INVESTIGATION OF 1,3-DIPOLAR CYCLOADDITION REACTIONS OF PHENANTHROLINIUM *N*-YLIDES

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INVESTIGATION OF 1,3-DIPOLAR CYCLOADDITION REACTIONS OF PHENANTHROLINIUM *N*-YLIDES

by
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THE GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES
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Approval of the Graduate School of Natural and Applied Science.

Prof. Dr. Nihat ÇELEBİ

Director

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

Doç.Dr.Azra BOZCAARMUTLU

Deputy Head of Department

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

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ABSTRACT

INVESTIGATION OF 1,3-DIPOLAR CYCLOADDITION REACTIONS OF PHENANTHROLINIUM N-YLIDES

Sağırlı, Akın
M.Sc. ,Department of Chemistry
Supervisor: Prof.Dr. Yaşar DÜRÜST

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In this study, 1,3-dipolar cycloadditions reactions of *(Z)* substituted arylidene oxazolones to phenanthrolinium *N*-ylides were carried out for the first time. In the first stage of the work a number of substituted arylidene oxazolones as dipolarophilic structures were prepared according to the literature procedures. Some of them are novel compounds and not reported previously. Both electron-withdrawing and electron-releasing groups were selected on the starting arylidene oxazolones. In the second part, the 1,3-dipolar cycloaddition reaction of phenanthrolinium ylides prepared from phenanthroline and phenacyl bromide with (*Z*)-substituted arylidene oxazolones afforded novel aryl substituted spiro[oxazole-4,10'-pyrrolo[1,2-a][

1,10]phenanthrolin]-5-ones, regioselectively. Totally, 15 novel aryl substituted spiro oxazolo [1,10] phenanthrolines including three chiral centers were obtained. The structures and stereochemical configurations of new aryl substituted spiro oxazolo [1,10] phenanthroline were elucidated by means of IR, NMR, 2D NMR, MASS, single crystal X-Ray Diffraction spectra and physical characteristics (melting points and R_f values).

Key words: 1,3-dipolar cycloaddition, phenanthrolinium *N*-ylide, arylidene oxazolone, spectroscopy

ÖZET

FENANTROLİNYUM *N*-İLİDLERİN 1,3-DIPOLAR HALKA KATILMA TEPKİMELERİNİN İNCELENMESİ

Sağırlı, Akın
Yüksek Lisans, Kimya Bölümü
Tez Danışmanı: Prof.Dr. Yaşar DÜRÜST

HAZİRAN 2010, 194 sayfa

Bu çalışmada, (*Z*)-substitue ariliden oksazolonların fenatrolinyum N-ilidlere 1,3-dipolar halka katılma tepkimeleri ilk defa çalışıldı. Çalışmanın ilk aşamasında dipolarofilik yapılar olarak bir seri substitue ariliden oksazolon literatürdeki yöntemlere göre hazırlandı. Bunların bazıları yenidir ve daha önce literatürde bildirilmemiştir. Başlangıç ariliden oksazolonlarda hem elektron çeken hem de elektron salan gruplar seçilmiştir.

İkinci bölümde, fenantrolin ve fenaçil bromürden hazırlanan fenatrolinyum fenaçil bromürün trietilamin etkisiyle tepkime ortamında oluşturulan fenatrolinyum ilidlerin (*Z*)-substitue ariliden oksazolonların 1,3-dipolar halkalı

tepkimeleri üzerinden stereoizomerik yeni substitue aril spiro[oksazol-4,10'-pirrolo[1,2-a][1,10]fenantrolin]-5-on bileşikleri, regioseçimli bir şekilde sentezlendiler. Toplam olarak üç kiral merkez taşıyan 15 yeni aril substitue spiro oxazolo [1,10] fenanthrolin elde edildi. Bu yeni aril substitue spiro oxazolo [1,10] fenanthrolin bileşiklerinin yapıları ve stereokimyasal konfigurasyonları IR, NMR, 2D NMR, Kütle, tek crystal X-Işını kırınımı spektrumları ve fiziksel sabitler (melting points and R_f values) yardımıyla aydınlatıldı.

Anahtar kelimeler: 1,3-dipolar halkalı katılma, fenantrolinyum *N*-ilid, ariliden oksazolon, spektroskopi

to my grandfather

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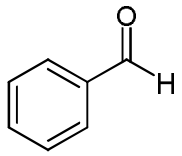
Finally I would like to thank my parents, for their unconditional love and support throughout my entire education. Everything I have accomplished has been derived from the values they taught me.

FORMULAE



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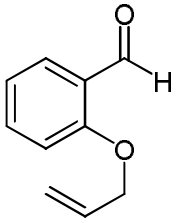

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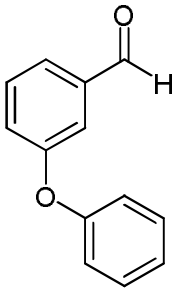

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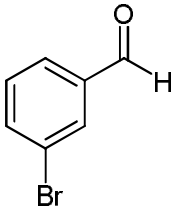

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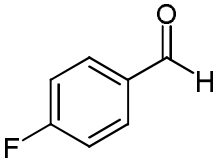

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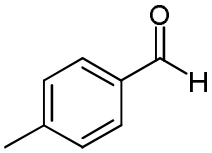

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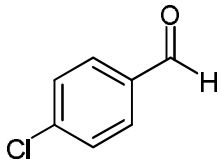

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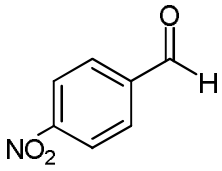

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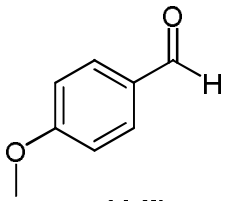

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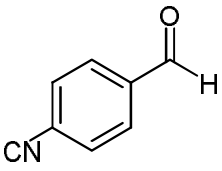

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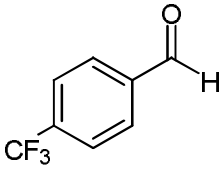

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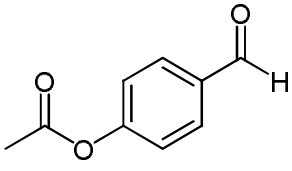

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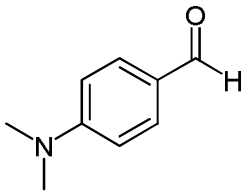

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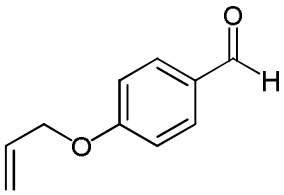

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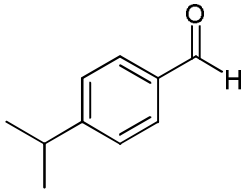

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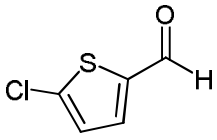

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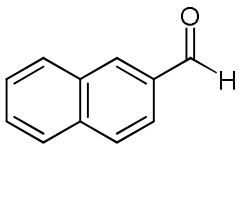

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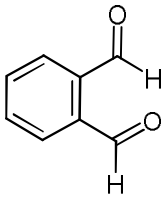

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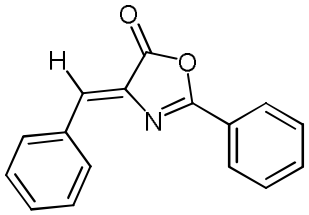

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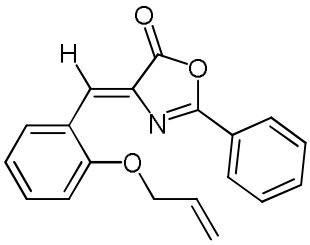

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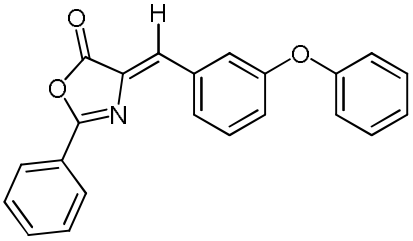

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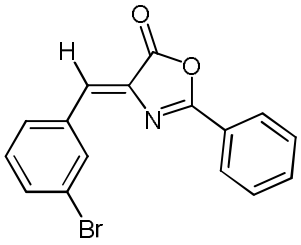

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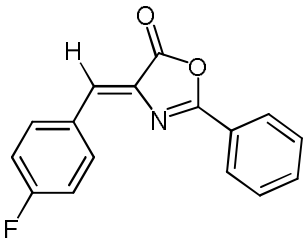

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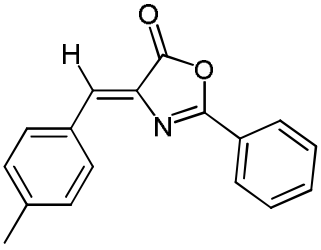

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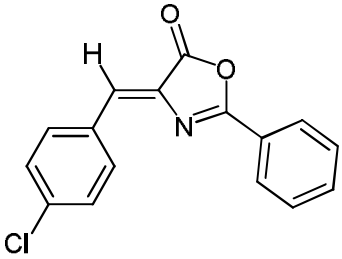

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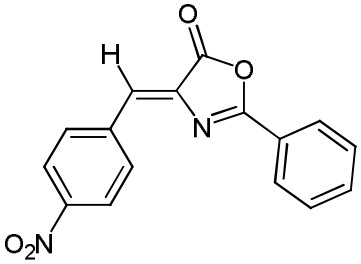

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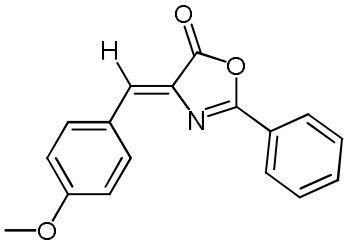

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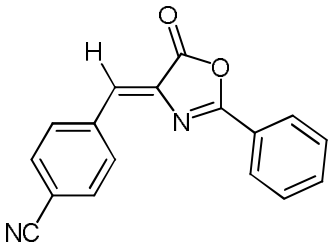

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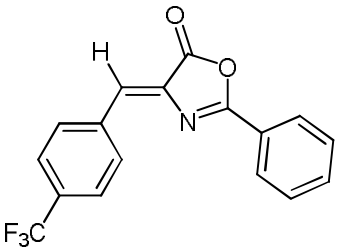

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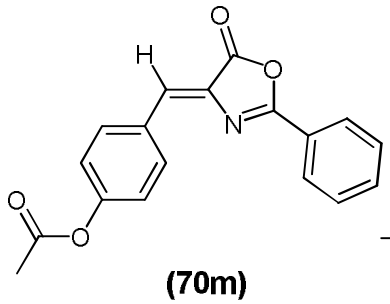

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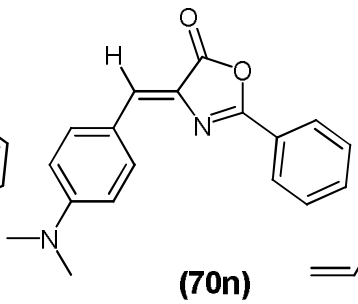

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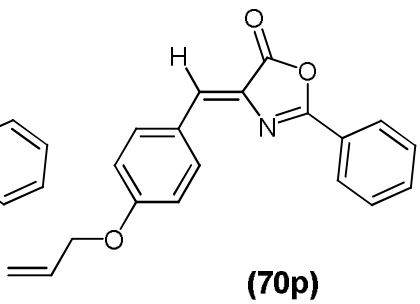

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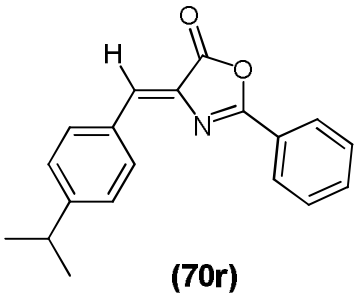

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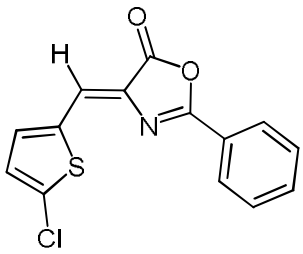

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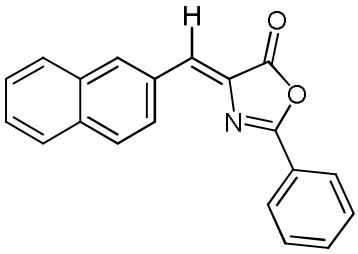

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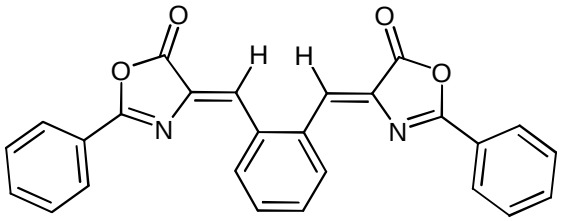

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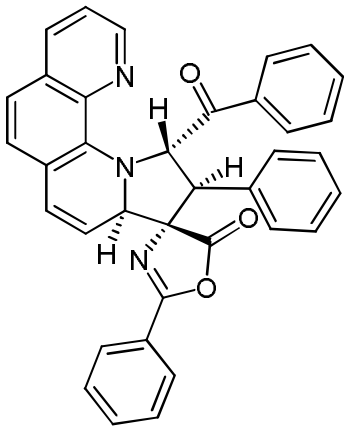

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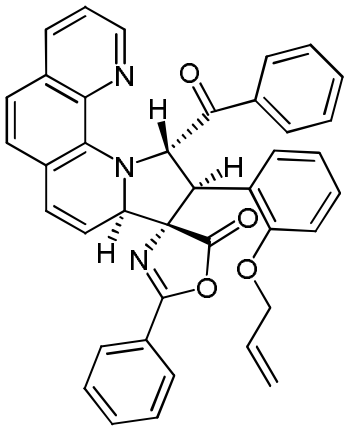

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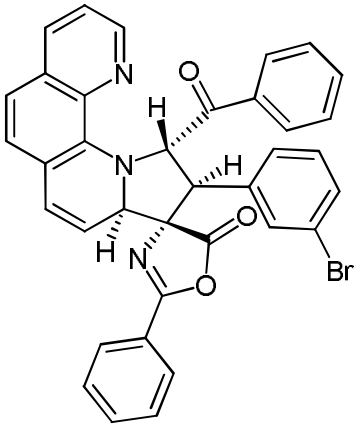

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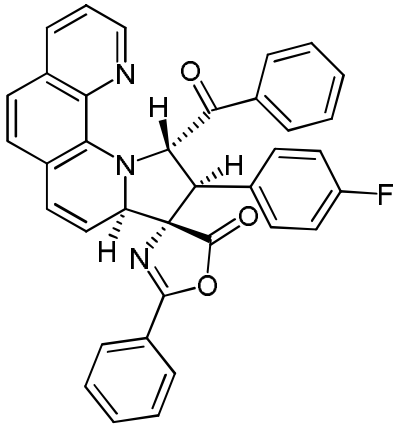

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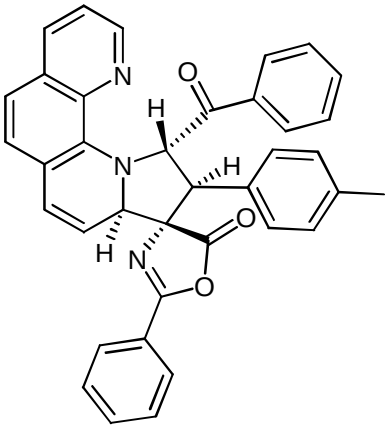

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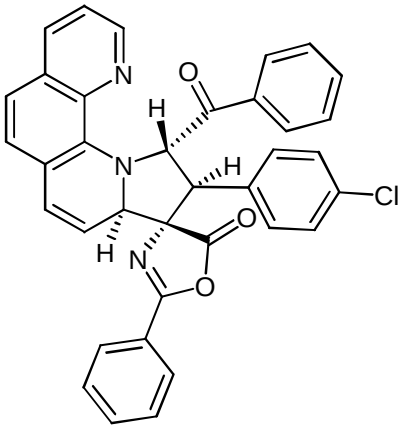

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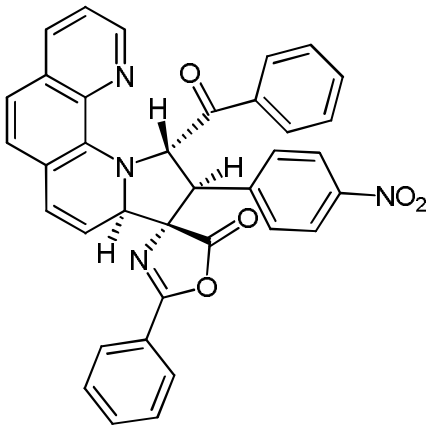

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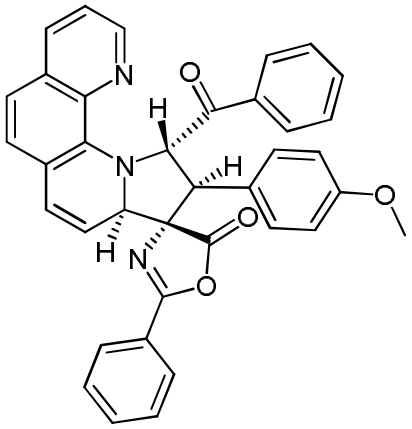

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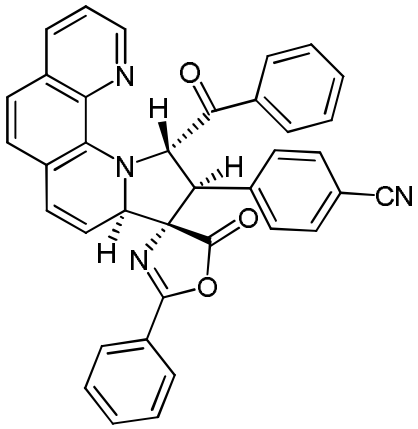

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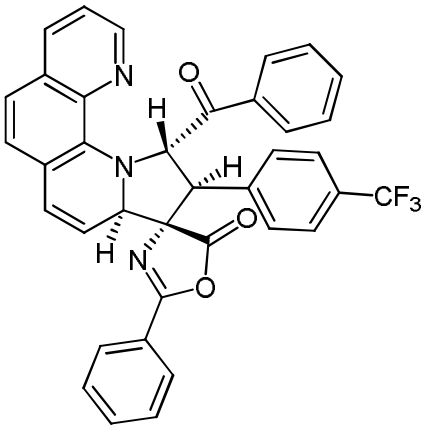

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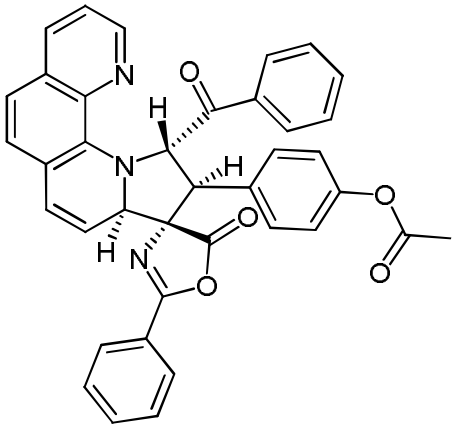

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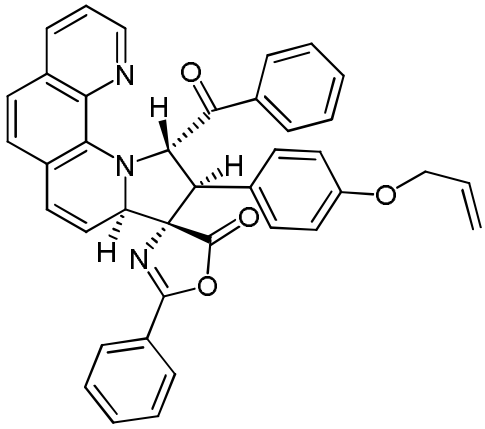

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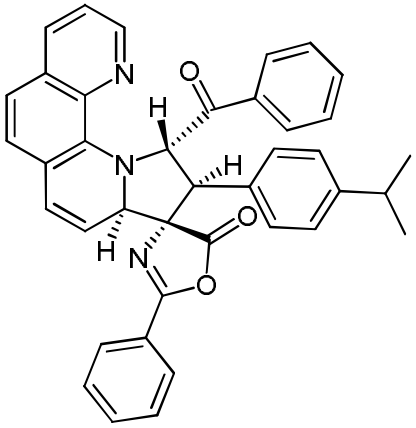

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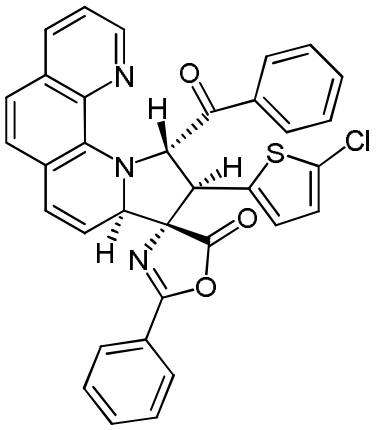

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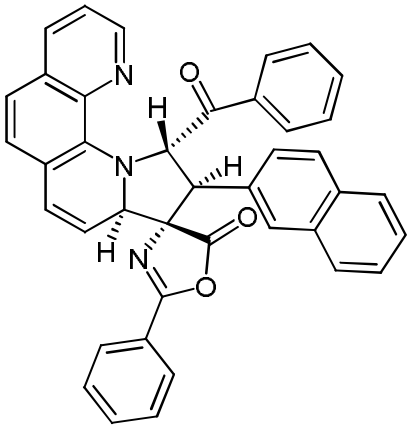

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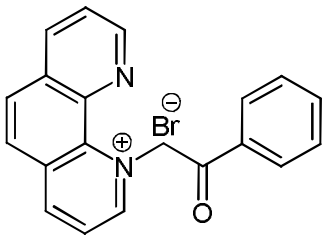

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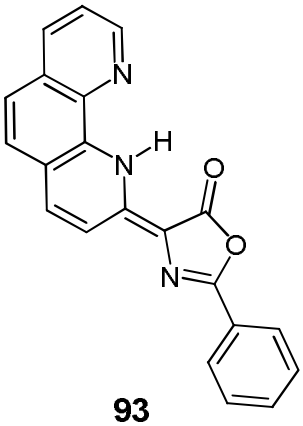

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ABBREVIATIONS

Ar	Aryl-
[1,3]-DC	[1,3]-Dipolar cycloadditions
DCM	Dichloromethane
AMY	Azomethine ylide
FMO	Frontier Molecular Orbital
COSY	Correlation spectroscopy
d	Doublet (NMR)
δ	Chemical shift (NMR)
dd	Doublet of doublets (NMR)
HMBC	Heteronuclear multiple bond correlation
HSQC	Heteronuclear single quantum correlation
IR	Infrared spectroscopy
m	Multiplet (NMR)
min	Minutes
m.p.	Melting point
LCMS	Liquid chromatography mass spectrometry
NMR	Nuclear magnetic resonance
NOESY	Nuclear Overhauser enhancement spectroscopy
Ph	Phenyl
ppm	Parts per million (NMR)
Rf	Retardation factor

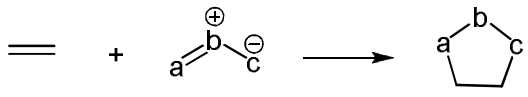
rt	Room temperature
s	Singlet (NMR)
t	Triplet (NMR)
TLC	Thin layer chromatography
LUMO	Lowest unoccupied molecular orbital
HOMO	Highest occupied molecular orbital
THF	Tetrahydrofuran
BuLi	Butyllithium
LDA	Lithiumdiisopropylamide
Me	Methyl
Δ	Heat
CH_3CN	Acetonitrile
Z	Conformation
E	Conformation
J	Coupling constant (NMR)
UV	Ultraviolet
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
NaOAc	Sodium acetate
EWG	Electron withdrawing
Hz	Hertz

CHAPTER I

INTRODUCTION

1.1. THE 1,3-DIPOLAR CYCLOADDITION REACTION

The addition of a 1,3-dipole to an alkene for the synthesis of five-membered rings is a classic reaction in organic chemistry (Scheme 1.1). The 1,3-dipolar cycloadditions (DC) reactions are used for the preparation of molecules of fundamental importance for both academia and industry. The general application of 1,3-dipoles in organic chemistry was first established by the systematic studies by Huisgen in the 1960s [1]. At the same time, the new concept of conservation of orbital symmetry, developed by Woodward and Hoffmann [2,3]. The chemistry of the 1,3-DC reaction has thus evolved for more than 100 years, and a variety of different 1,3-dipoles have been discovered.



1 **2** **3**

Scheme 1. 1 The simple representation of a 1,3-dipolar cycloaddition

1.1.1. The 1,3-dipole

A 1,3-dipole is a compound of the type a-het-b structure that undergoes 1,3-DC with multiply bonded systems and can best be described with a zwitterionic all octet lewis structure. Some important dipoles can be given an examples in Figure 1.1 [4].

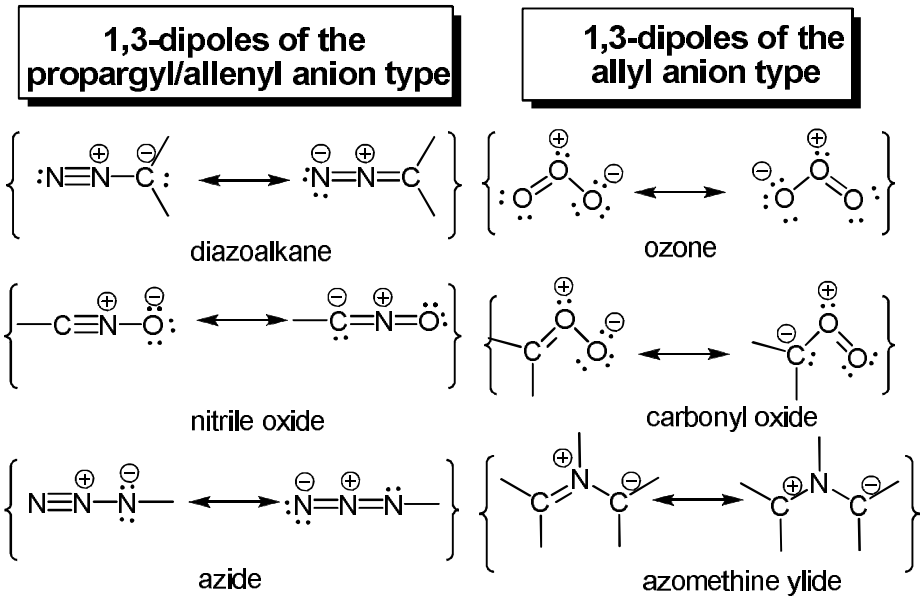


Figure 1. 1 Important 1,3-dipoles

Basically, 1,3 dipoles can be divided into two different types: the allyl anion type and the propargyl/allenyl anion type. 1,3 dipoles of the allyl anion type are bent just like allyl anions. The central atom can be an N, O or S atom, and this atom carries a formal positive charge in both all octet resonance forms. Centers *a* and *b* of the 1,3 dipole of the allyl anion type carry the formal negative charge , again one in each of the resonance forms. The 1,3 dipoles of the propargyl anion type contain a linearly coordinated central atom. The linearly coordinated central atom of these 1,3 dipoles is an N atom. This N atom carries a formal positive charge in both all octet resonance forms and it is connected to C atom and/or to other heteroatoms. These carry one in each of the resonance forms the formal negative charge,

this negative charge may be located on C atoms and/or a heteroatoms. The charge distribution of both 1,3 dipole type can be shown in Figure 1.2.

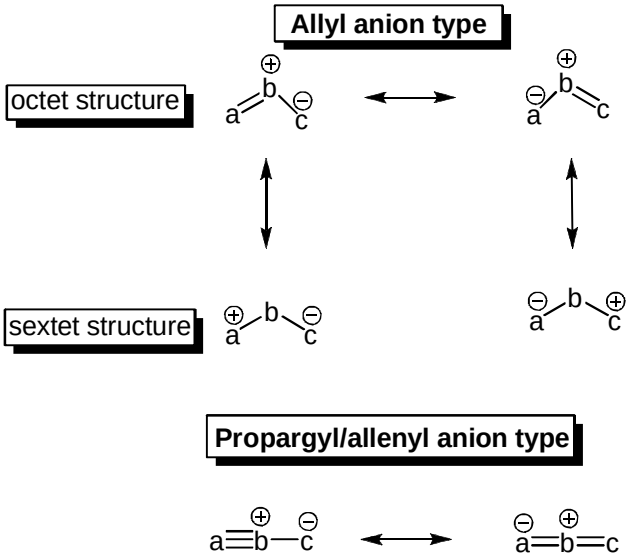


Figure 1. 2 Charge distribution of allyl anion and propargyl/allenyl anion type of 1,3 dipoles.

1.1.2. The dipolarophile

An unsaturated system that undergoes 1,3-DC with 1,3-dipoles is called dipolarophile. The dipolarophile can be almost any double or triple bond. The π electron system may be isolated, conjugated or part of cumulene system; it can even be enol form of a ketone or similar compound [5]. Some example of dipolarophile can be shown in (Figure 1.3) Alkenes, alkynes and their hetero derivatives may be regarded as dipolarophile. It can be possible to categorize dipolarophiles as an electron deficient, electron rich and conjugated one.

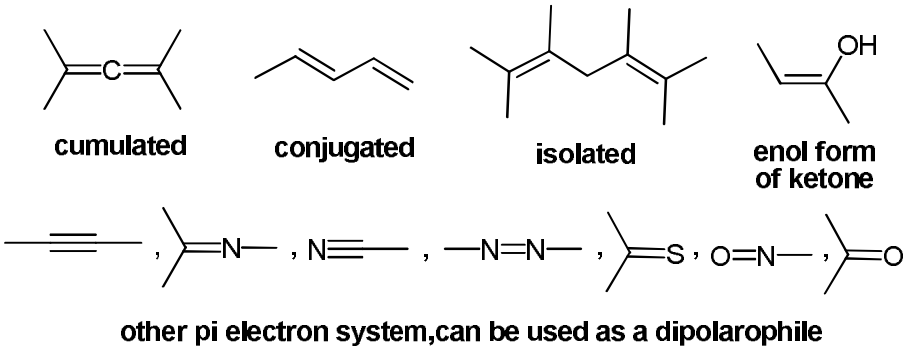


Figure 1. 3 Examples of some dipolarophiles.

1.1.3. The Reaction Mechanism of 1,3-Dipolar Cycloaddition

The transition state of the concerted 1,3-DC reaction is thus controlled by the frontier molecular orbitals (FMO) of the substrates. The $LUMO_{dipole}$ can interact with the $HOMO_{alkene}$ and the $HOMO_{dipole}$ with the $LUMO_{alkene}$. Sustman has classified 1,3-DC reactions into three types, on the basis of the relative FMO energies between the dipole and the alkene (Figure 1.4) [6-9].

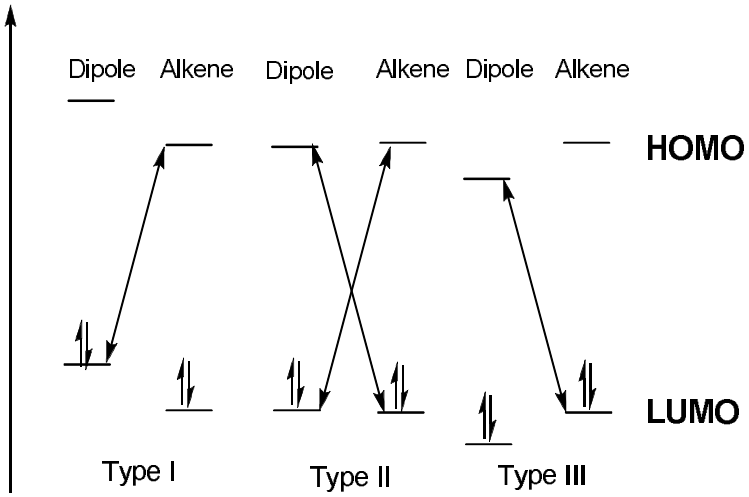


Figure 1. 4 The classification of 1,3-DC reactions on the basis of the FMOs: type I, a $HOMO_{dipole}$-$LUMO_{alkene}$ interaction; type II, interaction of both $HOMO_{dipole}$-$LUMO_{alkene}$ and $LUMO_{dipole}$-$HOMO_{alkene}$; type III, a $LUMO_{dipole}$-$HOMO_{alkene}$ interaction.

