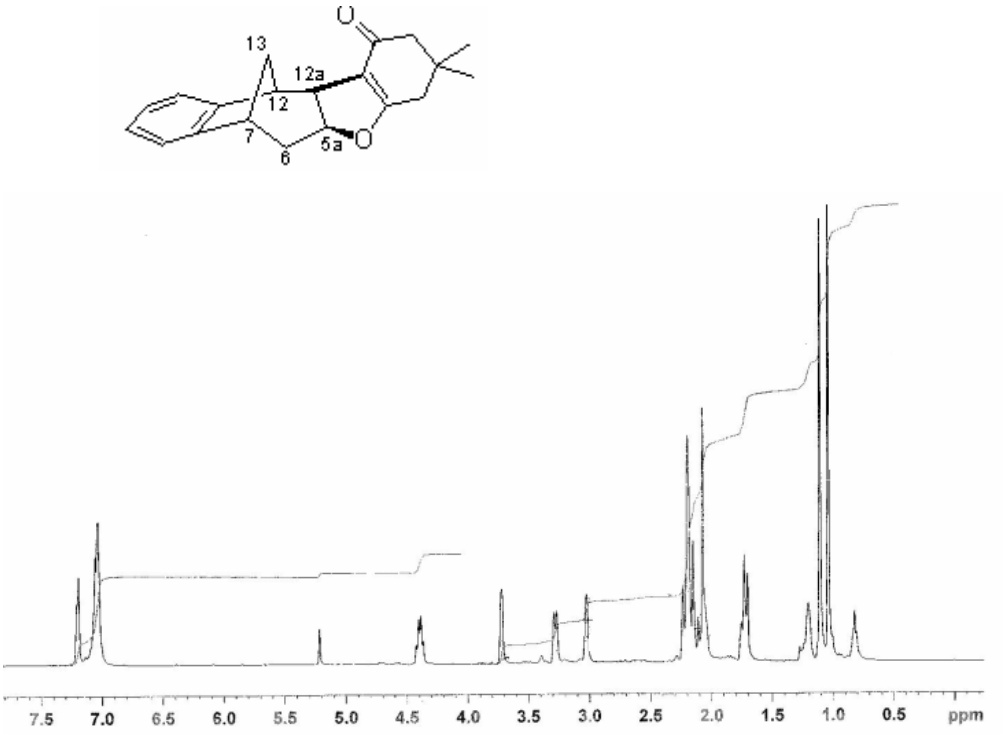


Figure A3 ^{1}H-NMR Spectrum of compound **108**

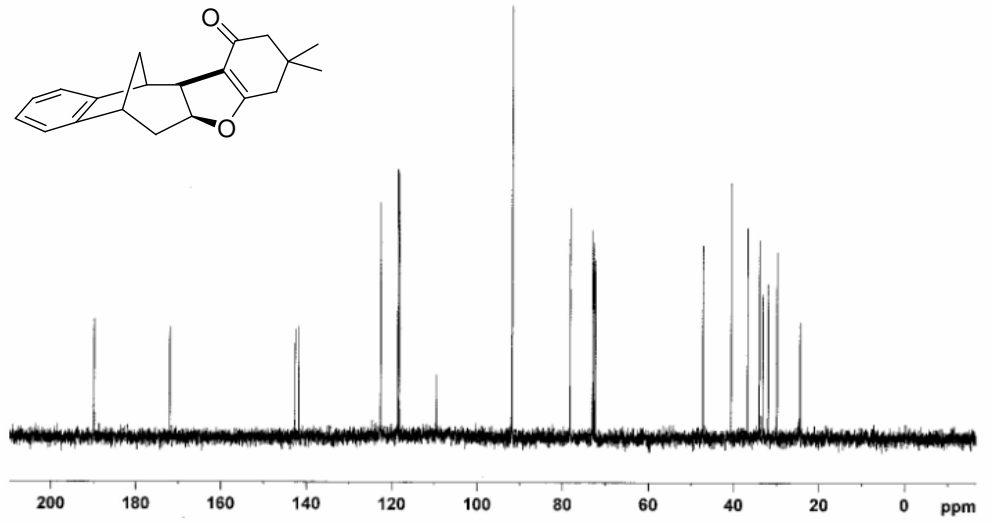


Figure A4 ^{13}C-NMR Spectrum of **108**

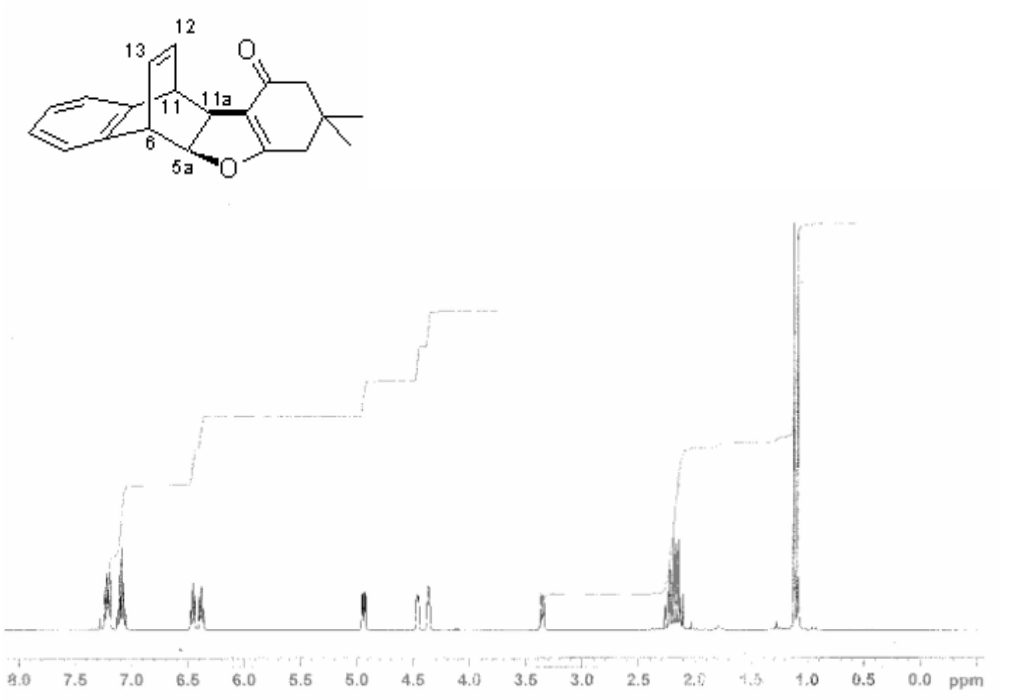


Figure A5 ^{1}H-NMR Spectrum of compound **109**.

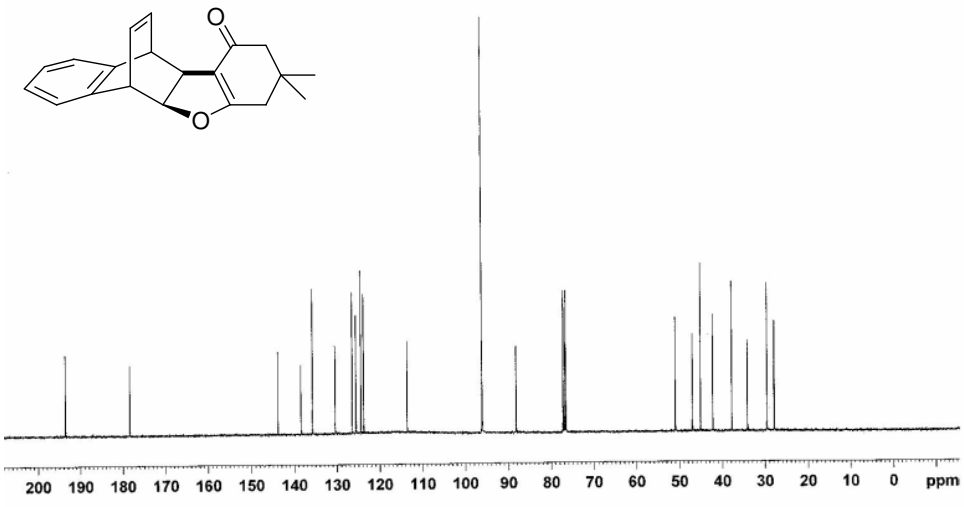


Figure A6 ^{13}C-NMR Spectrum of **109**

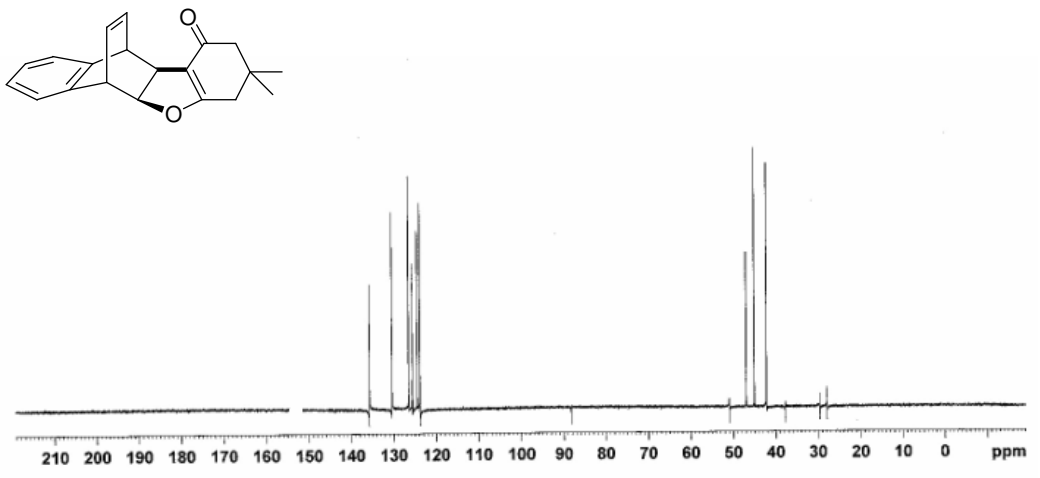


Figure A7 DEPT-90 Spectrum of **109**

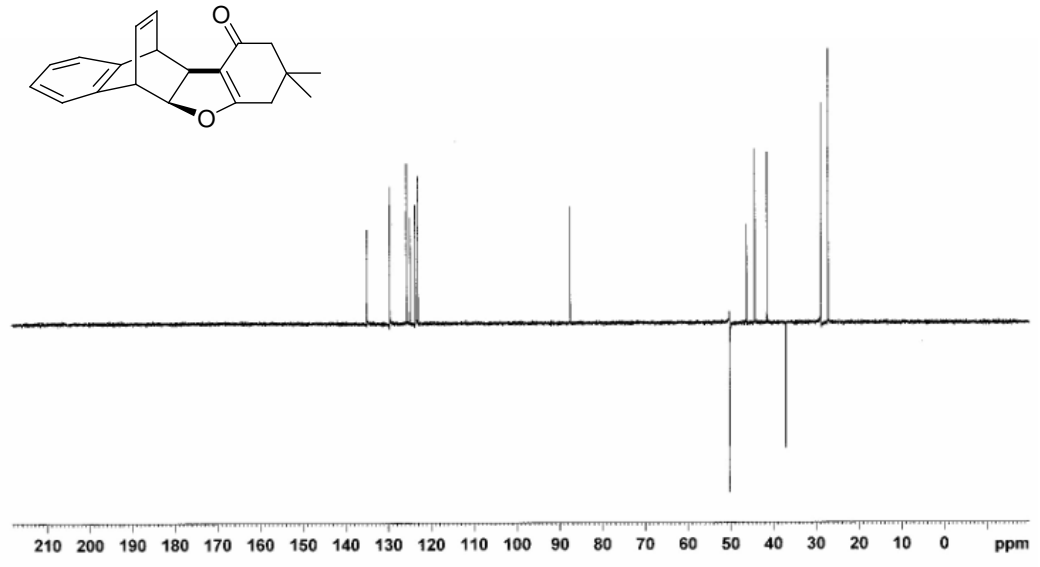


Figure A8 DEPT-135 Spectrum of **109**

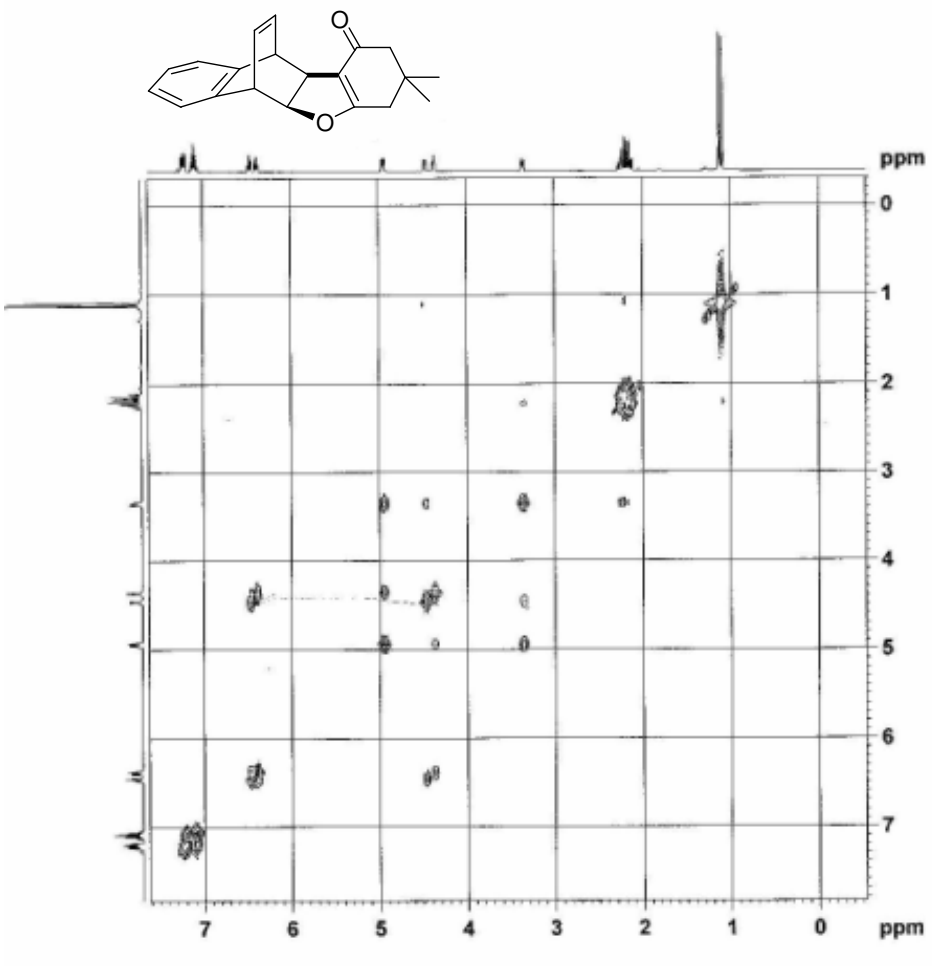


Figure A9 COSY Spectrum of **109**

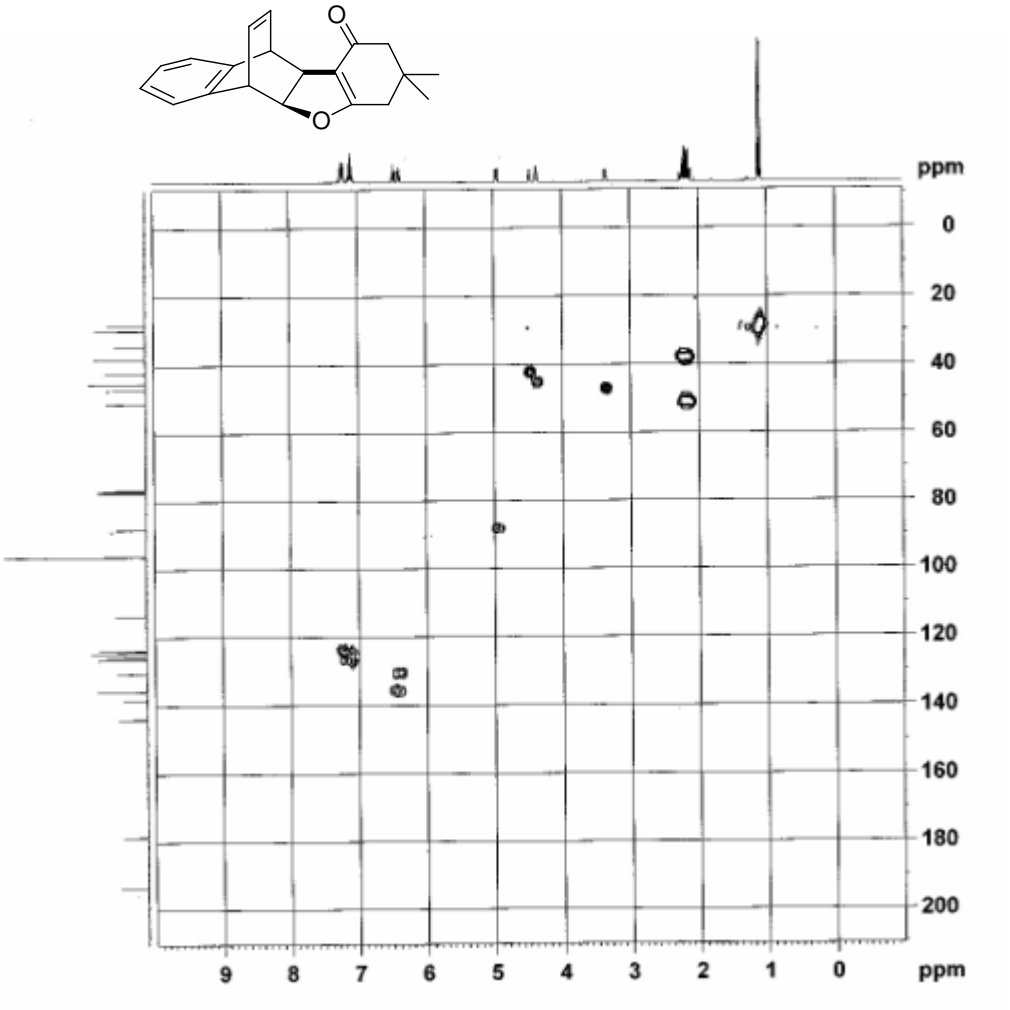


Figure A10 HMQC Spectrum of **109**

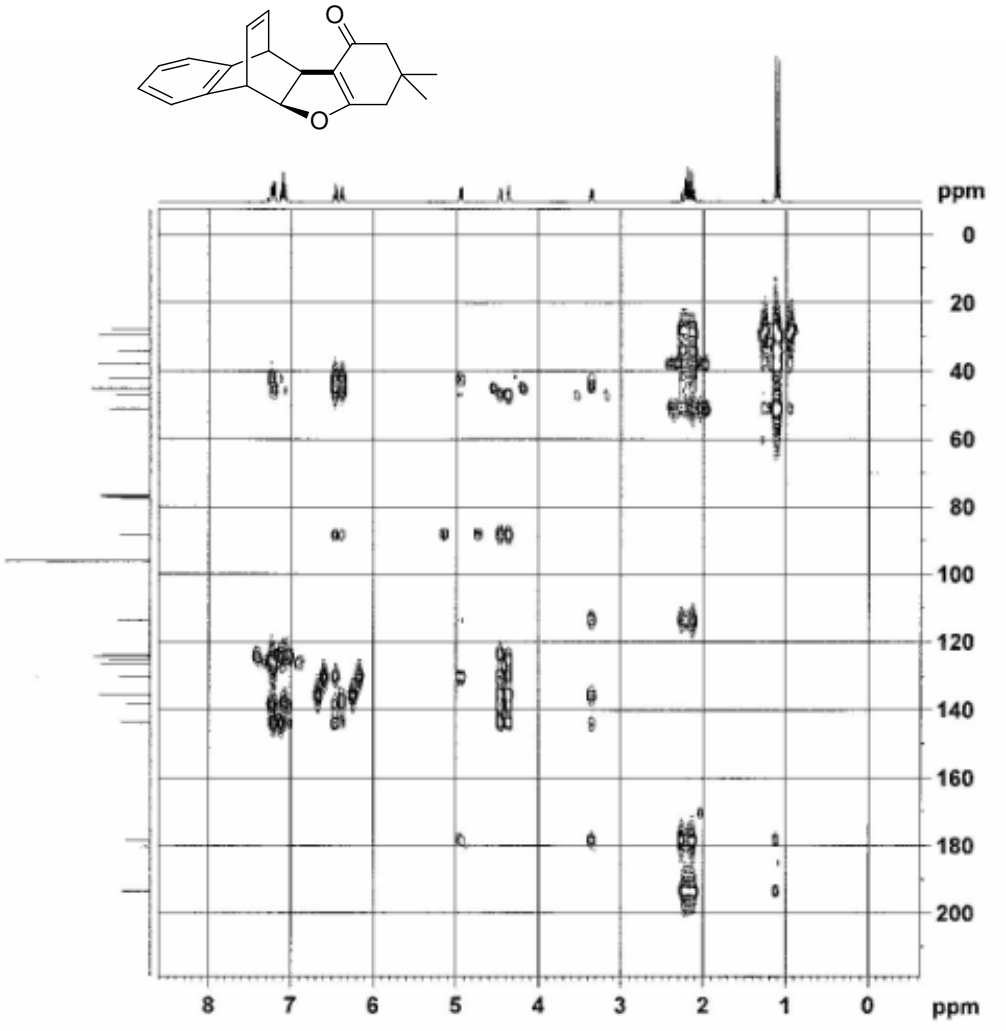


Figure A11 HMBC Spectrum of **109**

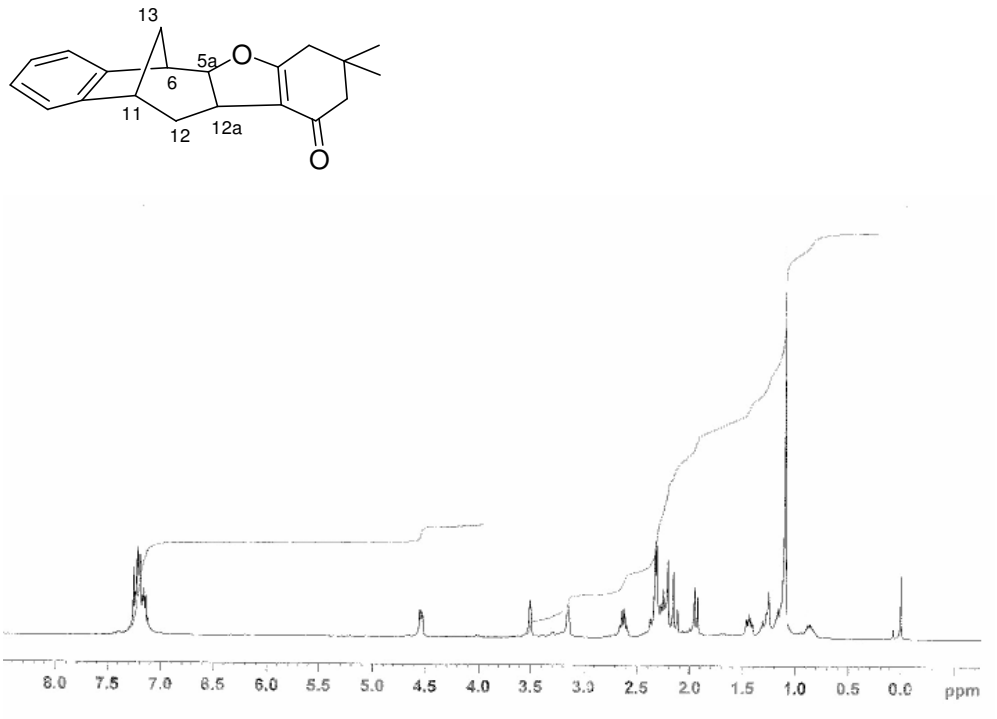


Figure A12 ^{1}H-NMR Spectrum of compound **110**.

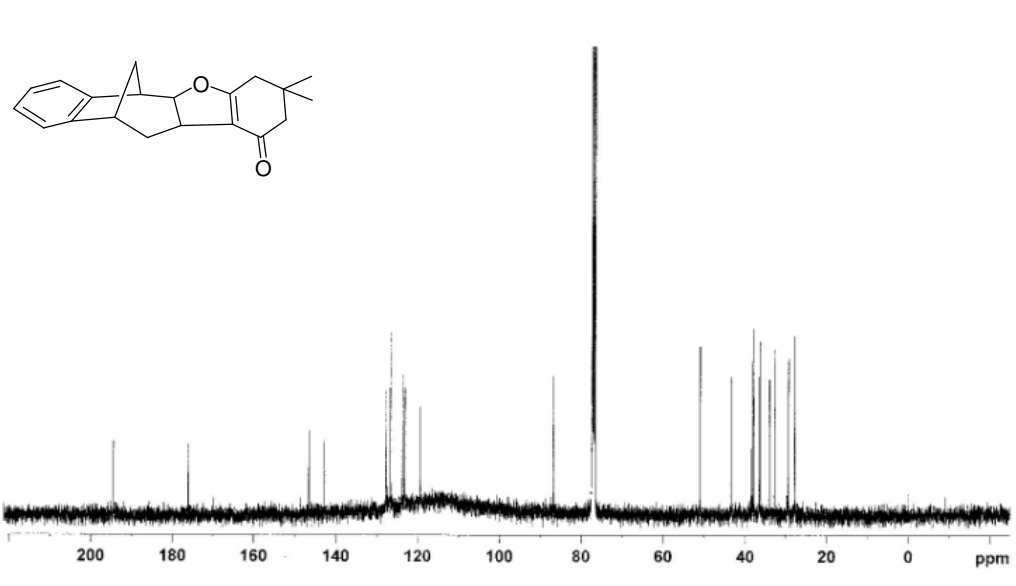


Figure A13 ^{13}C-NMR Spectrum of compound **110**.

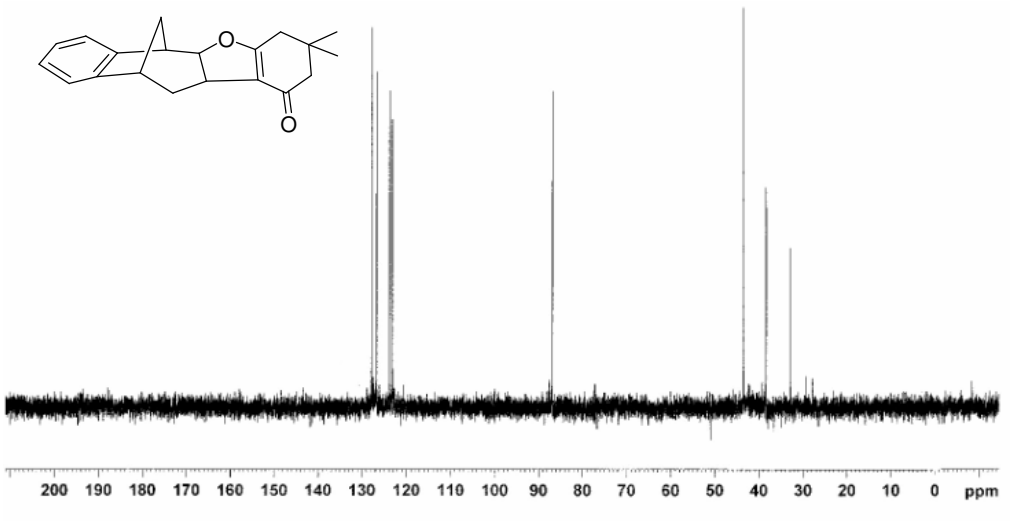


Figure A14 DEPT-90 Spectrum of **110**.

