$Mn(OAc)_3$ PROMOTED ADDITION OF AN ACTIVE METHYLENE COMPOUND TO ALKENES: MECHANISTIC STUDIES

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Approval of the thesis:

$Mn(OAc)_3$ PROMOTED ADDITION OF AN ACTIVE METHYLENE COMPOUND TO ALKENES: MECHANISTIC STUDIES

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ABSTRACT

$Mn(OAc)_3$ PROMOTED ADDITION OF AN ACTIVE METHYLENE COMPOUND TO ALKENES: MECHANISTIC STUDIES

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Radical cyclization of alkenes is one of the most important methods for the synthesis of cyclic compounds. The one electron oxidant $Mn(OAc)_3$ has been used for many years for the oxidative addition of acetic acid to alkenes to give lactones. In this thesis, various alkenes substituted at 1,2-positions by phenyl and thiophene rings were reacted with active methylene compounds in the presence of $Mn(OAc)_3 \cdot 2H_2O$. The regioselectivity of the addition were searched. The mechanism for the addition was studied in connection with the directing effect of the sulfur atom and substituents attached to the benzene ring. The regioselectivity was also discussed in terms of electron density distribution on the double bond.

Keywords: $Mn(OAc)_3$, directing effect of sulfur atom, substituents effect, radical cyclization, NBO calculations.

ÖZ

AKTİF METİLEN GRUBU İÇEREN BİLEŞİKLERİN $Mn(OAc)_3$ EŞLİĞİNDE ÇİFT BAĞLARA KATILMASI: MEKANİSTİK İNCELEME

Ceyhan, Selin

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Tez Yöneticisi: Prof. Dr. Metin Balcı

Eylül 2015, 142 sayfa

Alkenlerin radikalik siklizasyon reaksiyonları, siklik bileşiklerin sentezine uygulanan en önemli yöntemlerden birisidir. Tek elektron oksidantı $Mn(OAc)_3$ yıllardır asetik asitin alkenlere katılarak lakton oluşumuna başarılı bir şekilde uygulanmaktadır. Bu çalışmada 1,2- konumunda fenil ve tiyofen halkaları ile substitüe çift bağlar $Mn(OAc)_3 \cdot 2H_2O$ eşliğinde aktif metilen grubu içeren bileşiklerle reaksiyona sokularak katılmanın yer seçiciliği araştırıldı. Katılma reaksiyonunun mekanizmasına kükürt atomunun yönlendirici etkisi ile benzen halkasına bağlı olan sübstitüentlerin etkisi incelendi. Ayrıca katılımda gözlenen yer seçiciliği çift bağ üzerindeki elektron yoğunluğuna bağlı olarak da tartışıldı.

Anahtar kelimeler: $Mn(OAc)_3$, kükürt atomunun yönlendirici etkisi, sübstitüent etkisi , radikalik siklizasyon, NBO hesaplamaları.

To my beloved family…

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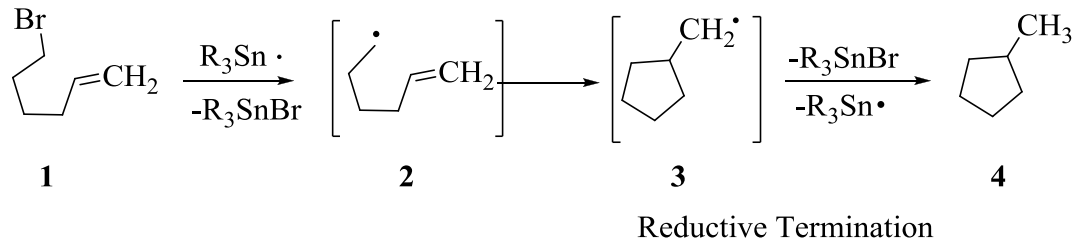
INTRODUCTION

1.1 Free Radicals in Organic Chemistry

The formation of a C-C bond using free radicals has pioneered a new era in the field of synthetic organic chemistry. With the developments in the last decade, the aspect of uncontrollability of free radical reactions has completely changed. After realizing that, free-radical reactions can be carried out in more precise and controllable way, synthetic organic chemists are more confident now. The works of Julia,[1] Walling and Beckwith[2] pioneered other synthetic organic chemists in the field of free-radical chemistry and these works end up with adding new aspects to the field of free-radical chemistry.[3]

1.1.1 Free Radical Cyclization Reactions

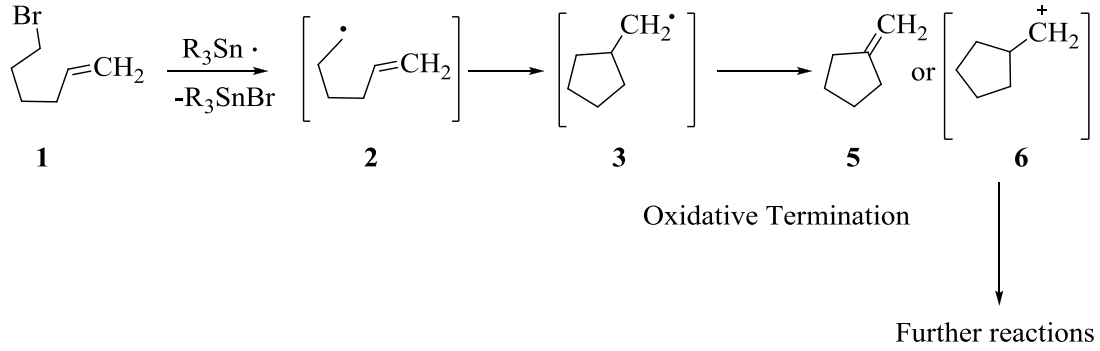
During past 30 years, the usage of free radical reactions for the alkene cyclization has become a valuable method for the synthesis of cyclic compounds.[4] Widely used procedure for the formation of cyclic compounds starts with the reduction of an alkyl halide **1** or other functional group to a radical by using R_3SnH. Initially formed radical **2** undergoes cyclization, then reduction of cyclic radical **3** in the propagation step forms compound **4** (Scheme 1).[5]



Scheme 1

This approach is limited due to the formation of unfunctionalized product, compound **4**, which is obtained from reductive termination.

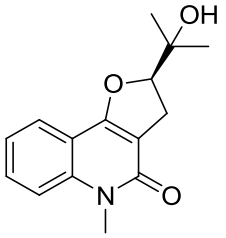
Oxidative free-radical cyclizations have considerable synthetic potential, because more functionalized products, compound **5** or intermediate **6**, can be prepared by generating the initial radical and terminating the cyclic radical oxidatively (Scheme 2).[5]



Scheme 2

1.2 General Knowledge on Manganese(III)Acetate

Transition metal catalysts especially $Mn(OAc)_3$ plays an important role for the synthesis of many biologically active molecules such as; araliopsine (**7**) and atanine (**8**).[6]



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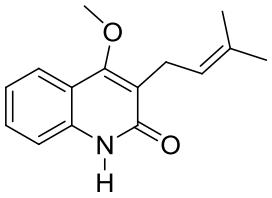


8

$Mn(OAc)_3$, one electron oxidant, is one of the most prominent reagent in the field of free radical chemistry. Due to the lower reduction potential of $Mn(OAc)_3$ compared to $Pb(OAc)_4$, $Cu(OAc)_2$, $(NH_4)_2Ce(NO_3)_6$ and $Fe(ClO_4)_3$, it shows moderate reactivity and higher selectivity.[7]

Anhydrous $Mn(OAc)_3$ and hydrated $Mn(OAc)_3 \cdot 2H_2O$ forms are commercially avaliable. Electrochemical oxidation of manganese(II)acetate with $KMnO_4$ and chlorine to give $Mn(OAc)_3 \cdot 2H_2O$ has been reported by Christensen.[8] Then in 1922, Weinland[9] proposed $[Mn_3(OAc)_6(H_2O)_2](OAc)_3 \cdot 4H_2O$ for the structure of $Mn(OAc)_3 \cdot 2H_2O$.[7]

Oxidations with manganese(III) acetate were divided into two pathways by de Klein[10];

• In direct oxidation pathway, radical intermediate is formed in the first step, then transformations such as; dimerization and disproportionation result in the formation of products (Scheme 3).[10]

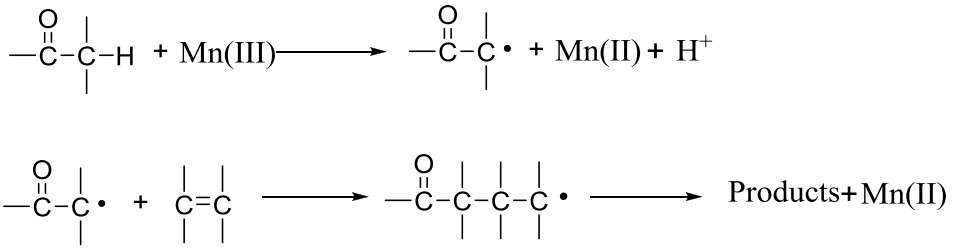
$$Mn(III) + \text{substrate} \longrightarrow \text{intermediate radical} + Mn(II)$$

$$Mn(III) + \text{intermediate } R\bullet \longrightarrow \text{product} + Mn(II)$$

Scheme 3

• In indirect oxidation pathway, a stabilized radical at an enolizable position is formed in the first step. Subsequent addition or substitution of initially formed radical to the aromatic systems or alkenes, results in the formation of a new radical.

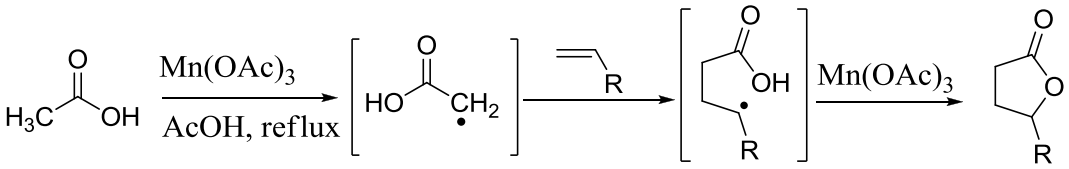
After the oxidation of final radical with excess $Mn(OAc)_3$, products are formed (Scheme 4).[10]



Scheme 4

1.3 Oxidative Free Radical Addition Reactions to Alkenes

Formation of lactones from alkenes and acetic acid in the presence of $Mn(OAc)_3$ was reported by Heiba-Dessau[11] and Bush-Finkbeiner[12] (Scheme 5).



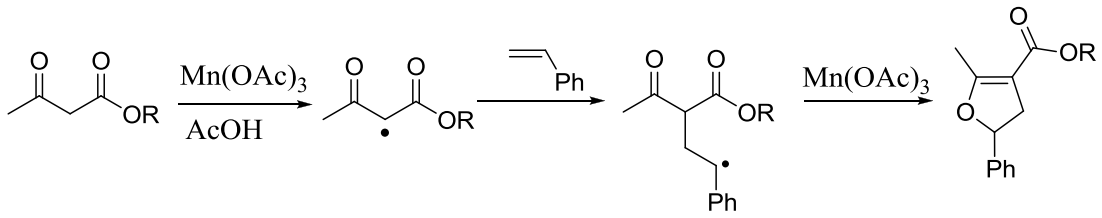
Scheme 5

Formation of radical **10** from acetic acid (**9**) was the initial step for the formation of lactone **12**. Subsequent addition of radical **10** to alkene leads to the formation of radical **11**. Lactone **12** was obtained from the oxidation of radical **11** with excess $Mn(OAc)_3$.

Unfortunately, $Mn(OAc)_3$ mediated cyclization reactions have some limitations. Optimal solvent for $Mn(OAc)_3$ reactions is acetic acid; therefore, the cyclization of unsaturated acids is not possible, due to the oxidation of acetic acid.[5]

1.3.1 Formation of dihydrofurans

Oxidation of β-ketoesters and 1,3-dicarbonyl compounds to radicals with $Mn(OAc)_3$ was reported by Heiba and Dessau[13] in 1974 (Scheme 6).



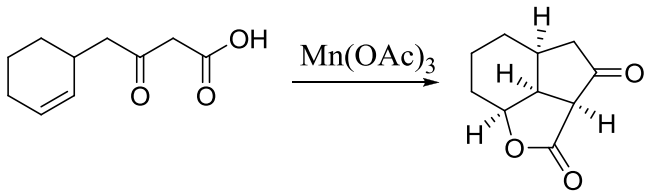
13 **14** **15** **16**

Scheme 6

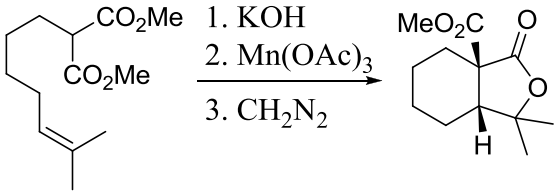
According to the proposed mechanism, the first step is the oxidative formation of radical **14**, which is then added to the alkene and resulting in the formation of radical **15**. Subsequent oxidation of radical **15** in the presence of excess $Mn(OAc)_3$ followed by cyclization produces dihydrofuran **16**.

1.3.2 Intramolecular Double Annulation Reactions of $Mn(OAc)_3$

Formation of cyclopentanone ring with intramolecular annulation reaction in the presence of $Mn(OAc)_3$ was reported by Corey[14] and Fristad[15] (Scheme 7).



17 **18**

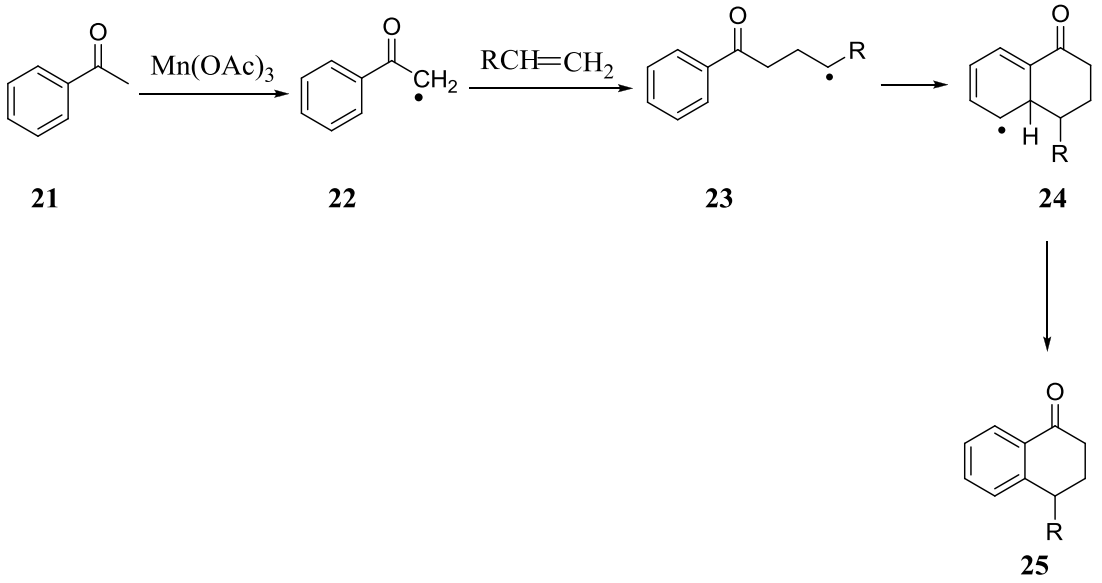


19 **20**

Scheme 7

1.3.3 Formation of Tetralones

In 1972 Heiba and Dessau[16] reported the formation of tetralones from the reaction of acetophenone and olefins in the presence of $Mn(OAc)_3$ (Scheme 8).



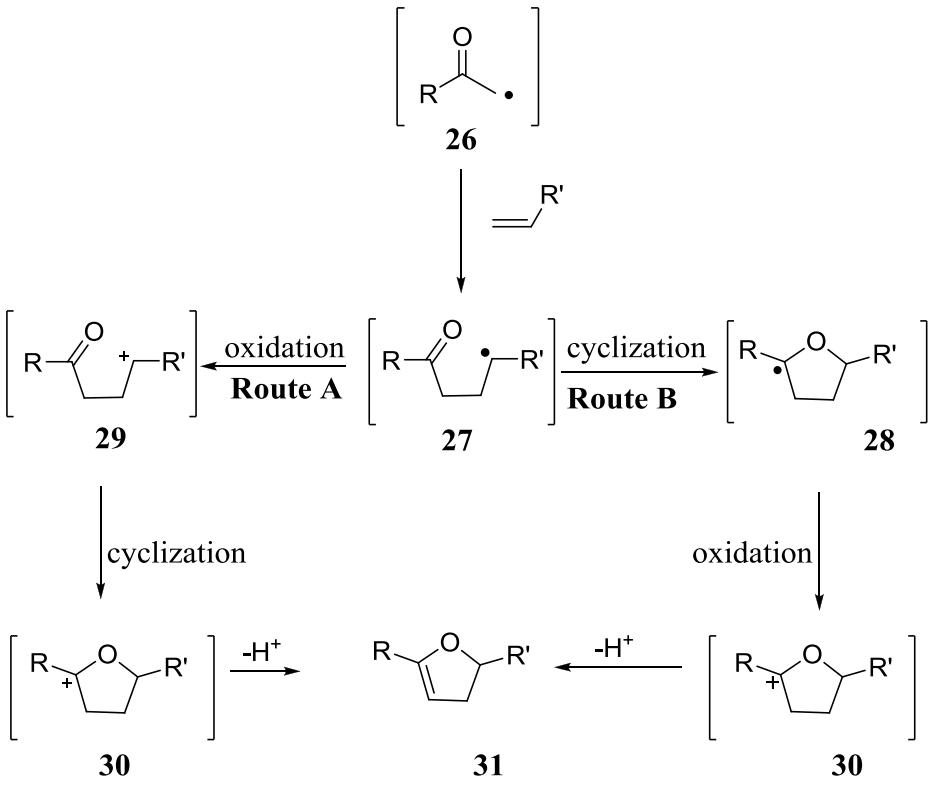
21 **22** **23** **24** **25**

Scheme 8

For the construction of tetralones, the first step is the formation of radical **22** oxidatively from acetophenone in the presence of $Mn(OAc)_3$. As a result of the addition of radical **22** to olefin, radical **23** is formed. Then radical **23** is converted to radical **24** via internal cyclization. Final step is the formation of tetralone derivative **25** in the presence of excess $Mn(OAc)_3$.

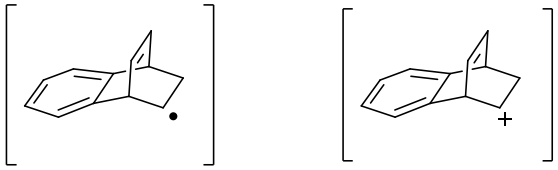
1.4 Mechanistic Considerations

In 1968 Heiba-Dessau[11] and Bush- Finkbeiner[12] reported the formation of lactones from alkenes and acetic acid in the presence of $Mn(OAc)_3$. There are two possible proposed mechanisms for the formation of lactones (Scheme 9).[17] The first step is the formation of a radical **26**, which is added to the alkene to produce radical **27**. Then, radical **27** may follow route **A** or route **B**. For the route **A**; radical **27** undergoes oxidation and forms carbocation **29** and then as a result of cyclization, carbocation **29** is converted to cyclic carbocation **30**. Finally, proton elimination gives compound **31**. For the route **B**; radical **27** undergoes cyclization and forms cyclic radical **28** and then radical **28** is oxidized to cyclic carbocation **30**. Subsequent proton elimination produces compound **31**. According to Heiba and Dessau[16] $Mn(OAc)_3$ reactions follow route **A**. According to Fristad and Peterson[18] $Mn(OAc)_3$ reactions follow route **B**.



Scheme 9

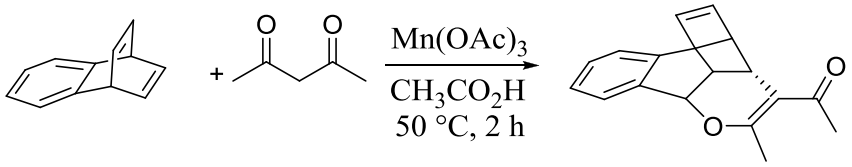
In order to finalize the confliction in the literature and enlighten the reaction mechanism, intermediates **32** and **33** are incorporated to the benzobarrelene system by Balci *et al.*[19]



32 **33**

It is well known that the radicals, which are formed at bicyclic systems, for example, benzobarrelene, do not have a tendency for rearrangement.[20] Therefore, it is expected that radical **32** cannot undergo rearrangement. On the other hand carbocations, which are formed at bicyclic systems can undergo rearrangement.[21] Therefore, carbocation **33** can undergo rearrangement and form a nonclassical carbocation.

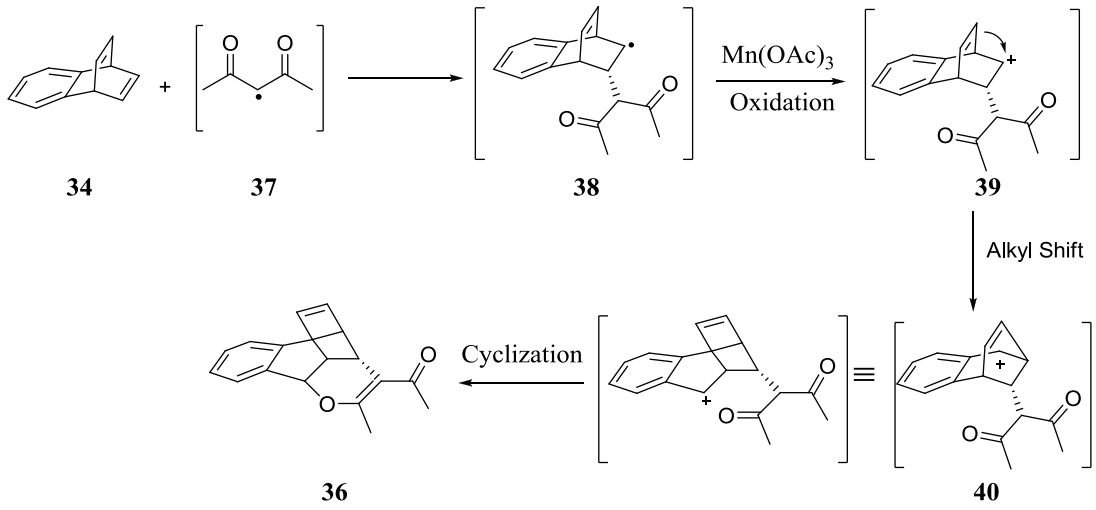
In the experimental study which is reported by Balci *et al*.[19] benzobarrelene (**34**) was reacted with acetylacetone (**35**) (Scheme 10).



34 **35** **36**

Scheme 10

At the end of the reaction, the formation of rearranged compound **36** was observed. Formation mechanism of compound **36** is shown in Scheme 11.[19]

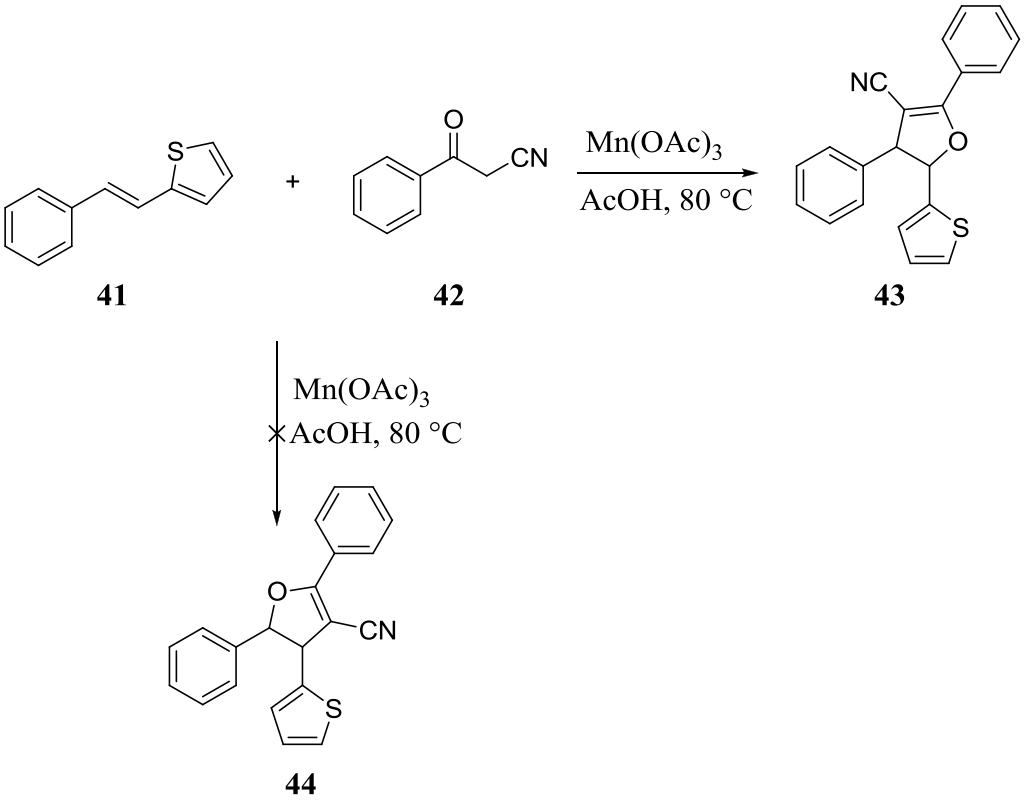


Scheme 11

Firstly, addition of acetylacetone radical to benzobarrelene results in the formation of radical **38**. In the presence of $Mn(OAc)_3$, radical **38** is oxidized to carbocation **39**. Wagner-Meerwein type rearrangement of carbocation **39** yields the formation of carbocation **40**. Subsequent cyclization of carbocation **40** generates the rearranged product compound **36**. Finally, it was proven that during $Mn(OAc)_3$ reactions cyclization occurs mainly after the oxidation of initially formed radical.

1.5 Aim of the thesis

Recently, Yilmaz *et al.*[22] reacted (*E*)-2-styrylthiophene (**41**) with 3-oxo-3-phenyl-propanenitrile (**42**) in the presence of $Mn(OAc)_3$ (Scheme 12). They proposed that only compound **43** was formed and any trace amount of compound **44** was not observed. Furthermore, they did not report or could not determine the exact configuration of the substituents attached to the dihydrofuran ring.

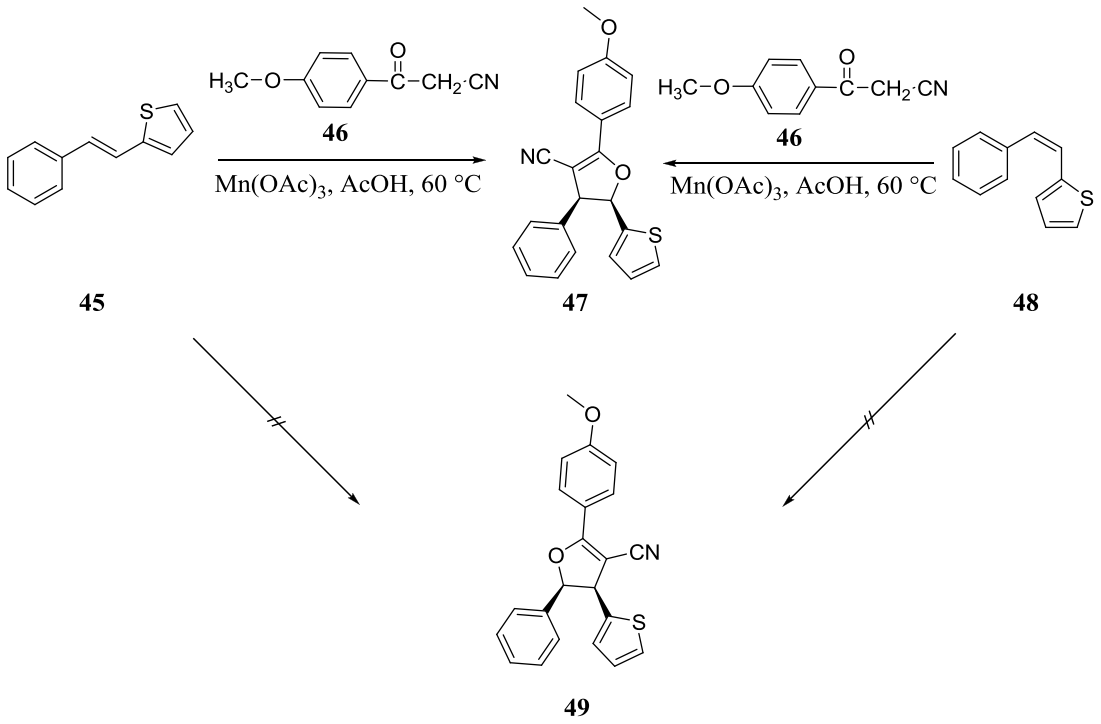


Scheme 12

Balci *et al.*[23] repeated this reaction as described by authors. They isolated a single product, compound **47** (Scheme 13).

Extensive NOE and 2D-NMR spectral measurements (COSY, HSQC and HMBC) revealed the constitution of the substituents attached to dihydrofuran ring as well as the configuration of the substituents. The structure **47** was assigned to the formed product.

Since thiophene electronically behaves like a benzene it was difficult to understand the exclusive formation of a single isomer **47**. Therefore, we were puzzled why **49** was not formed.



Scheme 13

The aim of this study was to reveal the reason and the mechanism for the formation of exclusively one regioisomer in the reaction of (*E*)-2-styrylthiophene (**45**) and (*Z*)-2-styrylthiophene (**48**) with compound **46** in the presence of $Mn(OAc)_3$ and enlighten the reaction mechanism by applying the same reaction to similar systems.

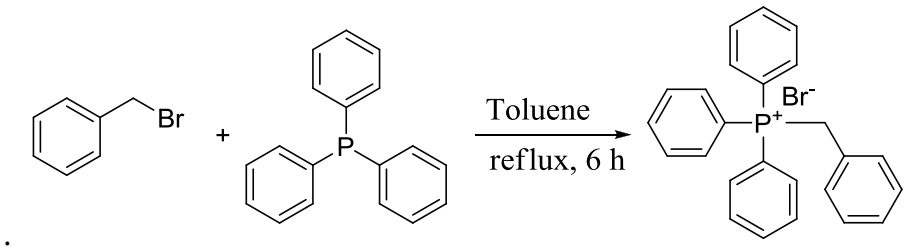
CHAPTER 2

RESULTS AND DISCUSSION

2.1 Reactions of 2-[(*E*)-2-phenylethenyl]thiophen & 2-[(*Z*)-2-phenylethenyl]-thiophen with $Mn(OAc)_3$

2.1.1 Synthesis of Benzyltriphenylphosphonium bromide

For the synthesis of starting alkenes **54** and **55**, it was started with the synthesis of benzyltriphenylphosphoniumbromide (**52**) according to a literature method.[24] Reaction of benzylbromide (**50**) and triphenylphosphine (**51**) in toluene gave starting material **52** in 96% yield (Scheme 14).



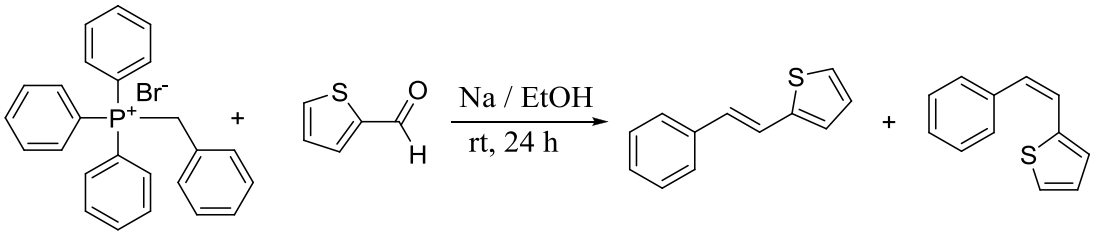
50 **51** **52** (96%)

Scheme 14

Characterization of compound **52** was done by using the NMR spectra. In ^{1}H NMR spectrum, methylene protons resonate at 5.79 ppm as a doublet. These protons couples with neighbour P atom and the coupling constant is J = 13.3 Hz.

2.1.2 Synthesis of 2-[(*E*)-2-phenylethenyl]thiophen & 2-[(*Z*)-2-phenylethenyl]-thiophen

After the synthesis of compound **52**, the synthesis of 2-[(*E*)-2-phenylethenyl]-thiophen (**54**) and 2-[(*Z*)-2-phenylethenyl]thiophen (**55**) were undertaken for future purposes. For this reason, Wittig reaction was performed by reacting thiophene-2-carbaldehyde (**53**) with benzyltriphenylphosphonium bromide (**52**) in Na/EtOH .[23] At the end of the reaction 2-[(*E*)-2-phenylethenyl]thiophen (**54**) and 2-[(*Z*)-2-phenylethenyl]thiophen (**55**) were obtained in yields of 51% and 38%, respectively (Scheme 15).



52 **53** **54** (51%) **55** (38%)

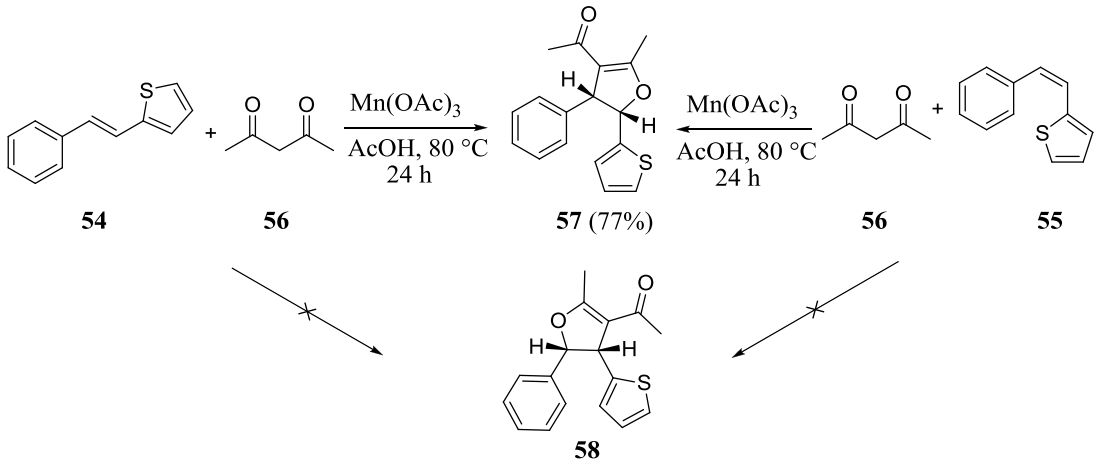
Scheme 15

To confirm the structures, ^{1}H-NMR and ^{13}C-NMR spectra were used. In the ^{1}H-NMR spectrum of compoud **54**, one of the olefinic proton resonates at 6.84 ppm as a doublet and the coupling constant is J = 16.1 Hz, which is in aggreement with the *trans* configuration. In the ^{1}H-NMR spectrum of compoud **55**, olefinic protons resonate at 6.61 and 6.48 ppm as an AB system and the coupling constant between the relevant proton is J = 12.0 Hz, which is in aggreement with the *cis* configuration

2.1.3 Cyclization of 2-[(*E*)-2-phenylethenyl]thiophen & 2-[(*Z*)-2-phenylethenyl]-thiophen

In order to enlighten the reaction mechanism, 2-[(*E*)-2-phenylethenyl]thiophen (**54**) and 2-[(*Z*)-2-phenylethenyl]thiophen (**55**) were reacted seperately with acetylacetone

(**56**) in the presence of $Mn(OAc)_3$ in acetic acid at 80 °C.[23] Both reactions gave only 1-(2-methyl-4-phenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl)ethanone (**57**) with the *cis* configuration in a yield of 77% (Scheme 16).



Scheme 16

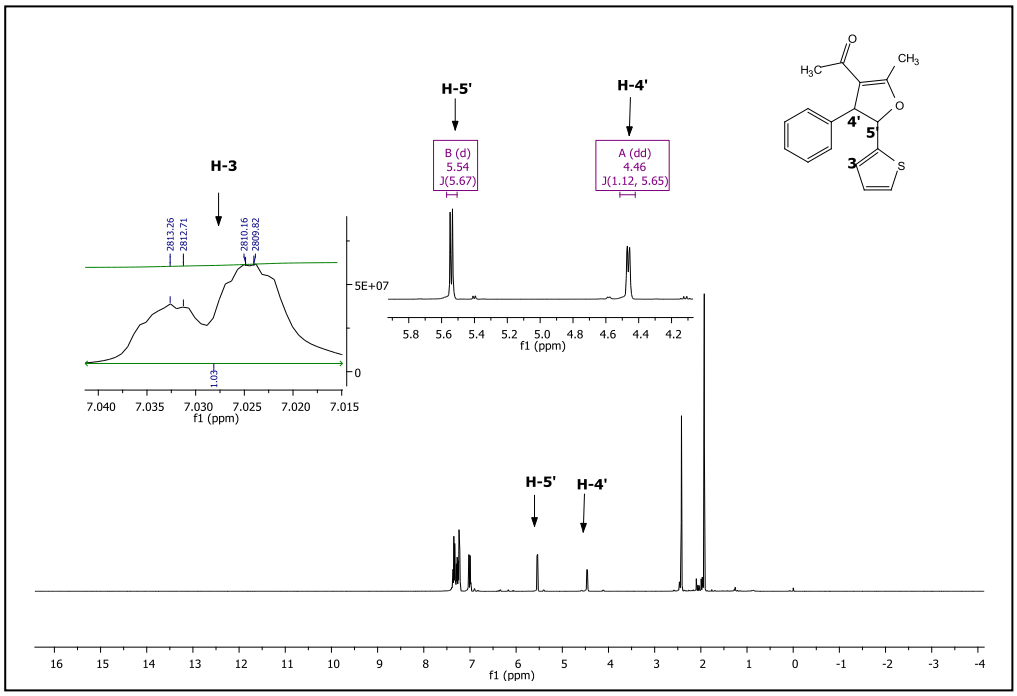


Figure 1 ^{1}H-NMR spectrum of compound **57**

The structure of compound **57** was determined by 1D and 2D spectral data. In the ^{1}H-NMR spectrum, the proton H-3 resonates at 7.03 ppm as doublet of doublets with coupling constants of J = 3.5 Hz and J = 0.5 Hz (Figure 1). The proton H-5' resonates at 5.54 ppm as a doublet, whereas the H-4' appears at 4.46 ppm as a doublet of doublets (Figure 1).

By using HSQC spectrum C-5' and C-4' carbon atoms were found (Figure 2).

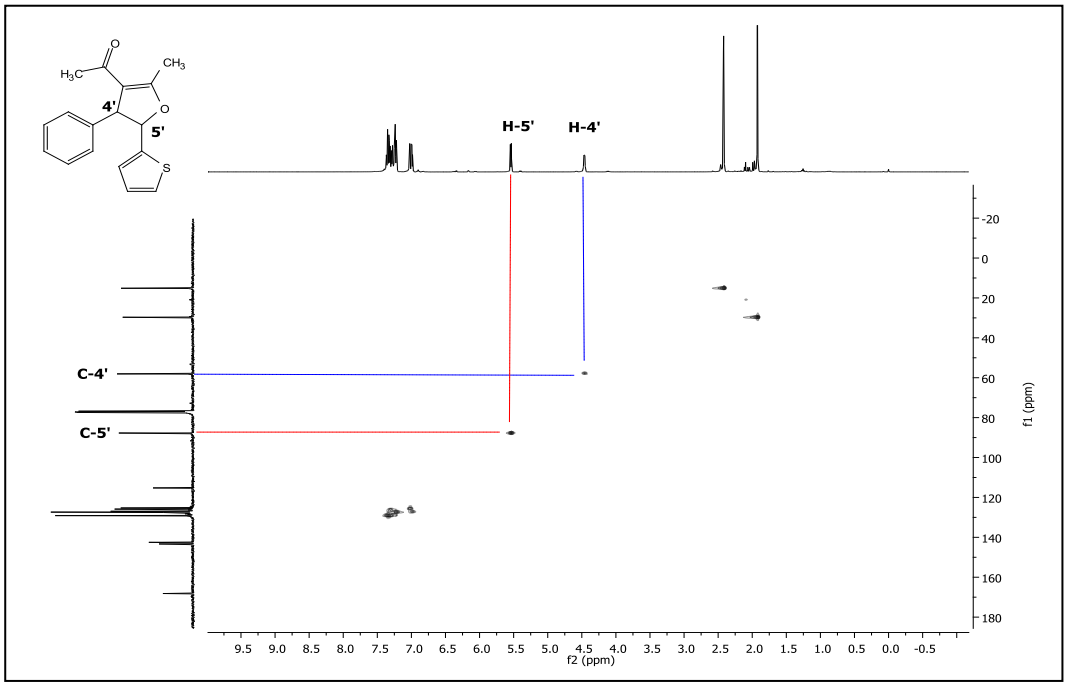


Figure 2 HSQC spectrum of compound **57**

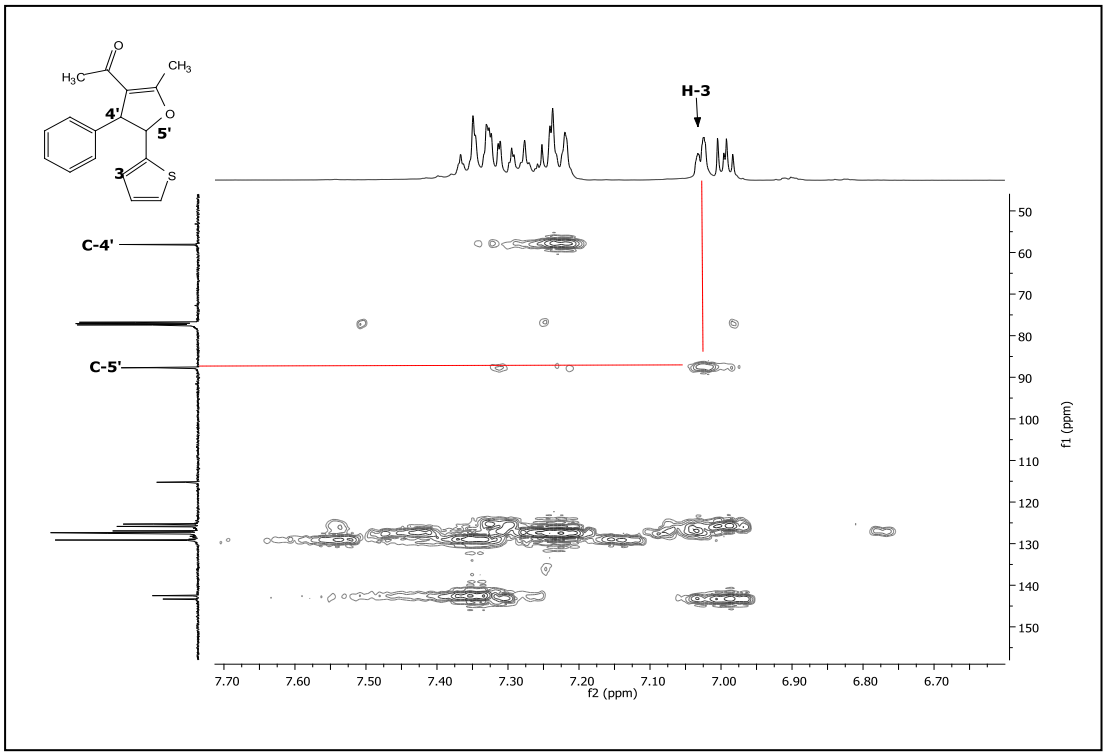
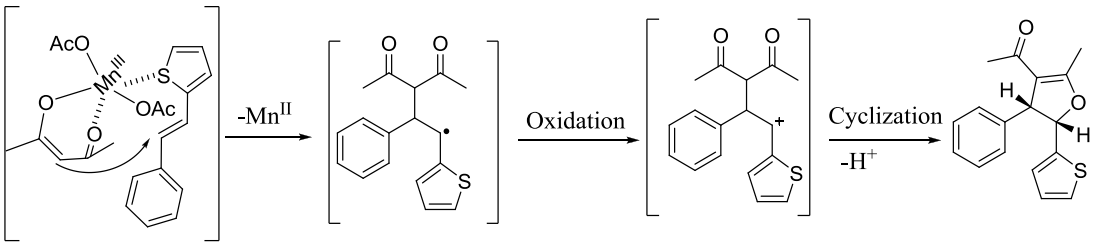


Figure 3 HMBC spectrum of compound **57**

The HMBC spectrum confirms the proposed structure without a question. The important part in the HMBC spectrum is the correlation between H-3 proton and C-5' carbon (Figure 3).

The formation of the regioisomer **58** was also expected. Examination of the reaction mixture did not indicate the formation of compound **58**. Balcı *et al.*[23] proposed the following reaction mechanism for similar reactions. According to this mechanism, first a complex **59** is formed between $Mn(OAc)_3$, alkene and acetylacetone (**56**) where sulfur atom of thiophene also undergoes an electronic interaction with the Mn atom of the $Mn(OAc)_3$. Then electron transfer from alkene to the Mn atom of the $Mn(OAc)_3$ occurs and carbon-carbon bond forms between the active carbon atom in acetylacetone and the olefinic carbon atom which is close to the benzene ring. Formation of carbon-carbon bond between the carbon atom which is close to the thiophene ring is hindered because of geometrical restrictions. After the formation of C-C bond, radical **60** is generated. Subsequent oxidation of radical **60** with $Mn(OAc)_3$, leads to the formation of carbocation **61**, which undergoes intramolecular cyclization reaction to give **57**. According to these mechanism, the position of the sulfur atom in the starting alkene affects the reaction mechanism and responsible for exclusive formation of final product **57** with the formation of complex **59** (Scheme 17).



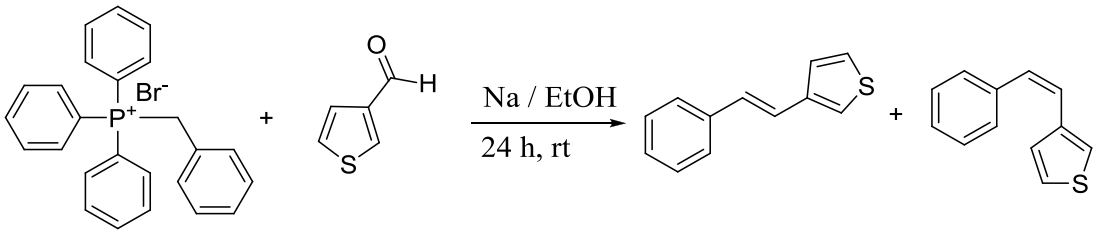
59 **60** **61** **57**

Scheme 17

2.2 Reactions of of 3-[(*E*)-2-phenylethenyl]thiophene & 3-[(*Z*)-2-phenylethenyl]-thiophene with $Mn(OAc)_3$

2.2.1 Synthesis of 3-[(*E*)-2-phenylethenyl]thiophene & 3-[(*Z*)-2-phenylethenyl]-thiophene

To strengthen the proposed mechanism, which indicates the importance of the position of the sulfur atom, position of the sulfur atom in the starting alkene was changed. For this purpose, we decided to synthesize the 3[(*E*)-2-phenylethenyl] thiophene (**63**) and 3[(*Z*)-2-phenylethenyl] thiophene (**64**) where the thiophen ring is bonded to the alkene at C-3 carbon atom of the thiophene ring. The target molecules were synthesized by reacting benzyltriphenylphosphonium bromide (**52**) and thiophene-3-carbaldehyde (**62**) in Na/EtOH.[25] 3-[(*E*)-2-phenylethenyl]thiophen (**63**) and 3-[(*Z*)-2-phenylethenyl] thiophen (**64**) were obtained in yields of 54% and 43%, respectively (Scheme 18).



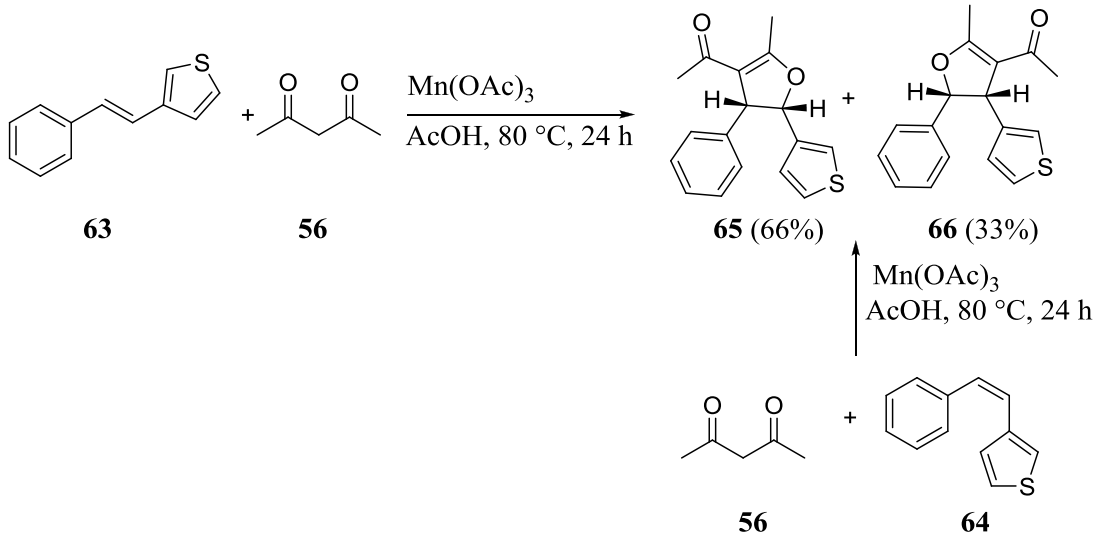
52 **62** **63** (54%) **64** (43%)

Scheme 18

In the ^{1}H-NMR spectrum of compoud **63** olefinic protons resonate at 7.12 and 6.94 ppm as an AB system with a coupling constant of J = 16.3 Hz, indicating the *trans* configuration of coupling product **63**. The olefinic protons in compoud **64** resonate at 6.57 and 6.53 ppm as an AB system with a coupling constant of J = 12.1 Hz, coupling constant clearly shows the *cis* configuration of coupling product **64**.

2.2.2 Cyclization Reactions of 3-[(*E*)-2-phenylethenyl]thiophene and 3-[(*Z*)-2-phenyl-ethenyl]thiophene

To observe the regioselectivity of the reaction when the position of the sulfur atom is moved to the third position, compounds **63** and compound **64** were reacted with acetylacetone (**56**) seperately in the presence of $Mn(OAc)_3$ in AcOH at 80 °C for 24 h. The formation of two regioisomeric cyclization products with *cis* configuration was observed (Scheme 19).



63 **56** **65** (66%) **66** (33%) **56** **64**

Scheme 19

The structures of compounds **65** and **66** were again determined by 1D and 2D spectral data. In the ^{1}H-NMR spectrum of compound **65** H-4' and H-5' resonate at 5.41 ppm and 4.34 ppm, respectively. Also H-4 proton resonates at 7.07 ppm as doublet of doublets with a coupling constants of J = 5.0 Hz and J = 1.2 Hz (Figure 4).

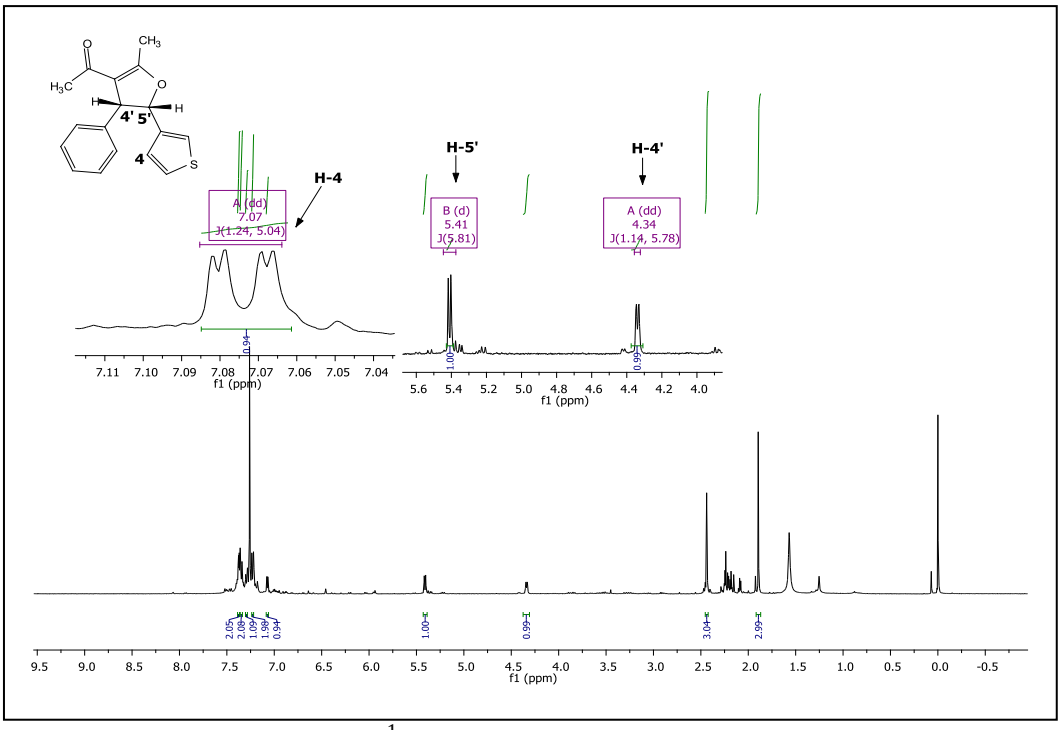


Figure 4 ^{1}H-NMR spectrum of compound **65**

First, we assigned the carbon resonances by using HSQC spectrum (Figure 5).

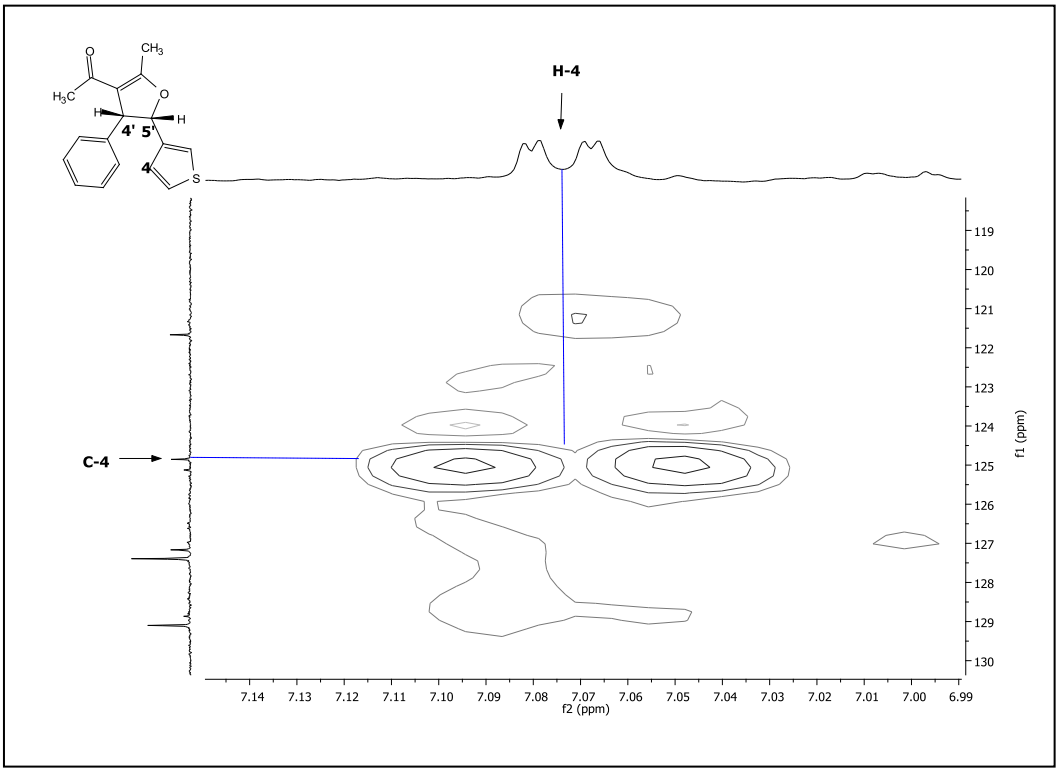


Figure 5 HSQC spectrum of compound **65**

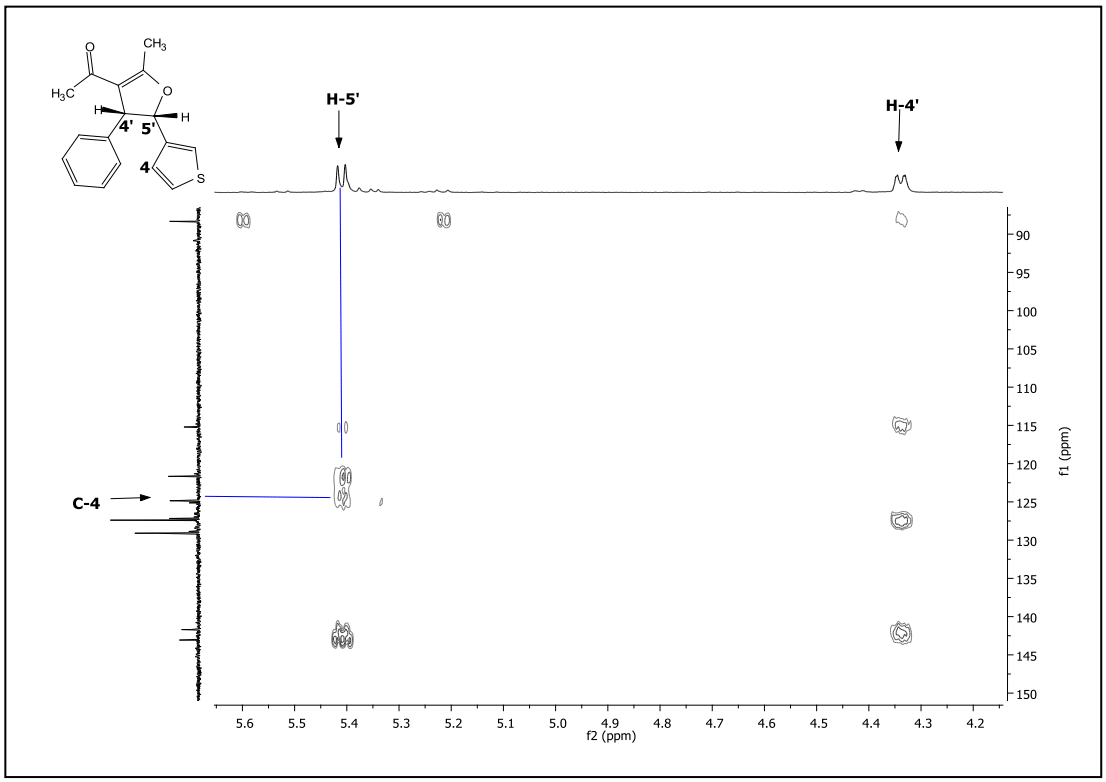
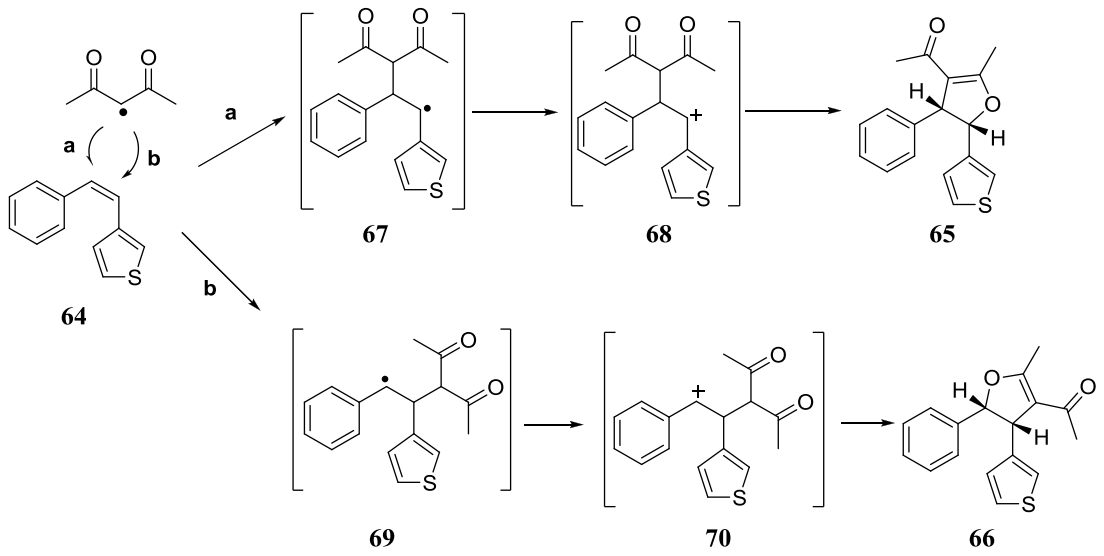


Figure 6 HMBC spectrum of compound **65**

With the help of HMBC spectrum we were able to distinguish between those isomers **65** and **66**. The important part in the HMBC spectrum was the correlation between H-5' proton and C-4 carbon of the thiophen ring. This correlation clearly shows that thiophene ring is bonded to the dihydrofuran ring from the same carbon atom as the oxygen functionality (Figure 6).