1,3-DC reactions of type I are typical for substrates such as azomethine ylides and azomethine imines, while reactions of nitrones are normally

classified as type II. 1,3-DC reactions of nitrile oxides are also classified as type II, but they are better classified as borderline to type III, since nitrile oxides have relatively low lying HOMO energies. Examples of type III interactions are 1,3-DC reactions of ozone and nitrous oxide.

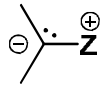
1.2. THE AZOMETHINE YLIDES

1.2.1. The History of Azomethine ylides

The history of 1,3-dipoles goes back to Curtius, who in 1883 discovered diazoacetic ester [10]. Five years later his younger colleague Buchner studied the reaction of diazoacetic ester with α,β-unsaturated esters and described the first 1,3-DC reaction [11]. In 1893 he suggested that the product of the reaction of methyl diazoacetate and methyl acrylate was a 1-pyrazoline and that the isolated 2-pyrazole was formed after rearrangement of the 1-pyrazole [12]. The general application of 1,3-dipoles in organic chemistry was first established by the systematic studies by Huisgen in the 1960s [1]. Huisgen mentioned about the classification of 1,3-dipoles and the concepts for 1,3-dipolar cycloaddition reactions, although it was not until 1976 that the first intramolecular 1,3-dipolar cycloadditions reaction of an azomethine ylide (AMY) was reported. At the same time, the new concept of conservation of orbital symmetry, developed by Woodward and Hoffmann, appeared [2-3].

1.2.2. The Structure of Azomethine ylides

Ylides are a large class of 1,3-dipoles. Most of them belong to allyl-type dipoles (except nitrile ylides).



where Z=N,P,As,Sb,S,Se

Figure 1. 5 Basic representation of structure of ylide

Among the ylides, azomethine ylide one of the most reactive and versatile classes of 1,3 dipoles and is trapped readily by a range of dipolarophiles, either inter or intramolecularly to form functionalized pyrrolidine and pyrrole containing molecules. These molecules are very important pharmaceuticals, natural alkaloids, organic catalysts, and building blocks in organic synthesis [13-14].

Azomethine ylides are 1,3-dipoles of the allyl anion type which composed of one nitrogen atom and two terminal sp^2 carbons, and have four π electrons spread over the three-atom C-N-C unit. They must be represented by a zwitterionic (or diradical) form. Four zwitterionic resonance forms of azomethine ylides can be drawn (Figure 1.6). The most common representation has a positive charge located on the nitrogen atom and a negative charge distributed over the two carbon atoms [15].

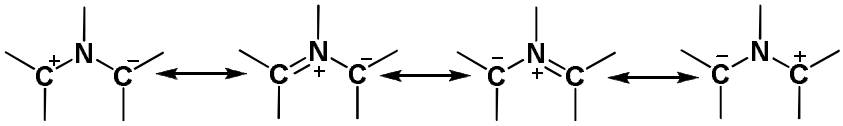
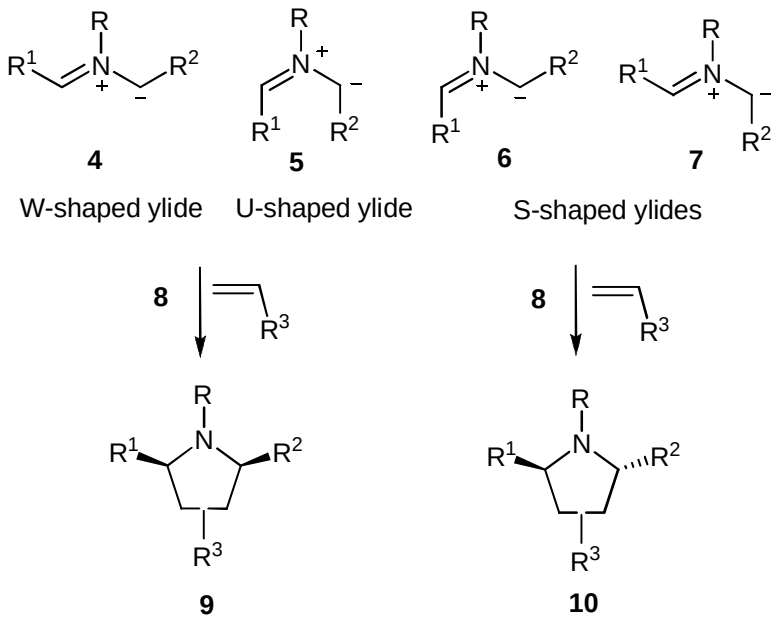


Figure 1. 6 Zwitterionic resonance forms of azomethine ylides

1.2.2.1 The Stereochemistry of Azomethine Ylide

The stereochemical outcome of the cycloaddition of azomethine ylide is dependent on the geometries of the dipoles as well as the dipolarophiles.There are four possible ylide geometries with the W- and U-shaped forms leading (for a suprafacial reaction) to the 2,5-cis-disubstituted

cyclic amine product **9** and the two S-shaped ylides leading to the 2,5-trans-disubstituted product **10** . The stereochemistry of cycloadducts which formed by ylides having different geometries can be shown in (Scheme 1.2). Mixture of stereoisomers can also result by the isomerization of the ylide. Similarly, 3,4-*cis*-disubstituted pyrrolidine product is derived from the *cis*-disubstituted alkenyl dipolarophiles, and the 3,4-*trans*-disubstituted pyrrolidine products arise from the *trans*-disubstituted alkenyl dipolarophiles due to the concertedness of the cycloaddition reaction [16].



Scheme 1. 2 Stereochemical examination of reaction between (W-U-S) shaped ylide and dipolarophile.

1.2.2.2. The Mechanical aspects

Depending on the nature of the dipole and the dipolarophile, the 1,3-dipolar cycloaddition reaction is controlled either by a LUMO(dipolarophile)-HOMO(dipole) or a LUMO(dipole)-HOMO(dipolarophile) interaction but in some cases a combination of both interactions is involved [17].

The reactivity and regiochemistry of 1,3-dipolar cycloaddition reactions based on relative frontier molecular orbital energies between the dipole and dipolarophile and classified azomethine ylide cycloadditions to a Type I class in which the dominant interaction involves the highest occupied molecular orbital (HOMO) of the azomethine ylide and the lowest unoccupied molecular orbital (LUMO) of the dipolarophile controlled by HOMO (represented by the solid line) as outlined in Figure 1.7. HOMO-controlled reactions are accelerated by electron-releasing substituents in the dipole and electron withdrawing groups in the dipolarophiles [18].

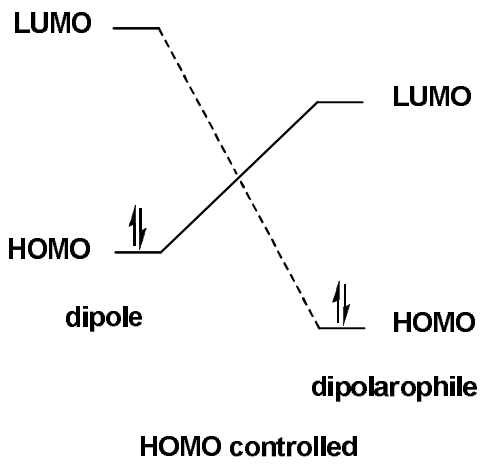


Figure 1. 7 HOMO controlled interaction between dipole and dipolarophile

The regioselectivity in the cycloadditions of azomethine ylide can be predicted on the basis of the unequal magnitude of the terminal coefficients of the HOMO and the LUMO ð orbitals of the dipoles and the direction of the reaction in which maximal frontier molecular orbital overlapping is allowed between the orbitals closest in energy [19-20]. The regioisomeric transition state **A** is more stable than **B** because of its more efficient overlap, see Figure 1.8, as dictated by the terminal coefficients. The favored regioisomer will be the one formed through the transition state in which atoms with larger

coefficients overlap, though there would be very small energy differences (0.1-5 kcal mol-1) between the two transition states [19].

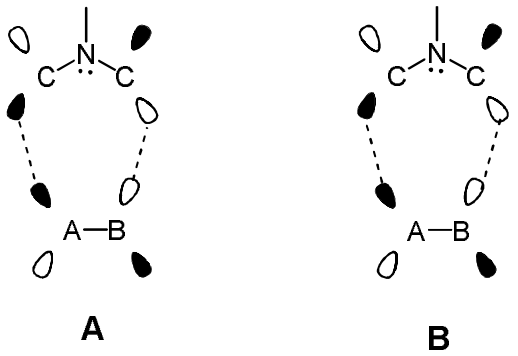
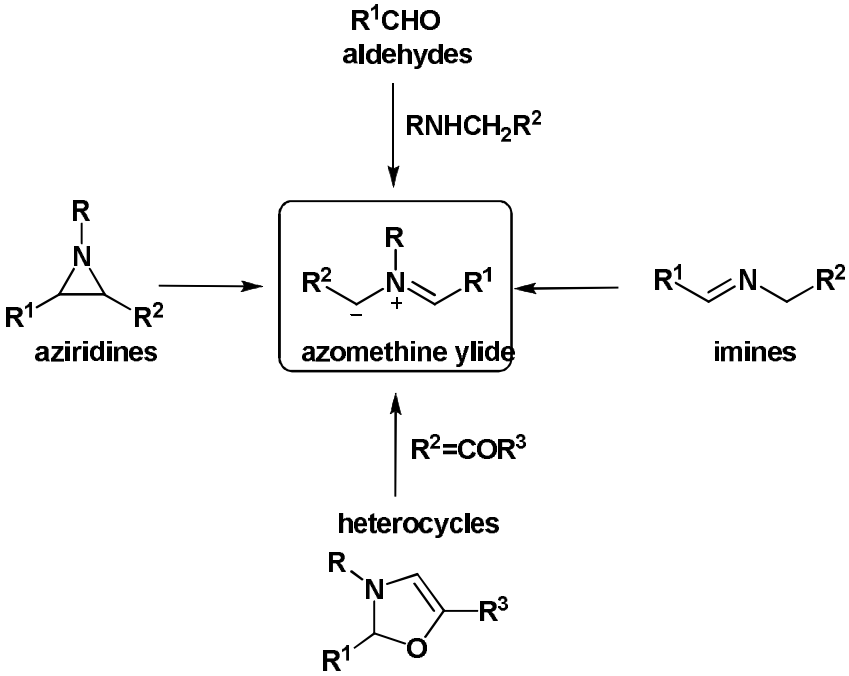


Figure 1. 8 Frontier molecular orbital overlapping of A and B with AMY

In general, there is overall acceleration of the rate of formation of both the regioisomers in the cycloaddition of the azomethine ylides due to excess negative charge on their terminal atom making double-bonded carbons of the dipolarophile either less negative or more positive. However, in the case of intramolecular cycloadditions, conformational constraints normally dictate that only one particular regioisomer can be formed [16].

1.2.3. The Preparation of Azomethine ylides

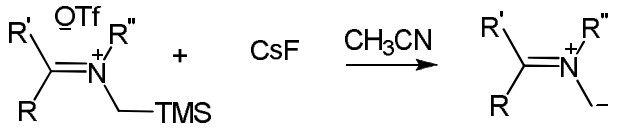
Although there are some examples of stable and isolable azomethine ylides, azomethine ylides are unstable species which have to be prepared *in situ*. A number of methods has been developed for the generation of azomethine ylides, such as proton abstraction from imine derivatives of α-amino acids, thermolysis or photolysis of aziridines, and dehydrohalogenation of imonium salts (Scheme 1.3) [21]. (methylation of imino ester,desilylation of α-trimethylsilylonium salts,deprotonation of amine N-oxides)



Scheme 1. 3 Different route of synthesis of azomethine ylide

1.2.3.1 The Desilylation Method

Desilylation is especially useful for generation of nonstabilized azomethine ylides which can be trapped by 1,3-dipolar addition [22-23].



11 **12** **13**

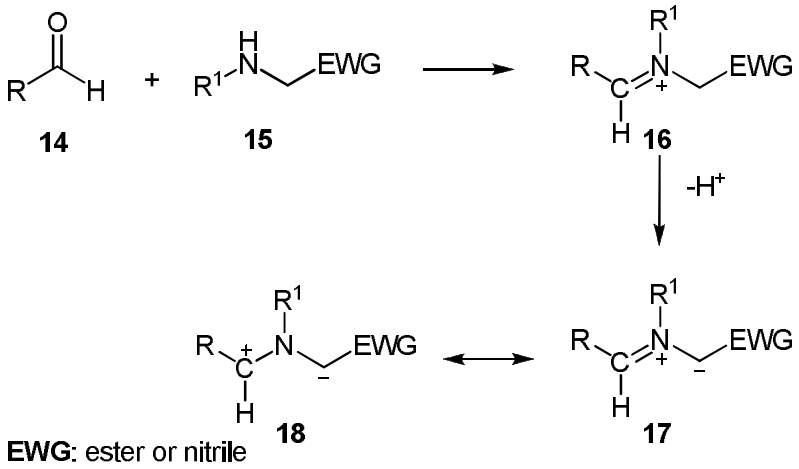
Scheme 1. 4 Generation of AMY by desilylation of α-amino organosilane.

1.2.3.2 The Ylides from Aldehyde

The most widely used azomethine ylide generation is in proton abstraction from imine derivatives of α-amino ester or α-amino acid.

1.2.3.2.1 With Secondary α-Amino Esters

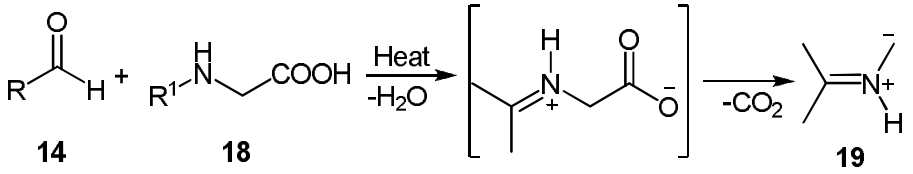
This AMY generation involves the condensation of α-amino ester or nitriles with aldehydes leading to iminium compounds, which spontaneously deprotonate at the position adjacent to the electron withdrawing group (EWG) to generate the ylides [24].



Scheme 1. 5 Condensation of α-amino ester to result nonstabilized AMY

1.2.3.2.2 With Secondary α-Amino Acids

An alternative procedure that generation of AMY lacking the carbonyl group uses α-amino acids rather than their esters. These react with aldehydes to form, after decarboxylation, the required unstabilized azomethine ylide generated [13].

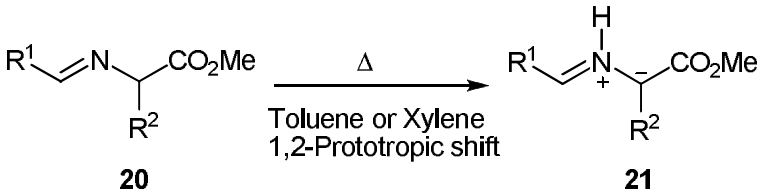


Scheme 1. 6 Decarboxylation of α-amino acid to result nonstabilized AMY

1.2.3.3 The Ylides from Imines

1.2.3.3.1 By Prototropy

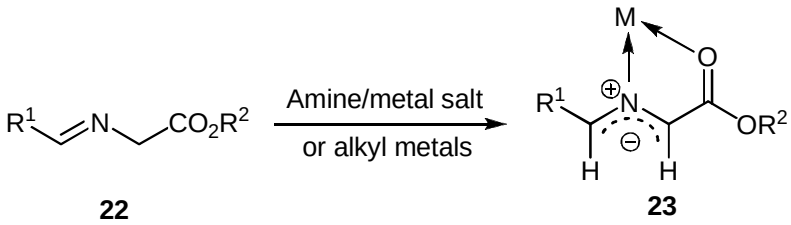
In this method AMYs are generated from imines by migration of a proton from the α-carbon to the N atom and it is called 1,2-prototropic shift [25-26].



Scheme 1. 7 1,2-prototropic shift of carboxymethyl imines.

1.2.3.3.2 By Metalation

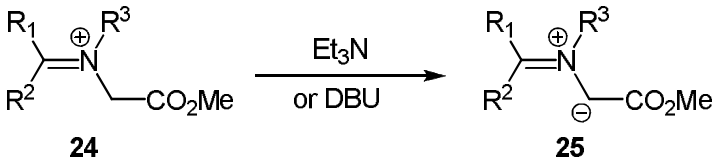
Another method for the generation of AMYs are the activation of imines for the formation of the required AMY by the addition of a metal salt. Iminic N atom and metal (such as lithium bromide (LiBr) or silver acetate (AgOAc)) coordinated in order to activate the substrate to deprotonation, thereby resulting in the N-metalated AMY [26].



Scheme 1. 8 Formation of stabilized N-metalated AMY

1.2.3.3.3 By Alkylation

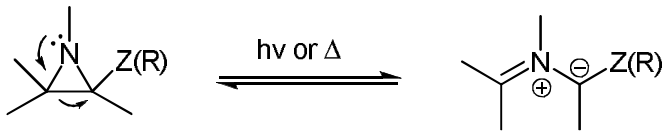
Alkylation of the nitrogen atom of an imine provides a method to prepare an iminium ion and hence, after subsequent deprotonation of the methine carbon of the iminium ion or desilylation, an azomethine ylide [27].



Scheme 1. 9 Deprotonation of iminium ion to generate AMY

1.2.3.4 The Aziridine Route

The well known, and extensively studied, carbon-carbon bond cleavage of aziridines generates an azomethine ylide (Scheme 1.10) with a determined geometry through a conrotatorial (thermolysis) or disrotatorial (photolysis) process [28-29]. This particular method of generation of 1,3-dipoles is limited by the harsh reaction conditions required, photolysis being the most versatile route and allowing for a more extensive study of the properties of these ylides.

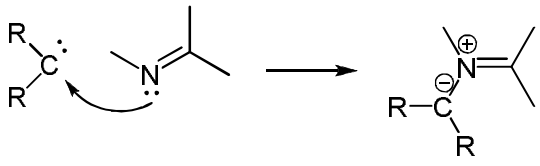


26 **27**

Scheme 1. 10 Generation of AMY by photolysis of aziridines.

1.2.3.5 The Carbene-Imine Route

Immonium ylides can be prepared by the reaction of simple halocarbenes and imines [30].



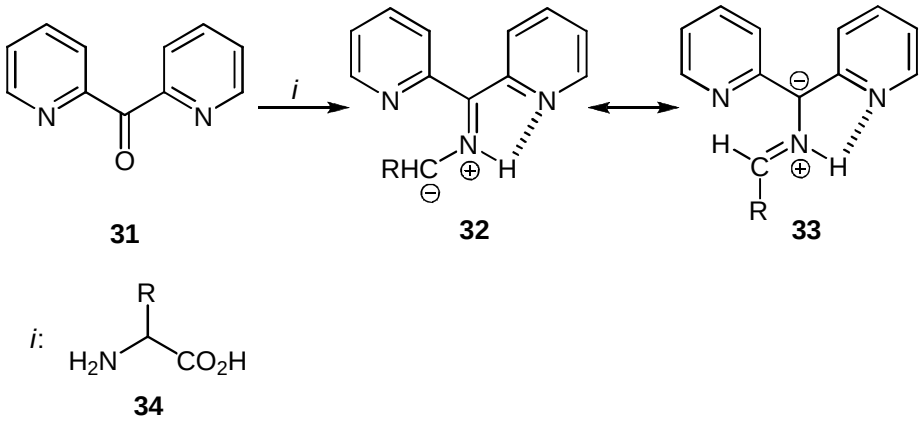
28 **29** **30**

Scheme 1. 11 Reaction of simple carbine and imine to form AMY

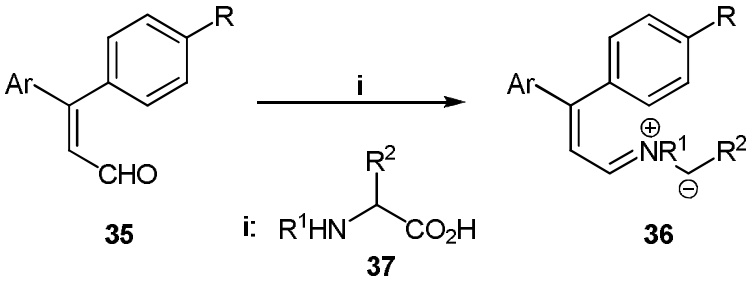
1.2.3.6 The Electrocyclisations

Azomethine ylides, generated by the Strecker degradation, underwent cyclocyclisations in some cases. 1,5-Electrocyclisations were observed when

2,2'-dipyridyl ketone **31** was allowed to react with acyclic α-amino acids in the absence of dipolarophiles (Scheme 1.12). After decarboxylation, two mesomeric forms were generated. 1,7-Electrocyclisation of non-stabilised azomethine ylides, generated by reaction of 3,3-diarylpropenals **35** and *N*-substituted α-amino acids (Scheme 1.13) [31-32].



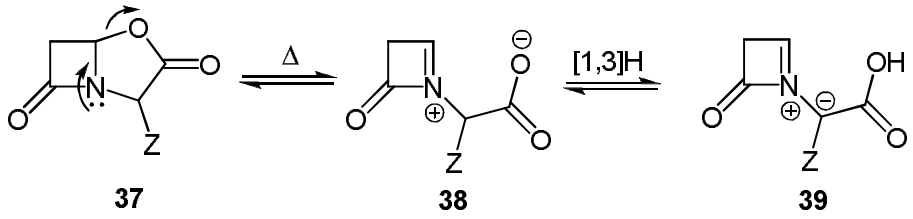
Scheme 1. 12 Example of generation of AMY by 1,5-Electrocyclisation



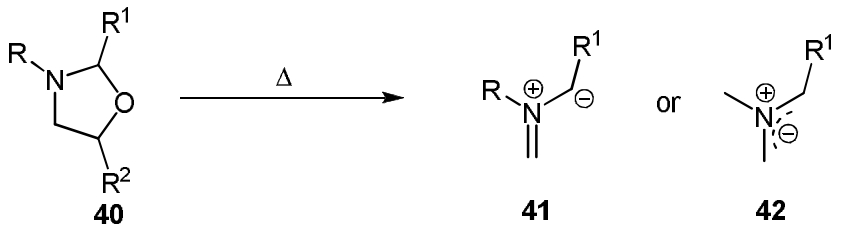
Scheme 1. 13 Example of generation of AMY by 1,7-Electrocyclisation

1.2.3.7 The Oxazole Derivative Routes

Oxazolidin-5-ones, oxazolidines, oxazoles and 2,3-dihydroisoxazoles can be considered as an oxazole derivative. They can be used as a precursor of azomethine ylide by different mechanism (see Scheme 1.14) [30].

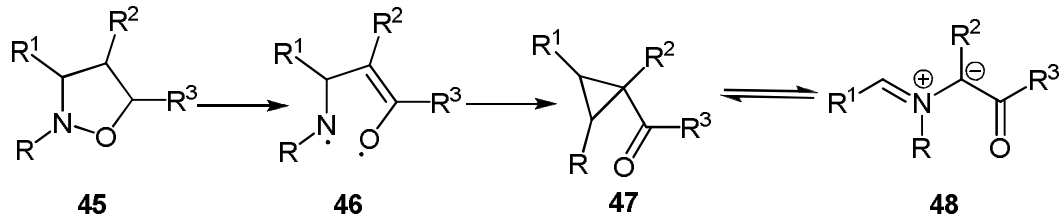


Route of generation of AMY from the oxazolidine-5-ones fused to β-lactam

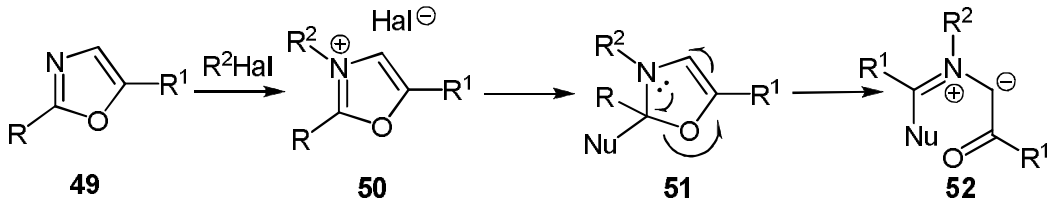


Generation of AMY by Flash Vacuum Thermolysis (FVT) of oxazolidine

Treatment of oxazoline with TMSOTf for generation of AMY



The photochemical or thermal rearrangement of 2,3-dihydroisoxazoles allows the intermediate aziridine then generated stabilized AMY

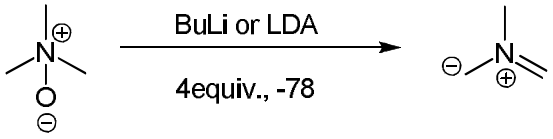


The route based on oxazole-oxazolium salt-oxazoline squence for the generation of AMY

Scheme 1. 14 Oxazole derivatives for the generation of AMY

1.2.3.8 The N-Oxide Route

Strong bases react with aliphatic tertiary amine *N*-oxides **53** to give an intermediate azomethine ylide **54** and this reaction was first reported as providing a new preparative method for aziridines [30].

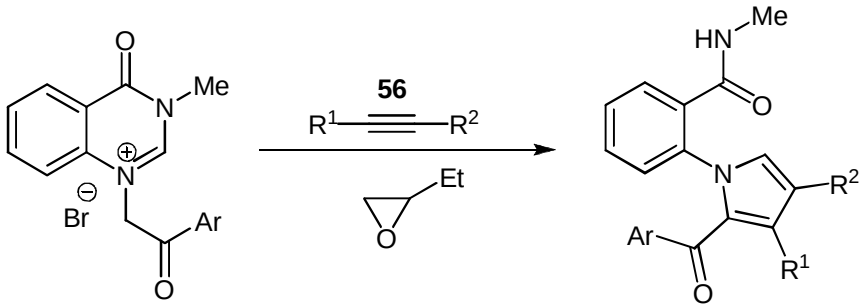


53 **54**

Scheme 1. 15 N-Oxide route of production of AMY

1.2.4. The Recent Publications

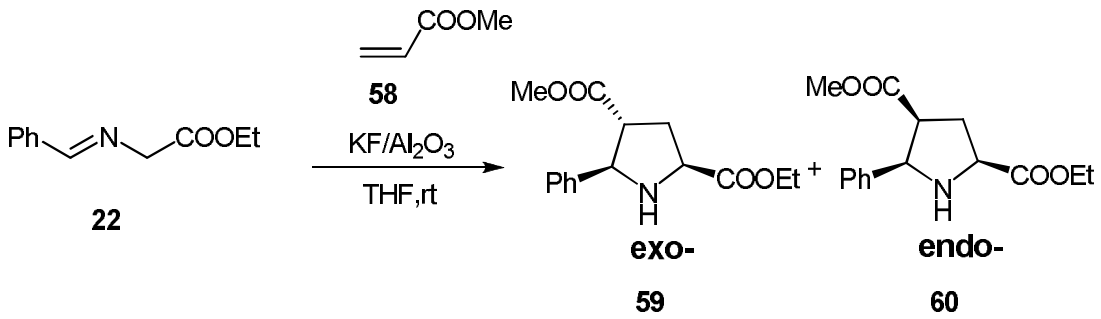
Treatment of quinazolin-4(3*H*)-one bromides **55** which generated by the means of 2-bromoacetophenone and 3-methyl-4(3*H*)-quinazolinone with acetylenic dipolarophiles in 1,2-epoxybutane medium gave, in good yields, *N*-arylpyrroles **57** instead of the corresponding pyrrolo[1,2-a]quinazolines [33].



55 **57**

Scheme 1. 16 Reaction of Quinazolinium Ylide and Acetylenic Dipolarophile to form *N*-arylpyrroles

Boruah et. al published that the novel procedure for the generation of AMY mediated by KF/Al_2O_3 as a solid supported reagent. This solid supported reagent is responsible for generation of AMY and also catalyzes the cycloaddition reactions [34].

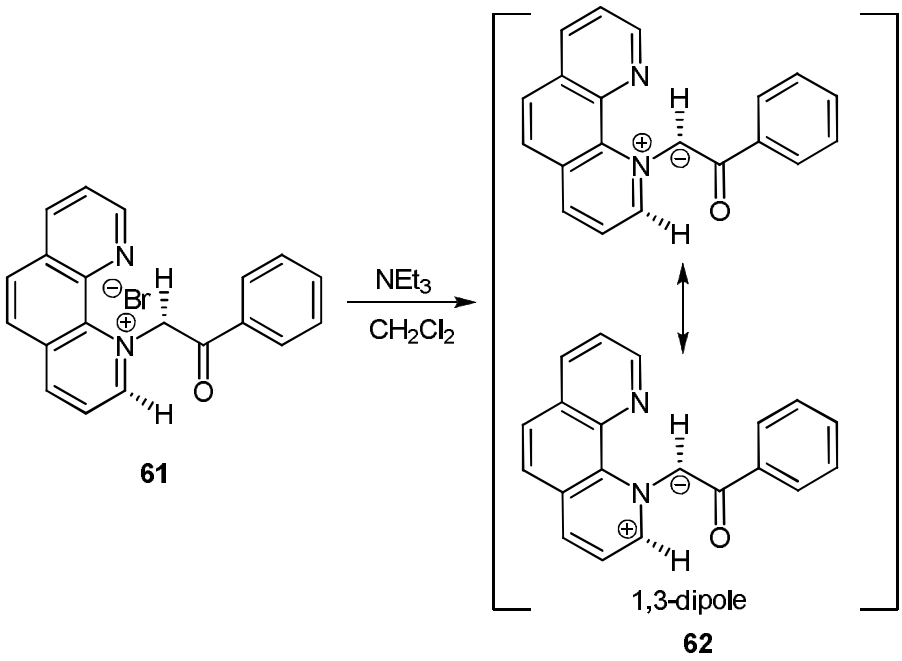


Scheme 1. 17 KF/Al_2O_3 mediated 1,3-dipolar cycloadditions of an AMY and a dipolarophile

1.2.5. The Phenanthrolinium *N*-ylide

1.2.5.1 The Structure of Phenanthrolinium *N*-ylide

The phenanthrolinium *N*-ylide which is used as a dipole in [3+2] dipolar cycloaddition reaction of 1,10-phenanthrolinium ylides with some dipolarophiles. First time phenanthrolinium *N*-ylides **61** were synthesized by reaction of 1,10-phenanthroline with reactive halide derivatives [35]. The generation of phenanthrolinium *N*-ylide is an example of ylides from imines by alkylation method (discussed in **1.2.2.3.1)**, which is obtained *in situ* by deprotonation of the corresponding cycloimmonium salt in the presence of base (mostly triethylamine) [36-37].