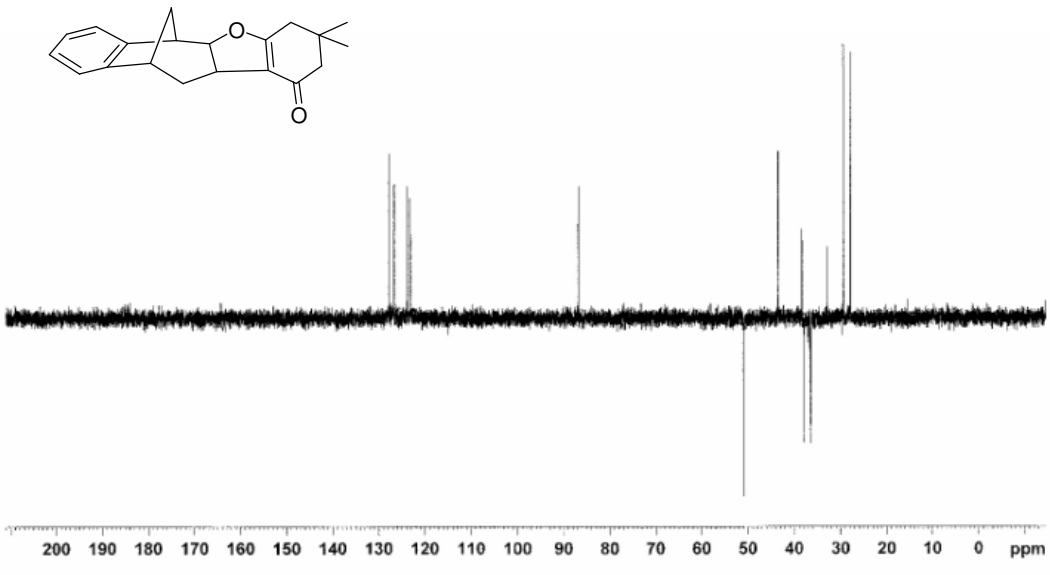


Figure A15 DEPT-135 Spectrum of **110**.

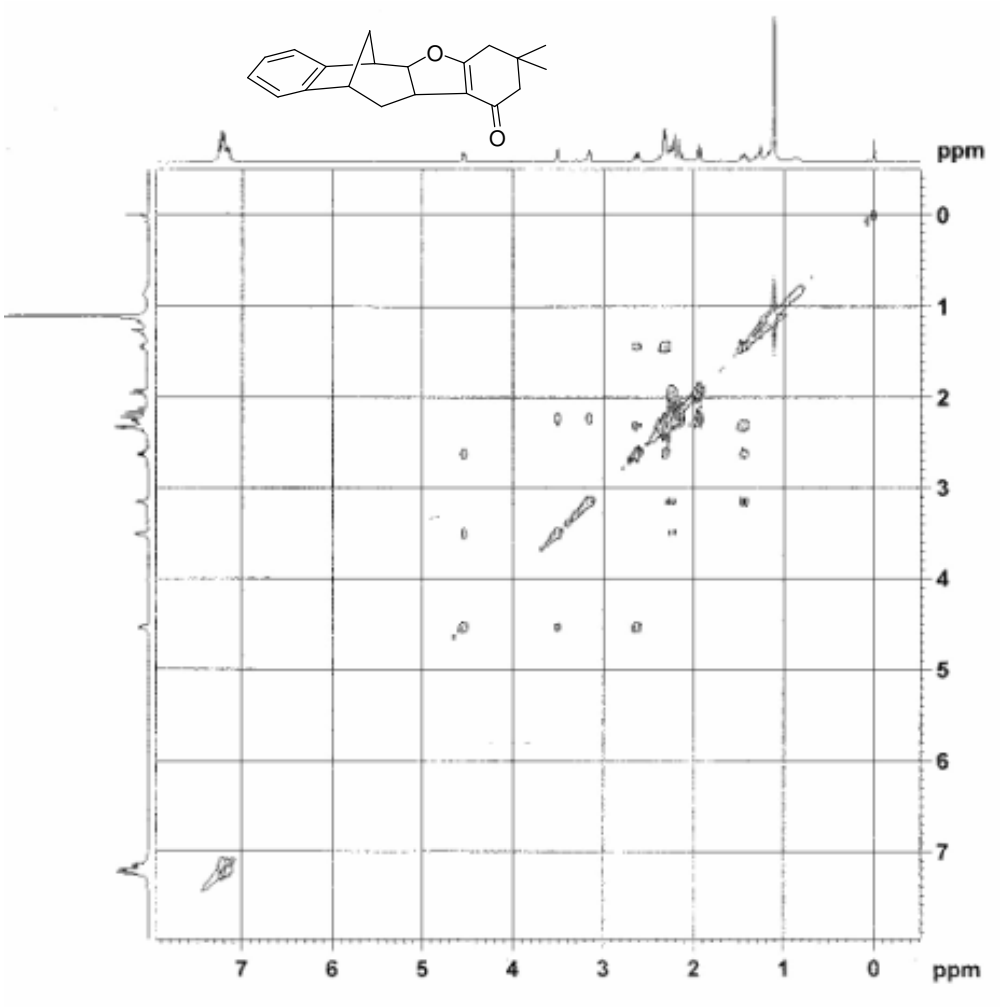


Figure A16 COSY Spectrum of **110**.

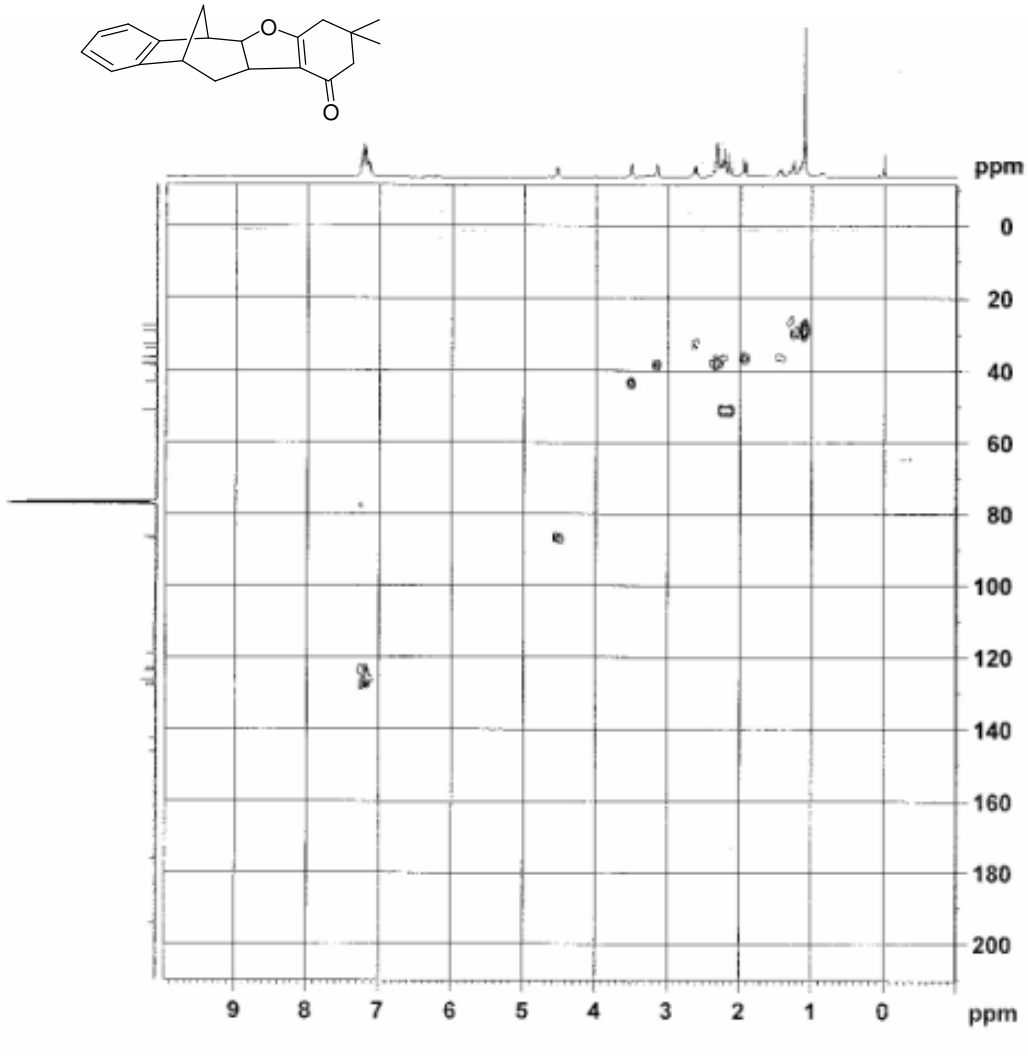


Figure A17 HMQC Spectrum of **110**.

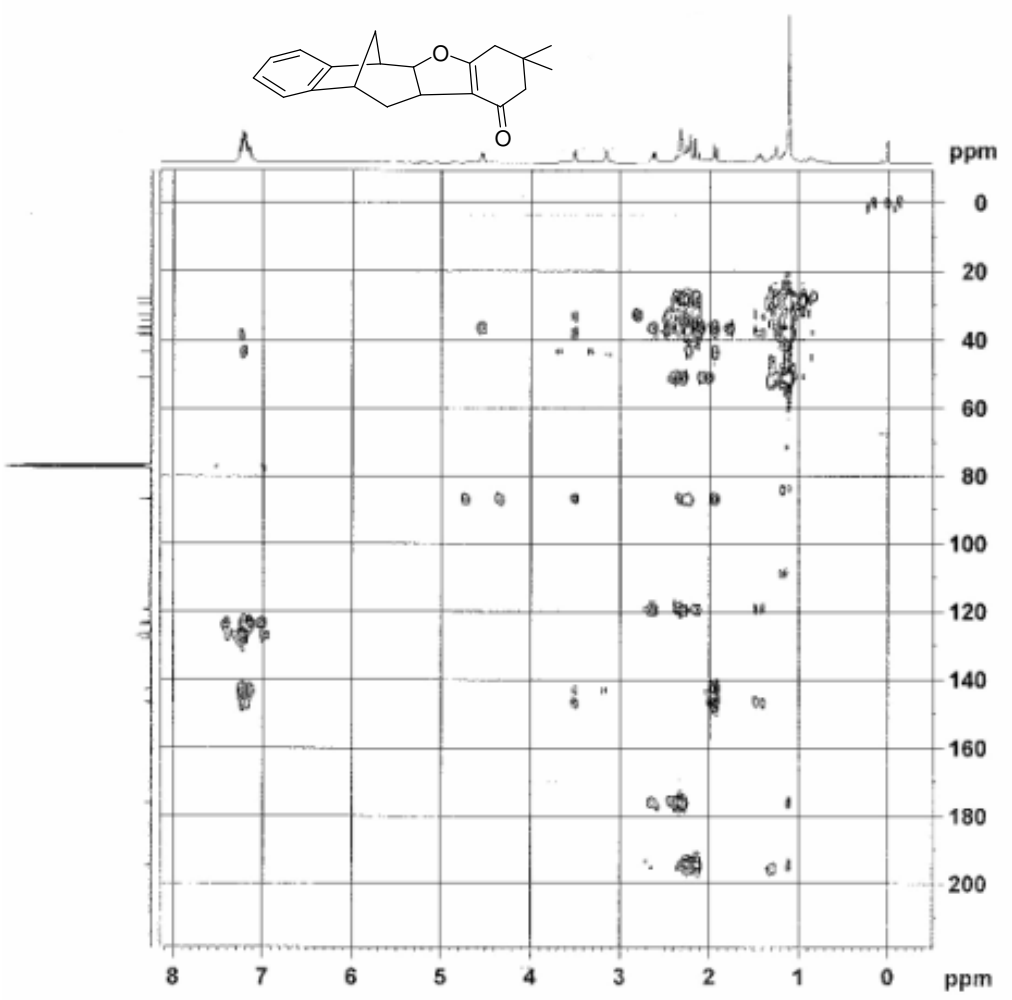


Figure A18 HMBC Spectrum of **110**

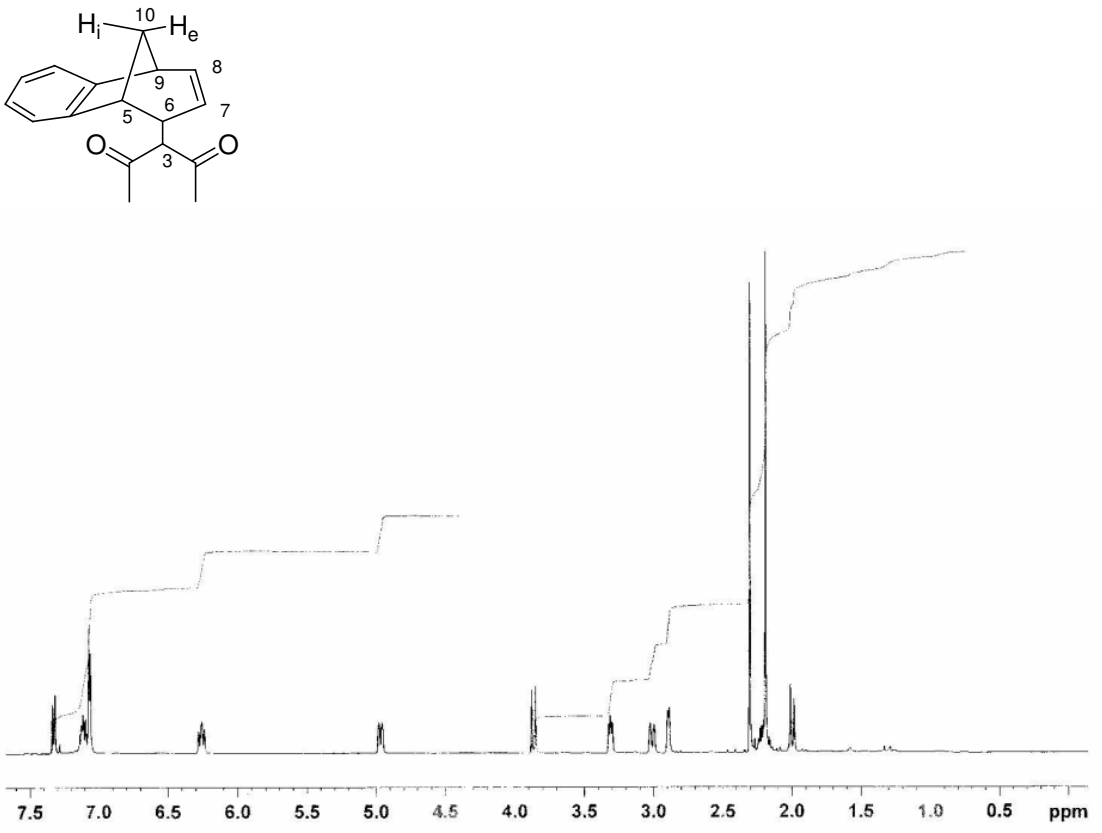


Figure A19 [1]H-NMR Spectrum of compound **131**.

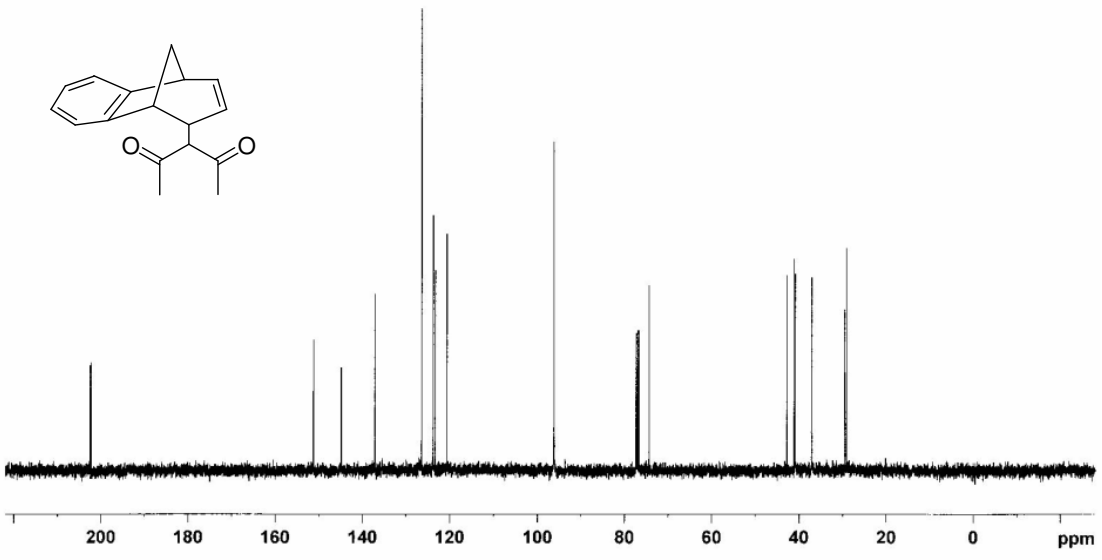


Figure A20 [13]C-NMR Spectrum of compound **131**

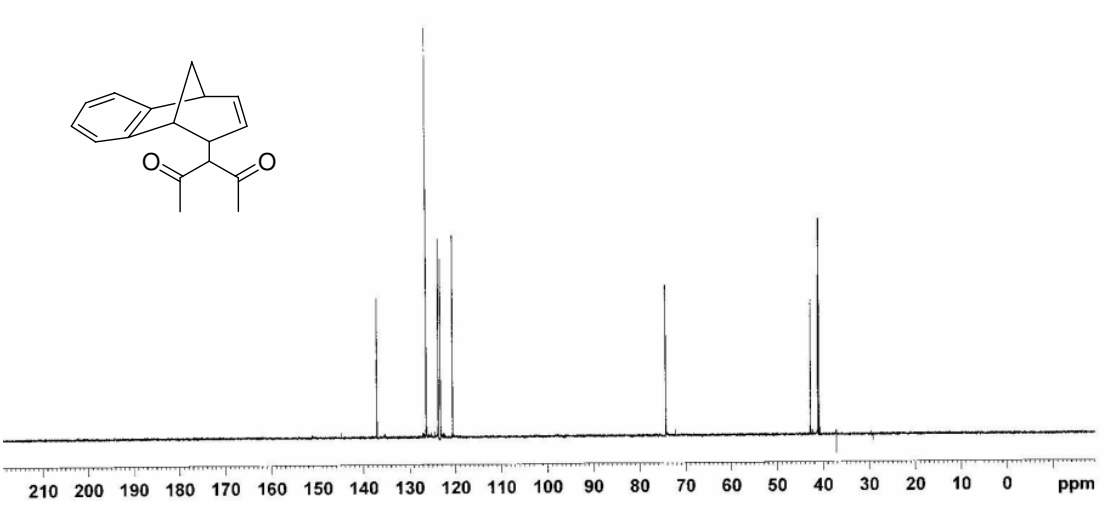


Figure A21 DEPT-90 Spectrum of **131**.

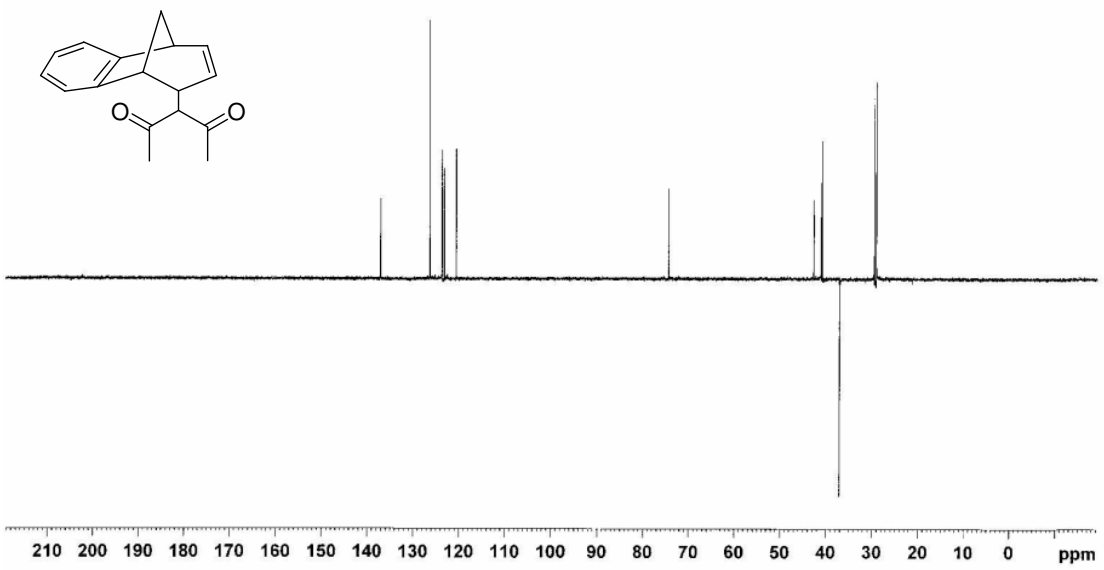


Figure A22 DEPT-135 Spectrum of **131**.

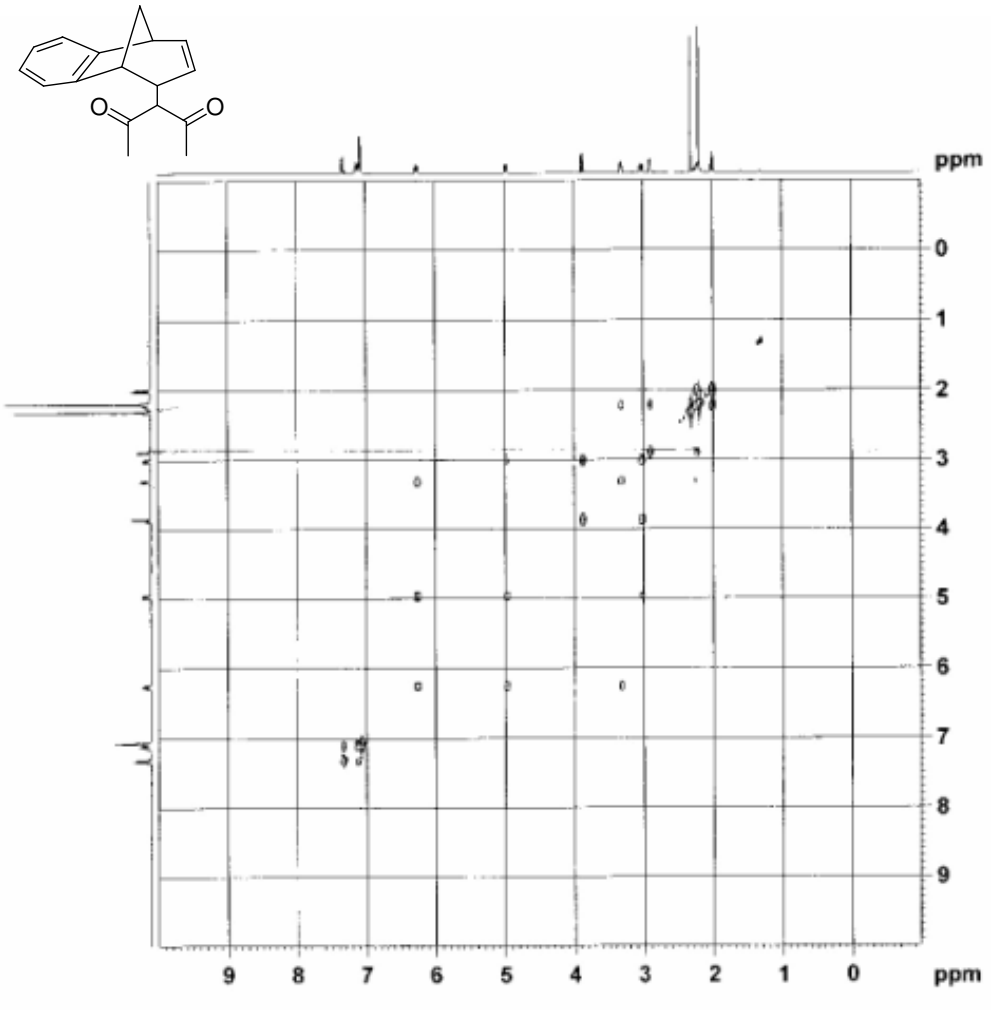


Figure A23 COSY Spectrum of **131**.

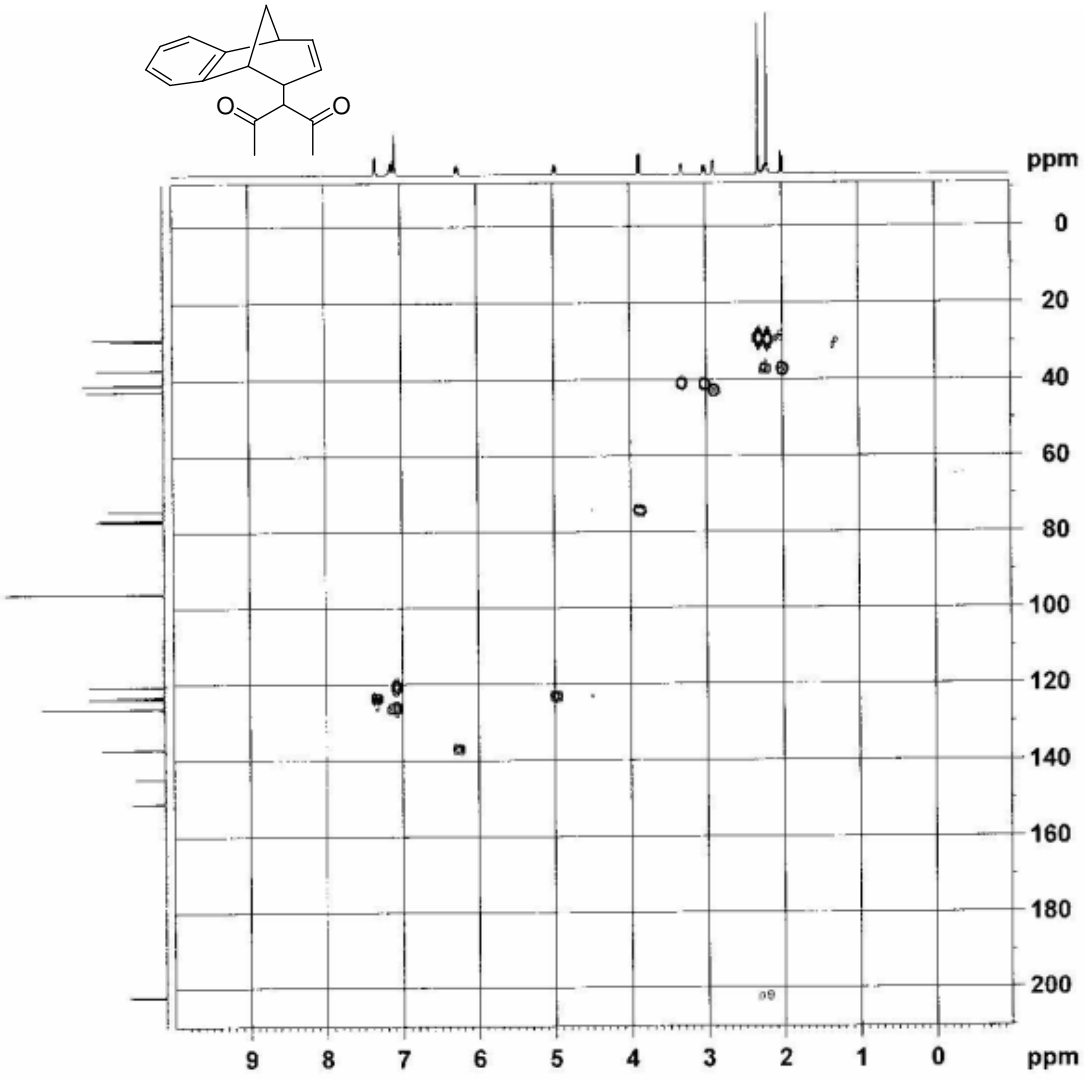


Figure A24 HMQC Spectrum of **131**.