In this case, the position of the sulfur atom was changed by moving the sulfur atom to the 3rd position. We assume that sulfur atom of the thiophene ring also forms a complex here. However, due to the large distance between the complex and double bond and geometrical reasons, this complex can not be responsible for the reaction. The sulfur atom doesn't have any directing effect in this case, so that a free diacetyl radical is acting as a reagent. Therefore, the radical can add to the both side of the double bond carbon atoms. As a result of the addition of radical to the both side of the double bond carbon atoms, compound **65** and compound **66** are formed in a ratio of 2:1 (Scheme 20).

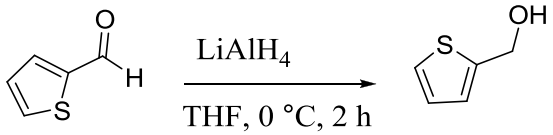


Scheme 20

2.3 Reactions of (*E*)-2-(2-(thiophen-3-yl)vinylthiophen & (*Z*)-2-(2-(thiophen-3-yl)vinylthiophen with $Mn(OAc)_3$

2.3.1 Synthesis of Thiophen-2-ylmethanol

After observing the formation of a single cyclization product **57**, by the reaction of compound **54** and compound **55** with $Mn(OAc)_3$ in presence of a 1,3-dicarbonyl compound, the formation of two cyclization products, compound **65** and compound **66** were observed upon moving the sulfur atom of the thiophene ring from second to the third position. After these results, we planned to synthesize an alkene that have two thiophene rings connected to the alkene moeity one at the C-2 and the other one at the C-3 carbon atoms. For the synthesis of the target molecule, we started with the synthesis of thiophene-2-ylmethanol (**71**) according to a literature method. Reduction of thiophen-2-carbaldehyde (**53**) with $LiAlH_4$ gave thiophene-2-ylmethanol (**71**) (Scheme 21).[26]



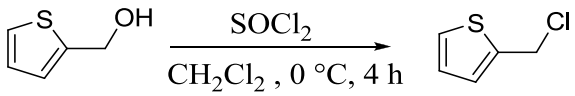
53 **71** (91%)

Scheme 21

The presence of broad signal (OH) at 3.66 ppm in ^{1}H-NMR spectrum and the disappearance of the aldehyde proton signal, proved the structure.

2.3.2 Chlorination of Thiophen-2-ylmethanol

To replace –OH group with –Cl atom, chlorination reaction was performed according to a literature method.[27] Thiophen-2-ylmethanol (**71**) was reacted with $SOCl_2$, 2-(chloromethyl)thiophene (**72**) was formed in 95% yield (Scheme 22).



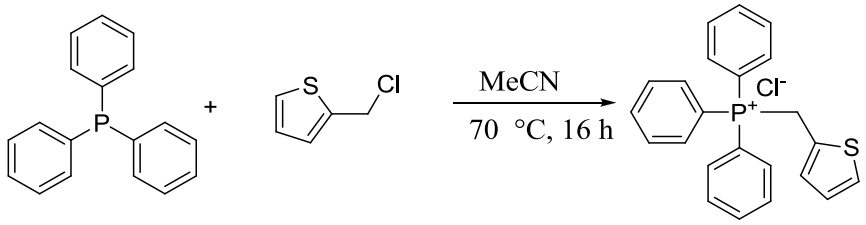
71 **72** (95%)

Scheme 22

Characterization of compound **72** was done with the help of the ^{1}H-NMR spectrum. The disappearance of broad –OH proton signal which resonates at 3.66 ppm and the presence of methylene protons signal at 4.70 ppm proved the structure of compound **72**.

2.3.3 Synthesis of Wittig Salt

To synthesize target salt **73**, 2-(chloromethyl)thiophene (**72**) was reacted with triphenylphosphine (**51**) in acetonitrile, triphenyl(thiophene-2-yl methyl) phosphonium chloride (**73**) was formed in 88% yield (Scheme 23).[28]



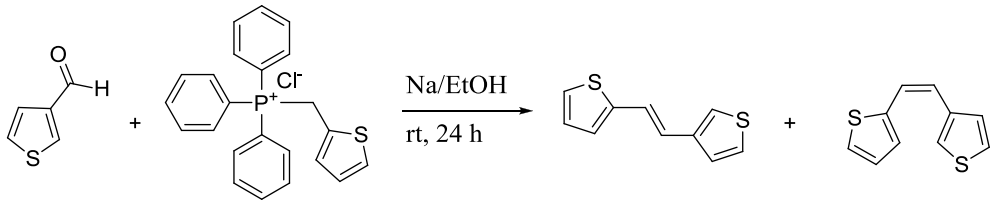
51 **72** **73**(88%)

Scheme 23

Characterization of compound **73** was established by using the ^{1}H-NMR spectrum. The methylene protons resonate at 5.79 ppm as doublet due to the coupling with neighbour phosphorous atom and the coupling constant is J = 13.3 Hz.

2.3.4 Synthesis of (*E*)-2-(2-(thiophen-3-yl)vinylthiophen & (*Z*)-2-(2-(thiophen-3-yl)vinyl-thiophen

After successful synthesis of the starting material **73**, thiophene-3-carbaldehyde (**62**) was reacted with triphenyl(thiophen-2-yl methyl)phosphonium chloride (**73**) in the presence of Na/EtOH. (*E*)-2-(2-(thiophen-3-yl)vinylthiophen (**74**) and (*Z*)-2-(2-(thiophen-3-yl)vinylthiophen (**75**) were formed in 55.5% and 30% yields, respectively (Scheme 24).



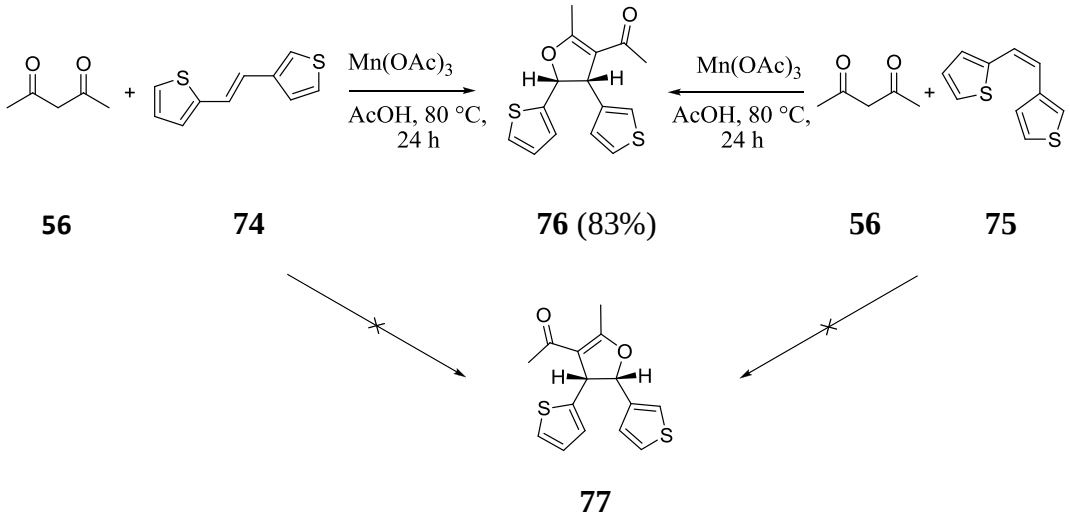
62 **73** **74** (55.5%) **75** (30%)

Scheme 24

In the ^{1}H-NMR spectrum of compound **74**, the presence of an AB system which appears at 7.01 and 6.87 ppm with a coupling constant of J = 16.1 Hz, indicates the *trans* configuration for compound **74**. In the ^{1}H-NMR spectrum of compound **75**, the presence of an AB system resonating at 6.55 and 6.37 ppm with a coupling constant of J = 11.9 Hz, is consistent with the *cis* configuration of compound **75**.

2.3.5 Cyclization Reactions of (*E*)-2-(2-(thiophen-3-yl)vinylthiophen and (*Z*)-2-(2-(thiophen-3-yl)vinyl-thiophen

(*E*)-2-(2-(thiophene-3-yl)vinylthiophene (**74**) and (*Z*)-2-(2-(thiophene-3-yl)vinyl thiophene (**75**) were seperately reacted with acetylacetone (**56**) in presence of $Mn(OAc)_3$. Analysis of the reaction mixture revealed the exclusive formation of a single product, 1-(2-methyl-5-(thiophen-2-yl)-4-(thiophen-3-yl)-4,5-dihyrofuran-3-yl)-ethanone (**76**), Careful analysis did not show the formation of any trace amount of isomer **77** (Scheme 25).



56 **74** **76** (83%) **56** **75**

77

Scheme 25

In ^{1}H-NMR spectrum of compound **76**, proton H-2 proton resonates at 6.41 ppm as doublet of doublets with the coupling constants of J = 2.9 Hz and J = 1.2 Hz which are characteristic thiophene couplings (Figure 7).

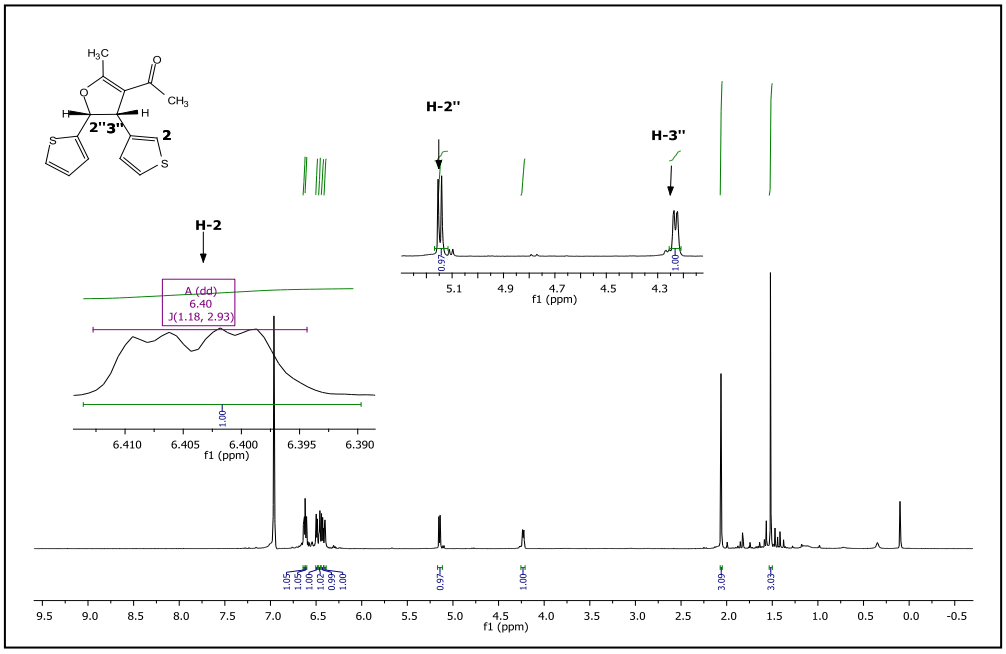


Figure 7 ^{1}H-NMR spectrum of compound **76**

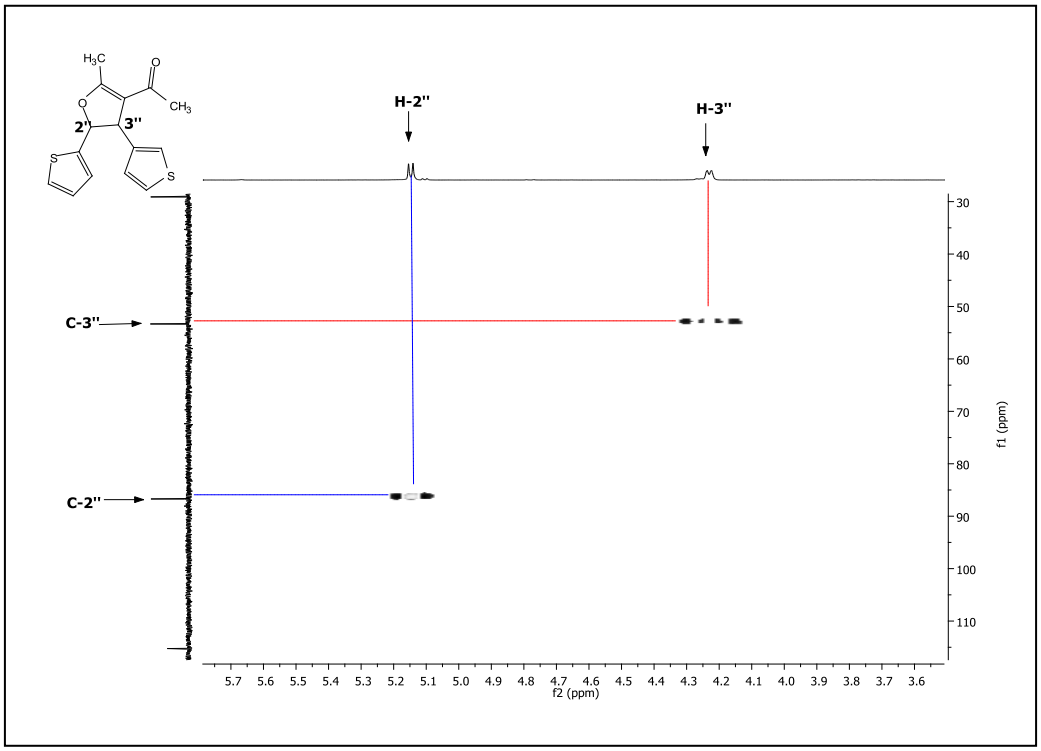


Figure 8 HSQC spectrum of compound **76**

By using HSQC spectrum C-2" and C-3" carbons were found (Figure 8).

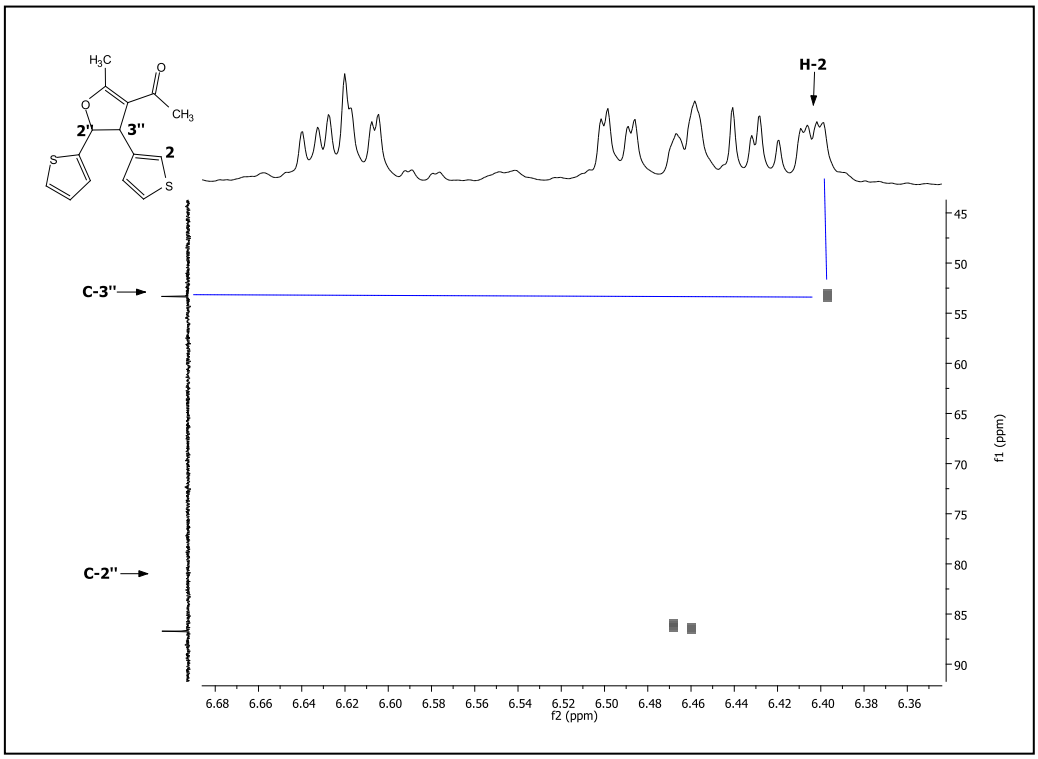
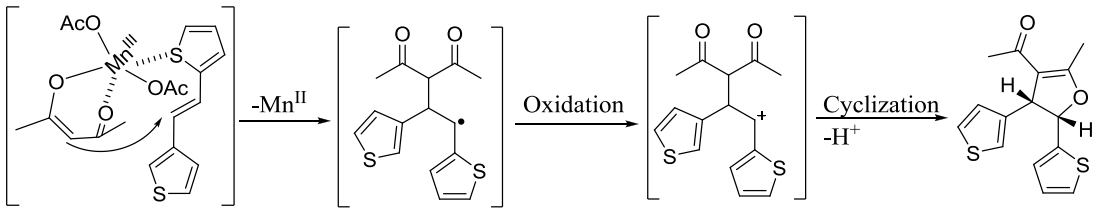


Figure 9 HMBC spectrum of compound **76**

With the help of the HMBC spectrum we were able to prove the structure of compound **76**. The important part in the spectrum was again the correlation between H-2 proton and C-3" carbon (Figure 9).

Exclusive formation of a single cyclization product **76** confirmed the proposed mechanism. (The starting alkenes **74** and **75** contain two thiophene rings attached from the different carbon atoms (C-2 and C-3) to the C=C double bond). The structure **76** shows that oxygen atom of the acetylacetone is bonded to the carbon atom which is connected to C-2 of thiophene ring (Scheme 26).



78 **79** **80** **76**

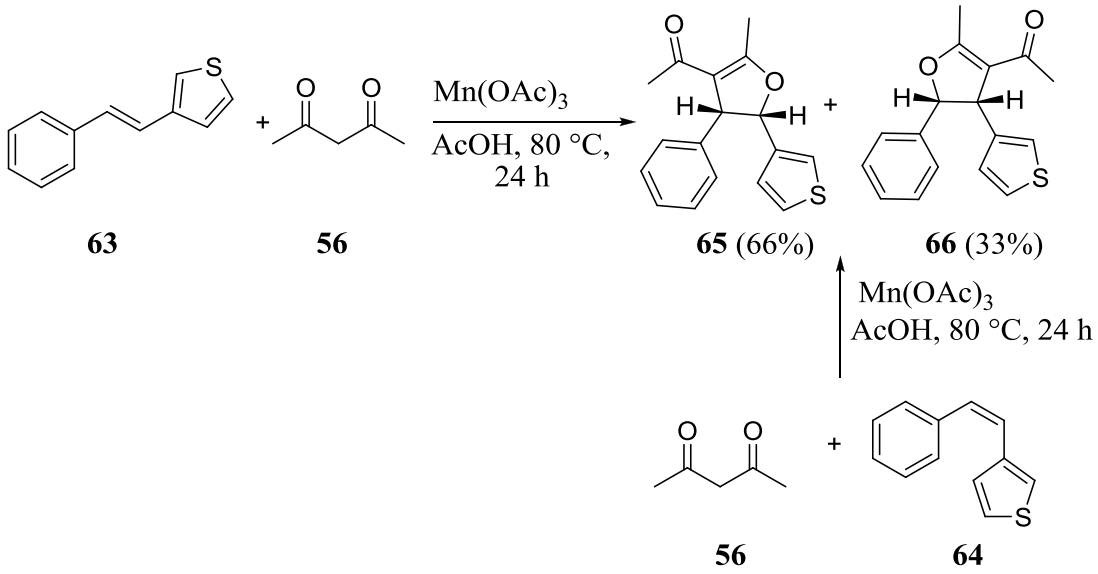
Scheme 26

All those results indicate that the position of sulfur atom, compared to the double

bond, plays an important role in determining the mode of the addition.

2.4 Theoretical Considerations

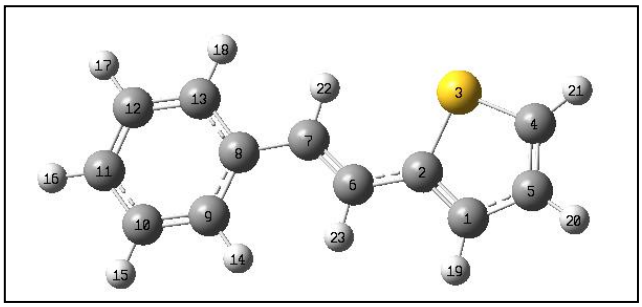
For the case in which the complex formation should not have any effect on the distribution of the adducts by changing the position of the sulfur atom (Scheme 27), the formation ratio of compounds **65** and compound **66** is 2:1. We assume that there can be some other factors that can affect the product distribution. To answer this question some theoretical calculations were done.

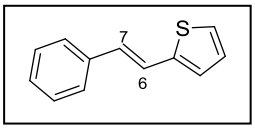


Scheme 27

The starting alkenes were optimized by using Gaussian 09L[29] programme and the optimizations were done at the level of M06 / TZVP.

It was thought that the electron densities on the olefinic carbon atoms can affect the final product distribution. For this reason natural bond orbital (NBO) analysis were carried out at the level of M06 / TZVP.

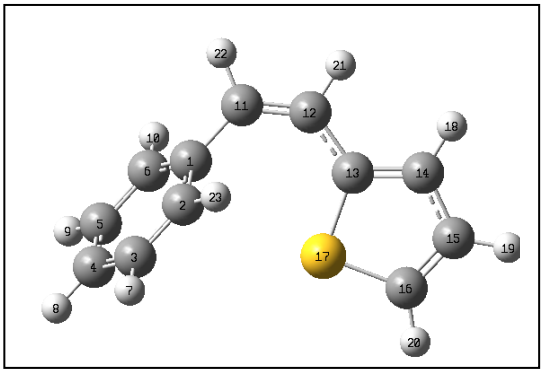


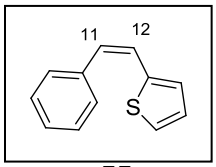


54

Figure 10 The optimized geometry for compound **54**

According to theoretical calculations which is done for compound **54**, the natural charge on C-7 atom is -0.172 Coulomb and natural charge on C-6 atom is -0.188 Coulomb. In compound **54** electron density on C-6 atom is higher than the electron density on C-7 atom (Figure 10).



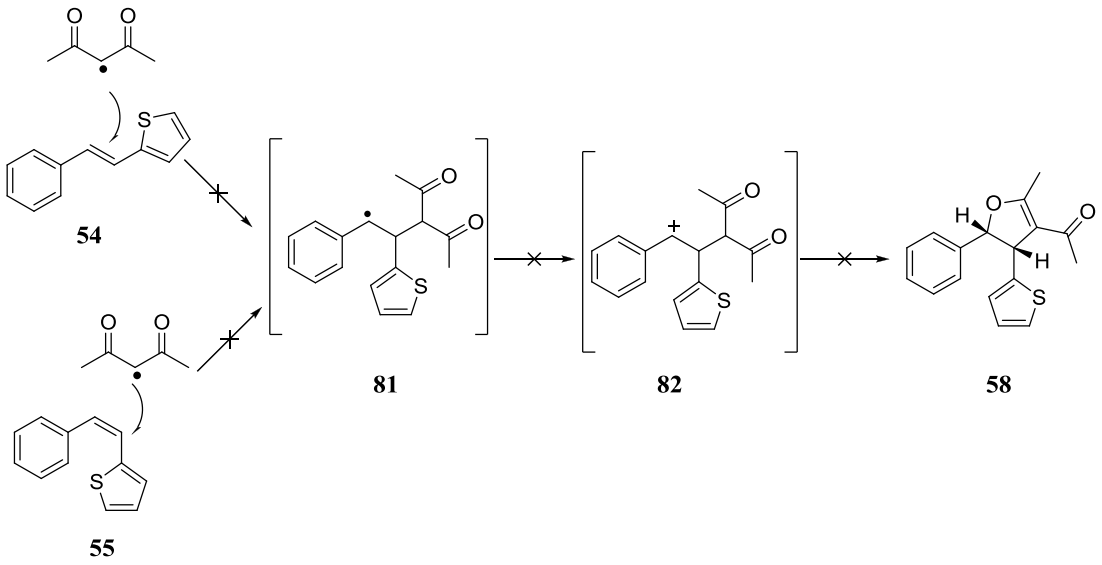


55

Figure 11 The optimized geometry for compound **55**

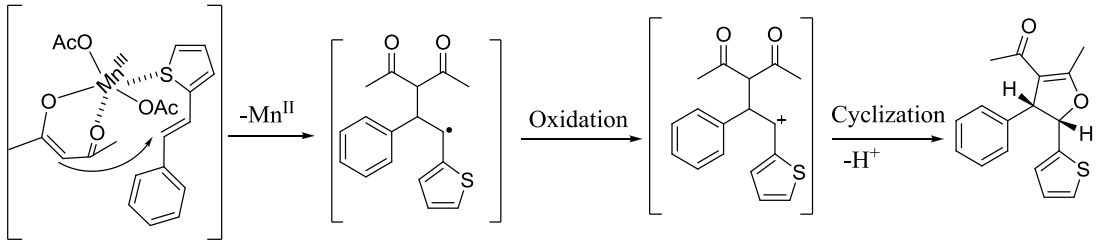
Natural charge on C-11 atom in compound **55** is -0.186 Coulomb; on the other hand natural charge on C-12 atom in compound **55** is -0.191 Coulomb. According to natural charge calculations it is obvious that the electron density on C-12 atom is higher than the electron density on C-11 atom (Figure 11).

On the basis of these theoretical calculations, we may propose that compound **58** should be formed as the major product with the addition of radical to the electron rich olefinic carbon atoms in both E and Z isomers (Scheme 28). However, no trace of compound **58** was not observed during experimental studies.



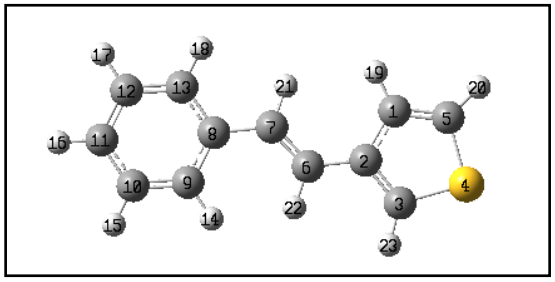
Scheme 28

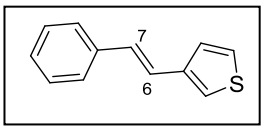
Formation of complex **59** explains the addition of radical to the electronically poor olefinic carbon atom and formation of compound **57** as a single product (Scheme 29).



Scheme 29

Natural bond orbital (NBO) analysis was carried out for compounds **63** and **64**

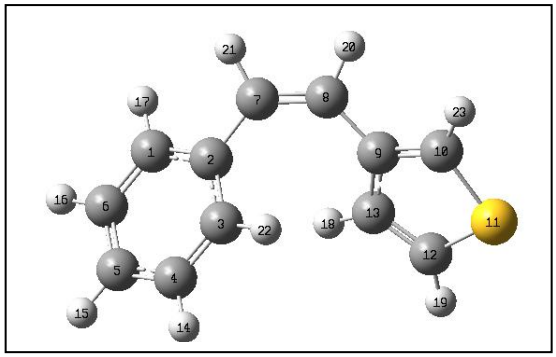


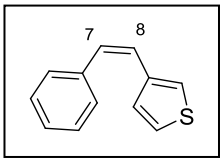


63

Figure 12 The optimized geometry of compound **63**

According to M06 / TZVP natural bond orbital (NBO) analysis; natural charge on the C-6 atom in compound **63** is –0.167 Coulomb; on the other hand, natural charge on the C-7 atom is -0.168 Coulomb. As a result, electron density on C-7 atom is more than the electron density on C-6 atom in compound **63** (Figure 12).



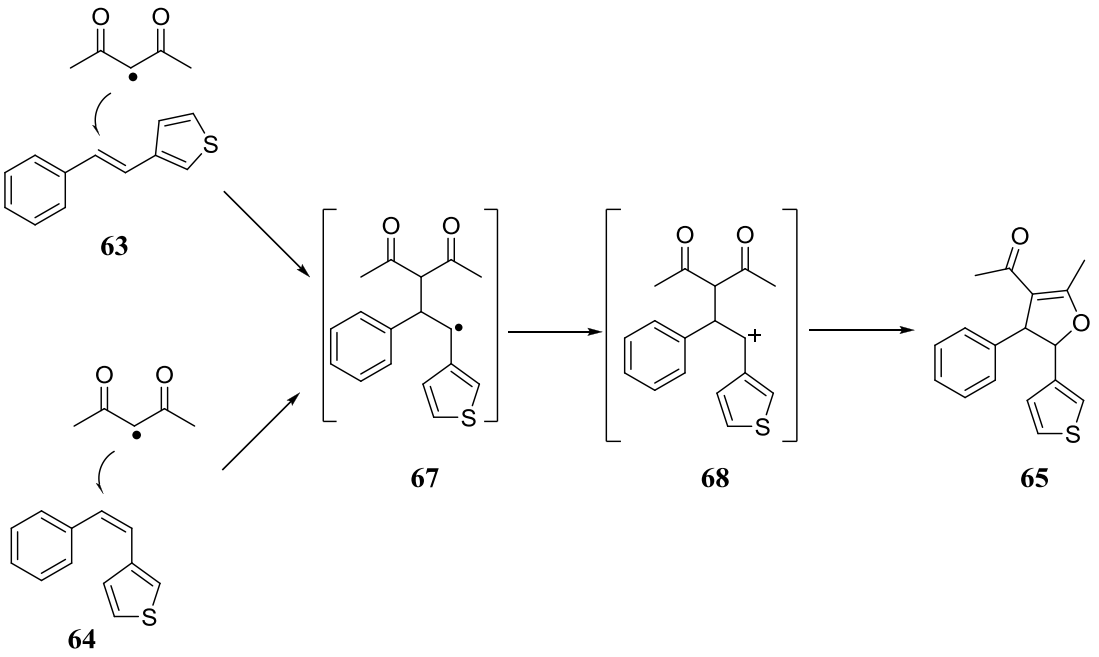


64

Figure 13 The optimized geometry for compound **64**

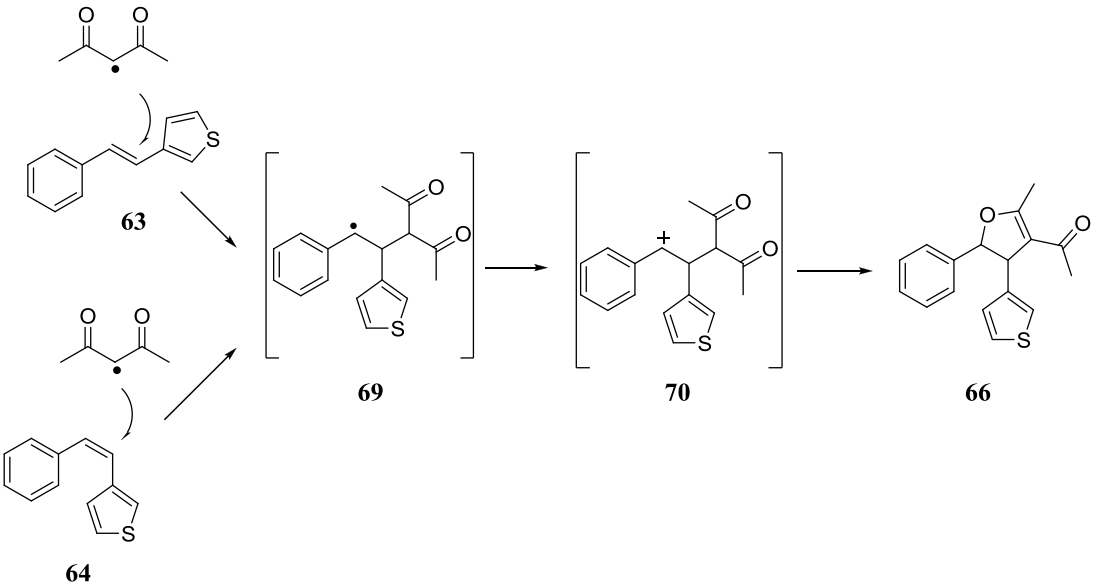
For the compound **64**, natural charge on the C-7 atom is -0.179 Coulomb and natural charge on the C-8 atom is -0.172 Coulomb. As a result, electron density on C-7 atom is higher than the electron density on the C-8 carbon atom in compound **64** (Figure 13).

According to the results of theoretical calculations, proposed mechanism for the formation of major product compound **65** is shown in Scheme 31. Compound **65** is formed as a result of the addition of radical to the electronically rich olefinic carbon atoms in both E and Z isomers.



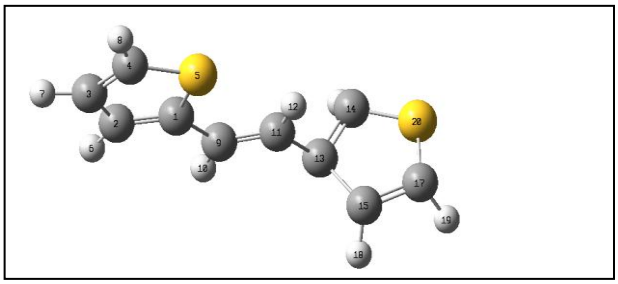
Scheme 30

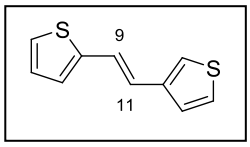
Compound **66** was formed as a minor product as a result of the adition of radical to the electronically poor olefinic carbon atoms in both E and Z isomers (Scheme 31).



Scheme 31

For the compounds **74** and **75** NBO analysis were carried out. According to the results of the compound **74** natural charge on C-11 carbon atom is -0.168 Coulomb and natural charge on C-9 carbon atom is -0.196 Coulomb. It is obvious that the electron density on C-9 carbon atom is higher than the electron density on C-11 carbon atom (Figure 14).

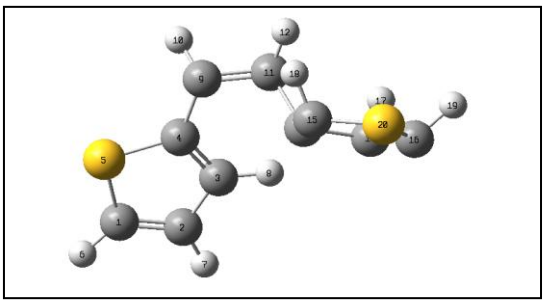


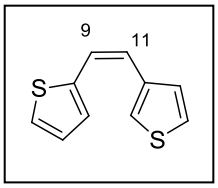


74

Figure 14 The optimized geometry for compound **74**

NBO analysis of compound **75** shows that the natural charge for the C-9 carbon atom is -0.188 Coulomb and for the C-11 carbon atom is -0.184 Coulomb. These calculations show that the electron density on the C-9 carbon atom is higher than the electron density on C-11 carbon atom (Figure 15).

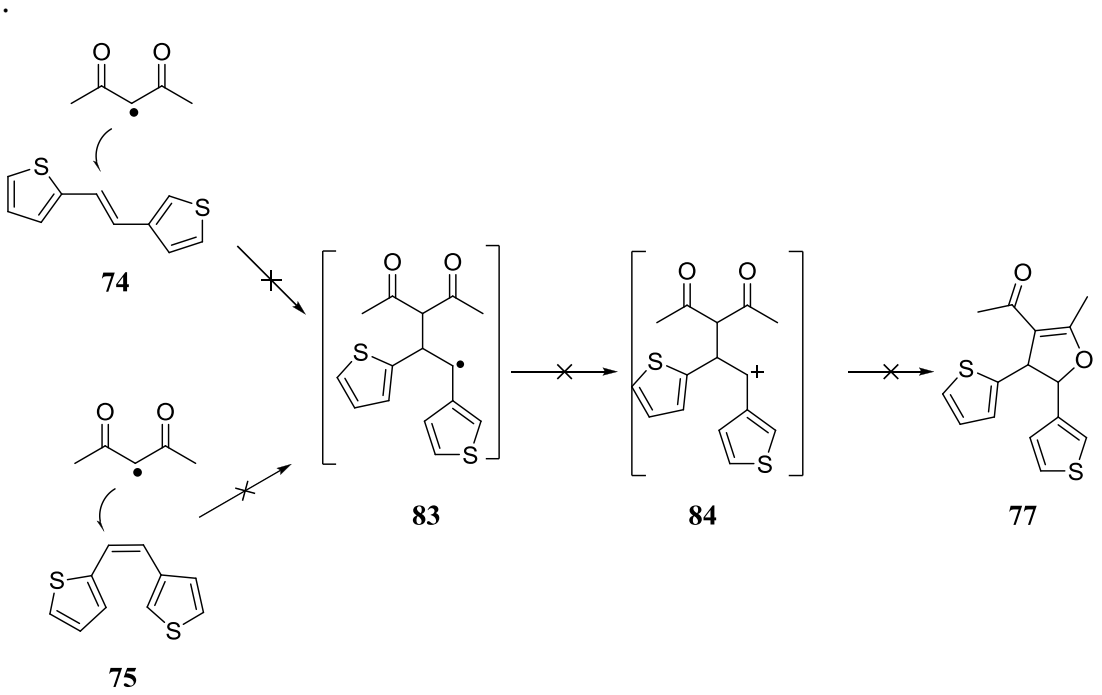




75

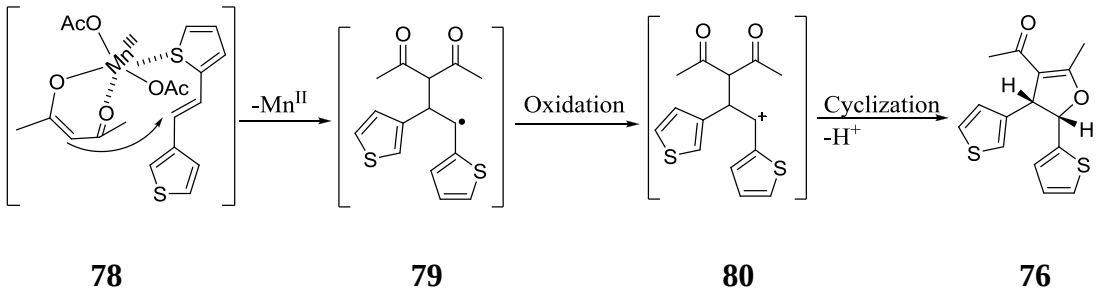
Figure 15 The optimized geometry for compound **75**

If we propose a mechanism according to the theoretical results, compound **77** should be formed as a major product. However, experimental results shows that no trace of compound **77** did not form during reaction (Scheme 32)



Scheme 32

For this reaction, again the complex formation is responsible for the formation of compound **76** as a single product (Scheme 33).



Scheme 33

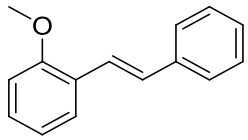
According to the experimental and theoretical results; for the cases in which the sulphur atom is close to the olefinic carbon atoms, formation of a complex such as **59** and **78** predominates and exclusively single cyclization products **57** or **76** are formed. For the cases in which the sulphur atom is not close to the olefinic carbon atoms, any complex formed can not be responsible for the addition because of the geometrical

reasons. In this case two cyclization products are formed and electronic effects determine the mode of the addition and the ratio of the product distribution.

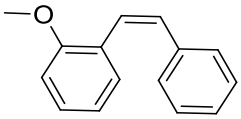
2.5 Reactions of (*E*)-1-methoxy-2-styrylbenzene and (*Z*)-1-methoxy-2-styryl benzene with $Mn(OAc)_3$

2.5.1 Synthesis of 2-methoxybenzaldehyde

To strengthen the proposed theory, which indicates the importance of a complex formation with the lone pair of sulfur atom and $Mn(OAc)_3$, we decided to synthesize stilbene derivatives having substituents in the ortho position of one of the benzene rings. Heteroatoms can also undergo interaction with $Mn(OAc)_3$ and determine the regioselectivity of the addition. Furthermore, we were interested in changing the electron density in one of the benzene rings in order to search whether the electron density at the double bond should have any effect on the mode of the addition reactions or not. First we introduced an electron donating methoxy group to the ortho position of one of the benzene ring in stilbene. For this purpose, we decided to synthesize (*E*)-1-methoxy-2-styrylbenzene (**88**) and (*Z*)-1-methoxy-2-styrylbenzene (**89**).

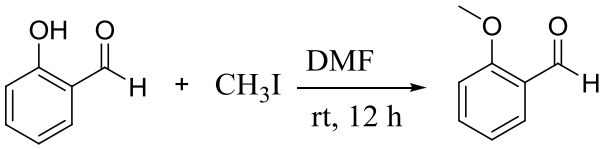


88



89

We started with the synthesis of 2-methoxybenzaldehyde (**87**). 2-Hydroxy benzaldehyde (**85**) was reacted with iodomethane (**86**) in DMF, at room temperature, for 12 h to obtain 2-methoxybenzaldehyde (**87**) (Scheme 34).[30]



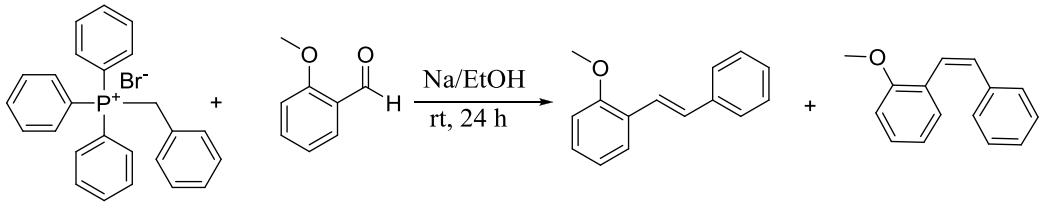
85 **86** **87** (97%)

Scheme 34

Disappearance of broad –OH proton signal and the presence of signal at 3.93 ppm, which belongs to methoxy protons, in the ^{1}H-NMR spectrum of compond **87** completely proves the structure.

2.5.2 Synthesis of (*E*)-1-methoxy-2-styrylbenzene and (*Z*)-1-methoxy-2-styryl benzene

(*E*)-1-methoxy-2-styrylbenzene (**88**) and (*Z*)-1-methoxy-2-styryl benzene (**89**) were synthesized by reacting 2-methoxybenzaldehyde (**87**) with benzyltriphenylphos phonium bromide (**52**) in Na/EtOH, at room temperature, for 24 hours (Scheme 35).[31]

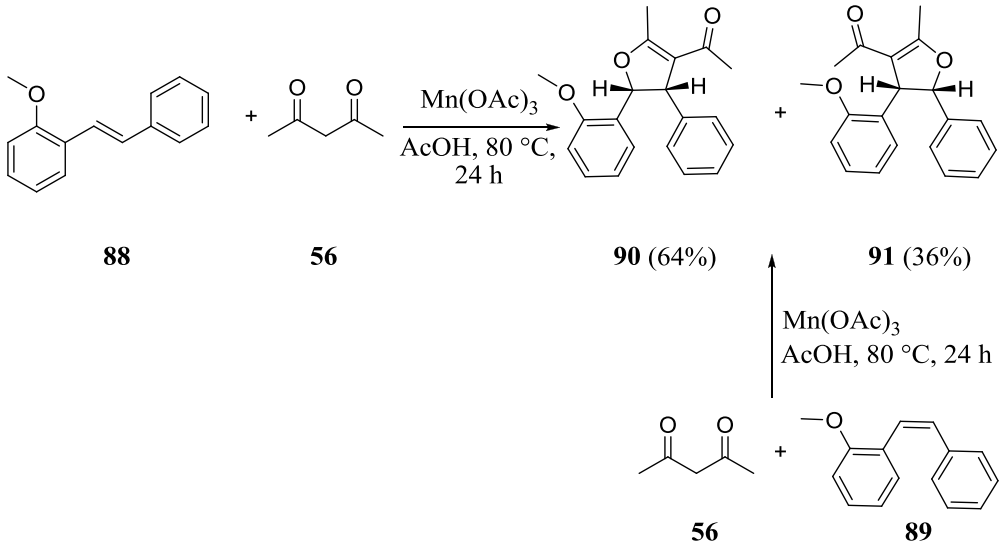


52 **87** **88** (49%) **89** (41%)

Scheme 35

In the ^{1}H-NMR spectrum of compound **88** olefinic protons resonate at 7.42 and 7.04 ppm as an AB system with a coupling constant of J = 16.5 Hz, indicating trans configuration of compound **88**. According to ^{1}H-NMR of compound **89** olefinic protons resonate at 6.62 and 6.56 ppm as an AB system with a coupling constant of J = 12.2 Hz, indicating the cis configuration of compound **89**.

2.5.3 Cyclization Reactions of (*E*)-1-methoxy-2-styrylbenzene and (*Z*)-1-methoxy-2-styryl benzene



Scheme 36

Compounds **88** and **89** were reacted with acetylacetone (**56**) seperately in presence of $Mn(OAc)_3$ in AcOH at 80 °C for 24 h. At the end of the reaction, the formation of two regioisomeric cyclization products **90** and **92** with cis configuration were obtained (Scheme 36).

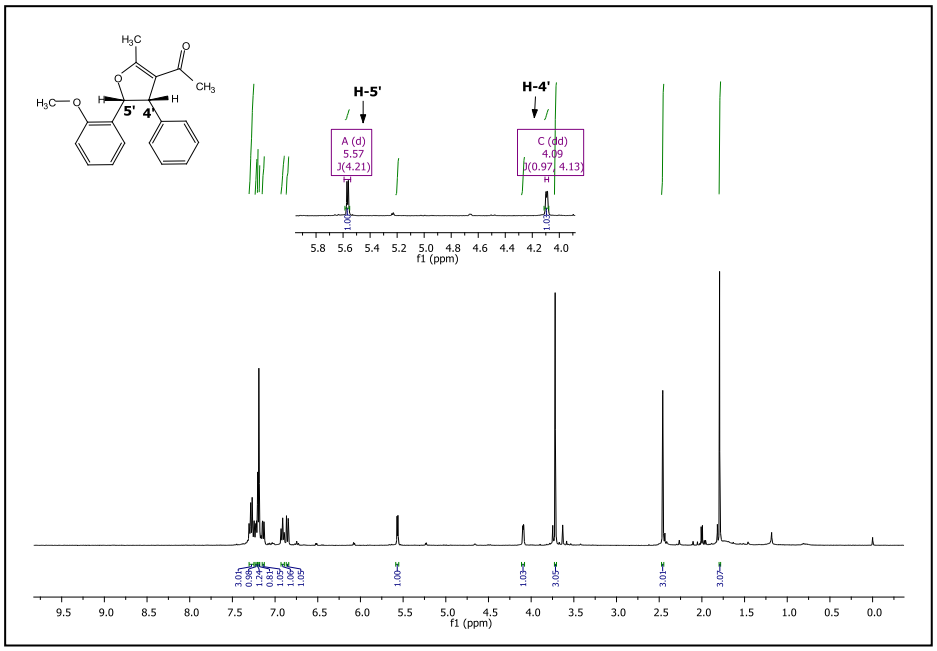


Figure 16 ^{1}H-NMR spectrum of compound **90**

In the ^{1}H-NMR spectrum of compound **90**, the protons H-5' and H-4' resonate at 5.57 and 4.09 ppm, respectively. The coupling constant observed between those protons is J = 4.2 Hz indicating the *cis* configuration of the substituents attached to the five membered ring in **90**. The methoxy protons resonate at 3.72 ppm as a singlet (Figure 16).

To determine the correct constitution of the isomers **90** and **91**, first we determined the exact resonance frequency of the C-2 carbon atom from the correlation between the –OCH_3 protons resonance and the C-2 carbon atom from the HMBC spectrum. Then we looked at the correlations between the C-2 carbon atom and proton resonances. Only the signal resonating at 5.57 ppm showed the correlation with the C-2 carbon atom not the signal appearing at 4.09 ppm. From this information we assigned the correct structure to **90** (Figure 17). In the case of minor isomer **91**, the C-2 carbon atom showed only correlation with H-4' proton not with H-5' proton.

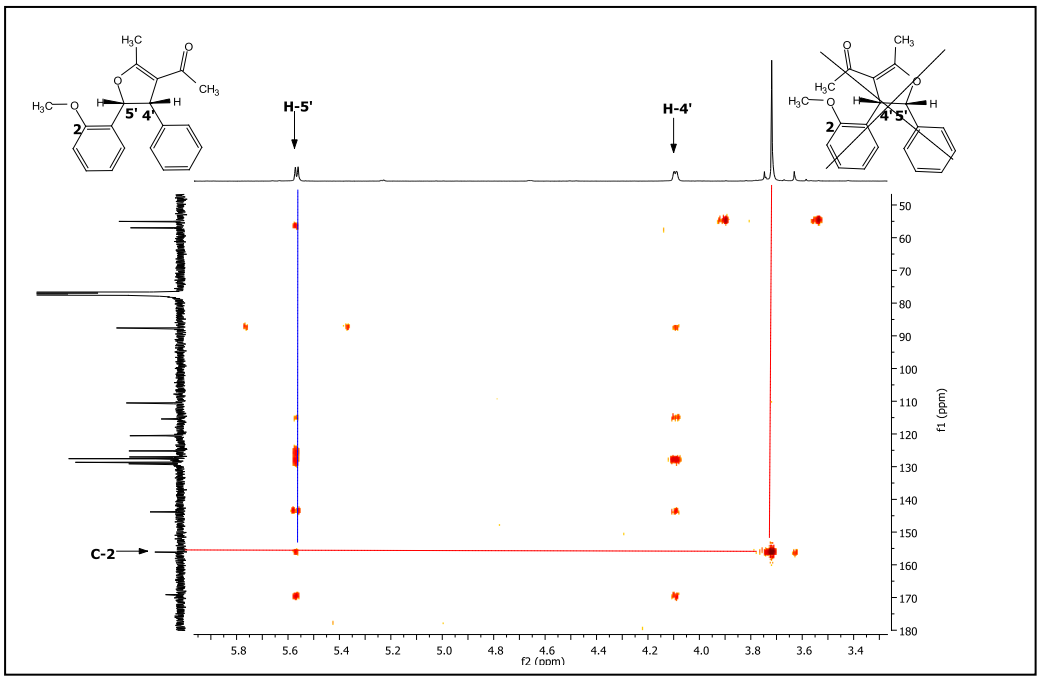


Figure 17 HMBC spectrum of compound **90**

For the starting alkenes of this reaction, optimization and natural bond orbital (NBO) analysis were done at the level of M06 / TZVP to get an idea about the mechanism of formation, which is based on the electron density on the olefinic carbon atoms.

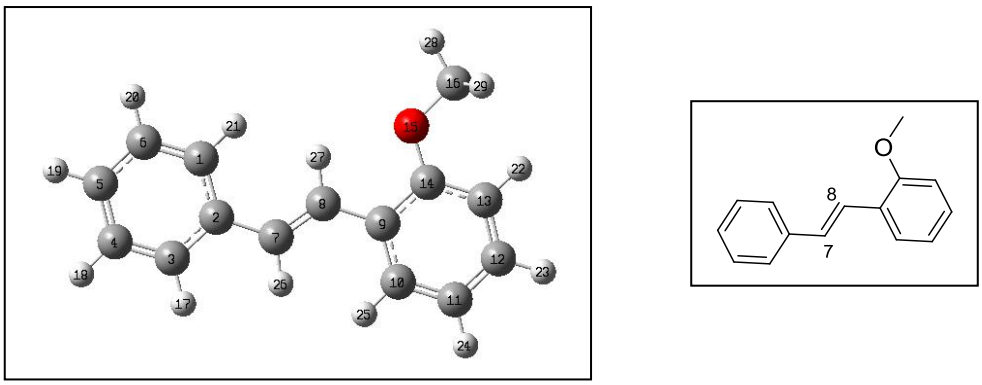


Figure 18 The optimized geometry for compound **88**

According to the NBO analysis result, the natural charge on C-8 atom in compound **88** is -0.171 Coulomb; on the other hand natural charge on C-7 atom is -0.170 Coulomb. These results shows that the electron density on C-8 atom is higher than the electron density on C-7 atom (Figure 18).

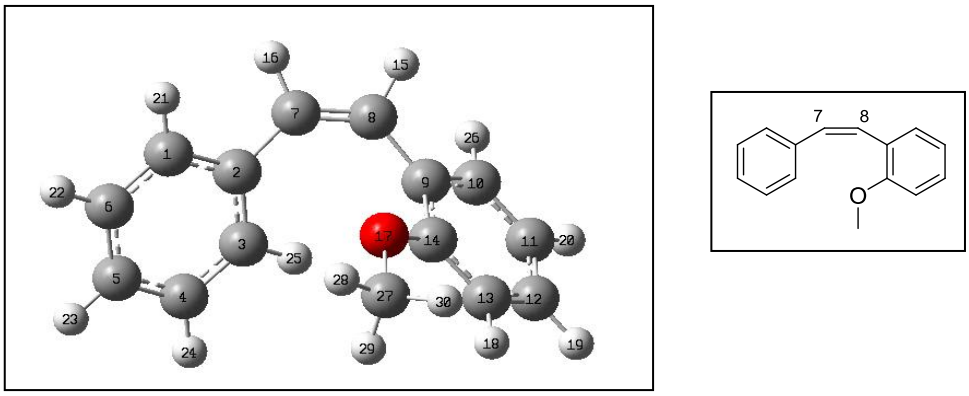
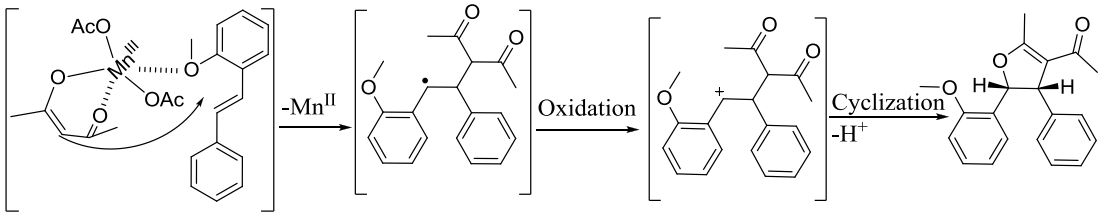


Figure 19 The optimized geometry for compound **89**

Same analysis was done to the isomer **89**. Natural charge on C-8 atom is -0.178 Coulomb and natural charge on C-7 atom is -0.164 Coulomb. NBO analysis shows that the electron density on C-8 atom is higher than the electron density on C-7 atom (Figure 19).

According to the results of theoretical calculations, compound **91** should be formed as a major product with the addition of radical to the electron rich olefinic carbon atoms in both E and Z isomers and compound **90** should be formed as the minor product.

These results indicate that electron density distribution on the double bonds in **88** as well as in **89** don't have any effect on the formation of products. For the formation of compound **90** as the major product we propose that the formation of a complex **92** between oxygen atom of methoxyl group, $Mn(OAc)_3$ and acetylacetone (**56**) is responsible for the mode of the reaction. An electron tansfer from the alkene to the Mn atom of the $Mn(OAc)_3$ occurs and carbon-carbon bond forms between the active carbon atom in acetylacetone (**56**) and the olefinic carbon atom which is close to the unsubstituted benzene ring. After the formation of carbon-carbon bond, the generated radical **93** undergoes subsequent oxidation to the carbocation **94** followed by intramolecular cyclization reaction to give regioisomer **90** (Scheme 37).



92 **93** **94** **90**

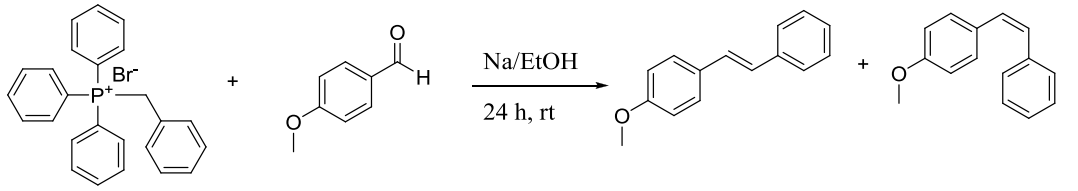
Scheme 37

2.6 Reactions of 1-methoxy-4-[(*Z*)-2-phenylethenyl]benzene and 1-methoxy-4-[(*E*)-2-phenylethenyl]benzene with $Mn(OAc)_3$

2.6.1 Synthesis of 1-methoxy-4-[(*E*)-2-phenylethenyl]benzene and 1-methoxy-4-[(*Z*)-2-phenylethenyl]benzene

To remove the effect of complex formation and to have deeper look into mechanism of formation of the products, we decided to move the electron donating methoxy group from the ortho position to the para position of the benzene ring in the starting alkene. For this purpose, we decided to synthesize the compounds **96** and **97**. Benzyltriphenylphosphonium bromide (**52**) was reacted with 4-methoxy benzaldehyde (**95**) in Na/EtOH as described above. 1-Methoxy-4-[(*E*)-2-phenyl

ethenyl]benzene (**96**) and 1-methoxy-4-[(*Z*)-2-phenylethenyl]benzene (**97**) were obtained in yields of 25% and 72%, respectively (Scheme 38).[29]

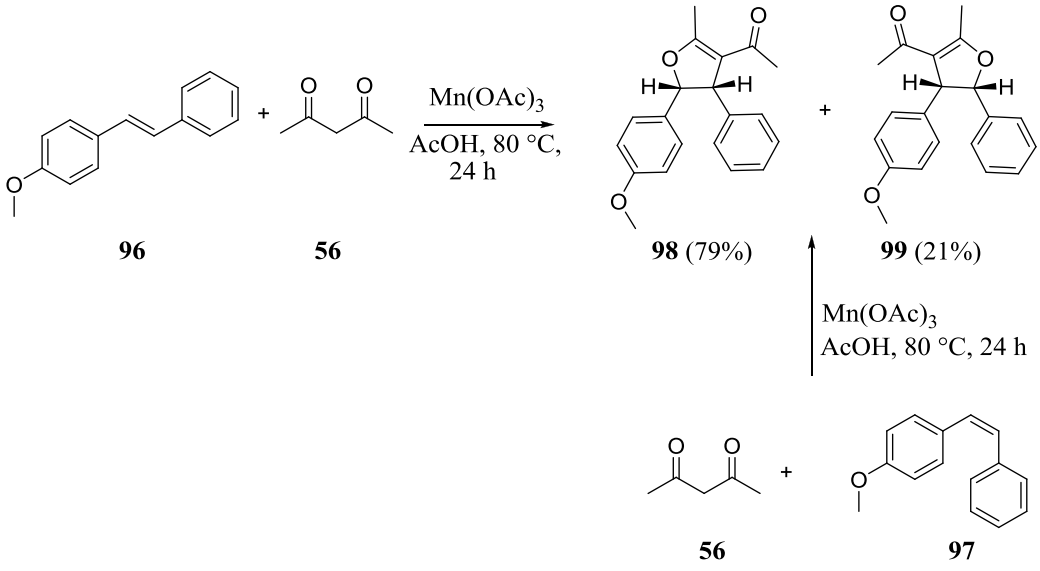


52 **95** **96** (72%) **97** (25%)

Scheme 38

The olefinic protons which resonate at 7.0 and 6.9 ppm as an AB system with a coupling constant of J = 16.3 Hz in ^{1}H-NMR spectrum, indicates the *trans* configuration for the compound **96**. On the other hand; in ^{1}H-NMR spectrum of compound **97**, olefinic protons resonate at 6.48 and 6.44 ppm as an AB system with a coupling constant of J = 12.1 Hz, clearly showing the *cis* configuration.