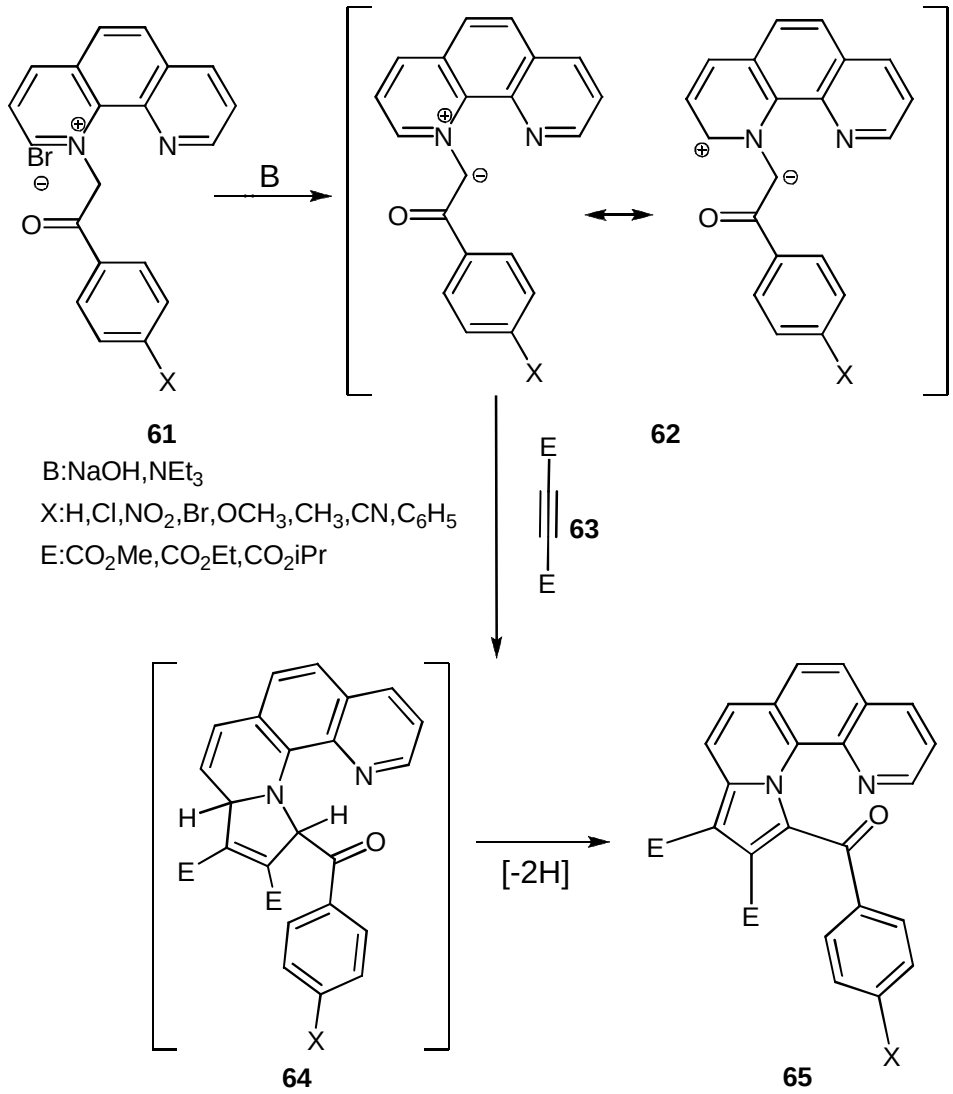


61 **62**

Scheme 1. 18 Zwitterionic structure of phenanthrolinium ylide

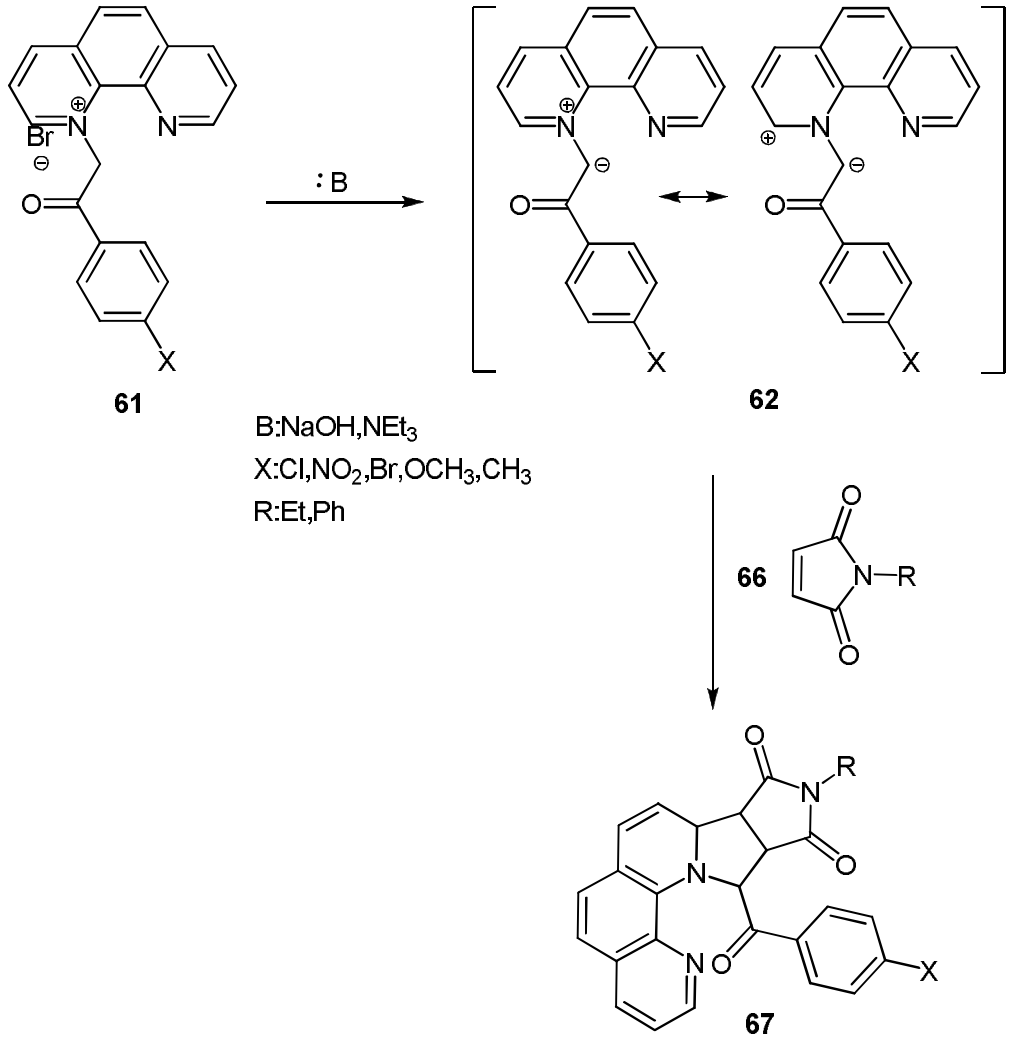
1.2.5.2 The Reactions of Phenanthrolinium *N*-ylide

The phenanthrolinium N-ylides obtained *in situ* which undergo cycloaddition reaction with acetylenic dipolarophiles resulting fused five membered nitrogen heterocycle was studied for the first time by Dumitraşcu et. al [38-40]. Similar study was investigated by Danac et.al who demonstrated that the formation of **65** was regioselective [41].(Scheme 1.19)



Scheme 1. 19 Reaction of Phenanthrolinium *N*-ylide and acetylenic dipolarophile to form pyrrolo[1,2-a][1,10]phenanthrolines.

The ability of 1,10-phenanthrolinium phenacylides **61** to react with maleimide derivatives **66** was examined and the new heterocyclic compound **67** was formed according to a semiempirical study, *via* a concerted nonsynchronous mechanism [42].(Scheme 1.20)



Scheme 1. 20 Cycloaddition Reaction of Phenanthrolinium *N*-ylide and maleimide derivatives.

1.3. THE AZLACTONE (Methylene Oxazolone)

1.3.1. The Structure and Formation of Azlactone

The oxazolones are very interesting heterocyclic compounds which have been used as a key material for synthesis of a variety of organic molecules. There are different structural classes of oxazolones possible that differ only position of double bond or position of N atom (Figure 1.9). The saturated analoques A, B, D, E do not have an exocyclic double bond, whereas the unsaturated analoques C, F do contain an exocyclic double bond [43].

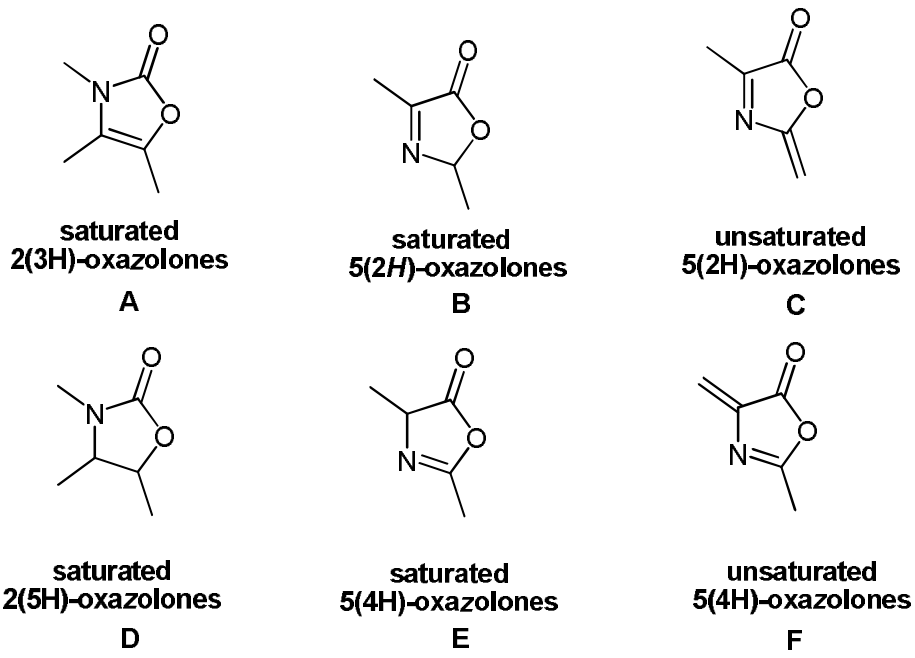
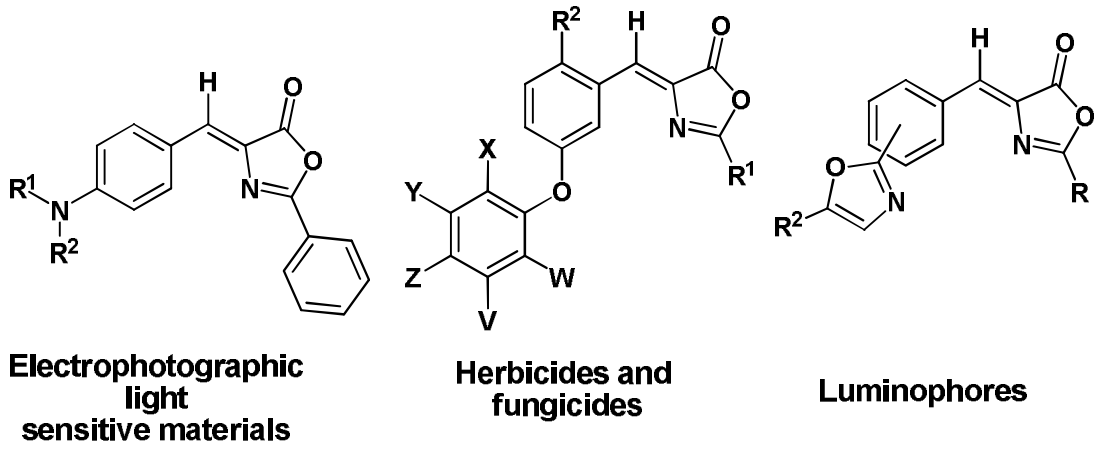


Figure 1. 9 General structure of different type oxazolones

Azlactones (Methylene Oxazolones) are very important reagents in organic chemistry for the preparation of many different nitrogen containing heterocycles [44]. There are wide application range of azlactones **70**, they can be used as herbicides and fungicides, organic luminophores, apocarotenoid derivatives, ultraviolet (UV)-absorbing layers, dyeing or printing synthetic fibers. Some of them exemplified in Figure 1.10 [45-53].



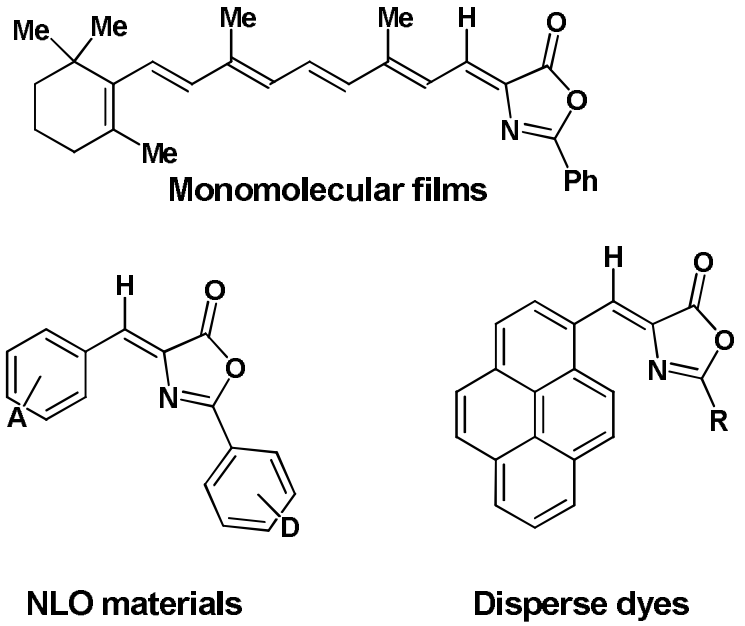
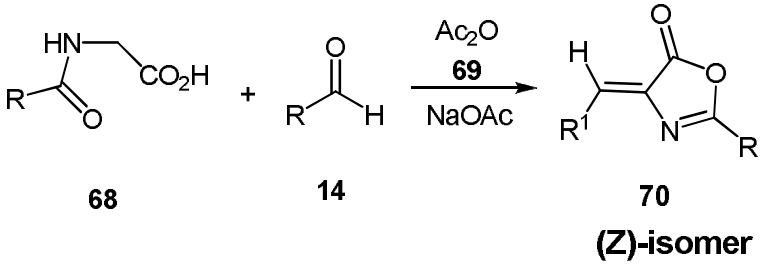


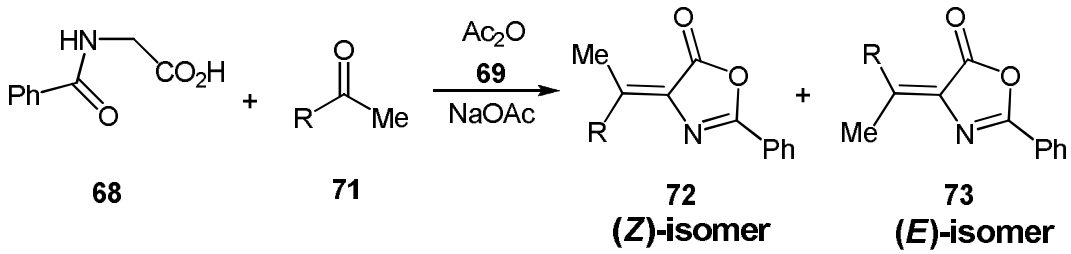
Figure 1. 10 Example of some unsaturated 5(4*H*)-oxazolones and their applications

The first procedure to prepare unsaturated 5(4H)-oxazolones was the Erlenmeyer synthesis that was described more than one hundred years ago and is still used extensively with some variations in the experimental conditions [54]. The well known route for generation of azlactones is Erlenmeyer-Plöchl azlactone synthesis which contains intramolecular condensation of acylglycines **68** in the presence of acetic anhydride **69** and a carbonyl compound **14**, usually an aldehyde. (Scheme 1.21) The Erlenmeyer synthesis usually proceeds with a very high degree of stereoselectivity to favor the thermodynamically more stable (*Z*) isomer. In some cases, the (*Z*) isomer is the only product obtained [55].



Scheme 1. 21 Erlenmeyer-Plöchl azlactone synthesis

A limited number of references have appeared that use ketones as the carbonyl component. The first example reported that acetophenones condense with N-benzoylglycine under Erlenmeyer conditions to afford a mixture of (*Z*)- and (*E*)- unsaturated 5(4*H*)-oxazolones **72** and **73** in which the (*Z*)-isomer **72** is the major compound [56].



Scheme 1. 22 Erlenmeyer-Plöchl azlactone synthesis by means of ketone.

1.3.1.1 The Structural Analysis of Azlactones

Spectroscopic studies of unsaturated 5(4*H*)-oxazolones have been performed in order to correlate spectroscopic behavior with a characteristic substituent parameter. Linear correlation of the IR frequency of the C=O group with substituent constants have been reported for some 4-arylidene-2-phenyl-5(4H)-oxazolones. The carbonyl group has a two-component band in the 1768–1812 cm^{-1} region that is sensitive to conformational changes and solvent effects. This would be expected for a high transmission of the substituent effect through the ring [57-58].

NMR is a useful technique to determine the stereochemistry of double bonds in this case it has been applied to the configurational assignment of geometric isomers of some unsaturated 5(4H)-oxazolones. For example, geometric isomers can be distinguished in ^{1}H NMR by benzene-induced

shifts. This technique was used to correctly assign the configuration of the (*E*, *Z*)- and (*E*, *E*)-geometric isomers of unsaturated 5(4*H*)-oxazolones prepared from (*E*)-cinnamaldehyde [59].The value of the long range ^{13}C-^{1}H coupling constants between olefinic proton and carbonyl carbon can be used to determine the configuration of (*Z*)- and (*E*)-unsaturated 5(4*H*) oxazolones because $^{1,3}J^{t}_{CH} > {}^{1,3}J^{c}_{CH}$ [60] (Figure 1.12).

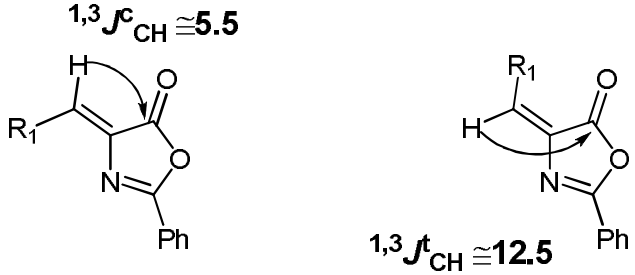


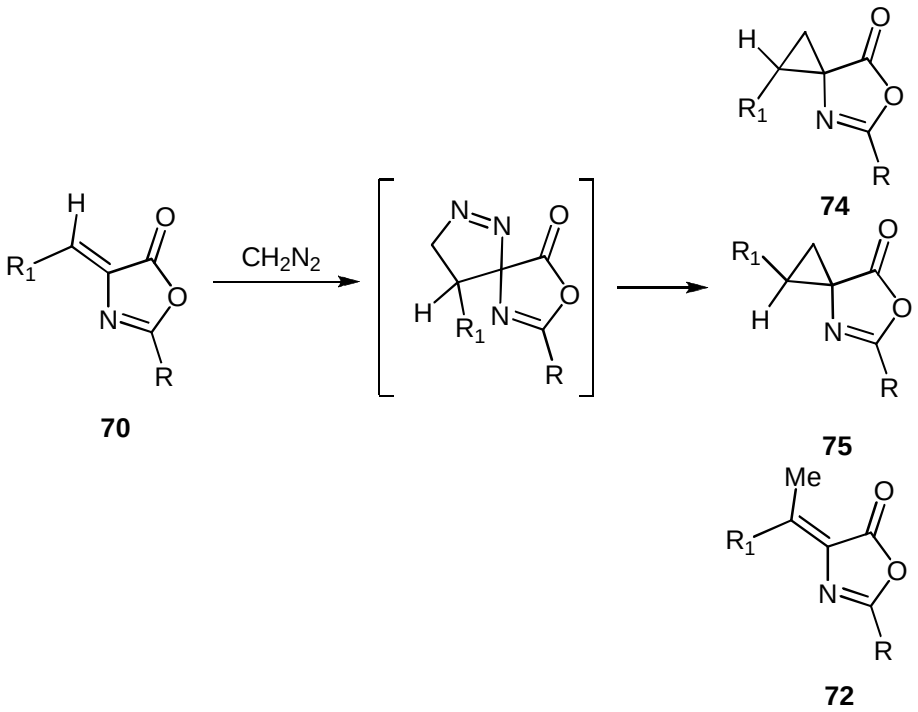
Figure 1. 11 The $^{1,3}J_{CH}$ coupling constants for (Z)- and (E)-unsaturated 5(4*H*) oxazolones

Studies of the UV–visible absorption spectra of 4-arylidene-2-phenyl-5(4*H*)-oxazolones show that the sign of the solvatochromism is substituent dependent in hydrogen-bonding solvents. On the other hand, in non-hydrogen-bonding solvents all substituents show a positive solvatochromism [61].Electron impact mass spectrometry is not useful for distinguish between (*Z*) and (*E*) isomer of 4-benzylidene-2-phenyl-5(4*H*)-oxazolones because there is minor differences in relative abundances of product ions in mass spectra. Therefore collision spectroscopy can be used instead of electron impact spectrometry because collisional mass spectra show clear differences for the (*Z*) and (*E*) isomers in the relative abundances of ions arising from competing fragmentations. For (*E*) isomers the $[M\text{-}CO]^{+}$ ion is the base peak in the spectrum, while for (*Z*) isomers the $PhCO^{+}$ ion is the base peak [62-63].

1.3.2. The Reactions Involving the Exocyclic Double Bond of Azlactones

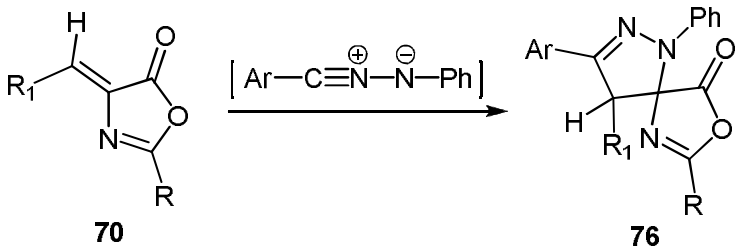
1.3.2.1 1,3-Dipolar Cycloadditions

1,3-Dipolar cycloaddition reaction with diazoalkane occurs to generate spiropyrazoline that in most cases has not been isolated. Therefore arising from the unstability of spiropyrazoline, it decomposes to form mixtures of *cis*- and *trans*- cyclopropane derivatives **74** and **75** homologation of the starting unsaturated 5(4*H*)-oxazolone **72** [64].



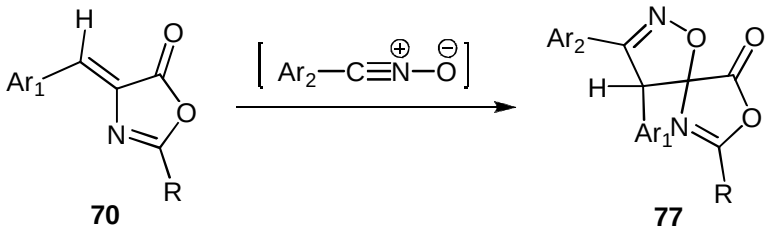
Scheme 1. 23 1,3-DC reaction of unsaturated 5(4*H*)-oxazolones with diazoalkane

Nitrile imines, generated *in situ* from the corresponding *N*-(phenyl)arylhydrazonoyl chlorides , react with unsaturated 5(4*H*)-oxazolones **70** to give the corresponding spiropyrazoline oxazolones **76**. The reaction is regioselective and in each case only one regioisomeric cycloadduct is formed [65-68].



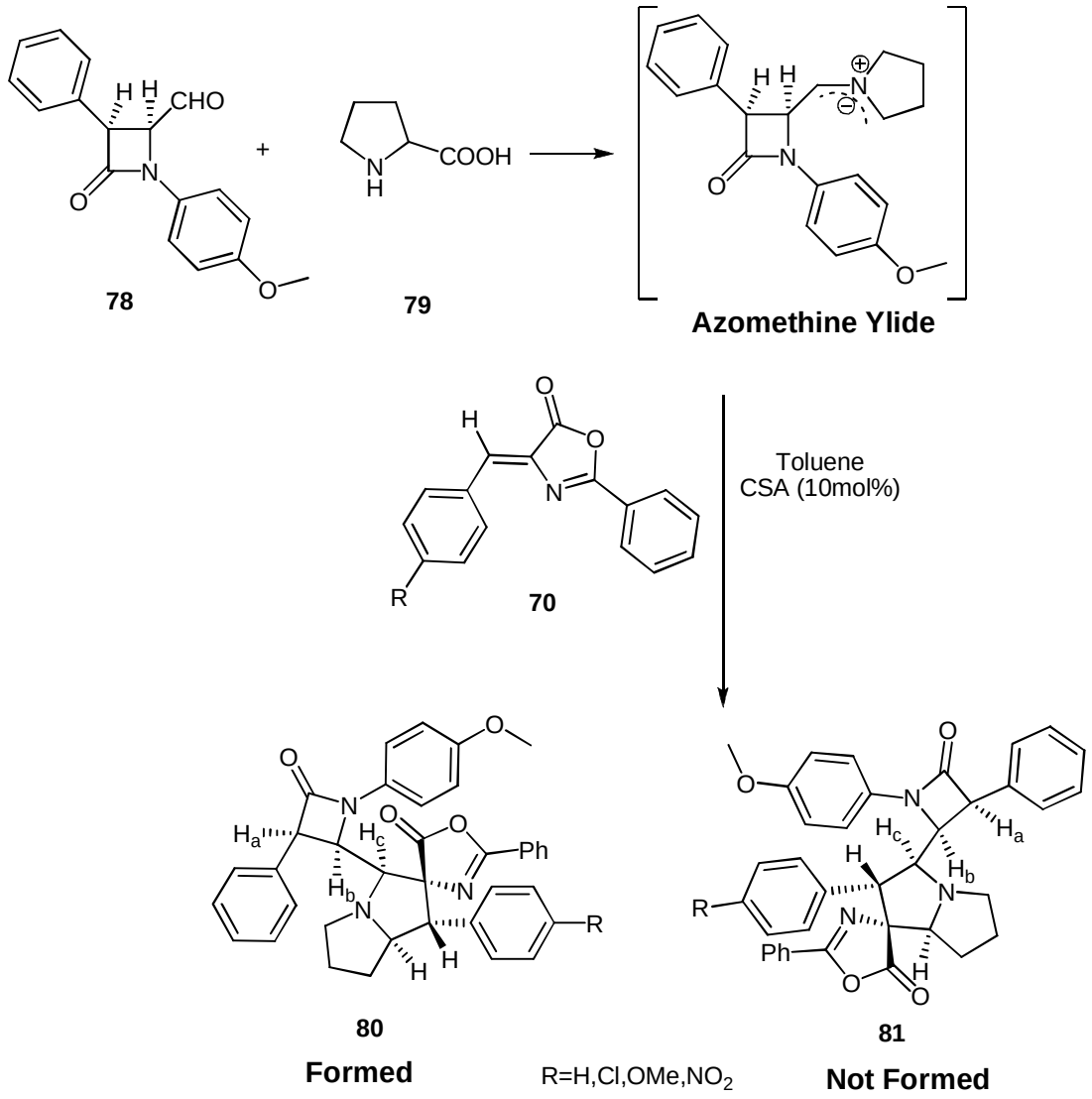
Scheme 1. 24 1,3-Dipolar Cycloaddition Reaction of Unsaturated 5(4*H*)-Oxazolones with Nitrile Imines

1,3-Dipolar cycloaddition reaction of Nitrile oxides with 4-arylmethylene-5(4*H*)-oxazolones has also been studied to form spiroisoxazoline oxazolones **77**. Examination of regiochemistry of this reaction shows that regiochemistry of the 1,3-dipolar cycloaddition of nitrile oxides is the same as that observed with nitrile imines [69-70].



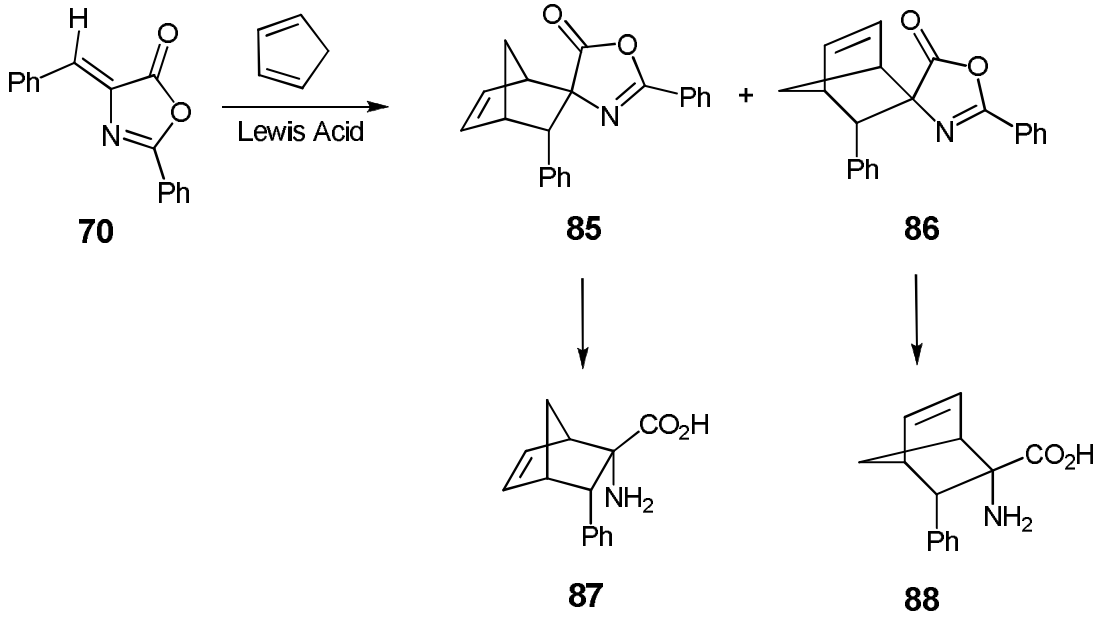
Scheme 1. 25 1,3-dipolar cycloaddition reaction of 4-arylmethylene-5(4*H*)-oxazolones with nitrile oxides

Raghunathan and coworkers reported that synthesis of substituted spiropyrrolidines **80** from unsaturated 5(4*H*)-oxazolone derivatives **70** through 1,3-DC reaction of AMY generated through decarboxylation route [71].



1.3.2.2 [4+2] Diels-Alder Reaction

Exocyclic double bond of unsaturated oxazolones has a great importance for Diels-Alder reaction. This exocyclic double bond can operate as a dienophile in the Diels-Alder reaction. (*Z*)-4-Benzylidene-2-phenyl-5(4*H*)-oxazolone **70** reacts with cyclopentadiene using a Lewis acid. The reaction leads to a mixture of cycloadducts **85** and **86** derived from endo and exo attack of the diene. Each endo- and exo-cycloadduct **86** and **85** was converted to the corresponding amino acid **88** and **87** by hydrogenation of the double bond and subsequent hydrolysis [72-73].



70 **85** **86** **87** **88**

Scheme 1. 26 [4+2] Cycloaddition of Azlactone with Cyclopentadiene further hydrolysis cycloadducts to afford the subsequent aminoacids.