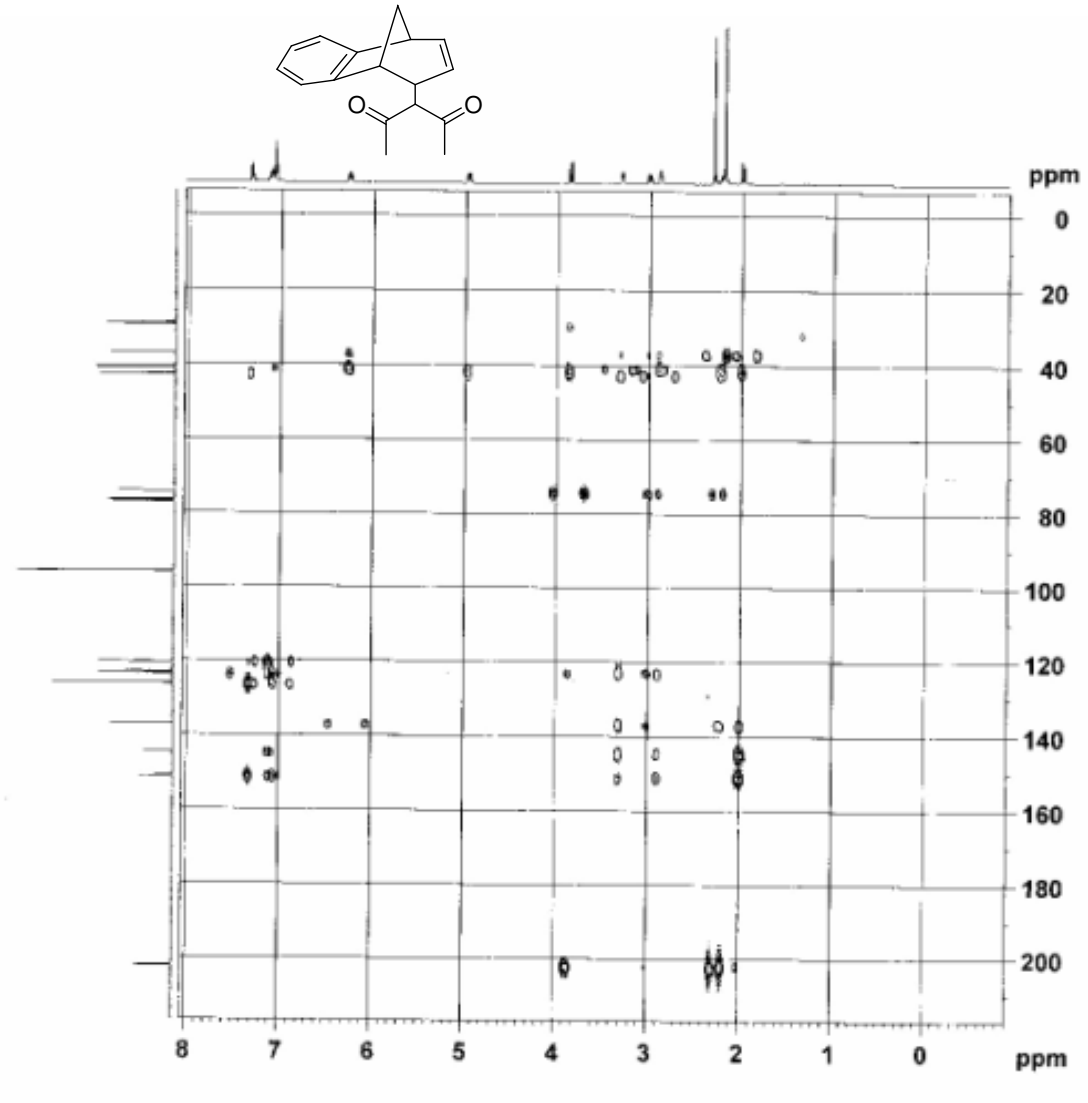


Figure A25 HMBC Spectrum of **131**.

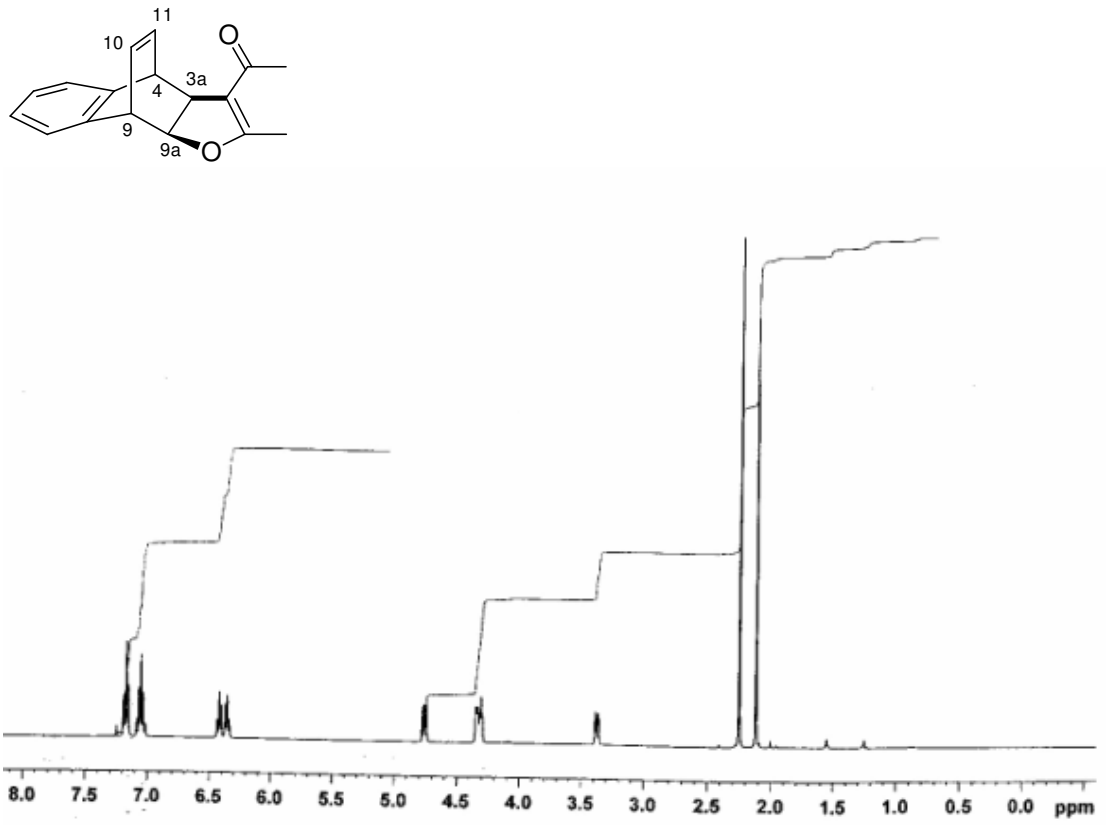


Figure A26 [1]H-NMR Spectrum of Compound **132**.

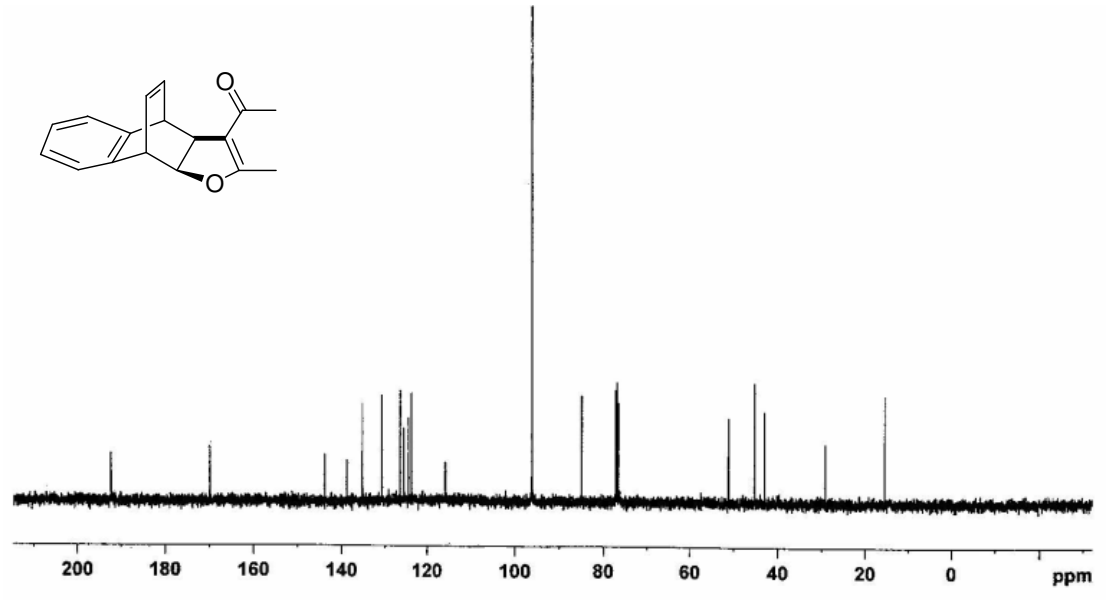


Figure A27 [13]C-NMR Spectrum of Compound **132**.

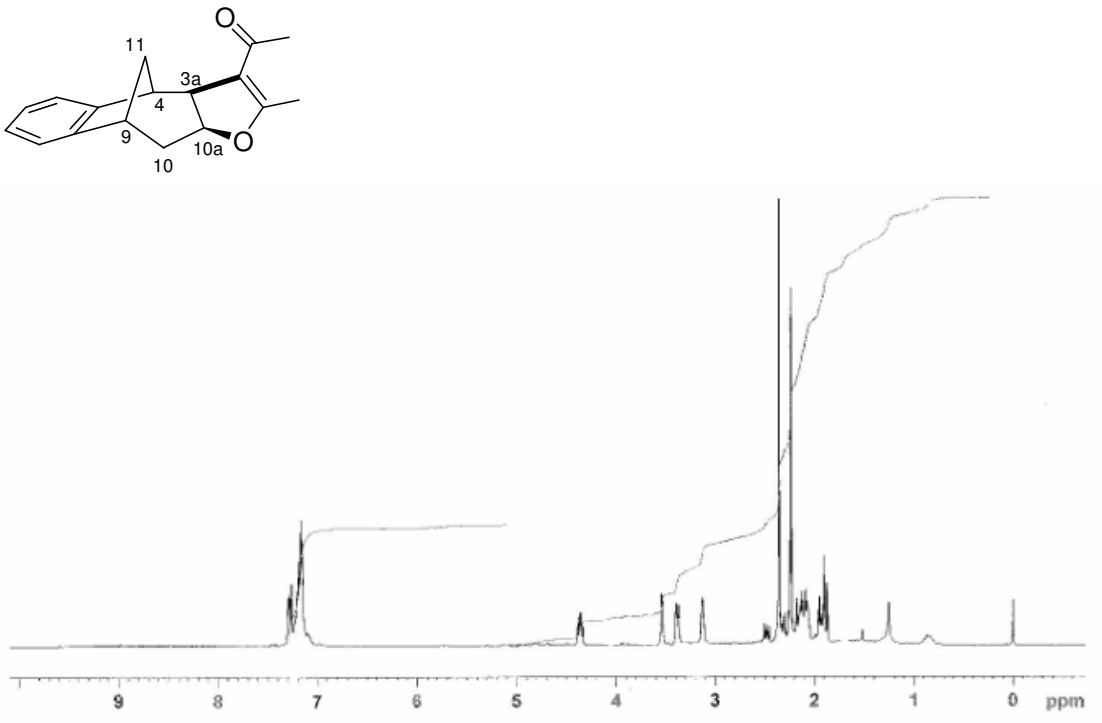
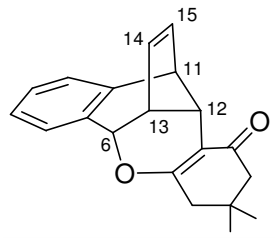


Figure A28 ^{1}H-NMR Spectrum of Compound **133**.



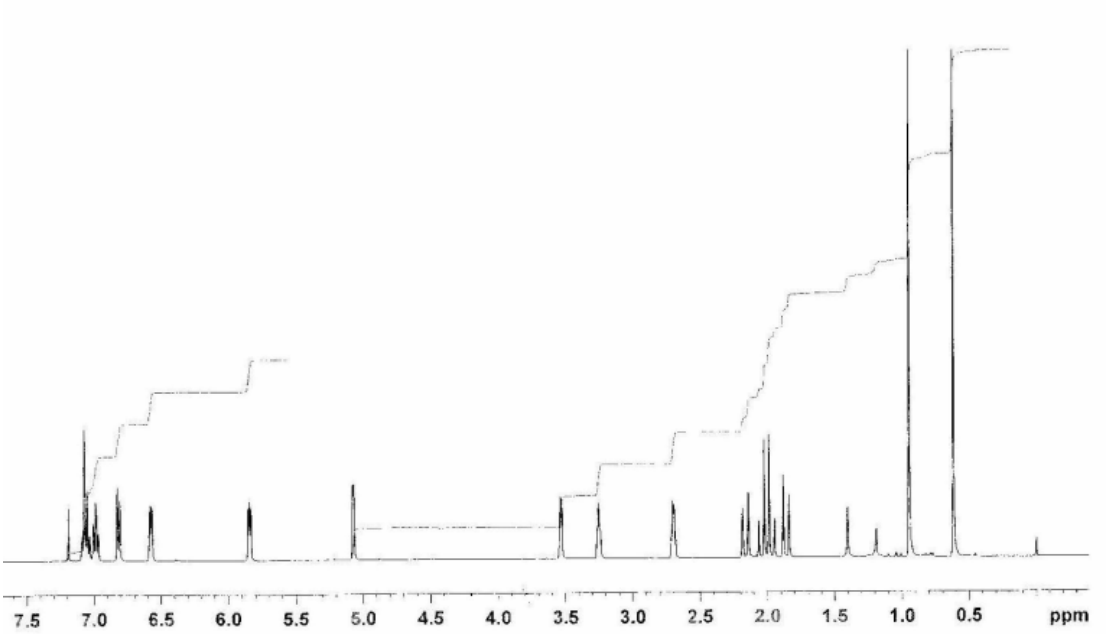


Figure A30 [1]H-NMR Spectrum of Compound **148**.

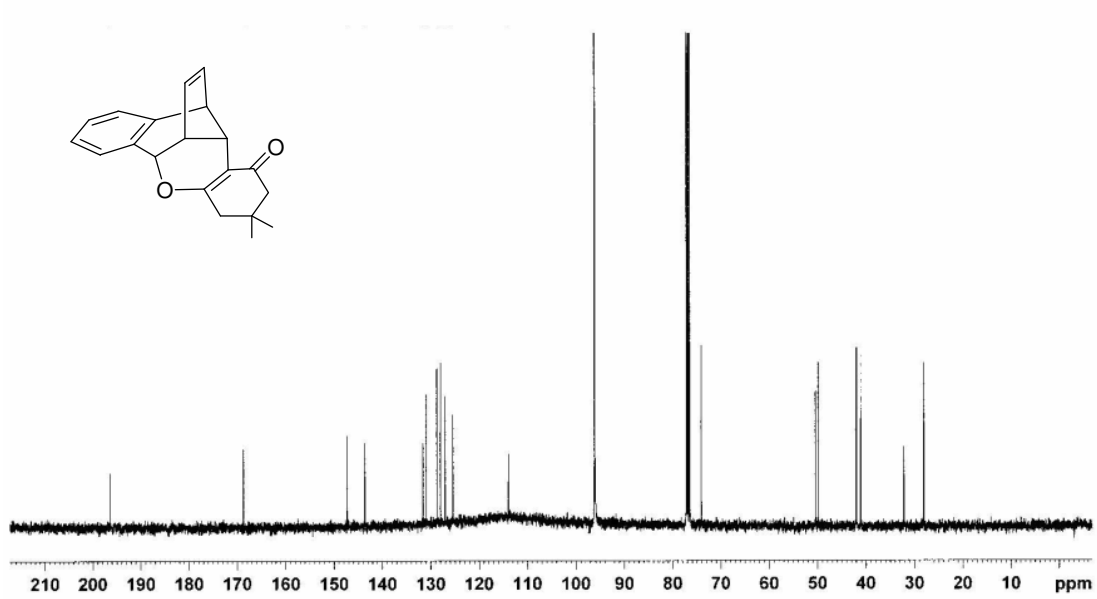


Figure A31 [13]C-NMR Spectrum of Compound **148**.

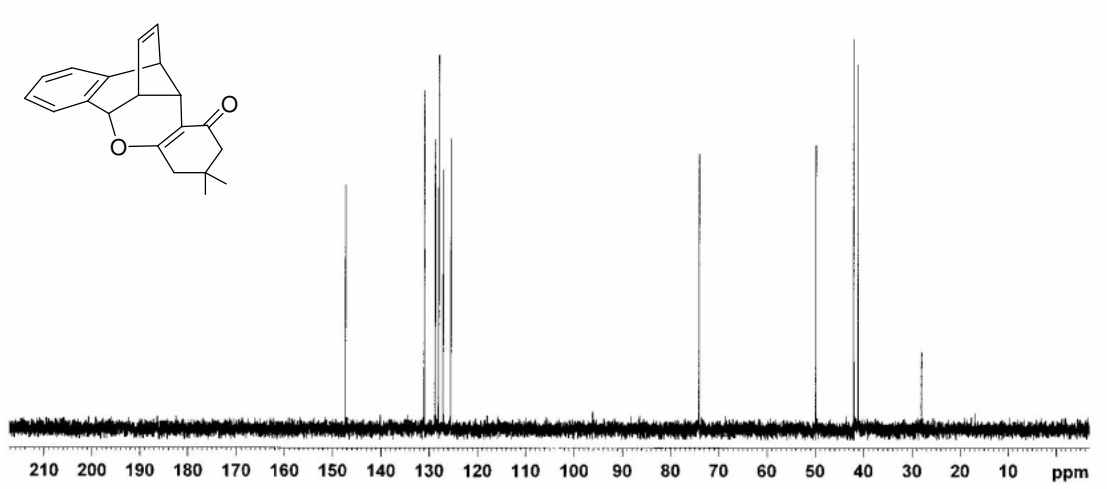


Figure A32 DEPT-90 Spectrum of Compound **148**.

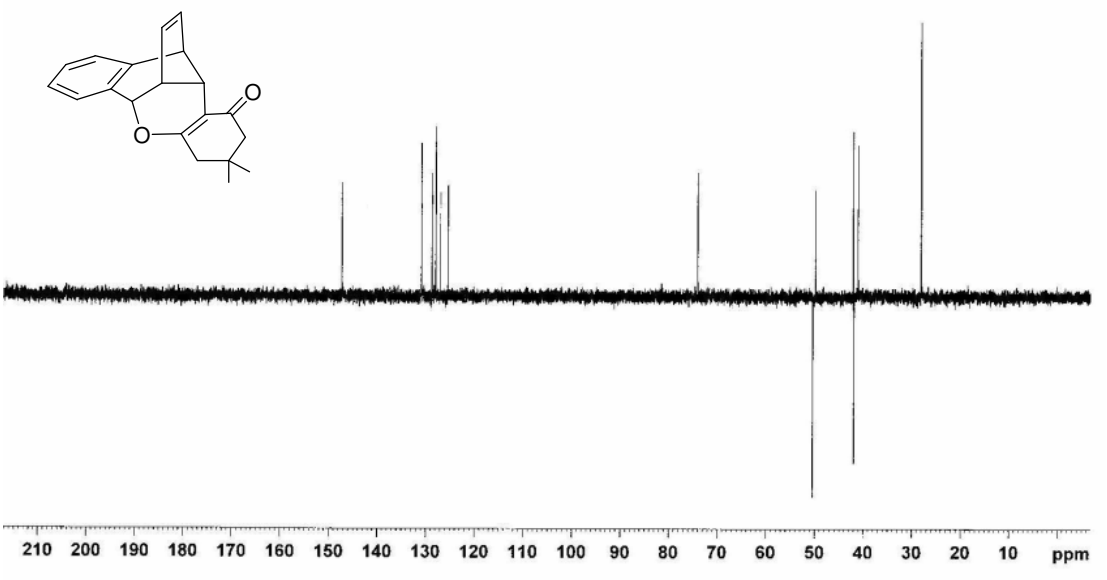


Figure A33 DEPT-135 Spectrum of Compound **148**.

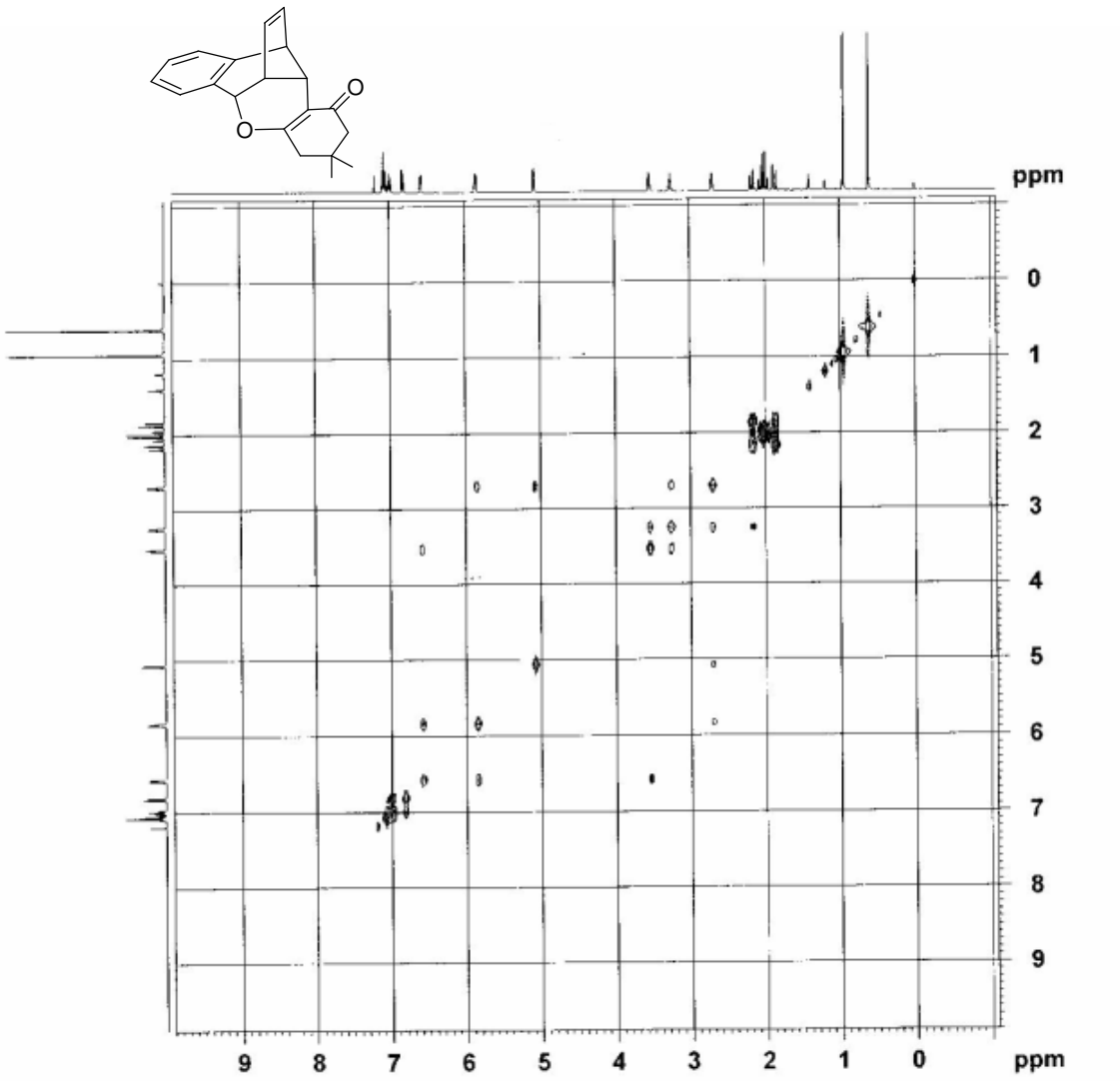


Figure A34 COSY Spectrum of **148**.

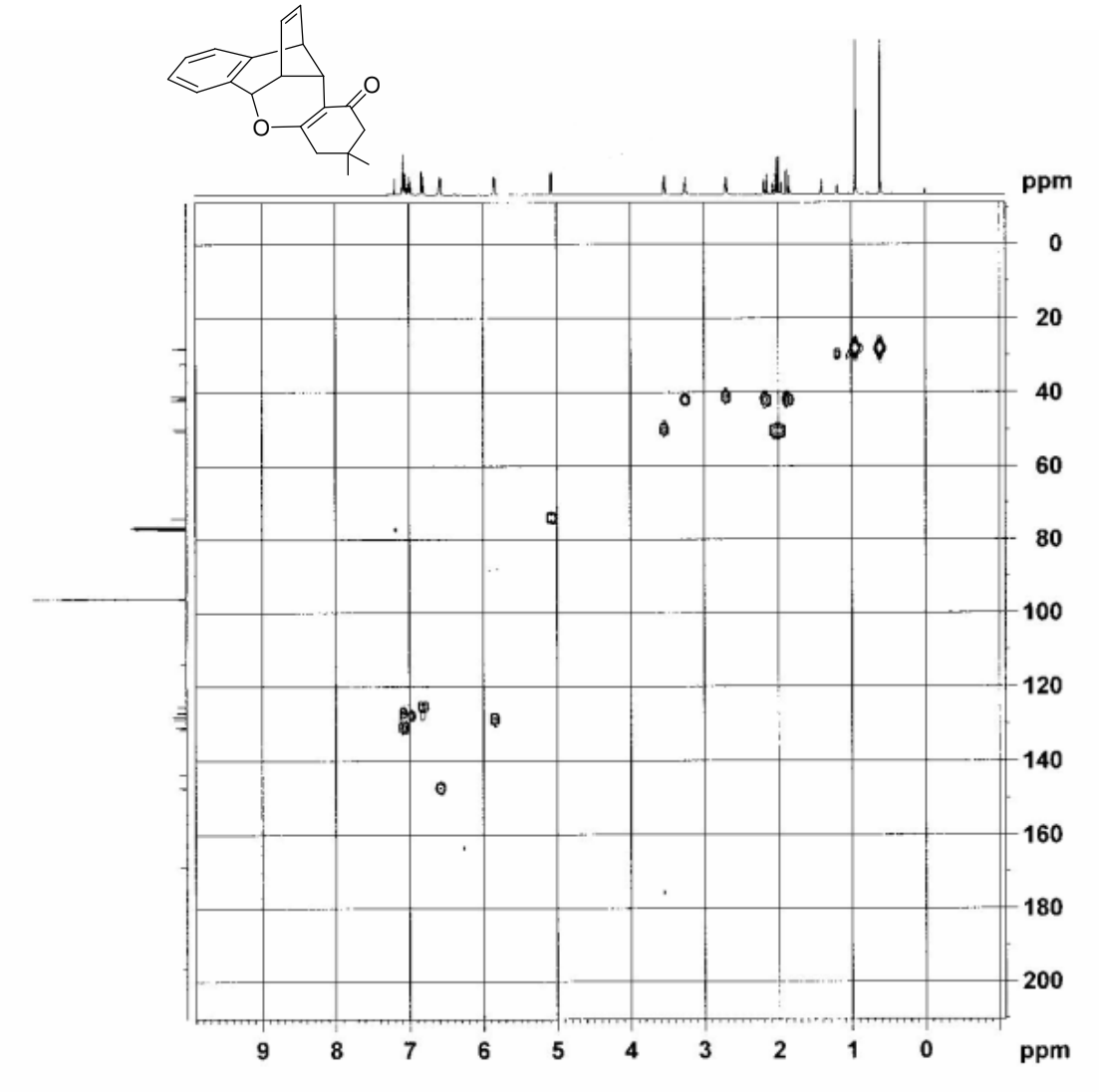


Figure A35 HMQC Spectrum of **148**.