2.6.2 Cyclization Reactions of 1-Methoxy-4-[(*E*)-2-phenylethenyl]benzene and 1-Methoxy-4-[(*Z*)-2-phenylethenyl]benzene



96 **56** **98** (79%) **99** (21%)

56 **97**

Scheme 39

The isomeric compouns **96** and **97** were reacted with acetylacetone (**56**) in presence of $Mn(OAc)_3$ in AcOH at 80 °C for 24 h. The formation of two regioisomeric cyclization products **98** and **99** with *cis* configuration of the substituents attached to the five membered ring were observed (Scheme 39).

In the ^{1}H-NMR spectrum of compound **98** the protons H-5' and H-4' resonate at 5.28 and 4.30 ppm, respectively. The H-3 protons in compound **98** are shifted to the high field because of the presence of methoxy groups at the ortho position (Figure 20). On the other hand; in the ^{1}H-NMR spectrum of compound **99** H-5' and H-4' protons resonate at 5.31 and 4.25 ppm, respectively.

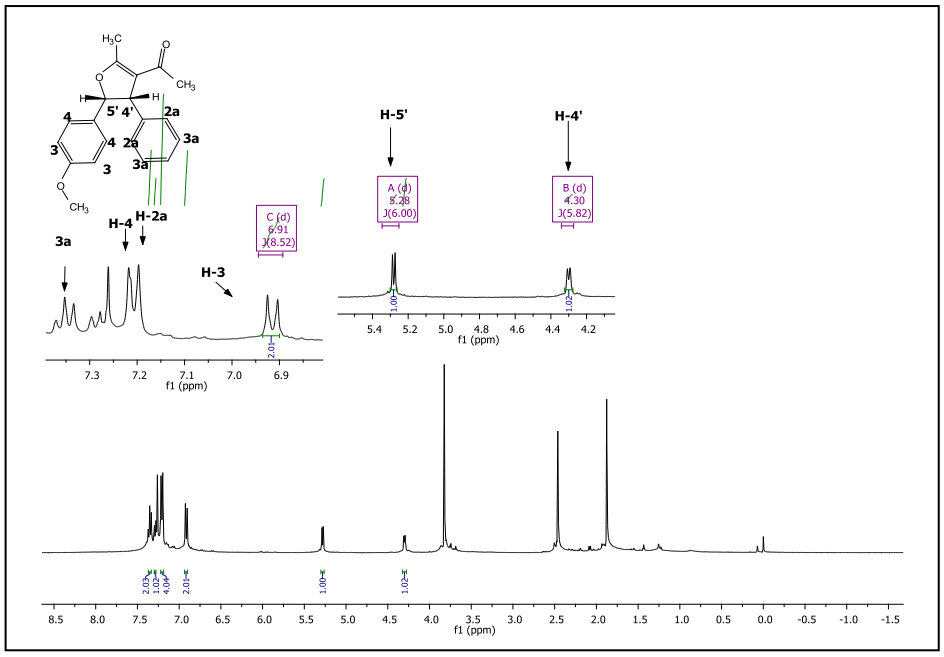


Figure 20 ^{1}H-NMR spectrum of compound **98**

Firstly, quaternary C-5 carbon atom is found from the correlation of H-3 protons, higher field aromatic protons, by using HMBC spectrum. Then the correlation of C-5 carbon atom with only H-4' proton not with H-5' proton completely proves the proposed structure for major product, compound **98,** (Figure 21). The other key correlation for the proposed structure for regioisomer **98**, is the correlation of C-1a and H-5'.

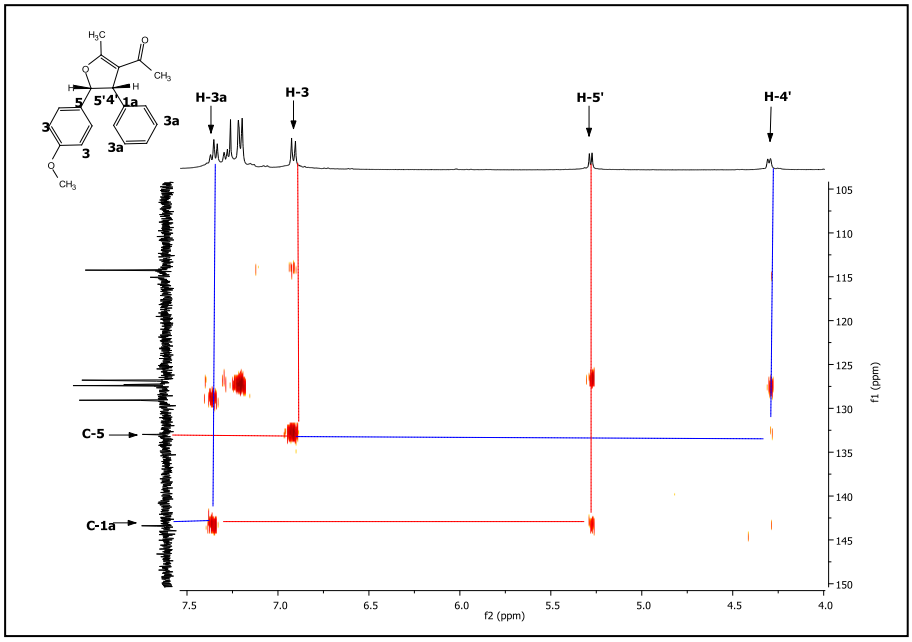


Figure 21 HMBC spectrum of compound **98**

NBO analysis for compound **96** shows that the electron density on C-7 atom is -0.162 Coulomb; on the other hand natural charge on C-8 atom is -0.183 Coulomb (Figure 22).

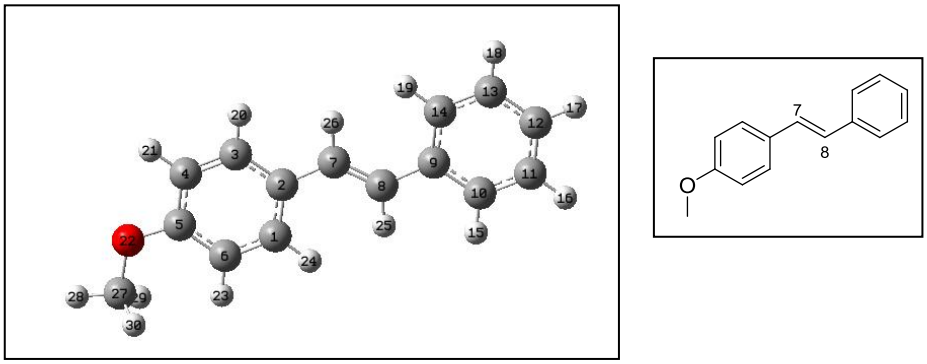


Figure 22 The optimized geometry for compound **96**

Natural charge on C-8 atom in compound **97** is -0.143 Coulomb; on the other hand natural charge on C-7 atom is -0.196 Coulomb. According to natural charge calculations it is obvious that the electron density on C-7 atom is higher than the electron density on C-8 atom (Figure 23).

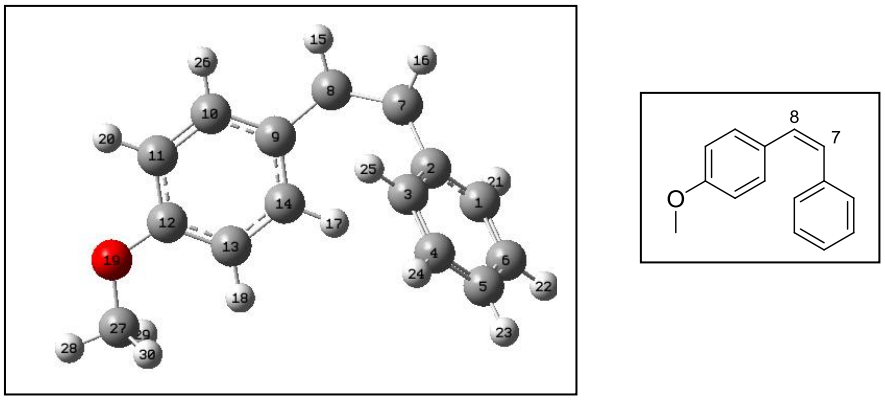


Figure 23 The optimized geometry for compound **97**

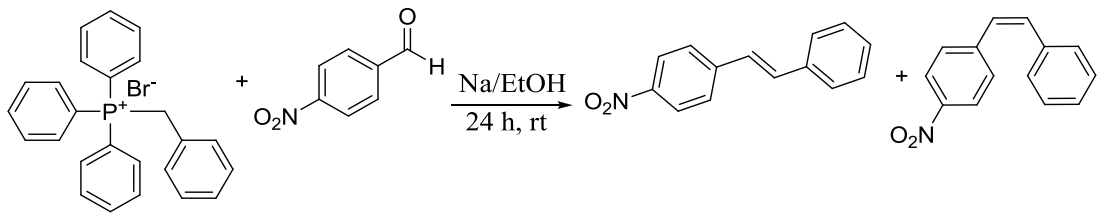
Theoretical calculations are in agreement with experimental results. According to the results, major cyclization product, compound **98**, is formed with the addition of radical to the electronically rich olefinic carbon atoms in both *E* and *Z* isomers.

The other regioisomeric cyclization product, compound **99**, is formed as a minor product with the additon of radical to the electronically poor olefinic carbon atom.

2.7 Reactions of (*E*)-1-nitro-4-styrylbenzene and (*Z*)-1-nitro-4-styrylbenzene with $Mn(OAc)_3$

2.7.1 Synthesis of (*E*)-1-nitro-4-styrylbenzene and (*Z*)-1-nitro-4-styrylbenzene

To search the effect of a strong electron withdrawing group, such as a nitro group, on the distribution of the addition products, we decided to introduce a nitro group to the para position of one of the benzene rings. Therefore, first we synthesized (*E*)-1-nitro-4-styrylbenzene (**101**) and (*Z*)-1-nitro-4-styrylbenzene (**102**) by reacting benzyltriphenylphosphoniumbromide (**52**) with 4-nitrobenzaldehyde (**100**) in Na/EtOH (Scheme 40).[32]



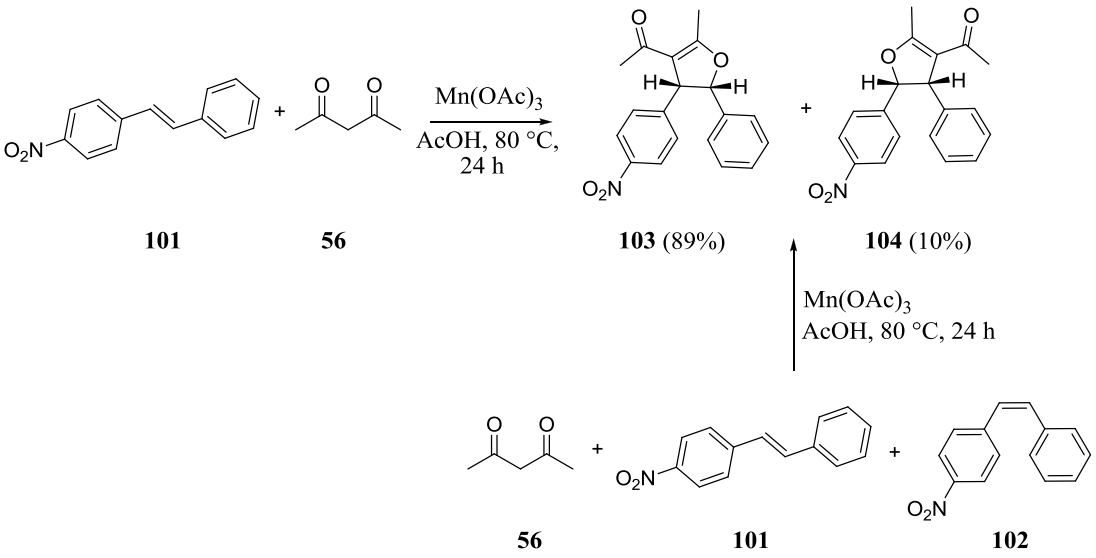
52 **100** **101** (64%) **102** (36%)

Scheme 40

In the ^{1}H-NMR spectrum of compound **101**, olefinic proton signals resonate at 7.30 and 7.15 ppm as an AB system with a coupling constant of J = 16.3 Hz, clearly showing the *trans* configuration. For the compound **102**, olefinic proton resonates at 6.82 and 6.62 ppm as an AB system with a coupling constant of J = 12.2 Hz, indicating the *cis* configuration of compound **102**.

2.7.2 Cyclization Reactions of (*E*)-1-nitro-4-styrylbenzene and (*Z*)-1-nitro-4-styrylbenzene

The stilbene derivatives **101** and **102** having a nitro group in the para position were reacted with acetylacetone (**56**) in presence of $Mn(OAc)_3$ in AcOH at 80 °C for 24 h. Again two regioisomeric cyclization products with *cis* configuration of the substituents attached to the dihydrofuran ring were isolated (Scheme 41).



Scheme 41

In ^{1}H-NMR spectrum of compound **103** H-5' and H-4' resonates at 5.20 and 4.34 ppm, respectively. The H-3 protons in compound **103** are shifted to the low field because of the presence of a nitro group at the ortho position. The H-4 proton resonates at 6.90 ppm (Figure 24).

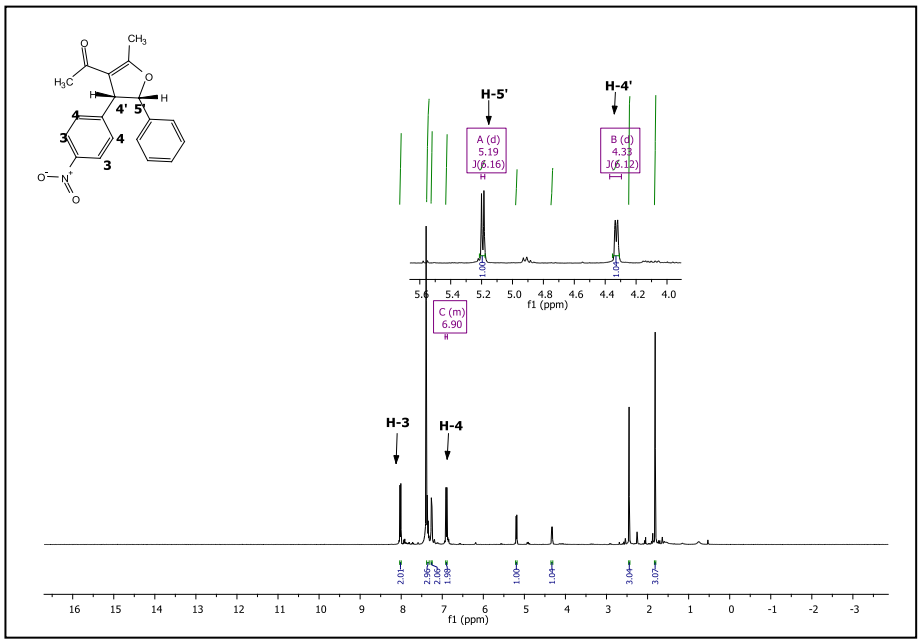


Figure 24 ^{1}H-NMR spectrum of compound **103**

Firstly, C-5' and C-4' carbon atoms were found from the HSQC spectrum (Figure 25).

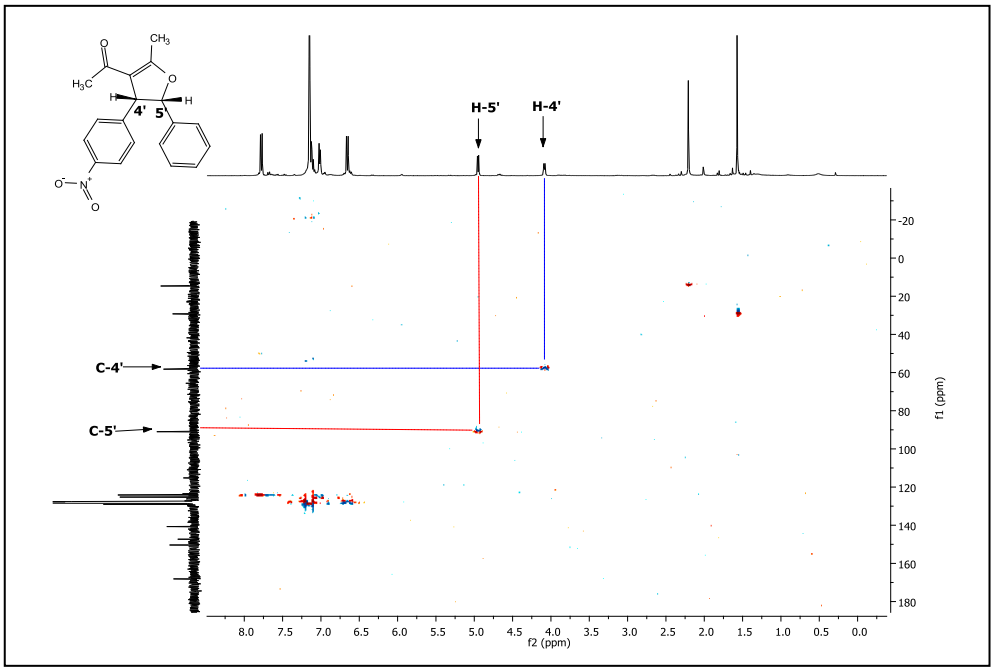


Figure 25 HSQC spectrum of compound **103**

The correlation of H-4 proton with only C-4' carbon atom not with the C-5' carbon atom in HMBC spectrum, completely proves the proposed structure for major product, compound **103**, (Figure 26). In the case of the minor product **104**, H-4 proton correlates with C-5' carbon atom not with C-4' carbon atom.

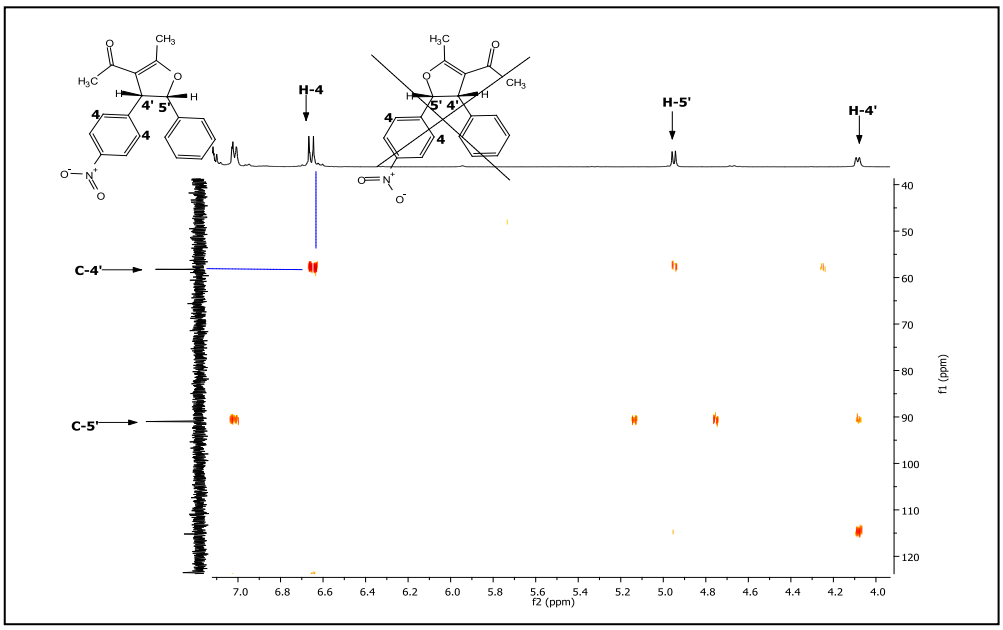


Figure 26 HMBC spectrum of compound **103**

According to the NBO analysis, natural charge on C-7 atom is -0.194 Coulomb and the natural charge on C-8 atom is -0.133 Coulomb in compound **101**. It can be seen that the electron density on C-7 atom is higher than the electron density on C-8 atom (Figure 27).

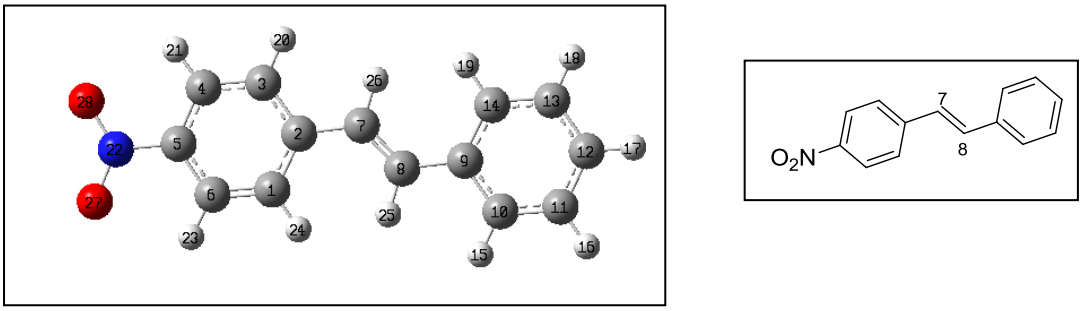


Figure 27 The optimized geometry for compound **101**

Same NBO analysis were done for compound **102**, according to these calculations the natural charge on C-8 atom is -0.200 Coulomb; on the other hand natural charge on C-7 atom is -0.148 Coulomb and the electron density on C-8 atom is higher than the electron density on C-7 atom (Figure 28).

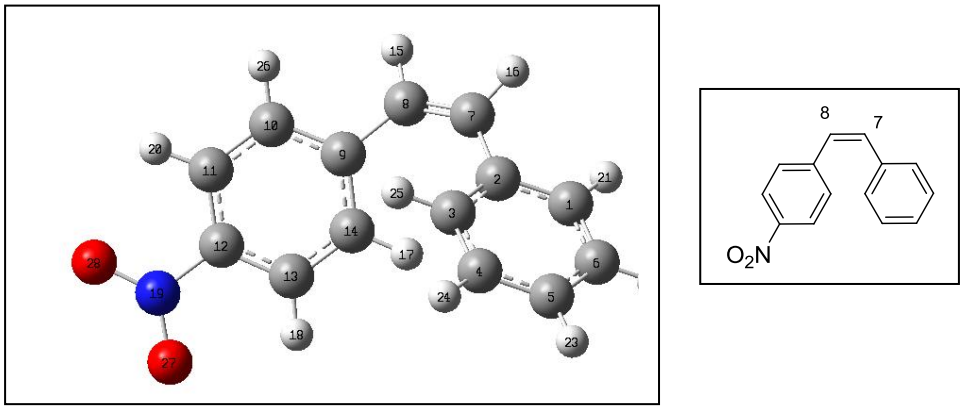


Figure 28 The optimized geometry for compound **102**

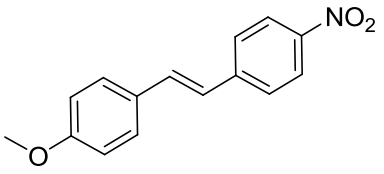
Theoretical calculations are in agreement with the experimental results. According to the results, electron density on the olefinic carbon atoms affects the reaction mechanism and product distribution. Major cyclization product, compound **103**, is formed with the addition of the radical to the electronically rich olefinic carbon atoms in both *E* and *Z* isomers from the same mechanism as shown in Scheme 30.

The other regioisomeric cyclization product, compound **104**, is formed as a minor product with the additon of radical to the electronically poor olefinic carbon atom.

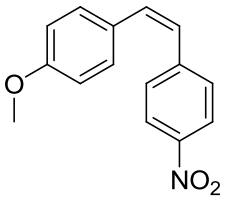
2.8 Reactions of (*E*)-1-Methoxy-4-(4-nitrostyryl)benzene and (*Z*)-1-Methoxy-4-(4-nitrostyryl)benzene with $Mn(OAc)_3$

2.8.1 Synthesis of (4-Methoxyphenyl)methanol

Finally, we were interested in the synthesis of a stilbene derivative substituted at one of the benzene ring with an electron-withdrawing group at the other one with the electron-donating group. Therefore, we planned the synthesis of **108** and **109**.

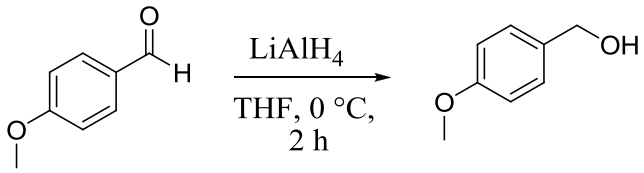


108



109

To synthesize the target molecule **108** and **109**, it was started with the synthesis of (4-methoxyphenyl)methanol (**105**) by reducing 4-methoxybenzaldehyde (**95**) with $LiAlH_4$ (Scheme 42). [33]



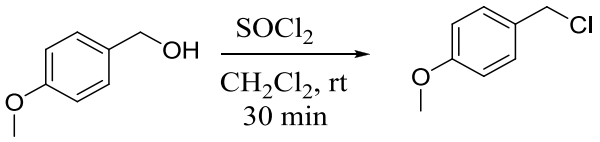
95 **105** (97%)

Scheme 42

Disappearance of aldehyde proton signal and the presence of broad -OH proton signal resonating at 3.56 ppm proved the structure for compound **105**.

2.8.2 Chlorination of (4-Methoxyphenyl)methanol

To replace –OH group with a chlorine atom, (4-Methoxyphenyl)methanol (**105**) was reacted with $SOCl_2$ as described in literature to give 1-(Chloromethyl)-4-methoxybenzene (**106**) (Scheme 43).[34]



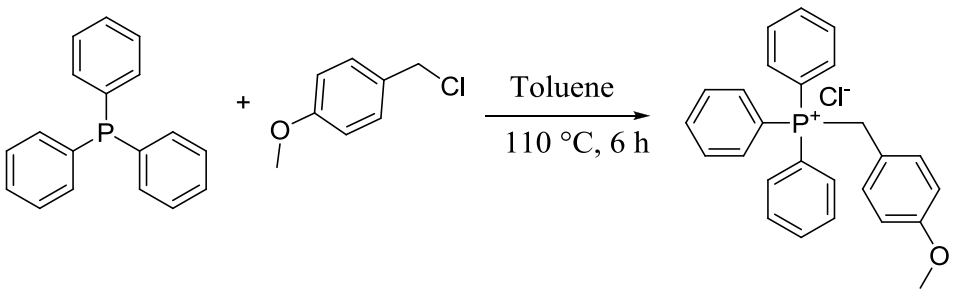
105 **106** (97%)

Scheme 43

Characterization of compound **106** was done by using the ^{1}H-NMR and ^{13}C-NMR spectral data. Disappearance of broad –OH proton signal, which resonates at 3.56 ppm, proved the proposed structure for compound **106**.

2.8.3 Synthesis of Wittig Salt

To perform Wittig reaction, it was started with the synthesis of Wittig salt **107**. To synthesize target salt 1-(chloromethyl)-4-methoxybenzene (**106**) was reacted with triphenylphosphine (**51**) in toluene. At the end of the reaction, (4-methoxybenzyl)triphenylphosphonium chloride (**107**) was formed (Scheme 44).[35]



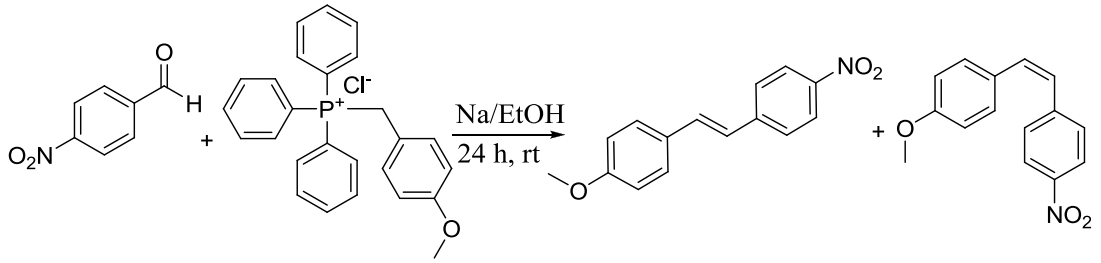
51 **106** **107** (84%)

Scheme 44

Methylene protons, resonating at 5.36 ppm as a doublet due to the coupling with neighbour phosphorous atom (J_{HP} = 13.8 Hz). [1] H-NMR spectrum of compound **107** completely proved the proposed structure.

2.8.4 Synthesis of (*E*)-1-methoxy-4-(4-nitrostyryl)benzene and (*Z*)-1-methoxy-4-(4-nitrostyryl)benzene

Target alkenes, compound **108** and compound **109**, were synthesized by reacting (4-Methoxybenzyl)triphenylphosphonium chloride (**107**) with 4-Nitrobenzaldehyde (**100**) in Na/EtOH solution (Scheme 45).[36]



100 **107** **108** (72%) **109** (25%)

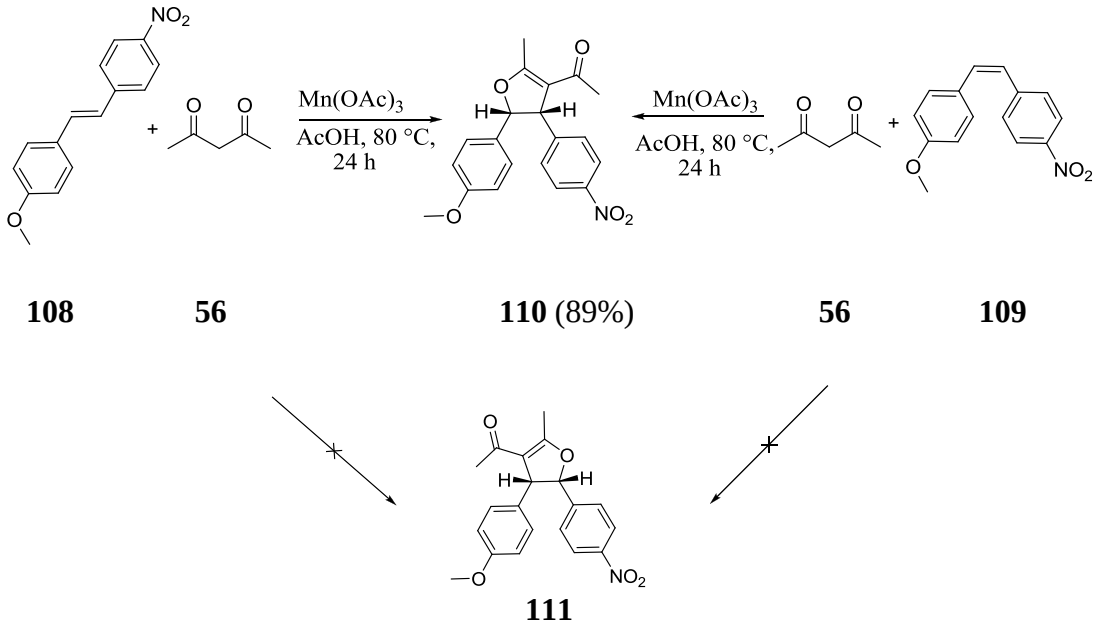
Scheme 45

Signals resonating at 7.25 and 7.03 ppm as an AB system with a coupling constant of J = 16.3 Hz, proved the proposed structure for compound **108**. In the ^{1}H-NMR spectrum of compound **109**, olefinic protons resonate at 6.75 and 6.53 ppm as an AB system with a coupling constant of J = 12.1 Hz, clearly showing the cis configuration.

2.8.5 Cyclization Reactions of (*E*)-1-Methoxy-4-(4-nitrostyryl)benzene and (*Z*)-1-Methoxy-4-(4-nitrostyryl)benzene

The stilbene derivatives having an electron-donating and electron-withdrawing groups, **108** and **109**, were seperately reacted with acetylacetone (**56**) in presence of

$Mn(OAc)_3$ for 24 h.[23] Careful analysis of the product indicated the formation of exclusively one regioisomer **110**. Formation of any trace amount of regioisomer **111** was not observed (Scheme 46).



108 **56** **110** (89%) **56** **109**

111

Scheme 46

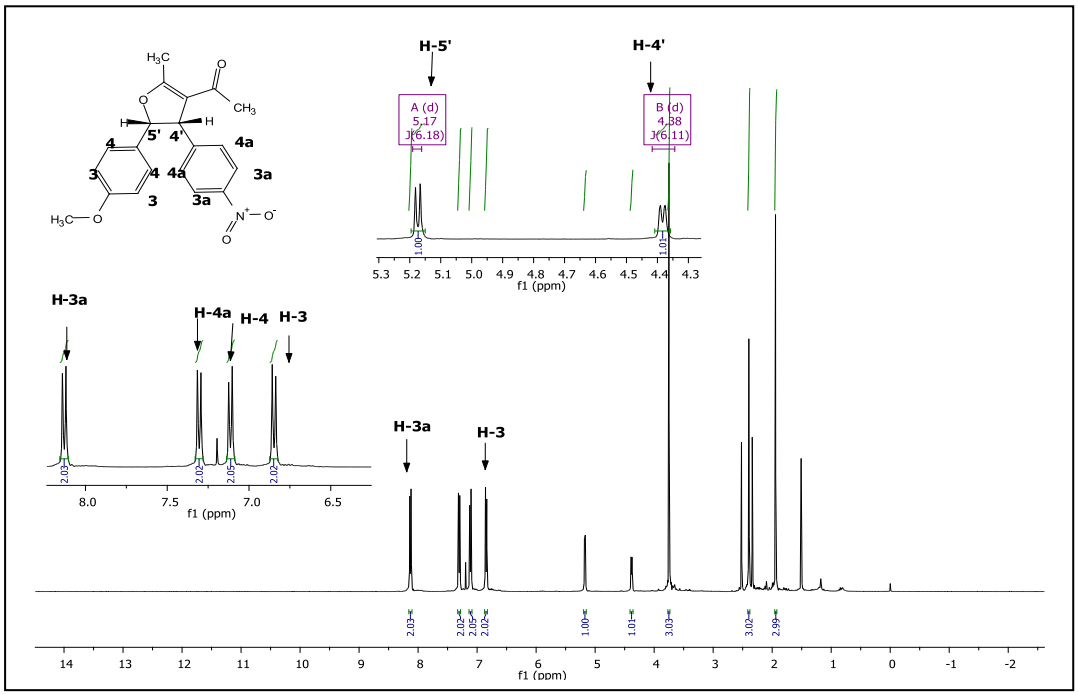


Figure 29 ^{1}H-NMR spectrum of compound **110**

In the ^{1}H-NMR of compound **110**, the H-5' proton resonates at 5.17 ppm and the proton H-4' resonates at 4.38 ppm. Due to the presence of methoxy group the H-3 protons are shifted to high field and they appear at 6.85 ppm. The H-3a protons are shifted to low field and they resonate at 8.13 ppm becasue of the presence of –NO_2 group (Figure 29).

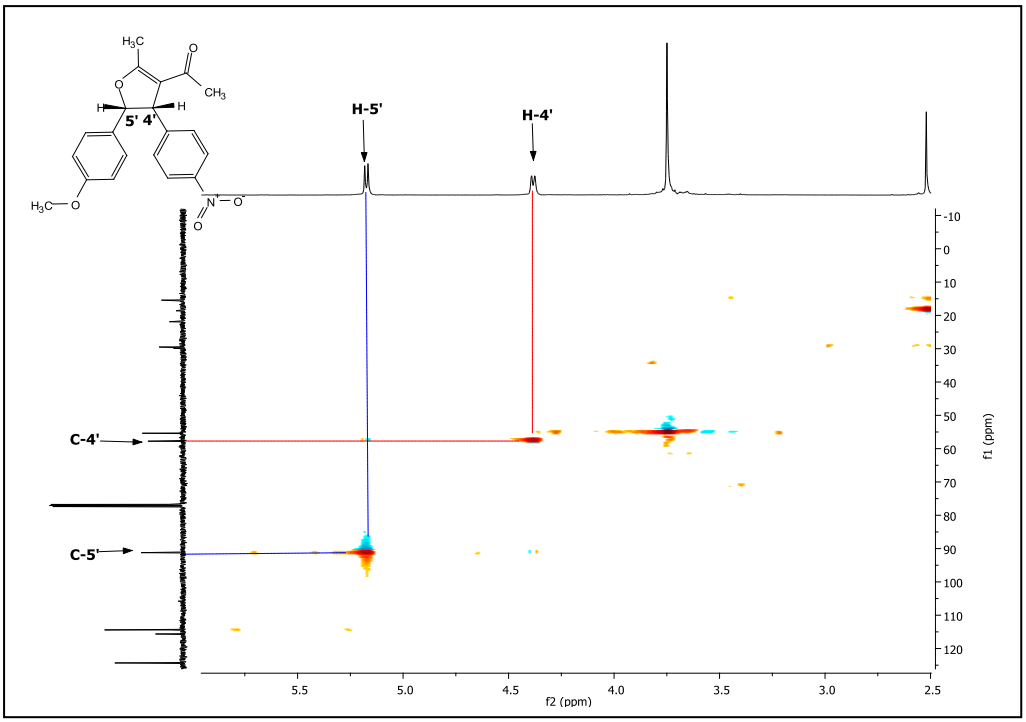


Figure 30 HSQC spectrum of compound **110**

First we determined the exact resonance frequencies of the carbon atoms C-4' and C-5' using the HSQC spectrum (Figure 30).

The HMBC spectrum of **110** shows that the H-4a proton resonance correlates with the C-4' carbon and the H-4 proton correlates with the C-5' carbon atom. On the basis of these findings we assigned the structure **110** to the isolated product (Figure 31).

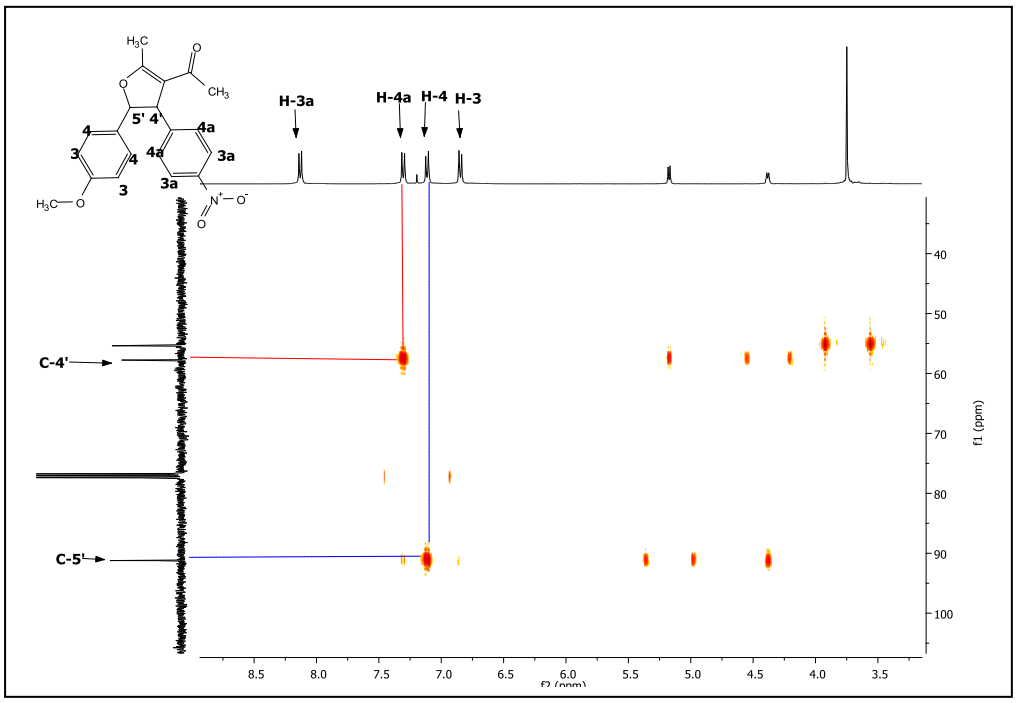
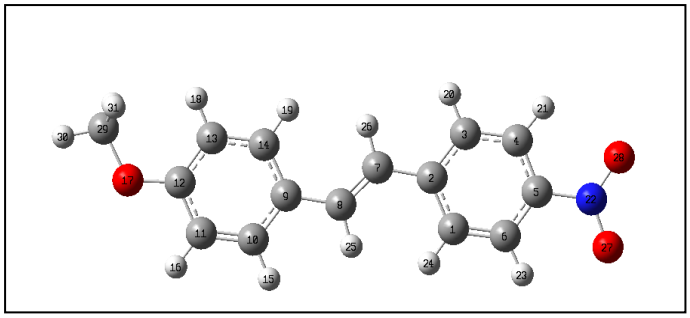


Figure 31 HMBC spectrum of compound **110**

For the starting alkenes **108** and **109**, optimization and natural bond orbital (NBO) analysis were done at the level of M06 / TZVP.



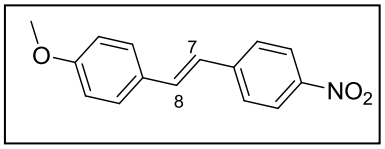


Figure 32 The optimized geometry for compound **108**

Natural charge on the C-7 carbon atom in compound **108** was found to be -0.207 Coulomb; on the other hand natural charge on C-8 atom in compound **108** is -0.125 Coulomb. According to natural charge calculations it is obvious that the electron density on the C-7 carbon atom is higher than the electron density on the C-8 carbon atom (Figure 32).

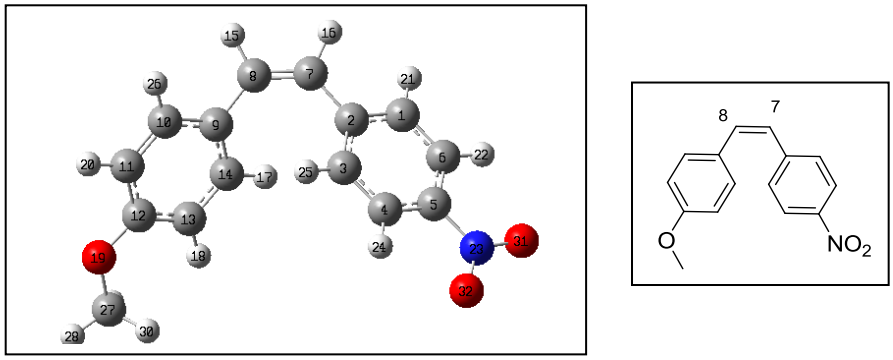


Figure 33 The optimized geometry for compound **109**

According to the NBO analysis of compound **109** natural charge on C-7 carbon atom is -0.214 Coulomb; on the other hand natural charge on C-8 carbon atom in is -0.139 Coulomb. It is obvious that the electron density on C-7 carbon atom is higher than the electron density on C-8 carbon atom (Figure 33).

Theoretical calculations are completely in agreement with the experimental results. According to the results, electronic effect dominates and only regioisomer **110** is formed during the reaction with the addition of radical to the electronically rich olefinic carbon atoms in both *E* and *Z* isomers from the same mechanism as shown in Scheme 30.

CHAPTER 3

EXPERIMENTAL

3.1 General

Nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra were recorded with Bruker Instrument Avance Series-Spectrospin DPX-400 Ultrashield instrument in $CDCl_3$ and C_6D_6 with TMS as internal reference. Chemical shifts (δ) were showed as parts per million (ppm). Spin multiplicities were expressed as singlet (s), doublet (d), doublet of doublet (dd), triplet (t), broad triplet (bt) triplet of triplet (tt) and multiplet (m) and coupling constants (J) were reported in Hertz (Hz).

Infrared spectra were recorded on a Matson FT-IR spectrometer and Vertex 70 series FT-IR spectrometer. Band positions were reported in reciprocal centimeters (cm^{-1}).

Mass spectra were recorded by Accurate-Mass Quadrupole Time-of-Flight (Q-TOF) LC/MS on Agilent 1200/6530.

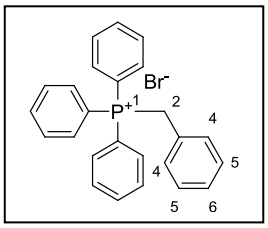
Column chromatograpies were performed by using Fluka Silica Gel 60 plates with a particle size of 0.063-0.20 mm. Thin layer chromatography (TLC) was performed by using 0.25 mm silica gel plates purchased from Fluka.

Compounds were named by using ACD Name Generator.

3.2 Benzyltriphenylphosphonium bromide (52)

Triphenylphosphine (**51**) (25 g, 0.095mol) was added to a solution of benzyl bromide (**50**) (19.1 g, 0.112 mol) in toluene (250 mL). The mixture was heated at reflux

temperature for 6 h and then cooled to room temperature. The product was filtered, recrystallized from EtOH/n-hexane mixture and 39.5 g (96 %) of (**52**) was collected as a white cubic crystals. M.p: 297-298 °C (lit. m.p. 288 °C).[24]



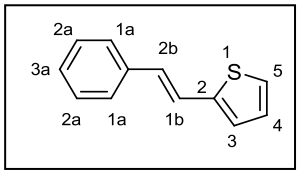
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.79-7.70 (m, 9H), 7.66-7.61 (m, 6H), 7.22 (tt, $J_{6,5}$ = 6.8 Hz, $J_{6,4}$ = 1.9 Hz, 1H, H-6), 7.14-7.09 (m, 4H), 5.37 (d, $J_{1,2}$ = 14.4 Hz, 2H, H-2).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 135.0 (3C), 134.3 (6C), 131.5 (2C), 130.2 (6C), 130.1 (3C), 128.8 (2C), 128.4, 117.7, 30.9

3.3 2-[(*E*)-2-phenylethenyl]thiophen (54) and 2-[(Z)-2-phenylethenyl]-thiophen (55)

Wittig salt **52** (4.5 g, 10.4 mmol) was added to a Na / EtOH solution, which is prepeared with the dissolution of metallic sodium (0.29 g, 12.5 mmol) in 50 mL of EtOH. After the dissolution of all Wittig salt (**52**), thiophene-2-carbaldehyde (**53**) (1.06 g, 9.46 mmol) was added to reaction media. The reaction mixture was stirred at room temperature for 24 h. After the evaporation of reaction solvent, water was added and the mixture was extracted with dichloromethane (3 × 50 mL). The organic extracts were dried over $MgSO_4$. Removal of solvent gave 1.74 g crude product, which was chromatographed over silica gel eluting with hexane. 2-[(*Z*)-2-phenylethenyl]thiophene (**55**) was isolated as the first fraction: colorless liquid 660 mg (38% isolated yield). 2-[(*E*)-2-phenylethenyl]thiophene (**54**) was isolated as the second fraction: white powder (from hexane), 890 mg (51% isolated yield), m.p 110 °C-111 °C.[23]

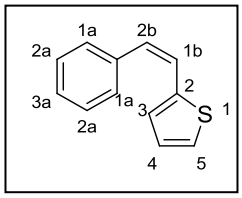
2-[(*E*)-2-phenylethenyl]thiophene(54)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 7.5 Hz, 2H, H-1a), 7.25 (t, J = 7.5 Hz, 2H, H-2a), 7.14 (m,2H), 7.09 (d, $J_{5,4}$ = 5.0 Hz, 1H, H-5), 6.97 (d, $J_{3,4}$ = 3.5 Hz, 1H, H-3), 6.91 (dd, $J_{4,5}$ = 5.0 Hz, $J_{4,3}$ = 3.5 Hz, 1H, H-4), 6.84 (d, J = 16.1 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 142.9, 137.0, 128.8 (2C), 128.4, 127.7 (2C), 126.4 (2C), 126.2, 124.4, 121.8.

2-[(*Z*)-2-phenylethenyl]thiophene (55)

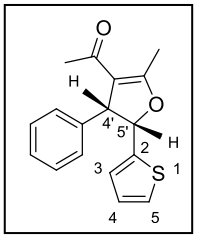


^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28-7.18 (m, 5H, benzene), 6.98 (d, $J_{5,4}$ = 5.0 Hz, 1H, H-5), 6.87 (d, $J_{3,4}$ = 3.5 Hz, 1H, H-3), 6.78 (dd, $J_{4,5}$ = 5.0 Hz, $J_{4,3}$ = 3.5 Hz, 1H, H-4), 6.61 (d, A part of AB system J = 12.0 Hz, 1H), 6.48 (d, B part of AB system J = 12.0 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 139.9, 137.4, 129.0, 128.9 (2C), 128.6 (2C), 128.2, 127.6, 126.5, 125.6, 123.4.

3.4 1-(2-Methyl-4-phenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl)ethanone (57)

$Mn(OAc)_3$ (2.89 g, 9.72 mmol) was dissolved in 30 mL of glacial acetic acid and the flask was heated to 80 °C under nitrogen. Then a mixture of -[(*E*)-2-phenylethenyl] thiophene(**54**) (0.67 g, 3.6 mmol) and acetylacetone (**56**) (7.218 g, 72.1 mmol) in 50 mL of glacial acetic acid was added dropwise to the $Mn(OAc)_3$ solution.The reaction mixture was stirred at 80 °C under nitrogen for 24 h. The reaction mixture was cooled to the room temperature and saturated $NaHCO_3$ solution was added to the reaction mixture. Then the solution was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of solvent under the reduced pressure afforded the residue, which was then separated by column chromatography on silica gel eluting with hexane / EtOAc (20:1) to yield 1-(2-Methyl-4-phenyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-yl)ethanone (**57**) as a pale yellow liquid (0.79 g, 77%).



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37-7.22 (m, 6H), 7.03 (br d, $J_{3,4}$ = 3.5 Hz, 1H, H-3), 6.99 (dd, $J_{4,5}$ = 5.0 Hz, $J_{4,3}$ = 3.5 Hz, 1H, H-4), 5.54 (d, $J_{5',4'}$ = 5.6 Hz, 1H, H-5'), 4.46 (dd, $J_{4',5'}$ = 5.6 Hz, J = 1.1, 1H, H-4'), 2.42 (d, J = 1,1 Hz, 3H), 1.93 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 195.0, 168.1, 143.3, 142.5, 129.1 (2C), 127.5, 127.4 (2C), 126.9, 125.8, 125.3, 115.2, 87.7, 58.1, 29.7, 15.1

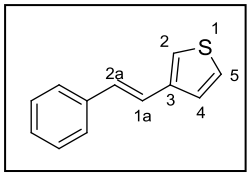
IR (ATR) 1669, 1593, 1372, 1309, 1217, 1127, 1075, 981, 929, 832, 770

HRMS for $C_{17}H_{16}O_2S$ $[M+H]^+$: 285.09493. Found: 285.09504

3.5 3-[(*E*)-2-phenylethenyl]thiophene (63) and 3-[(*Z*)-2-phenylethenyl]thiophene (64)

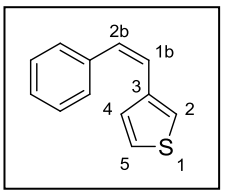
Wittig salt **52** (4.5 g, 10.4 mmol) was added to a Na / EtOH solution, which is prepeared by the dissolution of metallic sodium (0.29 g, 12.5 mmol) in 50 mL of EtOH. After the dissolution of all Wittig salt, thiophene-3-carbaldehyde (**62**) (1.06 g, 9.46 mmol) was added to reaction media. The reaction mixture was stirred at room temperature for 24 h. After the evaporation of reaction solvent, water was added and the mixture was extracted with dichloromethane (3 × 50 mL). The organic extracts were dried over $MgSO_4$. Evaporation of the solvent under the reduced pressure gave the residue, which was then separated by column chromatography on silica gel eluting with hexane. 3-[(*Z*)-2-phenylethenyl]thiophene (**64**) was isolated as a first fraction: colorless liquid, 740 mg (42.5% isolated yield). 3-[(*E*)-2-phenylethenyl]thiophene (**63**) was isolated as a second fraction: white powder (from hexane), 937 mg (53.5% isolated yield), m.p 123.5-124 °C.[25]

3-[(*E*)-2-phenylethenyl]thiophene (63)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 7.6 Hz, 2H), 7.35-7.29 (m, 4H), 7.25-7.22 (m, 2 H), 7.12 (d, A part of AB system J = 16.3 Hz, 1H), 6.94 (d, B part of AB system J = 16.3 Hz, 1H).

3-[(*Z*)-2-phenylethenyl]thiophene (64)



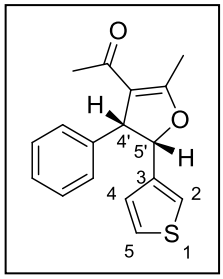
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30-7.22 (m, 5H), 7.12-7.09 (m, 2H), 6.86 (dd, $J_{4,5}$ = 4.7 Hz, $J_{4,2}$ = 1.5 Hz, 1H, H-4), 6.57 (d, A part of AB system J = 12.1 Hz, 1H), 6.53 (d, B part of AB system J = 12.1 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 138.3, 137.9, 129.6, 128.8 (2C), 128.4 (2C), 128.1, 127.3, 125.0, 124.5, 124.2.

^{13}C-NMR (100 MHz, $CDCl_3$) δ 140.2, 137.4, 128.7 (3C), 127.5, 126.3 (2C), 126.2, 125.0, 122.9, 122.4.

3.6 1-(2-Methyl-4-phenyl-5-(thiophen-3-yl)-4,5-dihydrofuran-3-yl)ethanone (65) and 1-(2-Methyl-5-phenyl-4-(thiophen-3-yl)-4,5-dihydrofuran-3-yl)ethanone (66)

$Mn(OAc)_3$ (0.890 g, 3.3 mmol) was dissolved in 30 mL of glacial acetic acid and the flask was heated to 80 °C under nitrogen. Then a mixture of 3-[(*E*)-2-phenylethenyl]thiophen (**63**) (0.206 g, 1,1 mmol) and acetylacetone (**56**) (2.21 g, 22 mmol) in 50 mL of glacial acetic acid was added dropwise to the $Mn(OAc)_3$ solution. The reaction mixture was stirred for 24 h at 80 °C under nitrogen. The reaction mixture was cooled to room temperature and saturated $NaHCO_3$ solution was added to the reaction mixture. Then the solution was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent under the reduced pressure afforded the residue, which was then separated by column chromatography on silica gel eluting with hexane / EtOAc (20:1) to yield 1-(2-Methyl-4-phenyl-5-(thiophen-3-yl)-4,5-dihydrofuran-3-yl)ethanone (**65**) as a first fraction: pale yellow liquid, 205 mg (66% crude yield). 1-(2-methyl-5-phenyl-4-(thiophen-3-yl)-4,5-dihydrofuran-3-yl)ethanone (**66**) can not be seperated. According to crude NMR of the mixture crude yield of the compound **66** was 33%.



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 4H), 7.31-7.28 (m, 1H), 7.23 (dd, J = 7.2 Hz, J = 1.5 Hz, 2H), 7.07 (dd, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.2 Hz, 1H, H-4), 5.41 (d, $J_{5',4'}$= 5.8 Hz, 1H, H-5'), 4.34 (dd, $J_{4',5'}$= 5.8 Hz, J = 1.1 Hz, 1H, H-4'), 2.44 (d, J = 1.1 Hz, 3H), 1.90 (s, 3H).

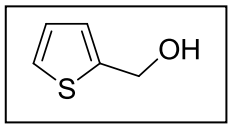
^{13}C-NMR (100 MHz, $CDCl_3$) δ 195.1, 168.6, 143.1, 141.7, 129.1 (2C), 127.4 (2C), 127.2, 125.1, 124.9, 121.7, 115.2, 88.3, 57.2, 29.7, 15.1

IR (ATR) 1715, 1669, 1595, 1517, 1346, 1217, 932, 851, 758, 699.

HRMS for $C_{17}H_{16}O_2S$ $[M+H]^+$: 285.09493 Found: 285.09910.

3.7 Thiophen-2-ylmethanol (71)

To a solution of $LiAlH_4$ (0.169 g, 4.46 mmol) in dry THF (10 mL), thiophene-2-carbaldehyde (**53**) (1.0 g, 8.92 mmol) was added dropwise in an ice-bath. After the reaction mixture was stirred for 2 h, and then the reaction mixture was quenched with sat. NH_4Cl solution. Then the extraction was performed with ethyl acetate (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$. Removal of solvent gave thiophen-2-ylmethanol (**71**) (930 mg, 91% isolated yield) as a yellow liquid.[26]



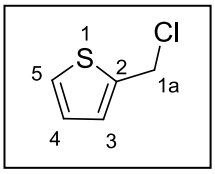
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, J = 3.9 Hz, J = 2.3 Hz, 1H), 7.00-6.99 (m, 2H), 4.73 (s, 2H), 3.66 (br s, 1H, -OH);

^{13}C-NMR (100 MHz, $CDCl_3$) δ 144.1, 126.9, 125.5 (2C), 59.5.

3.8 2-(Chloromethyl)thiophene (72)

Thiophene-2-ylmethanol (**71**) (9.42 g, 0.083 mol) was dissolved in dry CH_2Cl_2 (50 mL). The reaction flask was placed in a 0 °C ice bath. Then $SOCl_2$ (10.81 g, 0.091 mol) was added dropwise to the reaction mixture over 30 min. After the reaction

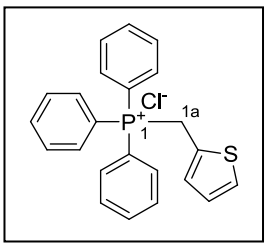
mixture was stirred for 4 h at 0 °C, removal of solvent gave 10.44 g 2-(Chloromethyl) thiophene (**72**) as a colorless liquid (10.44 g, 95%).[27]



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.20 (dd, $J_{5,4}$ = 5.1 Hz, $J_{5,3}$ = 0.9 Hz, 1H, H-5), 6.98 (br d, $J_{3,4}$ = 2.9 Hz, 1H, H-3), 6.85 (dd, $J_{4,5}$ = 5.1 Hz, $J_{4,3}$ = 3.6 Hz, 1H, H- 4), 4.70 (s, 2H, H-1a).
^{13}C-NMR (100 MHz, $CDCl_3$) δ 140.2, 127.8, 127.0 (2C), 40.5.