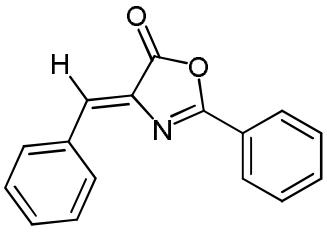
CHAPTER II

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a BRUKER AVANCE spectrometer (400 MHz for proton and 100 MHz for carbon). IR spectra were recorded on a SHIMADZU FTIR-8400S instruments (KBr pellet). Mass spectra were recorded on an Agilent LC-MS instrument. Chromatotron™ Centrifugal Thin-Layer Chromatograph System were used for isolation and purification of the reaction products. Melting points were determined on a MELTEMP apparatus and were uncorrected. TLC was done using precoated plates with fluorescent indicator (Merck 5735). The stain solutions of permanganate and iodine were used for visualization of the TLC spots. Arylidene oxazolones **70 a-u** were synthesized according to the methods described in the literature [74].

2.1. Synthesis of Arylidene Oxazolones 70 a-u

2.1.1. (*Z*)-4-Benzylidene-2-phenyloxazol-5(*4H*)-one (70a)

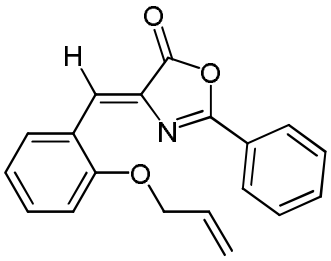


A mixture of benzaldehyde **(14a)** (1.144 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 mg, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, products recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.151 g (80%), m.p. 158 -160˚C.

R_f : 0.73 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1795 (C=O),1649 (C=N).

2.1.2. (*Z*)-4-(2-(Allyloxy)benzylidene)-2-phenyloxazol-5(*4H*)-one (70b)



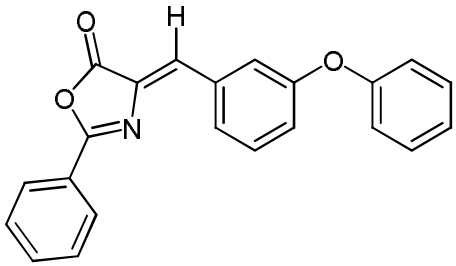
A mixture of 2-(allyloxy)benzaldehyde **(14b)** (1.750 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 mg, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, products recrystallized from acetone. A yellow crystalline solid was obtained; yield 3.063 g (93%), m.p. 146 -148˚C.

R_f : 0.81 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1790 (C=O),1643 (C=N).

^{1}H NMR (δ_H ,400 MHz, $CDCl_3$): 8.91 (dd, *J* = 1.7 , 6.2 Hz, 1H), 8.21 (d, *J* = 7.1 Hz, 2H), 7.93 (s, 1H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.0 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.17-6.08 (m,1H), 5.48 (d, *J* = 17.3 Hz, 1H), 5.37 (d, *J* = 11.9 Hz, 1H), 4.68 (d, *J* = 5.3 Hz, 2H).

2.1.3. (*Z*)-4-(3-Phenoxybenzylidene)-2-phenyloxazol-5(*4H*)-one (70c)



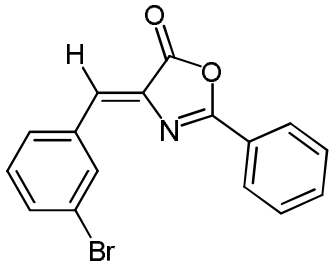
A mixture of 3-phenoxybenzaldehyde **(14c)** (3.683 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, products recrystallized with acetone. A yellow crystalline solid was obtained; yield 3.388 mg (92%), m.p. 175 -176˚C.

R_f : 0.77 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr): v (cm^{-1}) : 1784 (C=O),1657 (C=N).

^{1}H NMR (δ_H ,400 MHz, $CDCl_3$): 8.00 (s, 1H), 7.95 (d, *J* = 7.6 Hz, 2H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.40-7.34 (m, 3H), 7.21-7.15 (m, 2H), 7.12 (s, 1H), 7.07 (s, 1H), 7.09-7.06 (m, 3H).

2.1.4. (*Z*)-4-(3-Bromobenzylidene)-2-phenyloxazol-5(*4H*)-one (70d)



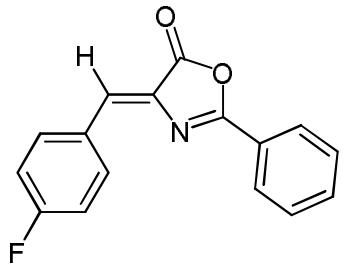
A mixture of 3-bromobenzaldehyde **(14d)** (1.998 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A yellow crystalline solid was obtained; yield 3.188 g (90%), m.p. 153 -155˚C.

R_f : 0.77 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1796 (C=O),1656 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): 8.36 (s, 1H), 8.12 (d, *J* = 7.2 Hz, 2H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.51-7.46 (m, 3H), 7.28 (t, *J* = 7.9 Hz, 1H), 7.07 (s, 1H).

2.1.5. (*Z*)-4-(4-Fluorobenzylidene)-2-phenyloxazol-5(*4H*)-one (70e)

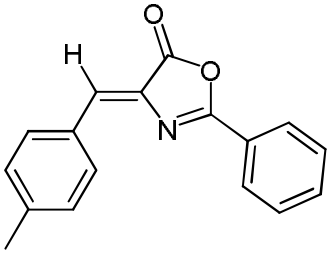


A mixture of 4-fluorobenzaldehyde **(14e)** (1.339 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, products recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.797 g (97%), m.p. 181 -183˚C.

R_f : 0.82 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1796 (C=O),1659 (C=N).

2.1.6. (*Z*)-4-(4-Methylbenzylidene)-2-phenyloxazol-5(*4H*)-one (70f)



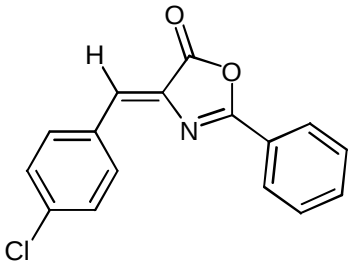
A mixture of 4-methylbenzaldehyde **(14f)** (1.296 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was

dried under vacuum for several hours. Finally, products recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.045 g (72%), m.p. 136 -138˚C.

R_f : 0.86 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1794 (C=O),1655 (C=N).

2.1.7. (*Z*)-4-(4-Chlorobenzylidene)-2-phenyloxazol-5(*4H*)-one (70g)



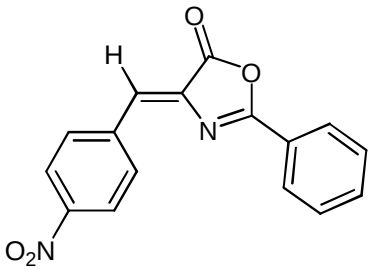
A mixture of 4-chlorobenzaldehyde **(14g)** (1.512 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.69 g (88 %), m.p. 195 -196˚C.

R_f : 0.76 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1797 (C=O),1654 (C=N).

^{1}H NMR (δ_H ,400 MHz, $CDCl_3$): δ= 8.19 (t, *J* = 11.1 Hz, 4H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.71 (s, 1H).

2.1.8. (*Z*)-4-(4-Nitrobenzylidene)-2-phenyloxazol-5(*4H*)-one (70h)

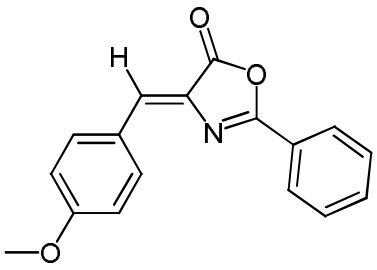


A mixture of 4-nitrobenzaldehyde **(14h)** (1.631 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 ml) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.985 g (94%), m.p. 234 -236˚C.

R_f : 0.67 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1798 (C=O),1655 (C=N).

2.1.9. (*Z*)-4-(4-Methoxybenzylidene)-2-phenyloxazol-5(*4H*)-one (70j)



A mixture of 4-methoxybenzaldehyde **(14j)** (1.469 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 ml) was stirred at 60 ˚C for 3h. After cooling the solution to room

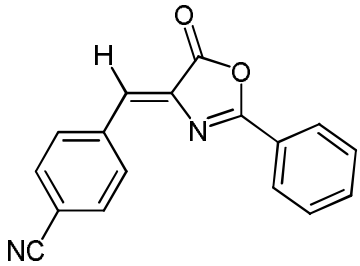
temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, products recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.380 mg (79%), m.p. 155 -157˚C.

R_f : 0.81 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1790 (C=O),1649 (C=N)

^1H NMR (δ_H , 400 MHz, $CDCl_3$): δ= 8.21 (t, *J* = 9.5 Hz, 4H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.25 (s, 1H), 7.02 (d, *J* = 14.5 Hz, 2H), 3.92 (s, 3H).

2.1.10. (*Z*)-4-((5-Oxo-2-phenyloxazol-4(*5H*)- ylidene)methyl) benzonitrile (70k)



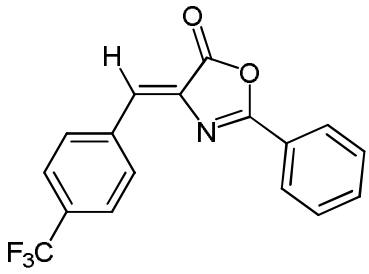
A mixture of 4-cyanobenzaldehyde **(14k)** (1.415 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.811 g (95%), m.p. 215 -217˚C.

R_f : 0.79 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 2220 (C≡N) ,1796 (C=O),1661 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): 8.32 (d, *J* = 8.3 Hz, 2H), 8.23 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.59 (t, *J* = 7.6 Hz , 2H), 7.21 (s, 1H).

2.1.11. (*Z*)-2-Phenyl-4-(4-(trifluoromethyl)benzylidene)oxazol-5(*4H*)-one (70l)



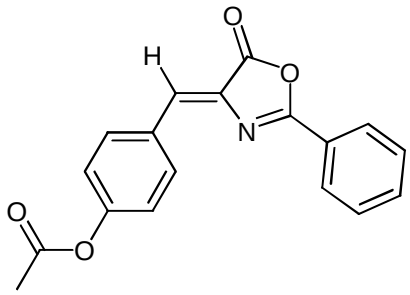
A mixture of 4-(trifluoromethyl)benzaldehyde **(14l)** (1.879 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A yellow crystalline solid was obtained; yield 3.013 g (88%), m.p. 168 -170˚C.

R_f : 0.92 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1801 (C=O),1658 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 8.33 (d, *J* = 8.2 Hz, 2H), 8.22 (d, *J* = 7.4 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.58 (t, *J* = 7.6 Hz 2H), 7.27 (d, *J* = 11.6 Hz, 1H).

2.1.12. (*Z*)-4-((5-Oxo-2-phenyloxazol-4(*5H*)-ylidene)methyl)phenyl acetate (70m)



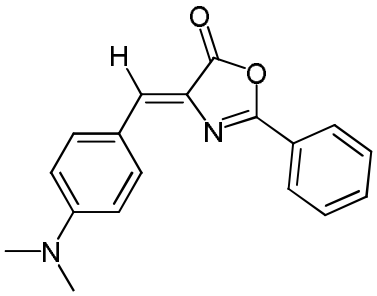
A mixture of 4-acetoxybenzaldehyde **(14m)** (1.771 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, products recrystallized from acetone. A yellow crystalline solid was obtained; yield 3.150 g (95%), m.p. 175 -176˚C.

R_f : 0.71 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1796, 1759 (C=O),1657 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 8.25 (d, *J* = 6.9 Hz, 2H), 8.19 (d, *J* = 7.1 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 2H), 7.24 (d, *J* = 9.0 Hz, 3H), 2.36 (s, 3H).

2.1.13. (*Z*)-4-(4-(Dimethylamino)benzylidene)-2-phenyloxazol-5(*4H*)-one (70n)



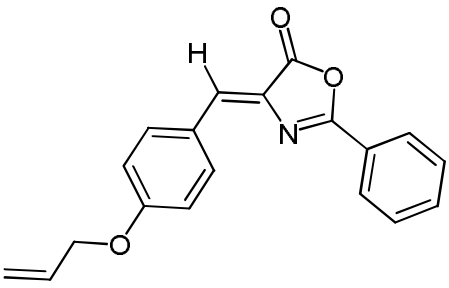
A mixture of 4-(*N,N*-dimethylamino)benzaldehyde **(14n)** (1.609 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A red needle crystalline solid was obtained; yield 2.554 g (81%), m.p. 207 -210˚C.

R_f : 0.62 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1786 (C=O),1643 (C=N).

^1H NMR (δ_H, 300 MHz, $CDCl_3$): δ= 8.18-8.15 (m, 4H), 7.59-7.50 (m, 3H), 7.23 (s, 1H), 6.77 (d, *J* = 9.1 Hz, 2H), 3.12 (s, 6H).

2.1.14. (*Z*)-4-(4-(Allyloxy)benzylidene)-2-phenyloxazol-5(*4H*)-one (70p)



A mixture of 4-(allyloxy)benzaldehyde **(14p)** (1.750 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic

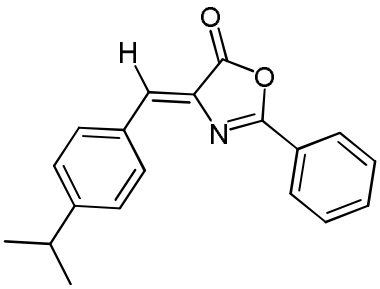
anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.536 g (77 %), m.p. 131-133˚C.

R_f : 0.81 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1786 (C=O),1649 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): 8.20 (t, *J* = 7.2 Hz, 4H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 2H), 7.26 (d, *J* = 16.1 Hz, 1H), 7.04 (d, *J* = 8.9 Hz, 2H), 6.13-6.08 (m,1H), 5.47 (d, *J* = 15.8 Hz, 1H), 5.37 (d, *J* = 10.5 Hz, 1H), 4.65 (d, *J* = 5.3 Hz, 2H).

2.1.15. (*Z*)-4-(4-Isopropylbenzylidene)-2-phenyloxazol-5(*4H*)-one (70r)



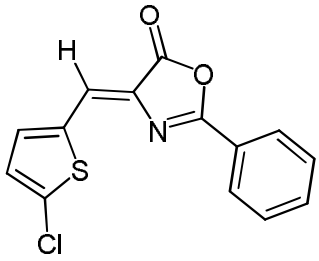
A mixture of 4-isopropylbenzaldehyde **(14r)** (1.598 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, products recrystallized from

acetone. A yellow crystalline solid was obtained; yield 2.923 g (93%), m.p. 112 -114˚C.

R_f : 0.90 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1797 (C=O),1654 (C=N).

2.1.16. (*Z*)-4-((5-Chlorothiophen-2-yl)methylene)-2-phenyloxazol-5(*4H*)-one (70s)



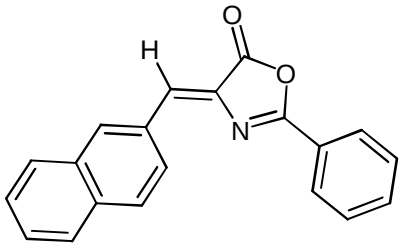
A mixture of 5-chlorothiophene-2-carbaldehyde **(14s)** (1.577 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, products recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.435 g (78%), m.p. 184 -187˚C.

R_f : 0.85 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1790 (C=O),1649 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 8.09 (d, *J* = 7.1 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 3.9 Hz, 2H), 6.91 (d, *J* = 4.0 Hz, 1H).

2.1.17. (*Z*)-4-(Naphthalen-2-ylmethylene)-2-phenyloxazol-5(*4H*)-one (70t)



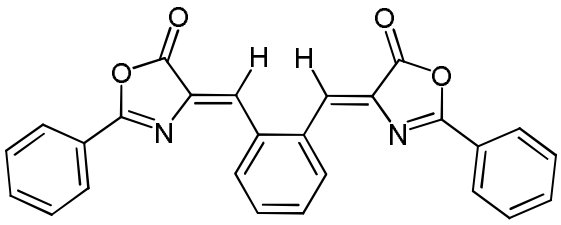
A mixture of 2-naphthaldehyde **(14t)** (1.685 g, 10.8 mmol), hippuric acid (2.212 g, 12.36 mmol) and sodium acetate (0.443 g, 5.4 mmol) in acetic anhydride (3 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A yellow crystalline solid was obtained; yield 2.906 g (90 %), m.p. 169 -170˚C.

R_f : 0.85 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1790 (C=O),1641 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 8.97 (d, *J* = 7.3 Hz, 1H), 8.25 (d, *J* = 8.5 Hz, 1H), 8.15 (d, *J* = 7.3 Hz, 2H), 8.07 (s, =CH, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.60-7.54 (m, 3H), 7.51-7.46 (m, 3H).

2.1.18. (4*Z*,4'*Z*)-4,4'-(1,2-phenylenebis(methan-1-yl-1-ylidene))bis(2-phenyloxazol-5(*4H*)-one) (70u)



A mixture of phthalaldehyde **(14u)** (2.790 g, 20.8 mmol), hippuric acid (4.424 g, 24.72 mmol) and sodium acetate (0.886 g, 10.8 mmol) in acetic anhydride (6 mL) was stirred at 60 ˚C for 3h. After cooling the solution to room temperature, water (30 mL) was added, and the crude azlactone was filtered and washed with two portions of water (50 mL). The product was dried under vacuum for several hours. Finally, product was recrystallized from acetone. A orange crystalline solid was obtained; yield 4.892 g (56 %), m.p. 201 - 204˚C.

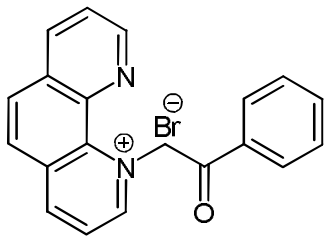
R_f : 0.75 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1801 (C=O),1643 (C=N).

^1H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 8.81 (dd, *J* = 3.5, 9.4 Hz, 2H), 8.21 (d, *J* = 7.1 Hz, 4H), 7.72 (s, =CH, 2H), 7.68-7.55 (m, 8H).

2.2. Synthesis of phenanthrolinium salt

2.2.1. 1-(2-Oxo-2-phenylethyl)-1,10-phenanthrolin-1-ium bromide (61)



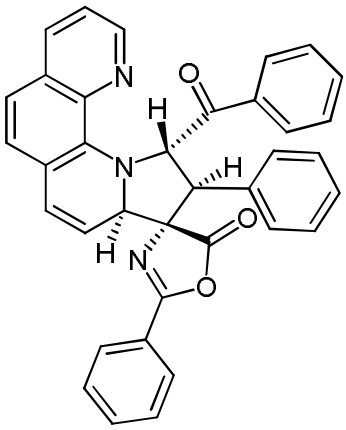
1,10-phenanthroline hydrate **89** (1.0 g, 5 mmol, 1 eq.) and 2-bromoacetophenone **90** (1.0 g, 5 mmol) were refluxed in acetone (20 mL) for 24 h. The precipitate formed was filtered by suction and washed with acetone (10 mL) .The product was dried under vacuum. An orange solid was obtained; yield 1.701 g (90 %), m.p. 225 -227˚C.

R_f : 0 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1686 (C=O)

2.3.Synthesis of cycloaddition products from the reaction of aryl substituted methylene oxazolones and phenanthrolinium ylides 3a-t

2.3.1. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-2,10'-diphenyl-10',11'-dihydro-*5H*,8a'*H*-spiro[oxazole-4,9'-pyrrolo[1,2- a][1,10] phenanthrolin]-5-one (91a)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-benzylidene-2-phenyloxazol-5(*4H*)-one **(70a)** (0.249 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A yellow solid was obtained; yield 0.164 g (30%), m.p. 152 -154˚C.

R_f : 0.60 (Ethyl Acetate-n-Hexane; 1:1)

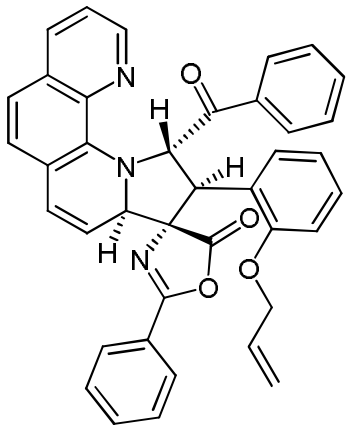
IR (KBr) : v (cm^{-1}) : 1805, 1677 (C=O),1649 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.97 (d, *J* = 7.0 Hz, 2H), 7.84 (dd, *J* = 1.5, 8.3 Hz, 1H), 7.70 (d, *J* = 7.4 Hz , 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.48-7.39 (m, 4H), 7.33-7.31 (m, 2H), 7.28-7.23 (m, 2H), 7.17 (t, *J* = 3.6 Hz, 1H), 7.11 (t, *J* = 3.1 Hz, 2H), 7.06 (t, *J* = 7.6 Hz, 1H), 7.00-6.95 (m, 2H), 6.67 (d, *J* = 9.2 Hz, 1H), 6.47 (dd, *J* = 1.7, 10.0 Hz ,1H), 6.23 (t, *J* = 2.0 Hz, 1H), 5.28 (dd, *J* = 2.4, 10.0 Hz, 1H), 4.00 (d, *J* = 9.2 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=196.4 (C=O), 175.1 (C=O),160.2 (C=N), 143.8, 139.0, 136.9, 135.7, 135.5, 133.2, 132.3, 131.5, 129.7, 129.3, 128.8, 128.2, 127.8, 127.6, 127.5, 126.5, 125.0, 119.9, 117.2, 116.3, 115.1, 80.6 (-CH), 72.5 (-CH), 72.3 (-CH), 57.4 (-CH).

LC-MS(55 eV):(*m/z*,%)= 548 (100) $[M]^+$, 549 (36), 580 (23), 299 (8).

2.3.2. (4*S*,8a'*R*,10'*R*,11'*S*)-10'-(2-(allyloxy)phenyl)-11'-benzoyl-2-phenyl-10',11'-dihydro-*5H*,8a'*H*-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91b)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(2-(allyloxy)benzylidene)-2-phenyloxazol-5(*4H*)-one **(70b)** (0.305 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction

mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour. There is no precipitate so reaction mixture was purified by chromatotron (1:5, ethyl acetate: hexane). The product was dried under vacuum. A red crystalline solid was obtained in DCM-Hexane mixture; yield 0.151 g (25%), m.p. 127 -129˚C.

R_f : 0.85 (Ethyl Acetate-n-Hexane; 1:1)

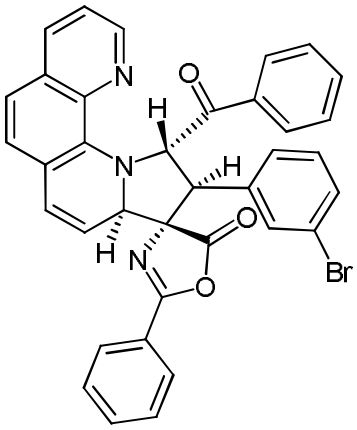
IR (KBr) : v (cm^{-1}) : 1803, 1708 (C=O),1656 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.95 (d, *J* = 7.2 Hz, 2H), 7.84 (dd, *J* = 1.7, 6.6 Hz, 1H), 7.77-7.69 (m, 3H), 7.56-7.52 (m, 2H), 7.46-7.39 (m, 4H), 7.28-7.23 (m, 2H), 7.08-7.02 (m, 2H), 6.98-6.95 (m, 2H), 6.85 (t, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 8.7 Hz, 1H), 6.52-6.44 (m, 2H), 6.24 (t, *J* = 2.1 Hz, 1H), 5.78-5.71 (m, 1H), 5.27 (dd, *J* = 2.4, 7.6 Hz, 1H), 5.15-5.10 (m, 2H), 4.82 (t, *J* = 6.9 Hz, 1H), 4.25 (dd, *J* = 5.0, 8.2 Hz, 1H), 4.01 (dd, *J* = 5.1, 8.1 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=196.9 (C=O), 175.8 (C=O),160.4 (C=N), 156.8, 144.5, 139.6, 137.6, 136.2, 136.0, 132.8, 132.6, 131.8, 130.3, 129.1, 128.8, 128.7, 128.6, 128.5, 128.1, 127.9, 127.0, 125.8, 123.0, 120.4, 120.3, 117.9, 117.0, 115.4, 111.8 (-CH), 80.1 (-CH), 73.0 (-CH), 68.9 (-CH).

LC-MS(55 eV):(*m/z*,%)= 604 (M^+,100) , 605 (42), 574 (30), 471 (22), 299 (63).

2.3.3. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-10'-(3-bromophenyl)-2-phenyl-10',11'-dihydro-*5H*,8a'*H*-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91d)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(3-bromobenzylidene)-2-phenyloxazol-5(*4H*)-one **(70d)** (0.328 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A yellow solid was obtained; yield 0.175 g (28%), m.p. 173 -174˚C.

R_f : 0.72 (Ethyl Acetate-n-Hexane; 1:1)

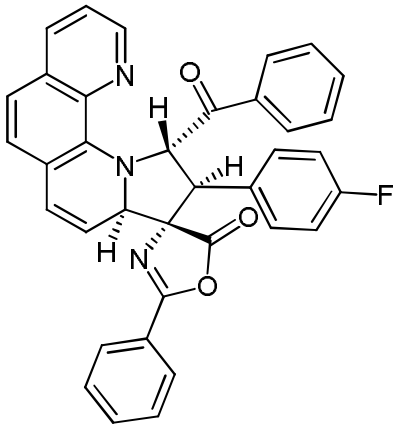
IR (KBr) : ν (cm^{-1}) : 1805, 1680 (C=O),1656 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.89 (d, *J* = 7.2 Hz, 2H), 7.77 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.61 (d, *J* = 7.3 Hz, 2H), 7.49-7.46 (m, 2H), 7.42-7.35 (m, 4H), 7.22-7.14 (m, 3H), 7.05 (d, *J* = 7.7 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.92-6.86 (m, 3H), 6.52 (d, *J* = 9.2 Hz, 1H), 6.38 (dd, *J* = 1.8, 10.0 Hz, 1H), 6.10 (t, *J* = 2.1 Hz, 1H), 5.17 (dd, *J* = 2.4, 10.0 Hz, 1H), 3.82 (d, *J* = 9.2 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=196.5 (C=O), 175.3 (C=O), 161.0 (C=N), 144.4, 139.3, 137.4, 136.3, 136.1, 133.0, 132.6, 131.2, 130.2, 129.8, 129.4, 128.7, 128.5, 128.1, 127.0, 125.3, 122.1, 120.5, 117.7, 116.5, 115.8 (-CH), 80.8 (-CH), 72.8 (-CH), 70.7 (-CH), 57.3 (-CH).

LC-MS(55 eV):(*m/z*,%)= 626 (100) $[M]^+$, 658 (95), 656 (79), 659 (37), 627 (35), 299 (5).

2.3.4. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-10'-(4-fluorophenyl)-2-phenyl-10',11'-dihydro-*5H*,8a'*H*-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91e)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(4-fluorobenzylidene)-2-phenyloxazol-5(*4H*)-one **(70e)** (0.267 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A yellow solid was obtained; yield 0.249 g (44%), m.p. 169 -171˚C.

R_f : 0.70 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1807, 1683 (C=O),1651 (C=N).

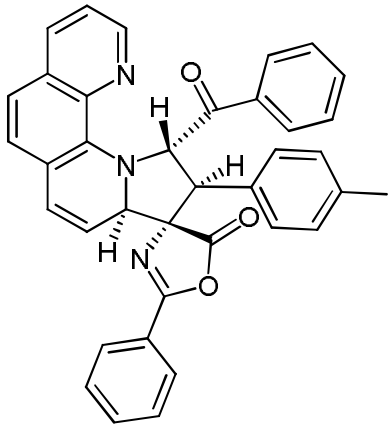
^1H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.96 (dd, *J* = 1.0, 1.4, 7.2 Hz, 2H), 7.85 (dd, *J* = 1.7, 6.6 Hz, 1H), 7.69 (dd, *J* = 0.9, 1.3, 7.2 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.48-7.41 (m, 4H), 7.27 (t, *J* = 6.9 Hz, 5H), 7.07 (d, *J* = 8.1 Hz, 1H),

7.00-6.96 (m, 2H), 6.80 (t, *J* = 8.7 Hz, 2H), 6.60 (d, *J* = 9.3 Hz, 1H), 6.47 (dd, *J* = 1.8, 8.2 Hz, 1H), 6.20 (t, *J* = 2.1 Hz, 1H), 5.26 (dd, *J* = 2.4, 10.0 Hz, 1H), 3.82 (d, *J* = 9.2 Hz, 1H).

^{13}C NMR (δ_C ,100 MHz, $CDCl_3$): δ=196.6 (C=O), 175.4 (C=O),161.0 (C=N), 144.3, 139.4, 137.4, 136.2, 136.0, 132.9, 132.0, 131.4, 131.3, 130.2, 129.6, 129.3, 128.7, 128.6, 128.1, 127.0, 125.4, 120.6, 117.7, 116.5, 115.7, 115.3, 115.1, 83.4 (-CH), 80.9 (-CH), 73.1 (-CH), 72.6 (-CH), 57.0 (-CH).

LC-MS(55 eV):(*m/z*,%)= 566 (100) $[M]^+$, 567 (42), 299 (16), 268 (13).

2.3.5. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-2-phenyl-10'-p-tolyl-10',11'-dihydro-*5H*,8a'*H*-spiro[oxazole-4,9'-pyrrolo[1,2- a][1,10] phenanthrolin]-5-one (91f)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(4-methylbenzylidene)-2-phenyloxazol-5(*4H*)-one **(70f)** (0.263 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated

by filtration. The product was dried under vacuum. A yellow solid was obtained; yield 0.163 g (29 %), m.p. 170 -171˚C.

R_f : 0.68 (Ethyl Acetate-n-Hexane; 1:1)

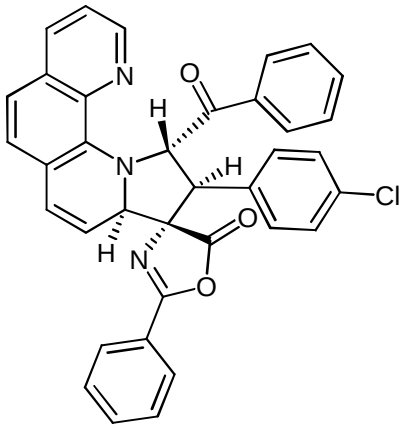
IR (KBr) : v (cm^{-1}) : 1803, 1678 (C=O),1651 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.98-7.93 (m, 2H), 7.82 (t, *J* = 6.8 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.47-7.40 (m, 4H), 7.30-7.18 (m, 5H), 7.06 (t, *J* = 8.1 Hz, 1H), 6.99-6.91 (m, 4H), 6.62 (d, *J* = 9.2 Hz, 1H), 6.45 (dd, *J* = 1.7, 10.0 Hz, 1H), 6.23-6.21 (m, 1H), 5.26 (dd, *J* = 2.4, 10.0 Hz, 1H), 3.97 (d, *J* = 9.2 Hz, 1H), 2.20 (d, *J* = 12.9 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=197.1 (C=O), 175.7 (C=O), 160.6 (C=N), 144.2, 136.3, 136.0, 132.7, 131.9, 130.6, 129.6, 129.3, 129.0, 128.7, 128.2, 128.1, 128.0, 127.0, 125.7, 120.4, 117.7, 116.8, 115.5, 83.7 (CH), 81.2 (CH), 73.0 (CH), 72.7 (-CH), 70.6 (-CH), 57.6 (-CH), 55.2 (-CH), 21.0 ($-CH_3$).

LC-MS (55 eV) : (*m/z*,%)= 562 (100) $[M]^+$, 563 (38), 484 (25), 299 (56), 264 (10).

2.3.6. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-10'-(4-chlorophenyl)-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91g)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(4-chlorobenzylidene)-2-phenyloxazol-5(*4H*)-one **(70g)** (0.283 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A yellow solid was obtained; yield 0.215 g (37%), m.p. 178 -179˚C.