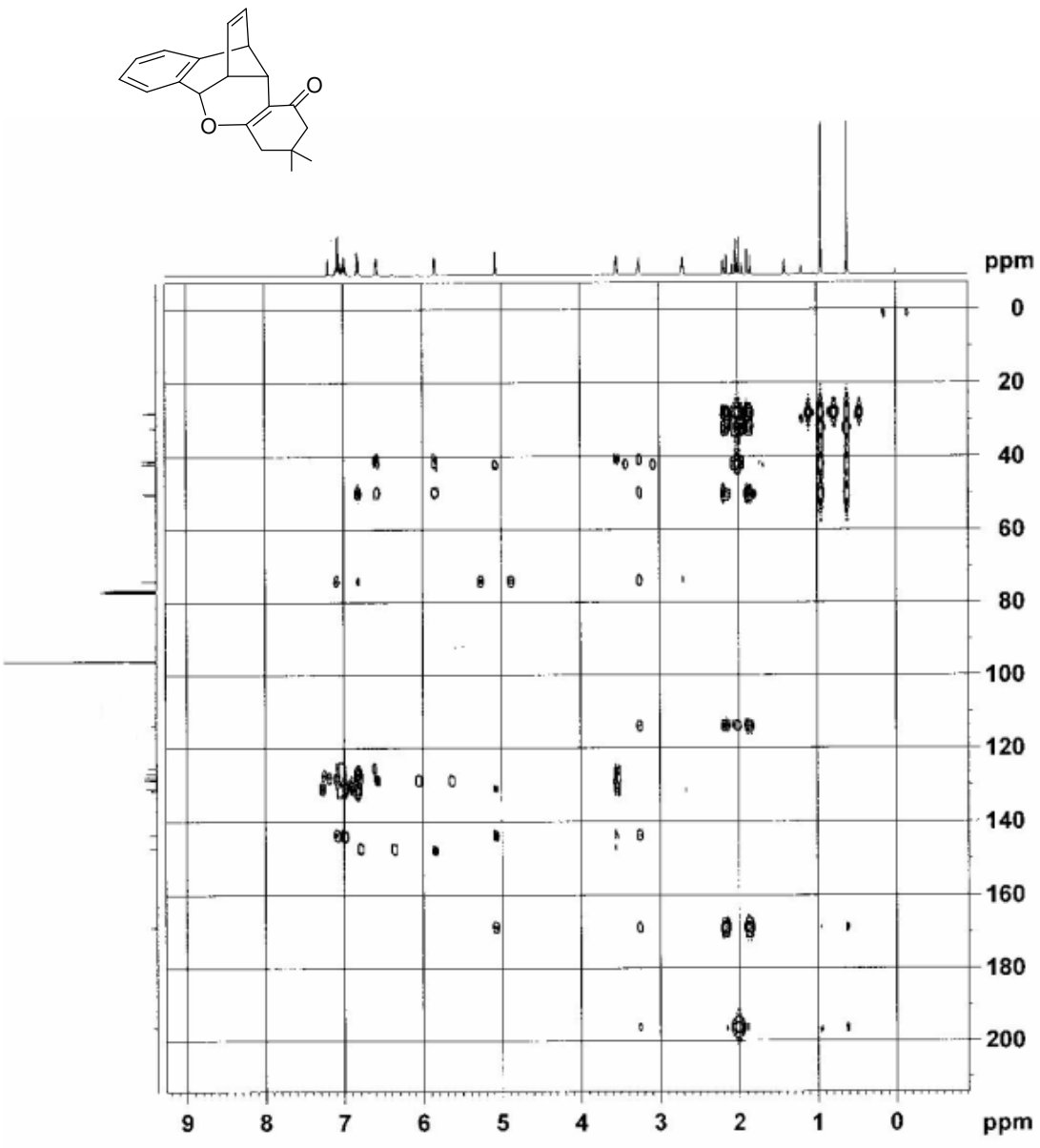
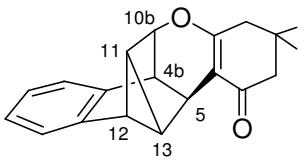


Figure A36 HMBC Spectrum of **148**.



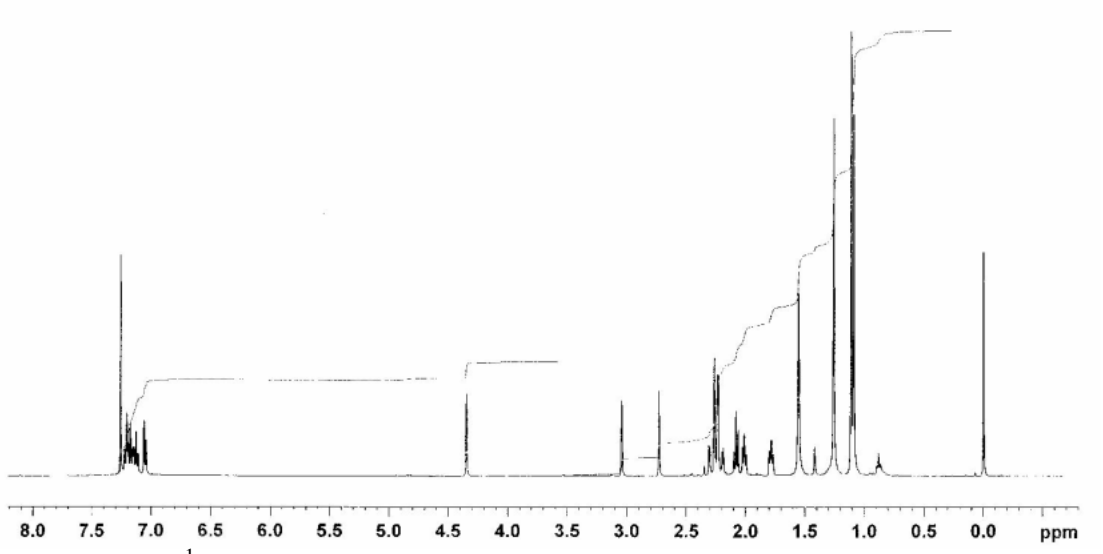


Figure A37 ^{1}H-NMR Spectrum of Compound **149**.

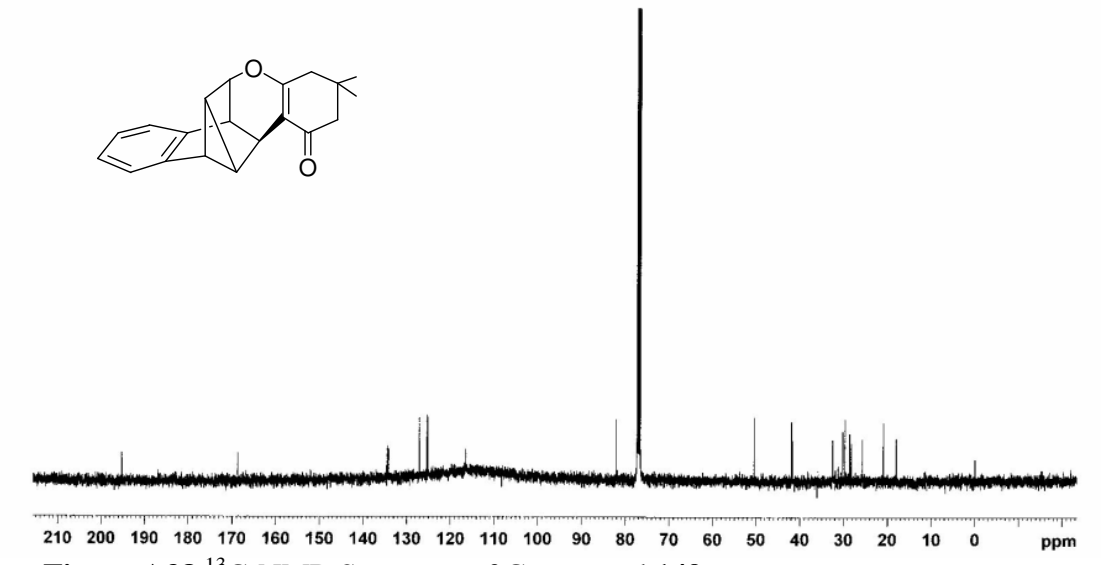


Figure A38 ^{13}C-NMR Spectrum of Compound **149**.

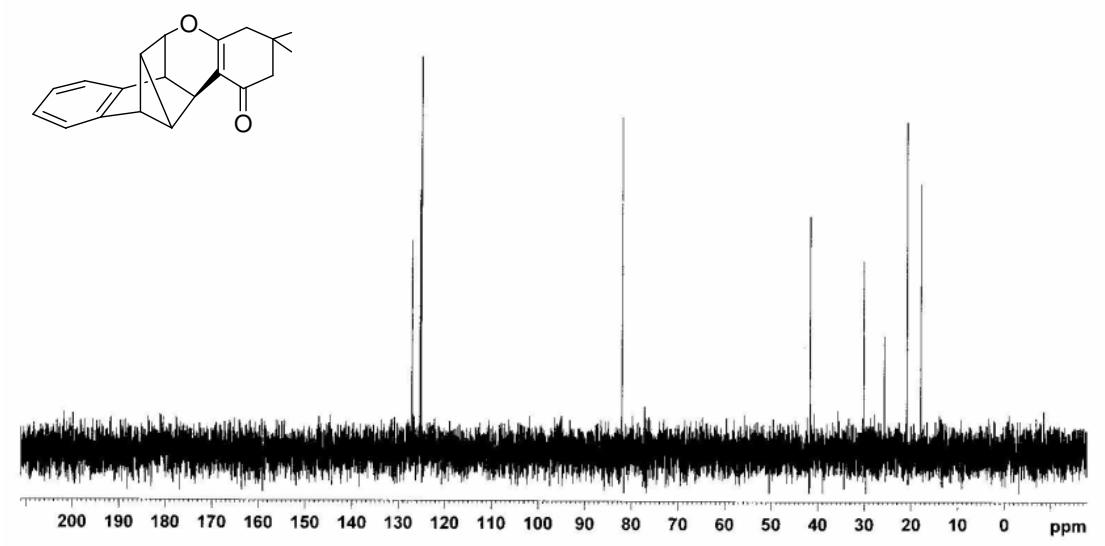


Figure A39 DEPT-90 Spectrum of **149**.

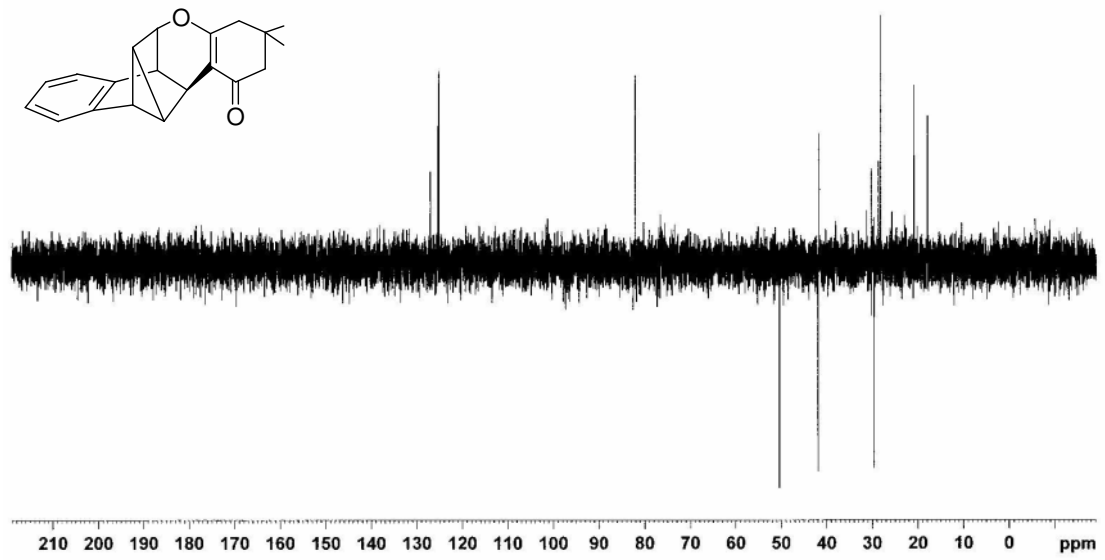


Figure A40 DEPT-135 Spectrum of **149**.

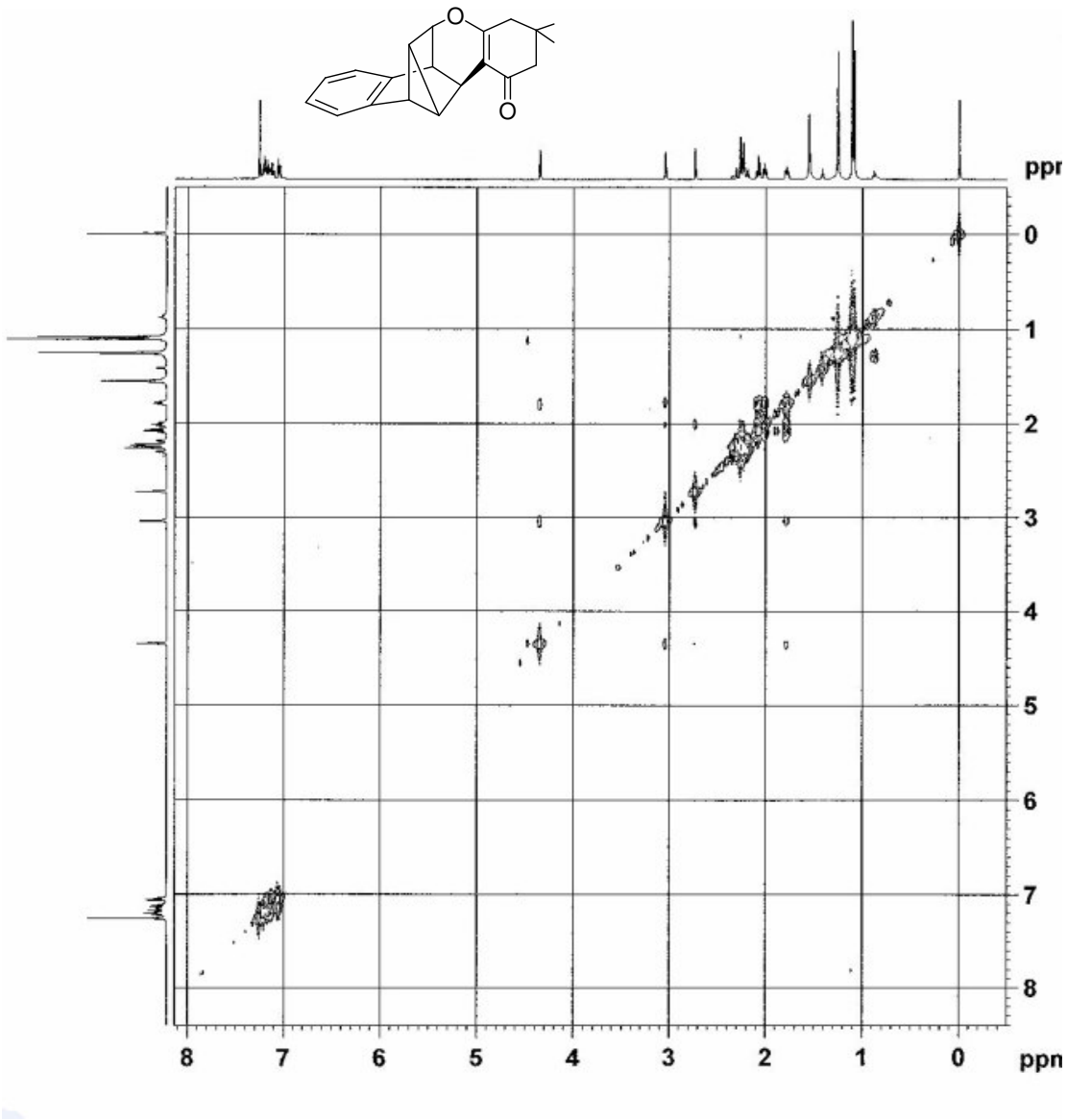


Figure A41 COSY Spectrum of **149**.

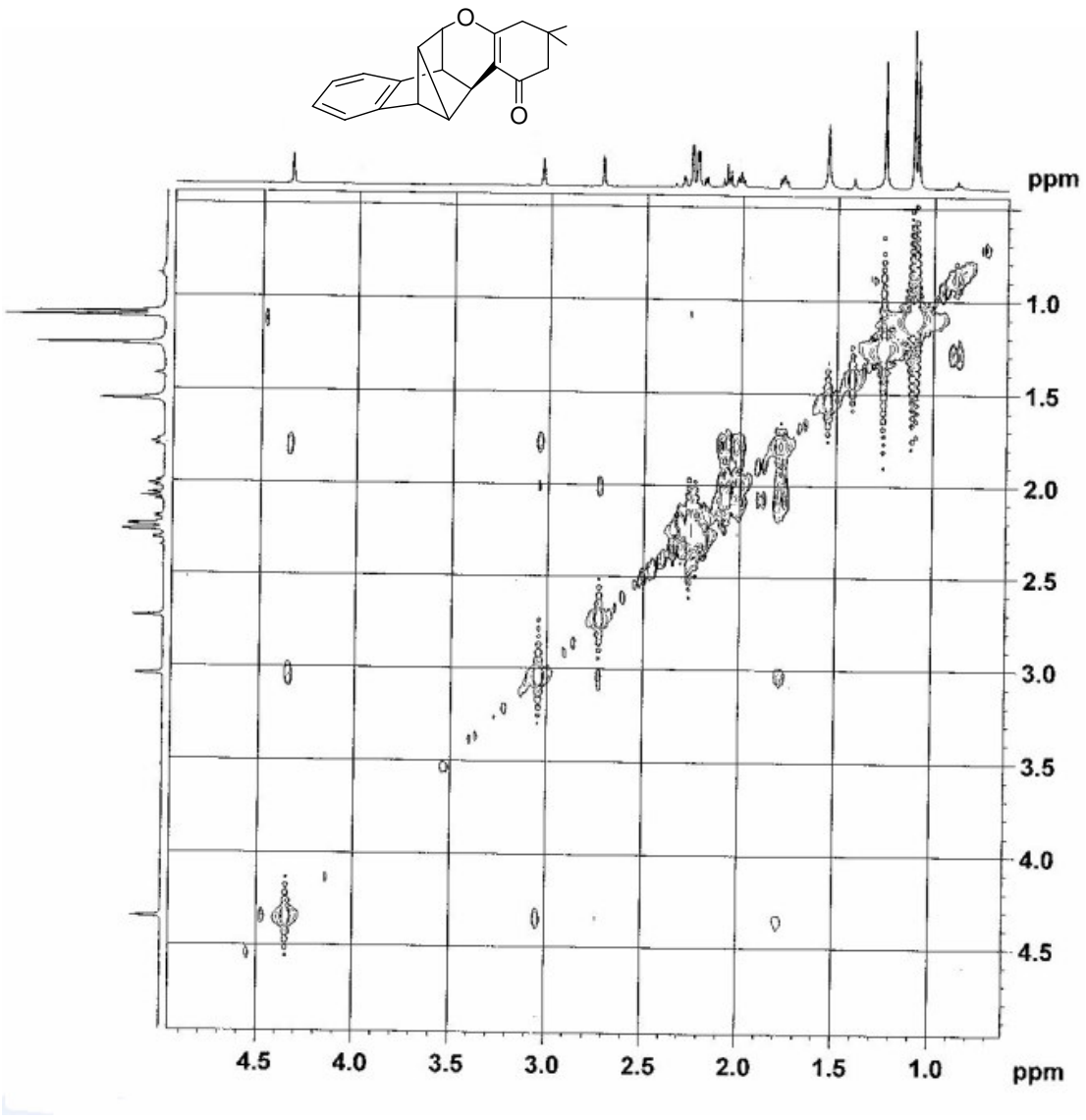


Figure A42 COSY Spectrum of **149**.

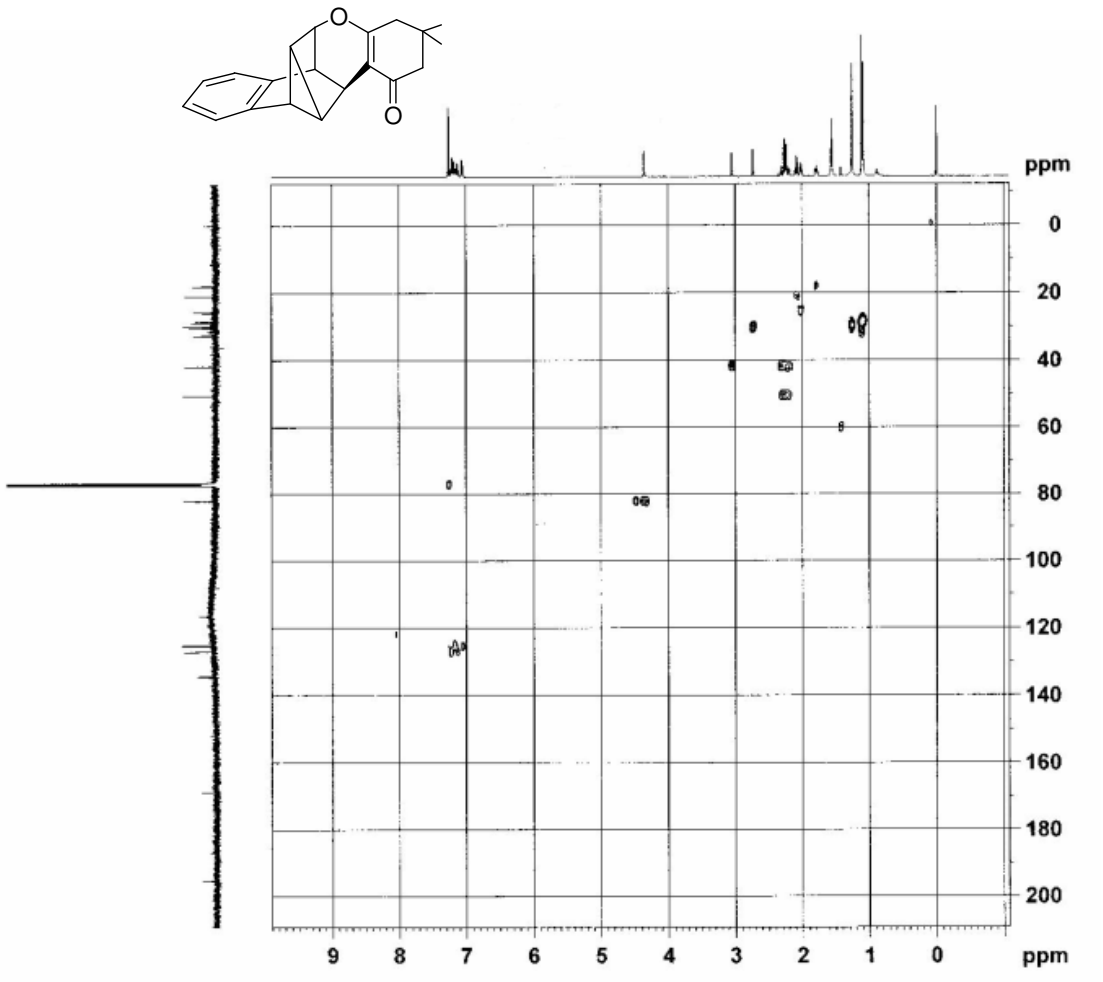


Figure A43 HMQC Spectrum of **149**.

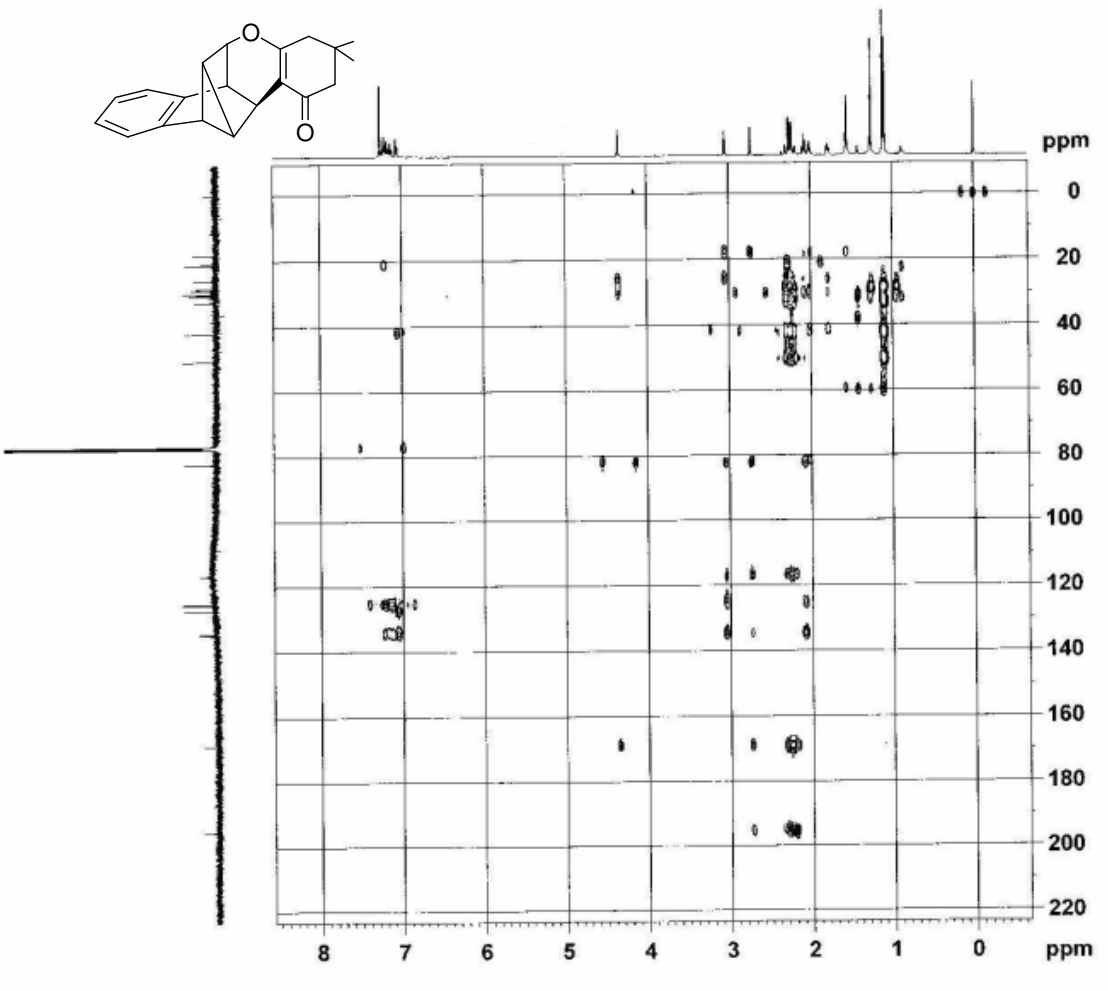


Figure A44 HMBC Spectrum of **149**.

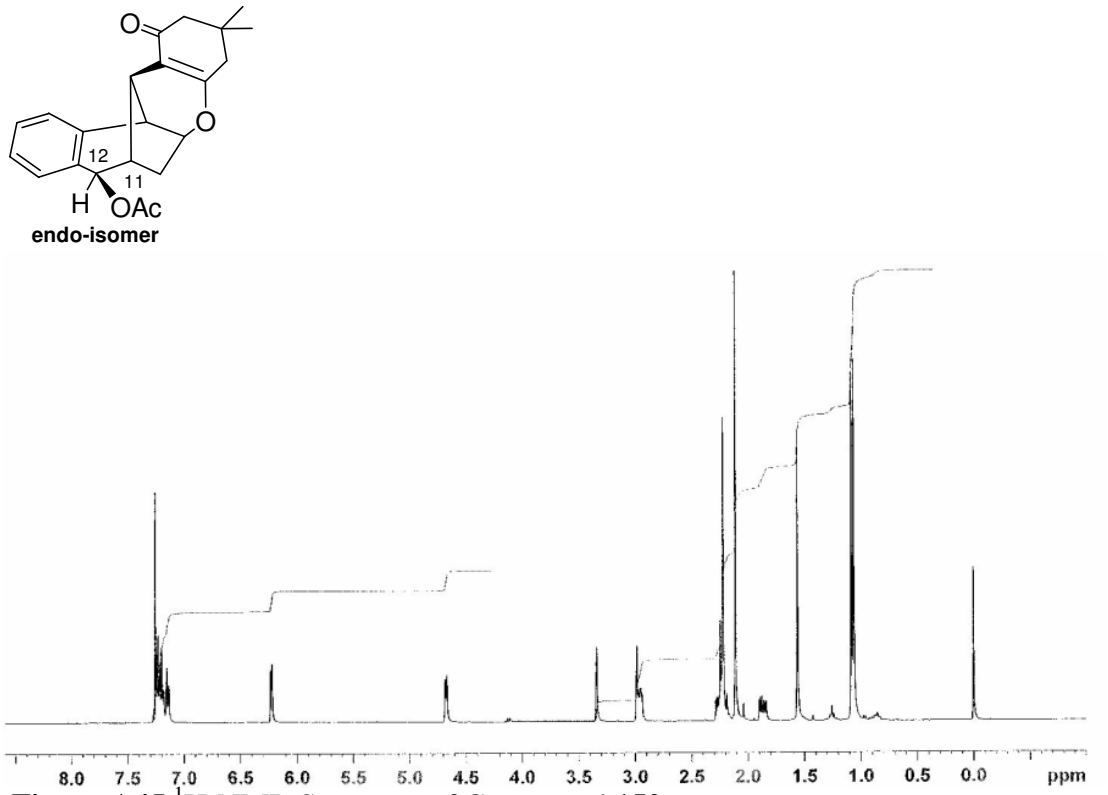


Figure A45 ^{1}H-NMR Spectrum of Compound **150**.