3.9 Triphenyl(thiophen-2-yl methyl)phosphonium chloride (73)

Triphenylphosphine (**51**) (2.76 g, 10.52 mmol) was added to a solution of (**72**) (0.93 g, 7.02 mmol) in acetonitrile (30 mL). The reaction mixture was heated at reflux temperature for 16 h and then cooled to room temperature. After the removal of solvent the product was washed with diethylether (50 mL) and Triphenyl(thiophen-2-yl methyl)phosphonium chloride (**73**) was collected (2.44 g, 88 %) as a light pink cubic crystals. M.p: 311-312°C.[28]



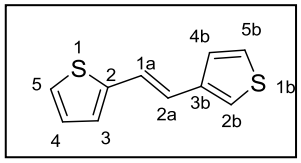
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.70 (m, 9H), 7.60-7.55 (m, 6H), 7.05 (m, 2H), 6.77 (bt, J = 4.3 Hz, 1H), 5.79 (d, $J_{1a,1}$ = 13.3 Hz , 2H, H-1a).
^{13}C-NMR (100 MHz, $CDCl_3$) δ 135.1 (3C), 134.3 (6C), 131.9, 130.3 (6C), 127.7, 127.4, 126.8, 117.8 (3C), 26.6.

3.10 (*E*)-2-(2-(thiophen-3-yl)vinylthiophen (74) and (*Z*)-2-(2-(thiophen-3-yl)vinyl thiophen (75)

Wittig salt **73** (1.73 g, 4.38 mmol) was added to a Na / EtOH solution, which is prepeared by the dissolution of metallic sodium (0.121 g, 5.26 mmol) in 50 mL of EtOH. After the dissolution of all Wittig salt, thiophene-3-carbaldehyde (**62**) (0.45 g, 4.01 mmol) was added to reaction media. The reaction mixture was stirred at room temperature for 24 h. After the evaporation of reaction solvent, water was added and

the reaction mixture was extracted with dichloromethane (3 × 50 mL). The organic extracts were dried over $MgSO_4$. Evaporation of the solvent under the reduced pressure gave the residue, which was then separated by column chromatography on silica gel eluting with hexane to yield (*Z*)-2-(2-(thiophen-3-yl)vinyl)thiophene (**75**) as a first fraction: colorless liquid, 230 mg (30 % isolated yield). (*E*)-2-(2-(thiophen-3-yl)vinyl)thiophene (**74**) was isolated as a second fraction: white needle (from hexane) 427 mg (55.5% isolated yield).

(*E*)-2-(2-(thiophen-3-yl)vinylthiophen (74)



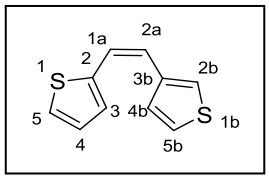
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.25-7.22 (m, 2H), 7.16 (bt, J = 1.9 Hz, 1H), 7.10 (d, J = 4.9 Hz, 1H), 7.00 (d, A part of AB system J = 16.1 Hz, 1H), 6.96 (d, $J_{3,4}$ = 3.3 Hz, 1H, H-3), 6.92 (dd, $J_{4,5}$ = 5.0 Hz, $J_{4,3}$ = 3.3 Hz, 1H, H-4), 6.90 (d, B part of AB system J = 16.1 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 142.8, 139.7, 127.6, 126.3, 125.7, 124.8, 124.1, 122.7, 122.2, 121.8.

IR (ATR) 3091, 1744, 1429, 1374, 1273, 1213, 1076, 1040, 951, 866, 856, 816, 769.

HRMS for $C_{10}H_8S_2$ $[M-H]^-$: 190.99892 Found: 191.00145

(Z)-2-(2-(thiophen-3-yl)vinyl thiophen (75)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.19-7.17 (m, 2H), 7.06 (d, J = 5.0 Hz, 1H), 6.95-6.92 (m, 1H), 6.92 (d, $J_{3,4}$ = 3.6 Hz, 1H, H-3), 6.83 (dd, $J_{4,5}$ = 4.9 Hz, $J_{4,3}$ = 3.5 Hz, 1H, H-4), 6.55 (d, A part of AB system J = 11.9 Hz, 1H), 6.37 (d, B part of AB system J = 11.9 Hz, 1H).

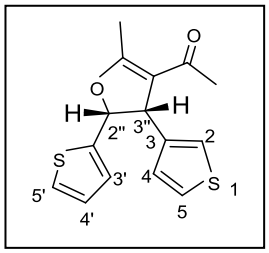
^{13}C-NMR (100 MHz, $CDCl_3$) δ 139.9, 137.8, 128.1, 128.0, 126.7, 125.7, 125.5, 124.2, 123.8, 123.3.

IR (ATR) 3102, 3011, 2923, 2853, 1732, 1435, 1411, 1350, 1261, 1214, 1108, 1079, 1044, 949, 855, 835, 807, 757.

HRMS for $C_{10}H_8S_2$ $[M-H]^-$: 190.99892 Found: 191.00145.

3.11 1-(2-Methyl-5-(thiophen-2-yl)-4-(thiophen-3-yl)-4,5-dihyrofuran-3-yl)ethanone (76)

$Mn(OAc)_3$ (1.59 g, 5.94 mmol) was dissolved in 30 mL of glacial acetic acid and the reaction flask was heated to 80 °C under nitrogen. Then a mixture of (*E*)-2-(2-(thiophen-3-yl)vinyl)thiophene (**74**) (0.381 g, 1,98 mmol) and acetylacetone (**56**) (3.97 g, 39.64 mmol) in 50 mL of glacial acetic acid was added dropwise to the $Mn(OAc)_3$ solution. The reaction mixture was stirred for 24 h at 80 °C under nitrogen. The reaction mixture was cooled to the room temperature and saturated $NaHCO_3$ solution was added. Then the solution was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent under the reduced pressure afforded the residue, which was then separated by column chromatography on silica gel eluting with hexane / EtOAc (20:1) to yield 1-(2-methyl-5-(thiophen-2-yl)-4-(thiophen-3-yl)-4,5-dihydro furan-3-yl)ethanone (**76**) as a pale yellow liquid, 477 mg (83% isolated yield).



^{1}H-NMR (400 MHz, C_6D_6) δ 6.63 (dd, $J_{5,4}$ = 5.0 Hz, $J_{5,2}$ = 3.0 Hz, 1H, H-5), 6.61 (dd, $J_{5',4'}$ = 5.0 Hz, $J_{5',3'}$ = 1.2 Hz, 1H, H-5'), 6.5 (dd, $J_{4,5}$ = 5.0 Hz, $J_{4,2}$ = 1.2 Hz, 1H, H-4), 6.47 (dd, $J_{3',4'}$= 3.5 Hz, $J_{3',5'}$ = 1.2 Hz,1H, H-3'), 6.43 (dd, $J_{4',5'}$ = 5.0 Hz, $J_{4',3'}$ = 3.6 Hz. 1H, H-4'), 6.41 (dd, $J_{2,5}$ = 2.9 Hz, $J_{2,4}$ = 1.2 Hz. 1H, H-2), 5.15 (d, $J_{2",3"}$ = 5.4 Hz, 1H, H-2"), 4.23 (dd, $J_{3",2"}$ = 5.4 Hz, J = 1.0 Hz, 1H, H-3"), 2.06 (d, J = 1.0 Hz, 3H), 1.52 (s, 3H).

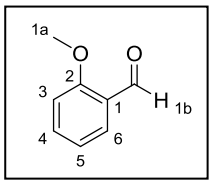
^{13}C-NMR (100 MHz, C_6D_6) δ 193.0, 166.8, 143.8, 143.7, 126.8,126.7, 126.5, 125.6, 125.1, 121.5, 115.2, 86.7, 53.3, 29.1, 14.7.

IR (ATR) 3096, 2962, 2921, 1744, 1668, 1592, 1417, 1370, 1326, 1260, 1227, 1119, 1078, 1017, 930, 857, 833, 793, 704.

HRMS for $C_{15}H_{14}O_2S_2$ $[M+H]^+$: 291.05135 Found: 291.05452

3.12 2-Methoxybenzaldehyde (87)

2-Hydroxybenzaldehyde (**85**) (1.46 g, 12.0 mmol) was methylated using methyl iodide (**86**) (1.7 g, 12 mmol) and anhydrous potassium carbonate (1.7 g, 12 mmol) in DMF (7 mL), by stirring at room temperature for 12 h. After the reaction eas complete, the reaction mixture was extracted with ethylacetate (3 × 50 mL). Removal of solvent gave crude product, which was chromatographed over silica gel eluting with hexane / EtOAc (10:1) to give the 2-Methoxybenzaldehyde (**87**) as a pale yellow liquid, 1.58 g (97% isolated yield).[30]



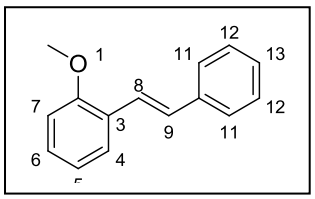
^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.41 (s, 1H, H-1b), 7.76 (dd, $J_{6,5}$ = 7.7 Hz, $J_{6,4}$ = 1.7 Hz, 1H, H-6), 7.49 (td, $J_{4,5}$ = 7.7 Hz, $J_{4,6}$ = 1.7 Hz, 1H, H-4), 6.98-6.91 (m, 2H), 3.84 (s, 3H, H-1a).
^{13}C-NMR (100 MHz, $CDCl_3$) δ 189.7, 161.8, 136.0, 128.3, 124.7, 120.6, 111.7, 55.6.

3.13 (*E*)-1-methoxy-2-styrylbenzene (88) and (*Z*)-1-methoxy-2-styryl benzene (89)

Wittig salt **52** (4.5 g, 10.4 mmol) was added to a Na / EtOH solution, which is prepeared by the dissolution of metallic sodium (0.29 g, 12.5 mmol) in 50 ml of EtOH. After the dissolution of all Wittig salt, 2-Methoxybenzaldehyde (**87**) (1.288 g, 9.46 mmol) was added to reaction mixture. The reaction mixture was stirred at room temperature for 24 h. After the evaporation of reaction solvent, water was added and the mixture was extracted with dichloromethane (3 × 50 mL). The organic extracts were dried over $MgSO_4$. Evaporation of the solvent under the reduced pressure gave

the residue, which was then separated by column chromatography on silica gel eluted with hexane. (Z)-1-methoxy-2-styryl benzene (**89**) was isolated as a first fraction: colorless liquid 810 mg, 41% (isolated yield). (*E*)-1-methoxy-2-styrylbenzene(**88**) was isolated as a second fraction: colorless liquid 970 mg, 49% (isolated yield).[31]

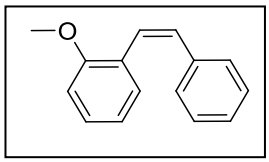
(*E*)-1-methoxy-2-styryl benzene (88)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, J = 7.7 Hz, J = 1.5 Hz, 1H), 7.46 (d, $J_{11,12}$ = 7.6 Hz, 2H, H-11), 7.42 (A part of AB system d, $J_{8,9}$ = 16.5 Hz, 1H, H-8), 7.27 (t, $J_{12,11}$ = 7.6 Hz, 2H, H-12), 7.20-7.15 (m, 2H), 7.04 (B part of AB system d, $J_{9,8}$ = 16.5 Hz, 1H, H-9), 6.90 (t, J = 7.5 Hz, 1H), 6.83 (d, J = 8.2 Hz, 1H), 3.82 (s, 3H).

^{13}C-NMR δ 156.9, 138.0, 129.1, 128.7, 128.6 (2C), 128.0, 127.4, 126.6 (2C), 126.4, 123.5, 120.8, 110.9, 55.5.

(*Z*)-1-methoxy-2-styryl benzene (89)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.18-7.08 (m, 7H), 6.82 (d, J = 8.2 Hz, 1H), 6.68 (t, J = 7.5 Hz, 1H), 6.62 (A part of AB system d, J = 12.3 Hz, 1H), 6.56 (B part of AB system d, J = 12.3 Hz, 1H), 3.76 (s, 3H).

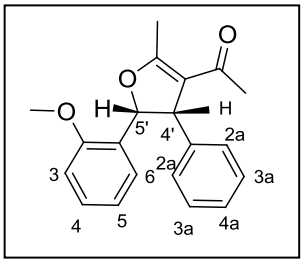
^{13}C-NMR (100 MHz, $CDCl_3$) δ 157.9, 139.0, 130.1, 129.7, 129.6 (2C), 129.0, 128.3, 127.5 (2C), 127.4, 124.5, 121.7, 111.9, 56.5.

3.14 1-(5-(2-Methoxyphenyl)-2-methyl-4-phenyl-4,5-dihydrofuran-3-yl)ethanone (90) and 1-(4-(2-Methoxyphenyl)-2-methyl-5-phenyl-4,5-dihydrofuran-3-yl)ethanone (91)

$Mn(OAc)_3$ (2.91 g, 10.8 mmol) was dissolved in 30 mL of glacial acetic acid and the flask was heated to 80 °C under nitrogen. Then a mixture of (*E*)-1-methoxy-2-styrylbenzene (**88**) (0.76 g, 3.6 mmol) and acetylacetone (**56**) (7.24 g, 72.3 mmol) in

50 mL of glacial acetic acid was added dropwise to the $Mn(OAc)_3$ solution. The reaction mixture was stirred for 24 h at 80 °C under nitrogen. The reaction mixture was cooled to the room temperature and saturated $NaHCO_3$ solution was added to the reaction mixture. Then the solution was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent gave the crude product, which was column chromatographed on silica gel eluting with (5:1 DCM/hexane). 1-(5-(2-Methoxyphenyl)-2-methyl-4-phenyl-4,5-dihydro furan-3-yl) ethanone (**90**) was isolated as a second fraction: pale yellow liquid (0.704 g (64% isolated yield). 1-(4-(2-Methoxyphenyl)-2-methyl-5-phenyl-4,5-dihydro furan-3-yl) ethanone (**91**) could not be seperated. According to crude NMR of the mixture, crude yield of the compound **91** was 36%.

1-(5-(2-Methoxyphenyl)-2-methyl-4-phenyl-4,5-dihydrofuran-3-yl)ethanone (90)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (m, 3H), 7.23-7.22 (m, 1 Hz), 7.19 (dd, J = 7.8 Hz, J = 1.7 Hz, 2H), 7.14 (dd, J = 7.5 Hz, J = 1.3 Hz, 1H), 6.91 (dt, J = 7.5 Hz, J = 0.7 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 5.57 (d, $J_{5'4'}$ = 4.2 Hz, 1H, H-5'), 4.09 (dd, $J_{4'5'}$ = 4.2 Hz, J = 1,0 Hz, 1H, H-4'), 3.72 (s, 3H), 2.45 (s, 3H), 1,79 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 195.5, 169.1, 156.1, 143.8, 129.2, 129.1, 128.7 (2C), 127.6 (2C), 127.0, 125.2, 120.5, 115.4, 110.5, 87.6, 57.0, 55.0, 29.5, 15.1.

IR (ATR) 2988, 2900,1669, 1438, 1491, 1455, 1378, 1286, 1188, 1075, 1066, 1050, 1027, 930, 753, 700, 653, 628.

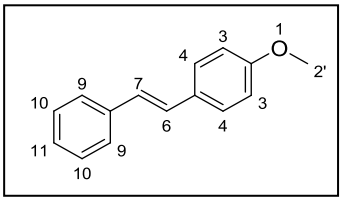
HRMS for $C_{20}H_{21}O_3$ $[M+H]^+$: 309,37894 Found: 309.15041

3.15 1-Methoxy-4-[(*E*)-2-phenylethenyl]benzene (96) and 1-Methoxy-4-[(*Z*)-2-phenylethenyl]benzene (97)

Wittig salt **52** (4.5 g, 10.4 mmol) was added to a Na / EtOH solution, which is prepeared by dissolution of metallic sodium (0.29 g, 12.5 mmol) in 50 mL of EtOH.

After the dissolution of all Wittig salt, 4-Methoxybenzaldehyde (**95**) (1.288 g, 9.46 mmol) was added to reaction media. The reaction mixture was stirred at room temperature for 24 h. After the evaporation of reaction solvent, water was added and the mixture was extracted with dichloromethane (3 × 50 mL). The organic extracts were dried over $MgSO_4$. Evaporation of the solvent under the reduced pressure gave the residue, which was then separated by column chromatography on silica gel eluted with hexane. 1-Methoxy-4-[(*Z*)-2-phenylethenyl]benzene (**96**) was isolated as a first fraction: colorless liquid 0.495 g (25% isolated yield). 1-Methoxy-4-[(*E*)-2-phenylethenyl]benzene (**97**) was isolated as a second fraction: white needles (from hexane) , 1.43 g (72% isolated yield), m.p 128-129 °C (Lit. 136 °C).[31]

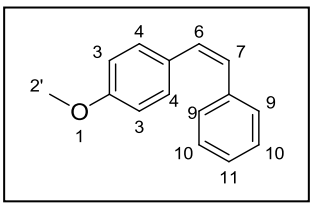
1-Methoxy-4-[(*E*)-2-phenylethenyl]benzene (96)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34 (br d, $J_{9,10}$ = 7.3 Hz, 2H, H-9), 7.26 (A part of AA'BB', quasi-d $J_{4,3}$ = 8.6 Hz, 2H, H-4), 7.16 (t, J = 7.6 Hz, 2H, H-10), 7.06 (t, J = 7.2 Hz, 1H, H-11), 7.01 (A part of AB system d, $J_{6,7}$ = 16.4 Hz, 1H, H-6), 6.91 (B part of AB system d, $J_{7,6}$ = 16.4 Hz, 1H, H-7), 6.76 (B part of AA'BB' quasi-d, $J_{3,4}$ = 8.7 Hz, 2H, H-3), 3.28 (s, 3H, H-2').

^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.3, 137.7, 130.2, 128.7 (2C), 128.2, 127.7 (2C), 127.2, 126.7, 126,3 (2C), 114.2 (2C), 55.3.

1-Methoxy-4-[(*Z*)-2-phenylethenyl]benzene (97)



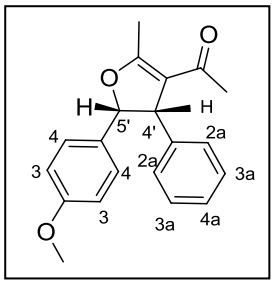
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, $J_{9,10}$ = 8.6 Hz, $J_{9,11}$ = 1.4 Hz, 2H, H-9), 7.20 (A part of AA'BB' system quasi-d, $J_{4,3}$ = 8.7 Hz, 2H, H-4), 7.05 (m, 2H, H-10), 6.98 (tt, $J_{11,10}$ = 7.3 Hz, $J_{11,9}$ = 1.4 Hz, 1H, H-11), 6.60 (B part of AA'BB' system quasi-d, $J_{3,4}$ = 8.7 Hz, 2H, H-3), 6.48 (A part of AB system d, $J_{6,7}$ = 12.2 Hz, 1H, H-6), 6.44 (B part of AB system d, $J_{7,6}$ = 12.2 Hz, 1H, H-7), 3.21 (s, 3H, H-2').

^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.8, 137.7, 130.3 (2C), 129.9, 129.7, 128.9 (2C), 128.8, 128.4 (2C), 127.0, 113.7 (2C), 55.2.

3.16 1-(5-(4-Methoxyphenyl)-2-methyl-4-phenyl-4,5-dihydrofuran-3-yl)ethanone (98) and 1-(4-(4-Methoxyphenyl)-2-methyl-5-phenyl-4,5-dihydrofuran-3-yl) etha none (99)

$Mn(OAc)_3$ (2.91 g, 10.8 mmol) was dissolved in 30 mL of glacial acetic acid and the flask was heated to 80 °C under nitrogen. Then a mixture of 1-methoxy-4-[(*E*)-2-phenylethenyl]benzene (**96**) (0.76 g, 3.6 mmol) and acetylacetone (**56**) (7.24 g, 72.3 mmol) in 50 mL of glacial acetic acid was added dropwise to the $Mn(OAc)_3$ solution. The reaction mixture was stirred for 24 h at 80 °C under nitrogen. The reaction mixture was cooled to the room temperature and saturated $NaHCO_3$ solution was added to the reaction mixture. Then the solution was extracted with ethyl acetate (3 ×5 0 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent gave the crude product ehich was column chromatographed on silica gel eluting with (5:1 DCM/hexane). 1-(5-(4-methoxyphenyl)-2-methyl-4-phenyl-4,5-dihydrofuran-3-yl)et hanone (**98**) was isolated as a second fraction: pale yellow liquid, 0.869 g (79% crude yield). 1-(4-(4-Methoxyphenyl)-2-methyl-5-phenyl-4,5-dihydrofuran-3-yl)etha none (**99**) can not be separated. According to crude NMR of the reaction mixture, crude yield of compound **99** was 21%.

1-(5-(4-Methoxyphenyl)-2-methyl-4-phenyl-4,5-dihydrofuran-3-yl)ethanone (98)



^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37-7.34 (m, 2H), 7.29-7.27 (m, 1H), 7.22-7.20 (m, 2H), 7.21(A part of AA'BB' system quasi-d, $J_{4,3}$ = 8.6 Hz, 2H, H-4), 6.92 (B part of AA'BB' system quasi-d, $J_{3,4}$ = 8.6 Hz, 2H, H-3), 5.28 (d, $J_{5',4'}$ = 6.0 Hz, 1H, H-5'), 4.30 (dd, $J_{4',5'}$ =6.0 Hz, J=1.0 Hz, 1H, H-4'), 3.83 (s, 3H), 2.46 (d, J = 1.2 Hz, 3H), 1.88 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 195.3, 168.9, 159.8, 143.4, 133.0, 129.1 (2C), 127.4 (2C), 127.3, 126.8 (2C), 115.1, 114.2 (2C), 91.9, 58.2, 55.3, 29.7, 15.2.

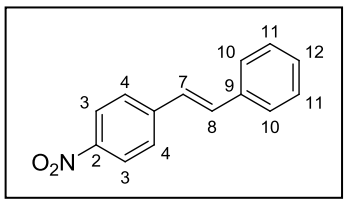
IR (ATR) 2932, 1741, 1667, 1593, 1512, 1422, 1377, 1304, 1243, 1174, 1128, 1111, 1076, 1029, 931, 826, 774, 750, 700, 645, 628, 606, 558.

HRMS for $C_{20}H_{21}O_3$ $[M+H]^+$: 309,37894 Found: 309.15023.

3.17(*E*)-1-Nitro-4-styrylbenzene (101) and (*Z*)-1-Nitro-4-styrylbenzene (102)

Wittig salt **52** (4.5 g, 10.4 mmol) was added to a Na / EtOH solution, which is prepeared by the dissolution of metallic sodium (0.29 g, 12.5 mmol) in 50 mL of EtOH. After the dissolution of all Wittig salt, 4-nitrobenzaldehyde (**100**) (1.43 g, 9.46 mmol) was added to reaction media. The reaction mixture was stirred at room temperature for 24 h. After the evaporation of reaction solvent, water was added and the mixture was extracted with dichloromethane (3×50 mL). The organic extracts were dried over $MgSO_4$. Evaporation of the solvent under the reduced pressure gave the residue, which was then separated by column chromatography on silica gel eluted with hexane. (*E*)-1-Nitro-4-styrylbenzene (**101**) was isolated as a second fraction: yellow needle (crystallized in hexane), 1.36 g (64% crude yield), m.p 159-161 °C (Lit. 157 °C).[32] (Z)-1-Nitro-4-styrylbenzene (**102**) can not be separated. According to crude NMR of the reaction mixture, crude yield of the compound **102** was 36%.

(*E*)-1-Nitro-4-styrylbenzene (101)



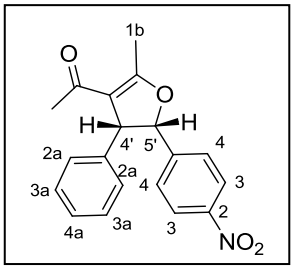
^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.22 (A part of AA'BB' system quasi-d, $J_{3,4}$ = 8.8 Hz, 2H, H-3), 7.6 (B part of AA'BB' system quasi-d, $J_{4,3}$ = 8.8 Hz, 2H, H-4), 7.56 (d, $J_{10,11}$ = 7.2 Hz, 2H, H-10), 7.41 (t, J = 7.3 Hz, 2H, H-11), 7.34 (bt, $J_{12,11}$ = 7.3 Hz, 1H, H-12), 7.27 (A part of AB system d, $J_{8,7}$ = 16.3 Hz, 1H, H-8), 7.14 (B part of AB system d, $J_{7,8}$ = 16.3 Hz, 1H, H-7).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 141.5, 138.6, 130.9, 128.1, 123.7 (2C), 123.6, 121.8 (2C), 121.6 (2C), 121.0, 119.0 (2C).

3.18 1-(2-Methyl-5-(4-nitrophenyl)-4-phenyl-4,5-dihydrofuran-3-yl)ethanone (103) and 1-(2-Methyl-4-(4-nitrophenyl)-5-phenyl-4,5-dihydrofuran-3-yl)ethan one (104)

$Mn(OAc)_3$ (1.163 g,4.33 mmol) was dissolved in 30 mL of glacial acetic acid and the flask was heated to 80 °C under nitrogen. Then a mixture of (*E*)-1-Nitro-4-styrylbenzene (**101**) (0.326 g, 1.4 mmol) and acetylacetone (**56**) (2.89 g, 28.9 mmol) in 50 mL of glacial acetic acid was added dropwise to the $Mn(OAc)_3$ solution. The reaction mixture was stirred for 24 h at 80 °C under nitrogen. The reaction mixture was cooled to the room temperature and saturated $NaHCO_3$ solution was added to the reaction mixture. Then the solution was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent gave the crude product which is column chromatographed on silica gel eluting with(10:1 hexane/EtOAc). 1-(2-Methyl-4-(4-nitrophenyl)-5-phenyl-4,5-dihydro furan-3-yl)ethan one (**103**) was isolated as a first fraction: pale yellow liquid, 0.41 g (90% isolated yield). 1-(2-Methyl-5-(4-nitrophenyl)-4-phenyl-4,5-dihydrofuran-3-yl)ethanone (**104**) was isolated as a second fraction: pale yellow liquid, 0.045 g (10% isolated yield).

1-(2-Methyl-5-(4-nitrophenyl)-4-phenyl-4,5-dihydrofuran-3-yl)ethanone (103)



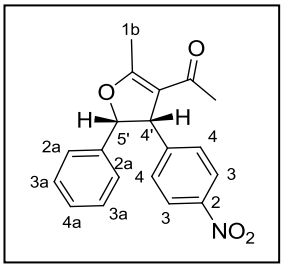
^{1}H-NMR (400 MHz, C_6D_6) δ 7.78 (A part of AA'BB' system quasi-d, $J_{3,4}$ = 8.6 Hz, 2H, H-3), 7.12-7.10 (m, 3H), 7.02 (bd, J = 6.6 Hz, 2H), 6.66 (B part of AA'BB' system quasi-d, $J_{4,3}$ = 8.6 Hz, 2H, H-4), 4.95 (d, $J_{5',4'}$ = 6.2 Hz, 1H, H-5'),4.09 ($J_{4',5'}$ = 6.2 Hz, 1H, H-4'), 2.21 (s, 3H), 1.57 (s, 3H).

^{13}C-NMR (100 MHz, C_6D_6) δ 192.9, 167,3, 147.9, 147.5, 143.0, 129.4 (2C), 128.4, 127.5 (2C), 125.6 (2C), 123.9 (2C), 115.1, 90.2, 58.7, 29.4, 14.5.

IR (ATR) 1715, 1669, 1595, 1517, 1346, 1217, 932, 851, 699.

HRMS for $C_{19}H_{18}NO_4$ $[M+H]^+$: 324.35052 Found: 324.12522

1-(2-Methyl-4-(4-nitrophenyl)-5-phenyl-4,5-dihydrofuran-3-yl)ethanone (104)



^{1}H-NMR (400 MHz, C_6D_6) δ 7.80 (A part of AA'BB' system quasi-d, $J_{3,4}$ = 8.7 Hz, 2H, H-3),7.11 (dd, $J_{2a,3a}$ = 7.4 Hz, $J_{2a,4a}$ = 1.5 Hz, 2H, H-2a), 7.08-7.04(m, 1H), 6.97-6.94 (m, 2H), 6.69 (B part of AA'BB' system quasi-d, $J_{4,3}$ = 8.7 Hz, 2H, H-4), 4.97 (d, $J_{5',4'}$ = 6.2 Hz, 1H, H-5'), 3.90 (dd, $J_{4',5'}$ = 6.2 Hz, $J_{4',1b}$ = 1.2 Hz, 1H, H-4'), 2,30 (d, $J_{1b,4'}$ = 1.2 Hz, 3H, H-1b), 1.6 (s, 3H).

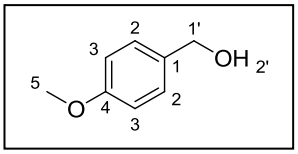
^{13}C-NMR (100 MHz, C_6D_6) δ 192.1, 168.1, 150.3, 147.3, 140.7, 129.0 (2C), 128.7, 128.0 (2C), 125.3 (2C), 124.2 (2C), 115.2, 91.0, 58.2, 29.2, 14.6.

IR (ATR) 1671, 1595, 1518, 1378, 1345, 1314, 1248, 1216, 1189, 1108, 1001, 930, 840, 751, 699, 650, 628

HRMS for $C_{19}H_{18}NO_4$ $[M+H]^+$: 324.35052 Found: 324.12465

3.19 (4-Methoxyphenyl)methanol) (105)

To a solution of $LiAlH_4$ (0.418 g, 0.011 mol) in dry THF (35 mL), 4-methoxybenzaldehyde (**95**) (3.0 g, 0.022 mol) was added drop wise in an ice-bath. After the reaction was stirred for 2 h, the mixture was quenched with sat. NH_4Cl solution. Then the extraction was performed with ethyl acetate (3 × 50mL) and dried over $MgSO_4$. Evaporation of solvent under the reduced pressure gave successively (4-Methoxyphenyl)methanol (**105**) as a colorless liquid, 2.94 g (97% isolated yield).[33]

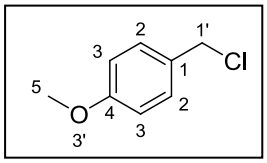


^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.24 (A part of AA'BB' system, quasi-d, $J_{2,3}$ = 8.6 Hz, 2H, H-2), 6.88 (B part of AA'BB' system, quasi-d, $J_{3,2}$ = 8.6 Hz, 2H, H-3), 4.5 (s, 2H, H-1'), 3.78 (s, 3H, H-5), 3.56 (bs, 1H, H-2').

^{13}C-NMR (100 MHz, $CDCl_3$) δ 158.9, 133.3, 128.6 (2C), 113.8 (2C), 64.5, 55.2.

3.20 1-(Chloromethyl)-4-methoxybenzene (106)

To a solution of (4-Methoxyphenyl)methanol (**105**) (2.33 g, 0.0168 mol) in dry CH_2Cl_2 (50 mL), $SOCl_2$ (4.02 g, 0.033 mol) was added slowly. The reaction was stirred for 30 min. After the completion of reaction the evaporation of solvent under the reduced pressure gave successively 1-(chloromethyl)-4-methoxybenzene (**106**) as a light brown liquid, 2.55 g (%97 isolated yield).[34]

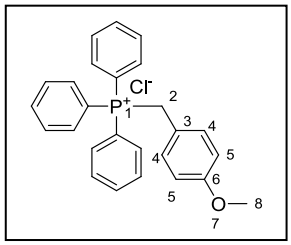


^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32 (A part of AA'BB' system, quasi-d, $J_{2,3}$ = 8.6 Hz, 2H, H-2), 6.88 (B part of AA'BB' system, quasi-d, $J_{3,2}$ = 8.6 Hz, 2H, H-3), 4.53 (s, 2H, H-1'), 3.79 (s, 3H, H-5).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.8, 130.2 (2C), 129.8, 114.2 (2C), 55.3, 45.4.

3.21 (4-Methoxybenzyl)triphenylphosphonium chloride (107)

Triphenylphosphine (**51**) (25 g, 0.095mol) was added to a solution of (**106**) (17.5 g, 0.112 mol) in toluene (250 mL). The mixture was heated to reflux for 6 h and then cooled to room temperature. The product was collected, recrystallized from ethanol-hexane mixture and 33.4 g (84% isolated yield) of (**107**) was collected as a white cubic crystals. M.p: 245-247 °C (Lit. 241-243 °C). [35]



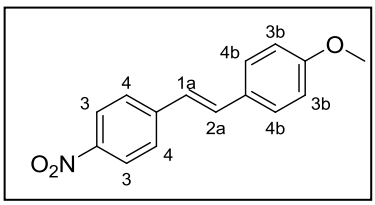
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.79-7.71 (m, 9H), 7.66-7.62 (m, 6H), 7.01 (dd, J = 8.7 Hz, J = 2.5 Hz, 2H), 6.66 (d, $J_{5,4}$ = 8.4 Hz, 2H, H-5), 5.36 (d, $J_{2,1}$ = 13.8 Hz, 2H, H-2), 3.73 (s, 3H, H-8).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.6, 134.9 (3C), 134.4 (6C), 132.7 (2C), 130.2 (6C), 118.6 , 117.9 (3C), 114.2 (2C), 55.2, 29.9.

3.22 (*E*)-1-Methoxy-4-(4-nitrostyryl)benzene (108) and (*Z*)-1-Methoxy-4-(4-nitro styryl)benzene (109)

(4-methoxybenzyl)triphenylphosphonium chloride (**107**) (4.35 g, 10.4 mmol) was added to a Na / EtOH solution, which is prepeared by the dissolution of metallic sodium (0.29 g, 12.5 mmol) in 50 mL of EtOH. After the dissolution of all Wittig salt **107**, 4-nitrobenzaldehyde (**100**) (1.43 g, 9.46 mmol) was added to reaction media. The reaction mixture was stirred at room temperature for 24 h. After the evaporation of reaction solvent, water was added and the mixture was extracted with dichloromethane (3 × 50 mL). The organic extracts were dried over $MgSO_4$. Evaporation of the solvent under the reduced pressure gave the residue, which was then separated by column chromatography on silica gel eluted with hexane. (*E*)-1-Methoxy-4-(4-nitrostyryl)benzene (**108**) was isolated as a second fraction: yellow needle (crystallized in hexane), 1.75 g (73% crude yield), m.p 135-137 °C (Lit. 130-131 °C).[36] (*Z*)-1-methoxy-4-(4-nitrostyryl)benzene (**109**) could not be separated. According to the crude NMR of the reaction mixture, the crude yield of the compound **109** was 27%.

(*E*)-1-methoxy-4-(4-nitrostyryl)benzene (108)

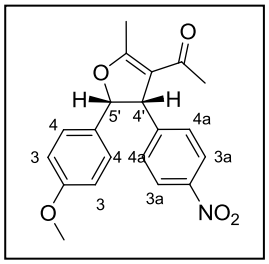


^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.13 (A part of AA'BB' system quasi-d, $J_{3,4}$ = 8.8 Hz, 2H, H-3), 7.52 (B part of AA'BB' system quasi-d, $J_{4,3}$ = 8.8 Hz, 2H, H-4), 7.43 (A part of AA'BB' system quasi-d, $J_{4b,3b}$ = 8.7 Hz, 2H, H-4b), 7.15 (A part of AB system d, $J_{2a,1a}$ = 16.3 Hz, 1H, H-2a), 6.93 (B part of AB system d, $J_{1a,2a}$ = 16.3 Hz, 1H, H-1a), 6.86 (B part of AA'BB' system quasi-d, $J_{3b,4b}$ = 8.7 Hz, 2H, H-3b), 3.78 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 160.3, 146.5, 144.3, 132.9, 128.9, 128.4 (2C), 126.5 (2C), 124.2 (2C), 124.1, 114.4 (2C), 55.4.

3.23 1-(5-(4-Methoxyphenyl)-2-methyl-4-(4-nitrophenyl)-4,5-dihydrofuran-3-yl) ethanone (110)

$Mn(OAc)_3$ (0.80 g, 2.98 mmol) was dissolved in 30 mL of glacial acetic acid and the flask was heated to 80 °C under nitrogen. Then a mixture of (*E*)-1-methoxy-4-(4-nitrostyryl)benzene (**108**) (0.254 g, 0.995 mmol) and acetylacetone (**56**) (1.99 g, 19.87 mmol) in 50 mL of glacial acetic acid was added dropwise to the $Mn(OAc)_3$ solution. The reaction mixture was stirred for 24 h at 80 °C under nitrogen. The reaction mixture was cooled to the room temperature and saturated $NaHCO_3$ solution was added to the reaction mixture. Then the solution was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent gave the crude product which was column chromatographed on silica gel eluting with (10:1 hexane/EtOAc) to yield 1-(5-(4-methoxyphenyl)-2-methyl-4-(4-nitrophenyl)-4,5-dihydrofuran-3-yl)ethanone (**110**) as a pale yellow liquid (312 mg, 89% isolated yield).



^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.12 (A part of AA'BB' system quasi-d, $J_{3a,4a}$ = 8.7 Hz, 2H, H-3a), 7.30 (B part of AA'BB' system quasi-d, $J_{4a,3a}$ = 8.7 Hz, 2H, H-4a), 7.11 (A part of AA'BB' system quasi-d, $J_{4,3}$ = 8.7 Hz, 2H, H-4), 6.84 (B part of AA'BB' system quasi-d, $J_{3,4}$= 8.7 Hz, 2H, H-3) 5.17 (d, $J_{5',4'}$ = 6.2 Hz, 1H, H-5'), 4.38 (d, $J_{4',5'}$ = 6.2 Hz, 1H, H-4'), 3.74 (s, 3H), 2.39 (s, 3H), 1.94 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 194.0, 169.5, 160.1, 150.8, 147.2, 131.9, 128.3(2C), 126.9 (2C), 124.3 (2C), 115.6, 114.4 (2C), 91.2, 57.8, 55.4, 29.5, 15.4.

IR (ATR) 2935, 2837, 1711, 1670, 1596, 1513, 1462, 1418, 1305, 1244, 1175, 1109, 1077, 1030, 982, 931, 851, 824, 767,745, 693, 631, 617.

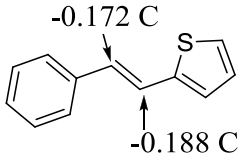
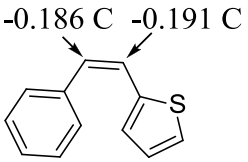
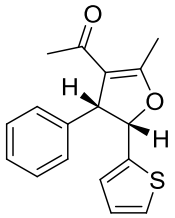
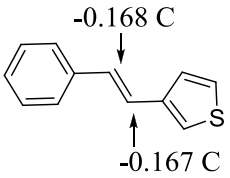
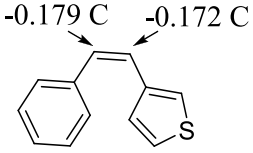
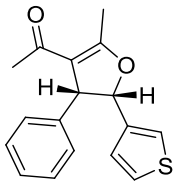
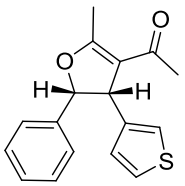
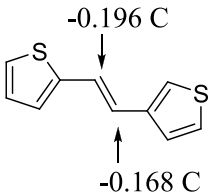
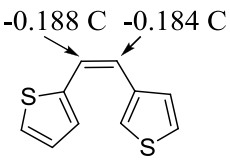
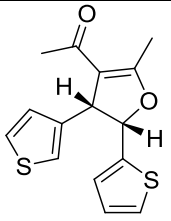
HRMS for $C_{17}H_{16}O_2S$ $[M+H]^+$: 354.37650. Found: 354.13519

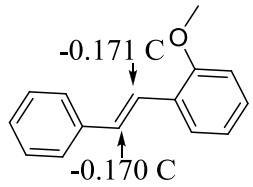
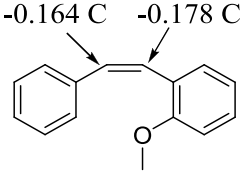
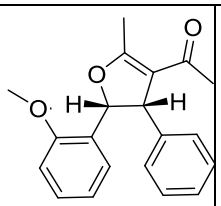
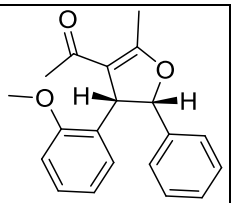
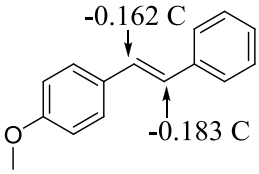
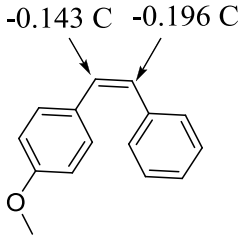
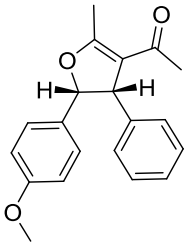
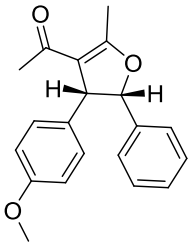
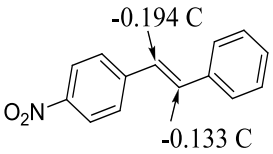
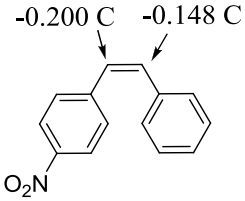
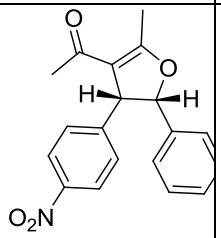
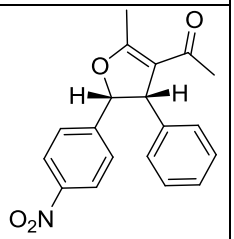
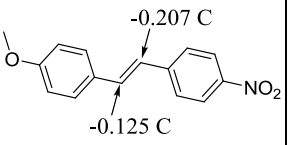
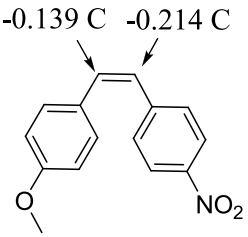
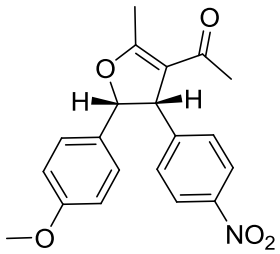
CHAPTER 4

CONCLUSION

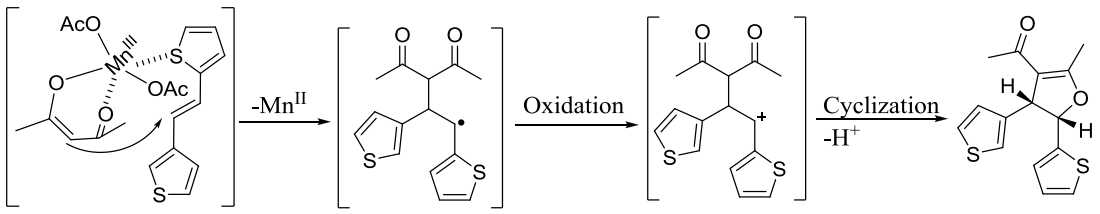
Radical cyclization of alkenes is one of the most important methods for the synthesis of cyclic compounds. In our study, in the presence of $Mn(OAc)_3$ active methylene compound was added to benzene and thiophene substituted alkenes and cyclization products were formed.

Table 1: Starting alkenes and cyclization product(s)

No	Alkene		Product(s)	
1	 **54**	 **55**	 **57** (77%)	
2	 **63**	 **64**	 **65** (66%)	 **66** (33%)
3	 **74**	 **75**	 **76** (83%)	

4	 **88**	 **89**	 **90** (64%)	 **91** (36%)
5	 **96**	 **97**	 **98** (79%)	 **99** (21%)
6	 **101**	 **102**	 **103** (89%)	 **104** (10%)
7	 **108**	 **109**	 **110** (89%)	

In the first part, directing effect of the sulfur atom on the regioselective addition of active methyelene compound to the benzene and thiophene substituted alkenes were studied. For the cases, in which the thiophene ring bonded to the olefine at C-2 position (Entry No: 1, 3) and for the ortho methoxy substituted stilbene derivative (Entry No: 4) complex formation is proposed and complex formation has the dominating effect on the formation of single regioisomer or product distribution.



78 **79** **80** **76**

For the case, in which the thiophene ring bonded to the olefine at C-3 position (Entry No:2) formation of two regioisomer observed. To search the reason for the formation of two regioisomeric cyclization products and their formation ratio, natural bond orbital (NBO) analysis were done to see whether the electron density on the olefinic carbon atoms have any affect on the reaction mechanism or not. For this reason, electron density on olefinic carbon atoms was changed by introducing electron-donating and electron-withdrawing groups to the benzene ring (Entry No: 5, 6 and 7) and the same reaction pathway was applied to these alkenes. Also NBO analysis were done for these molecules. According to the theoretical and experimental results; for the cases in which complex formation is hindered because of geometrical restrictions, electron density on olefinic carbon atoms have dominating effect on reaction mechanism and major cyclization product forms with the addition of radical to the electron rich olefinic carbon atom