R_f : 0.70 (Ethyl Acetate-n-Hexane; 1:1)

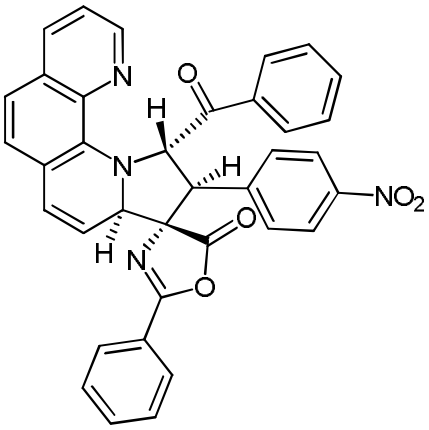
IR (KBr) : v (cm^{-1}) : 1807, 1685 (C=O),1657 (C=N)

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.97 (d, *J* = 7.1 Hz, 2H), 7.85 (dd, *J* = 1.7, 8.4 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.49-7.43 (m, 4H), 7.31-7.24 (m, 5H), 7.08 (t, *J* = 7.8 Hz, 3H), 7.01-6.96 (m, 2H), 6.61 (d, *J* = 9.2 Hz, 1H), 6.47 (dd, *J* = 1.8, 10.0 Hz, 1H), 6.21 (t, *J* = 2.1 Hz, 1H), 5.27 (dd, *J* = 2.5, 10.0 Hz, 1H), 3.96 (d, *J* = 9.2 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=196.6 (C=O), 175.4 (C=O), 160.9 (C=N), 144.4, 139.4, 137.4, 136.1, 134.0, 132.9, 132.5, 132.2, 131.0, 130.2, 129.4, 128.9, 128.8, 128.8, 128.7, 128.2, 127.0, 125.4, 120.5, 117.7, 116.6, 115.8, 88.8 (-CH), 83.5 (-CH), 80.9 (-CH), 73.1 (-CH), 57.1 (-CH).

LC-MS(55 eV):(*m/z*,%)= 582 (100) $[M]^+$, 584 (16), 583 (35).

2.3.7. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-10'-(4-nitrophenyl)-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2- a][1,10] phenanthrolin]-5-one (91h)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(4-nitrobenzylidene)-2-phenyloxazol-5(*4H*)-one **(70h)** (0.294 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A orange solid was obtained; yield 0.213 g (36 %), m.p. 148 -151˚C.

R_f : 0.54 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1813, 1687 (C=O),1649 (C=N).

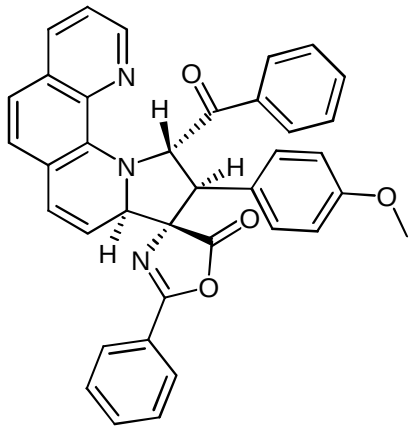
^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 8.03 (d, *J* = 8.8 Hz, 2H), 7.98-7.94 (m, 5H), 7.92 (s, 1H), 7.89 (dd, *J* = 1.7, 8.3 Hz, 2H), 7.82 (d, *J* = 7.2 Hz, 2H), 7.71 (d, *J* = 7.2 Hz, 2H), 7.61-7.42 (m, 14H), 7.32-7.24 (m, 7H), 7.09 (t, *J* = 8.2 Hz, 2H), 7.05-7.00 (m, 4H), 6.69 (d, *J* = 9.1 Hz, 1H), 6.51 (dd, *J* = 1.8, 10.0 Hz, 1H), 6.22 (dt, *J* = 2.2, 8.5 Hz, 2H), 5.29 (dd, *J* = 2.5, 10.0 Hz, 1H), 4.08 (t, *J* = 8.2 Hz, 2H).

^{13}C NMR (δ_C ,100 MHz, $CDCl_3$): δ=196.1 (C=O), 175.0 (C=O), 161.3 (C=N), 145.2, 141.9, 139.2, 136.2, 136.0, 133.2, 132.4, 131.2, 130.4, 130.0, 129.6,

128.9, 128.7, 128.3, 128.1, 127.0, 123.8, 123.4, 120.6, 117.8, 116.4, 116.1, 83.5 (-CH), 80.8 (-CH), 73.1 (-CH), 57.0 (-CH).

LC-MS(55 eV):(*m/z*,%)= 593 (100) $[M]^+$, 639 (10), 594 (45), 565 (8).

2.3.8. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-10'-(4-methoxyphenyl)-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91j)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(4-methoxybenzylidene)-2-phenyloxazol-5(*4H*)-one **(70j)** (0.279 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour. There is no precipitate so reaction mixture was purified by chromatotron (1:5, ethyl acetate: hexane). The product was dried under vacuum. A red solid was obtained; yield 0.156 mg (27%), m.p. 137 -139˚C.

R_f : 0.66 (Ethyl Acetate-n-Hexane; 1:1)

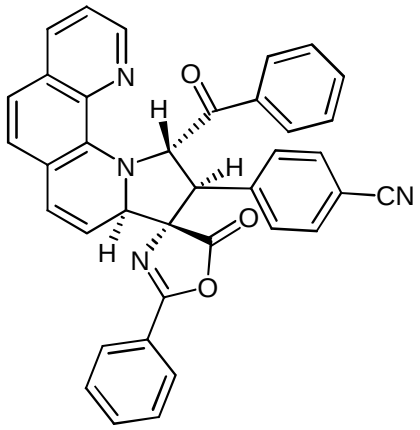
IR (KBr) : v (cm^{-1}) : 1807, 1691 (C=O),1631 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.98-7.93 (m, 2H), 7.83 (t, *J* = 8.8 Hz, 2H), 7.70 (d, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 6.7 Hz, 1H), 7.48-7.40 (m, 4H), 7.27-7.21 (m, 2H), 7.05 (t, *J* = 7.3 Hz, 1H), 6.99-6.94 (m, 2H), 6.22-6.20 (m, 1H), 3.98-3.92 (m, 1H), 3.70 (d, *J* = 18.9 Hz, 3H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=197.0 (C=O), 175.7 (C=O), 160.6 (C=N), 159.3, 143.4, 139.5, 136.3, 132.6, 131.9, 130.9, 130.1, 128.7, 128.2, 127.0, 125.6, 120.4, 117.7, 116.8, 115.5, 97.6 (-CH), 81.2 (-CH), 77.3 (-CH), 72.8 (-CH), 57.3 (-CH).

LC-MS(55 eV):(*m/z*,%)= 578 (100) $[M]^+$, 580 (10), 579 (41), 340 (9), 79 (35).

2.3.9. 4-((4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-5-oxo-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2- a][1,10] phenanthroline]-10'-yl)benzonitrile (91k)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-((5-oxo-2-phenyloxazol-4(*5H*)-ylidene)methyl)benzonitrile **(70k)** (0.274 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated

by filtration. The product was dried under vacuum. A orange solid was obtained; yield 0.172 g (30%), m.p. 155 -157˚C.

R_f : 0.70 (Ethyl Acetate-n-Hexane; 1:1)

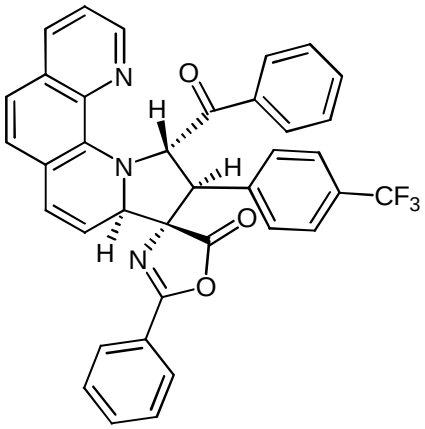
IR (KBr) : v (cm^{-1}) : 1809, 1687 (C=O),1649 (C=N)

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.97-7.80 (m, 4H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.60-7.42 (m, 9H), 7.34-7.27 (m, 2H), 7.10-7.01 (m, 3H), 6.83 (d, *J* = 9.1 Hz, 1H), 6.66 (d, *J* = 9.1 Hz, 1H), 6.53 (dd, *J* = 9.8, 16.0 Hz, 1H), 6.22 (d, *J* = 7.9 Hz, 1H), 5.41 (d, *J* = 9.9 Hz, 1H), 5.28 (d, *J* = 9.9 Hz, 1H), 4.02 (t, *J* = 8.1 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=196.1 (C=O), 175.0 (C=O), 161.2 (C=N), 144.5, 139.8, 136.2, 135.9, 133.2, 132.4, 132.0, 130.5, 130.3, 130.2, 129.8, 129.5, 128.9, 128.8, 128.6, 128.3, 128.1, 127.0, 125.0, 120.6, 118.3, 117.9, 117.7, 116.5, 116.4, 116.3, 116.0, 112.2, 112.0 (C=N), 83.4 (-CH), 80.7 (-CH), 73.0 (-CH), 57.3 (-CH).

LC-MS(55 eV):(*m/z*,%)= 573 (100) $[M]^+$, 574 (45), 275 (23), 181 (13).

2.3.10. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-2-phenyl-10'-(4-(trifluoromethyl)phenyl)-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10]phenanthrolin]-5-one (91l)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-2-phenyl-4-(4-(trifluoromethyl)benzylidene)oxazol-5(*4H*)-one **(70l)** (0.317 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A yellow solid was obtained; yield 0.277 g (45%), m.p. 170 -171˚C.

R_f : 0.81 (Ethyl Acetate-n-Hexane; 1:1)

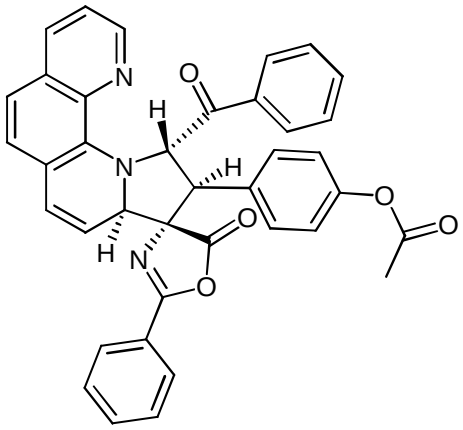
IR (KBr) : v (cm^{-1}) : 1809, 1684 (C=O),1654 (C=N)

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.98 (d, *J* = 7.3 Hz, 2H), 7.87 (dd, *J* = 1.5, 6.8 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.52 (dd, *J*=1.6, 2.4 Hz, 1H), 7.48-7.36 (m, 7H), 7.28-7.24 (m, 2H), 7.09 (d, *J* = 8.1 Hz, 1H), 7.03-6.98 (m, 2H), 6.66 (d, *J* = 9.2 Hz, 1H), 6.50 (dd, *J* = 1.7, 10.0 Hz, 1H), 6.22 (s, 1H), 5.28 (dd, *J* = 2.4, 10.0 Hz, 1H), 4.03 (d, *J* = 9.2 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=196.4 (C=O), 175.2 (C=O), 161.1 (C=N), 144.4, 139.3, 138.4, 137.4, 136.2, 133.1, 132.2, 130.3, 129.5, 128.8, 128.6, 128.1, 127.0, 125.7, 125.2, 120.6 (-CF_3), 117.7, 116.5, 116.0, 80.8 (-CH), 73.1 (-CH), 70.8 (-CH), 57.2 (-CH).

LC-MS(55 eV):(*m/z*,%)= 616 (100) $[M]^+$, 618 (10), 617 (42).

2.3.11. 4-((4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-5-oxo-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2- a][1,10] phenanthroline]-10'-yl)phenyl acetate (91m)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-((5-oxo-2-phenyloxazol-4(*5H*)-ylidene)methyl)phenyl acetate **(70m)** (0.307 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A yellow solid was obtained; yield 0.242 g (40%), m.p. 157 -158˚C.

R_f : 0.71 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1815, 1764, 1685 (C=O),1658 (C=N)

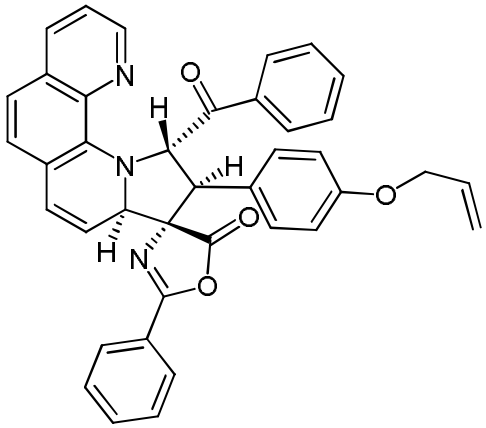
^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.99 (d, *J* = 7.4 Hz, 2H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 7.5 Hz, 2H), 7.56 (t, *J* = 7.1 Hz, 1H), 7.45 (t, *J* = 7.0 Hz, 4H), 7.34-7,27 (m, 4H), 7.07 (d, *J* = 8.0 Hz, 1H), 7.00-6.96 (m, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.63 (d, *J* = 9.2 Hz, 1H), 6.47 (d, *J* = 9.9 Hz, 1H), 6.21 (s, 1H), 5.27 (d, *J* = 9.9 Hz, 1H), 3.99 (d, *J* = 9.2 Hz, 1H), 2,22 (s, 3H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=196.8 (C=O), 184.2 (C=O), 175.5 (C=O), 169.0 (C=N), 160.9, 154.1, 150.5, 144.4, 139.5, 137.4, 136.0, 132.9, 132.1, 131.6, 130.9, 130.3, 129.4, 128.7, 128.6, 128.2, 127.0, 125.5, 121.5, 120.5,

117.7, 116.6, 115.7 (-CH), 81.0 (-CH), 73.6 (-C-), 73.0 (-CH), 63.8 (-CH), 57.1 (- CH_3).

LC-MS(55 eV):(*m/z*,%)= 606 (100) $[M]^+$, 608 (18), 607 (42), 576 (10), 572 (8).

2.3.12. (4*S*,8a'*R*,10'*R*,11'*S*)-10'-(4-(allyloxy)phenyl)-11'-Benzoyl-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91p)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(4-(allyloxy)benzylidene)-2-phenyloxazol-5(*4H*)-one **(70p)** (0.305 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour. There is no precipitate so reaction mixture was purified by chromatotron (1:5, ethyl acetate: hexane).The product was dried under vacuum. A red crystalline solid was obtained in DCM-Hexane mixture; yield 0.163 g (27 %), m.p. 144 -146˚C.

R_f : 0.70 (Ethyl Acetate-n-Hexane; 1:1)

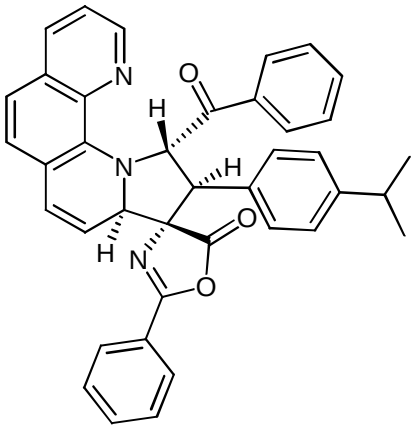
IR (KBr) : v (cm^{-1}) : 1807, 1691 (C=O),1649 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.98-7.93 (m, 2H), 7.69 (dd, *J* = 1.8, 8.4 Hz, 2H), 7.70 (d, *J* = 7.2 Hz, 1H), 7.58-7.53 (m, 1H), 7.48-7.40 (m, 4H), 7.32-7.20 (m, 4H), 7.05 (t, *J* = 7.3 Hz, 1H), 6.99-6.94 (m, 2H), 6.66 (d, *J* = 8.8 Hz, 2H), 6.46 (dd, *J* = 1.8, 11.9 Hz, 1H), 6.22-6.20 (m, 1H), 6.01-5.91 (m, 1H), 5.38-5.21 (m, 3H), 4.43-4.38 (m, 2H), 3.96 (d, *J* = 9.3 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=197.1 (C=O), 175.7 (C=O), 160.6 (C=N), 158.3, 144.2, 139.6, 137.4, 136.3, 136.0, 133.0, 132.7, 131.9, 130.8, 130.1, 129.2, 128.7, 128.1, 127.0, 125.8, 125.6, 120.4, 117.7, 116.8, 115.5, 114.8, 114.5, 83.7 (-CH), 81.2 (-C-), 73.1 (-CH), 68.5 (-CH), 57.3 ($-CH_2$).

LC-MS (55 eV):(*m/z*,%)= 604 (100) $[M]^+$, 605 (49), 316 (8), 296 (7), 79 (65).

2.3.13. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-10'-(4-isopropylphenyl)-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91r)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(4-isopropylbenzylidene)-2-phenyloxazol-5(*4H*)-one **(70r)** (0.291 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The

residue was refluxed in ethanol for an hour. There is no precipitate so reaction mixture was purified by chromatotron (1:5, ethyl acetate: hexane). The product was dried under vacuum. A orange solid was obtained; yield 0.165 g (28 %), m.p. 156 -158˚C.

R_f : 0.65 (Ethyl Acetate-n-Hexane; 1:1)

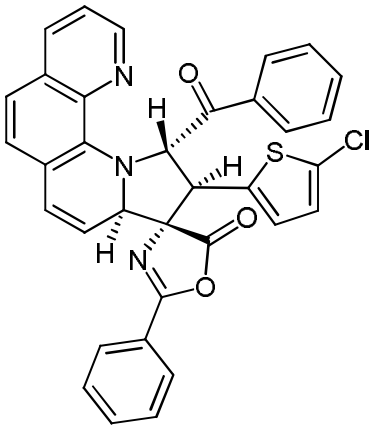
IR (KBr) : v (cm^{-1}) : 1809, 1686 (C=O),1649 (C=N)

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 8.00-7.94 (m, 2H), 7.83 (dd, *J* = 1.7, 6.6 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.59-7.54 (m, 1H), 7.48-7.42 (m, 3H), 7.40-7.37 (m, 1H), 7.27-7.20 (m, 4H), 7.05-6.94 (m, 5H), 6.24-6.21 (m, 1H), 3.97 (dd, *J* = 2.3, 9.4 Hz, 1H), 2.80-2.71 (m, 1H), 1.16-1.10 (m, 6H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=197.1 (C=O), 175.6 (C=O), 162.3 (C=N), 148.8, 144.2, 139.6, 137.4, 136.3, 136.0, 132.6, 131.8, 131.1, 130.9, 130.3, 130.4, 130.1, 129.8, 129.0, 128.7, 128.2, 127.9, 127.0, 126.8, 125.7, 125.4, 124.7, 120.4, 117.7, 116.7, 115.5, (-CH), 83.6 (-CH-), 81.2 (-CH), 57.6 (-CH), 33.7 (-CH-aliphatic), 23.8 ($-CH_3$).

LC-MS(55 eV):(*m/z*,%)= 590 (100) $[M]^+$, 605 (13), 604 (31), 591 (37), 578 (12), 301 (18), 299 (57).

2.3.14. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-10'-(5-chlorothiophen-2-yl)-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91s)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-((5-chlorothiophen-2-yl)methylene)-2-phenyloxazol-5(*4H*)-one **(70s)** (0.289 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A yellow solid was obtained; yield 247 mg (42 %), m.p. 161 -162˚C.

Rf : 0.54 (Ethyl Acetate-n-Hexane; 1:1)

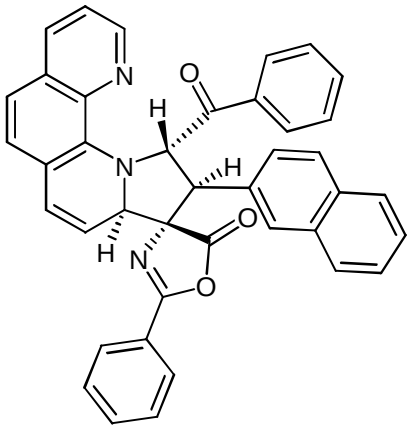
IR (KBr) : v (cm^{-1}) : 1805, 1678 (C=O),1657 (C=N).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 8.09 (d, *J* = 7.2 Hz, 2H), 7.85 (dd, *J* = 1.7, 6.6 Hz, 1H), 7.78 (d, *J* = 7.3 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 3H), 7.45 (dd, *J* = 1.7, 2.4 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 1H), 7.01-6.96 (m, 2H), 6.48-6.39 (m, 4H), 6.16 (t, *J* = 2.1 Hz, 1H), 5.27 (dd, *J* = 2.5, 9.9 Hz, 1H), 4.24 (d, *J* = 9.3 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=196.3 (C=O), 175.4 (C=O),161.9 (C=N), 144.3, 139.2, 137.3, 136.6, 136.1, 134.6, 133.2, 132.2, 131.2, 130.2, 129.6, 129.0, 128.9, 128.5, 128.3, 127.0, 125.4, 125.1, 120.5, 117.6, 116.2, 115.9 (-CH), 80.4 (-CH), 74.0 (-CH), 72.6 (-CH), 53.5 (-CH).

LC-MS(55 eV):(*m/z*,%)= 588 (100) $[M]^+$, 634 (7), 591 (16), 590 (45).

2.3.15. (4*S*,8a'*R*,10'*R*,11'*S*)-11'-Benzoyl-10'-(naphthalen-2-yl)-2-phenyl-10',11'-dihydro-5H,8a'H-spiro[oxazole-4,9'-pyrrolo[1,2-a][1,10] phenanthrolin]-5-one (91t)



Phenanthrolinium salt **61** (0.379 g, 1 mmol) was suspended in dichloromethane (5 mL) and then (*Z*)-4-(naphthalen-2-ylmethylene)-2-phenyloxazol-5(*4H*)-one **(70t)** (0.299 g, 1 mmol). Under vigorous stirring, triethylamine (0.14 mL) was added dropwise. After 20 min the reaction mixture was washed twice with water (10 mL) and solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was isolated by filtration. The product was dried under vacuum. A orange solid was obtained; yield 0.299 g (50%), m.p. 172 -173˚C.

R_f : 0.66 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1805, 1692 (C=O),1643 (C=N).

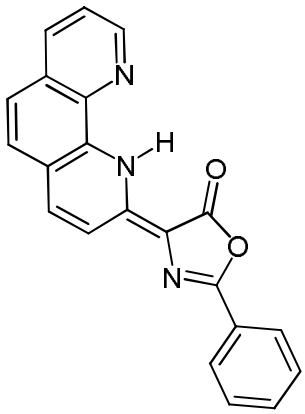
^1H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 7.97 (d, *J* = 6.7 Hz, 1H), 7.85-7.82 (m, 2H), 7.77 (dd, *J* = 1.7, 6.6 Hz, 1H), 7.55 (t, *J* = 9.5 Hz, 2H), 7.49-7.42 (m, 3H), 7.37-7.20 (m, 8H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.94-6.86 (m, 4H), 6.70 (d, *J* = 9.0 Hz, 1H), 6.41 (dd, *J* = 1.8, 10.0 Hz, 1H),

6.31 (t, *J* = 2.1 Hz, 1H), 5.21 (dd, *J* = 2.5, 10.0 Hz, 1H), 5.00 (d, *J* = 9.1 Hz, 1H).

^{13}C NMR (δ_C, 100 MHz, $CDCl_3$): δ=197.6 (C=O), 175.9 (C=O), 160.7 (C=N), 144.4, 139.6, 137.5, 136.1, 133.7, 133.5, 132.8, 132.5, 131.9, 131.8, 130.3, 129.9, 129.3, 128.7, 128.4, 128.1, 127.9, 127.7, 127.0, 125.5, 124.5, 123.4, 122.1, 120.5, 118.1, 117.1, 117.8, 117.1, 115.9, 115.7 (CH), 80.4 (CH), 74.8 (CH), 73.5 (-CH), 50.1 (-CH).

LC-MS(55 eV):(*m/z*,%)= 598 (100) $[M]^+$, 599 (44), 391 (50), 300 (69), 299 (50).

2.4.1. (*E*)-4-(1,10-phenanthrolin-2(*1H*)-ylidene)-2-phenyloxazol-5(*4H*)-one (93)



The side product **96** which was obtained upon chromatography with ethyl acetate-n-hexane mixture. It was isolated by filtration and dried under vacuum. The fine red needles were obtained; yield trace, m.p. decom. 260˚C.

R_f : 0.66 (Ethyl Acetate-n-Hexane; 1:1)

IR (KBr) : v (cm^{-1}) : 1691 (C=O),1637 (C=N), 3443 (N-H).

^{1}H NMR (δ_H, 400 MHz, $CDCl_3$): δ= 13.30 (s, 1H) N-H, 9.13 (dd, *J* = 1.6, 4.3 Hz, 1H), 8.26 (dd, *J* = 1.6, 8.3 Hz, 1H), 8.07 (dd, *J* = 1.5, 8.3 Hz, 2H), 7.93 (s, 2H), 7.67-7.64 (m, 3H), 7.50-7.43 (m, 3H).

CHAPTER III

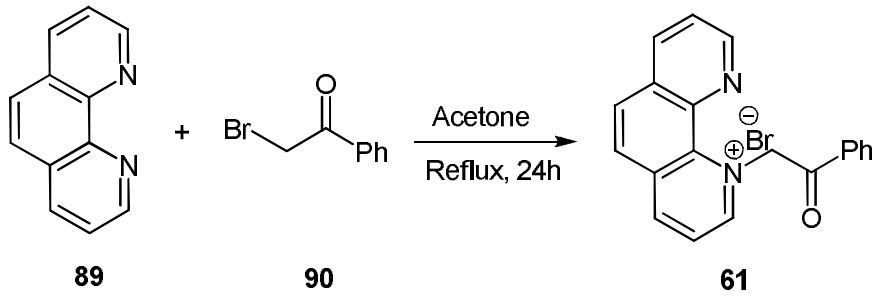
RESULT DISCUSSION

1,3-Dipolar cycloaddition reactions are widely used in synthetic organic chemistry, in particular, for the synthesis of various five-membered heterocyclic systems that are used in industry, medicine and as synthons for fine organic synthesis [75].

Taking into account of importance of [3+2] cycloaddition reactions, to our best knowledge of literature survey, 1,3-dipolar cycloadditions reactions of *(Z)*-substituted arylidene oxazolone with phenanthrolinium *N*-ylide was performed for the first time in our work, although study of cycloaddition reactions of phenanthrolinium *N*-ylides with substituted alkene and alkyne derivatives were reported previously. For this reason, we have been focused, in this study, to obtain pyrrolidine heterocycles starting from both phenanthrolinium *N*-ylide and substituted azlactones.

The work under investigation is essentially consisted of three parts.

In the first part of the study, phenanthroline **89** was reacted with 2-bromoacetophenone **90** to give phenanthrolinium phenacyl bromide **61** according to procedure described in the literature (Scheme 3.1) [38].

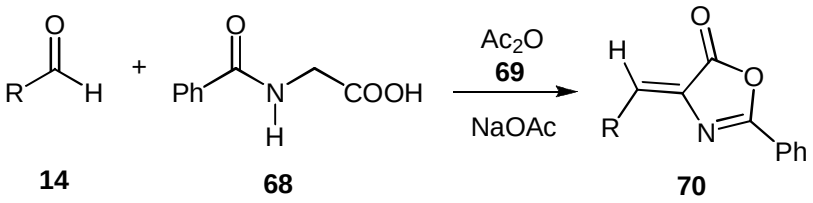


89 90 61

Scheme 3. 1 Synthesis of phenanthrolinium phenacyl bromide

Data for this salt (IR, m.p. and R_f) were found to be in consistent with the literature values. During the reaction, the precipitation of cycloimmonium salt in the reaction medium is the proof of the generation of this salt. The C=O absorption at around 1686 cm^{-1} in the IR spectrum is the another indication for the generation of phenanthrolinium phenacyl bromide. This salt is used in the proceeding steps where it has been converted into ylide *in situ* by the effect of triethyl amine as a base.

In the second part, the synthesis of arylidene azlactones (arylidene oxazolones) were carried out by the condensation of hippuric acid **68** in the presence of acetic anhydride **69** and the corresponding substituted aromatic aldehydes **14** carrying electron-withdrawing and electron donating groups (Scheme 3.2) [74].



14 **68** **70**

	R
70a	4-H-C_6H_4-
70b	2-OCH_2CHCH_2-C_6H_4-
70c	3-$OC_6H_5C_6H_4$
70d	3-Br-C_6H_4-
70e	4-F-C_6H_4-
70f	4-CH_3-C_6H_4-
70g	4-Cl-C_6H_4-
70h	4-NO_2-C_6H_4-
70j	4-OCH_3-C_6H_4-
70k	4-CN-C_6H_4-
70l	4-CF_3-C_6H_4-
70m	4-CH_3COO-C_6H_4-
70n	4-$N(CH_3)_2$-C_6H_4-
70p	4-OCH_2CHCH_2-C_6H_4
70r	4-$CH(CH_3)_2$-C_6H_4
70s	5-Cl-2-thienyl-
70t	2-naphthyl-

Scheme 3. 2 Synthesis and structures of arylidene oxazolones (azlactones)

Substituted arylidene azlactones were identified based on the spectroscopic (IR, NMR) and physical (m.p., R_f) data. In the IR spectrum, the disappearance of C=O absorption of the corresponding aldehyde and appearance of lactone C=O absorbtion at between 1801-1784 cm^{-1} and C=N double bond absorption at between 1661-1640 cm^{-1} are major descriptive indication of the formation of azlactones. In addition, ^1H NMR spectra exhibited the olefinic protons at 7.0-8.2 ppm (Figure 3.1).

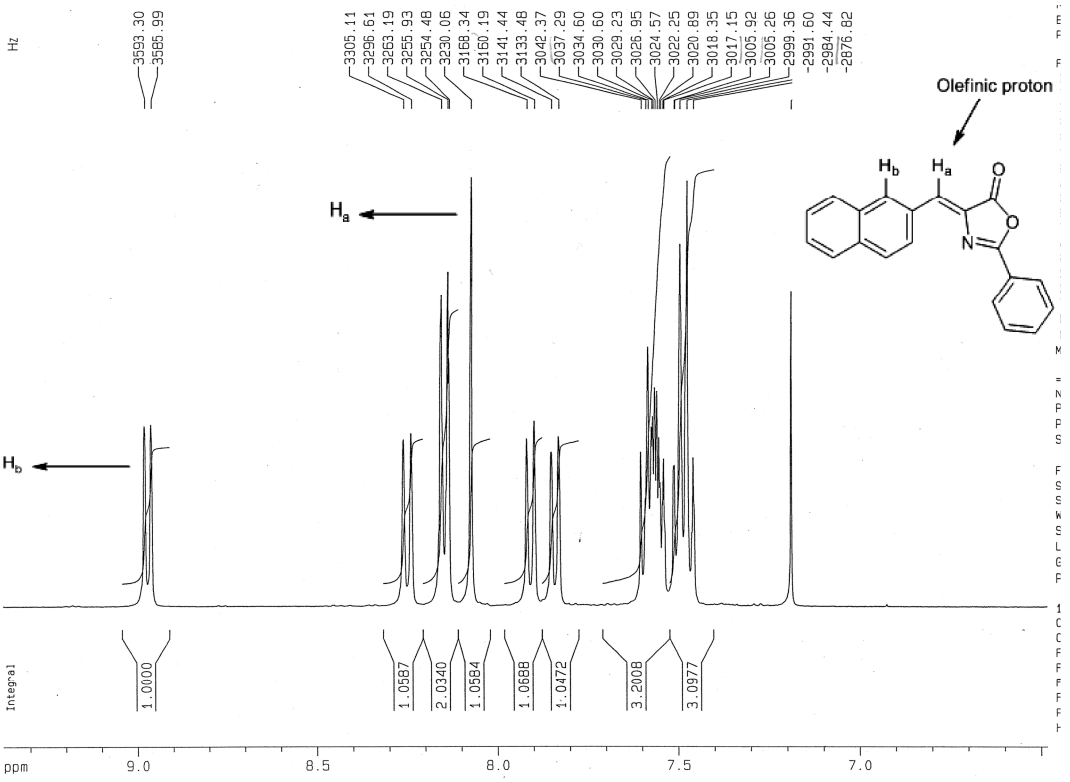


Figure 3. 1 Expanded ^{1}H NMR spectra of **70t**

The recrystallization of compound **70b** and **70u** from acetone gave crystals and the structure of compounds were elucidated by single crystal X-ray diffraction (Figure 3.2 and 3.3). These were also the proof of the *Z* conformation of synthesized azlactones instead of *E* ones.