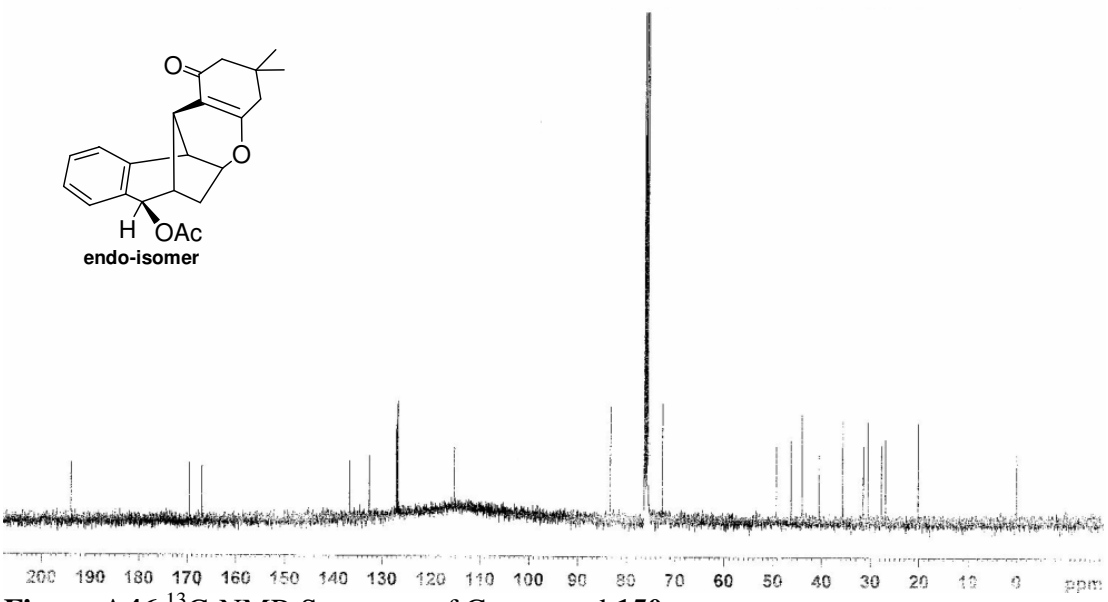


Figure A46 ^{13}C-NMR Spectrum of Compound **150**.

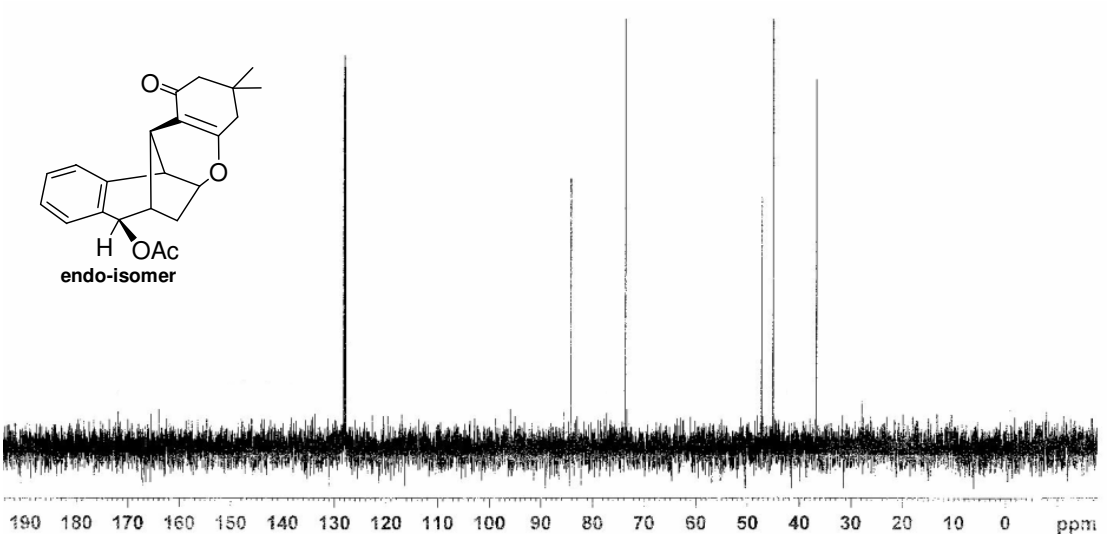


Figure A47 DEPT-90 Spectrum of **150**.

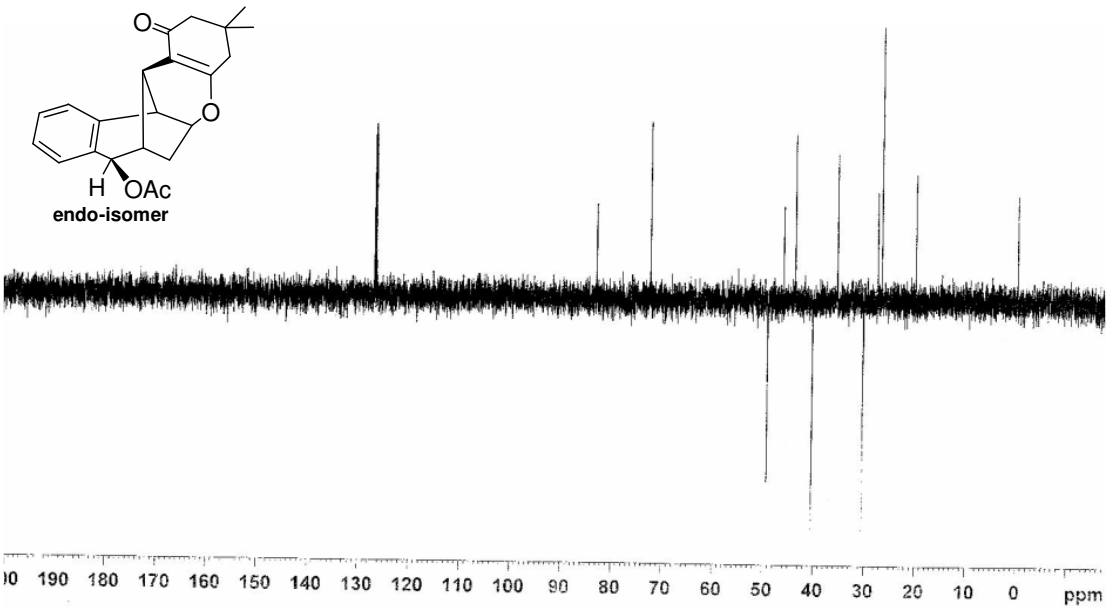


Figure A48 DEPT-135 Spectrum of **150**.

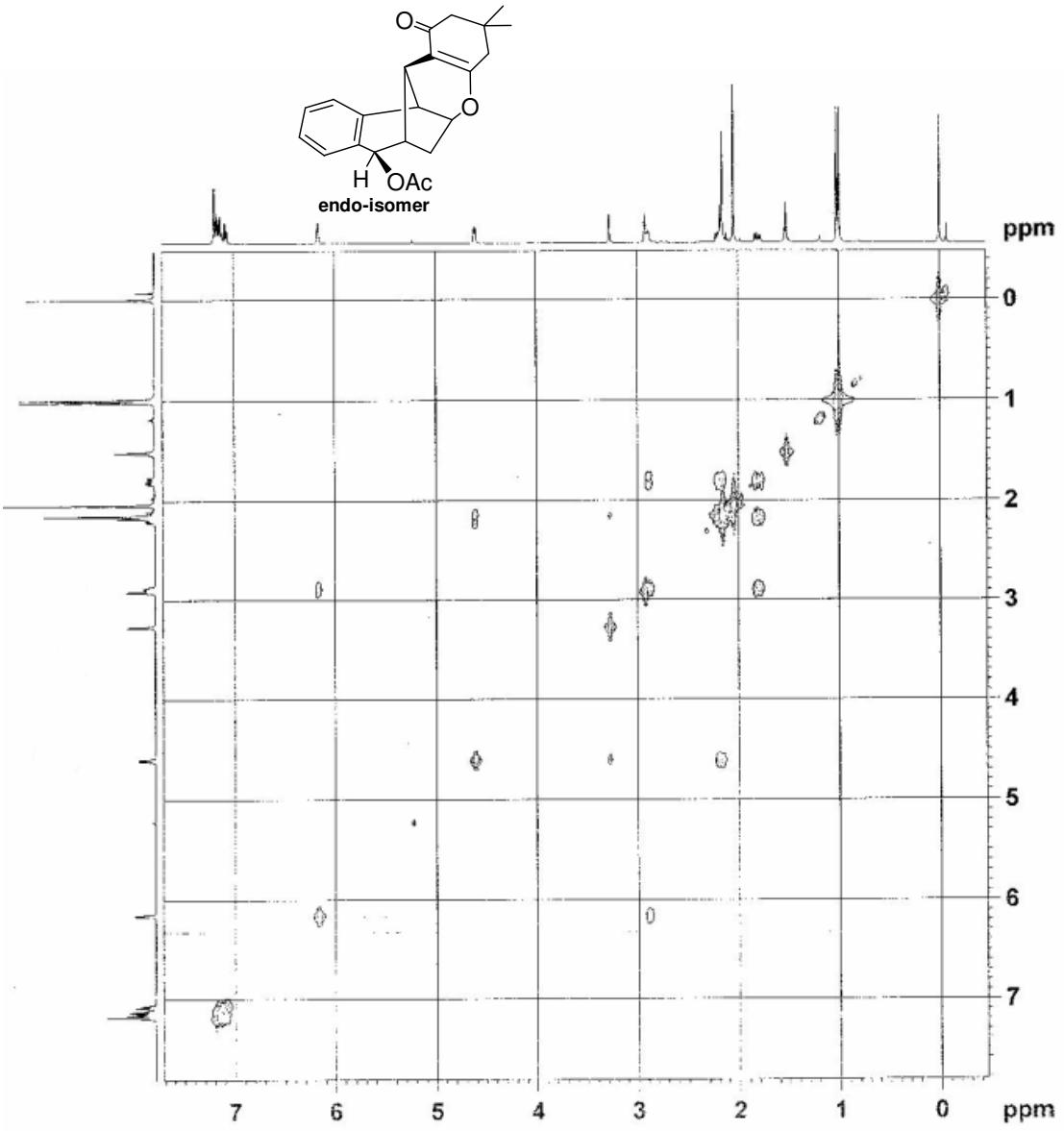


Figure A49 COSY Spectrum of **150**.

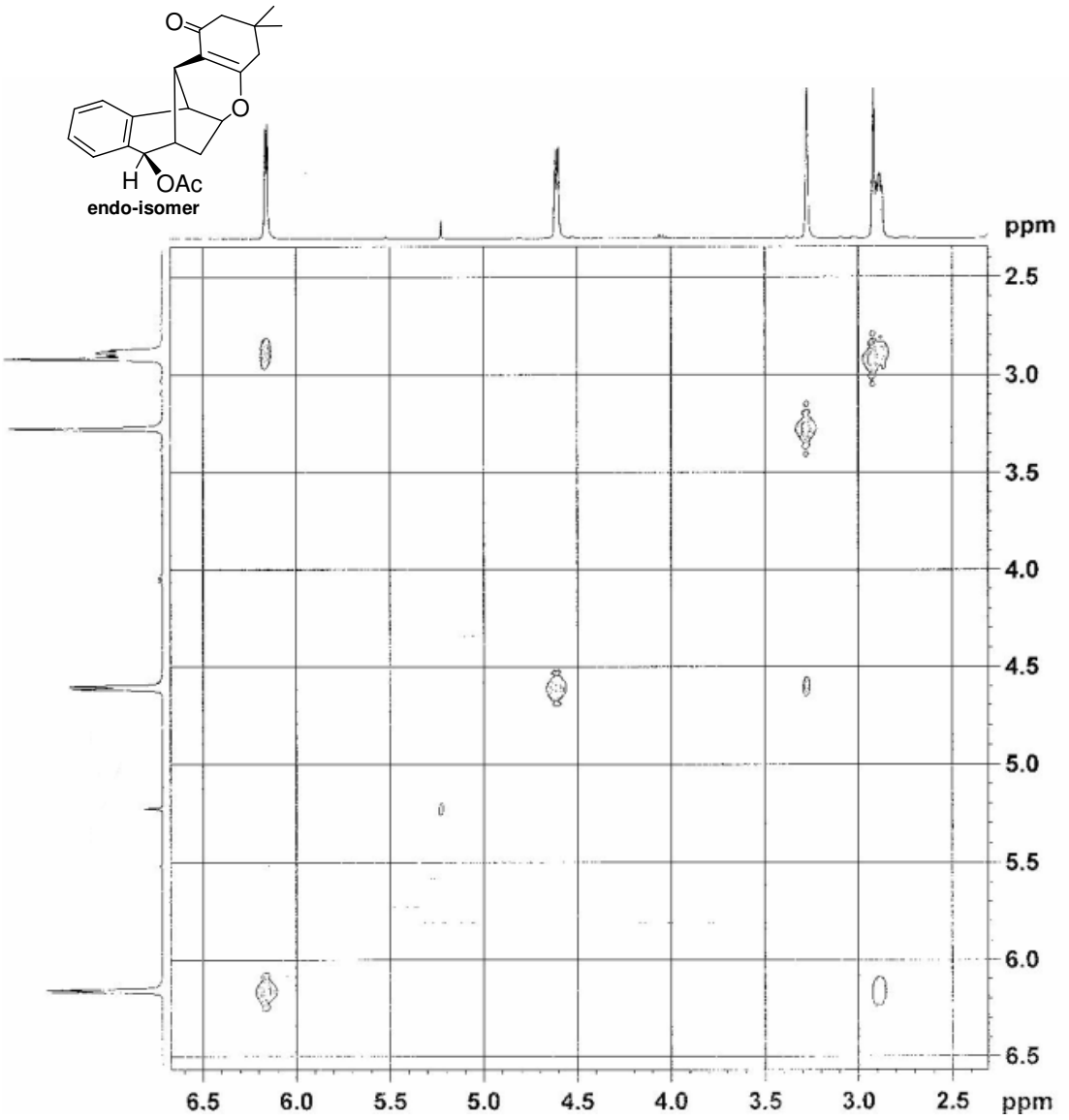


Figure A50 COSY Spectrum of **150**.

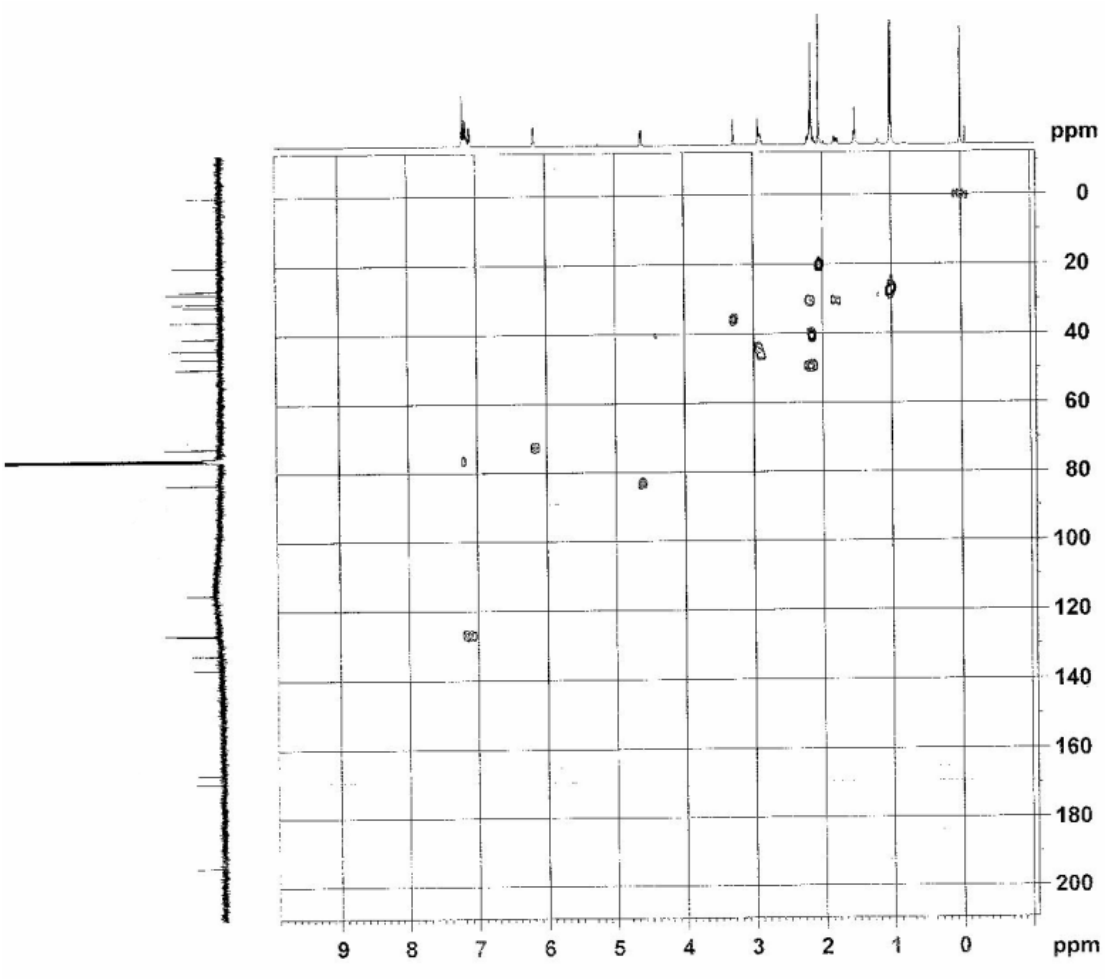


Figure A51 HMQC Spectrum of **150**.

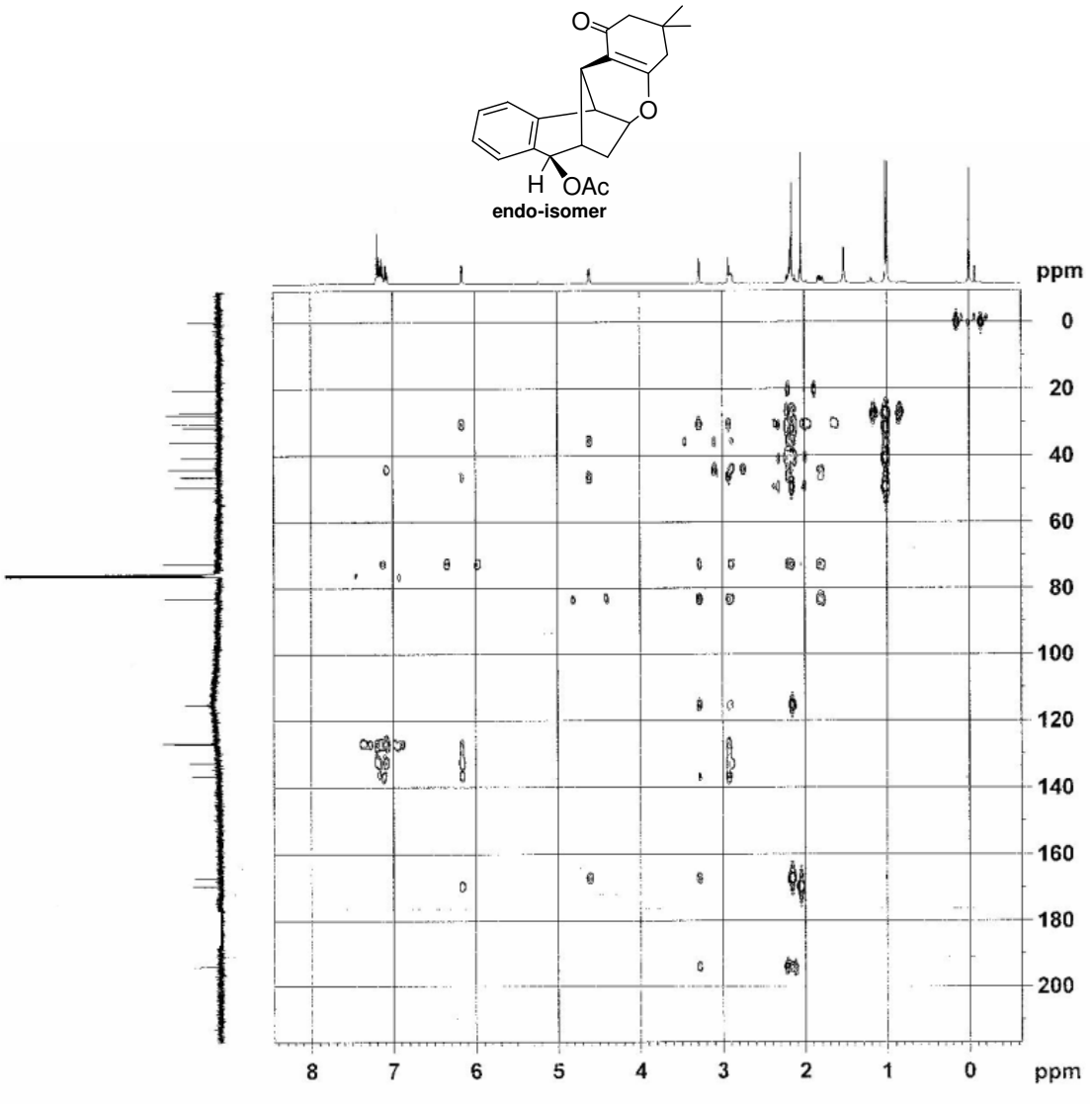


Figure A52 HMBC Spectrum of **150**.

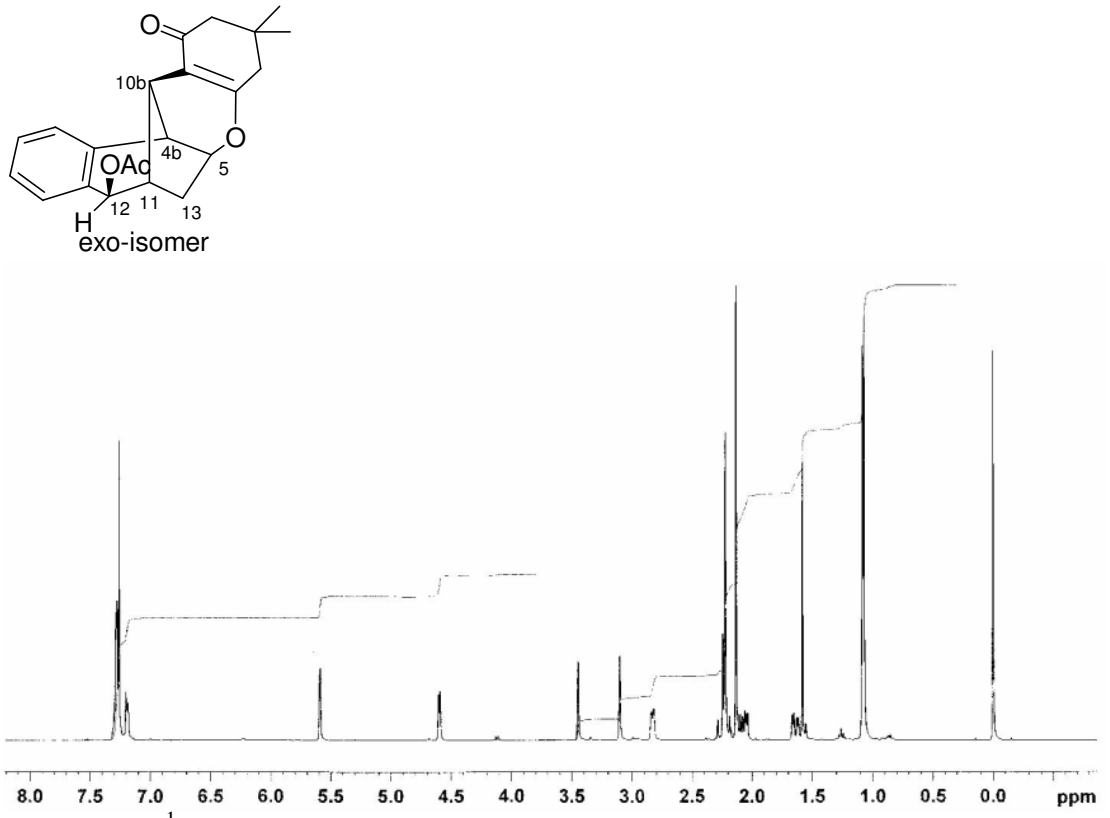


Figure A53 ^{1}H-NMR Spectrum of Compound **151**

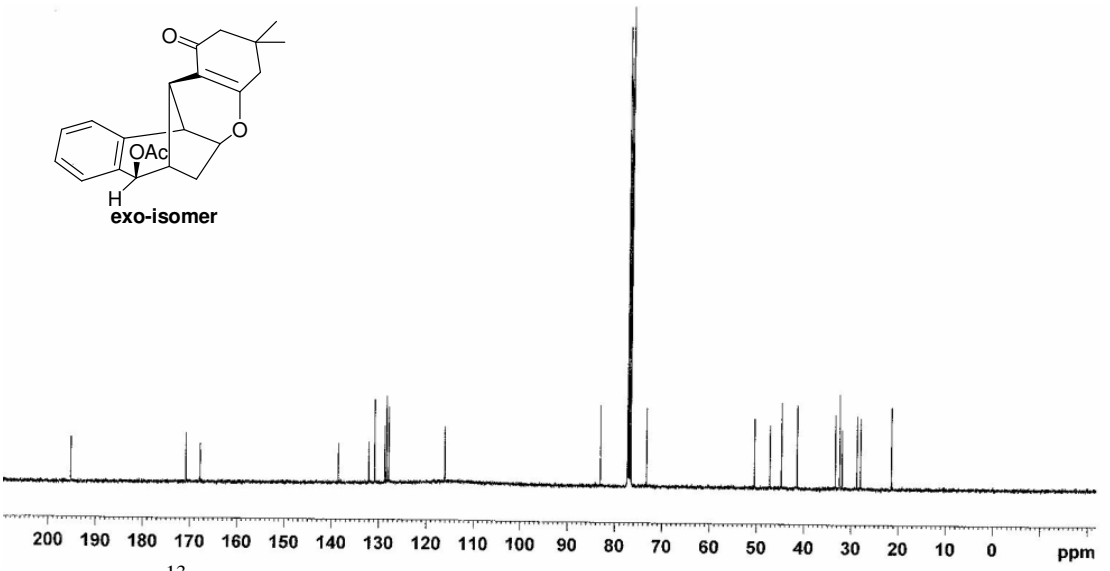


Figure A54 ^{13}C-NMR Spectrum of Compound **151**

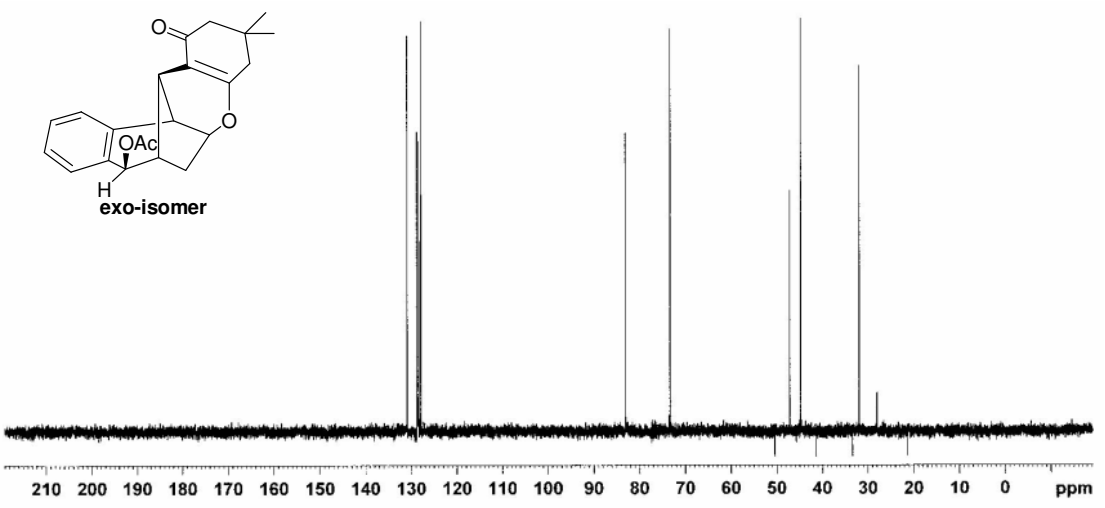


Figure A55 DEPT-90 Spectrum of **151**.