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APPENDICES

SPECTRAL DATA

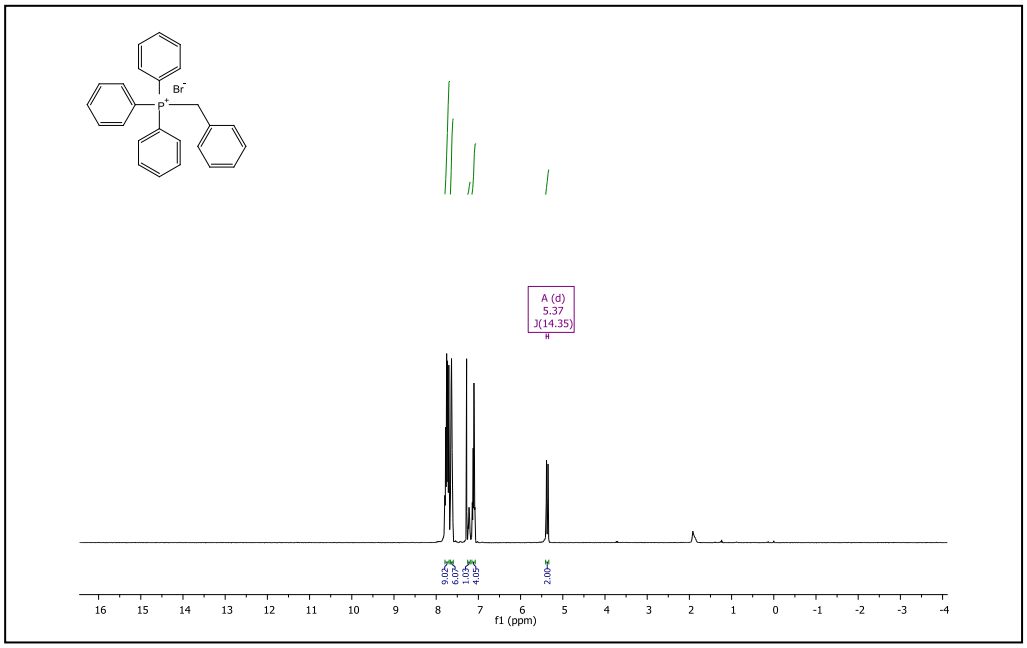

Figure A 1 ^{1}H NMR spectrum of compound **52**

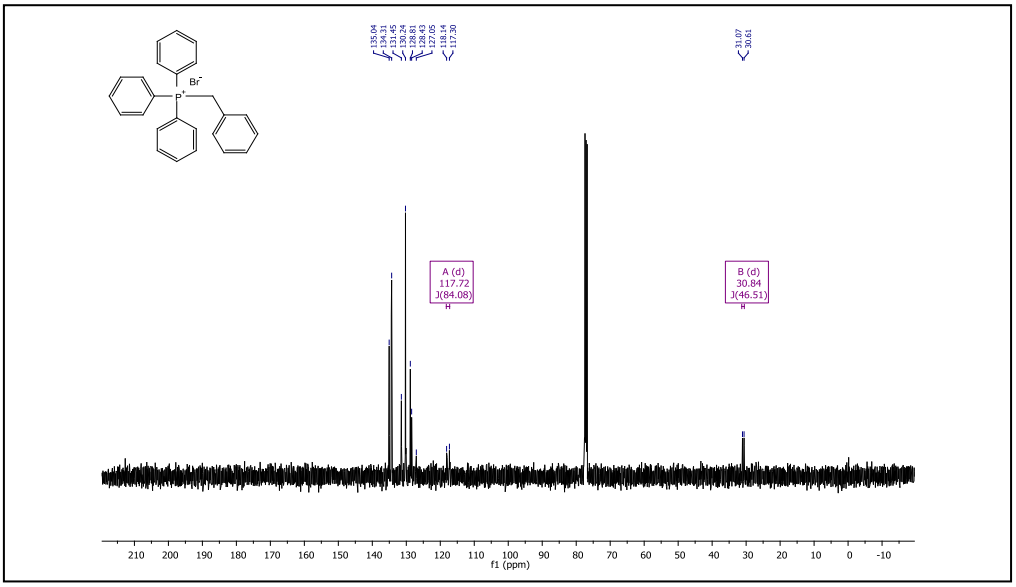

Figure A 2 ^{13}C NMR spectrum of compound **52**

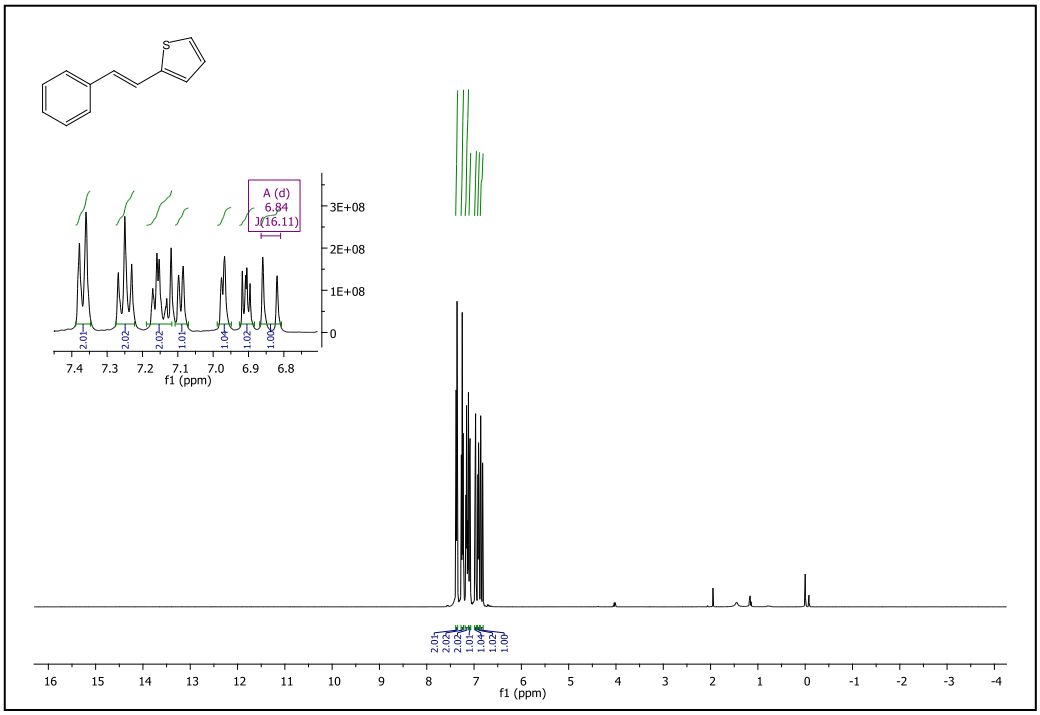

Figure A 3 ^{1}H NMR spectrum of compound **54**

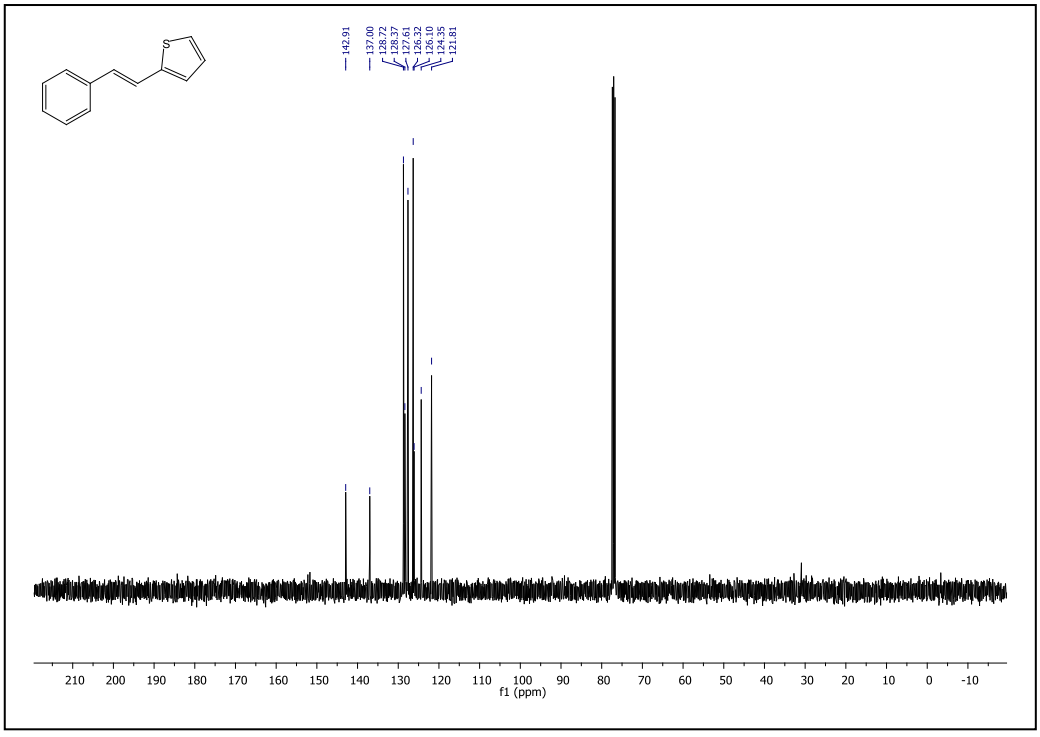

Figure A 4 ^{13}C NMR spectrum of compound **54**

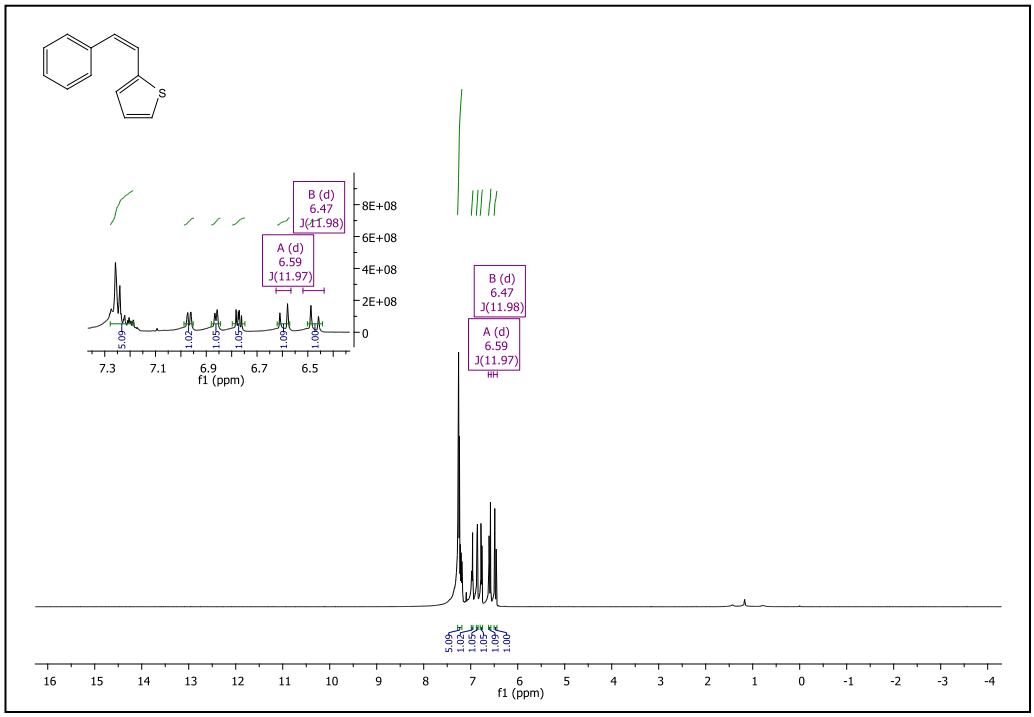

Figure A 5 ^{1}H NMR spectrum of compound **55**

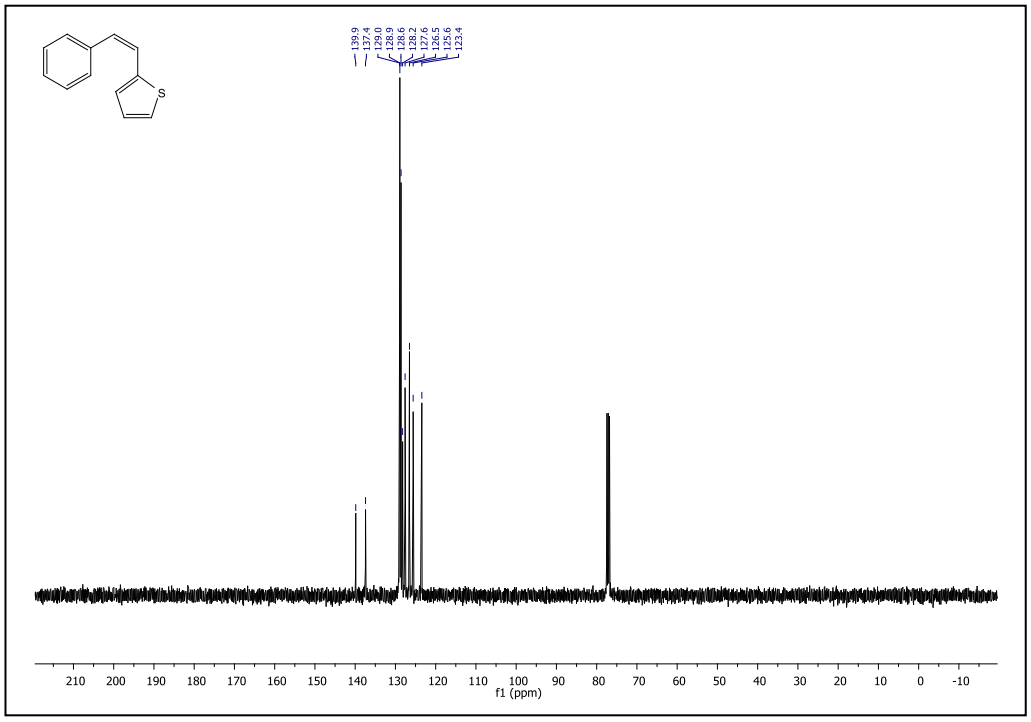

Figure A 6 ^{13}C NMR spectrum of compound **55**

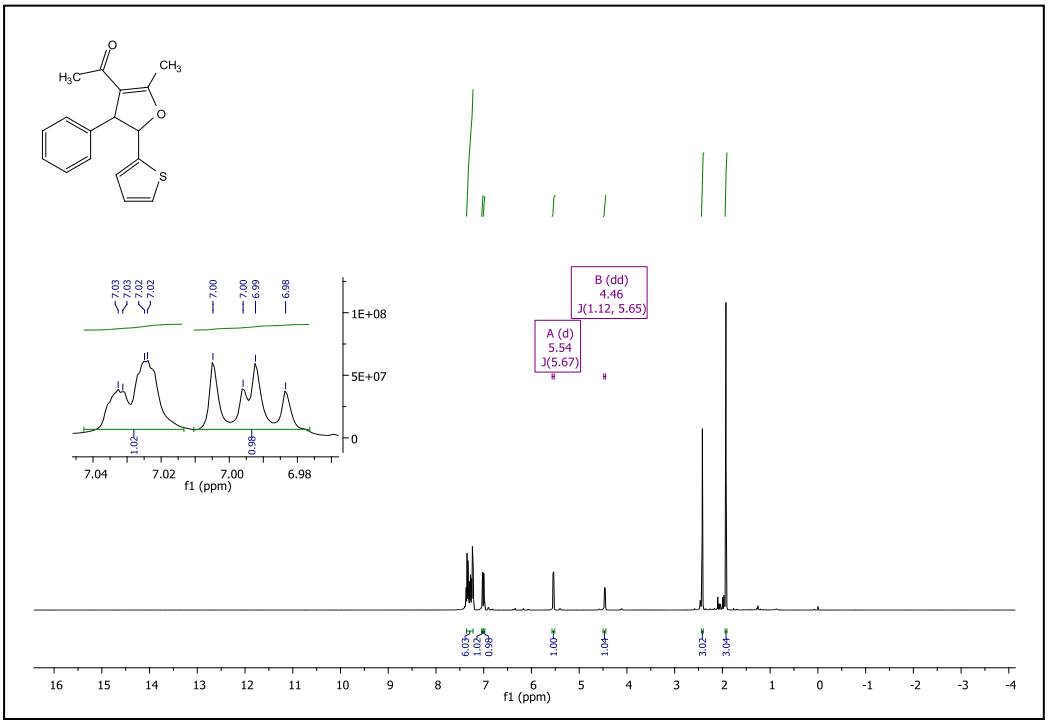

Figure A 7 ^{1}H NMR spectrum of compound **57**

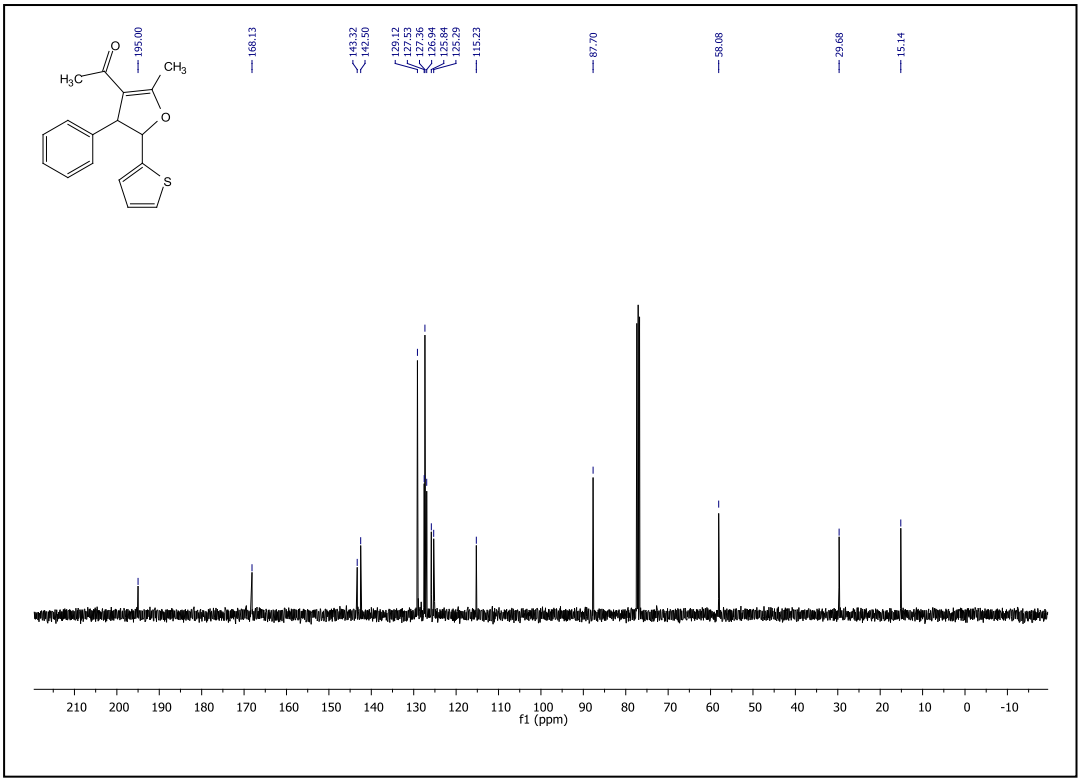

Figure A 8 ^{13}C NMR spectrum of compound **57**

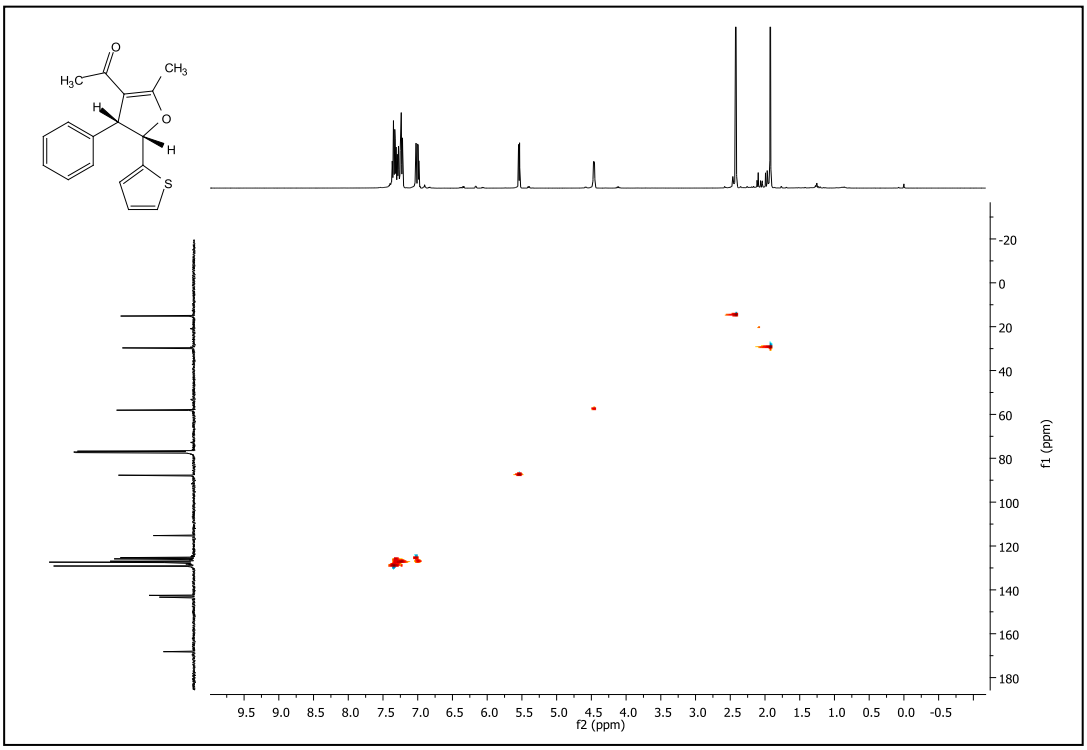

Figure A 9 HSQC spectrum of compound **57**

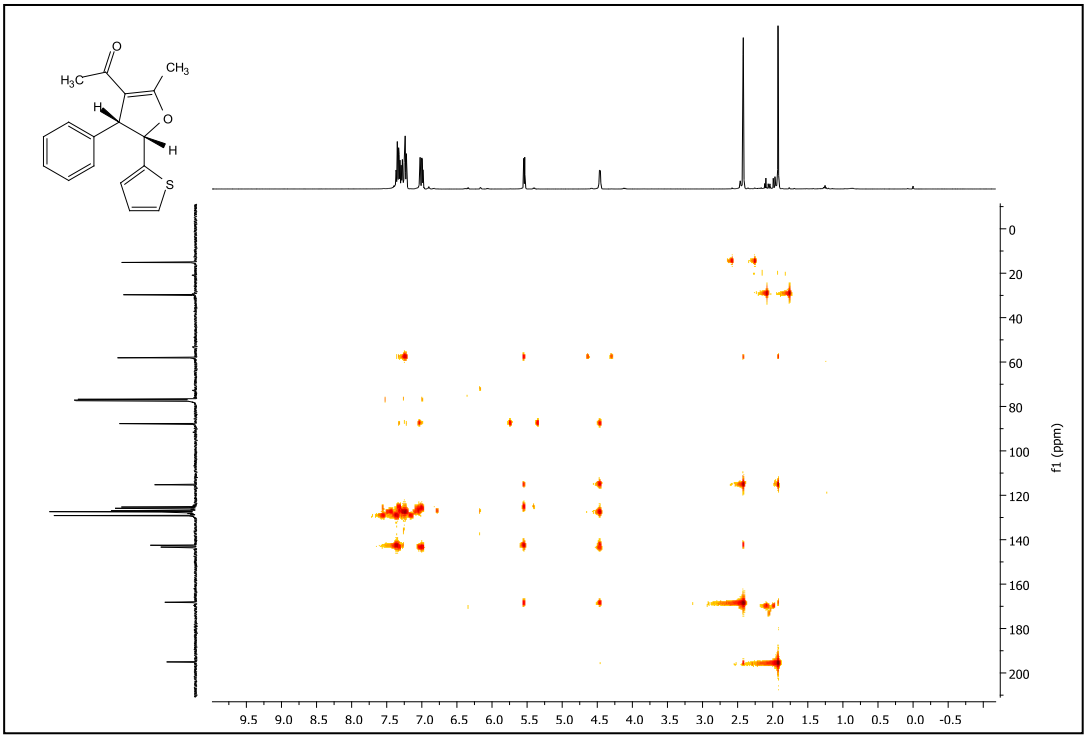

Figure A 10 HMBC spectrum of compound **57**

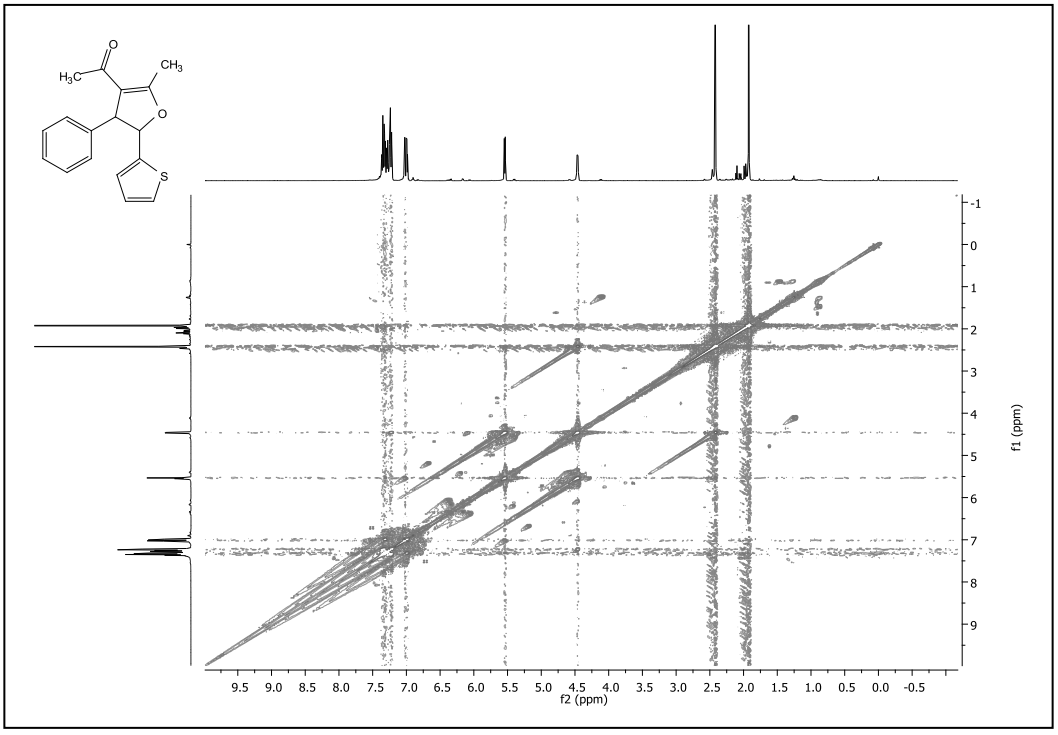

Figure A 11 COSY spectrum of compound **57**

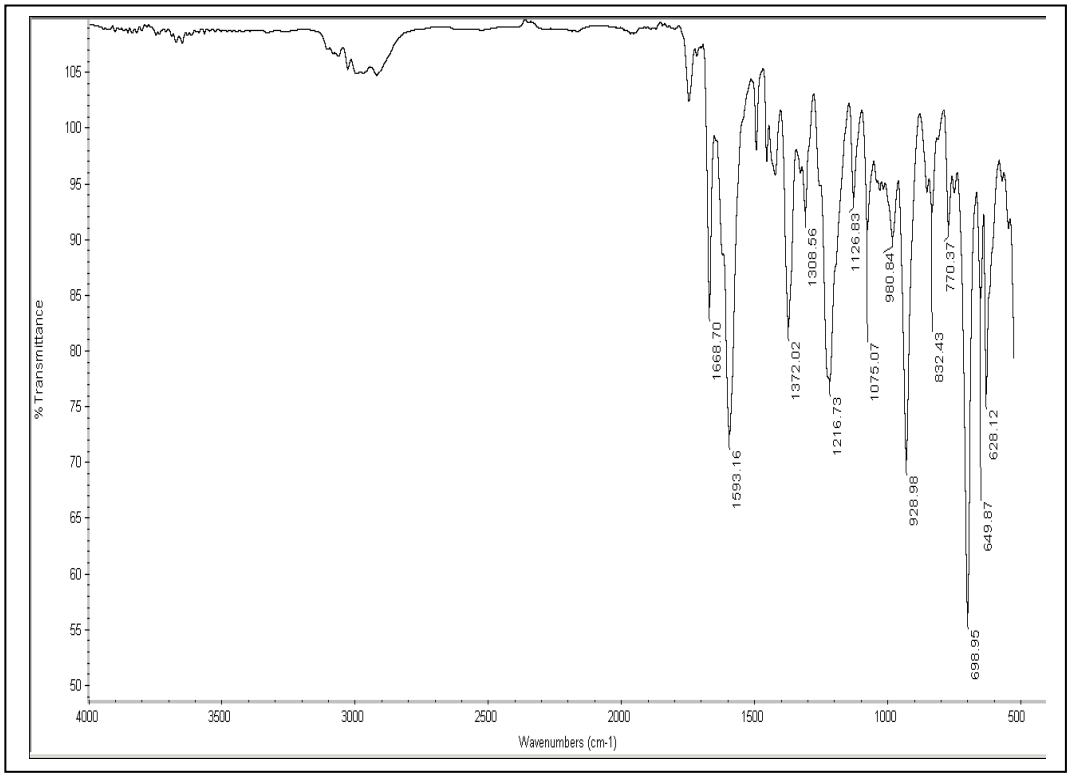

Figure A 12 IR spectrum of compound **57**

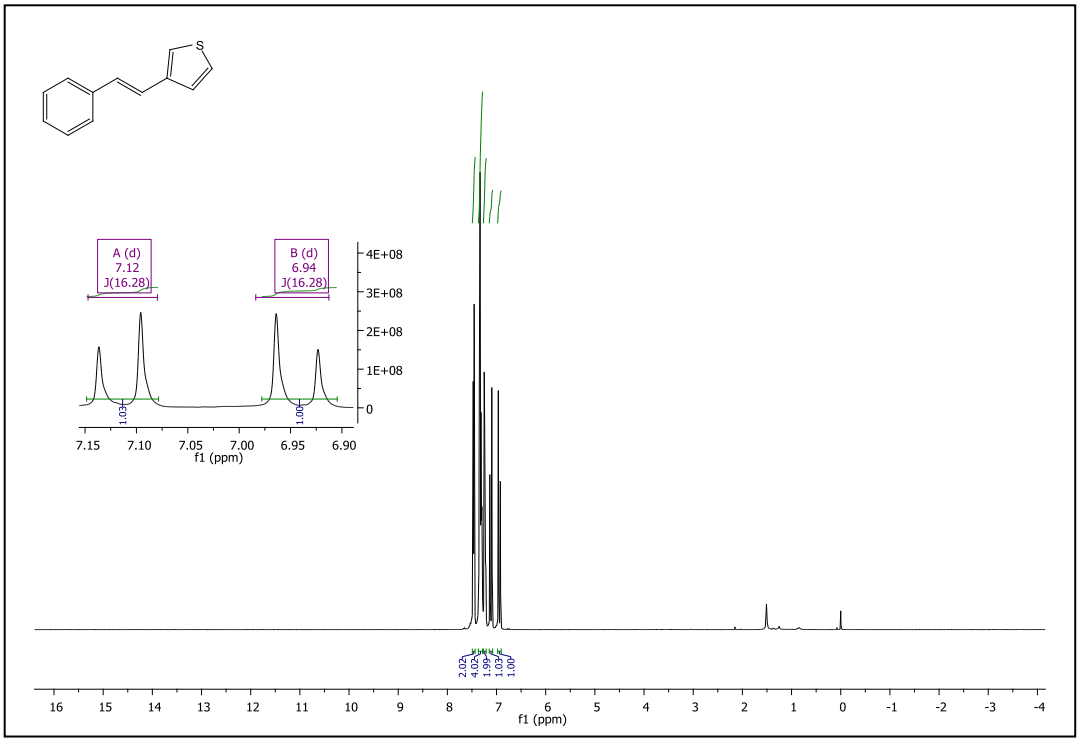

Figure A 13 ^{1}H NMR spectrum of compound **63**

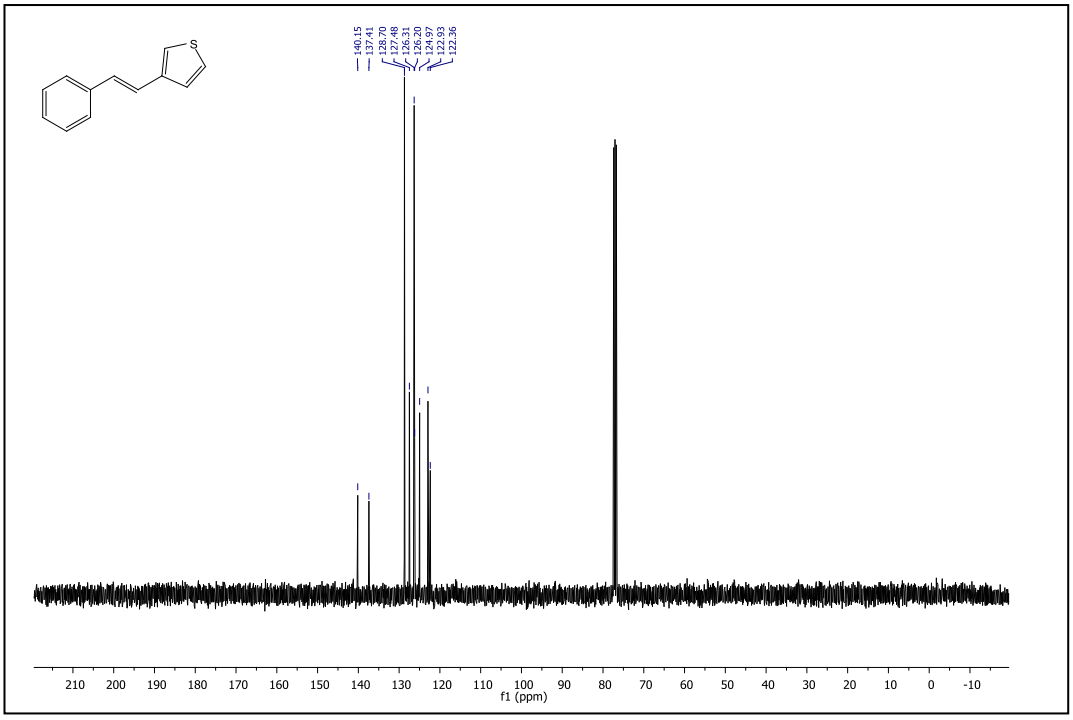

Figure A 14 ^{13}C NMR spectrum of compound **63**

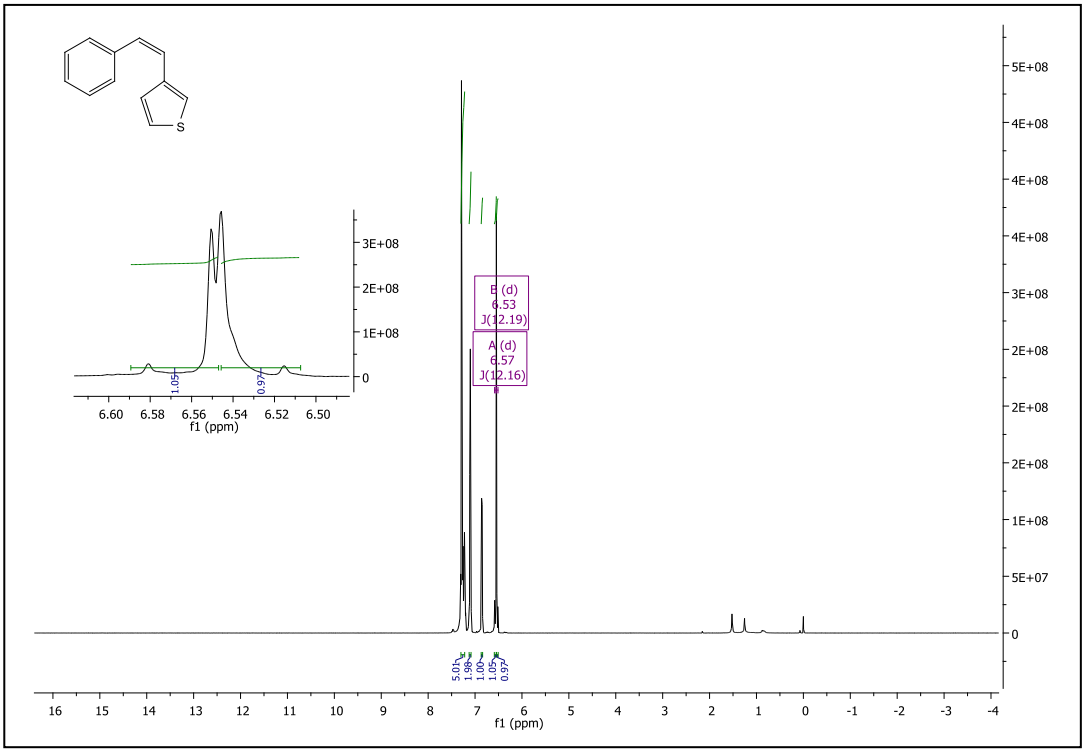

Figure A 15 ^{1}H NMR spectrum of compound **64**

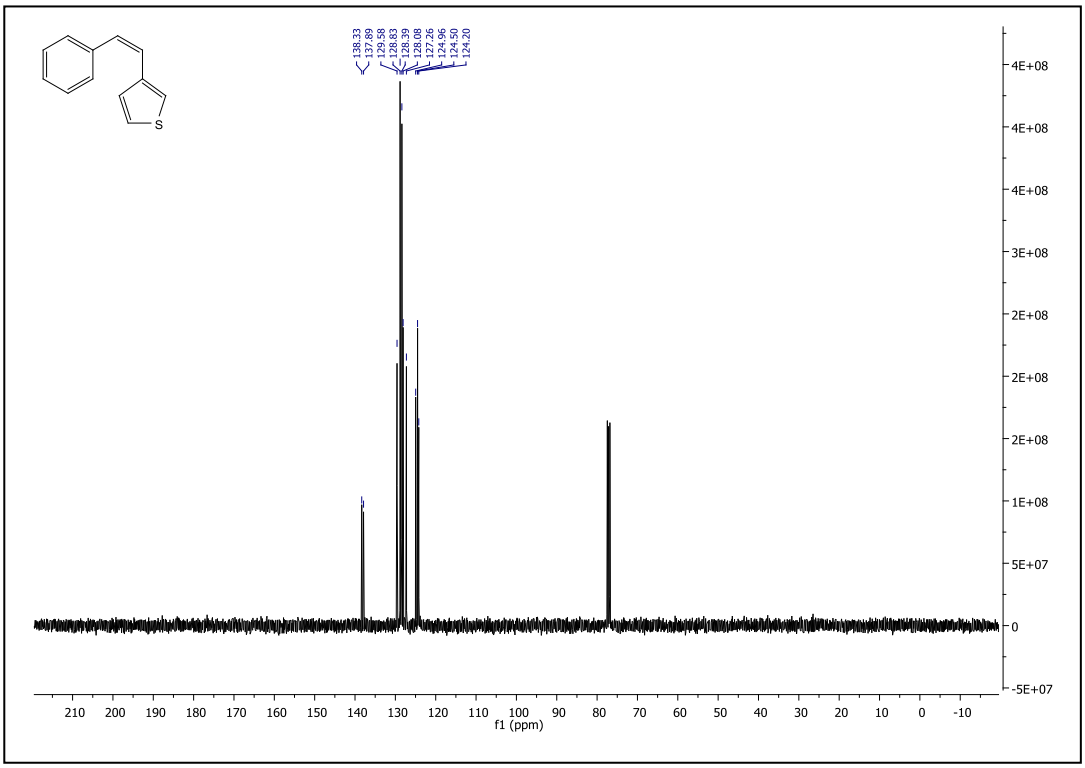

Figure A 16 ^{13}C NMR spectrum of compound **64**

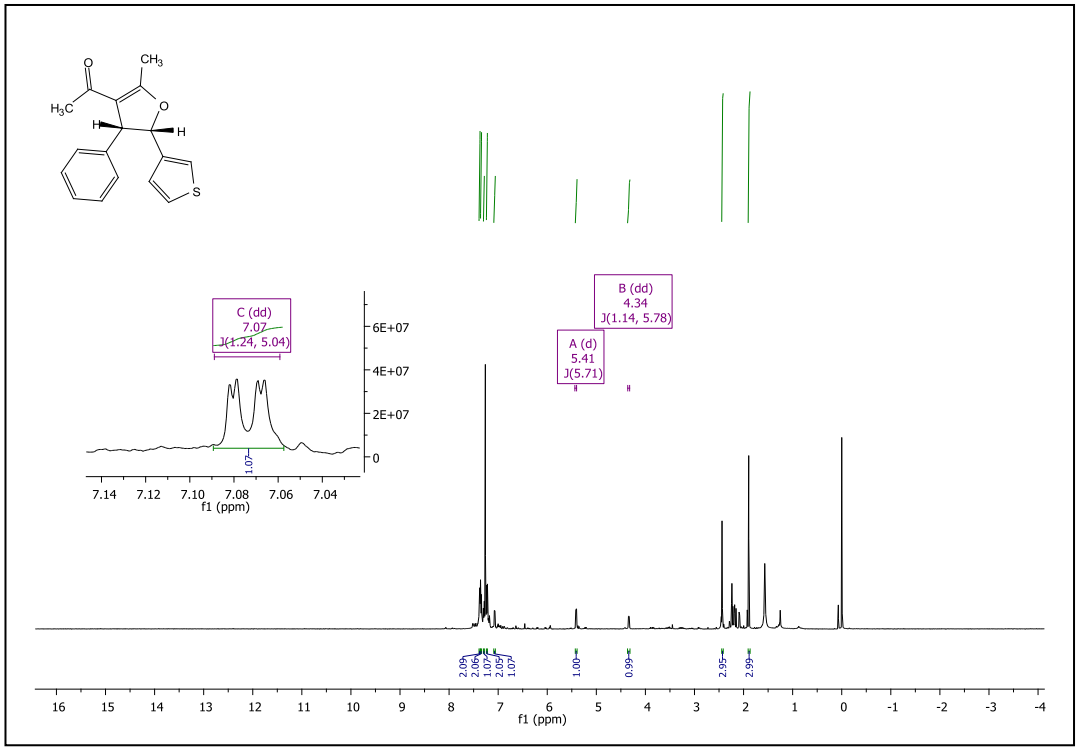

Figure A 17 ^{1}H NMR spectrum of compound **65**

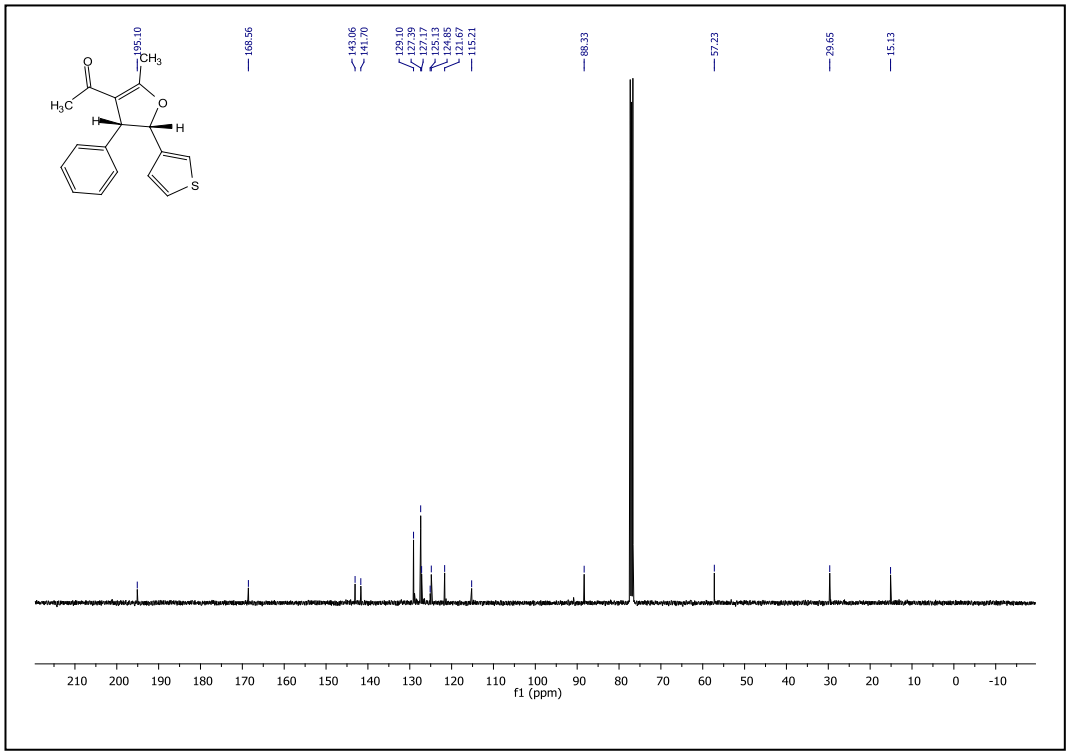

Figure A 18 ^{13}C NMR spectrum of compound **65**

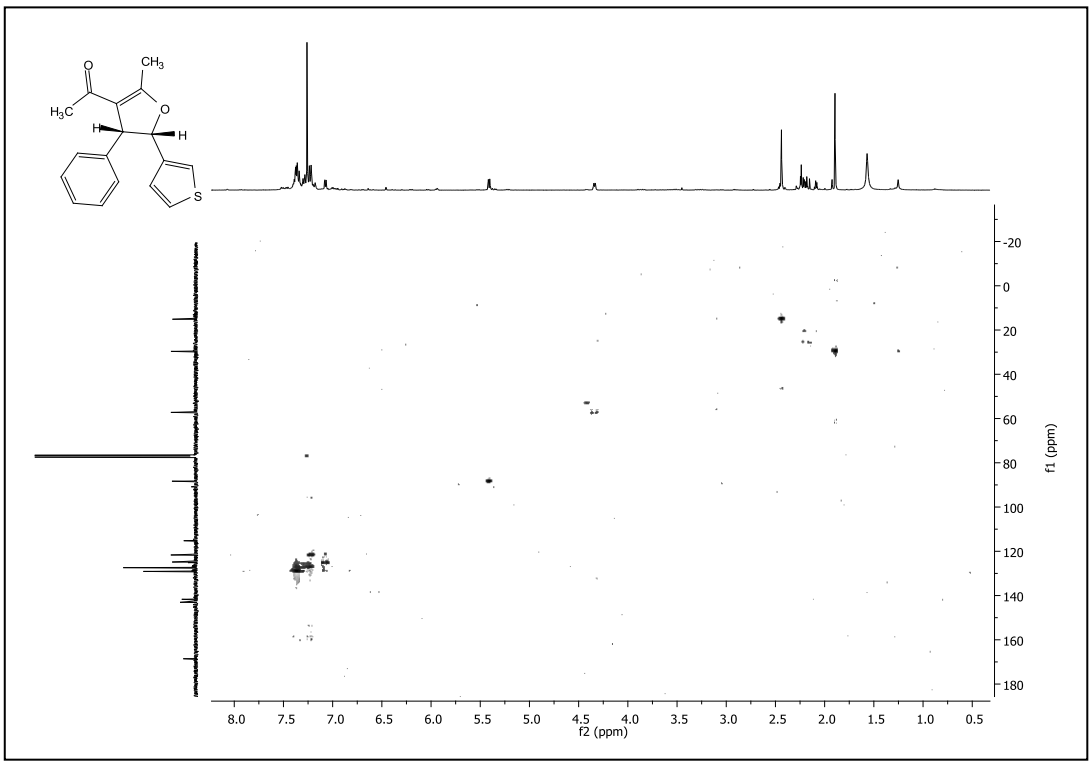

Figure A 19 HSQC spectrum of compound **65**

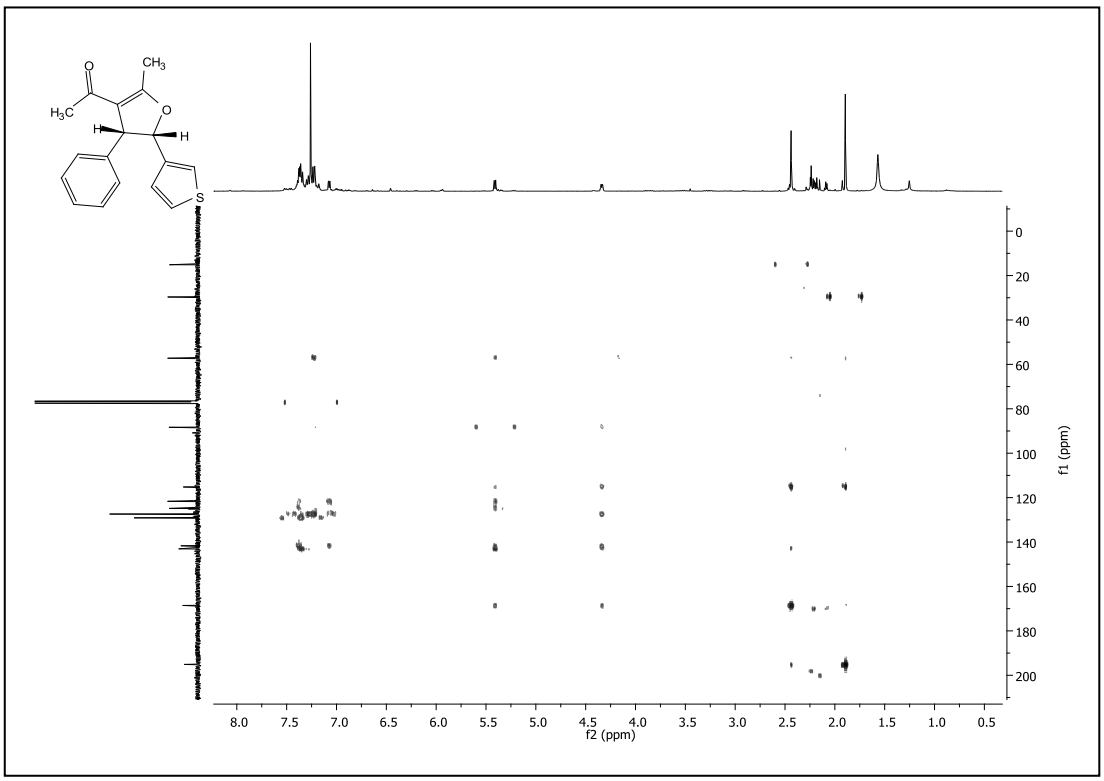

Figure A 20 HMBC spectrum of compound **65**

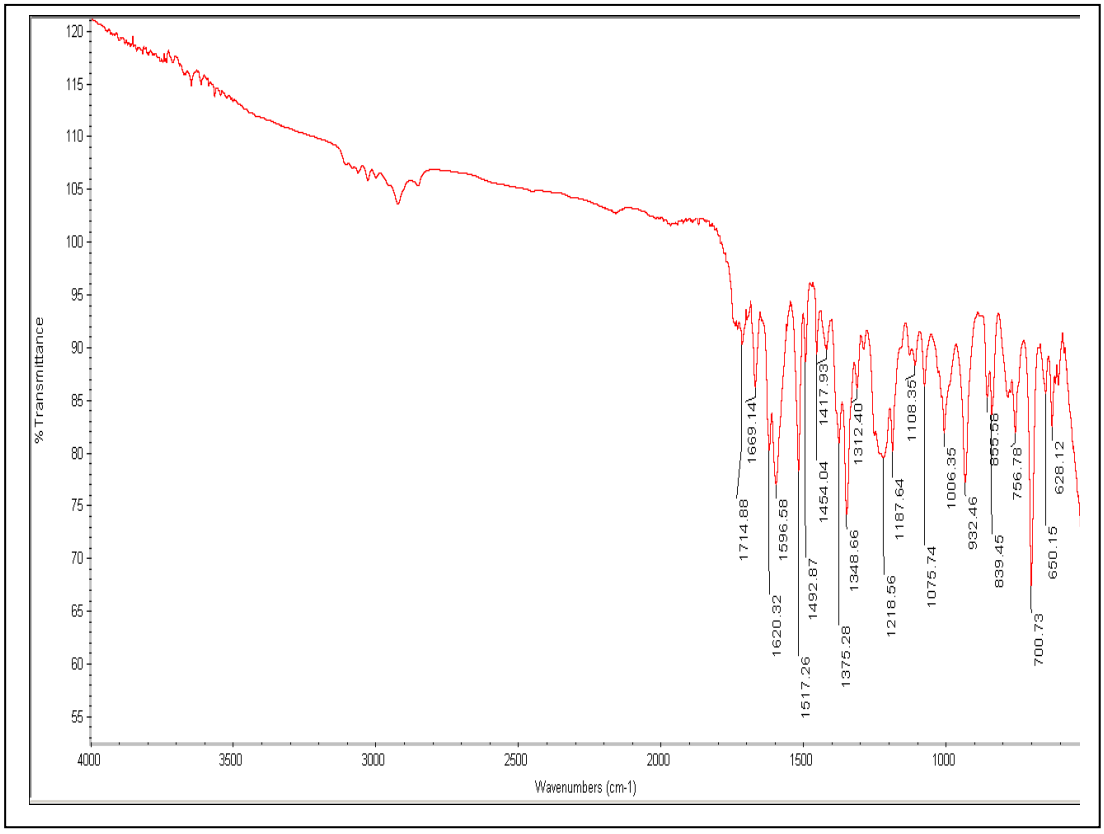

Figure A 21 IR spectrum of compound **65**

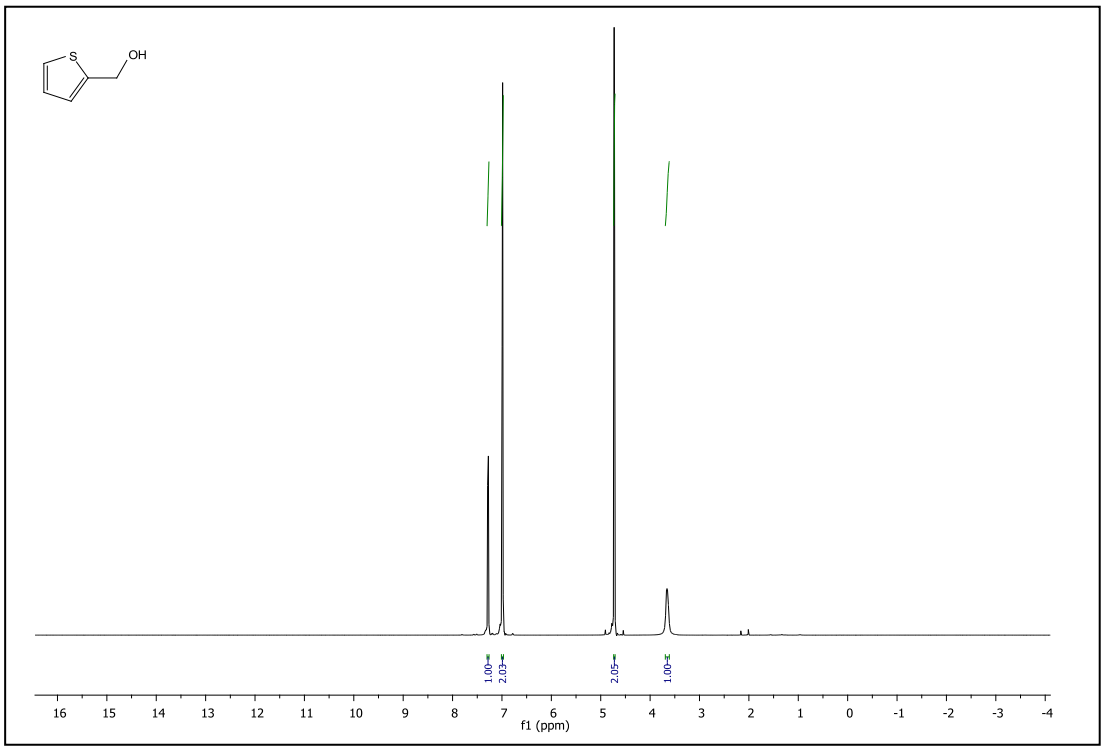

Figure A 22 ^{1}H NMR spectrum of compound **71**

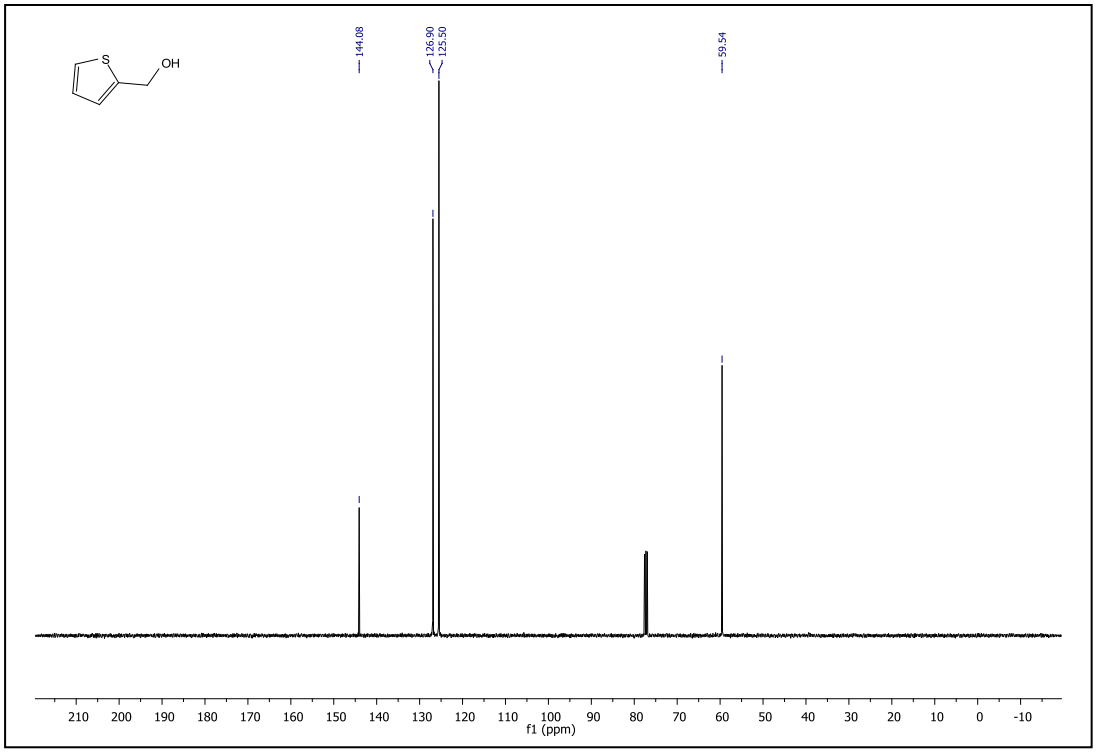

Figure A 23 ^{13}C NMR spectrum of compound **71**

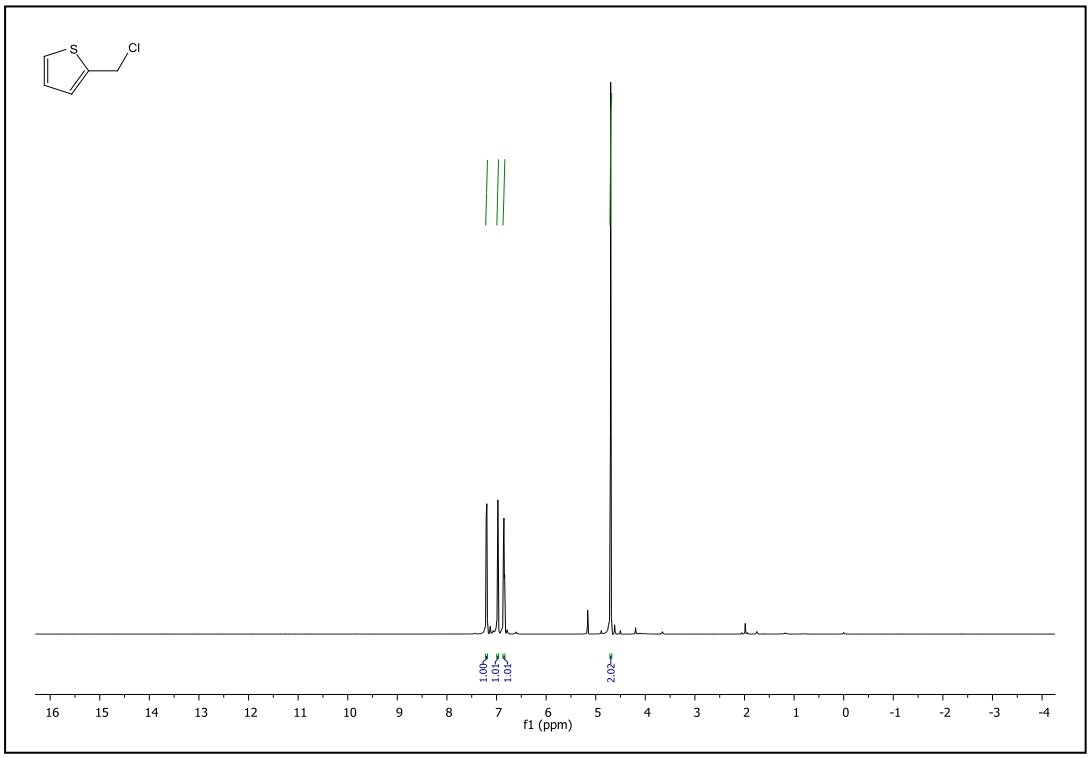

Figure A 24 ^{1}H NMR spectrum of compound **72**

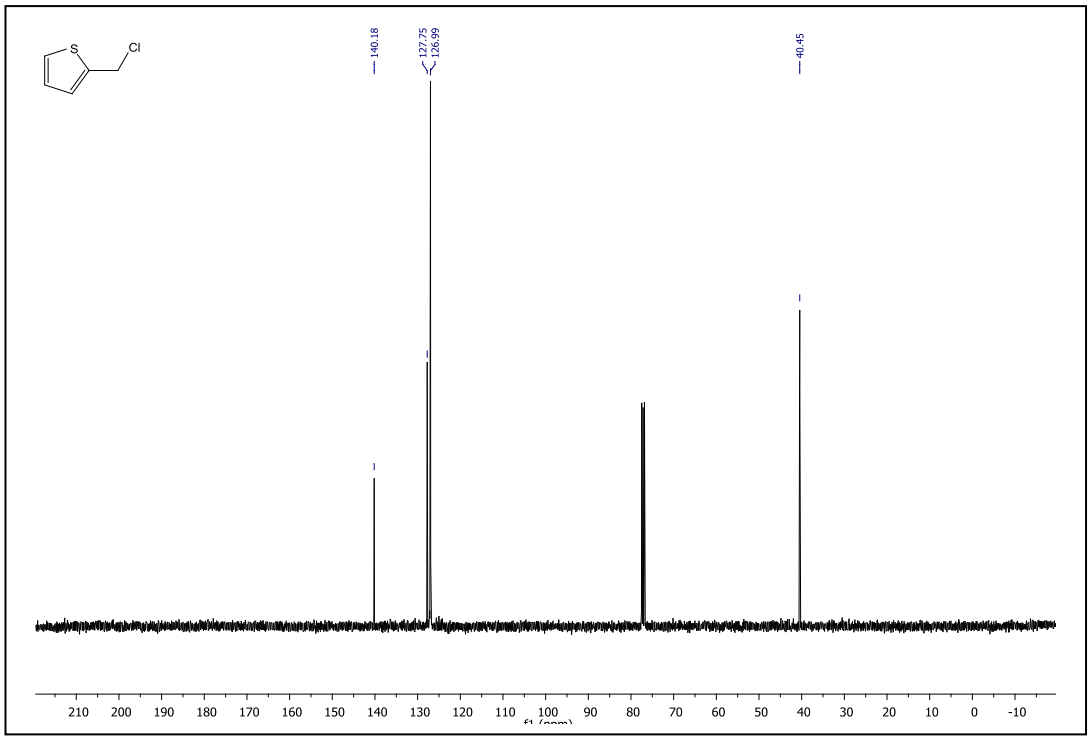

Figure A 25 ^{13}C NMR spectrum of compound **72**

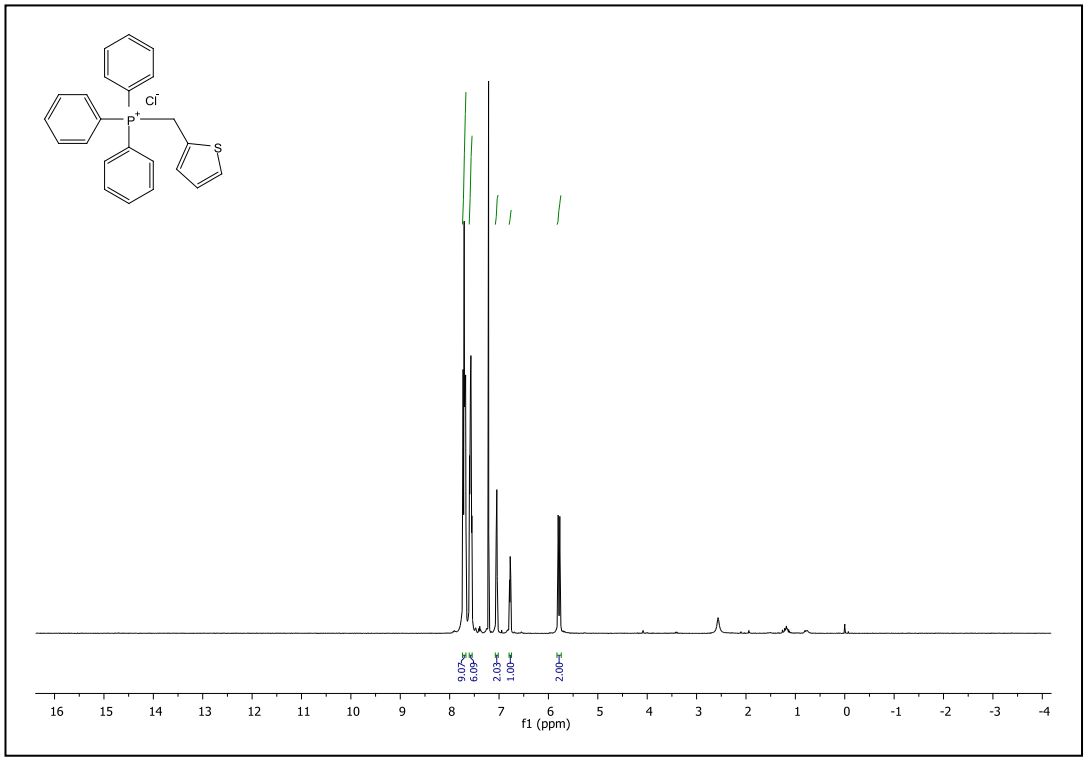

Figure A 26 ^{1}H NMR spectrum of compound **73**

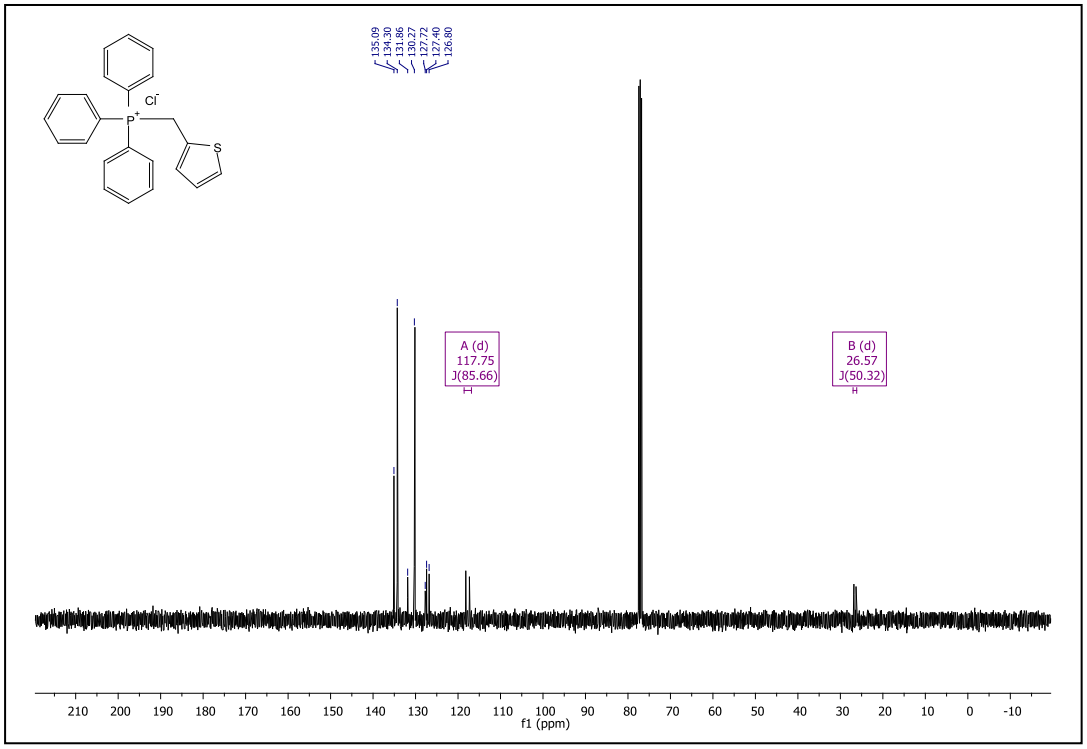

Figure A 27 ^{13}C NMR spectrum of compound **73**

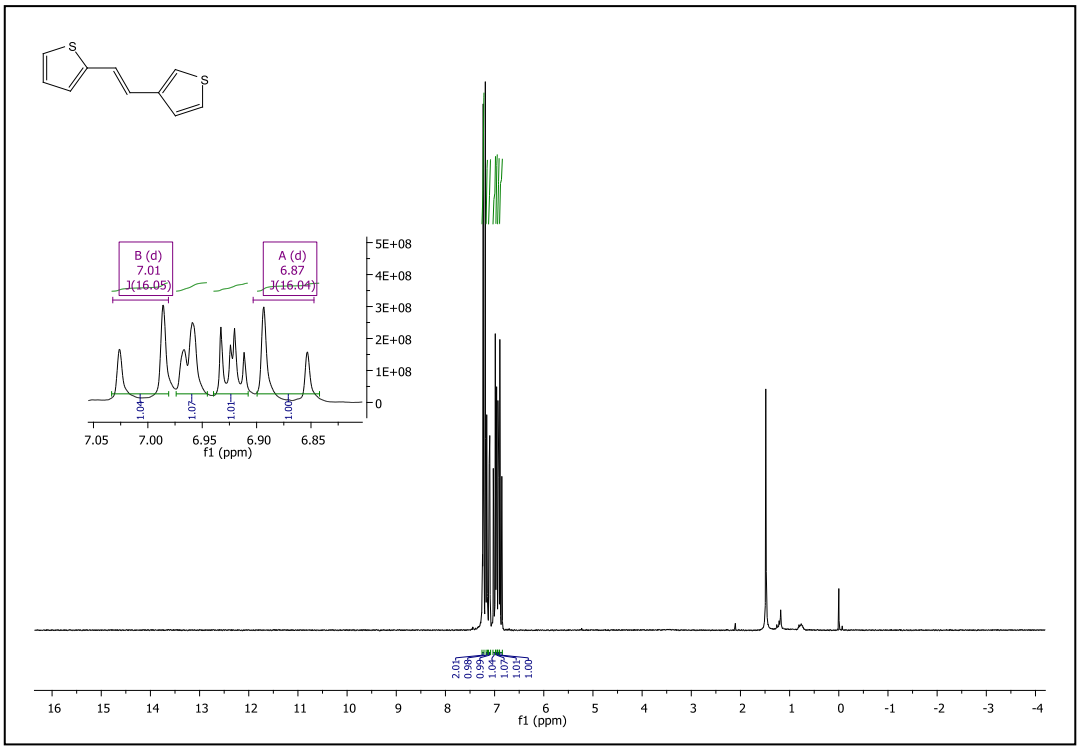

Figure A 28 ^{1}H NMR spectrum of compound **74**

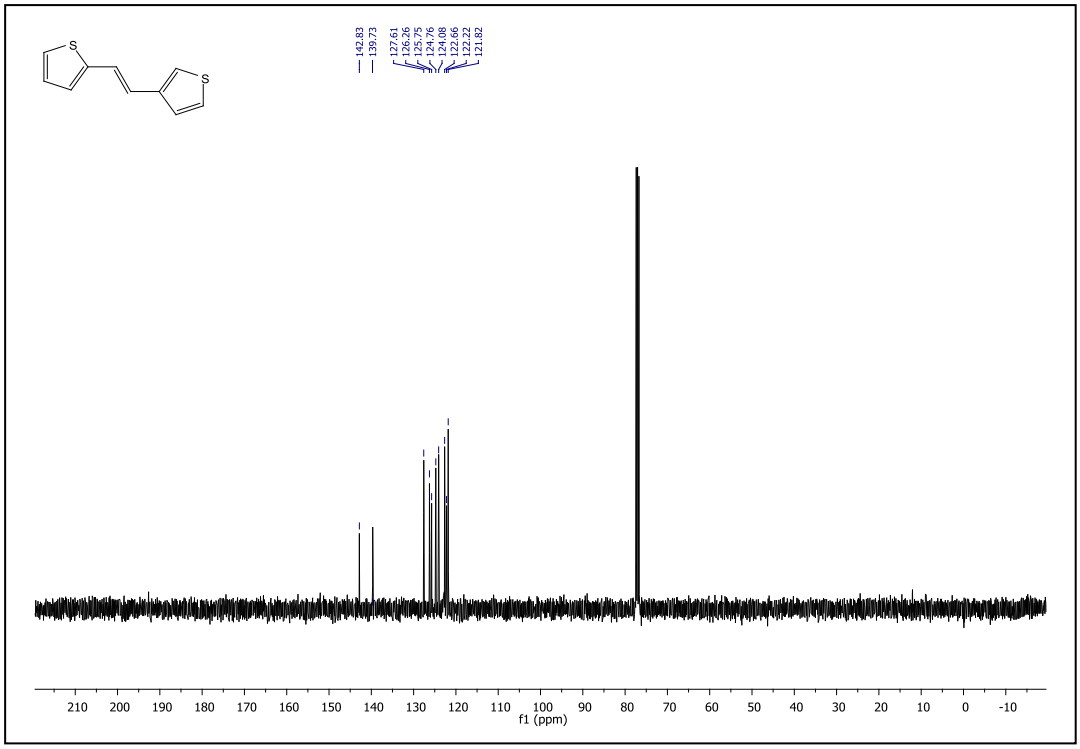

Figure A 29 ^{13}C NMR spectrum of compound **74**

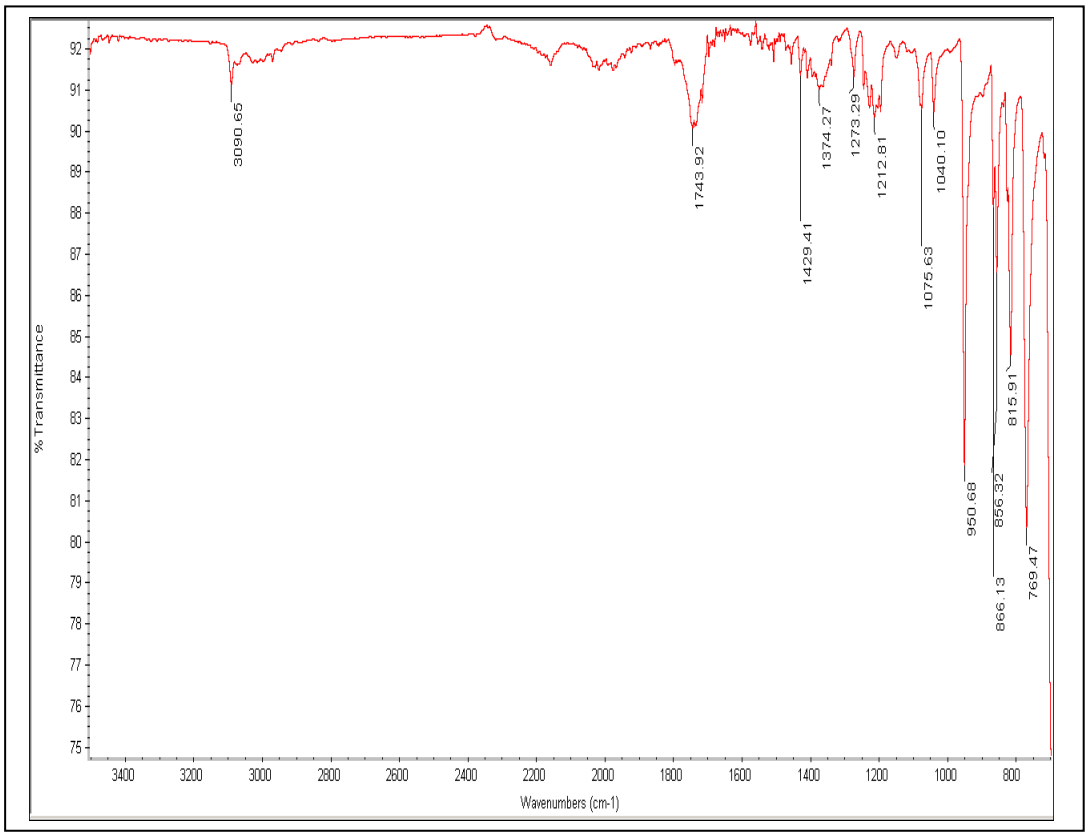

Figure A 30 IR spectrum of compound **74**

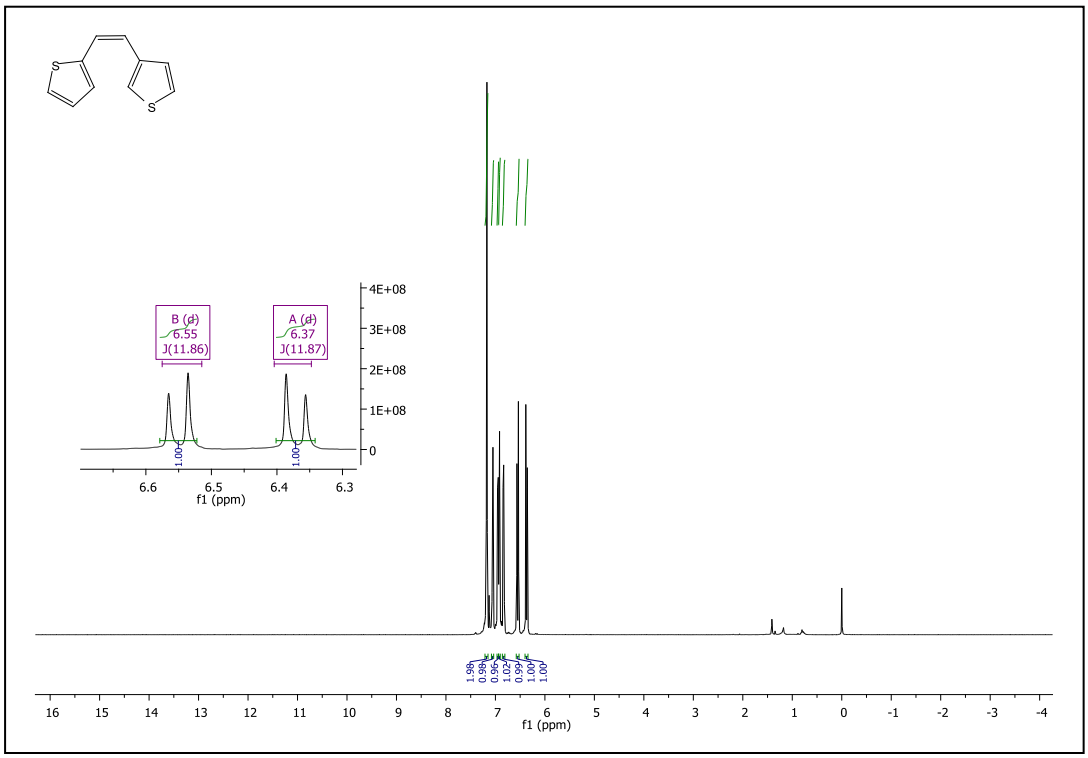

Figure A 31 ^{1}H NMR spectrum of compound **75**

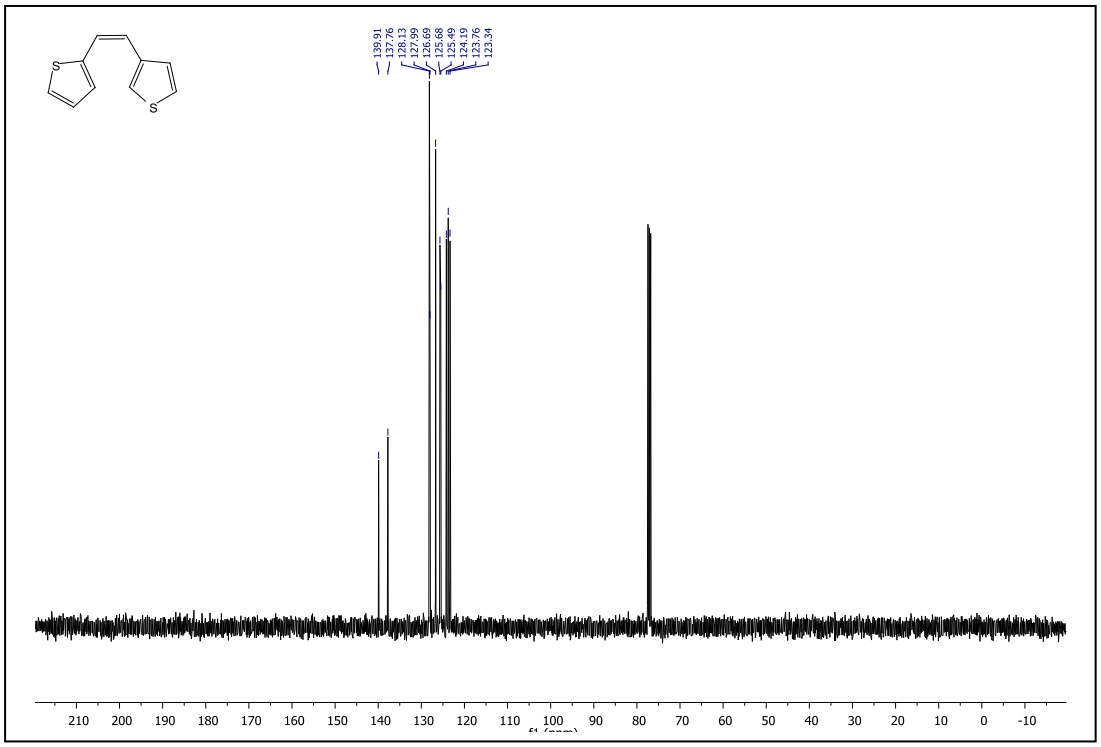

Figure A 32 ^{13}C NMR spectrum of compound **75**

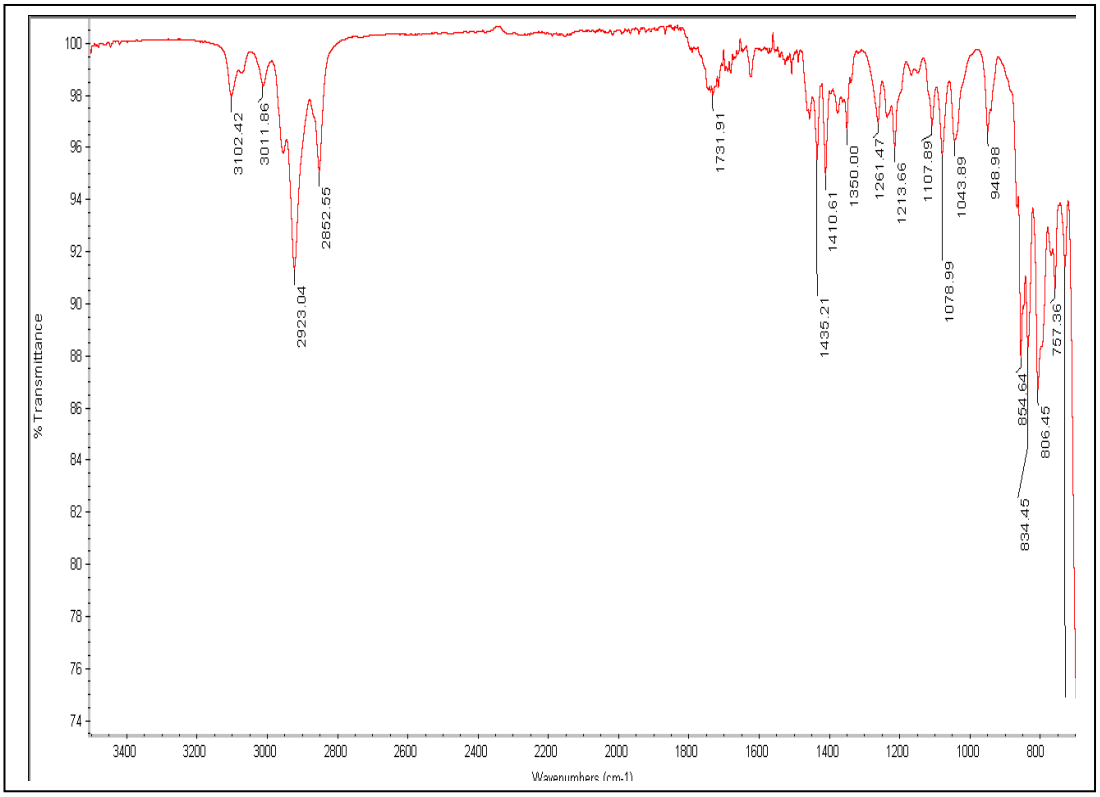

Figure A 33 IR spectrum of compound **75**

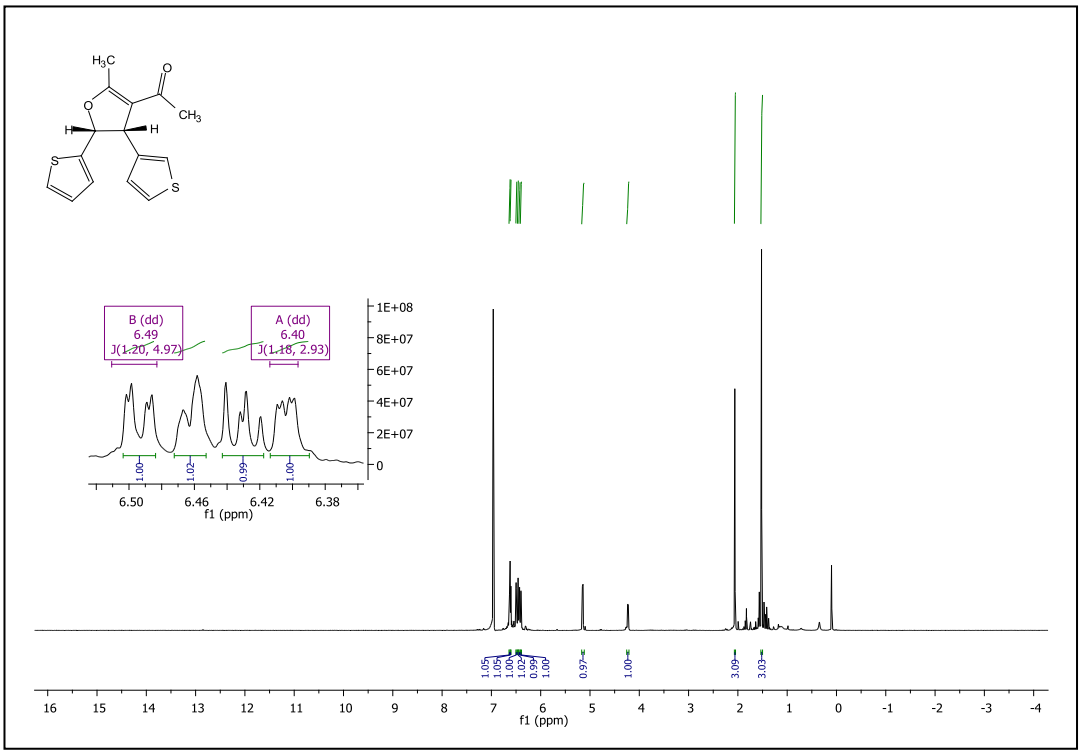

Figure A 34 ^{1}H NMR spectrum of compound **76**

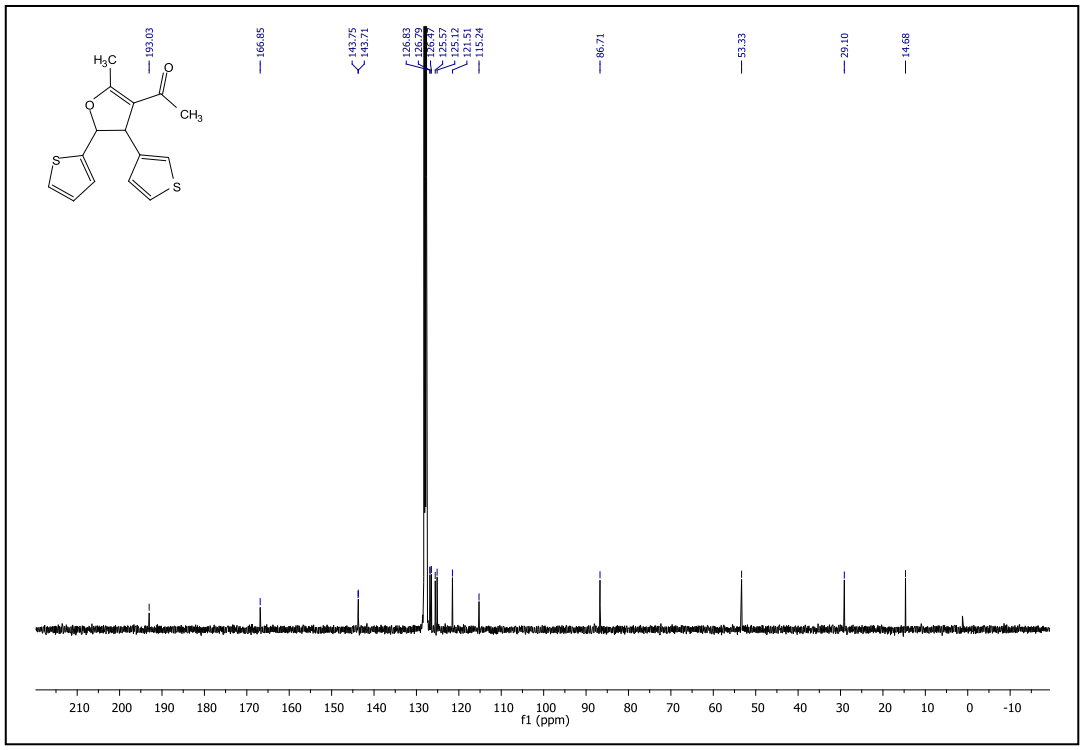

Figure A 35 ^{13}C NMR spectrum of compound **76**

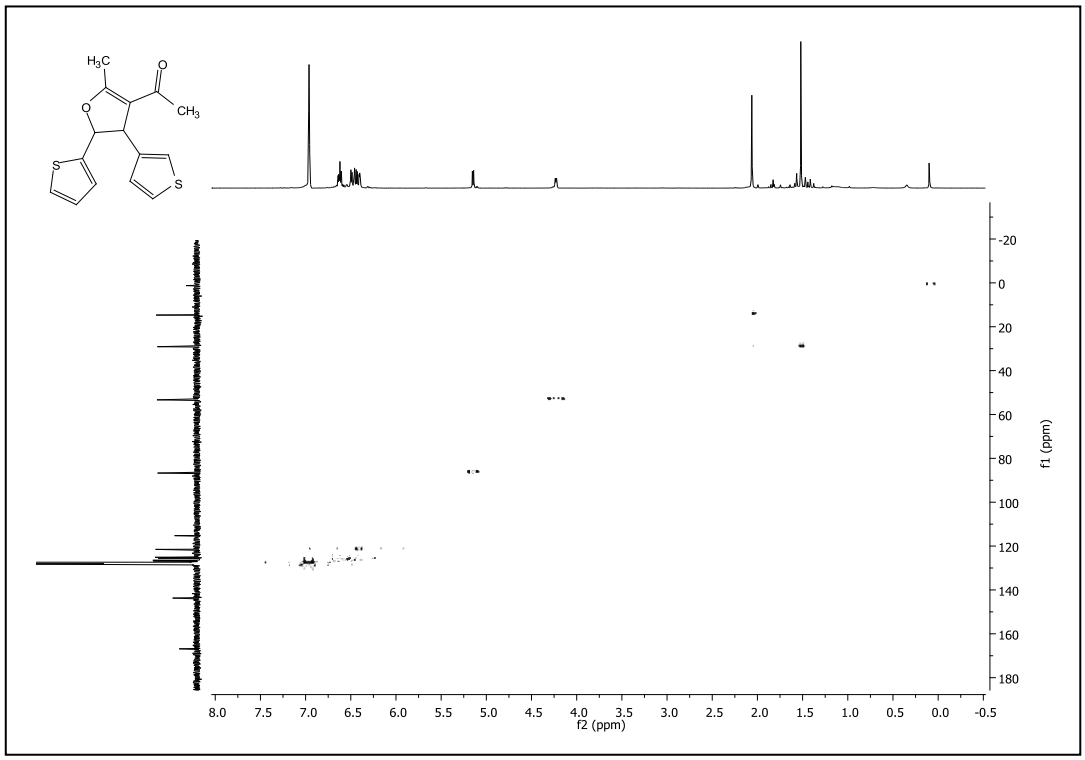

Figure A 36 HSQC spectrum of compound **76**

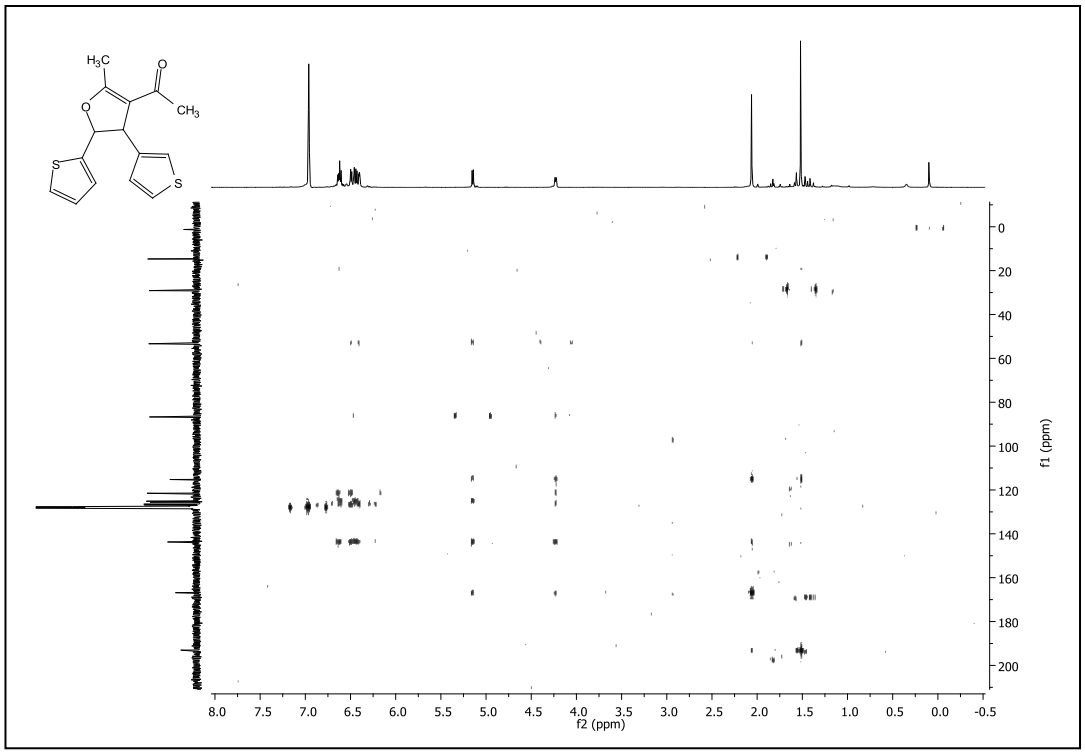

Figure A 37 HMBC spectrum of compound **76**

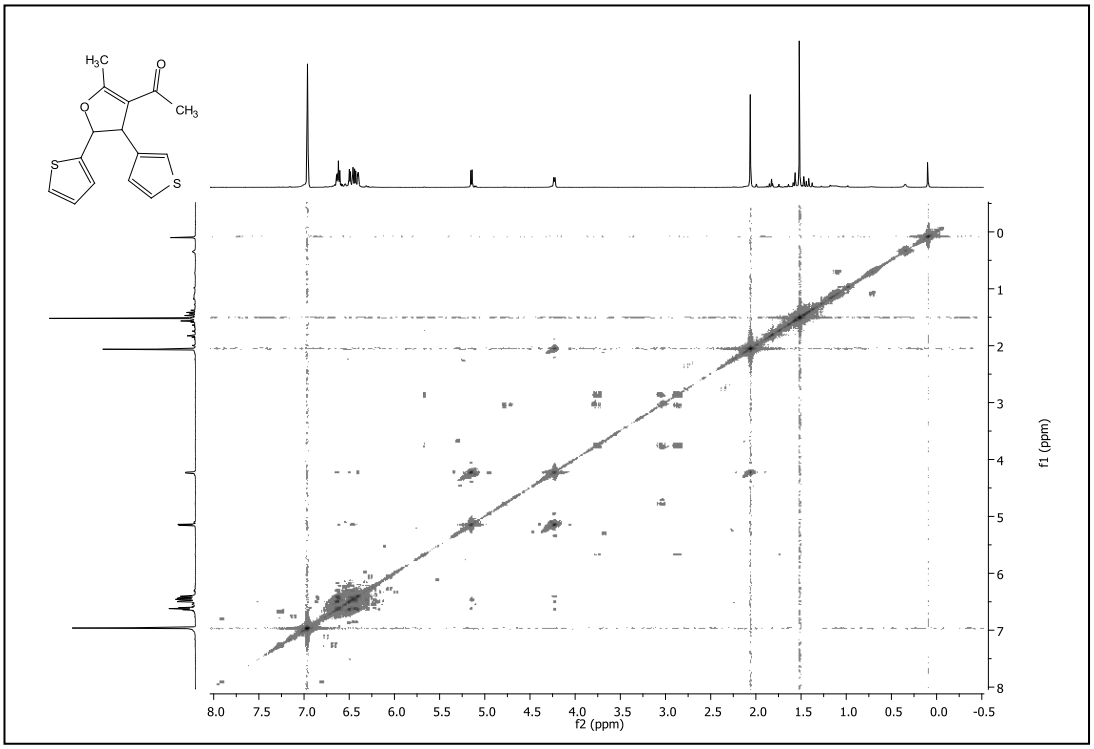

Figure A 38 COSY spectrum of compound **76**

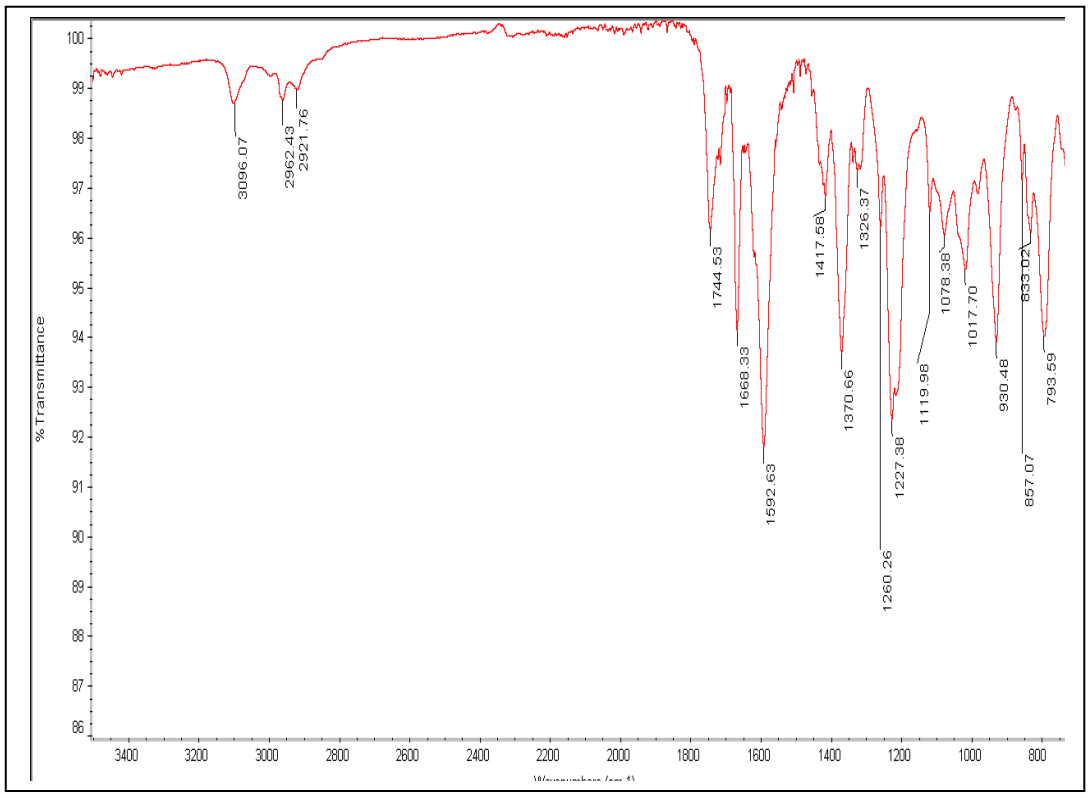

Figure A 39 IR spectrum of compound **76**

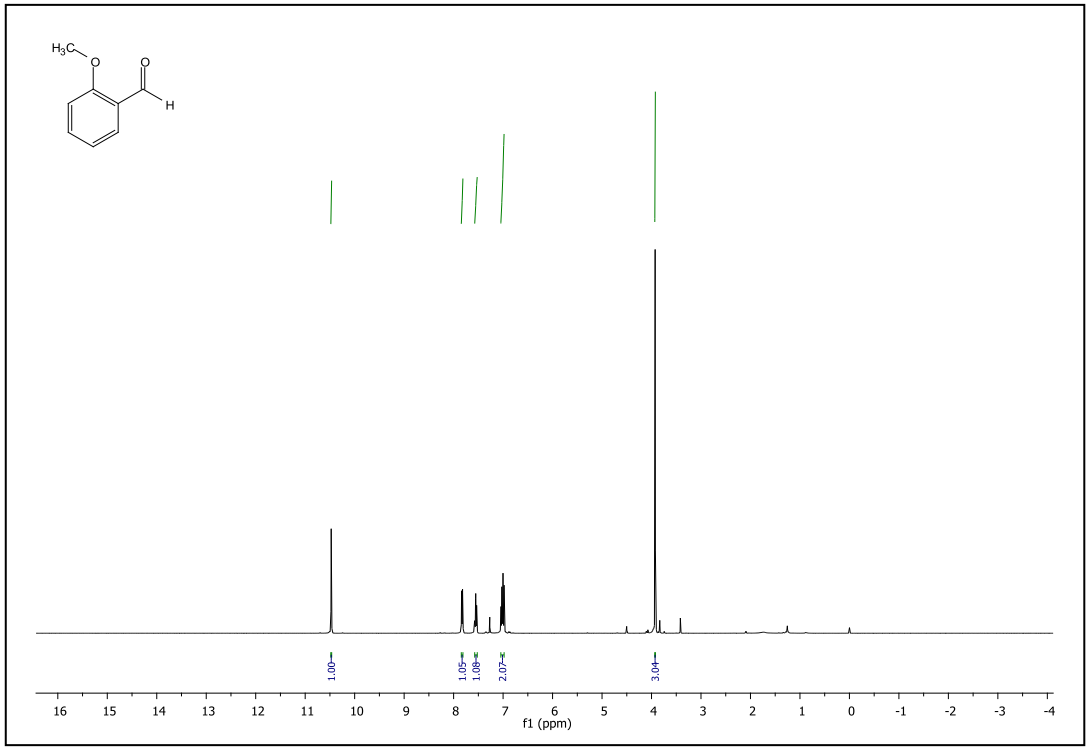

Figure A 40 ^{1}H NMR spectrum of compound **87**

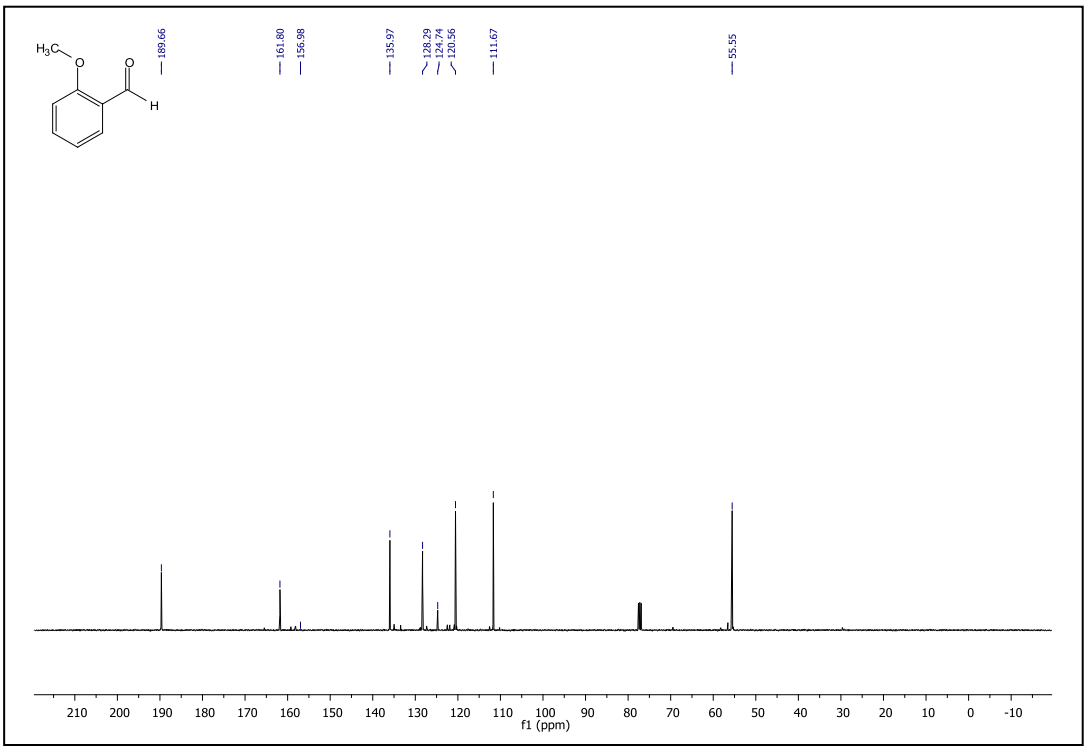

Figure A 41 ^{13}C NMR spectrum of compound **87**

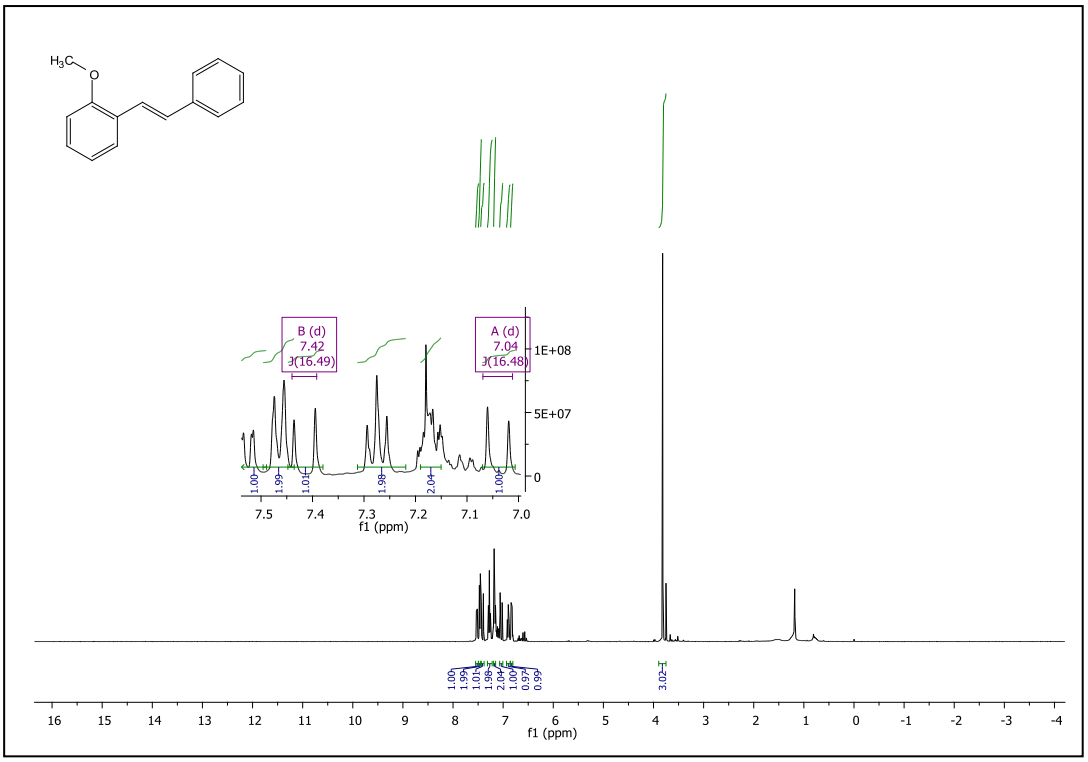

Figure A 42 ^{1}H NMR spectrum of compound **88**

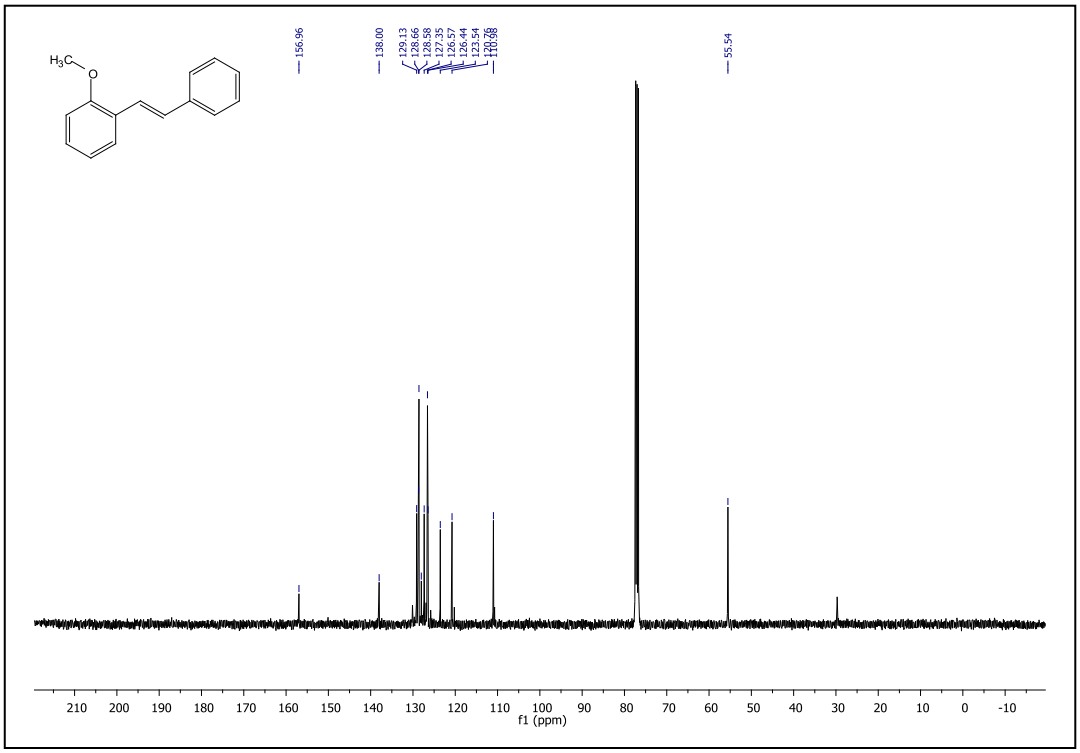

Figure A 43 ^{13}C NMR spectrum of compound **88**

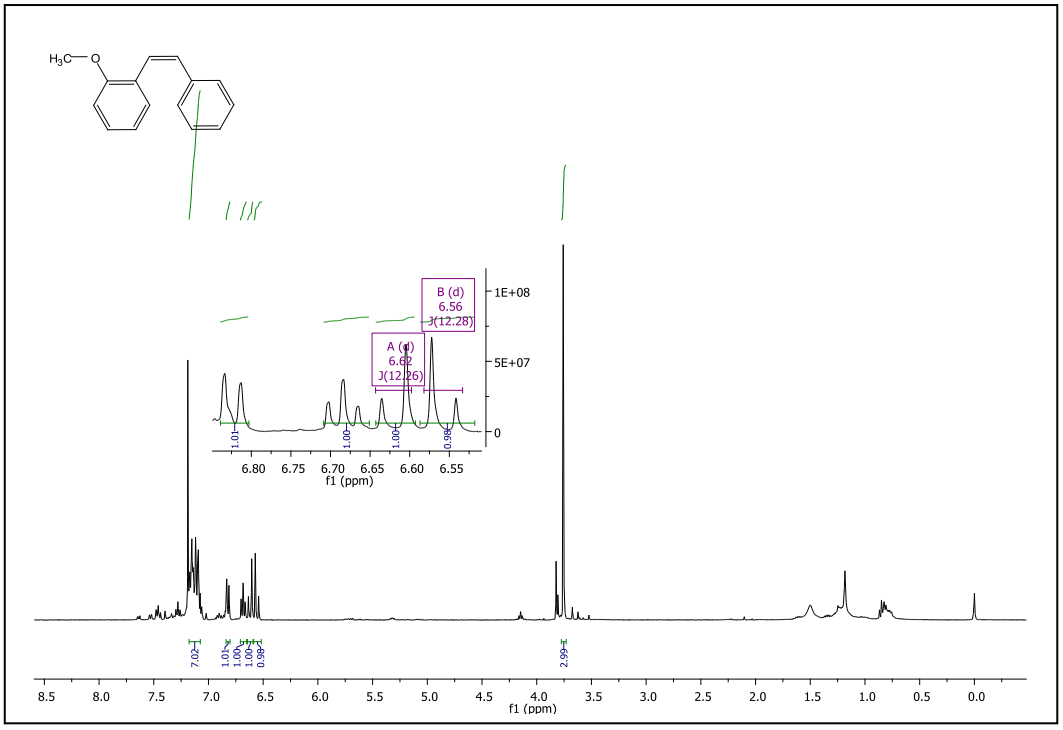

Figure A 44 ^{1}H NMR spectrum of compound **89**

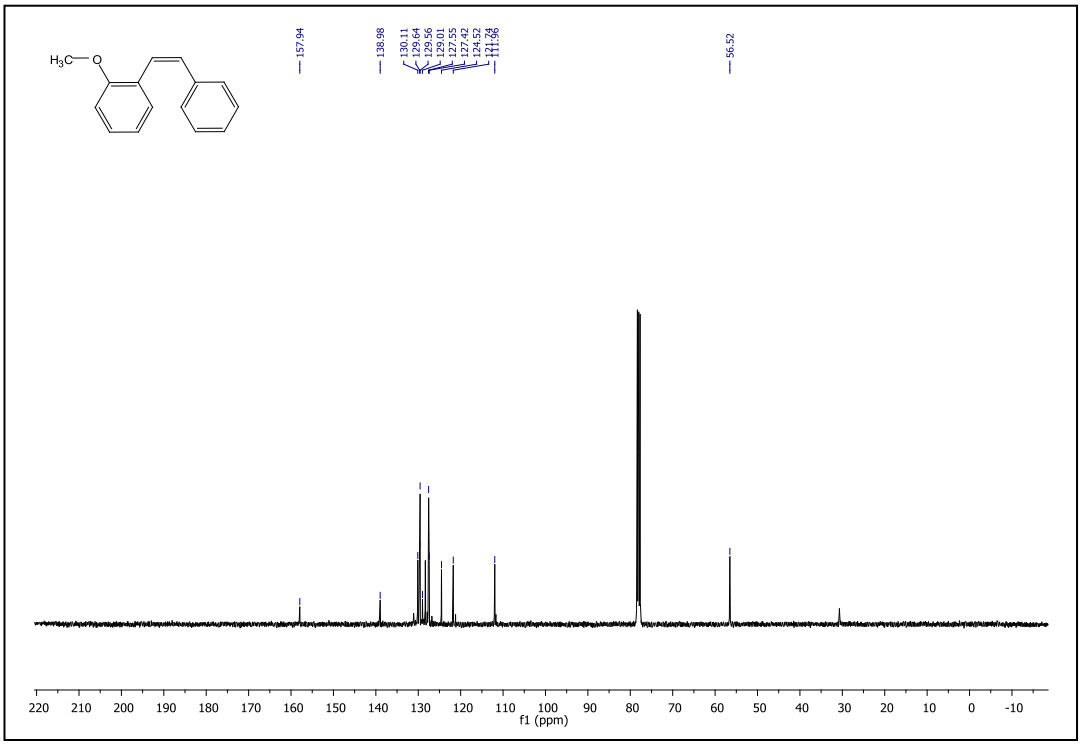

Figure A 45 ^{13}C NMR spectrum of compound **89**

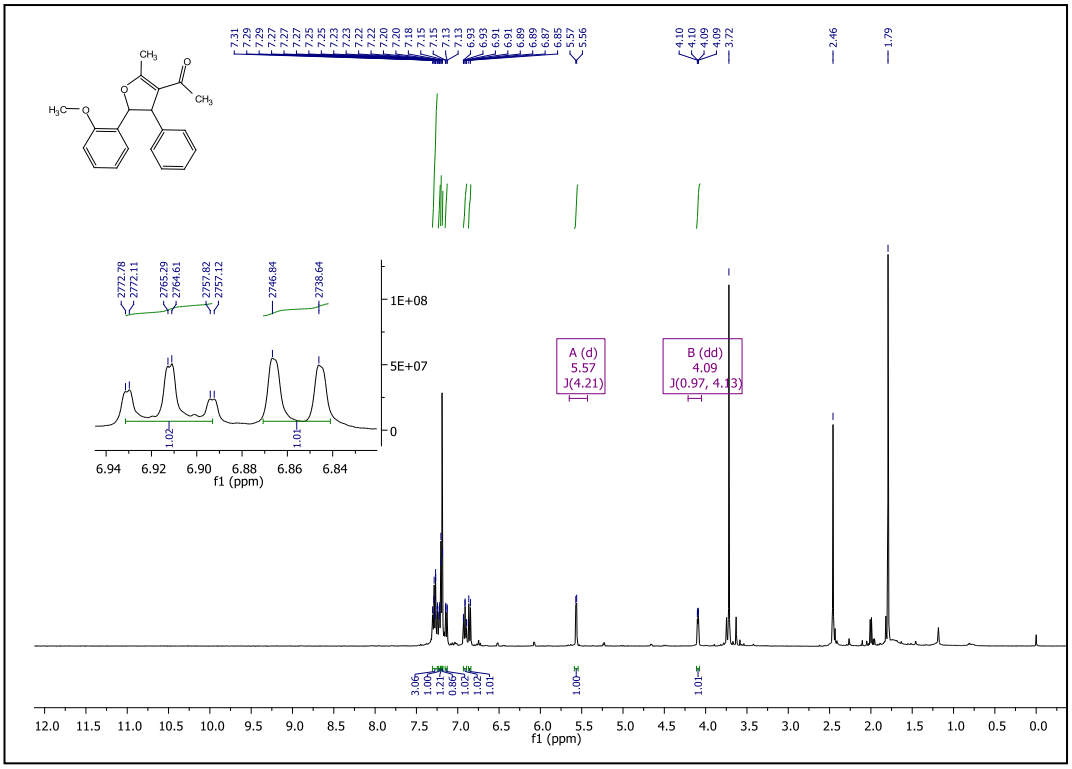

Figure A 46 ^{1}H NMR spectrum of compound **90**

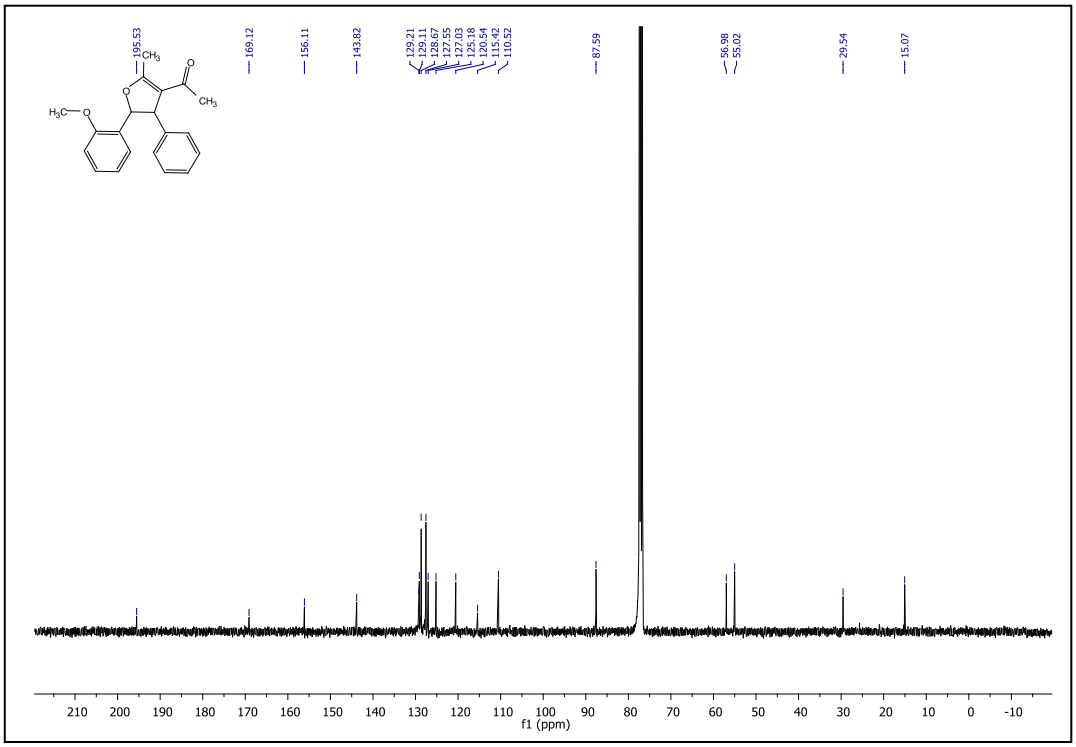

Figure A 47 ^{13}C NMR spectrum of compound **90**

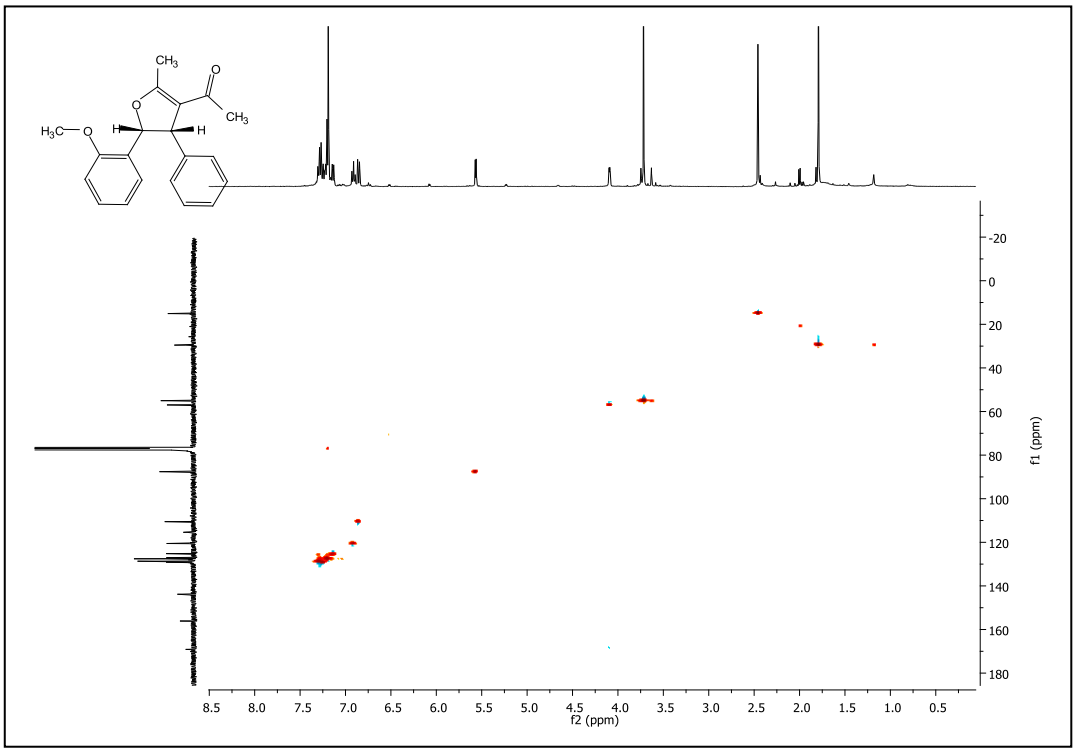

Figure A 48 HSQC spectrum of compound **90**

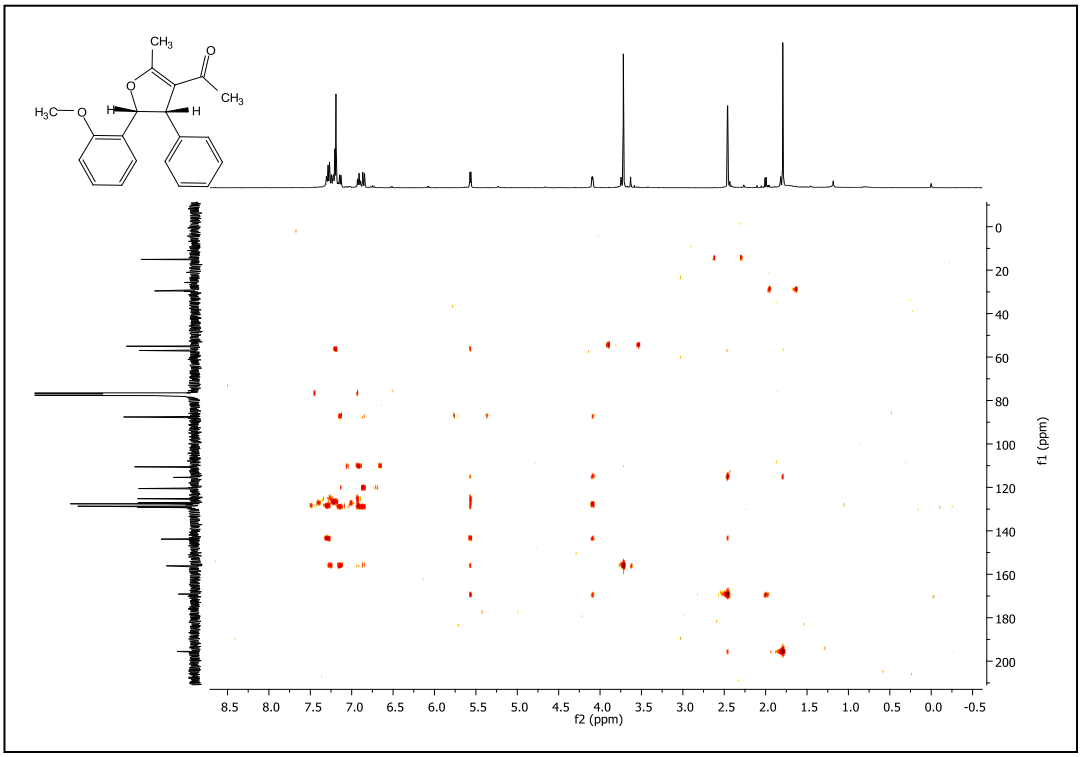

Figure A 49 HMBC spectrum of compound **90**

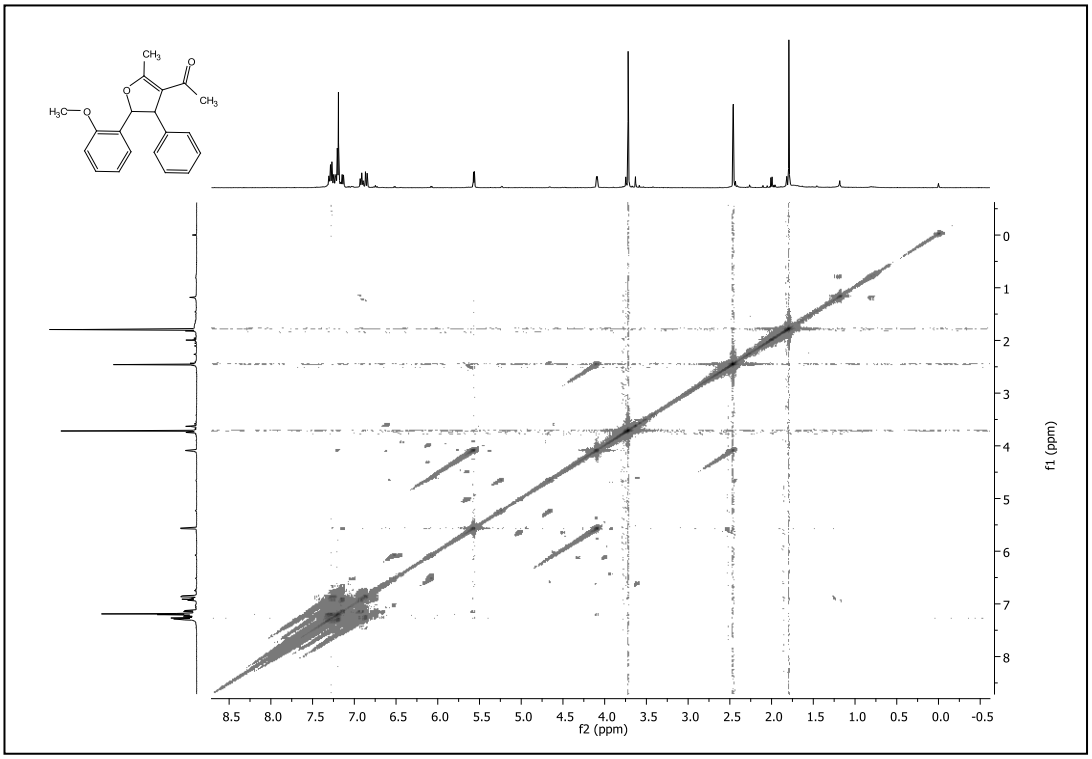

Figure A 50 COSY spectrum of compound **90**

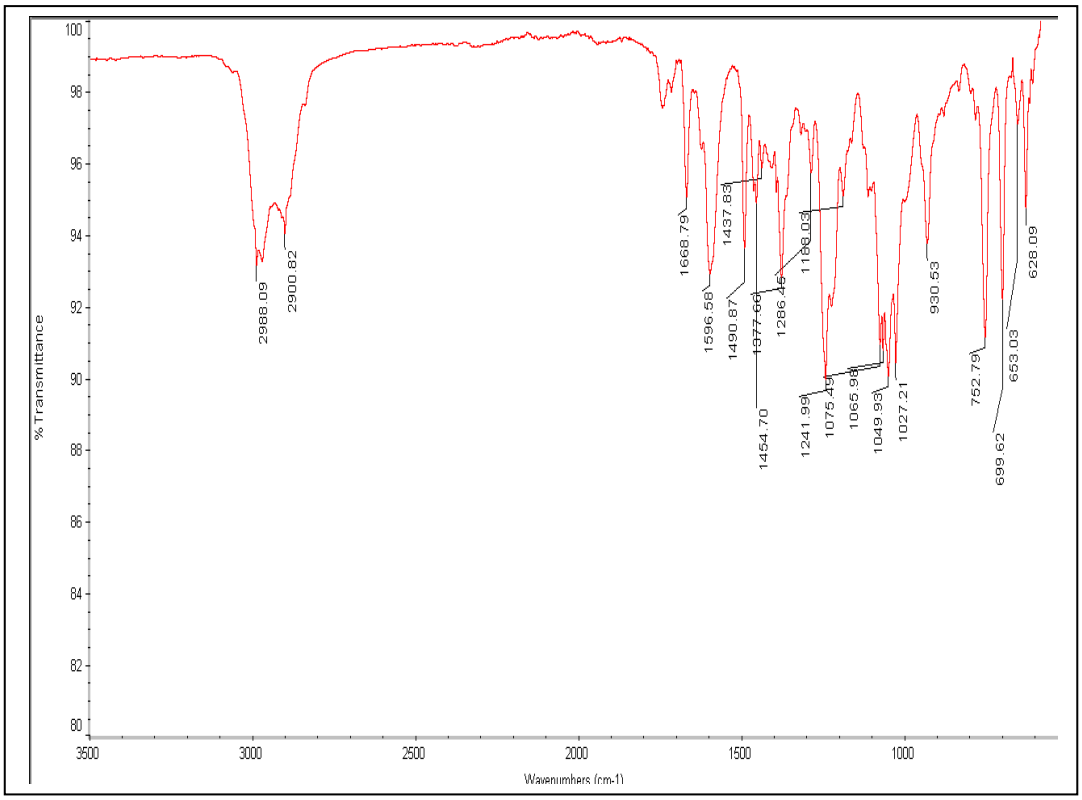

Figure A 51 IR spectrum of compound **90**

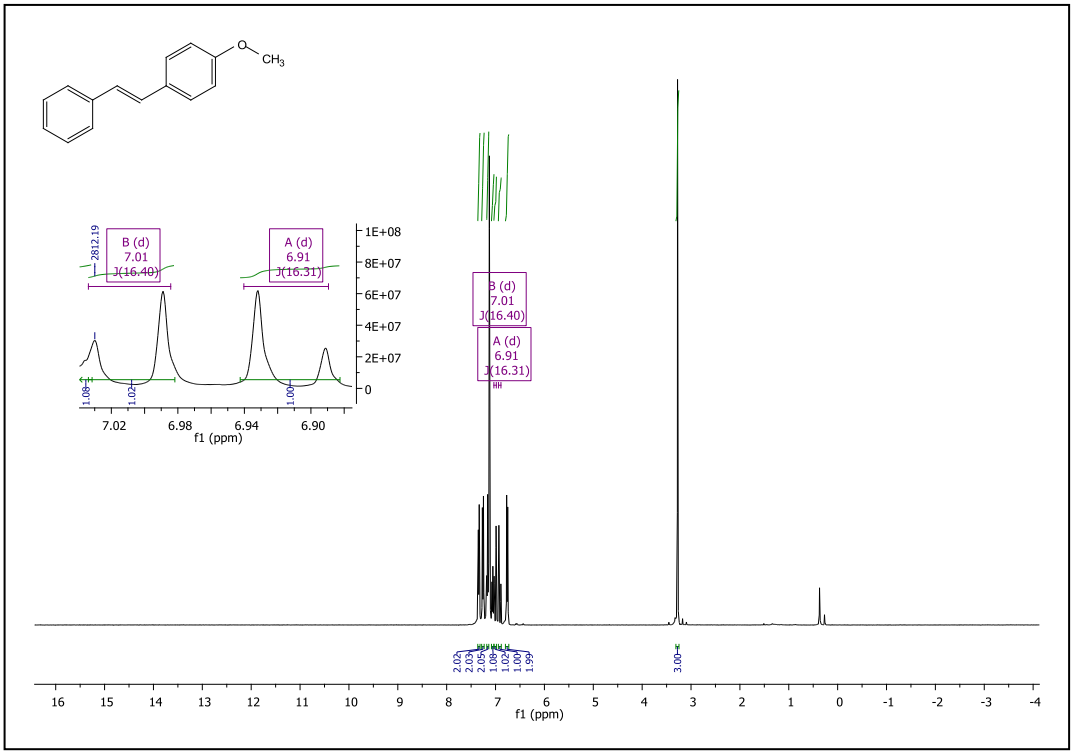

Figure A 52 ^{1}H NMR spectrum of compound **96**