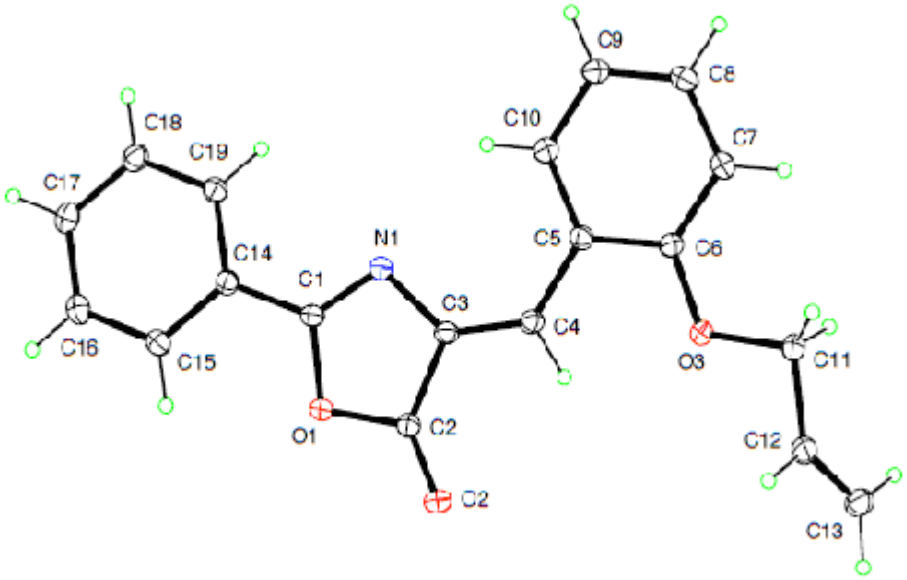


Figure 3. 2 X-ray diffraction for compound **70b**

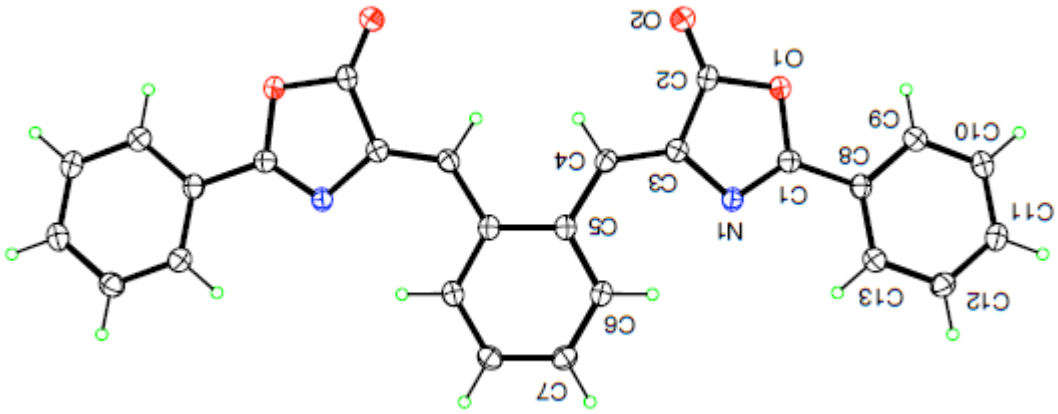
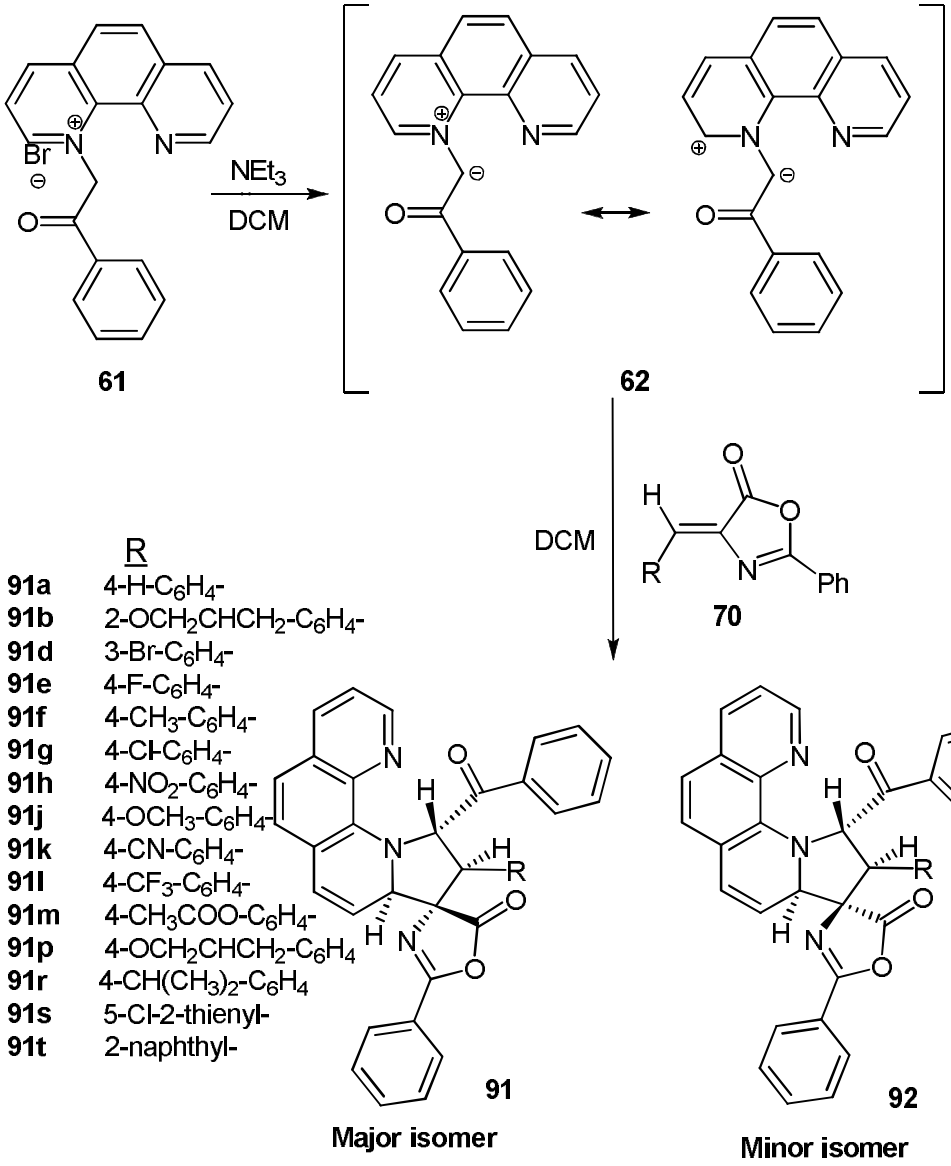


Figure 3. 3 X-ray diffraction for compound **70u**

In the last part of this work, we have been focused on the 1,3-dipolar cycloaddition reaction of phenanthrolinium *N*-ylide, which is prepared *in situ* by deprotonation of phenanthrolinium phenacyl bromide **61** by the effect of triethylamine to the substituted arylidene oxazolones in dichloromethane at room temperature. The reaction seemed to have been proceeded regioselectively and 15 novel substituted spiro oxazolo [1,10] phenanthrolines **91a-t** yielded upon work-up and purification (Scheme 3.3)

[38]. In some cases, stereoisomers which differ only in the spiro junction chiral carbon were obtained that was confirmed by X-Ray diffraction spectra.



Scheme 3. 3 Synthesis of cycloadducts

The structure elucidations of the new cycloadducts were performed by means of spectroscopic methods, especially by ^{1}H NMR, ^{13}C NMR, 2D NMR spectra, LC-MS and X-ray diffraction measurements. The stereochemistry of **91** and **92** has been established by X-ray diffraction ORTEP view of **91b** and

91p (Figure 3.4 and 3.5) and also HSQC, HMBC and NOESY spectra were made use in these assignments.

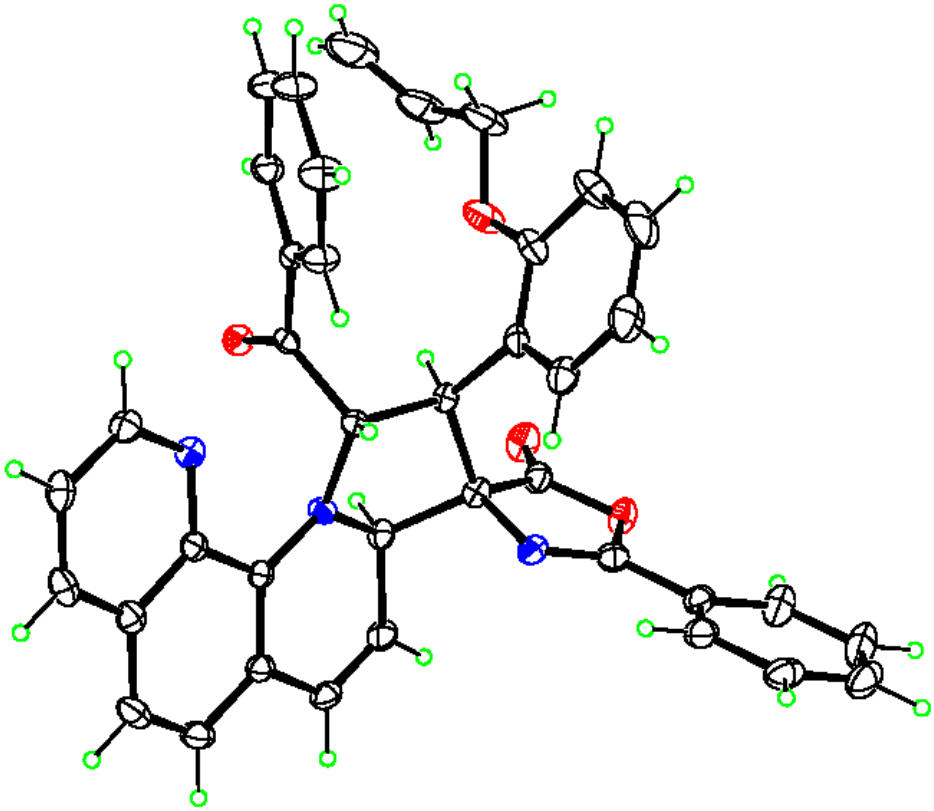


Figure 3. 4 X-ray diffraction of minor stereoisomers of **91b**

Durust46

Yaşar Dürüst

(AS25)

Crystal data

$C_{39}H_{29}N_3O_4$	$F(000)$ = 1264
M_r = 603.65	D_x = 1.296 Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, λ = 0.71073 Å
Hall symbol: -P 2ybc	Cell parameters from 8291 reflections
a = 20.863 (3) Å	θ = 2.5–28.9°
b = 9.5092 (14) Å	μ = 0.09 mm^{-1}
c = 16.8550 (15) Å	T = 90 K
β = 112.328 (8)°	Plate fragment, Orange
V = 3093.2 (7) Å^3	0.27 × 0.20 × 0.10 mm
Z = 4	

Data collection

Nonius KappaCCD (with Oxford Cryostream) diffractometer	5193 reflections with $I > 2\sigma(I)$
Radiation source: fine-focus sealed tube	R_{int} = 0.058
graphite	θ_{max} = 28.9°, θ_{min} = 2.6°
ω and φ scans	h = −28→28
47226 measured reflections	k = −12→12
8066 independent reflections	l = −22→22

Refinement

Refinement on F^2	Secondary atom site location: Difference Fourier map
Least-squares matrix: Full	Hydrogen site location: Inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)]$ = 0.053	H-atom parameters constrained
$wR(F^2)$ = 0.115	$w = 1/[\sigma^2(F_o^2) + (0.0395P)^2 + 1.0581P]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 1.02	$(\Delta/\sigma)_{max} < 0.001$
8066 reflections	$\Delta\rho_{max}$ = 0.36 e Å^{-3}
416 parameters	$\Delta\rho_{min}$ = −0.22 e Å^{-3}
0 restraints	Extinction correction: *SHELXL*, $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Primary atom site location: Structure-invariant direct methods	Extinction coefficient: 0.0031 (4)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for

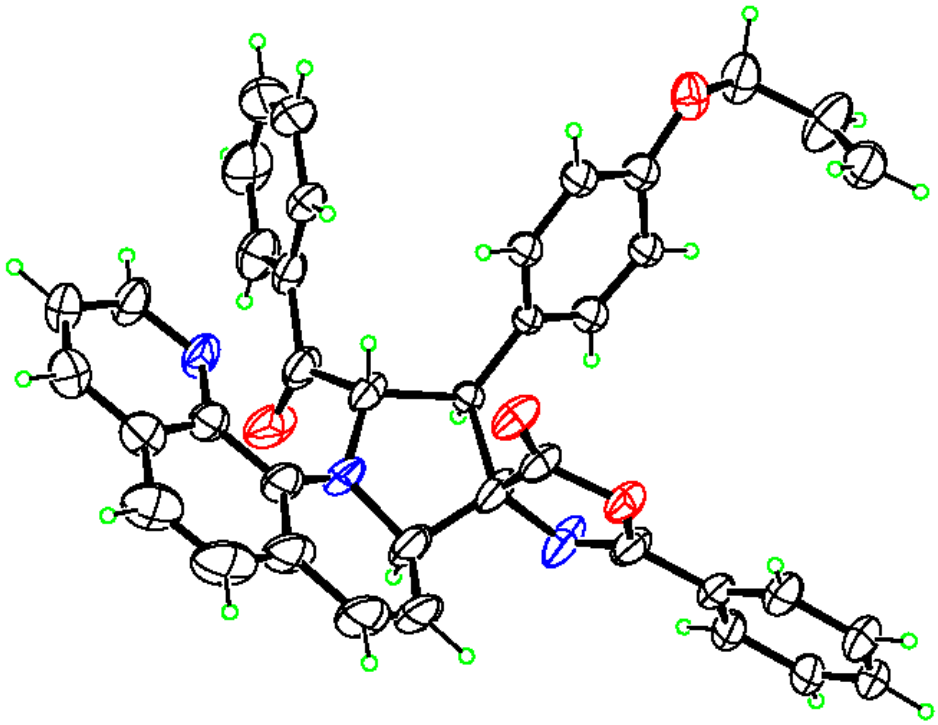


Figure 3. 5 X-ray diffraction of major stereoisomer of **91p**

Durust41Cu

Yaşar Dürüst

(AS54)

Crystal data

$C_{39}H_{29}N_3O_4$	$F(000) = 1264$
$M_r = 603.65$	$D_x = 1.318$ Mg m^{-3}
Monoclinic, $P2_1/c$	Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å
Hall symbol: -P 2ybc	Cell parameters from 4036 reflections
$a = 19.3349$ (6) Å	$\theta = 5.8–64.8°$
$b = 8.2351$ (2) Å	$\mu = 0.69$ mm^{-1}
$c = 19.3989$ (5) Å	$T = 100$ K
$\beta = 99.925$ (2)°	Fragment, orange
$V = 3042.56$ (14) Å^3	0.24 × 0.22 × 0.12 mm
$Z = 4$	

Data collection

Bruker Kappa Apex-II CCD area detector diffractometer	5353 independent reflections
Radiation source: fine-focus sealed tube	4076 reflections with $I > 2\sigma(I)$
graphite	$R_{int} = 0.061$
phi and ω scans	$\theta_{max} = 66.9°$, $\theta_{min} = 5.5°$
Absorption correction: multi-scan SADABS (Sheldrick, 2002)	$h = -22\rightarrow23$
$T_{min} = 0.852$, $T_{max} = 0.922$	$k = -9\rightarrow9$
30477 measured reflections	$l = -22\rightarrow23$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.076$	H-atom parameters constrained
$wR(F^2) = 0.206$	$w = 1/[\sigma^2(F_o^2) + (0.0745P)^2 + 3.1283P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{max} < 0.001$
5353 reflections	$\Delta\rho_{max} = 0.33$ e Å^{-3}
446 parameters	$\Delta\rho_{min} = -0.30$ e Å^{-3}
24 restraints	Extinction correction: SHELXL, $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$

Depending on the substitutent existing in dipolarophiles, 1,3-dipolar cycloaddition reaction can be supposed to generate either *cis* or *trans* stereoisomers which can be explained by transition state of formation stereoisomers (Figure 3.6).

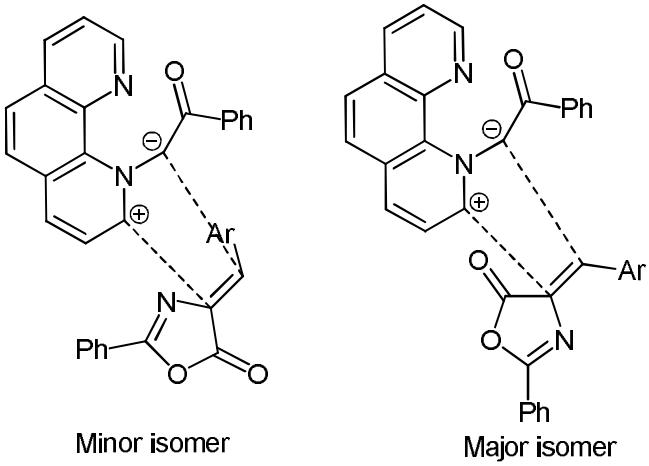


Figure 3. 6 Transition states leading to the formation of stereoisomers **91a-t**

Based on the relative positions of the peaks and *J* coupling constants of the relevant protons in the ^{1}H NMR and carbon chemical shift values in ^{13}C NMR spectra for the **91** and **92**, it revealed that the major isomers are **91** which are observed in all cases, the minor ones are observed for all of them except **91m** and **91e** shown in Table 3.1.

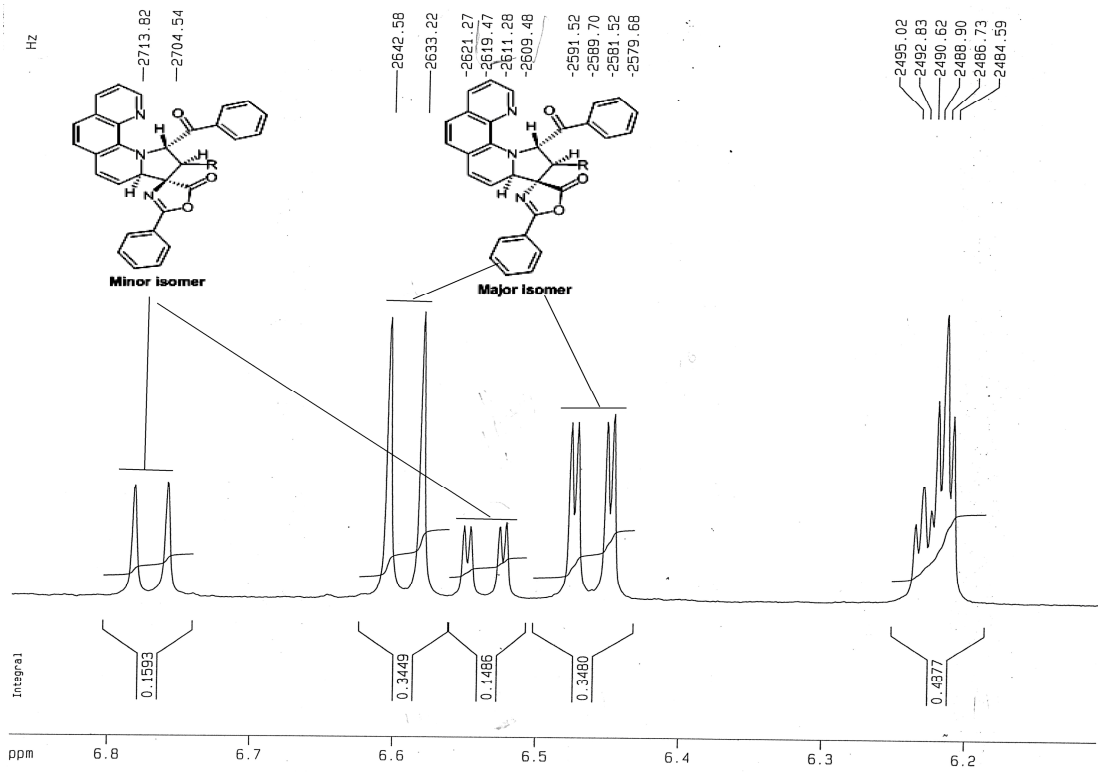


Figure 3. 7 Partial ^{1}H NMR Spectrum of compounds **91r**

Compound	R	Major isomer	Minor isomer	Ratio
91a	4-H-C_6H_4-	+	+	0.20
91b	2-OCH_2CHCH_2-C_6H_4-	+	+	0.35
91d	3-Br-C_6H_4-	+	+	0.47
91e	4-F-C_6H_4-	+	-	-
91f	4-CH_3-C_6H_4-	+	+	0.27
91g	4-Cl-C_6H_4-	+	+	0.08
91h	4-NO_2-C_6H_4-	+	+	0.85
91j	4-OCH_3-C_6H_4-	+	+	0.60
91k	4-CN-C_6H_4-	+	+	0.80
91l	4-CF_3-C_6H_4-	+	+	0.06
91m	4-CH_3COO-C_6H_4-	+	-	-
91p	4-OCH_2CHCH_2-C_6H_4-	+	+	0.30
91r	4-$CH(CH_3)_2$-C_6H_4-	+	+	0.38
91s	5-Cl-2-thienyl-	+	+	0.34
91t	2-naphthyl-	+	+	0.08

Table 3. 1 Stereoisomeric ratios in the cycloadducts **91a-t**

In the IR spectra of these heterocycles, the benzoyl C=O stretching vibration arises around at 1695-1670 cm^{-1}, lactone C=O stretching vibration appears at 1815-1800 cm^{-1} and stretching vibration for C=N double bond is found between at 1660-1630 cm^{-1}.

The chemical shift positions of the H_a proton of cycloadducts **91a-t** appeared as quite deshielded around 6.30-6.10 ppm because of being vicinity to benzoyl carbonyl and nitrogen atom. H_a proton is splitted into triplet caused by neighbourhood proton and an ortho proton of the aromatic ring (benzoyl). Interestingly, H_c proton arises as a doublet of doublet, probably, caused by adjacent and neighbourhood olefinic protons.

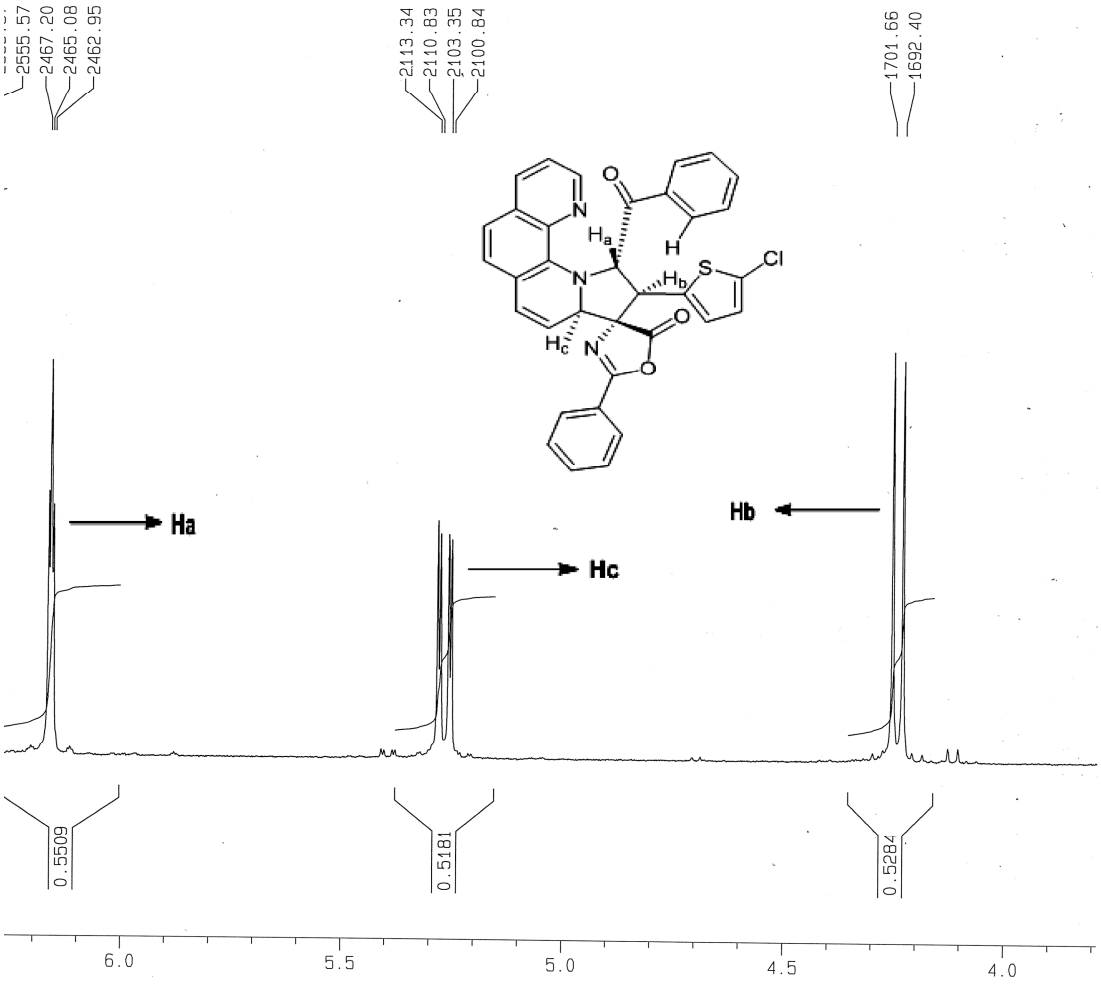


Figure 3. 8 Expanded ^{1}H NMR spectrum of **91s**

In the ^{13}C NMR spectra, two carbonyl and a C=N carbon chemical shifts were observed between 200-160 ppm. The carbon chemical shift of C_a of cycloadducts which belongs to benzoyl carbonyl appeared between 197-195 ppm, C_b, indicates the lactone carbonyl at around 176-175 ppm and C_c shows the iminic carbon, C=N of azlactone at around 169-160 ppm. As it can be seen from the spectra there are also a second and smaller carbon signals along with the bigger ones. Those can be regarded as the carbon chemical signals regarding the minor stereoisomer of the reaction products.

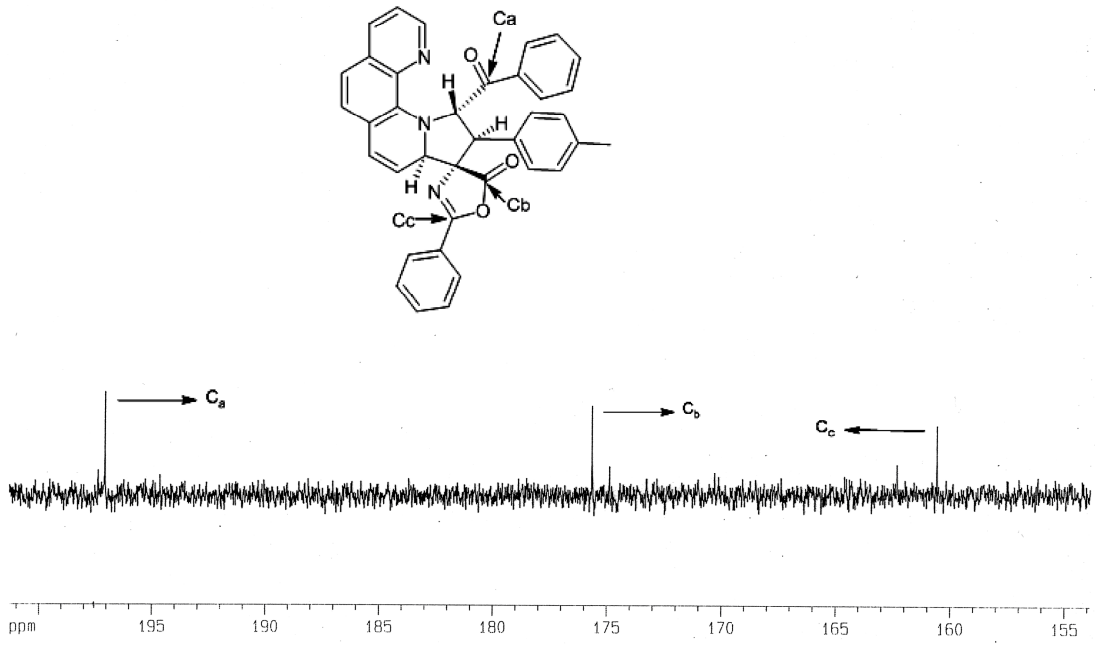


Figure 3. 9 Expanded ^{13}C NMR of **91f**

Upon examination of liquid chromatography-mass spectra (LC-MS) run at atmospheric pressure and mostly chemical ionisation mode of the cycloadducts **91a-t** , the base peaks were found to be protonated molecular ion $[M+H]^+$ due to positive ionization mode.