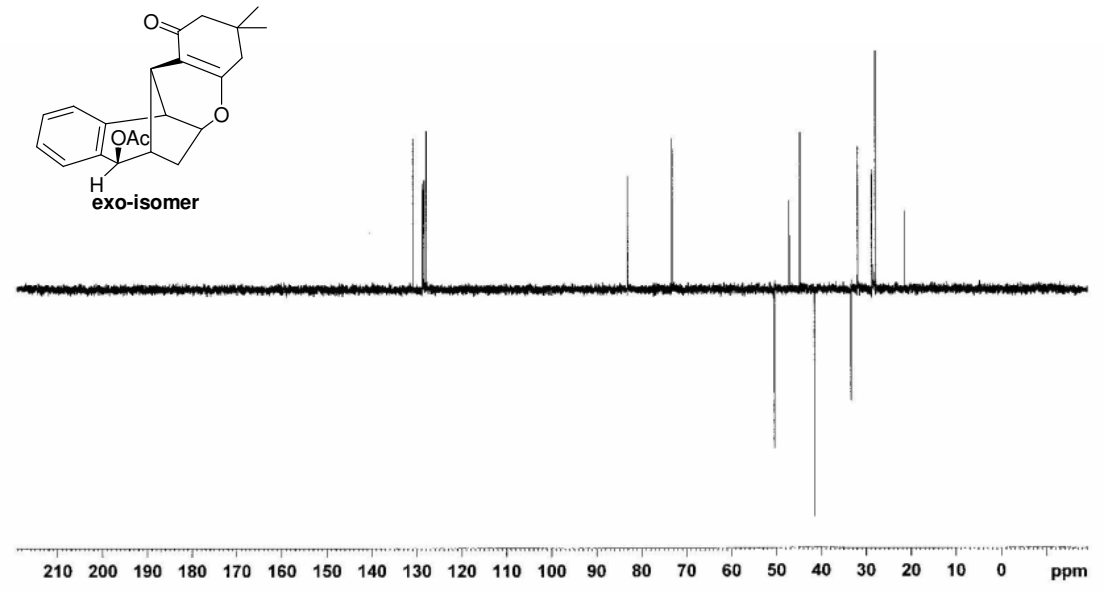


Figure A56 DEPT-135 Spectrum of **151**.

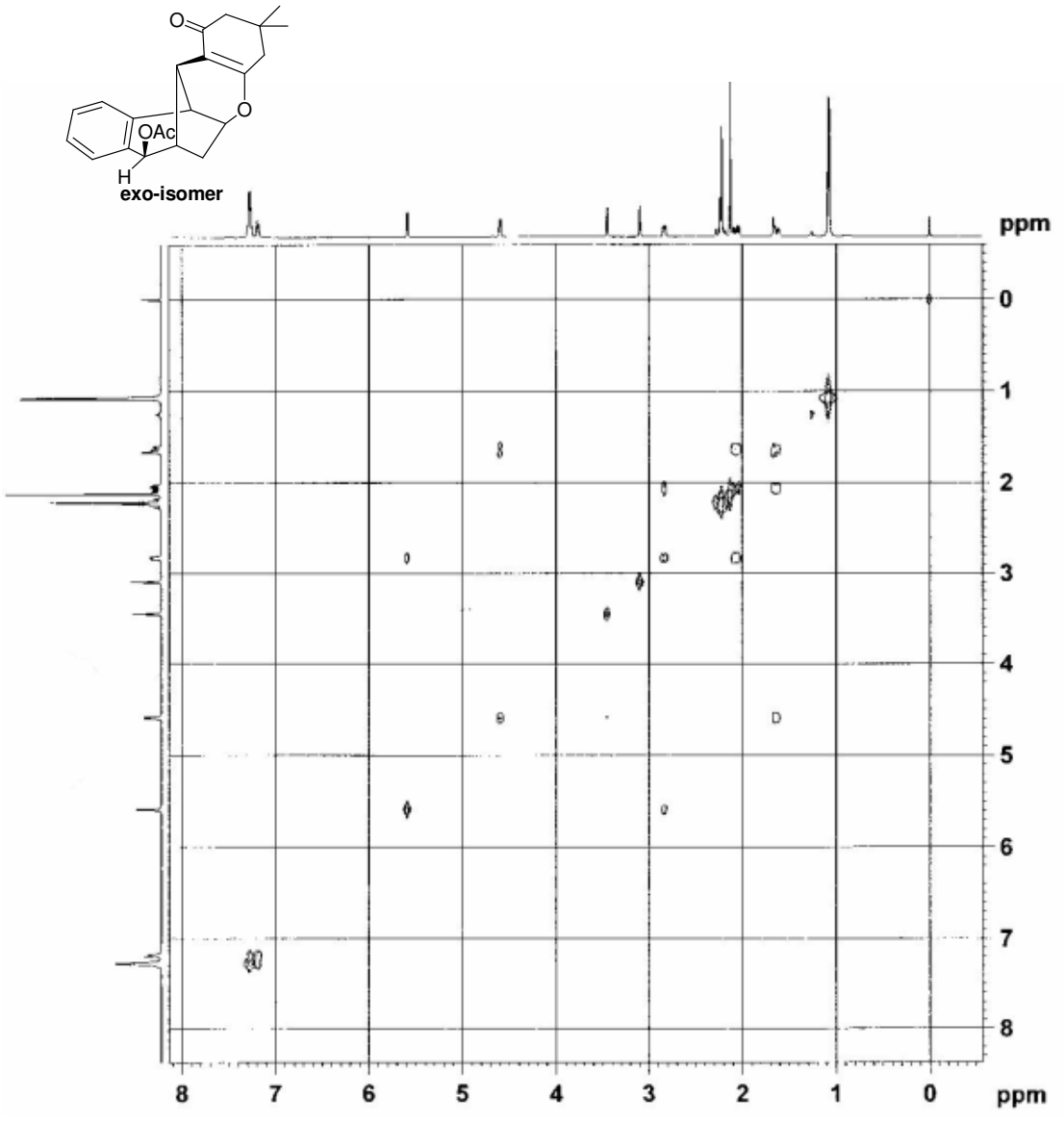


Figure A57 COSY Spectrum of **151**.

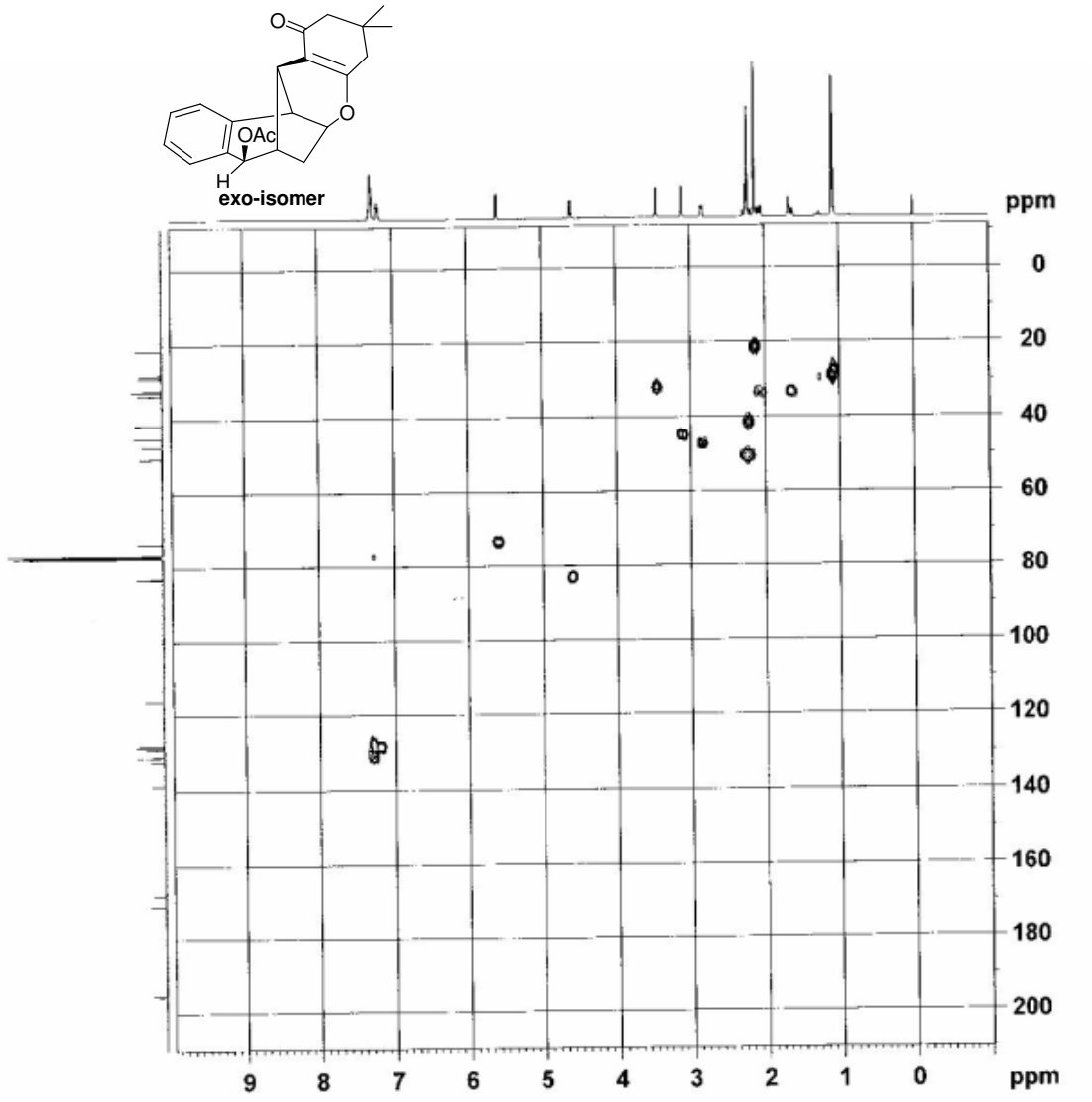


Figure A58 HMQC Spectrum of **151**.

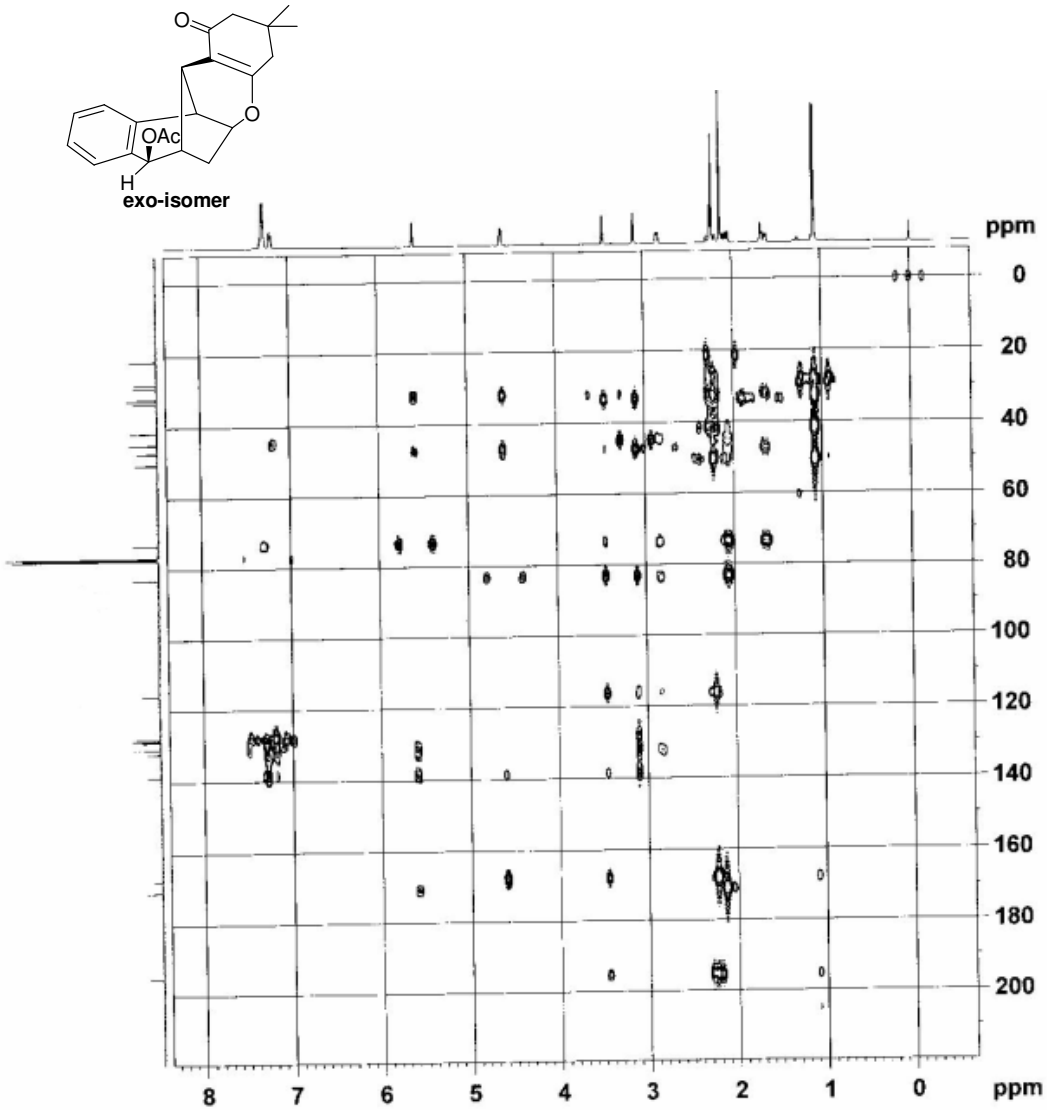


Figure A59 HMBC Spectrum of **151**.

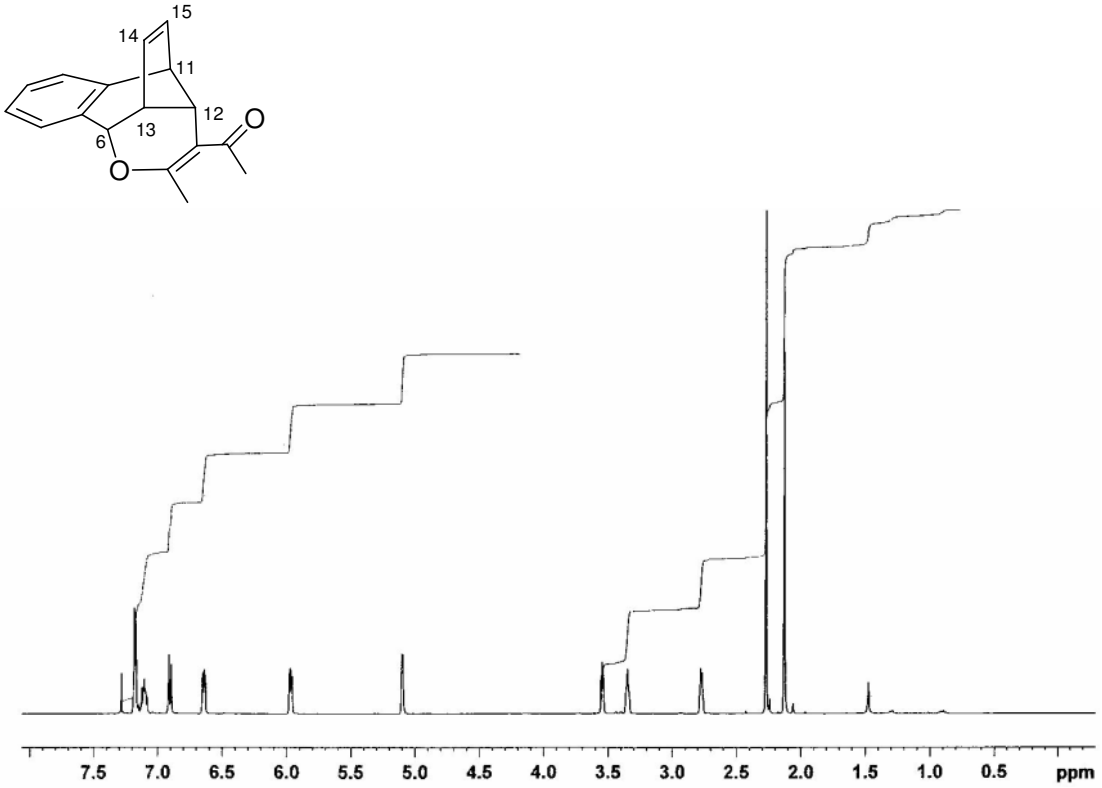


Figure A60 ^{1}H-NMR Spectrum of Compound **169**.

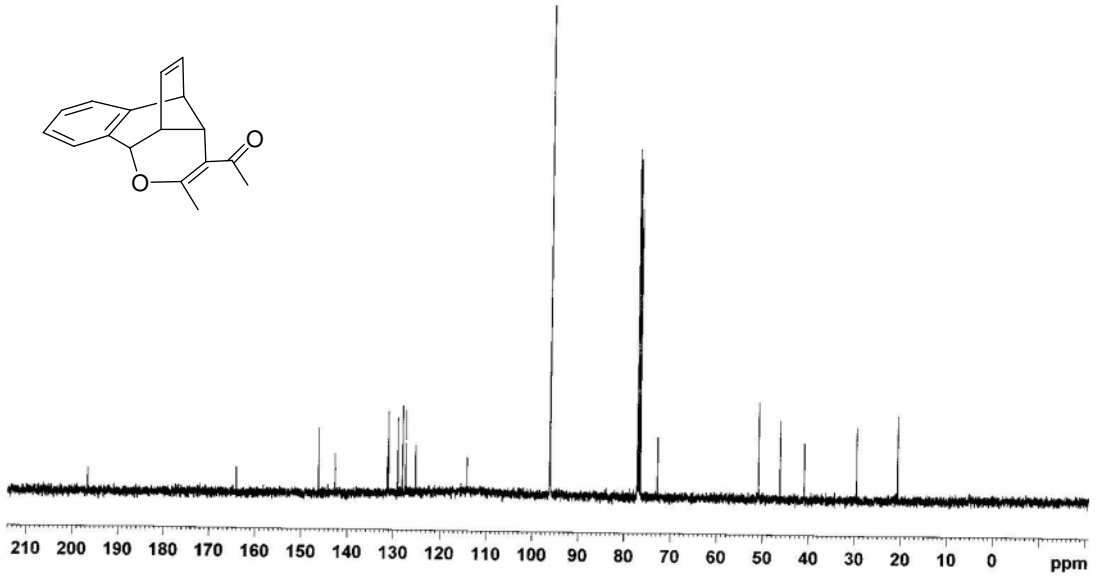


Figure A61 ^{13}C-NMR Spectrum of Compound **169**.

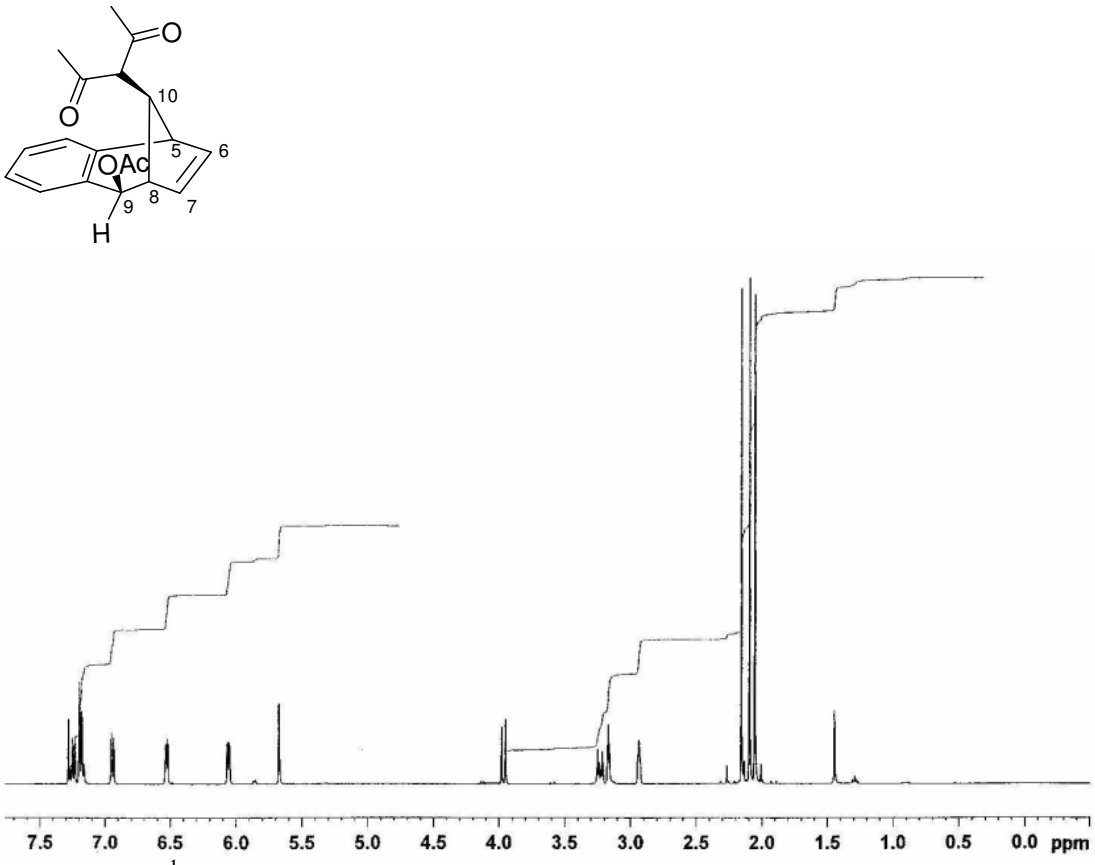


Figure A62 ^{1}H-NMR Spectrum of Compound **170**.

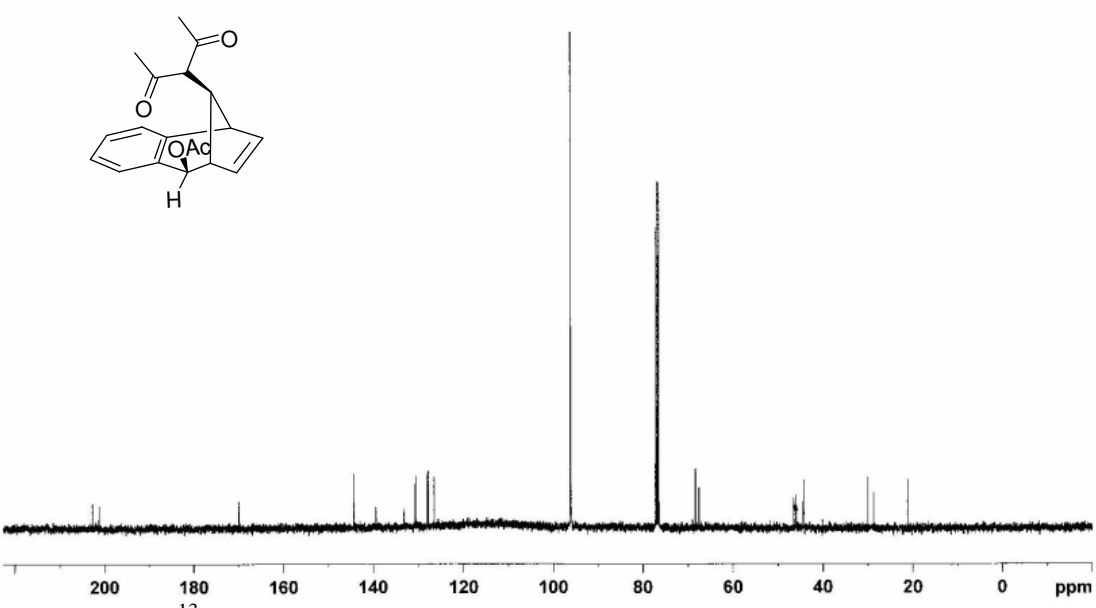


Figure A63 ^{13}C-NMR Spectrum of Compound **170**.

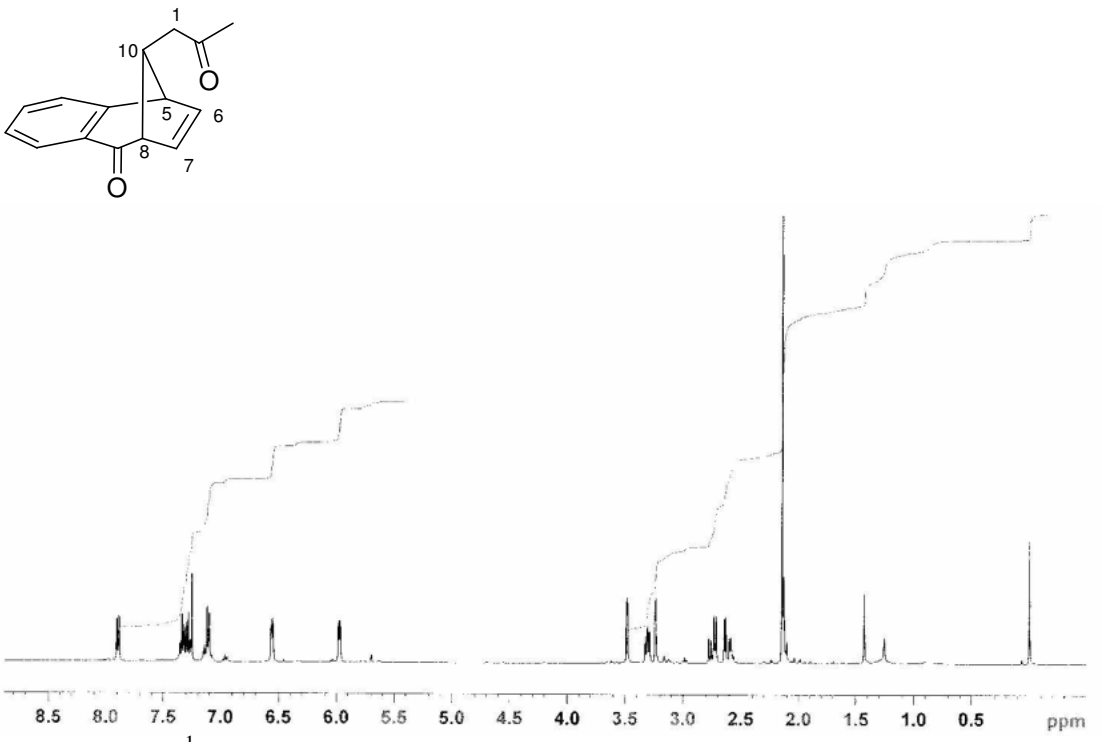


Figure A64 [1]H-NMR Spectrum of Compound **174**.