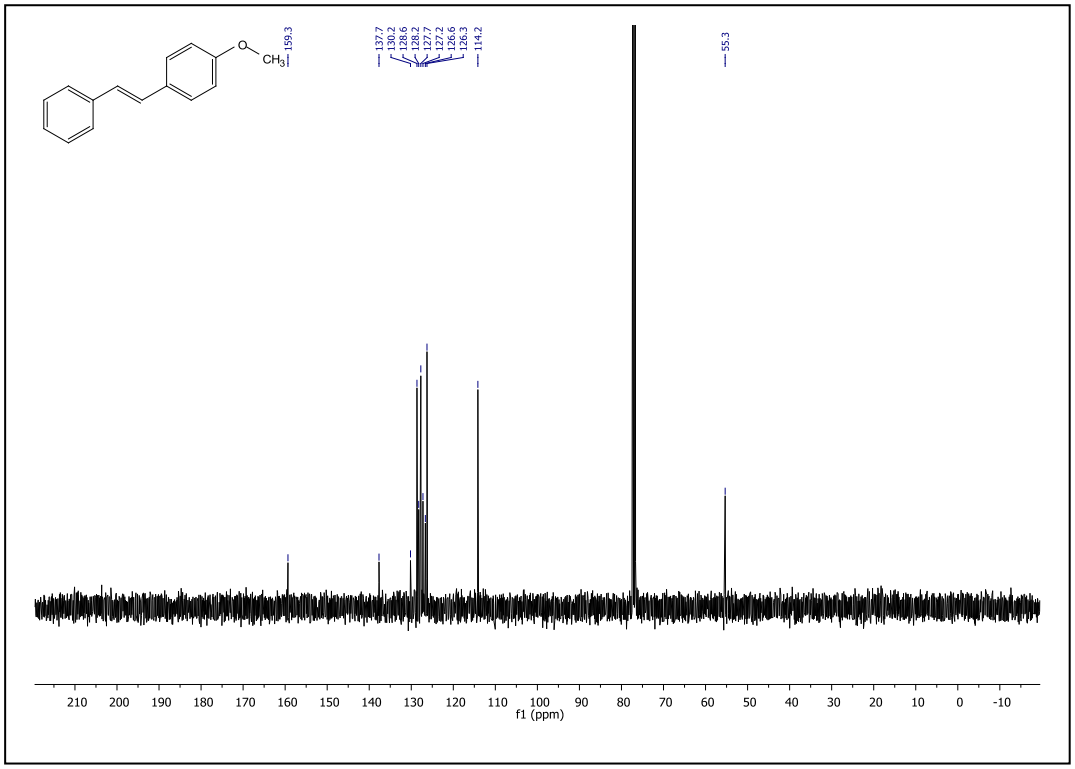

Figure A 53 ^{13}C NMR spectrum of compound **96**

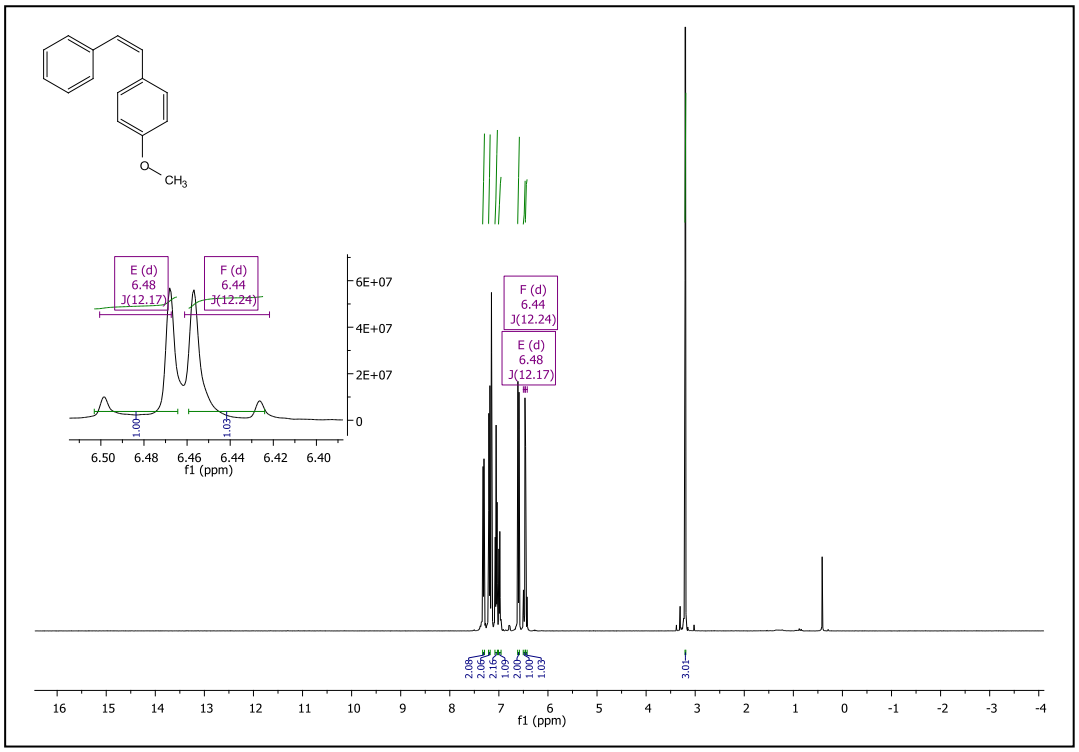

Figure A 54 ^{1}H NMR spectrum of compound **97**

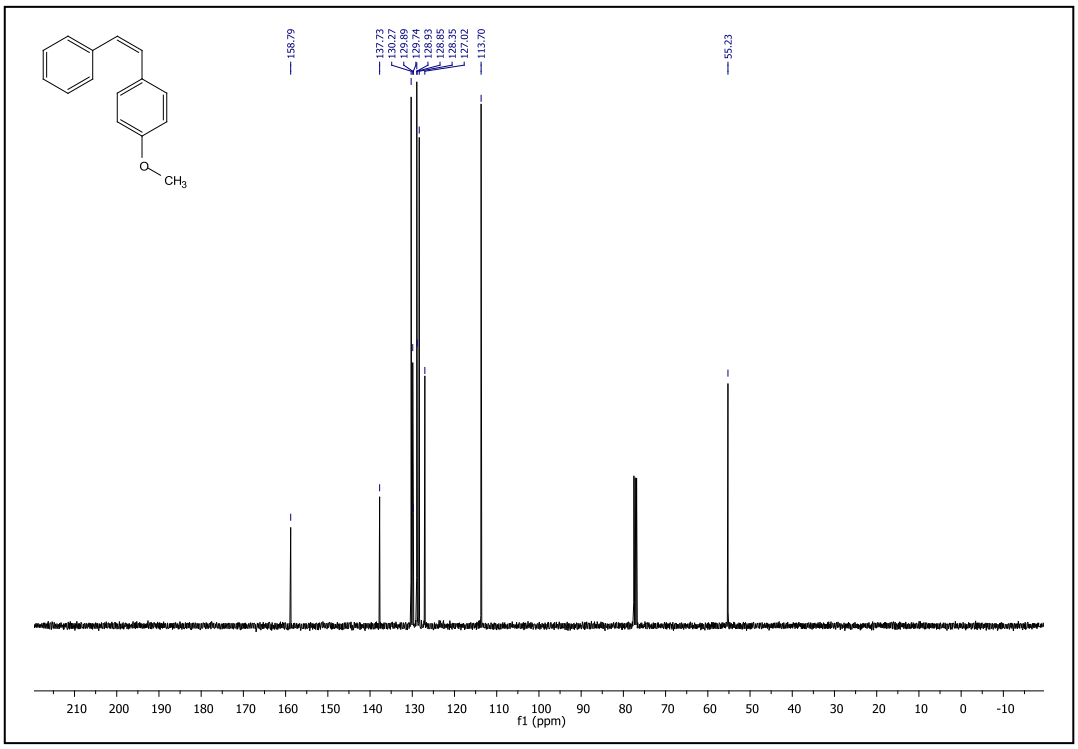

Figure A 55 ^{13}C NMR spectrum of compound **97**

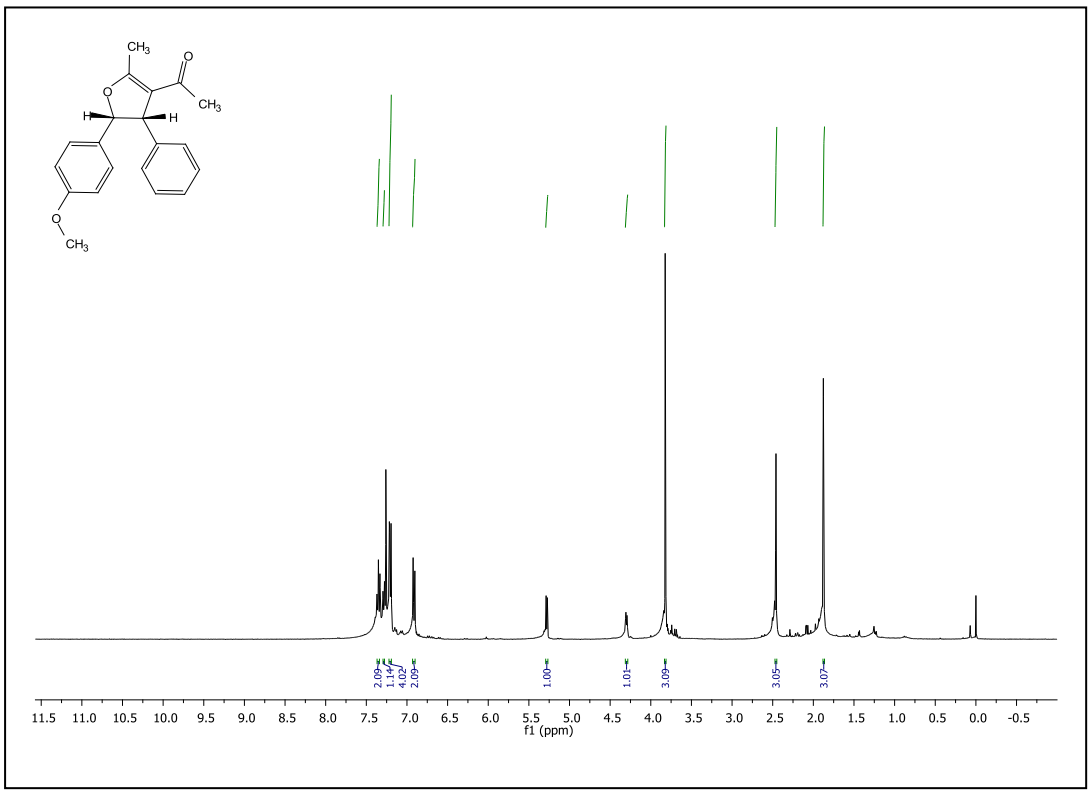

Figure A 56 ^{1}H NMR spectrum of compound **98**

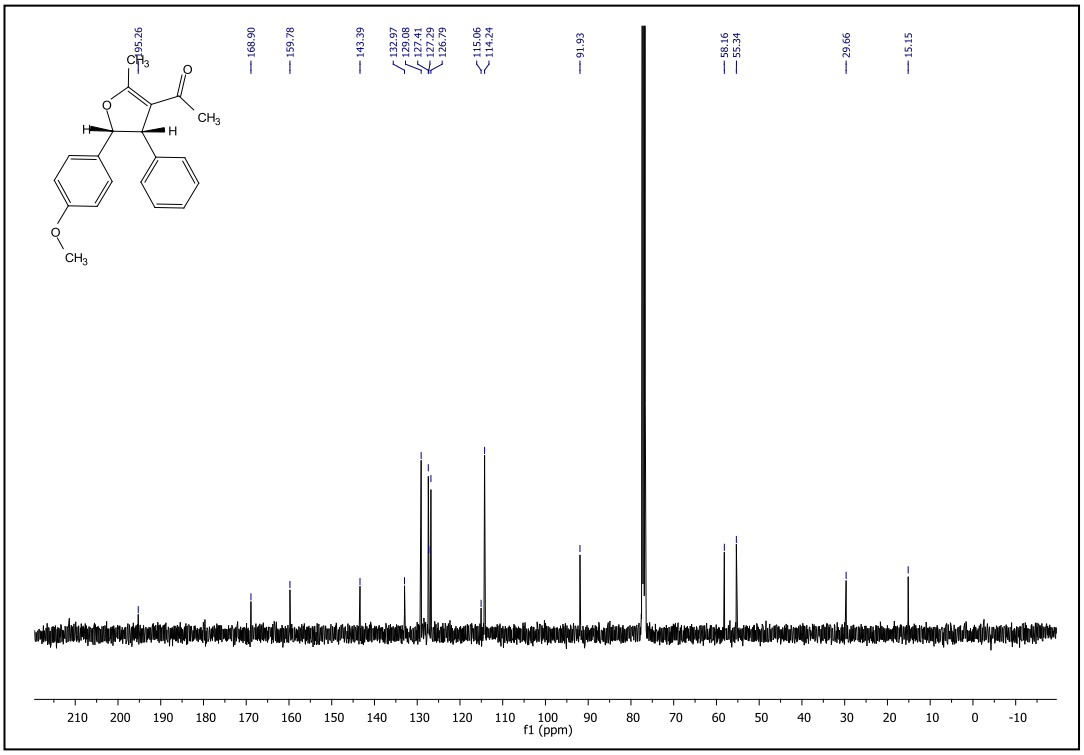

Figure A 57 ^{13}C NMR spectrum of compound **98**

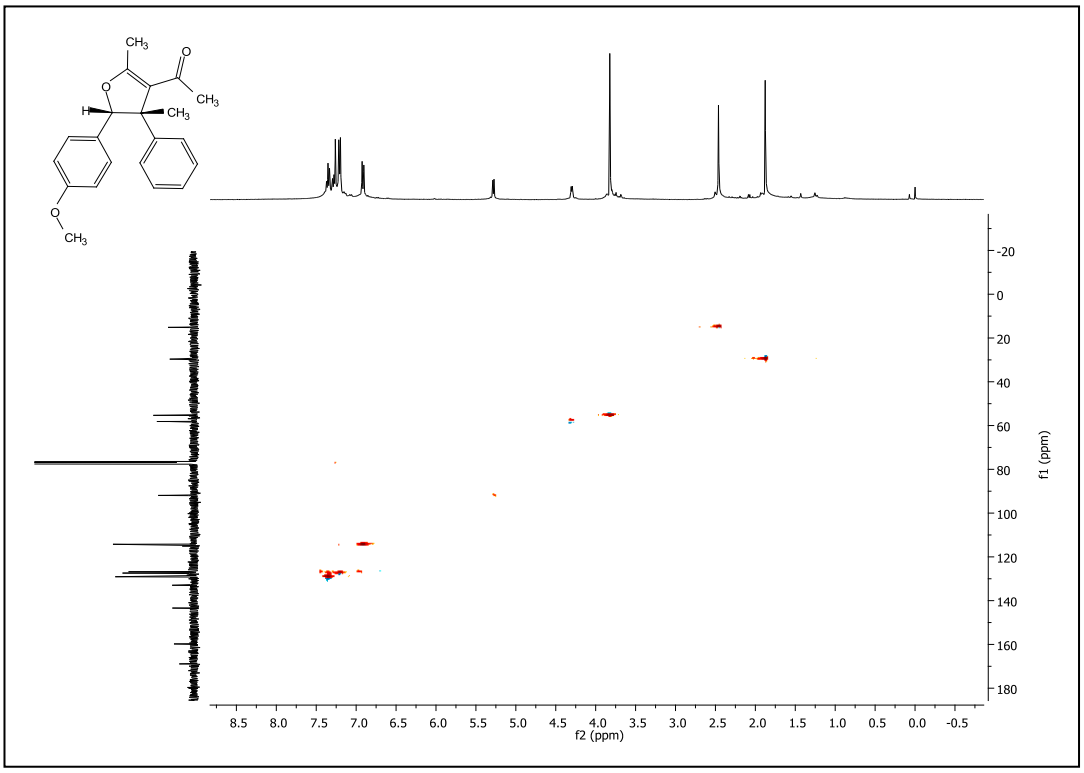

Figure A 58 HSQC spectrum of compound **98**

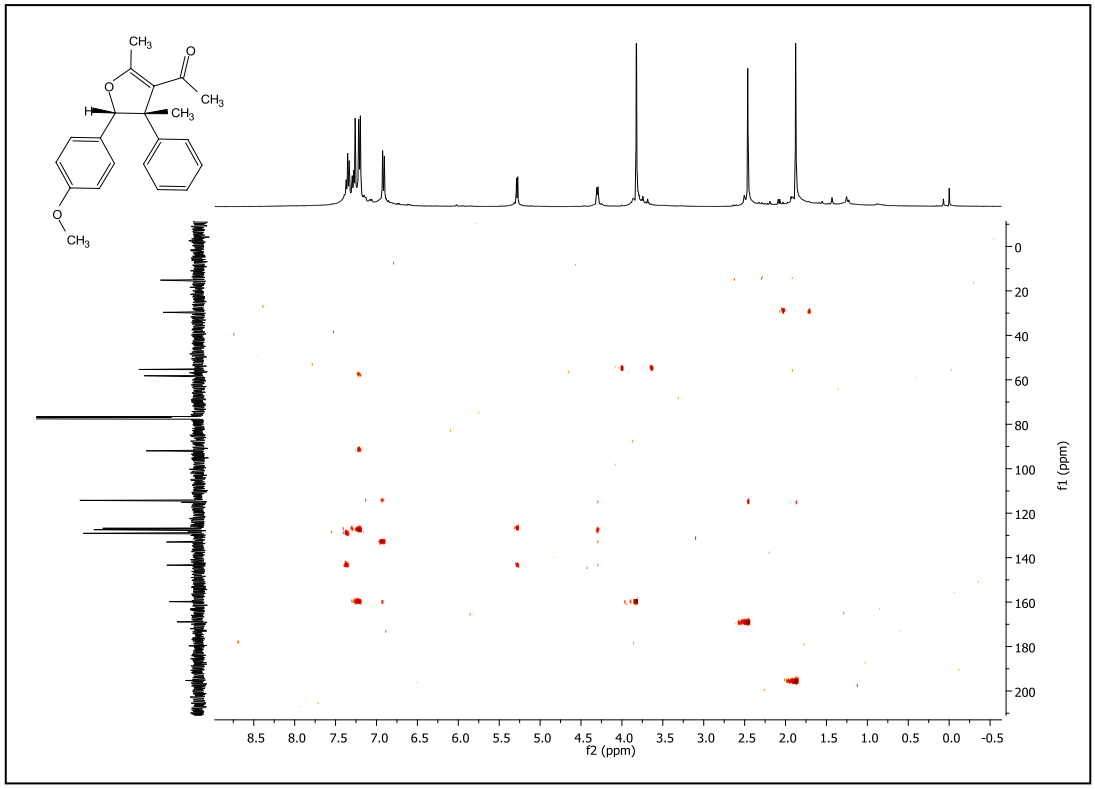

Figure A 59 HMBC spectrum of compound **98**

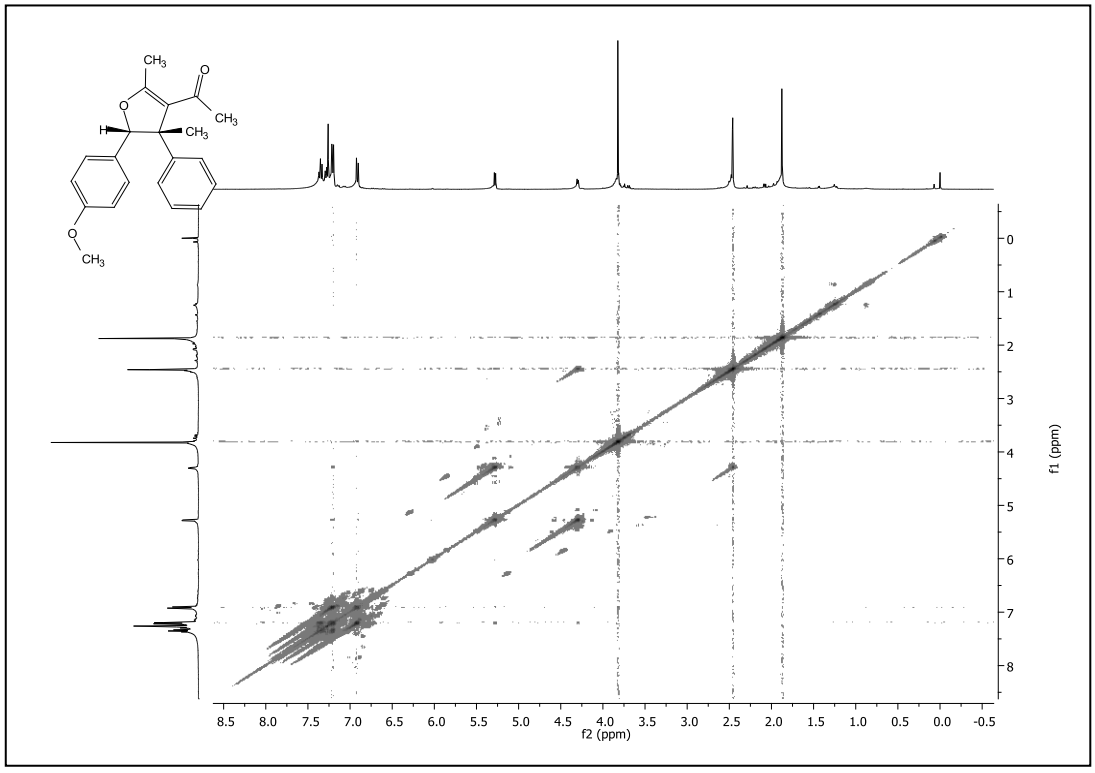

Figure A 60 COSY spectrum of compound **98**

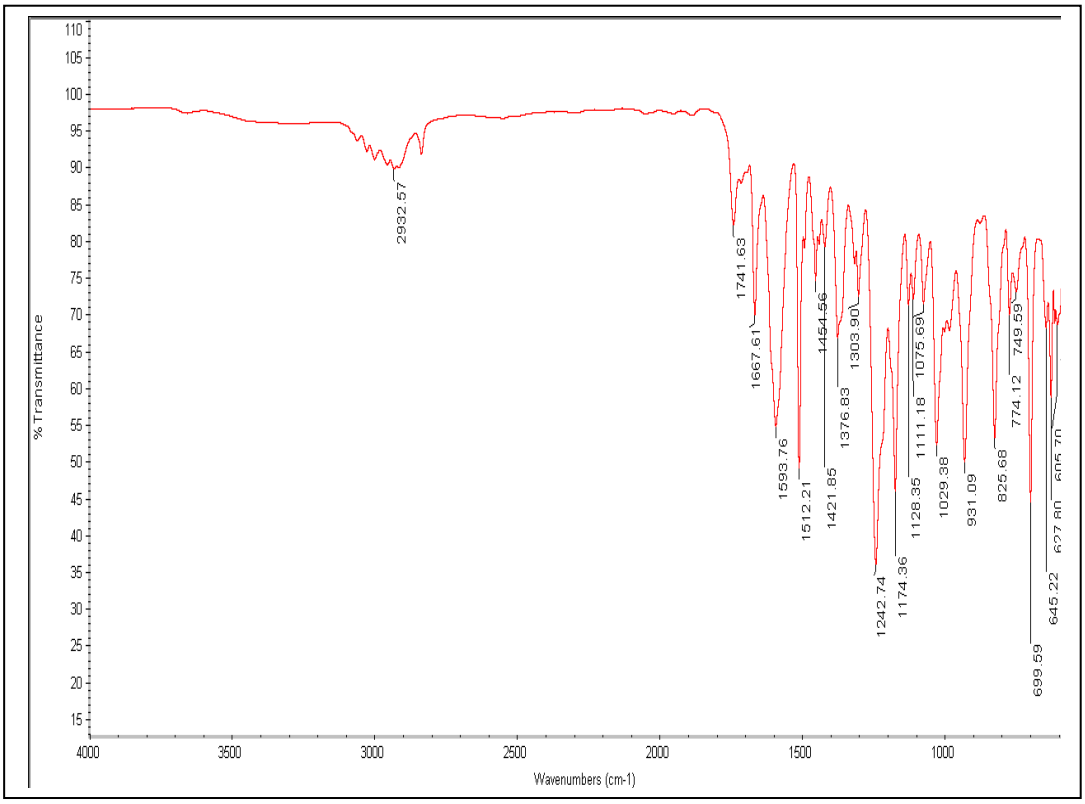

Figure A 61 IR spectrum of compound **98**

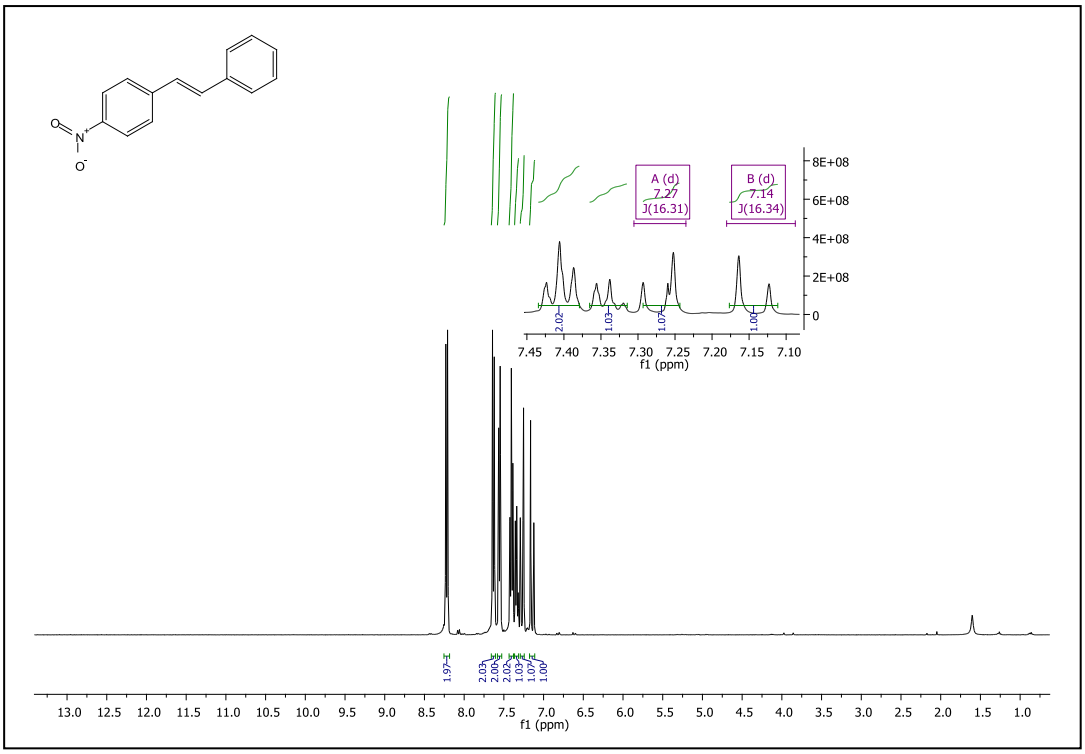

Figure A 62 ^{1}H NMR spectrum of compound **101**

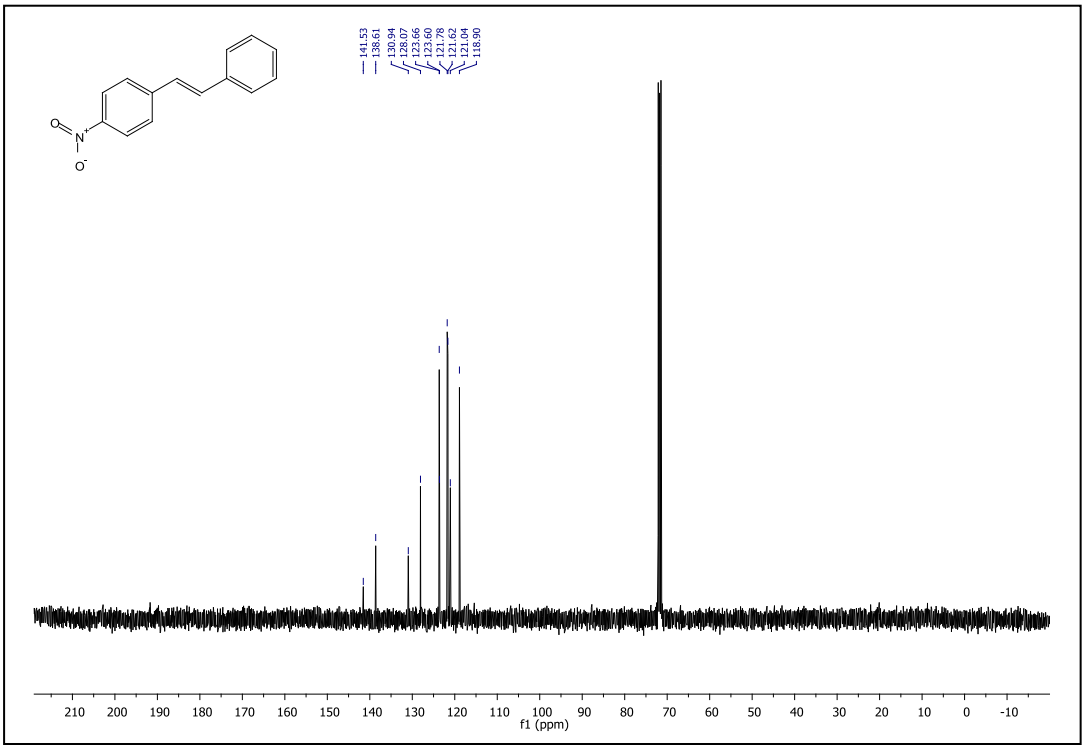

Figure A 63 ^{13}C NMR spectrum of compound **101**

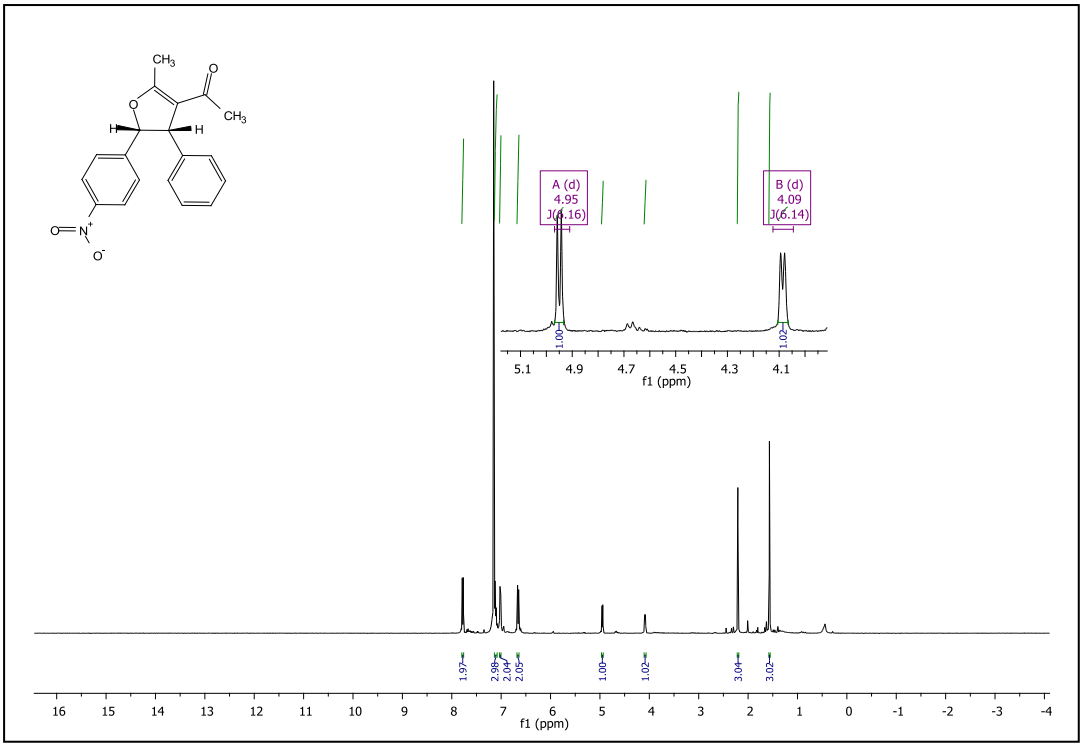

Figure A 64 ^{1}H NMR spectrum of compound **104**

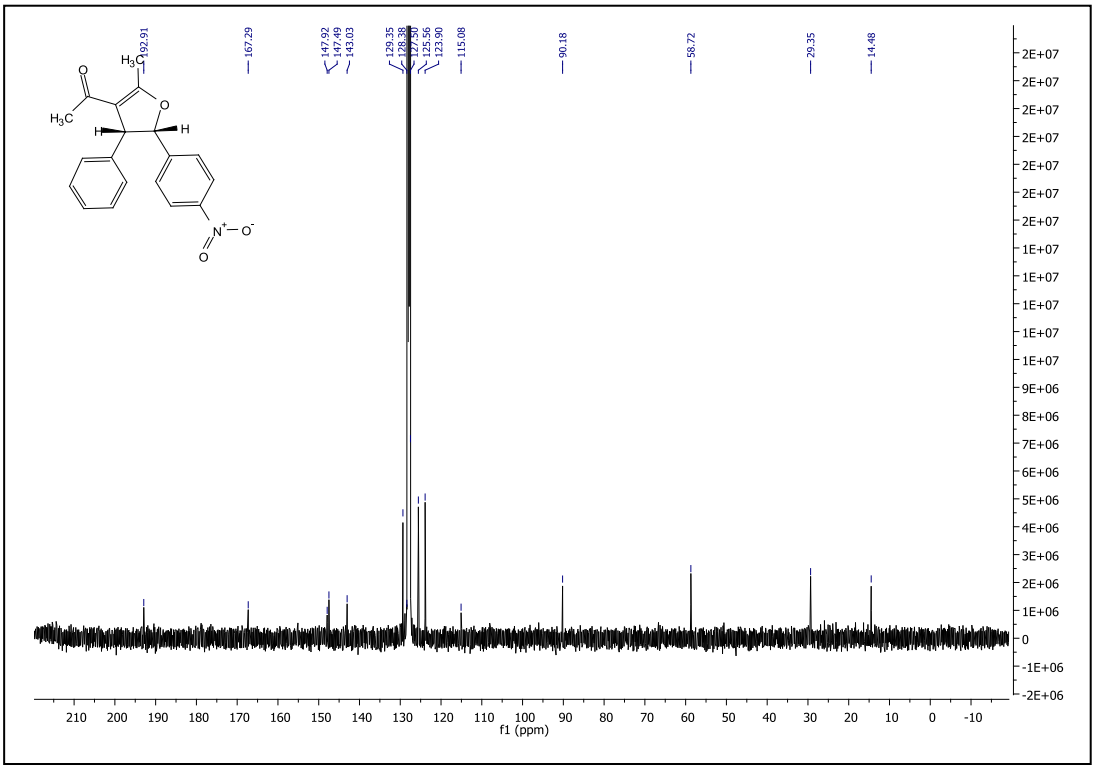

Figure A 65 ^{13}C NMR spectrum of compound **104**

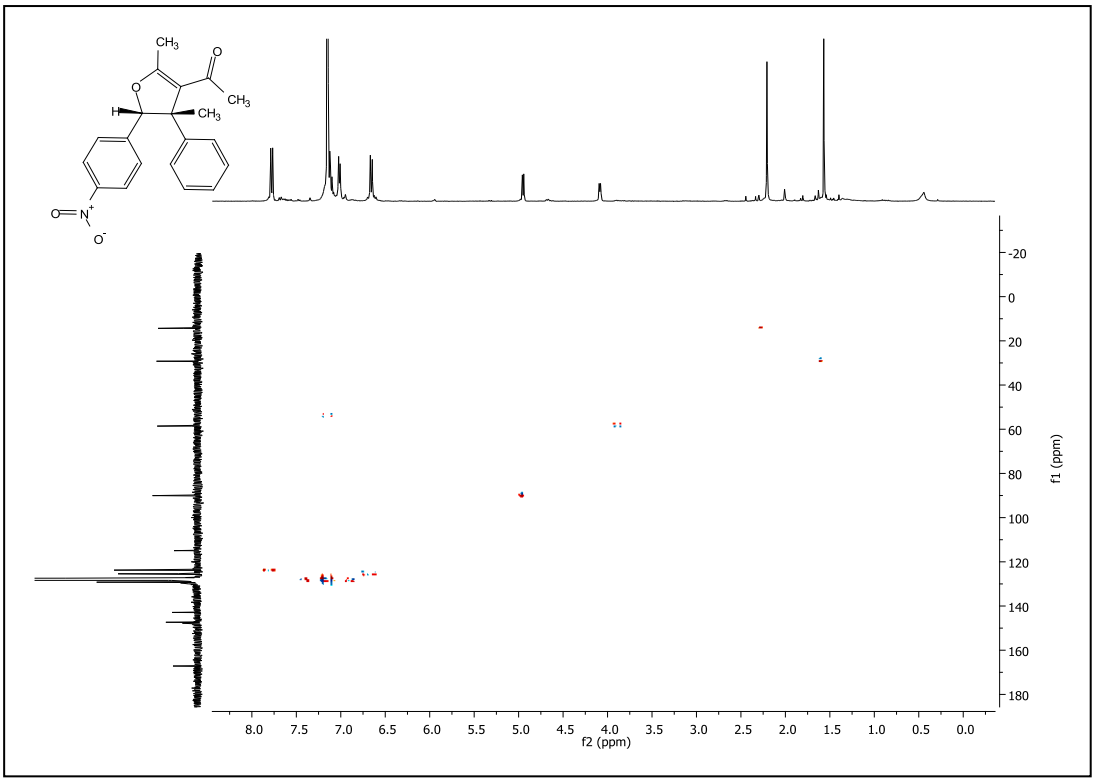

Figure A 66 HSQC spectrum of compound **104**

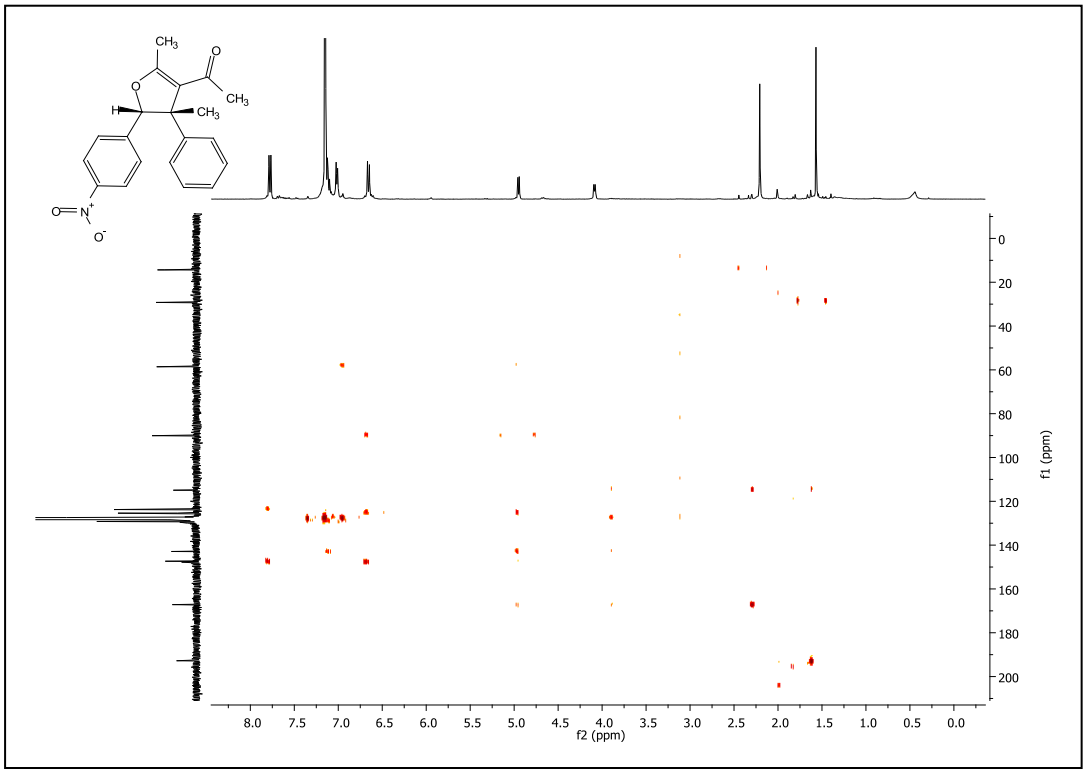

Figure A 67 HMBC spectrum of compound **104**

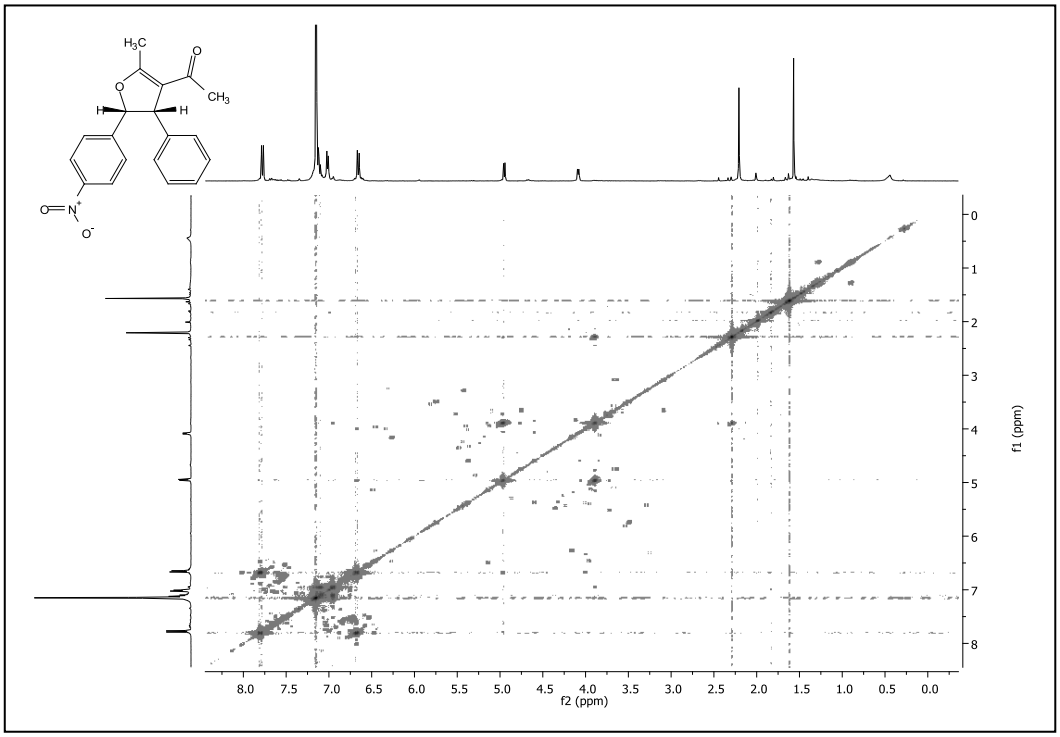

Figure A 68 COSY spectrum of compound **104**

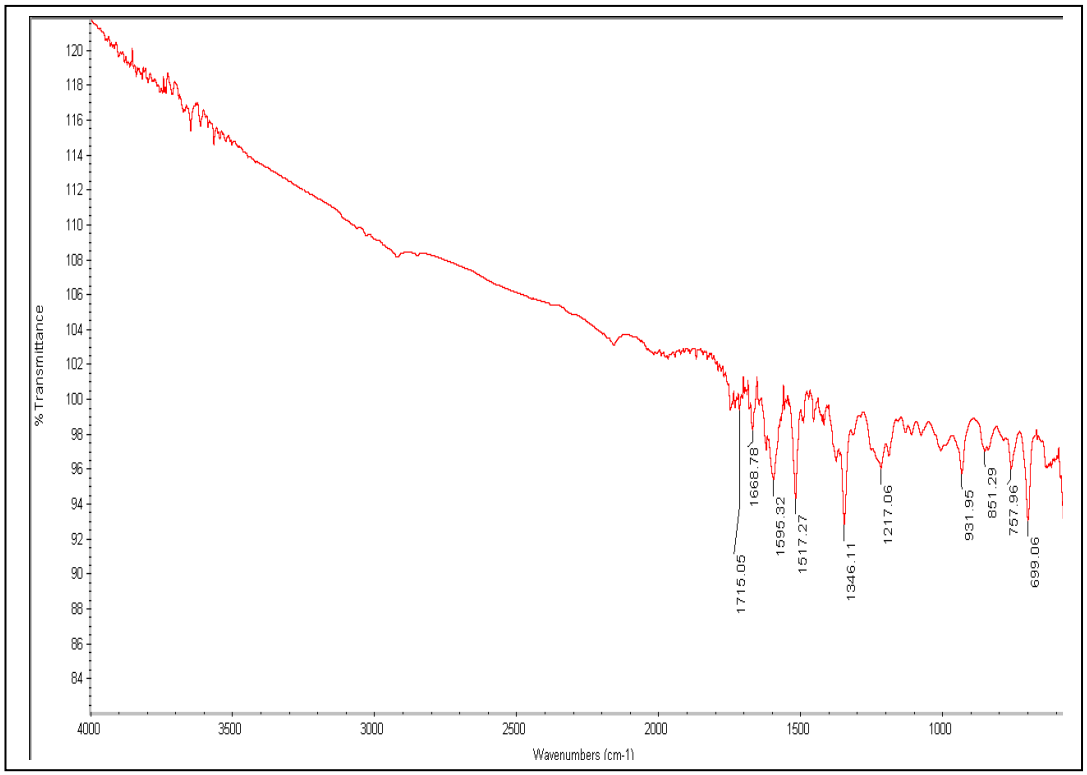

Figure A 69 IR spectrum of compound **104**

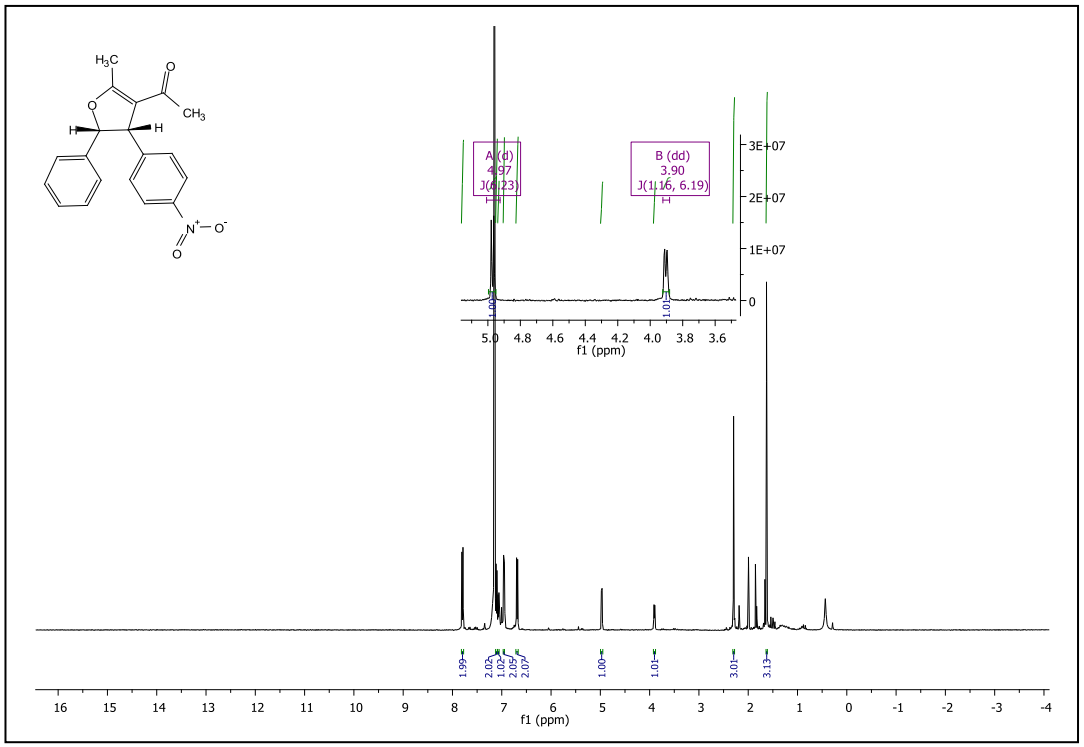

Figure A 70 ^{1}H NMR spectrum of compound **103**

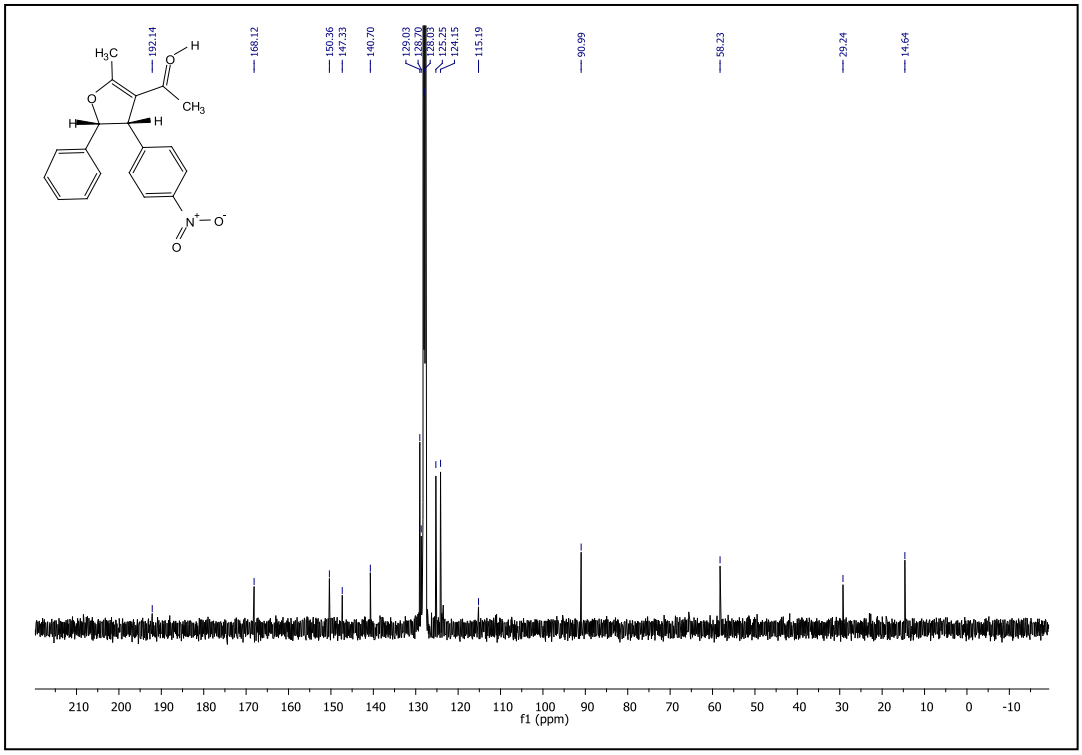

Figure A 71 ^{13}C NMR spectrum of compound **103**

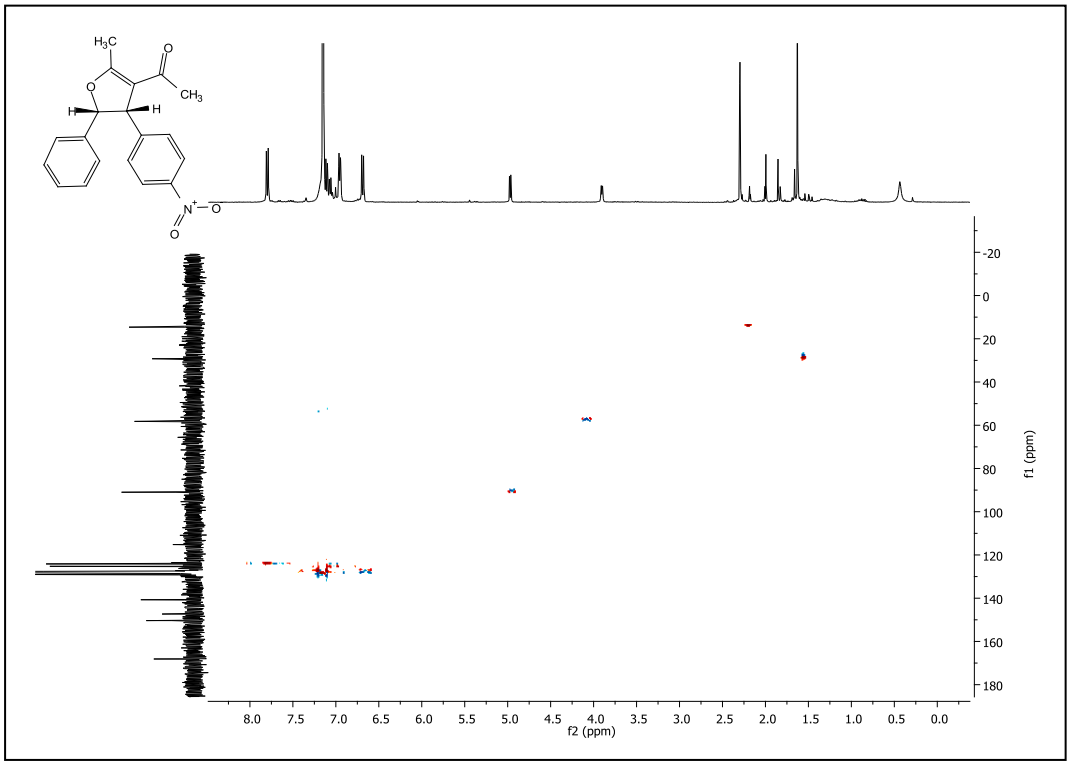

Figure A 72 HSQC spectrum of compound **103**

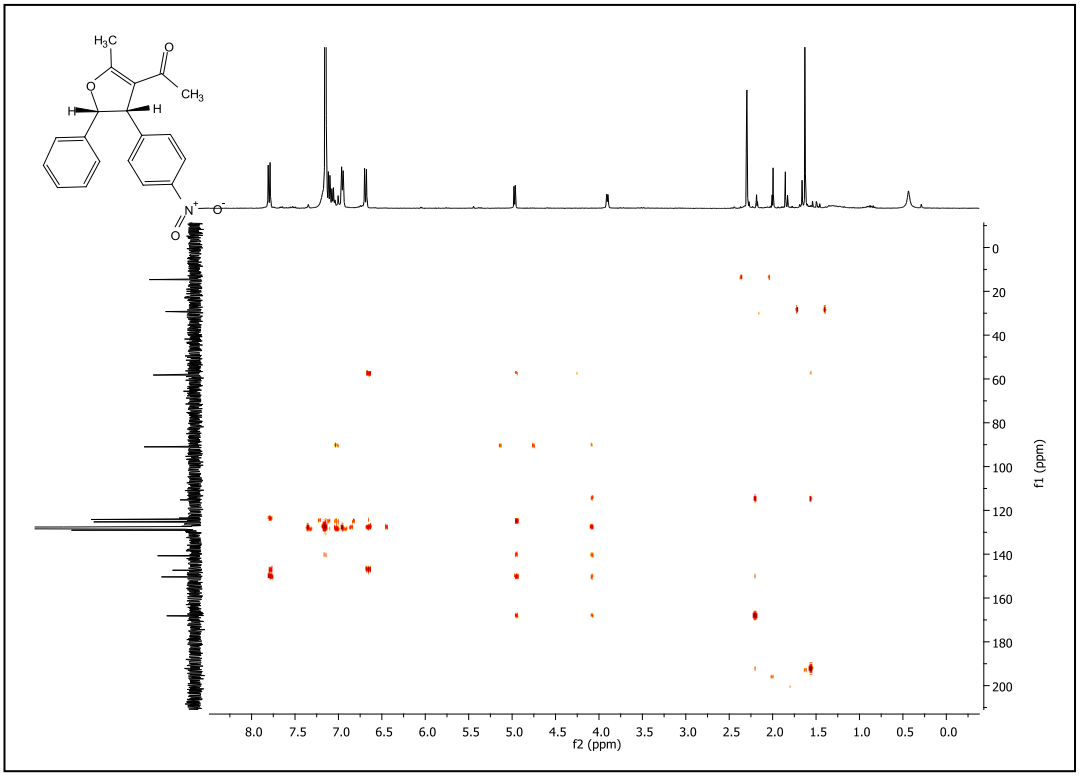

Figure A 73 HMBC spectrum of compound **103**

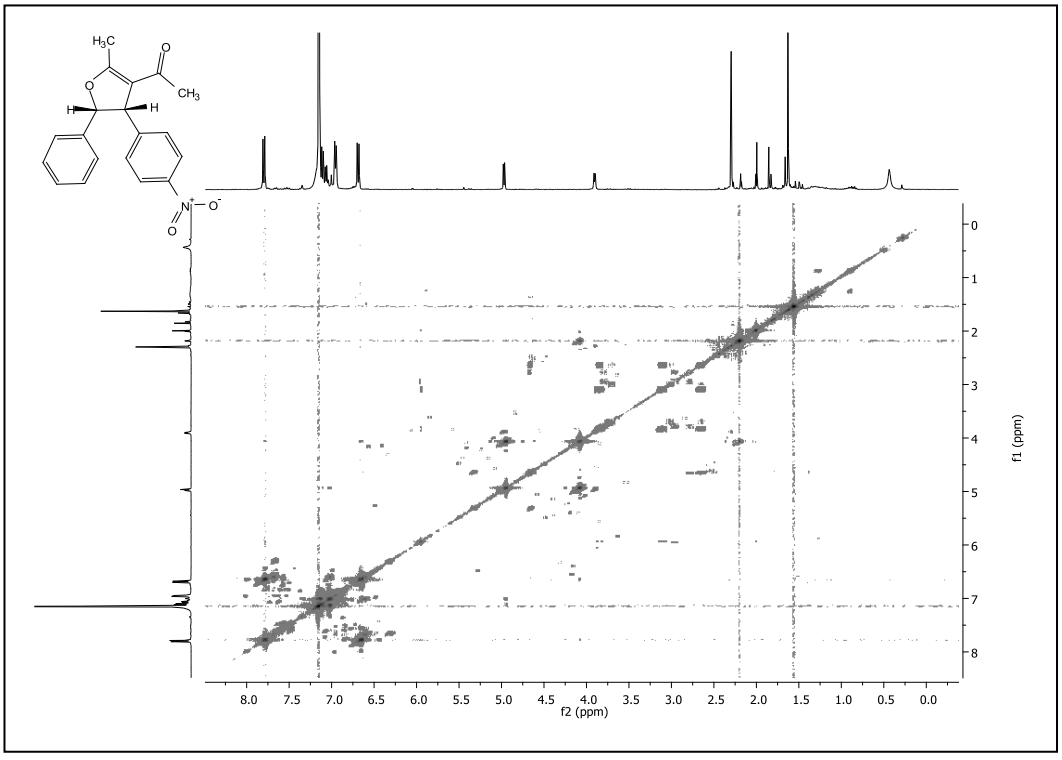

Figure A 74 COSY spectrum of compound **103**

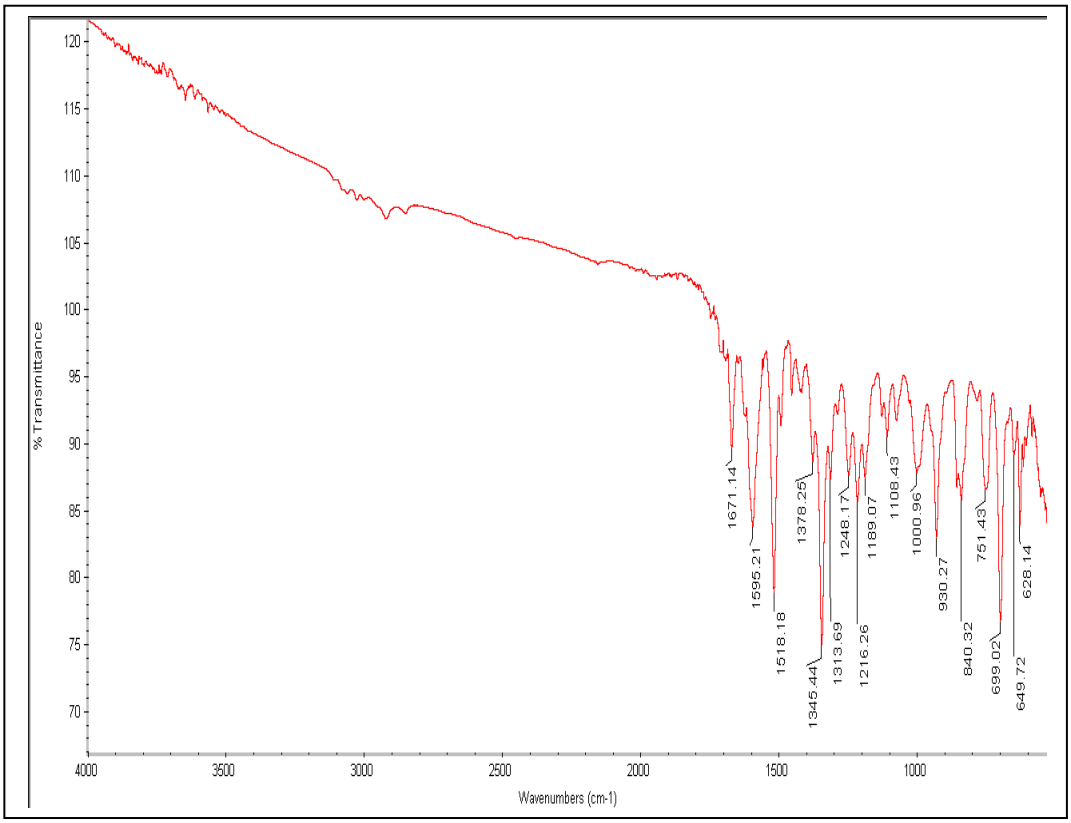

Figure A 75 IR spectrum of compound **103**

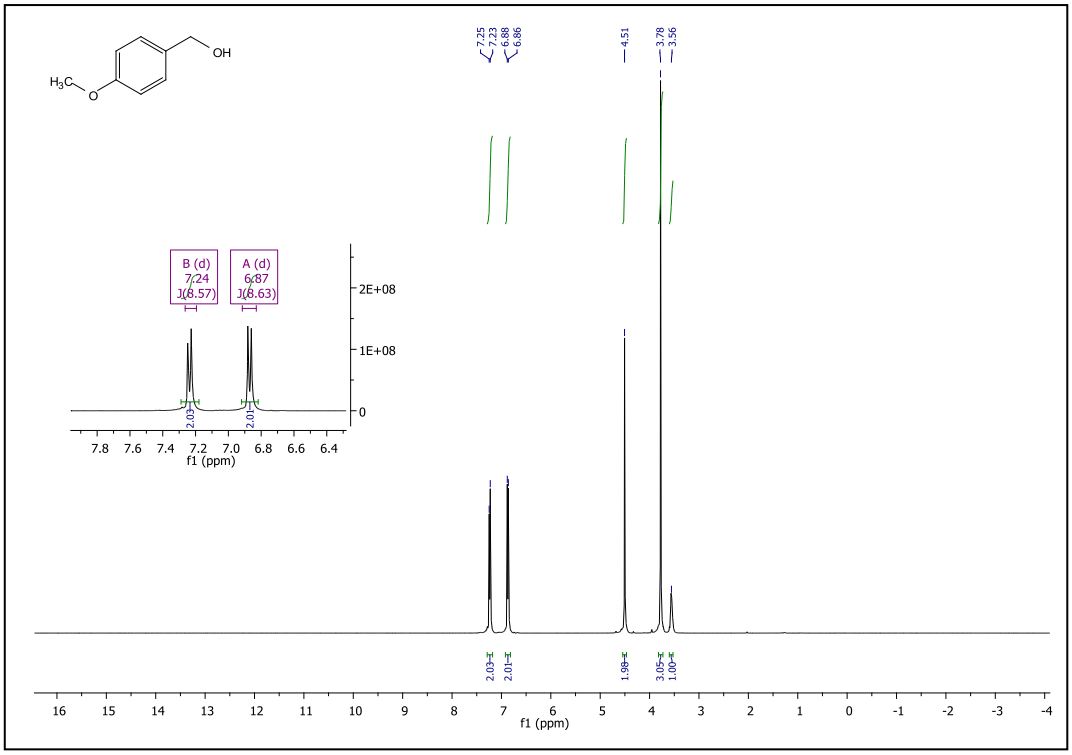

Figure A 76 ^{1}H NMR spectrum of compound **105**

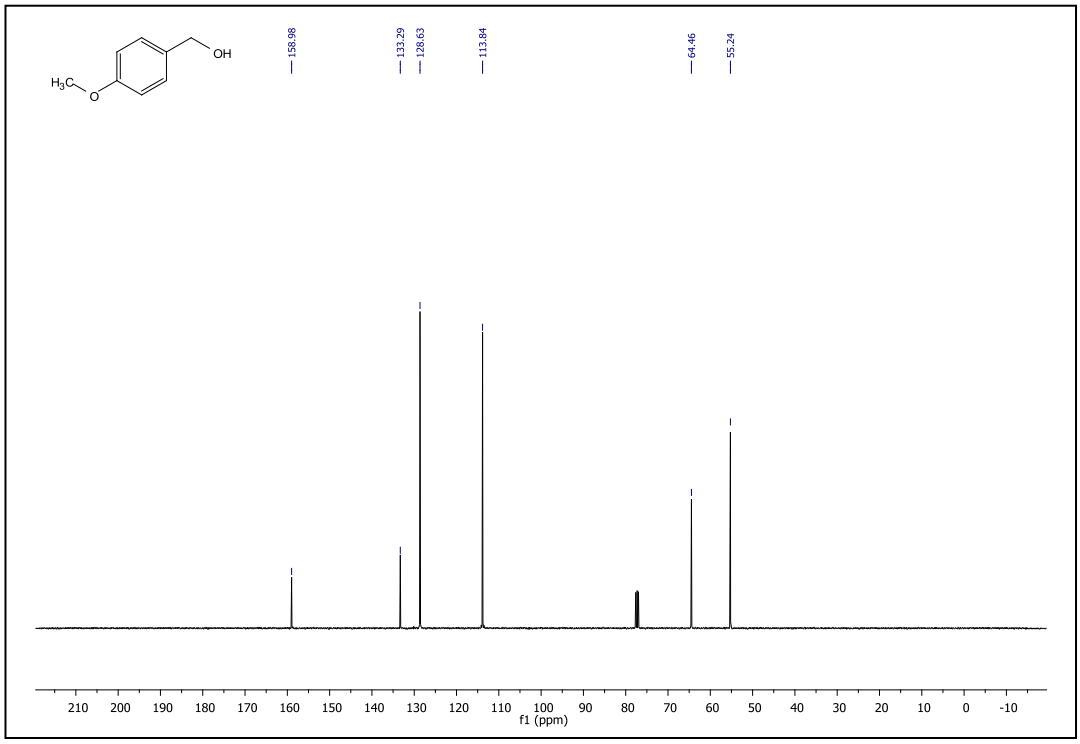

Figure A 77 ^{13}C NMR spectrum of compound **105**

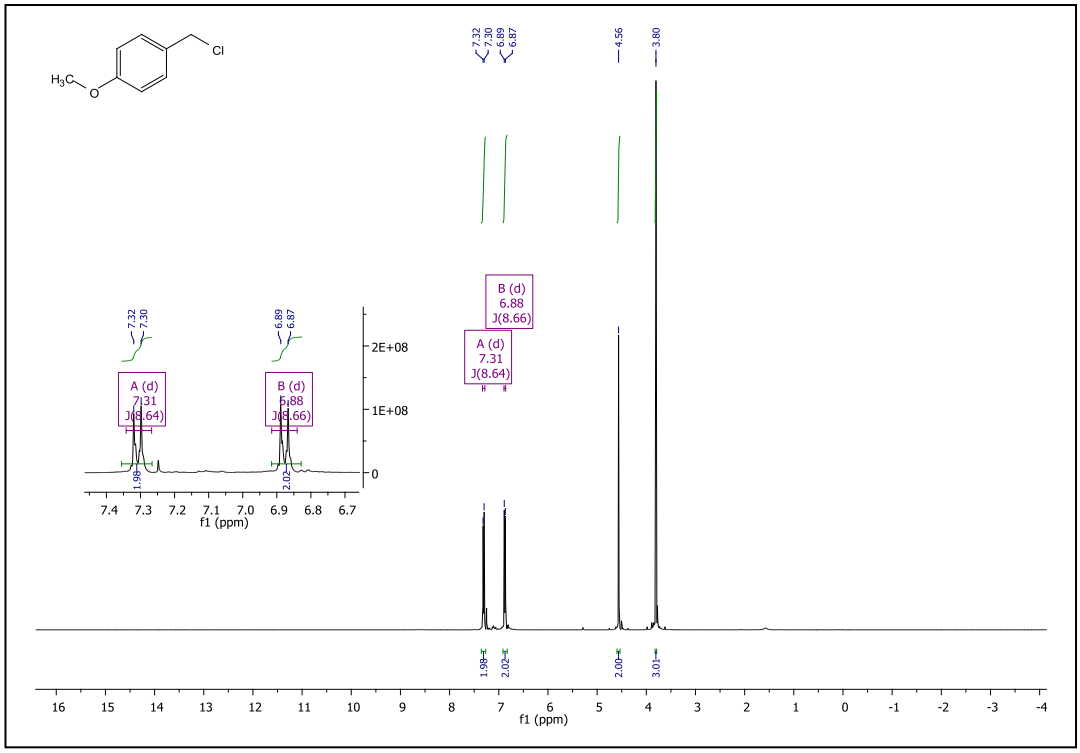

Figure A 78 ^{1}H NMR spectrum of compound **106**

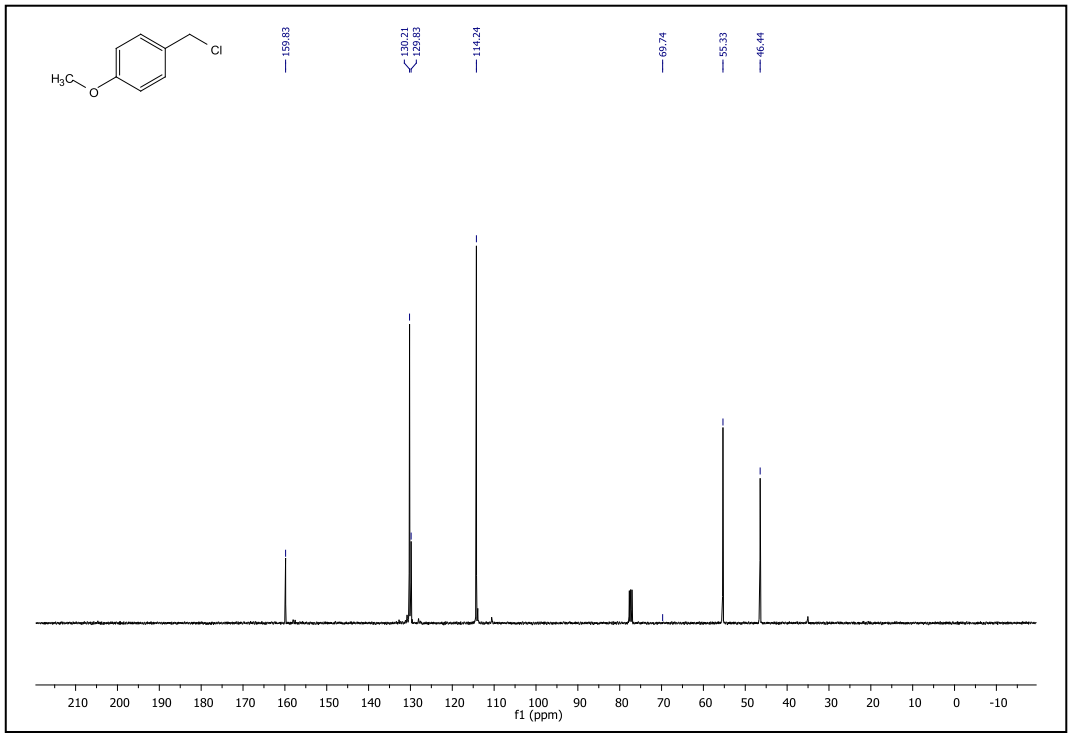

Figure A 79 ^{13}C NMR spectrum of compound **106**

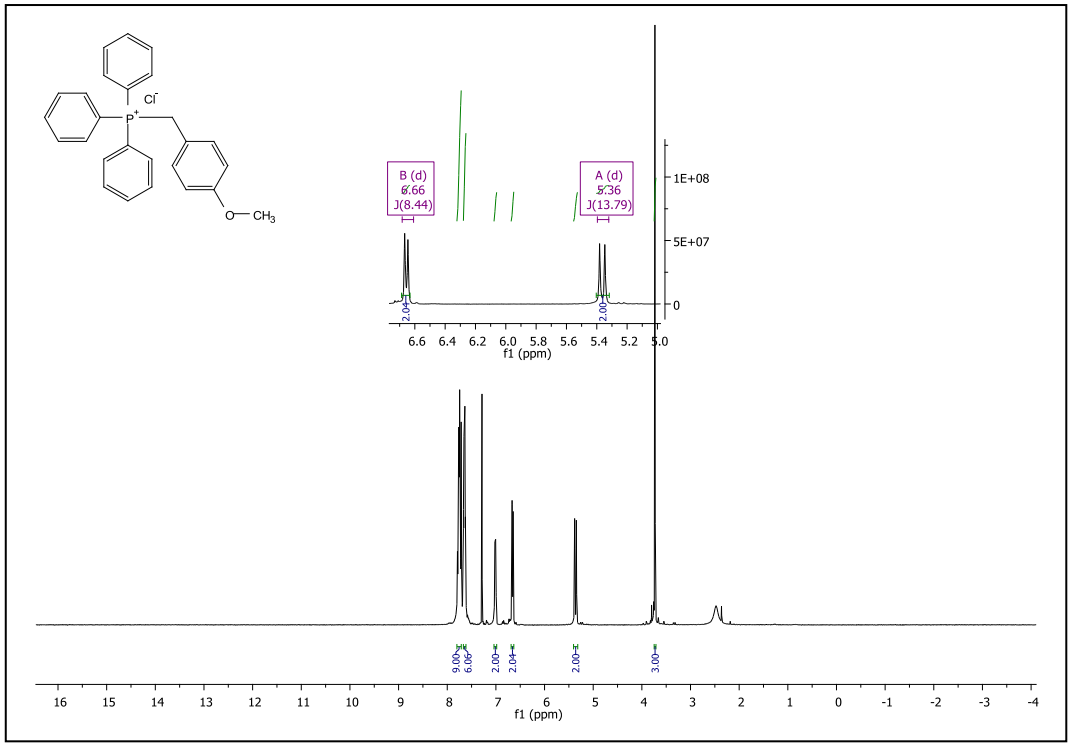

Figure A 80 ^{1}H NMR spectrum of compound **107**

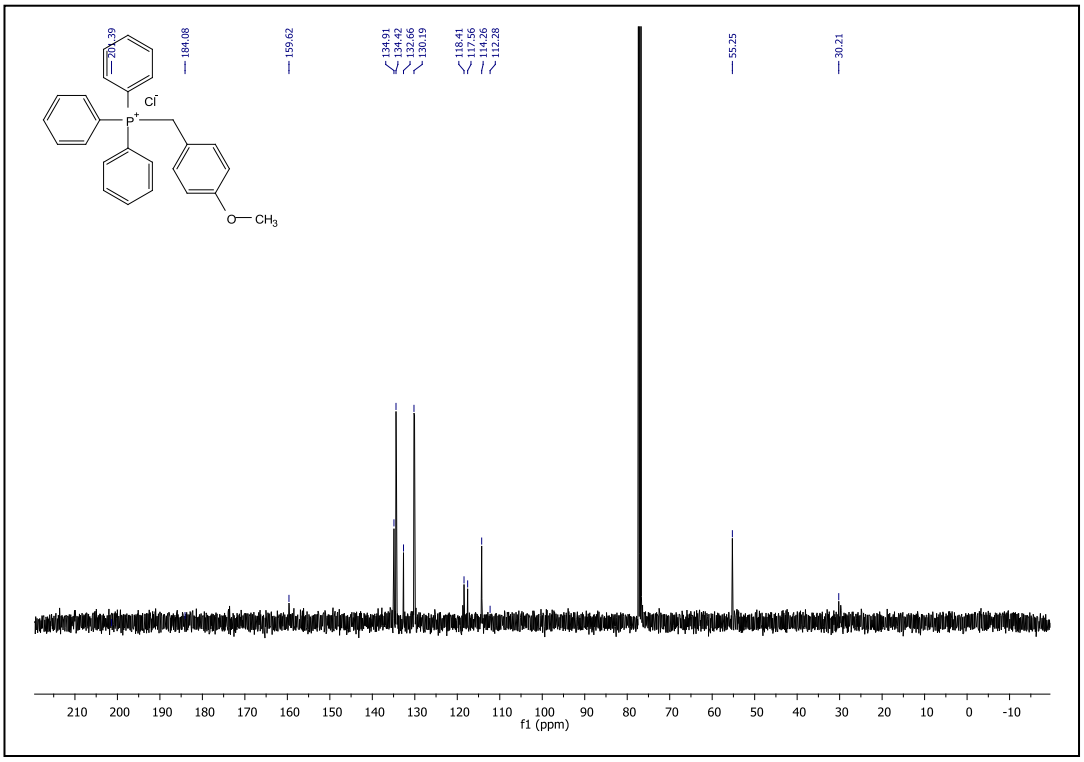

Figure A 81 ^{13}C NMR spectrum of compound **107**

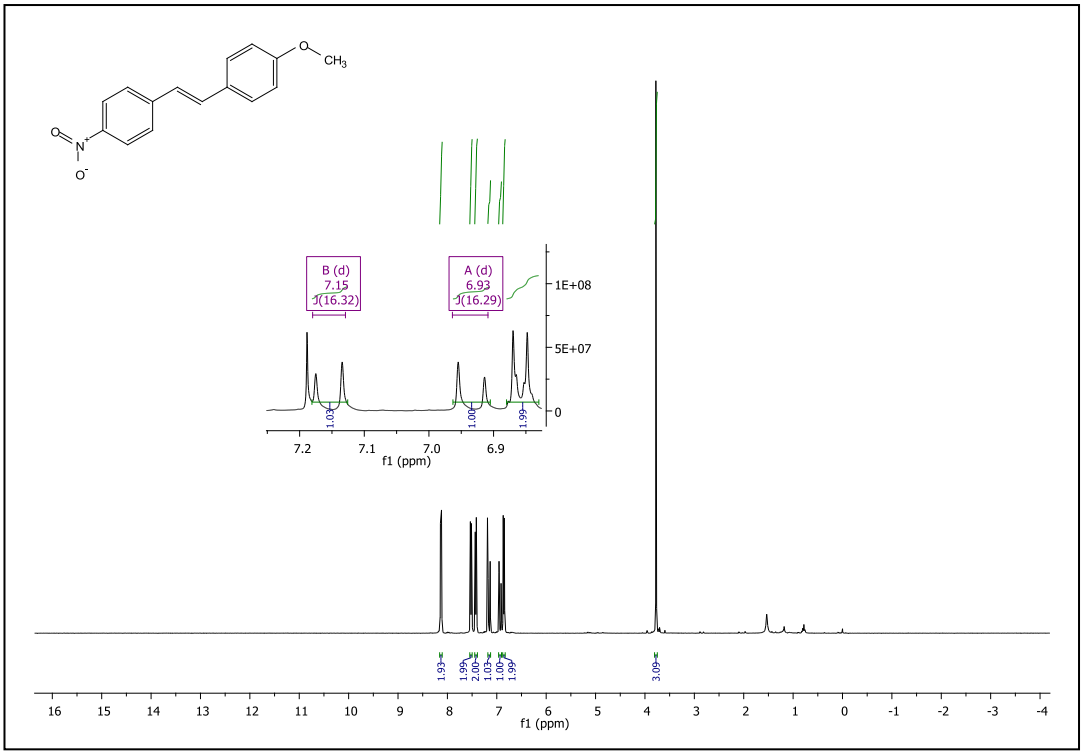

Figure A 82 ^{1}H NMR spectrum of compound **108**

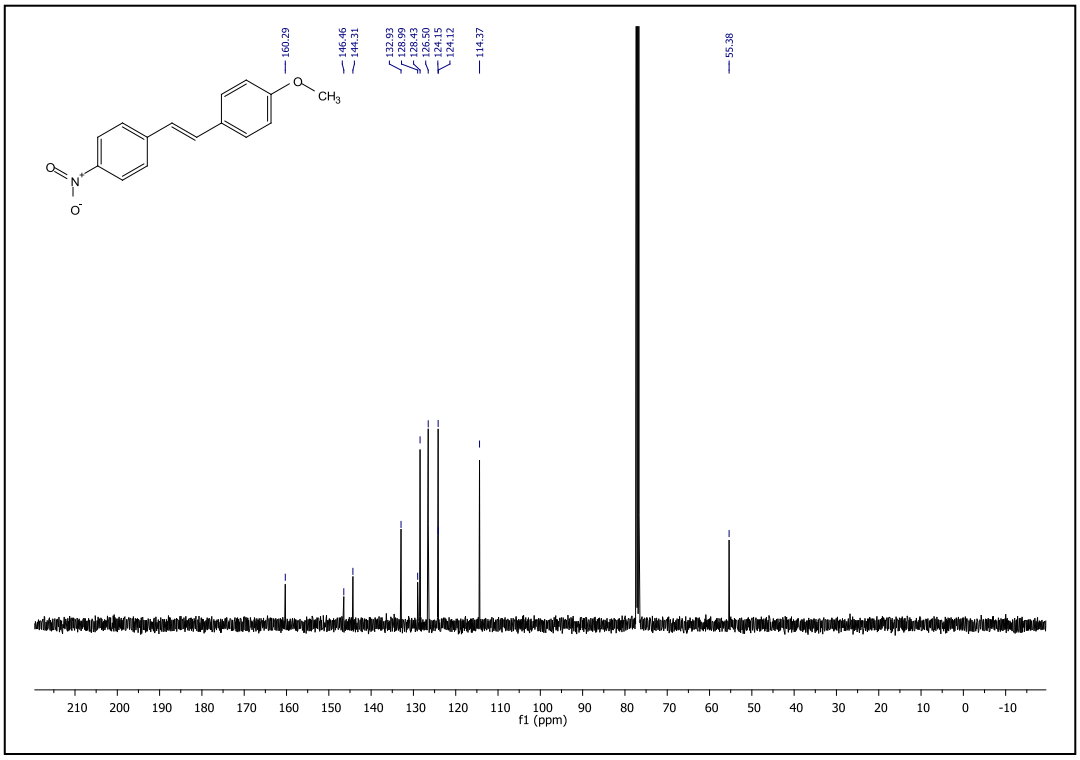

Figure A 83 ^{13}C NMR spectrum of compound **108**

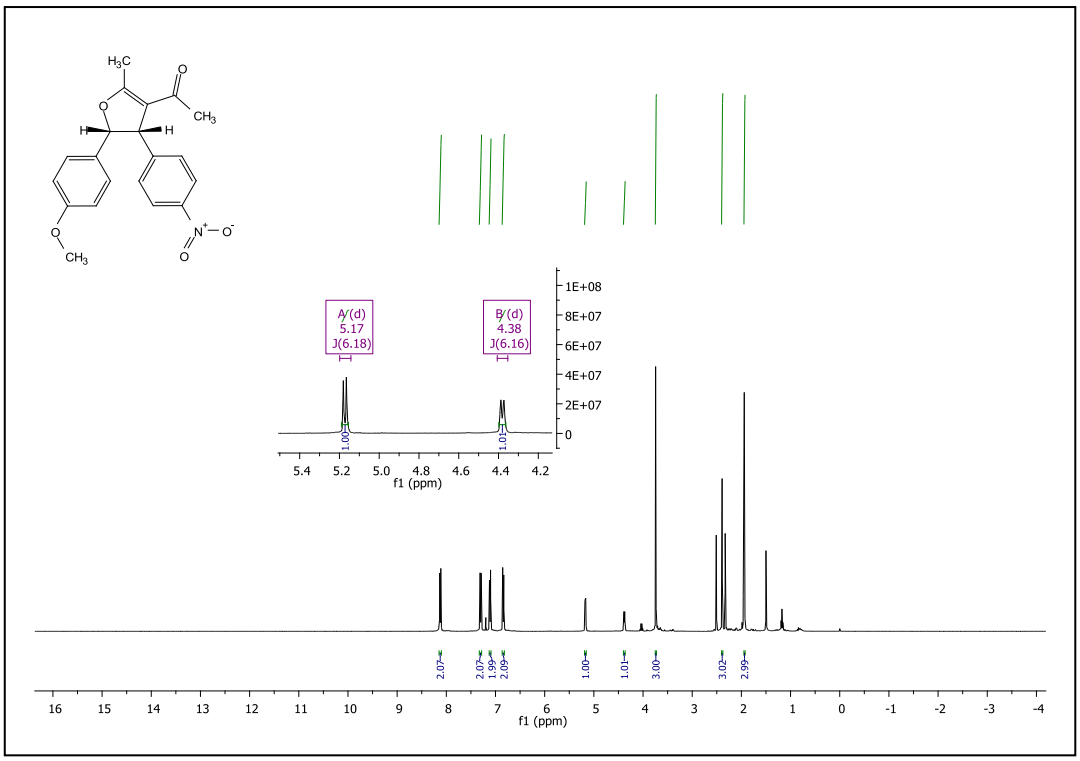

Figure A 84 ^{1}H NMR spectrum of compound **110**

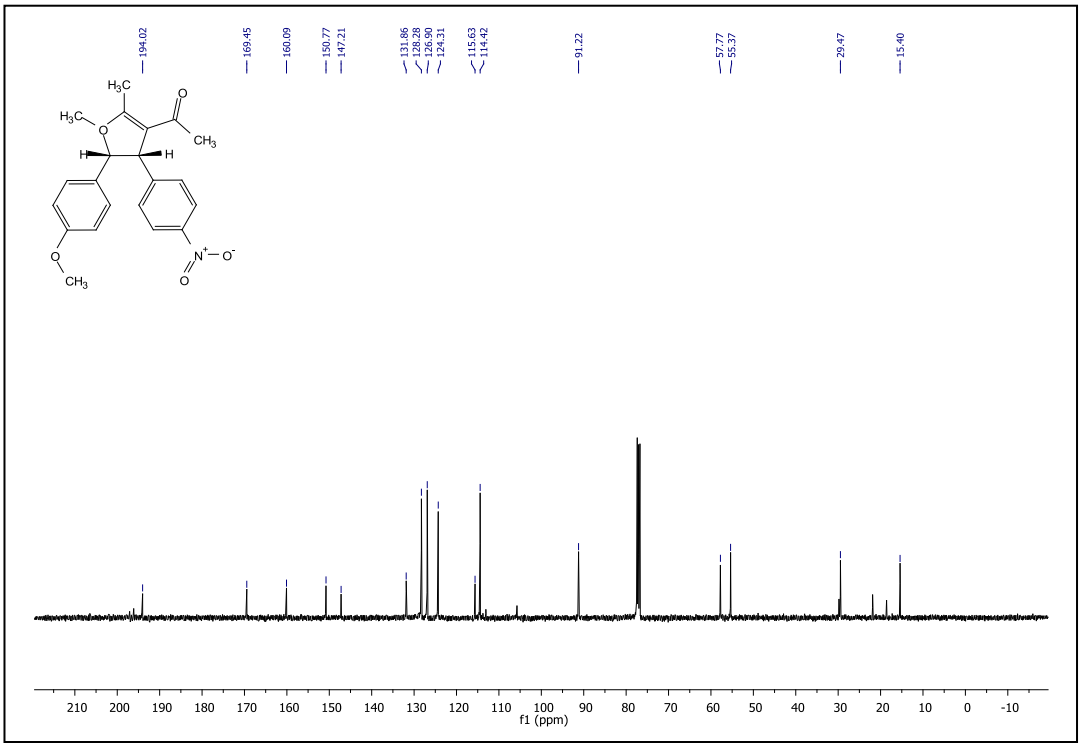

Figure A 85 ^{13}C NMR spectrum of compound **110**

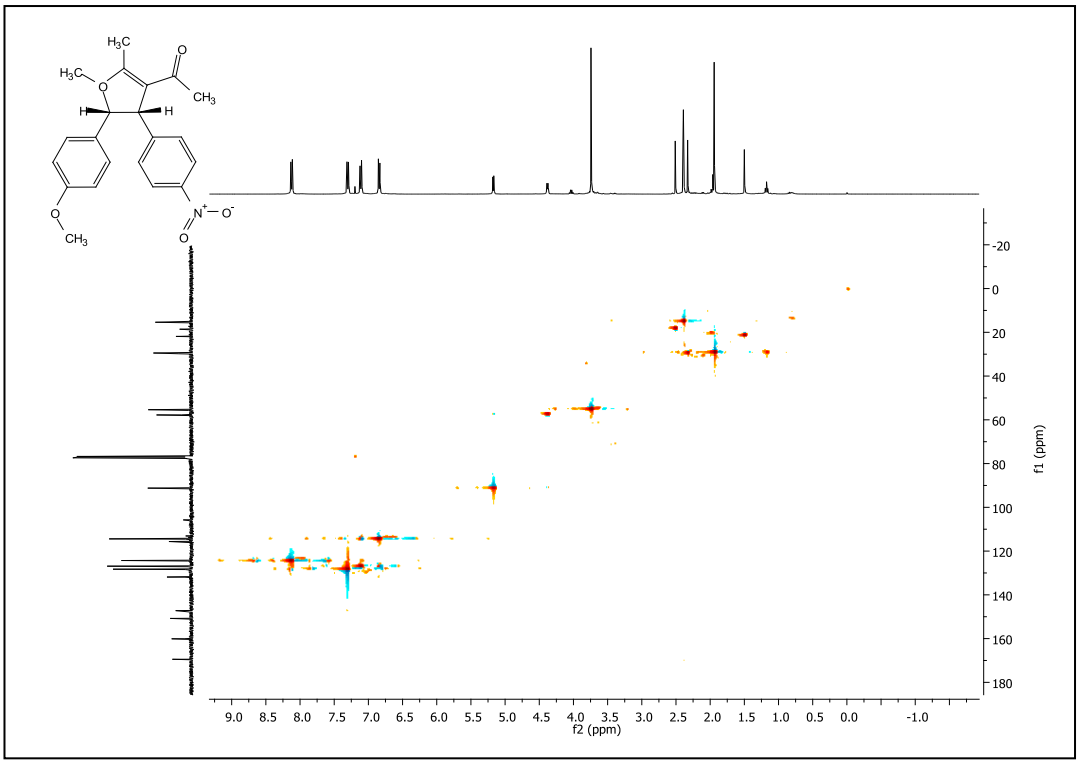

Figure A 86 HSQC spectrum of compound **110**

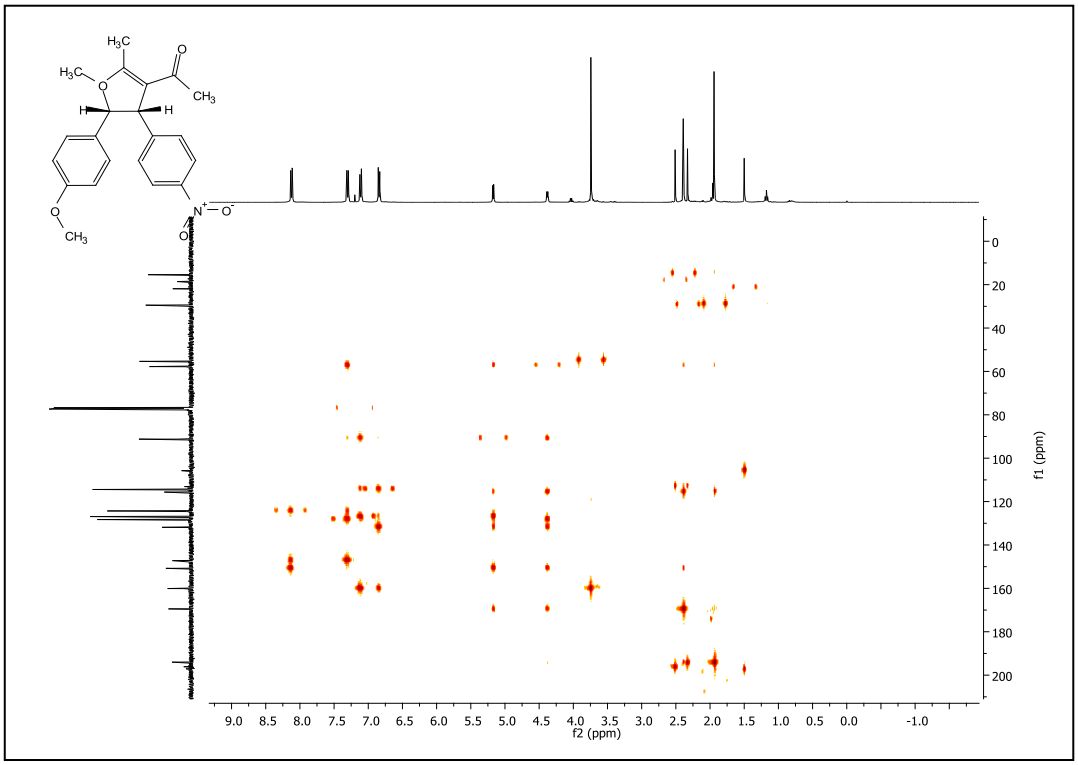

Figure A 87 HMBC spectrum of compound **110**

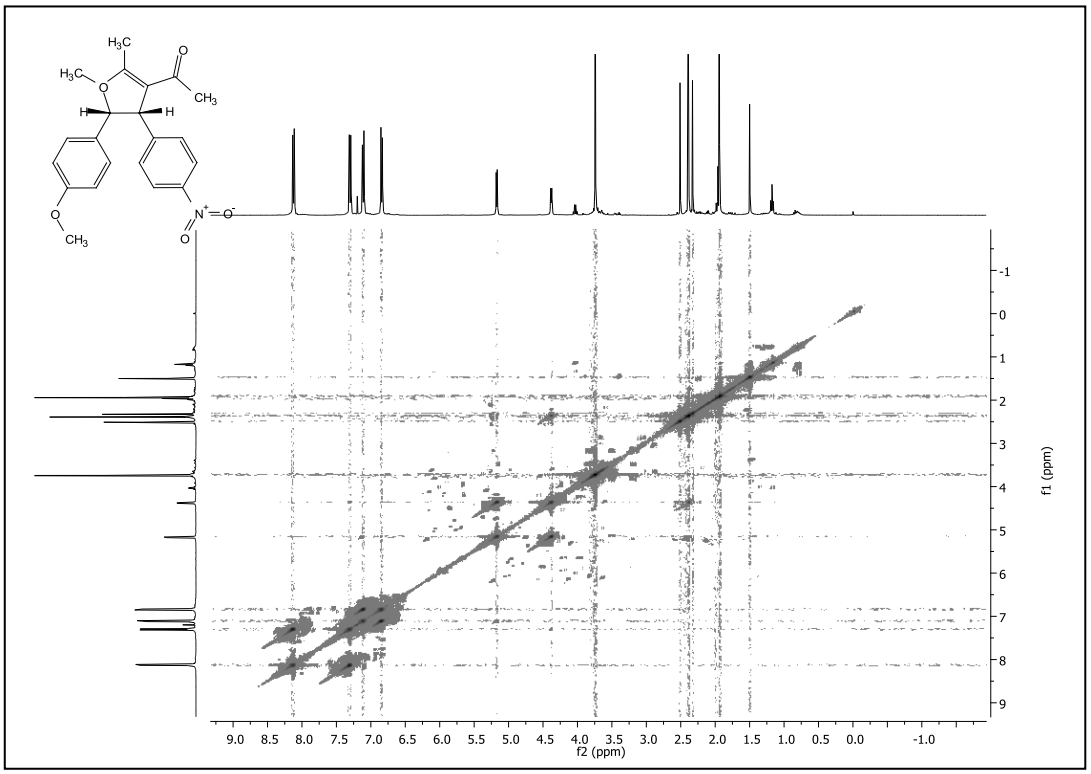

Figure A 88 COSY spectrum of compound **110**

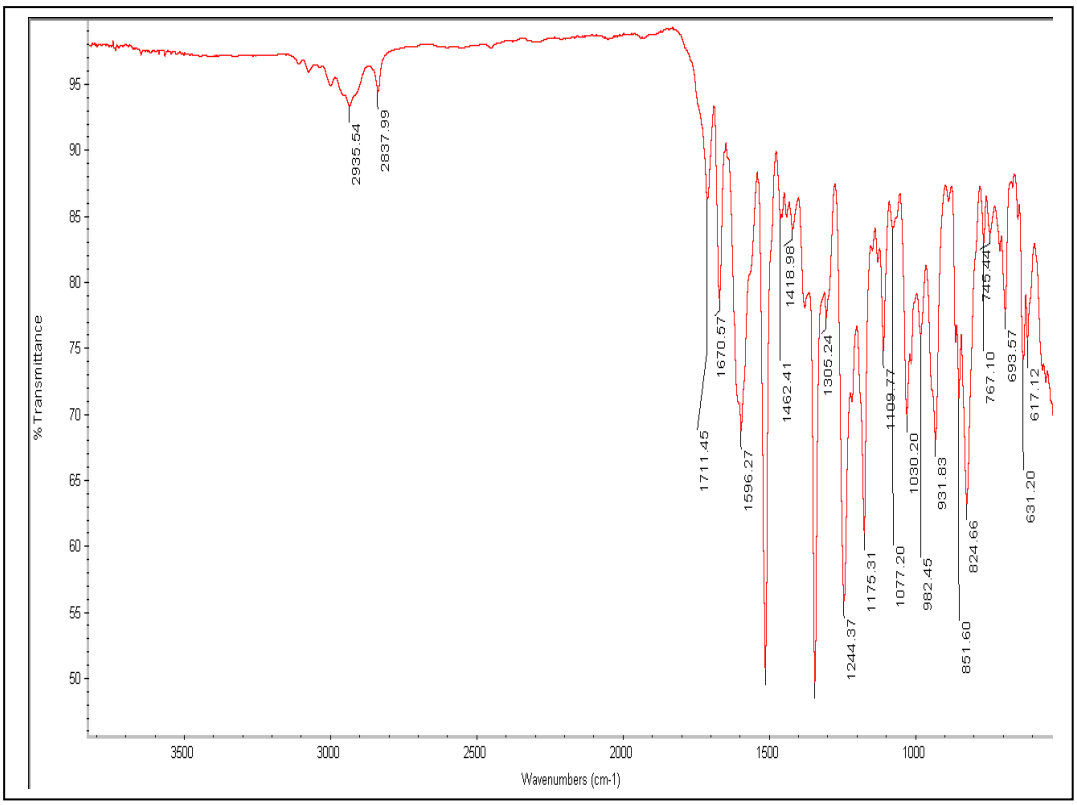

Figure A 89 IR spectrum of compound **110**

THEORETICAL CALCULATIONS

Cartesian Coordinates for the Optimized Structure of Compound 54

	X	Y	Z
C	-0.664342	-3.151499	0.000000
C	-0.848894	-1.795597	0.000000
S	-2.559136	-1.418124	0.000000
C	-2.970296	-3.099680	0.000000
C	-1.868146	-3.891864	0.000000
C	0.178574	-0.790154	0.000000
C	0.000000	0.536190	0.000000
C	1.033231	1.560032	0.000000
C	2.401527	1.271455	0.000000
C	3.339940	2.283937	0.000000
C	2.941239	3.613732	0.000000
C	1.590473	3.918381	0.000000
C	0.650720	2.903307	0.000000
H	2.737159	0.240090	0.000000
H	4.395441	2.036087	0.000000
H	3.681389	4.405340	0.000000
H	1.266040	4.952723	0.000000
H	-0.407220	3.147102	0.000000
H	0.322974	-3.597235	0.000000
H	-1.913800	-4.972640	0.000000
H	-4.008546	-3.394452	0.000000
H	-1.019689	0.920604	0.000000
H	1.188274	-1.197077	0.000000

Cartesian Coordinates for the Optimized Structure of Compound 55

	X	Y	Z
C	-1.443494	0.903648	0.099576
C	-1.593900	0.059122	1.197169
C	-2.527000	-0.962929	1.178462
C	-3.324917	-1.155922	0.061990
C	-3.192944	-0.314096	-1.031308
C	-2.264713	0.712611	-1.009488
H	-2.631041	-1.612946	2.039765
H	-4.052723	-1.959030	0.045361
H	-3.816612	-0.458715	-1.906181
H	-2.157303	1.369588	-1.866511
C	-0.449717	1.990068	0.114960
C	0.879116	1.856081	0.133432
C	1.705955	0.672585	0.055389
C	3.071064	0.672963	0.162000
C	3.663210	-0.595889	-0.017206
C	2.746816	-1.564672	-0.273521
S	1.131771	-0.946471	-0.290171