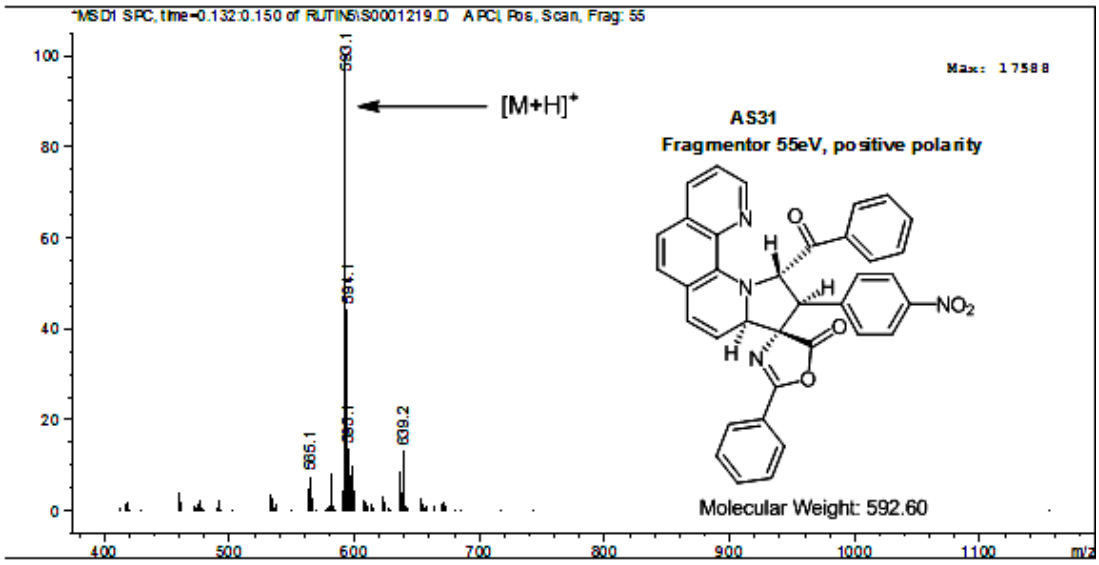
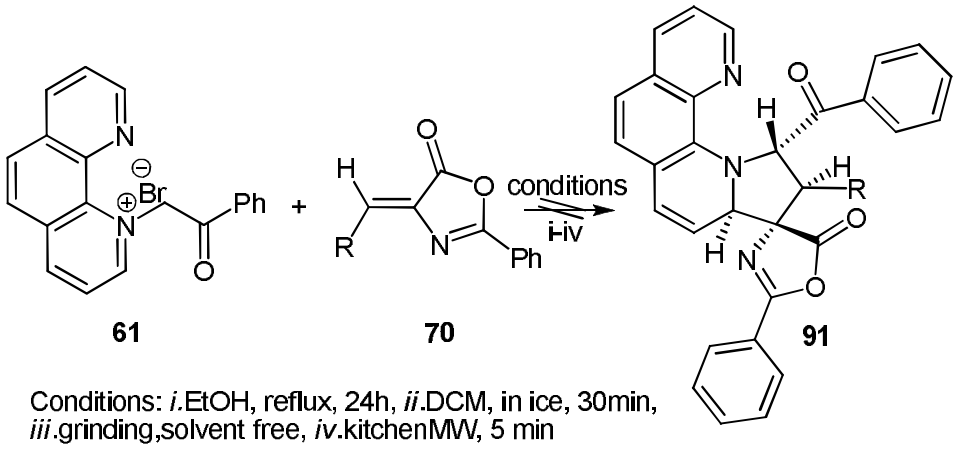


Figure 3. 10 LC-MS spectra of **91h**

In our cycloaddition chemistry, 1,3-DC reaction of phenanthrolinium *N*-ylide and azlactones to afford cycloadducts **91a-t** were successful although the yields of **91a-t** were moderate. In optimization studies the reactions were carried out in different solvents and conditions. It was observed that DCM and acetonitrile gave similar yields, the best yields were achieved when the reaction was performed in DCM at room temperature. The reaction did not take place when the domestic kitchen type microwave oven was used. Even we tried different solvents and conditions to increase the yield but none of conditions were successful (Scheme 3.4).



Scheme 3. 4 Trial conditions for increasing yield of cycloadducts **91a-t**

The best reaction conditions and yield of cycloadducts **91a-t** can be seen in Table 3.2.

Compound	R	Condition	Yield %
91a	4-H-C_6H_4-	DCM,rt,30 min	30
91b	2-OCH_2CHCH_2-C_6H_4-		25
91d	3-Br-C_6H_4-		28
91e	4-F-C_6H_4-		44
91f	4-CH_3-C_6H_4-		29
91g	4-Cl-C_6H_4-		37
91h	4-NO_2-C_6H_4-		36
91j	4-OCH_3-C_6H_4-		27
91k	4-CN-C_6H_4-		30
91l	4-CF_3-C_6H_4-		45
91m	4-CH_3COO-C_6H_4-		40
91p	4-OCH_2CHCH_2-C_6H_4-		27
91r	4-$CH(CH_3)_2$-C_6H_4-		28
91s	5-Cl-2-thienyl-		42
91t	2-naphthyl-		50

Table 3. 2 Substituents and reaction yields

The moderate yields of cycloadducts **91a-t** can be accounted for the transformation of the reaction product, during crystallization, into the compound **93.** A color change of solution into red-brown timely appeared. And this side product was obtained upon chromatography with ethyl acetate-n-hexane mixture, surprisingly as fine red needles **93.** We were able to identify fully the compound **93** by IR, ^{1}H NMR and X-ray diffraction spectra. It was postulated that the formation of **93** could be possible through some kind of rearrangement-type conversion of cycloadduct in solvent. Although we are unable to give a definitive mechanism, the following route (Scheme 3.5) may be plausible, and is supported by experimental data.

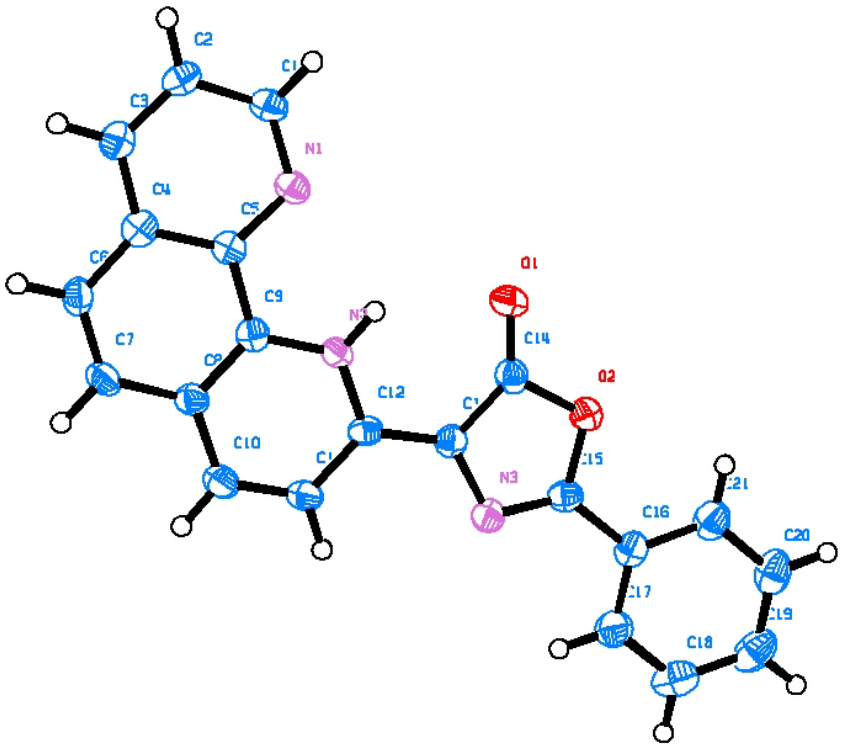
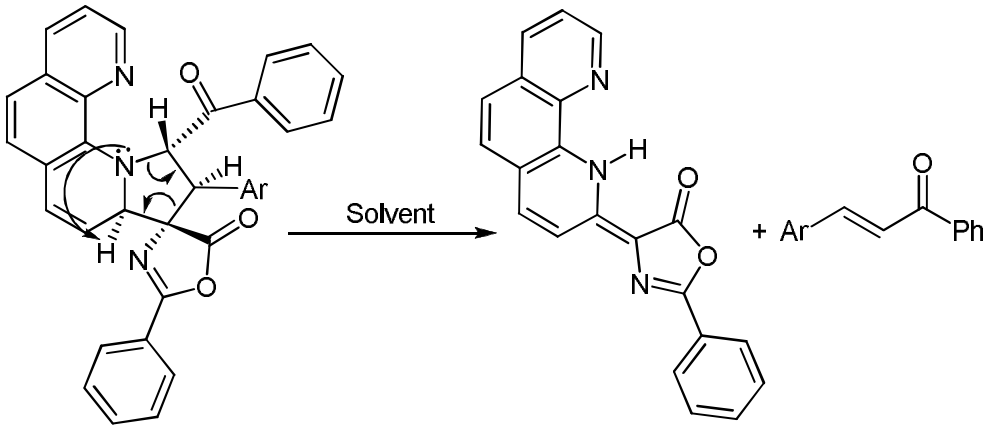


Figure 3. 11 X-ray diffraction ORTEP view of compound **93**



91 **93** **94**

Scheme 3. 5 Proposed mechanism for the formation of **93**

However, we could not detect the compound **94**, further detailed investigation is needed to make a clear comment on this.

CONCLUSION

In this work, we have demonstrated the synthesis of 15 novel aryl substituted spiro oxazolo [1,10] phenanthrolines including four chiral centers from phenanthrolinium ylides and (*Z*)-substituted arylidene oxazolones which some of them are novel compounds. The structures and stereochemical configurations of cycloadducts were identified by means of IR, NMR, 2D NMR, MASS, single crystal X-Ray Diffraction spectra.