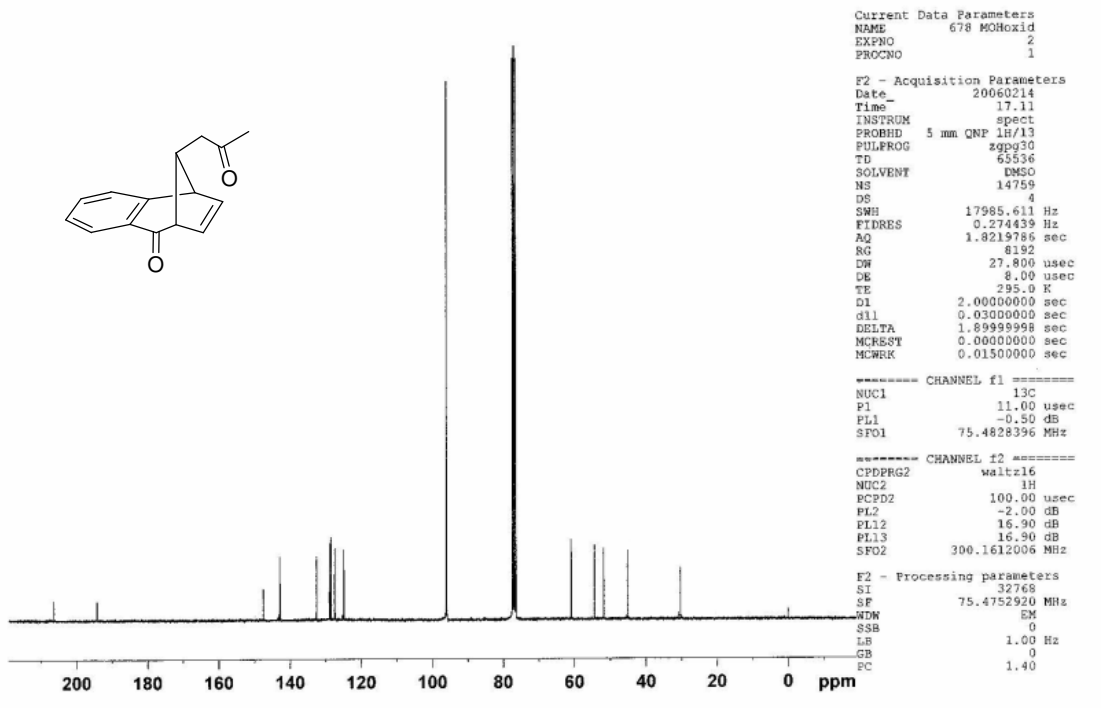
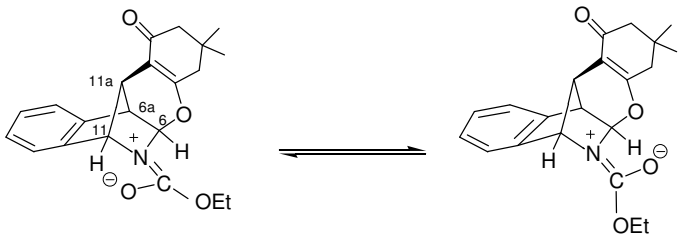


Figure A65 [13]C-NMR Spectrum of Compound **174**.

30 °C [1]H-NMR



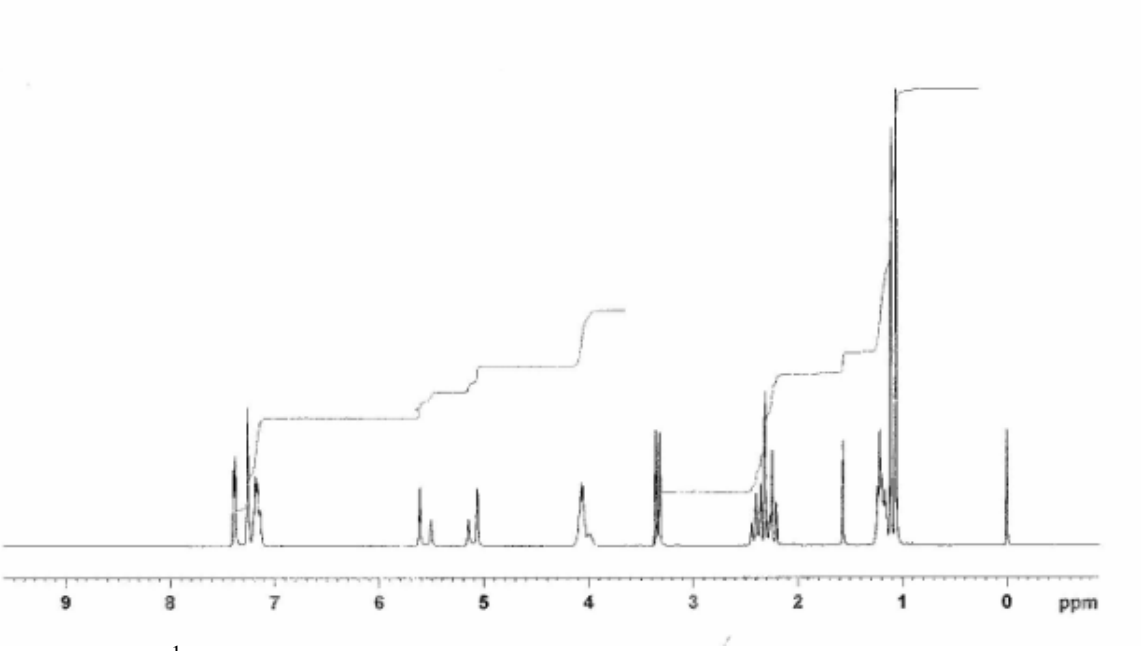
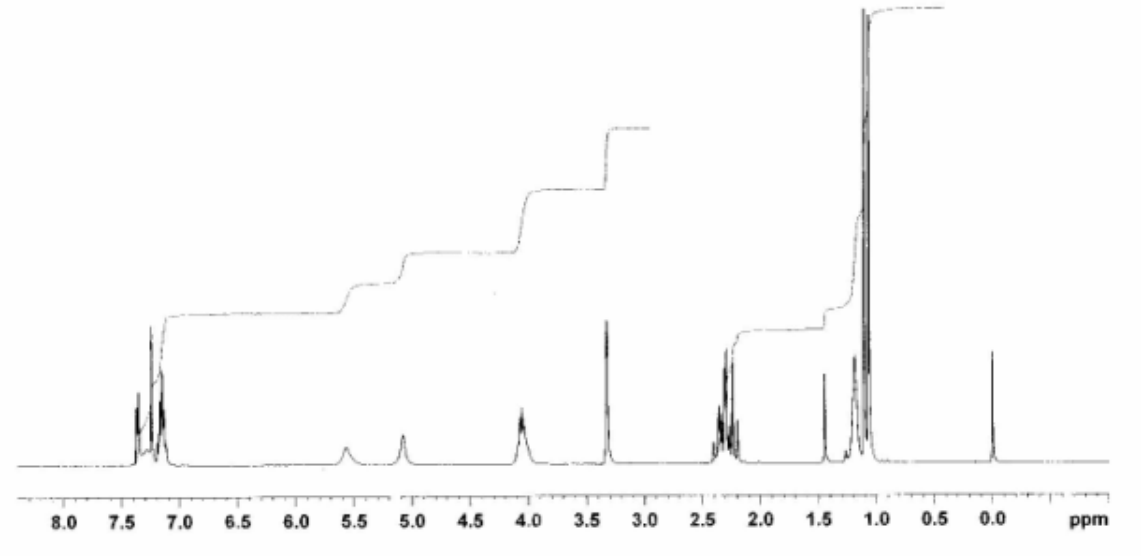


Figure A66 ^{1}H-NMR Spectrum of Compound **189**.

60 ℃ ^{1}H-NMR



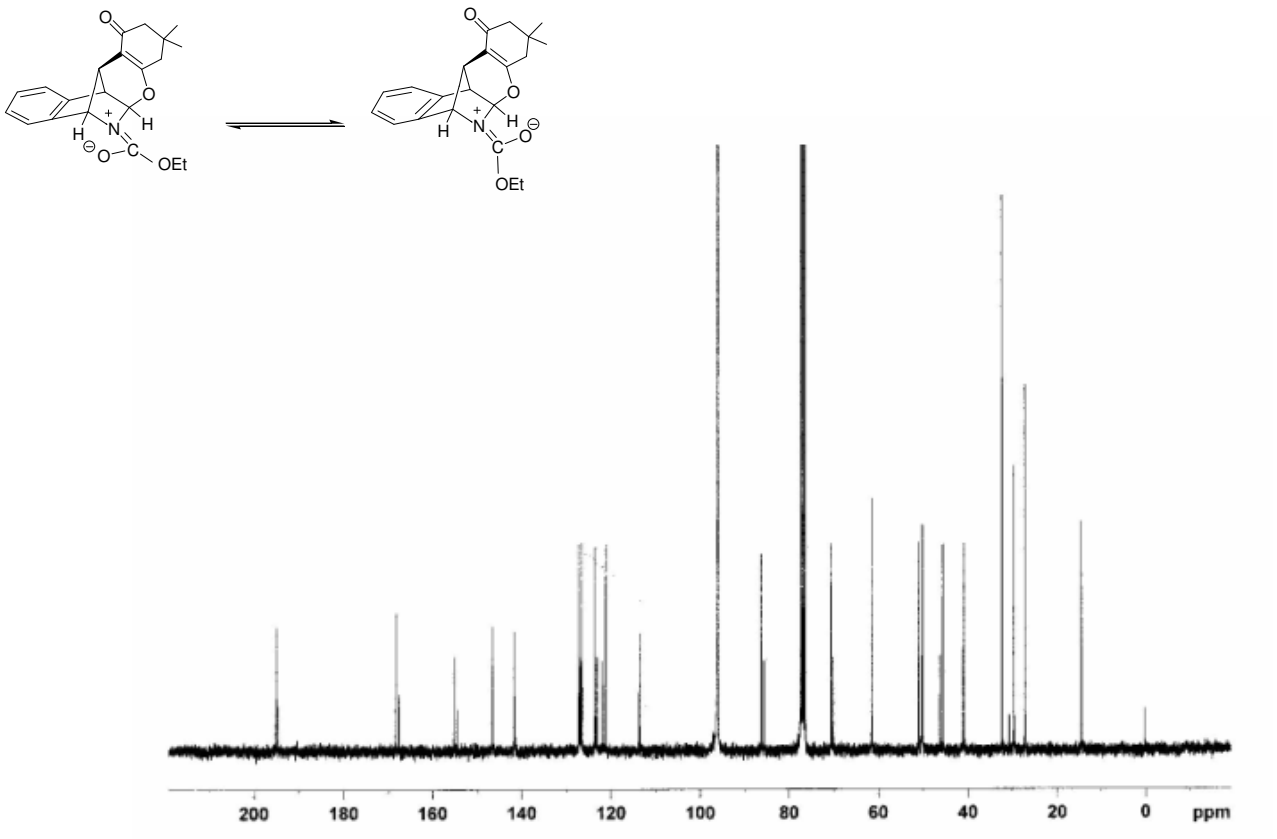


Figure A67 ^{13}C-NMR Spectrum of Compound **189**.

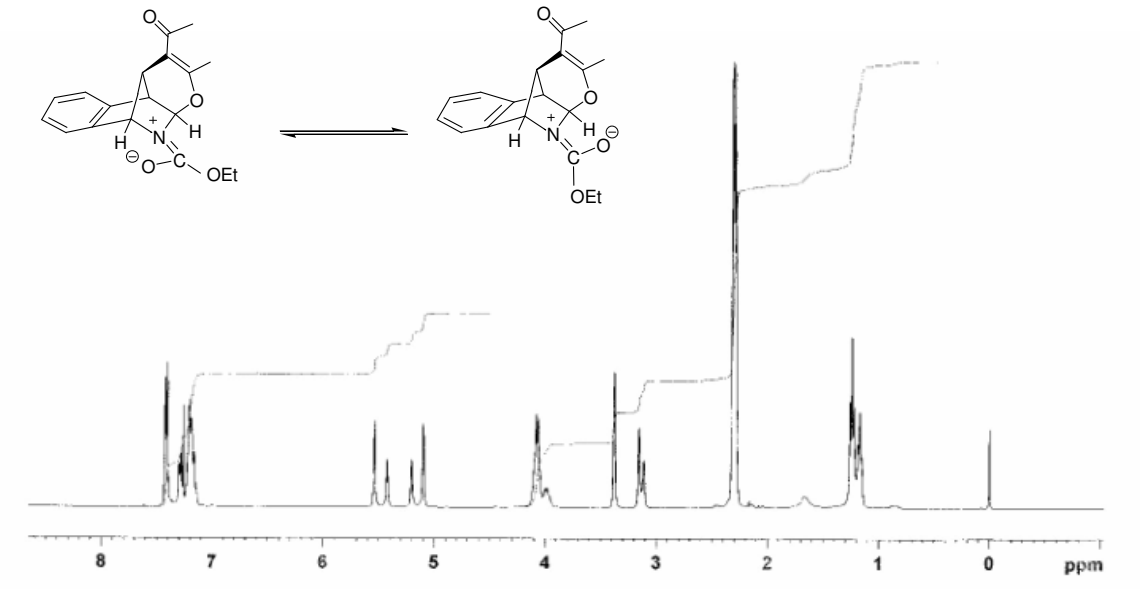


Figure A68 ^{1}H-NMR Spectrum of Compound **195**.

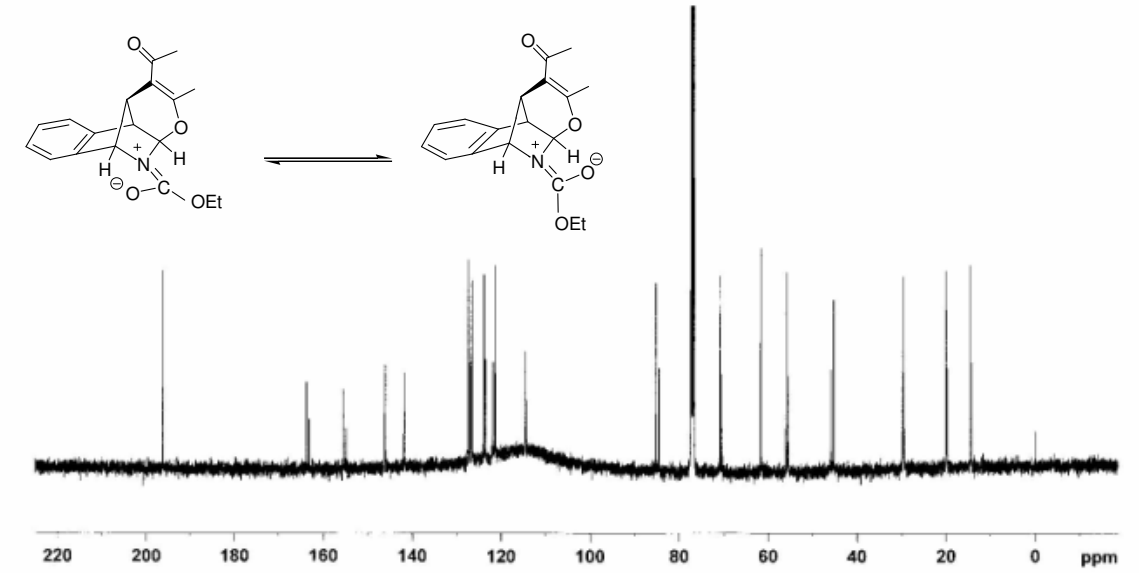


Figure A69. ^{13}C-NMR Spectrum of Compound **195**.

APPENDIX B

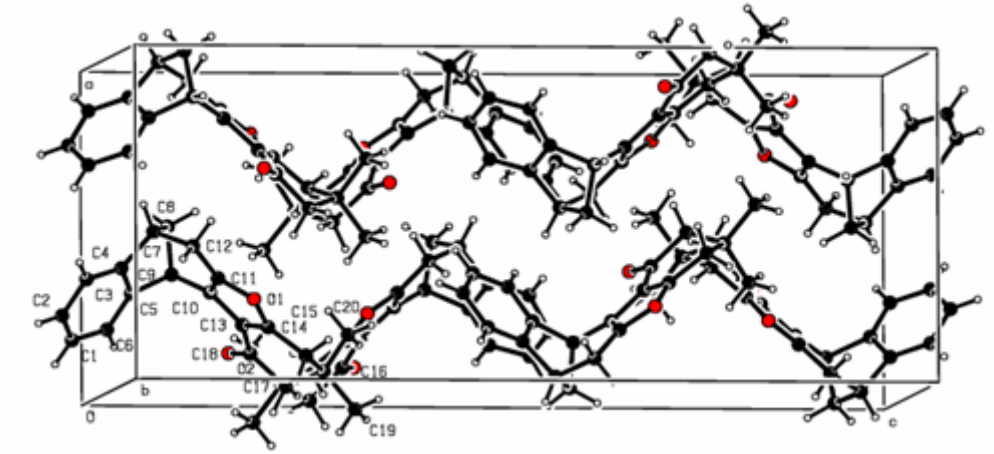


Figure A70 Crystal lattice of compound **107** .

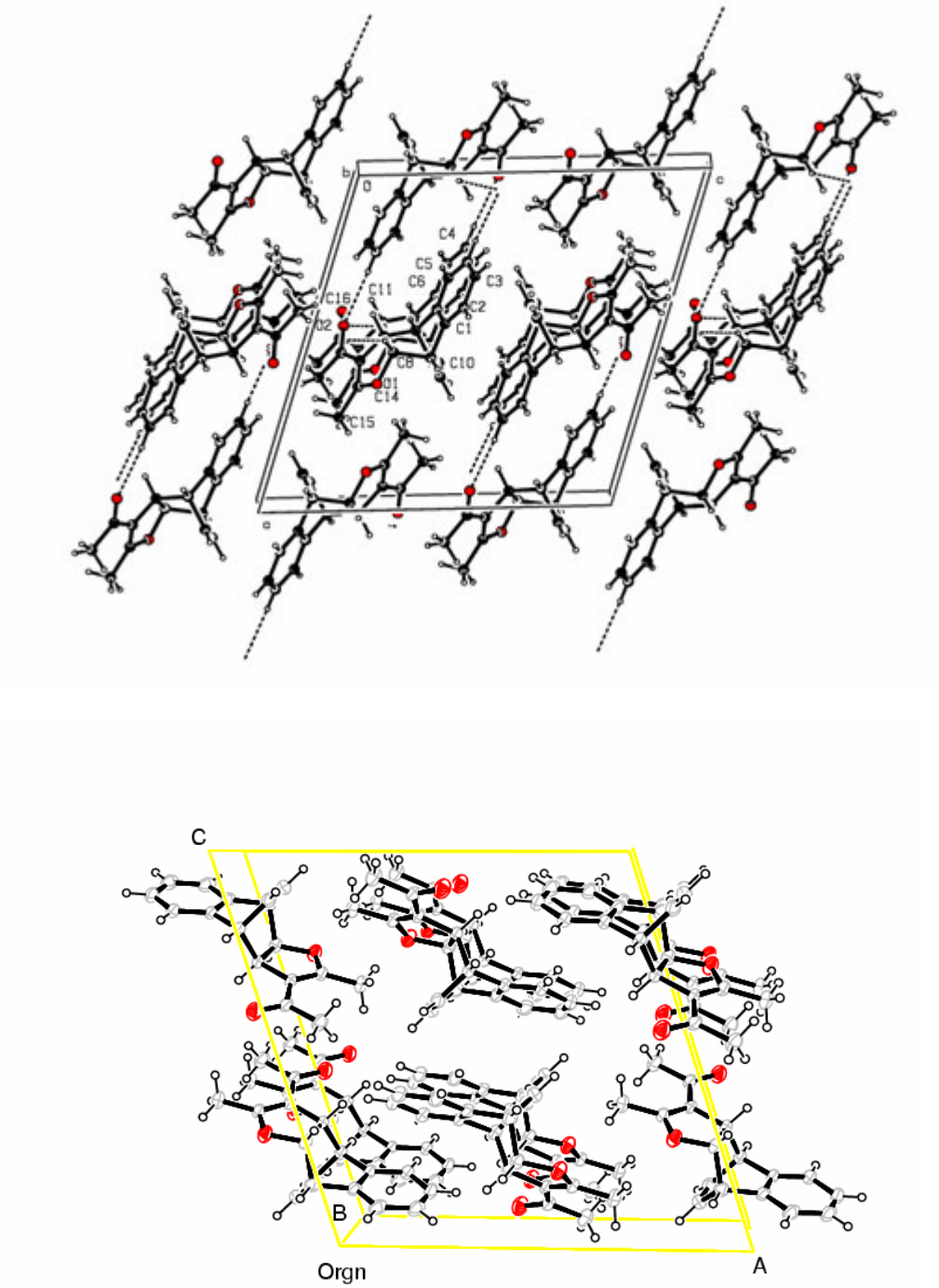


Figure A71 Crystal lattice of compound **132** .

X-RAY Data of Compound 107

Table A1. Fractional atomic coordinates and isotropic temperature factors (Angstrom squared), with standard deviations in the least significant digits in parentheses. For anisotropic atoms, the equivalent isotropic temperature factors are shown.

	x/a	y/b	z/c	U
O(1)	0.25779(15)	0.27726(11)	0.33774(5)	0.053
O(2)	0.12487(18)	-0.08352(13)	0.34517(7)	0.070
C(5)	0.2887(2)	0.0833(2)	0.4775(1)	0.048
C(14)	0.1803(2)	0.1992(2)	0.3150(1)	0.046
C(13)	0.19500(19)	0.10099(16)	0.34015(7)	0.043
C(9)	0.3488(2)	0.0469(2)	0.4247(1)	0.050
C(18)	0.1158(2)	0.0072(2)	0.3244(1)	0.048
C(11)	0.3243(2)	0.2239(2)	0.3787(1)	0.050
C(16)	0.0549(2)	0.1194(2)	0.2406(1)	0.055
C(10)	0.29011(19)	0.11762(16)	0.38158(7)	0.045
C(15)	0.0932(2)	0.2263(2)	0.2698(1)	0.055
H(15A)	0.13689	0.27582	0.24527	0.066
H(15B)	0.01613	0.26307	0.28312	0.066
C(4)	0.3566(2)	0.1748(2)	0.4960(1)	0.054
C(12)	0.4157(3)	0.2844(2)	0.4140(1)	0.063
H(12A)	0.37211	0.34642	0.43067	0.075
H(12B)	0.48819	0.31223	0.39332	0.075
C(3)	0.3190(3)	0.2262(2)	0.5429(1)	0.067
H(3)	0.36399	0.28723	0.55561	0.080
C(7)	0.4644(2)	0.2030(2)	0.4573(1)	0.063
C(17)	0.0156(2)	0.0324(2)	0.2818(1)	0.055
H(17A)	-0.06316	0.05683	0.29937	0.066
H(17B)	-0.00447	-0.03549	0.26302	0.066
C(2)	0.2130(3)	0.1852(2)	0.5708(1)	0.071
H(2)	0.18668	0.21933	0.60225	0.086
C(6)	0.1831(2)	0.0431(2)	0.5052(1)	0.057
H(6)	0.13727	-0.01751	0.49244	0.068
C(8)	0.4891(2)	0.0895(2)	0.4321(1)	0.067
H(8A)	0.53846	0.04218	0.45587	0.081
H(8B)	0.53397	0.09586	0.39819	0.081
C(1)	0.1467(3)	0.0948(2)	0.5523(1)	0.067
H(1)	0.07650	0.06791	0.57164	0.081
C(19)	-0.0598(3)	0.1450(3)	0.2035(1)	0.086
H(19A)	-0.08534	0.07911	0.18503	0.130
H(19B)	-0.03450	0.20004	0.17792	0.130
H(19C)	-0.13128	0.17199	0.22431	0.130
C(20)	0.1688(3)	0.0776(3)	0.2072(1)	0.077
H(20A)	0.24103	0.06227	0.23020	0.116
H(20B)	0.19300	0.13280	0.18153	0.116
H(20C)	0.14383	0.01141	0.18878	0.116
H(9)	0.34490	-0.03280	0.41770	0.048(6)
H(7)	0.54270	0.24220	0.47258	0.077(7)

Table A2. Vibration parameters (Angstrom squared) in the expression:

-2(pi squared)(U11((h.a*)squared) + U22((k.b*)squared) + U33((l.c*)squared) + 2.U12.h.k.a*.b* + 2.U13.h.l.a*.c* + 2.U23.k.l.b*.c*)

	U11	U22	U33	U12	U13	U23
O(1)	0.066(1)	0.048(1)	0.047(1)	-0.009(1)	-0.001(1)	0.005(1)
O(2)	0.085(1)	0.051(1)	0.074(1)	-0.012(1)	-0.007(1)	0.005(1)
C(5)	0.052(1)	0.052(1)	0.040(1)	0.003(1)	-0.003(1)	0.005(1)
C(14)	0.048(1)	0.046(1)	0.044(1)	-0.002(1)	0.002(1)	0.001(1)
C(13)	0.043(1)	0.044(1)	0.041(1)	0.000(1)	0.003(1)	0.001(1)
C(9)	0.056(1)	0.052(1)	0.043(1)	0.004(1)	-0.004(1)	0.001(1)
C(18)	0.048(1)	0.050(1)	0.046(1)	-0.002(1)	0.005(1)	0.004(1)
C(11)	0.057(1)	0.053(1)	0.039(1)	-0.008(1)	0.001(1)	0.002(1)
C(16)	0.045(1)	0.074(2)	0.047(1)	0.006(1)	-0.007(1)	0.003(1)
C(10)	0.049(1)	0.048(1)	0.037(1)	-0.002(1)	0.001(1)	0.002(1)
C(15)	0.052(1)	0.063(1)	0.051(1)	0.006(1)	-0.003(1)	0.011(1)
C(4)	0.058(1)	0.066(1)	0.040(1)	-0.005(1)	-0.005(1)	0.001(1)
C(12)	0.069(2)	0.071(2)	0.048(1)	-0.028(1)	0.002(1)	0.001(1)
C(3)	0.089(2)	0.069(2)	0.042(1)	-0.003(1)	-0.007(1)	0.003(1)
C(7)	0.057(1)	0.084(2)	0.050(1)	-0.021(1)	-0.006(1)	0.000(1)
C(17)	0.045(1)	0.060(1)	0.061(1)	-0.004(1)	-0.003(1)	0.009(1)
C(2)	0.093(2)	0.081(2)	0.040(1)	0.019(2)	0.007(1)	0.003(1)
C(6)	0.059(1)	0.058(1)	0.054(1)	-0.003(1)	-0.001(1)	0.013(1)
C(8)	0.051(1)	0.097(2)	0.053(1)	0.005(1)	0.000(1)	0.004(1)
C(1)	0.068(2)	0.080(2)	0.054(1)	0.009(1)	0.013(1)	0.019(1)
C(19)	0.066(2)	0.117(2)	0.076(2)	0.007(2)	-0.028(1)	0.003(2)
C(20)	0.066(2)	0.114(2)	0.052(1)	0.011(2)	0.007(1)	0.010(1)

Table A3. Complete listing of bond distances (Angstroms)

O(1) C(14)	1.362(3)	O(1) - C(11)	1.391(3)
O(2) - C(18)	1.221(3)	C(5) - C(9)	1.525(3)
C(5) - C(4)	1.391(4)	C(5) - C(6)	1.379(4)
C(14) - C(13)	1.356(3)	C(14) - C(15)	1.480(3)
C(13) - C(18)	1.455(3)	C(13) - C(10)	1.441(3)
C(9) - C(10)	1.504(3)	C(9) - H(9)	0.983(3)
C(18) - C(17)	1.514(4)	C(11) - C(10)	1.339(3)
C(11) - C(12)	1.486(4)	C(16) C(17)	1.531(4)
C(16) - C(19)	1.535(4)	C(16) - C(20)	1.528(4)
C(15) - H(15A)	0.970(3)	C(15) - H(15B)	0.970(3)
C(4) - C(3)	1.383(4)	C(4) - C(7)	1.512(4)
C(12) - H(12A)	0.970(3)	C(12) - H(12B)	0.970(3)
C(3) - H(3)	0.930(3)	C(3) - C(2)	1.388(4)
C(7) - C(8)	1.535(4)	C(7) - H(7)	1.012(3)
C(17) - H(17A)	0.970(3)	C(17) - H(17B)	0.970(3)
C(2) - H(2)	0.930(3)	C(2) - C(1)	1.372(4)
C(6) - H(6)	0.930(3)	C(6) - C(1)	1.387(4)
C(8) - H(8A)	0.970(3)	C(8) - H(8B)	0.970(3)
C(1) - H(1)	0.930(3)	C(19) - H(19A)	0.960(4)
C(19) - H(19B)	0.960(4)	C(19) - H(19C)	0.960(3)