H	3.629298	1.580034	0.360776
H	4.727612	-0.780752	0.040022
H	2.915574	-2.616707	-0.447746
H	1.467211	2.770831	0.179075
H	-0.847212	3.002255	0.104053
H	-0.959998	0.207571	2.065385

Cartesian Coordinates for the Optimized Structure of Compound 63

	X	Y	Z
C	2.852561	-1.287801	0.001150
C	2.000443	-0.181517	-0.000103
C	2.583019	1.089636	-0.001386
C	3.954949	1.241517	-0.001289
C	4.786490	0.129957	0.000042
C	4.227776	-1.136749	0.001255
C	0.560672	-0.401435	-0.000080
C	-0.397151	0.529996	0.000320
C	-1.829790	0.292620	0.000205
C	-2.774115	1.364106	0.001597
C	-4.064078	0.953157	0.001267
S	-4.176588	-0.773574	-0.000811
C	-2.460179	-0.922577	-0.001230
H	1.954225	1.973060	-0.002581
H	4.384037	2.237304	-0.002319
H	5.863181	0.253382	0.000090
H	4.865977	-2.013107	0.002257
H	2.419134	-2.283349	0.002093
H	-2.479229	2.406459	0.002827
H	-4.961533	1.552309	0.002101
H	0.264065	-1.449465	-0.000285
H	-0.114489	1.580755	0.000892
H	-2.013555	-1.905626	-0.002581

Cartesian Coordinates for the Optimized Structure of Compound 64

	X	Y	Z
C	2.913567	0.862193	0.567571
C	1.704551	0.733718	-0.117313
C	1.471554	-0.444415	-0.829099
C	2.401619	-1.467592	-0.825997
C	3.586544	-1.335907	-0.117114
C	3.840678	-0.164693	0.578198
C	0.763775	1.856165	-0.125021
C	-0.573440	1.847809	-0.115826
C	-1.497636	0.730627	0.038742
C	-2.770348	0.766090	-0.458817
S	-3.671684	-0.656646	-0.084413
C	-2.322122	-1.310445	0.785611
C	-1.257520	-0.476069	0.766812
H	2.205140	-2.372304	-1.390349
H	4.314103	-2.139341	-0.117345
H	4.769007	-0.047970	1.125959
H	3.118978	1.783242	1.104663
H	-0.324777	-0.693600	1.269653
H	-2.410192	-2.271412	1.269024
H	-1.060870	2.815636	-0.210964
H	1.238158	2.835280	-0.153782
H	0.554382	-0.547864	-1.398383
H	-3.224315	1.559784	-1.034337

Cartesian Coordinates for the Optimized Structure of Compound 88

	X	Y	Z
C	-2.752738	1.033577	-0.000847
C	-2.387299	-0.316274	0.000778
C	-3.410972	-1.266734	0.001798
C	-4.742750	-0.891785	0.001040
C	-5.085201	0.449705	-0.000621
C	-4.081312	1.408797	-0.001554
C	-1.003966	-0.773217	0.001669
C	0.090943	-0.005369	-0.001636
C	1.472097	-0.466002	-0.001014
C	1.826205	-1.813648	-0.001616
C	3.144728	-2.227578	-0.000919
C	4.154914	-1.282352	0.000183
C	3.845214	0.068153	0.000539
C	2.518652	0.479130	-0.000010
O	2.146713	1.782393	0.000373
C	3.146052	2.768043	0.001311
H	-3.147588	-2.320071	0.003235
H	-5.516355	-1.651321	0.001838
H	-6.126749	0.749140	-0.001207
H	-4.340346	2.461692	-0.002705
H	-1.987006	1.801168	-0.001371
H	4.645052	0.797107	0.001360
H	5.194162	-1.589889	0.000614
H	3.382204	-3.284548	-0.001435
H	1.042298	-2.562498	-0.003000
H	-0.894389	-1.856318	0.005431
H	-0.025886	1.072994	-0.005038
H	2.633256	3.728373	0.001607
H	3.779752	2.703689	0.893271

H	3.780488	2.704667	-0.890200

Cartesian Coordinates for the Optimized Structure of Compound 89

	X	Y	Z
C	2.897460	0.868203	-0.552474
C	1.630230	0.975185	0.019289
C	1.318609	0.136876	1.091210
C	2.230707	-0.796126	1.547762
C	3.476269	-0.913214	0.946517
C	3.808225	-0.072779	-0.103422
C	0.702065	1.980061	-0.497823
C	-0.632943	1.960316	-0.559835
C	-1.588257	0.908779	-0.193776
C	-2.754398	1.271393	0.473565
C	-3.696302	0.337361	0.870776
C	-3.484873	-0.997363	0.580059
C	-2.352421	-1.390469	-0.116935
C	-1.414699	-0.448359	-0.520481
H	-1.106820	2.873390	-0.915892
H	1.185942	2.876935	-0.880343
O	-0.322382	-0.756292	-1.250751
H	-2.212518	-2.435456	-0.362805
H	-4.208373	-1.745404	0.883529
H	-4.585251	0.651616	1.404185
H	3.161999	1.530105	-1.371462
H	4.783776	-0.146078	-0.571028
H	4.189377	-1.645920	1.306787
H	1.971606	-1.433947	2.385816
H	0.350743	0.226424	1.573259
H	-2.905663	2.321899	0.703028
C	0.081653	-2.099220	-1.330117

H	1.051836	-2.100316	-1.825311
H	0.193238	-2.541613	-0.332877
H	-0.618776	-2.705158	-1.916775

Cartesian Coordinates for the Optimized Structure of Compound 96

	X	Y	Z
C	0.724838	-1.666101	0.000000
C	1.015762	-0.303240	0.000000
C	2.367663	0.059931	0.000000
C	3.372189	-0.880485	0.000000
C	3.057747	-2.236381	0.000000
C	1.721322	-2.625294	0.000000
C	0.000000	0.738134	0.000000
C	-1.326520	0.572851	0.000000
C	-2.339665	1.619065	0.000000
C	-3.687459	1.252863	0.000000
C	-4.692543	2.203590	0.000000
C	-4.373618	3.551016	0.000000
C	-3.039228	3.934112	0.000000
C	-2.037186	2.984344	0.000000
H	-3.943466	0.197676	0.000000
H	-5.730376	1.890217	0.000000
H	-5.156980	4.299909	0.000000
H	-2.779158	4.986739	0.000000
H	-1.002304	3.308755	0.000000
H	2.627374	1.114099	0.000000
H	4.416704	-0.592445	0.000000
O	4.105248	-3.091675	0.000000
H	1.447618	-3.672575	0.000000
H	-0.307839	-1.997745	0.000000
H	-1.728275	-0.439178	0.000000

H	0.399172	1.751240	0.000000
C	3.832880	-4.469804	0.000000
H	4.795992	-4.976955	0.000000
H	3.271225	-4.771966	0.891703
H	3.271225	-4.771966	-0.891703

Cartesian Coordinates for the Optimized Structure of Compound 97

	X	Y	Z
C	3.560033	0.249951	-0.787593
C	2.465752	0.578970	0.011667