C(20) - H(20A)	0.960(3)	C(20) - H(20B)	0.960(3)
C(20) - H(20C)	0.960(3)		

Table A4. Complete listing of bond angles (degrees)

C(14)-O(1)-C(11)	105.8(2)	C(9)-C(5)-C(4)	108.3(2)
C(9)-C(5)-C(6)	130.7(2)	C(4)-C(5)-C(6)	120.9(2)
O(1)-C(14)-C(13)	110.6(2)	O(1)-C(14)-C(15)	121.3(2)
C(13)-C(14)-C(15)	128.1(2)	C(14)-C(13)-C(18)	119.9(2)
C(14)-C(13)-C(10)	106.6(2)	C(18)-C(13)-C(10)	133.4(2)
C(5)-C(9)-C(10)	106.9(2)	C(5)-C(9)-H(9)	115.0(2)
C(10)-C(9)-H(9)	114.7(2)	O(2)-C(18)-C(13)	123.1(2)
O(2)-C(18)-C(17)	122.2(2)	C(13)-C(18)-C(17)	114.6(2)
O(1)-C(11)-C(10)	111.0(2)	O(1)-C(11)-C(12)	121.4(2)
C(10)-C(11)-C(12)	127.6(2)	C(17)-C(16)-C(19)	110.0(2)
C(17)-C(16)-C(20)	110.0(3)	C(19)-C(16)-C(20)	109.3(2)
C(13)-C(10)-C(9)	135.1(2)	C(13)-C(10)-C(11)	106.0(2)
C(9)-C(10)-C(11)	118.8(2)	C(14)-C(15)-H(15A)	109.8(2)
C(14)-C(15)-H(15B)	109.8(2)	H(15A)-C(15)H(15B)	108.2(3)
C(5)-C(4)-C(3)	120.0(3)	C(5)-C(4)-C(7)	109.7(2)
C(3)-C(4)-C(7)	130.3(3)	C(11)-C(12)-H(12A)	110.1(3)
C(11)-C(12)-H(12B)	110.1(2)	H(12A)-C(12)H(12B)	108.4(3)
C(4)-C(3)-H(3)	120.5(3)	C(4)-C(3)-C(2)	119.0(3)
H(3)-C(3)-C(2)	120.5(3)	C(4)-C(7)-C(8)	100.5(2)
C(4)-C(7)-H(7)	116.8(3)	C(8)-C(7)-H(7)	116.3(3)
C(18)-C(17)-C(16)	115.6(2)	C(18)-C(17)-H(17A)	108.4(2)
C(18)-C(17)-H(17B)	108.4(2)	C(16)-C(17)-H(17A)	108.4(2)
C(16)-C(17)-H(17B)	108.4(2)	H(17A)-C(17)H(17B)	107.4(3)
C(3)-C(2)-H(2)	119.7(3)	C(3)-C(2)-C1)	120.7(3)
H(2)-C(2)-C(1)	119.7(3)	C(5)-C(6)-H(6)	120.7(3)
C(5)-C(6)-C(1)	118.7(3)	H(6)-C(6)-C(1)	120.7(3)
C(7)-C(8)-H(8A)	111.5(3)	C(7)-C(8)-H(8B)	111.5(3)
H(8A)-C(8)-H(8B)	109.3(3)	C(2)-C(1)-C(6)	120.8(3)
C(2)-C(1)-H(1)	119.6(3)	C(6)-C(1)-H(1)	119.6(3)
C(16)-C(19)-H(19A)	109.5(3)	C(16)-C(19)-H(19B)	109.5(3)
C(16)-C(19)-H(19C)	109.5(3)	H(19A)-C(19)H(19B)	109.5(3)
H(19A)-C(19)-H(19C)	109.5(3)	H(19B)-C(19)H(19C)	109.5(4)
C(16)-C(20)-H(20A)	109.5(3)	C(16)-C(20)-H(20B)	109.5(3)
C(16)-C(20)-H(20C)	109.5(3)	H(20A)-C(20)H(20B)	109.5(3)
H(20A)-C(20)-H(20C)	109.5(3)	H(20B)-C(20)H(20C)	109.5(3)

X-RAY Data of Compound 132

Table A5. Fractional atomic coordinates and isotropic temperature factors (Angstrom squared), with standard deviations in the least significant digits in parentheses. For anisotropic atoms, theequivalent isotropic temperature factors are shown.

	x/a	y/b	z/c	U
O(1)	0.60818(10)	−0.34250(22)	0.22377(10)	0.045
O(2)	0.45813(11)	0.26304(26)	0.08899(12)	0.053
C(11)	0.47640(11)	−0.10229(28)	0.20663(11)	0.034
C(6)	0.39937(12)	−0.09459(30)	0.33516(12)	0.037
C(8)	0.53309(13)	−0.33805(29)	0.35454(13)	0.039
C(7)	0.46711(12)	0.03157(28)	0.29457(12)	0.036
C(1)	0.43469(13)	−0.29450(30)	0.36668(12)	0.039
C(14)	0.62188(12)	−0.17017(29)	0.17453(12)	0.037
C(10)	0.59958(13)	−0.15881(33)	0.40095(13)	0.041
C(12)	0.51604(13)	−0.32160(28)	0.24422(13)	0.037
C(16)	0.53488(12)	0.16761(29)	0.10331(12)	0.038
C(13)	0.55048(11)	−0.02487(28)	0.16012(11)	0.035
C(9)	0.56568(13)	0.03077(31)	0.37057(13)	0.040
C(15)	0.71198(14)	−0.18441(37)	0.14566(16)	0.049
H(15A)	0.69563	−0.22197	0.07829	0.070
H(15B)	0.75396	−0.28961	0.18426	0.070
H(15C)	0.74444	−0.05084	0.15583	0.070
C(17)	0.61041(16)	0.25186(37)	0.06106(16)	0.051
H(01D)	0.58719	0.37926	0.02604	0.072
H(01E)	0.62322	0.14957	0.01768	0.072
H(01F)	0.66900	0.28050	0.11248	0.072
C(5)	0.30969(13)	−0.03102(38)	0.34089(13)	0.045
H(5)	0.28531	0.10132	0.31895	0.052
C(2)	0.38073(16)	−0.43322(36)	0.40383(14)	0.049
H(2)	0.40380	−0.56755	0.42367	0.056
C(4)	0.25666(14)	−0.16897(45)	0.38011(15)	0.055
H(4)	0.19709	−0.12696	0.38571	0.064
C(3)	0.29173(16)	−0.36713(43)	0.41070(15)	0.057
H(3)	0.25526	−0.45757	0.43624	0.065
H(7)	0.4408(15)	0.1752(37)	0.2733(16)	0.038(6)
H(11)	0.4100(17)	−0.1132(38)	0.1568(17)	0.044(6)
H(10)	0.5616(17)	−0.4775(39)	0.3810(17)	0.046(6)
H(12)	0.4755(16)	−0.4389(38)	0.2081(17)	0.043(6)
H(9)	0.5996(18)	0.1606(40)	0.3930(18)	0.048(6)
H(8)	0.661(2)	−0.182(4)	0.449(2)	0.058(7)

Table A6. Vibration parameters (Angstrom squared) in the expression: −2(pi squared) (U11((h.a*)squared) + U22((k.b*)squared) +U33((l.c*)squared) + 2.U12.h.k.a*.b* + 2.U13.h.l.a*.c* 2.U23.k.l.b*.c*)

	U11	U22	U33	U12	U13	U23
O(1)	0.0441(7)	0.0397(7)	0.0503(7)	0.0089(5)	0.0251(6)	0.0041(6)

O(2)	0.0477(8)	0.0527(9)	0.0566(8)	0.0130(7)	0.0253(7)	0.0144(7)
C(11)	0.0295(6)	0.0382(8)	0.0311(7)	0.0018(6)	0.0133(5)	0.0013(6)
C(6)	0.0321(7)	0.0450(9)	0.0315(7)	.0031(6)	0.0143(6)	-0.0021(6)
C(8)	0.0406(8)	0.0351(8)	0.0384(8)	0.0020(7)	0.0146(7)	0.0055(7)
C(7)	0.0349(7)	0.0337(8)	0.0366(7)	0.0018(6)	0.0176(6)	0.0005(6)
C(1)	0.0393(8)	0.0425(9)	0.0329(7)	-.0074(7)	0.0152(6)	0.0004(6)
C(14)	0.0336(7)	0.0412(9)	0.0357(7)	0.0013(6)	0.0153(6)	-0.0031(6)
C(10)	0.0330(7)	0.0511(10)	0.0357(8)	-.0007(7)	0.0089(6)	0.0009(7)
C(12)	0.0367(8)	0.0341(8)	0.0392(8)	0.0003(6)	0.0170(6)	-0.0022(6)
C(16)	0.0371(8)	0.0407(9)	0.0334(7)	-.0004(7)	0.0164(6)	-0.0010(6)
C(13)	0.0313(7)	0.0388(8)	0.0323(7)	0.0016(6)	0.0156(6)	0.0006(6)
C(9)	0.0355(8)	0.0426(9)	0.0382(8)	-.0076(7)	0.0151(6)	0.0067(7)
C(15)	0.0361(8)	0.0574(12)	0.0534(11)	0.0064(8)	0.0236(8)	-.0015(9)
C(17)	0.050(1)	0.051(1)	0.050(1)	-0.004(1)	0.027(1)	0.007(1)
C(5)	0.0346(8)	0.0637(12)	0.0349(8)	-.0004(8)	0.0155(6)	-.0029(8)
C(2)	0.054(1)	0.051(1)	0.038(1)	-0.018(1)	0.019(1)	0.000(1)
C(4)	0.0347(8)	0.0879(17)	0.0410(9)	-.0124(10)	0.0181(7)	-.0080(10)
C(3)	0.050(1)	0.078(2)	0.040(1)	-0.027(1)	0.021(1)	-0.004(1)

Table A7. Complete listing of bond distances (Angstroms)

O(1) - C(14)	1.354(3)	O(2) - C(16)	1.227(3)
C(11) - C(13)	1.512(3)	C(11) - H(11)	1.01(3)
C(6) - C(7)	1.517(3)	C(6) - C(1)	1.394(3)
C(6) - C(5)	1.387(3)	C(8) - C(1)	1.514(3)
C(8) - C(10)	1.511(3)	C(8) - H(10)	1.00(3)
C(7) - C(9)	1.513(3)	C(7) - H(7)	1.00(3)
C(1) - C(2)	1.390(3)	C(14) - C(13)	1.355(3)
C(14) - C(15)	1.489(3)	C(10) - C(9)	1.325(3)
C(10) - H(8)	0.96(3)	C(12) - H(12)	0.99(3)
C(16) - C(13)	1.453(3)	C(16) - C(17)	1.505(3)
C(9) - H(9)	0.96(3)	C(15) - H(15A)	0.960(3)
C(15) - H(15B)	0.960(3)	C(15) - H(15C)	0.960(3)
C(17) - H(01D)	0.960(3)	C(17) - H(01E)	0.960(3)
C(17) - H(01F)	0.960(3)	C(5) - H(5)	0.930(3)
C(5) - C(4)	1.395(4)	C(2) - H(2)	0.930(3)
C(2) - C(3)	1.388(4)	C(4) - H(4)	0.930(3)
C(4) - C(3)	1.380(4)	C(3) - H(3)	0.930(3)

Table A8. Complete listing of bond angles (degrees)

C(13)-C(11)-H(11)	110.7(14)	C(7)-C(6)-C(1)	113.1(2)
C(7)-C(6)-C(5)	126.7(2)	C(1)-C(6)-C(5)	120.2(2)
C(1)-C(8)-C(10)	107.8(2)	C(1)-C(8)-H(10)	114.1(14)
C(10)-C(8)-H(10)	111.4(14)	C(6)-C(7)-C(9)	107.2(2)
C(6)-C(7)-H(7)	111.8(13)	C(9)-C(7)-H(7)	114.4(13)
C(6)-C(1)-C(8)	113.2(2)	C(6)-C(1)-C(2)	120.7(2)

C(8)-C(1)-C(2)	126.1(2)	O(1)-C(14)-C(13)
113.9(2)		
O(1)-C(14)-C(15)	112.3(2)	C(13)-C(14)-C(15)
133.8(2)		
C(8)-C(10)-C(9)	114.7(2)	C(8)-C(10)-H(8)
122.1(17)		
C(9)-C(10)-H(8)	123.3(17)	O(2)-C(16)-C(13)
119.2(2)		
O(2)-C(16)-C(17)	119.3(2)	C(13)-C(16)-C(17)
121.5(2)		
C(11)-C(13)-C(14)	108.8(2)	C(11)-C(13)-C(16)
121.1(2)		
C(14)-C(13)-C(16)	129.9(2)	C(7)-C(9)-C(10)
114.6(2)		
C(7)-C(9)-H(9)	120.8(15)	C(10)-C(9)-H(9)
124.6(15)		
C(14)-C(15)-H(15A)	109.5(2)	C(14)-C(15)-H(15B)
109.5(2)		
C(14)-C(15)-H(15C)	109.5(2)	H(15A)-C(15)-H(15B)
109.5(3)		
H(15A)-C(15)-H(15C)	109.5(3)	H(15B)-C(15)-H(15C)
109.5(2)		
C(16)-C(17)-H(01D)	109.5(2)	C(16)-C(17)-H(01E)
109.5(2)		
C(16)-C(17)-H(01F)	109.5(2)	H(01D)-C(17)-H(01E)
109.5(3)		
H(01D)-C(17)-H(01F)	109.5(3)	H(01E)-C(17)-H(01F)
109.5(3)		
C(6)-C(5)-H(5)	120.6(2)	C(6)-C(5)-C(4)
118.9(3)		
H(5)-C(5)-C(4)	120.6(2)	C(1)-C(2)-H(2)
120.7(3)		
C(1)-C(2)-C(3)	118.6(3)	H(2)-C(2)-C(3)
120.7(3)		
C(5)-C(4)-H(4)	119.7(3)	C(5)-C(4)-C(3)
120.7(2)		
H(4)-C(4)-C(3)	119.7(3)	C(2)-C(3)-C(4)
120.8(3)		
C(2)-C(3)-H(3)	119.6(3)	C(4)-C(3)-H(3)
119.6(3)		

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Table A9. Fractional atomic coordinates and isotropic temperature factors
(Angstrom squared), with standard deviations in the least significant digits in parentheses. For anisotropic atoms, the equivalent isotropic temperature factors are shown.

	x/a	y/b	z/c	U
O(3)	0.2662(2)	0.3004(1)	−0.0053(2)	0.062
O(2)	0.3883(2)	0.3954(1)	0.0216(2)	0.073
C(21)	0.3562(3)	0.3396(1)	0.0703(3)	0.054
C(22)	0.3041(4)	0.4094(2)	−0.1365(3)	0.090
H(22A)	0.36476	0.39996	−0.19211	0.104
H(22B)	0.21515	0.38280	−0.17574	0.104
C(23)	0.2636(7)	0.4747(2)	−0.1529(5)	0.156
H(23A)	0.21302	0.48489	−0.08915	0.234
H(23B)	0.19832	0.48309	−0.25506	0.234
H(23C)	0.35174	0.50079	−0.12577	0.234
O(4)	0.49177(16)	0.22726(7)	0.32545(17)	0.047
N(1)	0.4433(2)	0.3321(1)	0.2200(2)	0.046
C(12)	0.6969(2)	0.2934(1)	0.4695(3)	0.044
C(9)	0.4027(2)	0.2850(1)	0.3066(3)	0.045
H(9)	0.29564	0.27508	0.25975	0.051
C(13)	0.5937(2)	0.3471(1)	0.4692(3)	0.045
H(13)	0.63896	0.37505	0.55678	0.052
C(11)	0.6397(2)	0.2366(1)	0.4038(2)	0.044
C(8)	0.4429(2)	0.3195(1)	0.4573(3)	0.047
H(8)	0.44620	0.29249	0.54086	0.053
O(1)	0.9139(2)	0.3502(1)	0.6105(3)	0.076
C(15)	0.8754(3)	0.1759(1)	0.5451(3)	0.051
C(7)	0.5216(3)	0.3866(1)	0.3230(3)	0.049
H(7)	0.58962	0.41257	0.29425	0.056
C(14)	0.7290(3)	0.1782(1)	0.4065(3)	0.053
H(14A)	0.75081	0.17774	0.31782	0.060
H(14B)	0.67052	0.14015	0.40405	0.060
C(16)	0.9525(3)	0.2412(1)	0.5601(3)	0.061
H(16A)	1.03822	0.24222	0.65523	0.070
H(16B)	0.98996	0.24451	0.48202	0.070
C(17)	0.8576(3)	0.2993(1)	0.5510(3)	0.053
C(6)	0.4010(3)	0.4226(1)	0.3516(3)	0.053
C(1)	0.3496(3)	0.3796(1)	0.4302(3)	0.052
C(5)	0.3349(3)	0.4822(1)	0.3069(3)	0.069
H(5)	0.36839	0.51056	0.25329	0.082
C(19)	0.9734(3)	0.1220(1)	0.5272(3)	0.066
H(19A)	0.99711	0.13092	0.44271	0.093
H(19B)	0.92063	0.08181	0.51191	0.093
H(19C)	1.06403	0.11927	0.61587	0.093
C(2)	0.2313(3)	0.3954(2)	0.4666(3)	0.068
H(2)	0.19620	0.36686	0.51842	0.078
C(4)	0.2161(3)	0.4980(2)	0.3453(4)	0.081
H(4)	0.16982	0.53792	0.31782	0.097

C(18)	0.8431(3)	0.1622(1)	0.6838(3)	0.071
H(18A)	0.93536	0.16126	0.77093	0.099
H(18B)	0.79357	0.12144	0.67258	0.099

	x/a	y/b	z/c	U
H(18C)	0.77999	0.19555	0.69481	0.099
C(3)	0.1663(3)	0.4556(2)	0.4232(4)	0.082
H(3)	0.08695	0.46748	0.44757	0.095

Table A10. Vibration parameters (Angstrom squared) in the expression:

-2(pi squared)(U11((h.a*)squared) + U22((k.b*)squared) + U33((l.c*)squared) + 2.U12.h.k.a*.b* + 2.U13.h.l.a*.c* + 2.U23.k.l.b*.c*)

	U11	U22	U33	U12	U13	U23
O(3)	0.053(1)	0.073(1)	0.045(1)	0.010(1)	0.010(1)	-0.005(1)
O(2)	0.093(1)	0.065(1)	0.045(1)	0.011(1)	0.00.015(1)	
C(21)	0.048(1)	0.058(2)	0.046(1)	0.016(1)	0.018(1)	0.005(1)
C(22)	0.121(3)	0.086(2)	0.043(2)	0.025(2)	0.023(2)	0.020(2)
C(23)	0.235(6)	0.098(3)	0.078(3)	0.053(4)	0.004(3)	0.028(2)
O(4)	0.0396(8)	0.0440(9)	0.0456(9)	0.0008(7)	0.0092(7)	.0006(7)
N(1)	0.044(1)	0.047(1)	0.038(1)	0.003(1)	0.013(1)	0.006(1)
C(12)	0.037(1)	0.047(1)	0.040(1)	0.003(1)	0.012(1)	0.003(1)
C(9)	0.035(1)	0.047(1)	0.044(1)	0.003(1)	0.013(1)	0.003(1)
C(13)	0.040(1)	0.045(1)	0.040(1)	-0.001(1)	0.011(1)	0.002(1)
C(11)	0.037(1)	0.046(1)	0.038(1)	0.002(1)	0.011(1)	0.003(1)
C(8)	0.042(1)	0.050(1)	0.039(1)	0.000(1)	0.015(1)	0.001(1)
O(1)	0.046(1)	0.061(1)	0.096(2)	-0.006(1)	0.006(1)	0.017(1)
C(15)	0.044(1)	0.052(1)	0.048(1)	0.011(1)	0.018(1)	0.006(1)
C(7)	0.045(1)	0.044(1)	0.047(1)	-0.001(1)	0.013(1)	0.004(1)
C(14)	0.047(1)	0.050(1)	0.051(1)	0.005(1)	0.016(1)	0.003(1)
C(16)	0.039(1)	0.060(2)	0.070(2)	0.005(1)	0.017(1)	0.003(1)
C(17)	0.041(1)	0.056(1)	0.050(1)	0.000(1)	0.013(1)	0.002(1)
C(6)	0.046(1)	0.051(1)	0.048(1)	0.006(1)	0.005(1)	0.004(1)
C(1)	0.042(1)	0.060(2)	0.044(1)	0.005(1)	0.010(1)	0.007(1)
C(5)	0.059(2)	0.053(2)	0.071(2)	0.009(1)	0.004(1)	0.003(1)
C(19)	0.055(2)	0.061(2)	0.071(2)	0.015(1)	0.027(1)	0.004(1)
C(2)	0.050(1)	0.087(2)	0.056(2)	0.007(1)	0.018(1)	0.019(1)
C(4)	0.061(2)	0.063(2)	0.091(2)	0.018(1)	0.000(2)	0.026(2)
C(18)	0.075(2)	0.069(2)	0.057(2)	0.018(1)	0.030(1)	0.014(1)
C(3)	0.054(2)	0.092(2)	0.080(2)	0.018(2)	0.013(2)	0.035(2)

Table A11. Complete listing of bond distances (Angstroms)

O(3) – C(21)	1.208(4)	O(2) – C(21)	1.336(4)
C(21) – N(1)	1.374(4)	C(22) – H(22A)	0.970(4)
C(22) – H(22B)	0.970(4)	C(22) – C(23)	1.403(6)
C(23) – H(23A)	0.960(6)	C(23) – H(23B)	0.960(5)
C(23) – H(23C)	0.960(6)	O(4) – C(11)	1.350(3)
N(1) – C(9)	1.449(3)	C(12) – C(13)	1.503(4)
C(12) – C(11)	1.352(4)	C(12) – C(17)	1.453(4)
C(9) – H(9)	0.980(3)	C(13) – H(13)	0.980(3)
C(13) – C(8)	1.540(4)	C(11) – C(14)	1.488(4)
C(8) – H(8)	0.980(3)	C(8) – C(1)	1.504(4)
O(1) – C(17)	1.224(4)	C(15) – C(14)	1.526(4)
C(15) – C(16)	1.530(4)	C(15) – C(19)	1.527(4)
C(15) – C(18)	1.535(4)	C(7) – H(7)	0.980(3)
C(7) – C(6)	1.513(4)	C(14) – H(14A)	0.970(3)
C(14) – H(14B)	0.970(3)	C(16) – H(16A)	0.970(3)
C(16) – H(16B)	0.970(3)	C(16) – C(17)	1.503(4)
C(6) – C(1)	1.396(4)	C(6) – C(5)	1.383(4)
C(1) – C(2)	1.377(4)	C(5) – H(5)	0.930(3)
C(5) – C(4)	1.393(5)	C(19) – H(19A)	0.960(3)
C(19) – H(19B)	0.960(3)	C(19) – H(19C)	0.960(3)
C(2) – H(2)	0.930(3)	C(2) – C(3)	1.389(5)
C(4) – H(4)	0.930(4)	C(4) – C(3)	1.373(5)
C(18) – H(18A)	0.960(4)	C(18) – H(18B)	0.960(3)
C(18) – H(18C)	0.960(4)	C(3) – H(3)	0.930(4)

Table A12. Complete listing of bond angles (degrees)

O(3)-C(21)-O(2)	125.7(3)	O(3)-C(21)-N(1)	124.2(3)
O(2)-C(21)-N(1)	110.1(3)	H(22A)-C(22)-H(22B)	108.3(4)
H(22A)-C(22)-C(23)	109.9(4)	H(22B)-C(22)-C(23)	109.8(4)
C(22)-C(23)-H(23A)	109.5(5)	C(22)-C(23)-H(23B)	109.5(4)
C(22)-C(23)-H(23C)	109.5(5)	H(23A)-C(23)-H(23B)	109.5(6)
H(23A)-C(23)-H(23C)	109.5(5)	H(23B)-C(23)-H(23C)	109.5(5)
C(21)-N(1)-C(9)	119.9(2)	C(13)-C(12)-C(11)	119.8(2)
C(13)-C(12)-C(17)	121.0(3)	C(11)-C(12)-C(17)	119.0(3)
N(1)-C(9)-H(9)	111.1(2)	C(12)-C(13)-H(13)	111.7(2)
C(12)-C(13)-C(8)	110.1(2)	H(13)-C(13)-C(8)	111.7(2)
O(4)-C(11)-C(12)	122.6(2)	O(4)-C(11)-C(14)	112.3(2)
C(12)-C(11)-C(14)	125.1(2)	C(13)-C(8)-H(8)	116.0(2)
C(13)-C(8)-C(1)	101.4(2)	H(8)-C(8)-C(1)	116.0(3)
C(14)-C(15)-C(16)	107.8(3)	C(14)-C(15)-C(19)	109.2(3)
C(14)-C(15)-C(18)	109.7(3)	C(16)-C(15)-C(19)	110.8(2)
C(16)-C(15)-C(18)	110.2(3)	C(19)-C(15)-C(18)	109.0(3)
H(7)-C(7)-C(6)	116.5(3)	C(11)-C(14)-C(15)	112.1(3)
C(11)-C(14)-H(14A)	109.2(3)	C(11)-C(14)-H(14B)	109.2(3)
C(15)-C(14)-H(14A)	109.2(3)	C(15)-C(14)-H(14B)	109.2(3)
H(14A)-C(14)-H(14B)	107.9(3)	C(15)-C(16)-H(16A)	108.3(3)
C(15)-C(16)-H(16B)	108.3(3)	C(15)-C(16)-C(17)	116.1(2)
H(16A)-C(16)-H(16B)	107.4(3)	H(16A)-C(16)-C(17)	108.3(3)
H(16B)-C(16)-C(17)	108.3(3)	C(12)-C(17)-O(1)	120.9(3)
C(12)-C(17)-C(16)	118.0(3)	O(1)-C(17)-C(16)	121.1(3)
C(7)-C(6)-C(1)	105.1(3)	C(7)-C(6)-C(5)	133.2(3)
C(1)-C(6)-C(5)	121.4(3)	C(8)-C(1)-C(6)	107.6(2)
C(8)-C(1)-C(2)	131.6(3)	C(6)-C(1)-C(2)	120.7(3)

C(6)-C(5)-H(5)	121.3(3)	C(6)-C(5)-C(4)	117.4(3)
H(5)-C(5)-C(4)	121.3(3)	C(15)-C(19)-H(19A)	109.5(3)
C(15)-C(19)-H(19B)	109.5(3)	C(15)-C(19)-H(19C)	109.5(3)
H(19A)-C(19)-H(19B)	109.5(3)	H(19A)-C(19)-H(19C)	109.5(3)
H(19B)-C(19)-H(19C)	109.5(3)	C(1)-C(2)-H(2)	121.1(4)
C(1)-C(2)-C(3)	117.7(3)	H(2)-C(2)-C(3)	121.2(3)
C(5)-C(4)-H(4)	119.5(4)	C(5)-C(4)-C(3)	120.9(4)
H(4)-C(4)-C(3)	119.5(4)	C(15)-C(18)-H(18A)	109.5(3)
C(15)-C(18)-H(18B)	109.5(3)	C(15)-C(18)-H(18C)	109.5(3)
H(18A)-C(18)-H(18B)	109.5(3)	H(18A)-C(18)-H(18C)	109.5(3)
H(18B)-C(18)-H(18C)	109.5(4)	C(2)-C(3)-C(4)	121.8(3)
C(2)-C(3)-H(3)	119.1(4)	C(4)-C(3)-H(3)	119.1(4)

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