C	2.055004	-0.339583	0.978912
C	2.697406	-1.556356	1.115610
C	3.766953	-1.881364	0.294019
C	4.198569	-0.971210	-0.656675
C	1.830308	1.892620	-0.145371
C	0.533617	2.218859	-0.134017
C	-0.657999	1.372164	-0.080296
C	-1.838752	1.897107	0.456100
C	-2.997977	1.157794	0.514614
C	-3.022277	-0.140789	0.013266
C	-1.869907	-0.674430	-0.554056
C	-0.710283	0.080639	-0.597709
H	0.311366	3.283133	-0.192739
H	2.532015	2.712275	-0.288610
H	0.173754	-0.347330	-1.056533
H	-1.865554	-1.672066	-0.974036
O	-4.204121	-0.792029	0.110727
H	-3.908558	1.564911	0.938336
H	3.904392	0.965098	-1.528483
H	5.041146	-1.210743	-1.295608
H	4.268477	-2.836079	0.403865

H	2.366681	-2.254923	1.876170
H	1.226581	-0.088129	1.632248
H	-1.835363	2.912460	0.840738
C	-4.280703	-2.105106	-0.381644
H	-5.299611	-2.444430	-0.203844
H	-4.074277	-2.148589	-1.457381
H	-3.586544	-2.774959	0.139110

Cartesian Coordinates for the Optimized Structure of Compound 101

	X	Y	Z
C	-1.400370	0.777128	0.000000
C	0.000000	0.756592	0.000000
C	0.675137	1.982050	0.000000
C	-0.006950	3.180748	0.000000
C	-1.388579	3.157368	0.000000
C	-2.095130	1.965432	0.000000
C	0.780846	-0.469951	0.000000
C	0.303128	-1.719017	0.000000
C	1.076827	-2.951737	0.000000
C	0.397610	-4.171821	0.000000
C	1.083162	-5.373262	0.000000
C	2.467498	-5.380349	0.000000
C	3.159266	-4.176427	0.000000
C	2.474537	-2.978245	0.000000
H	-0.687937	-4.169253	0.000000
H	0.534009	-6.307746	0.000000
H	3.008700	-6.319296	0.000000
H	4.243174	-4.175444	0.000000
H	3.034380	-2.049576	0.000000
H	1.759814	1.984864	0.000000
H	0.511051	4.130796	0.000000

N	-2.129617	4.430109	0.000000
H	-3.176913	1.990161	0.000000
H	-1.956661	-0.152730	0.000000
H	-0.775178	-1.867380	0.000000
H	1.858094	-0.318733	0.000000
O	-3.342114	4.373823	0.000000
O	-1.483773	5.457742	0.000000

Cartesian Coordinates for the Optimized Structure of Compound 102

	X	Y	Z
C	3.833334	0.233219	-0.738931
C	2.729904	0.572587	0.043374
C	2.284458	-0.342815	0.997153
C	2.902713	-1.571670	1.136618
C	3.979308	-1.908975	0.329838
C	4.445220	-1.000759	-0.606647
C	2.113387	1.892276	-0.124826
C	0.820279	2.230241	-0.139517
C	-0.369594	1.378577	-0.115259
C	-1.545216	1.886886	0.443390
C	-2.707843	1.144150	0.468178
C	-2.697733	-0.118824	-0.092965
C	-1.561076	-0.645661	-0.682096
C	-0.404980	0.104826	-0.692340
H	0.598757	3.294049	-0.193367
H	2.824106	2.707557	-0.247133
H	0.484817	-0.294673	-1.163704
H	-1.601920	-1.630222	-1.129357
N	-3.935000	-0.921217	-0.077109
H	-3.619214	1.527528	0.907666
H	4.204381	0.947596	-1.467387

H	5.294112	-1.251922	-1.232190
H	4.461295	-2.873368	0.440918
H	2.547304	-2.269375	1.886315
H	1.453182	-0.080072	1.642325
H	-1.537560	2.884132	0.870364
O	-3.891306	-2.029899	-0.568100
O	-4.920846	-0.424732	0.426787

Cartesian Coordinates for the Optimized Structure of Compound 108

	X	Y	Z
C	2.429921	-0.169905	0.000000
C	1.415629	0.797159	0.000000
C	1.796699	2.143867	0.000000
C	3.123563	2.519285	0.000000
C	4.093818	1.534283	0.000000
C	3.758257	0.189391	0.000000
C	0.000000	0.471138	0.000000
C	-0.532979	-0.756700	0.000000
C	-1.941879	-1.105947	0.000000
C	-2.307357	-2.457752	0.000000
C	-3.624855	-2.850761	0.000000
C	-4.637250	-1.894124	0.000000
C	-4.300832	-0.542058	0.000000
C	-2.971263	-0.165375	0.000000
H	-1.527571	-3.212952	0.000000
H	-3.903370	-3.897653	0.000000
O	-5.900372	-2.367319	0.000000
H	-5.069256	0.220521	0.000000
H	-2.736305	0.893389	0.000000
H	1.026345	2.907582	0.000000
H	3.417535	3.560322	0.000000

N	5.513458	1.920610	0.000000
H	4.543002	-0.555347	0.000000
H	2.176568	-1.223280	0.000000
H	0.137971	-1.614085	0.000000
H	-0.663336	1.333586	0.000000
O	6.339306	1.030256	0.000000
O	5.774823	3.106496	0.000000
C	-6.959003	-1.441910	0.000000
H	-7.878586	-2.023838	0.000000
H	-6.941037	-0.805760	0.892172
H	-6.941037	-0.805760	-0.892172

Cartesian Coordinates for the Optimized Structure of Compound 109

	X	Y	Z
C	2.494079	1.724447	-0.715564
C	1.295132	1.581923	-0.011687
C	1.120558	0.439144	0.776516
C	2.089682	-0.538929	0.831969
C	3.251074	-0.376359	0.094736
C	3.469838	0.749401	-0.677003
C	0.313369	2.664936	-0.063805
C	-1.022757	2.615379	-0.004328
C	-1.927715	1.468288	-0.004657
C	-3.138211	1.555125	0.691969
C	-4.030304	0.508547	0.717220
C	-3.751348	-0.663245	0.016939
C	-2.570848	-0.758331	-0.714151
C	-1.679510	0.300567	-0.720135
H	-1.529347	3.578407	0.033394
H	0.755899	3.654822	-0.153271
H	-0.772945	0.218598	-1.309330

H	-2.342536	-1.644589	-1.292055
O	-4.683650	-1.635969	0.097276
H	-4.961517	0.571323	1.267655
H	2.652754	2.617570	-1.310490
H	4.394650	0.848186	-1.229989
N	4.285722	-1.424677	0.145569
H	1.966968	-1.422983	1.443645
H	0.213707	0.327712	1.358891
H	-3.371097	2.466687	1.233769
C	-4.447959	-2.843219	-0.584178
H	-5.300375	-3.487050	-0.376783
H	-4.373014	-2.689683	-1.666681
H	-3.534923	-3.335301	-0.230392
O	5.308452	-1.237568	-0.480454
O	4.051603	-2.413587	0.809378