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APPENDICES

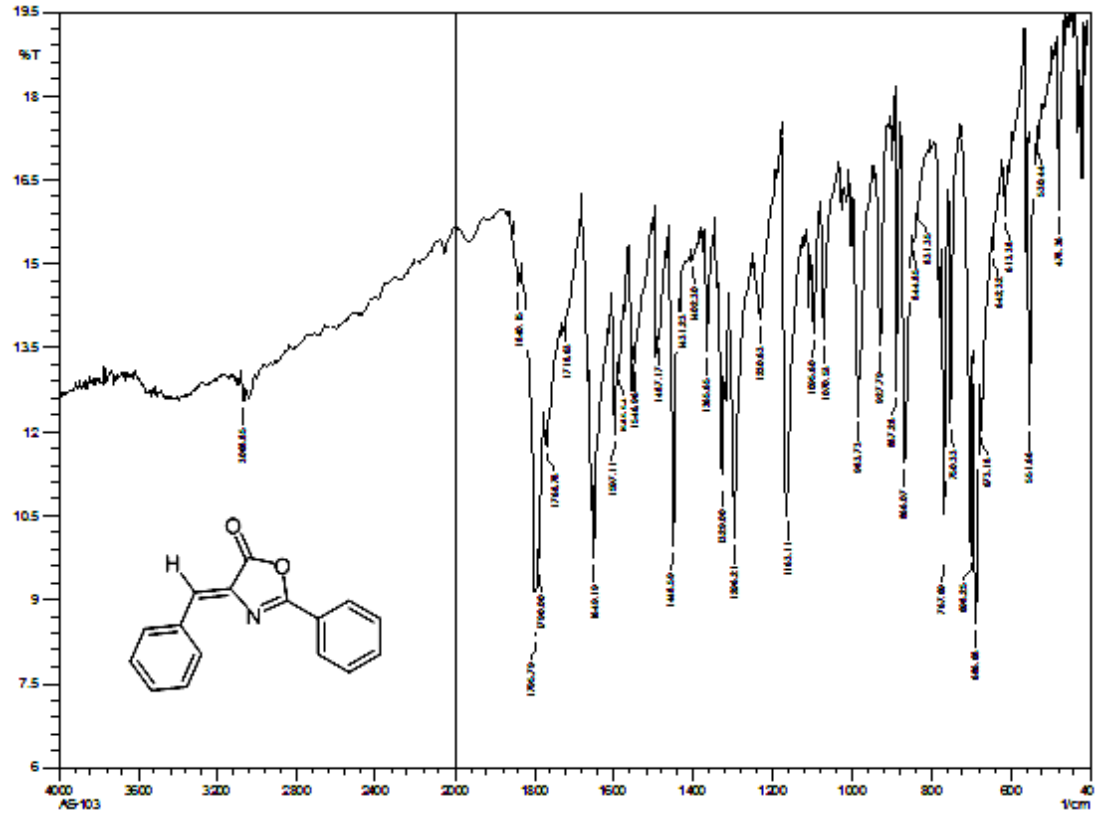

Figure 4. 1 IR Spectrum of **70a**

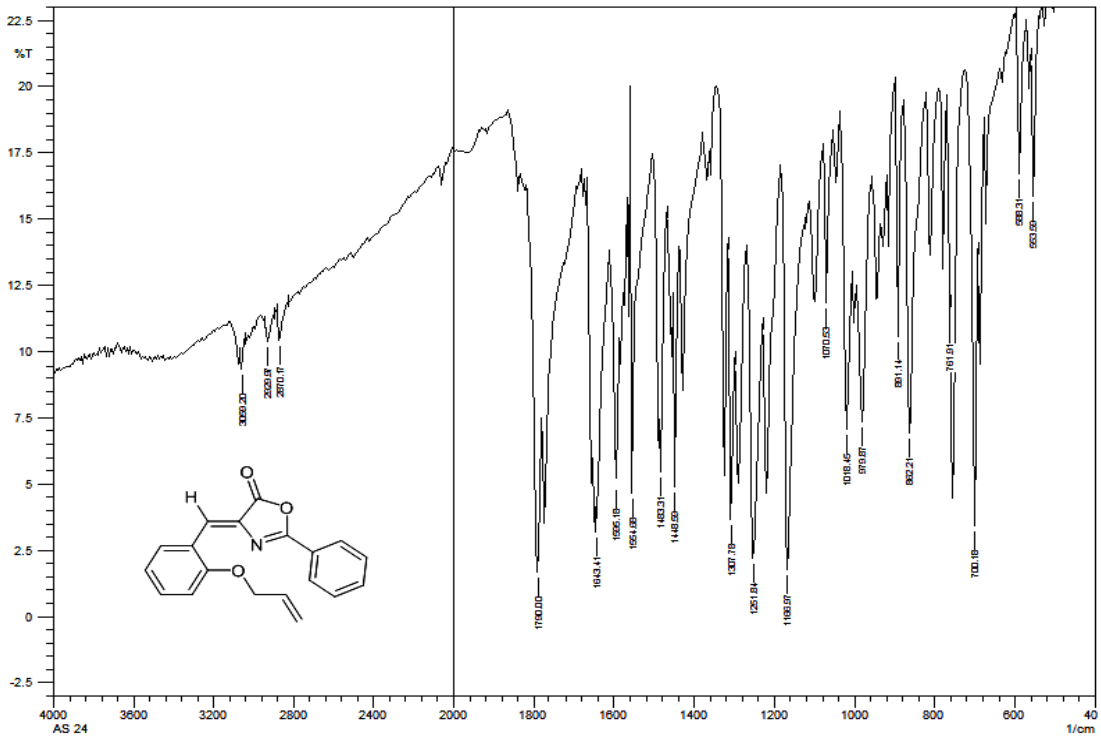

Figure 4. 2 IR Spectrum of **70b**

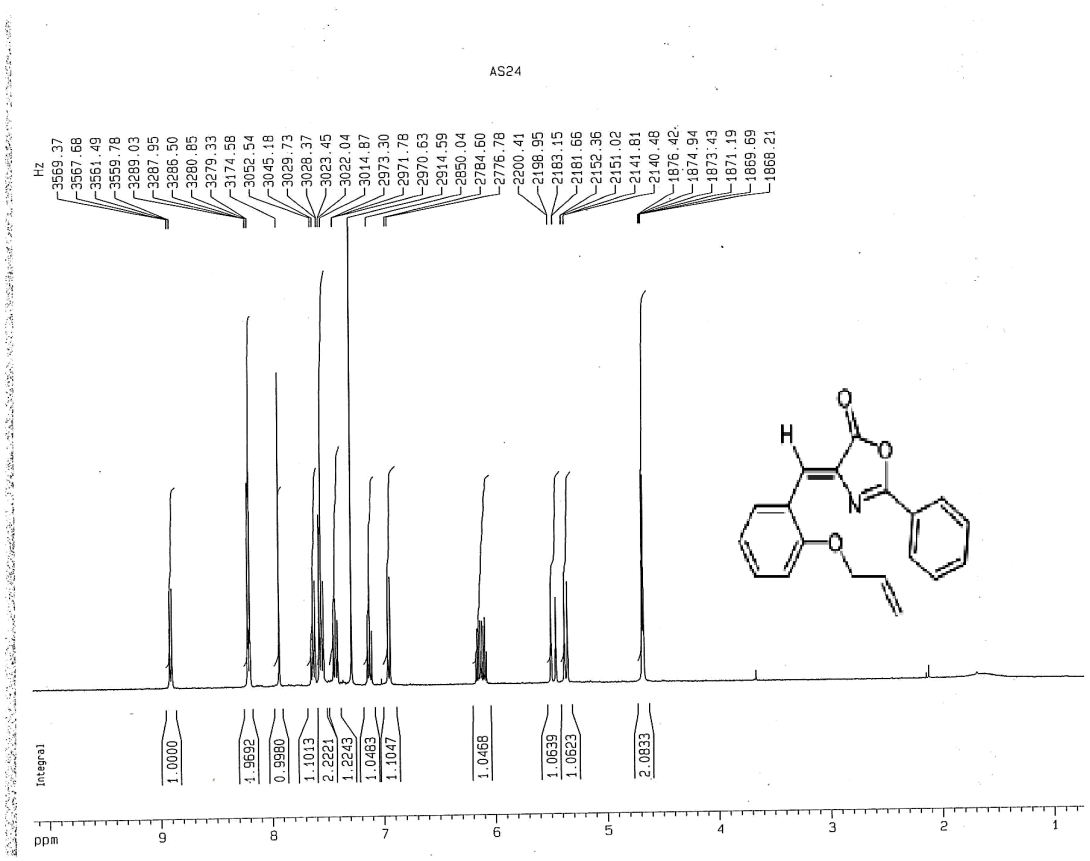

Figure 4. 3 ^{1}H NMR Spectrum of **70b**

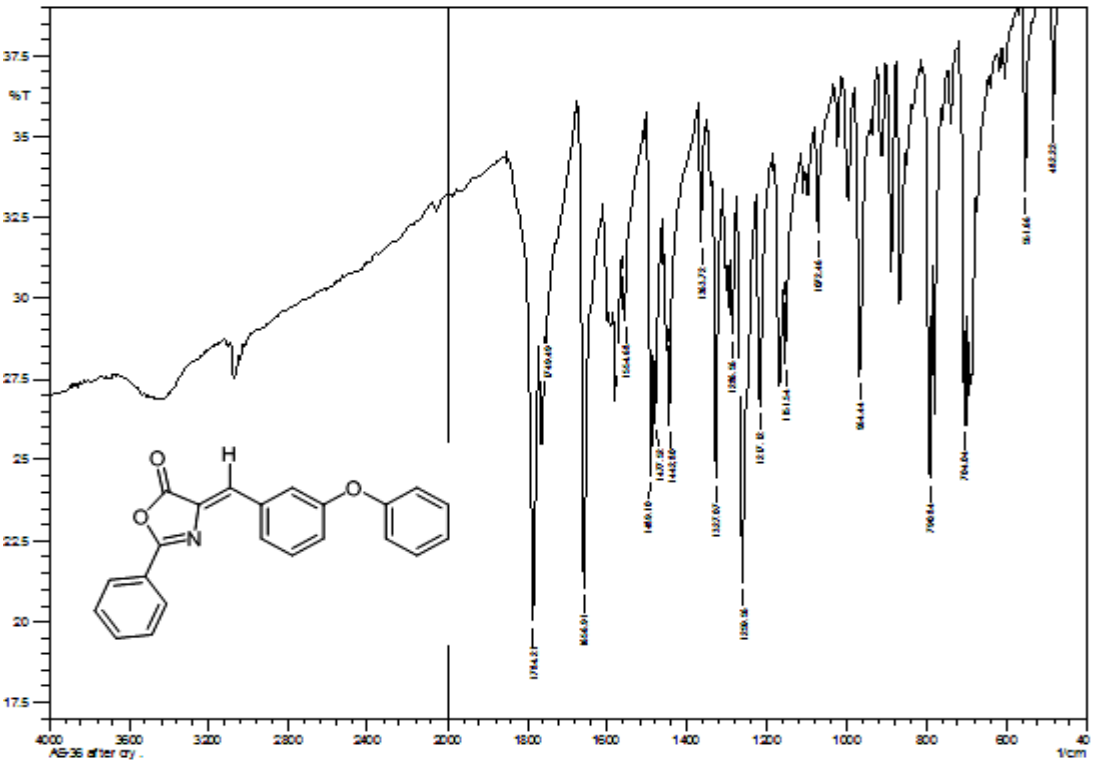

Figure 4. 4 IR Spectrum of **70c**

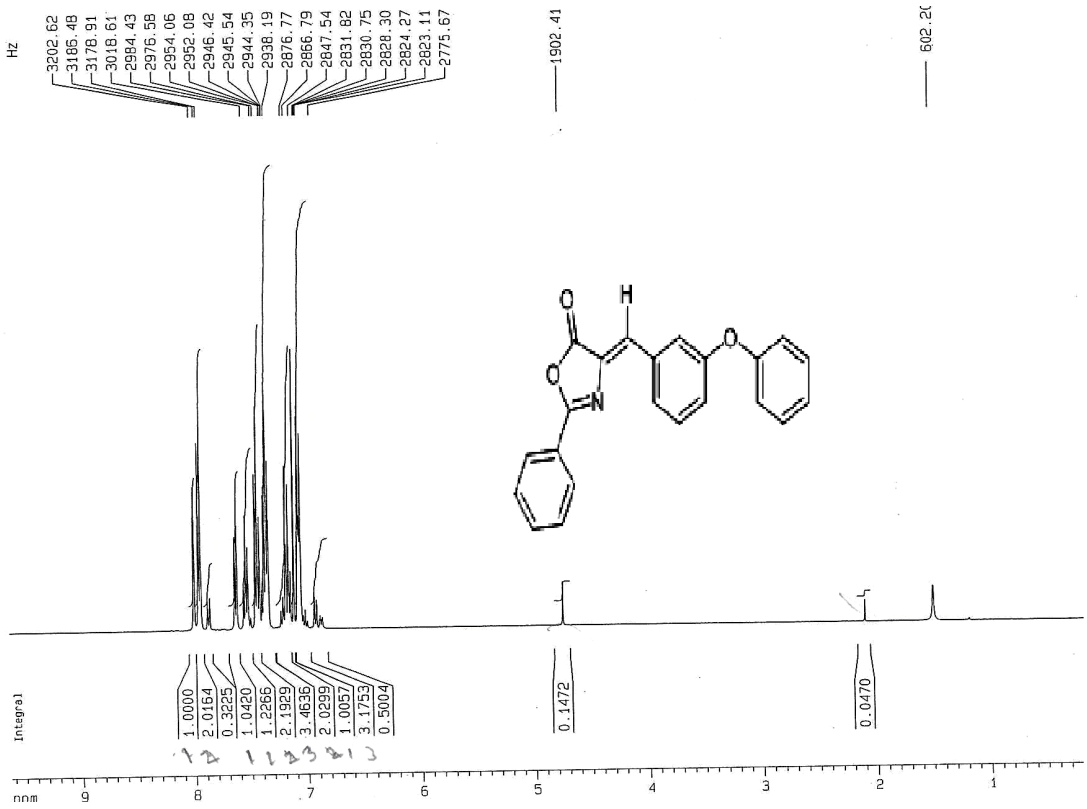

Figure 4. 5 ^{1}H NMR Spectrum of **70c**

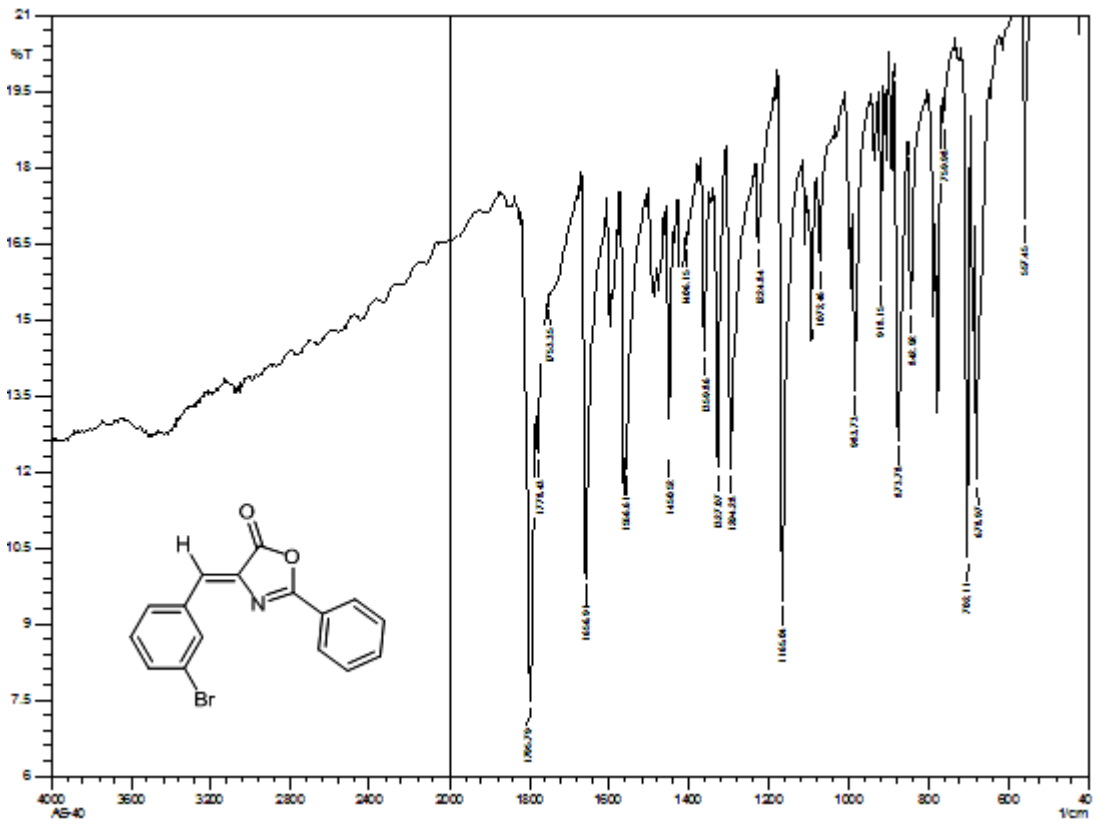

Figure 4. 6 IR Spectrum of **70d**

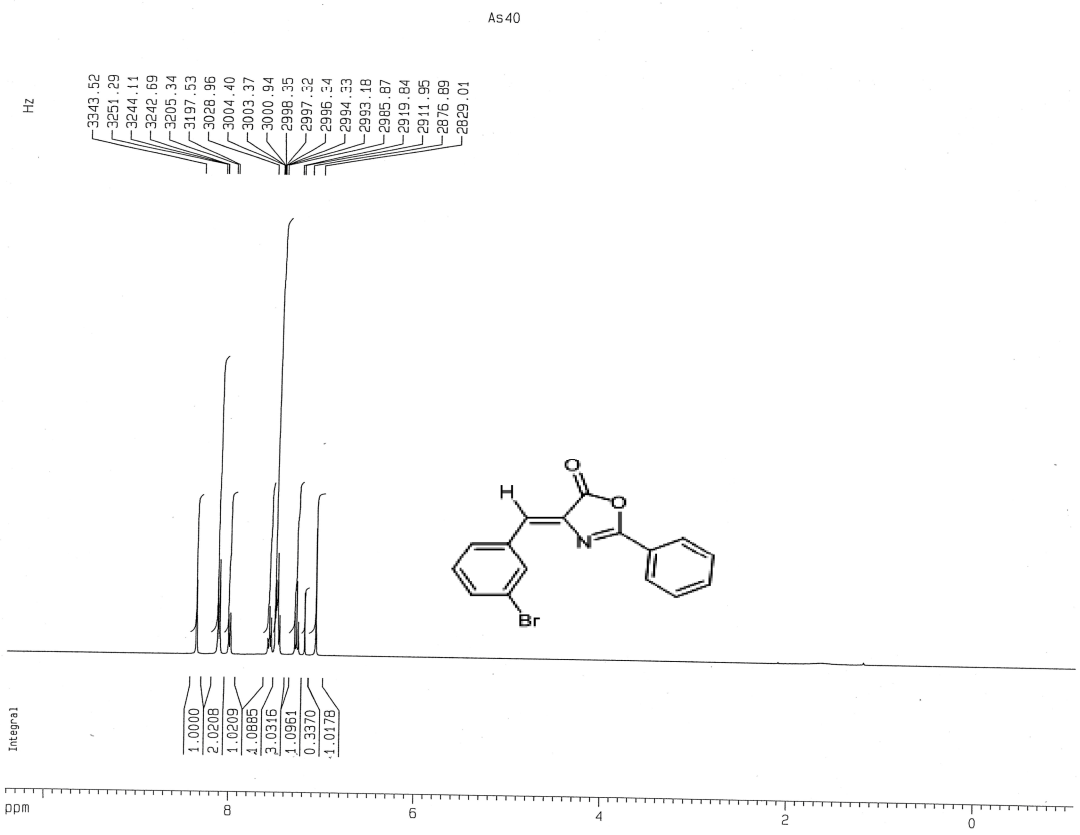

Figure 4. 7 ^{1}H NMR Spectrum of **70d**

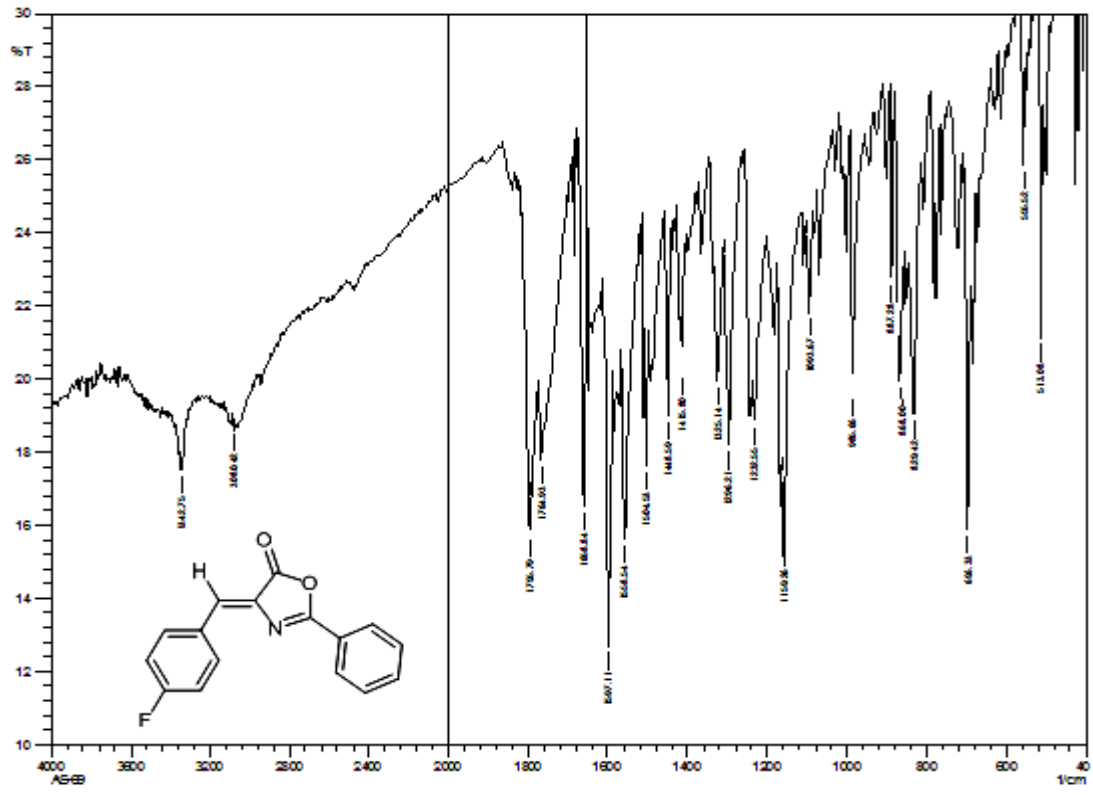

Figure 4. 8 IR Spectrum of **70e**

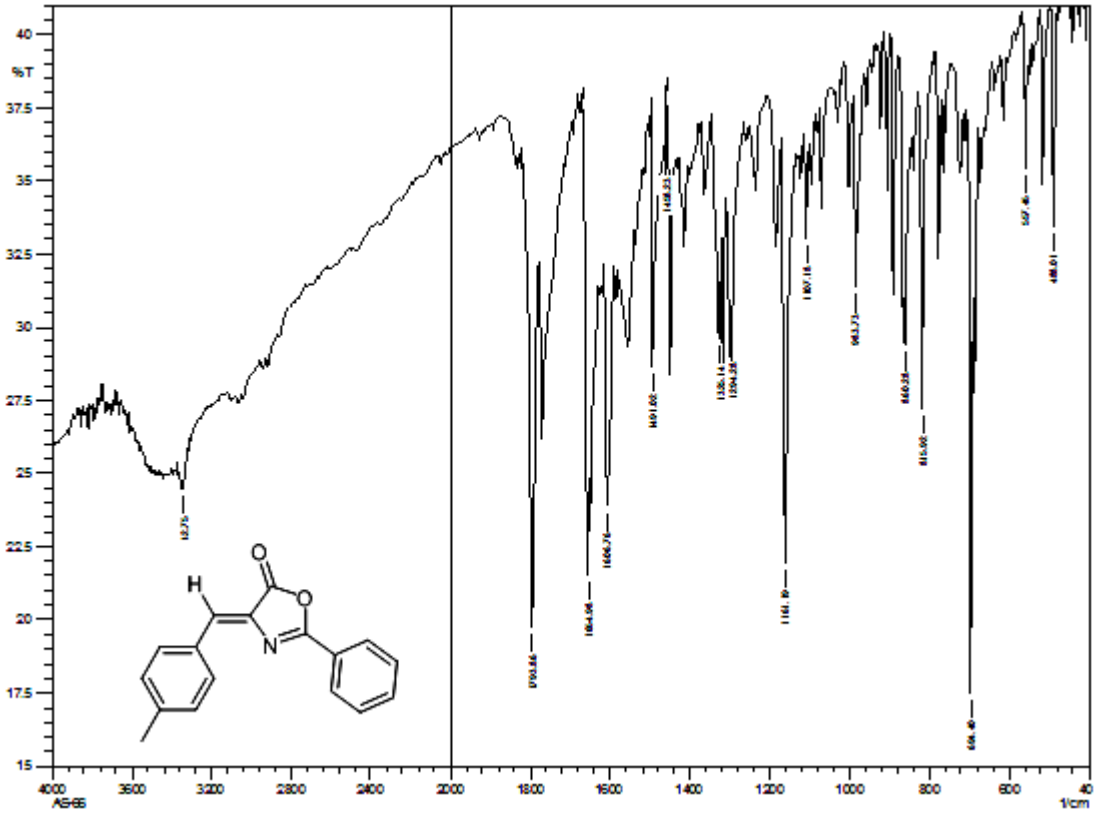

Figure 4. 9 IR Spectrum of **70f**

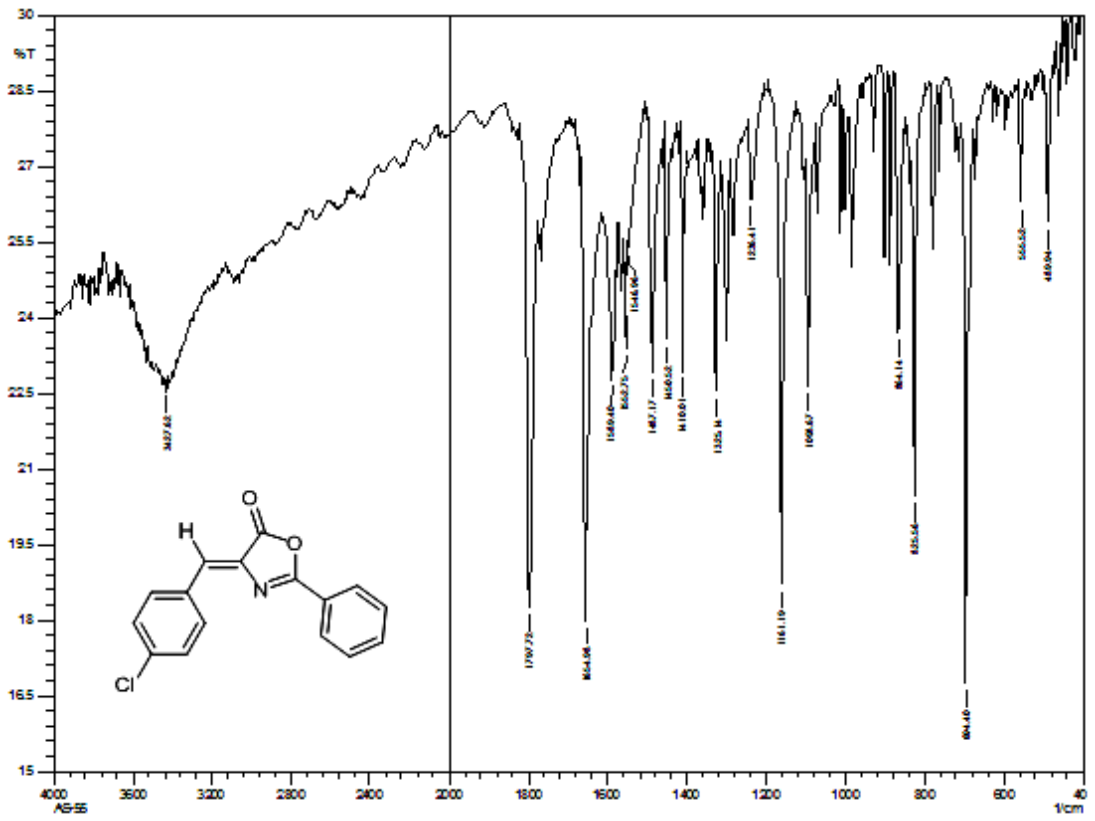

Figure 4. 10 IR Spectrum of **70g**

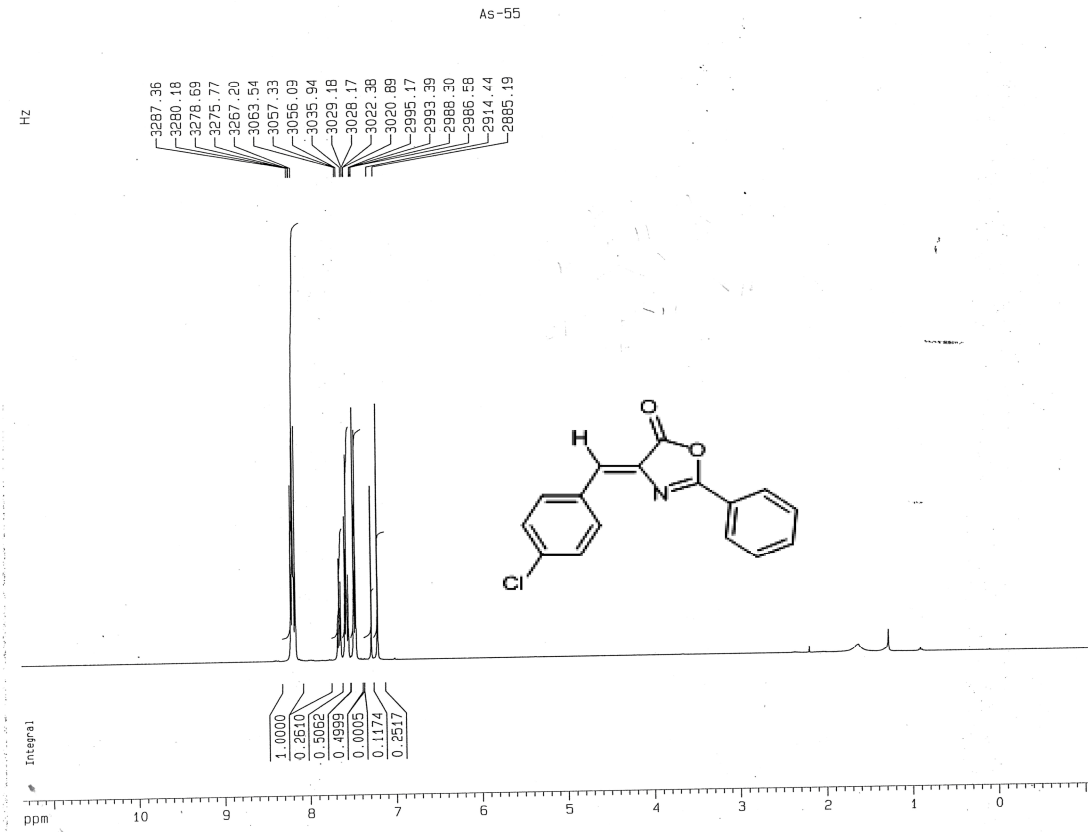

Figure 4. 11 ^{1}H NMR Spectrum of **70g**

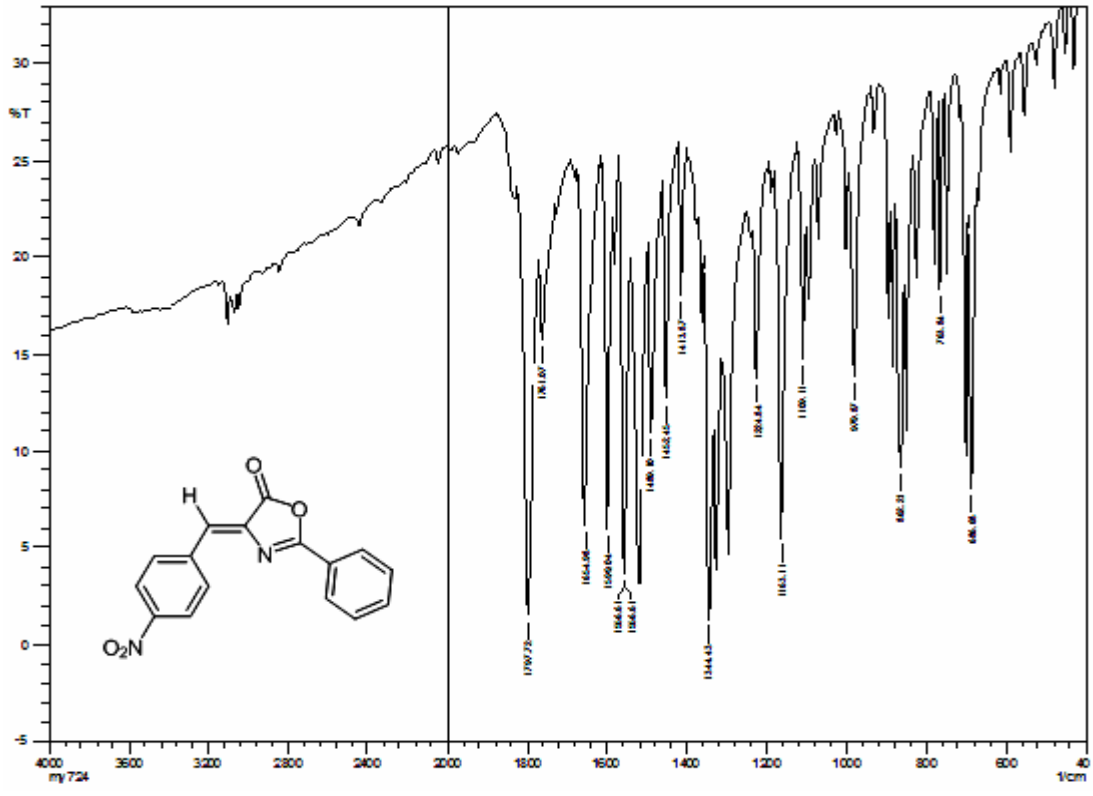

Figure 4. 12 IR Spectrum of **70h**

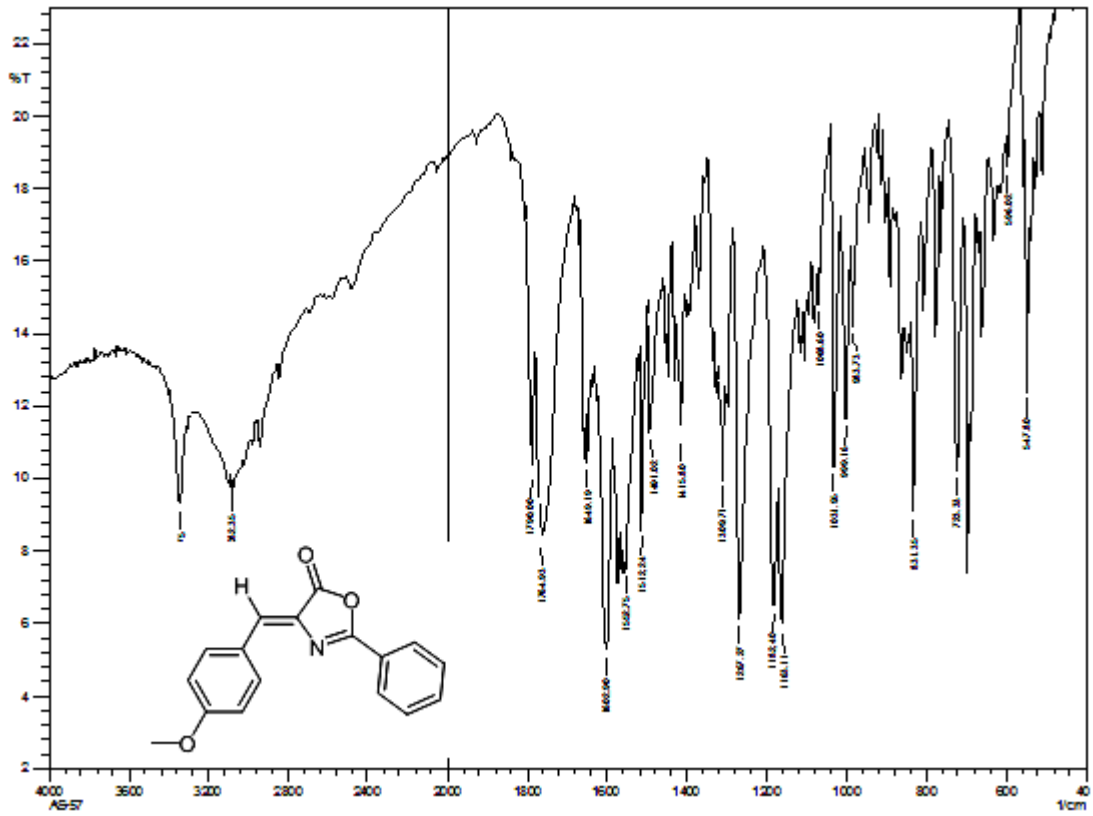

Figure 4. 13 IR Spectrum of **70j**

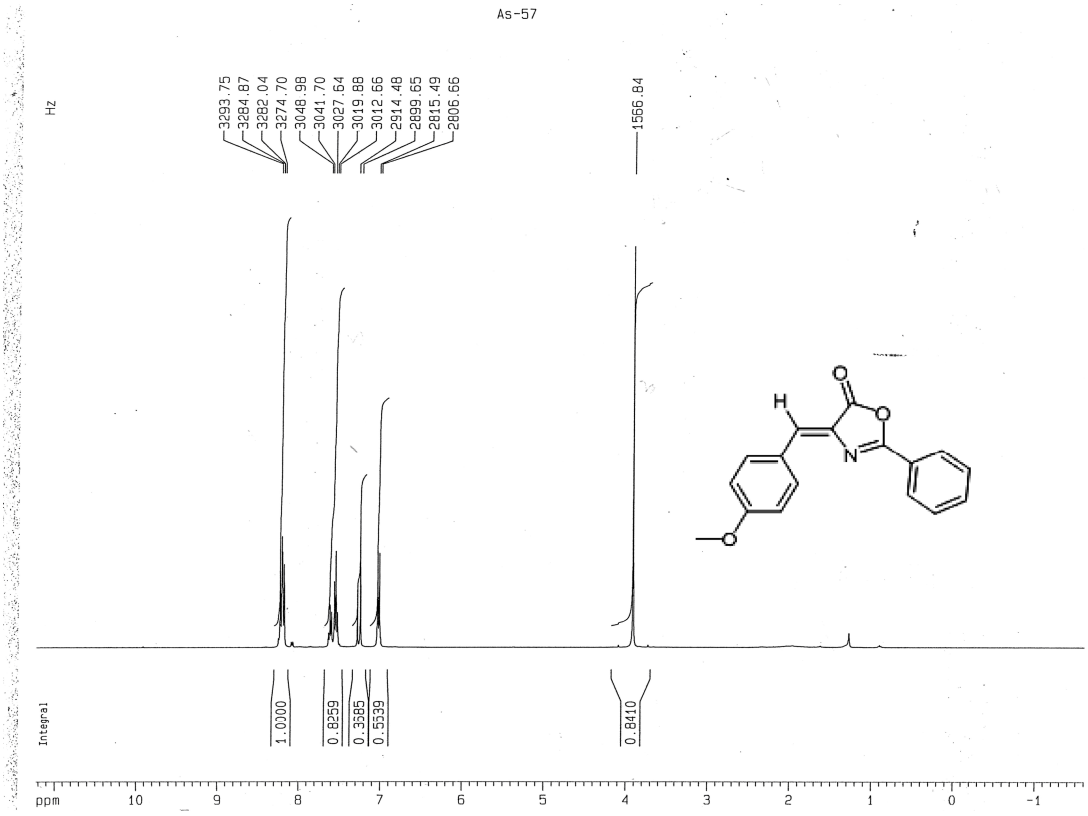

Figure 4. 14 ^{1}H NMR Spectrum of **70j**

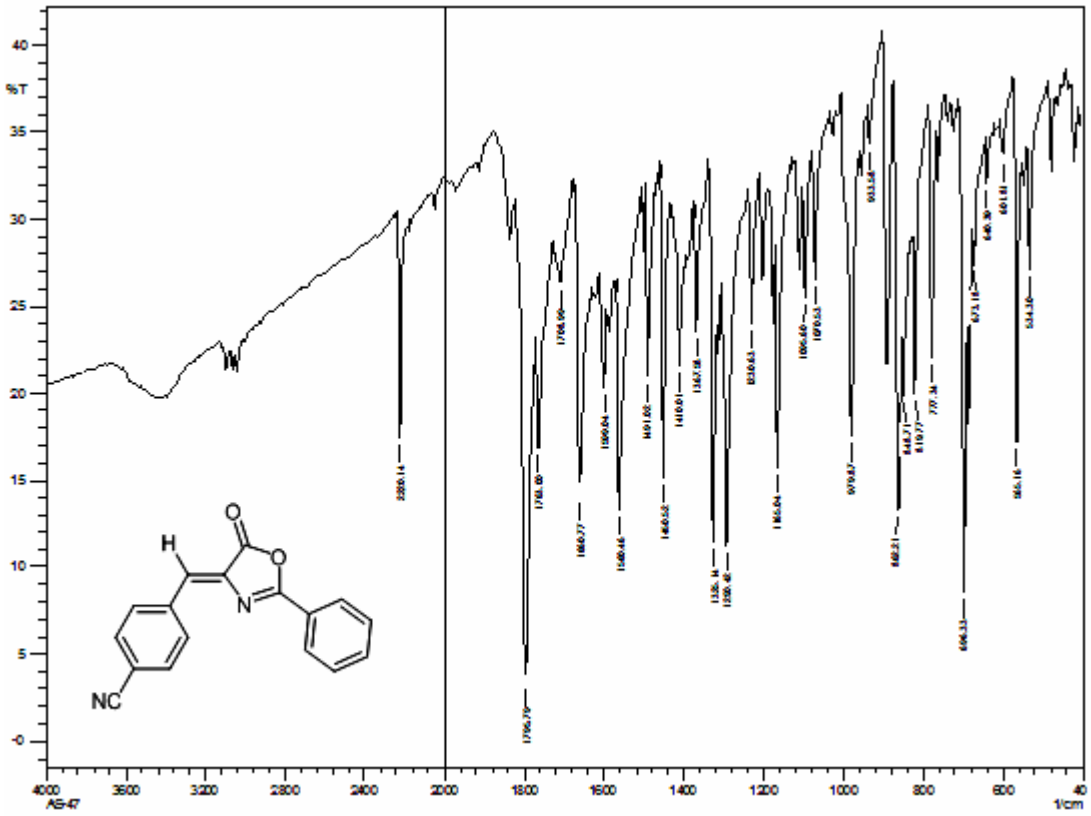

Figure 4. 15 IR Spectrum of **70k**

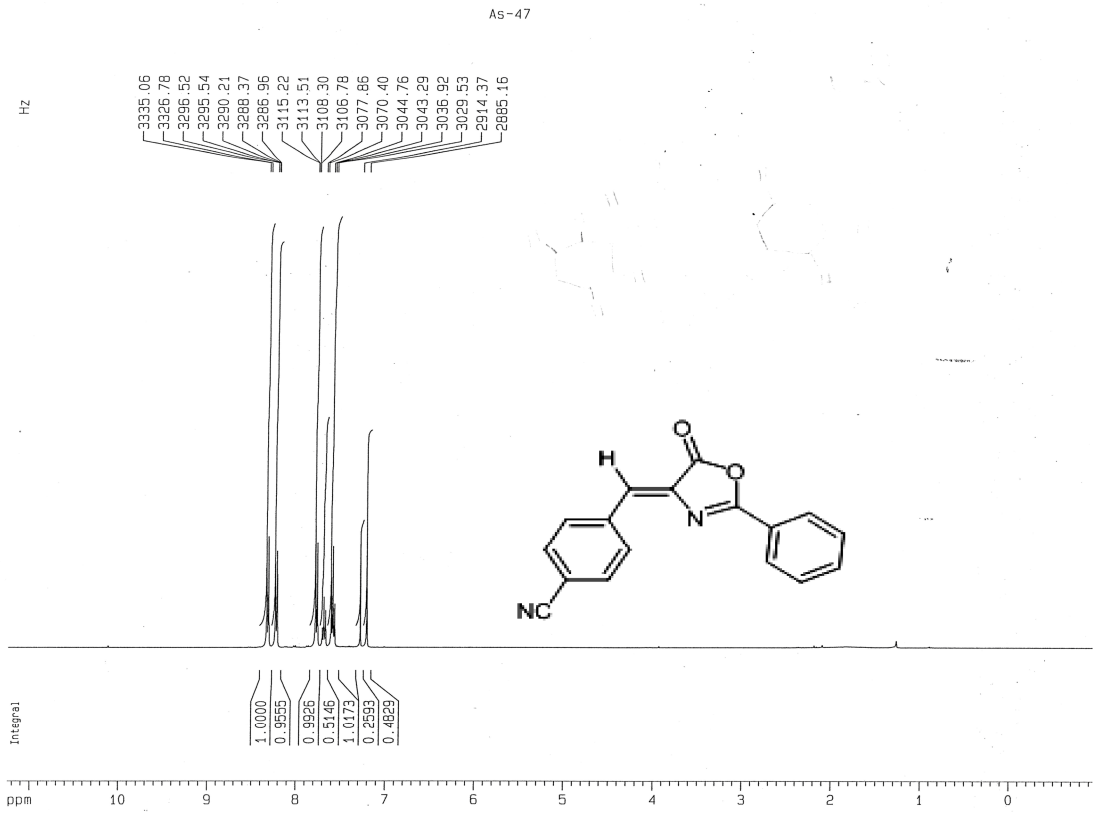

Figure 4. 16 ^{1}H NMR Spectrum of **70k**

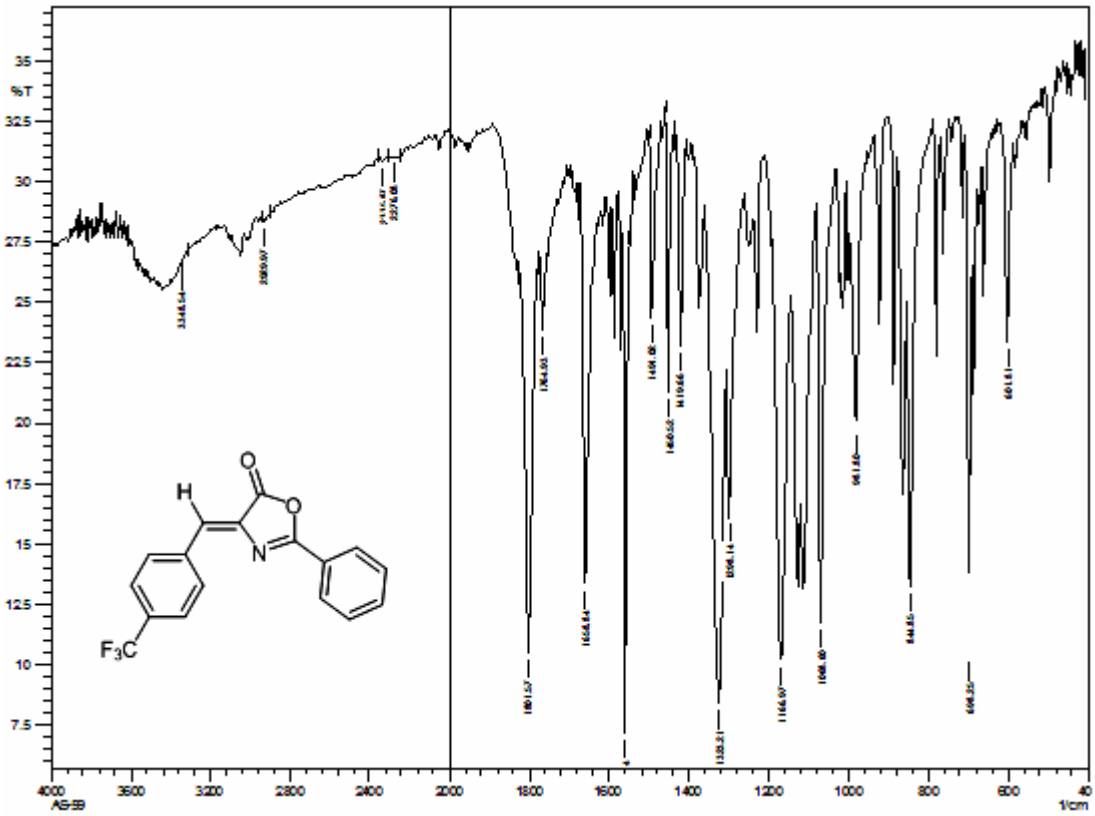

Figure 4. 17 IR Spectrum of **70l**

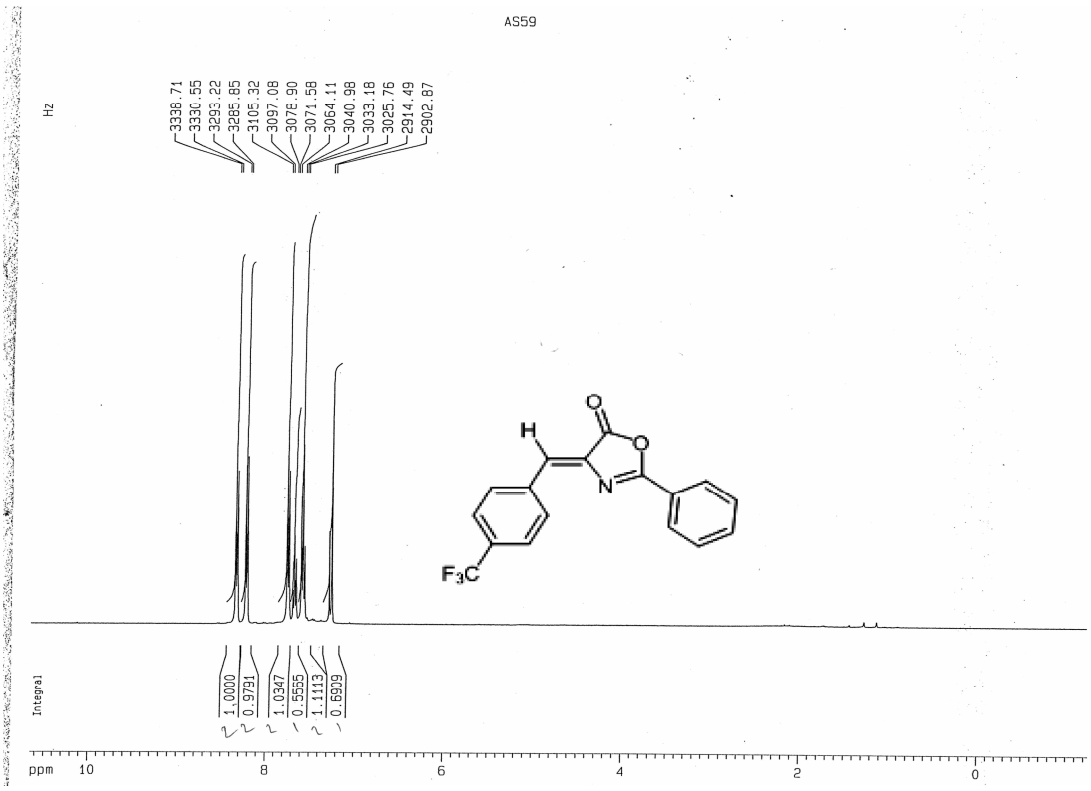

Figure 4. 18 ^{1}H NMR Spectrum of **70l**

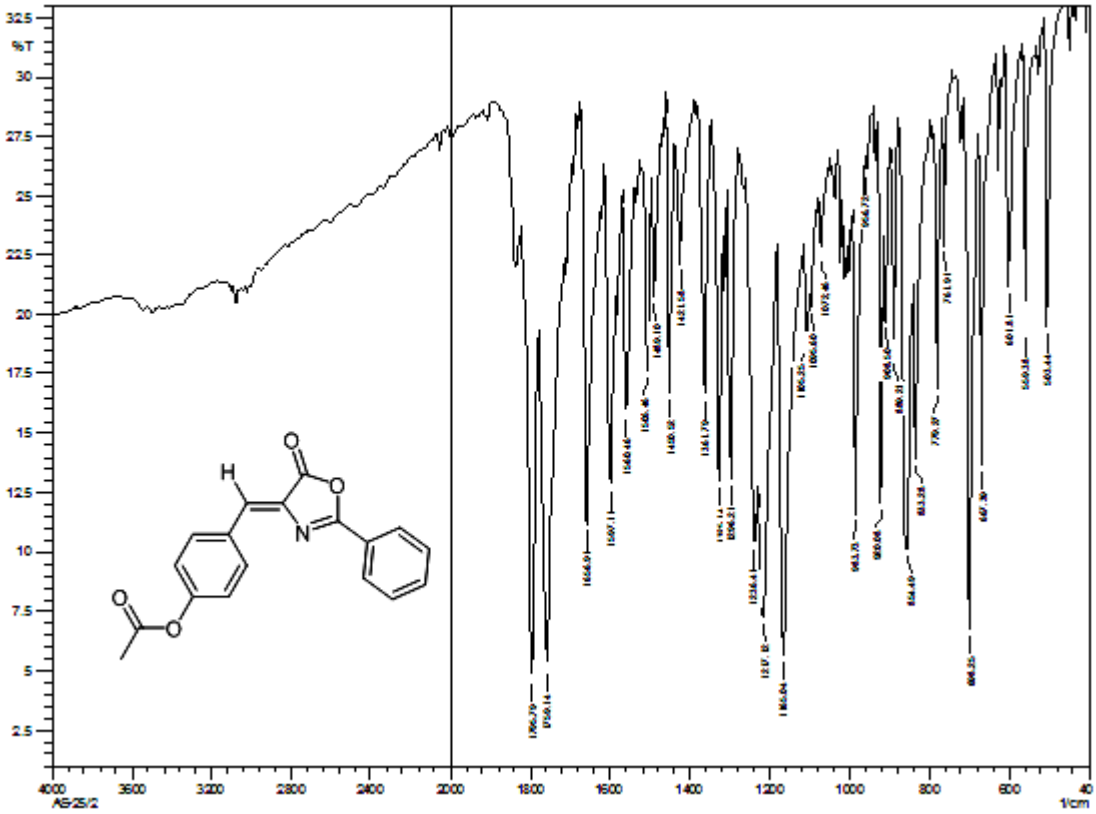

Figure 4. 19 IR Spectrum of **70m**

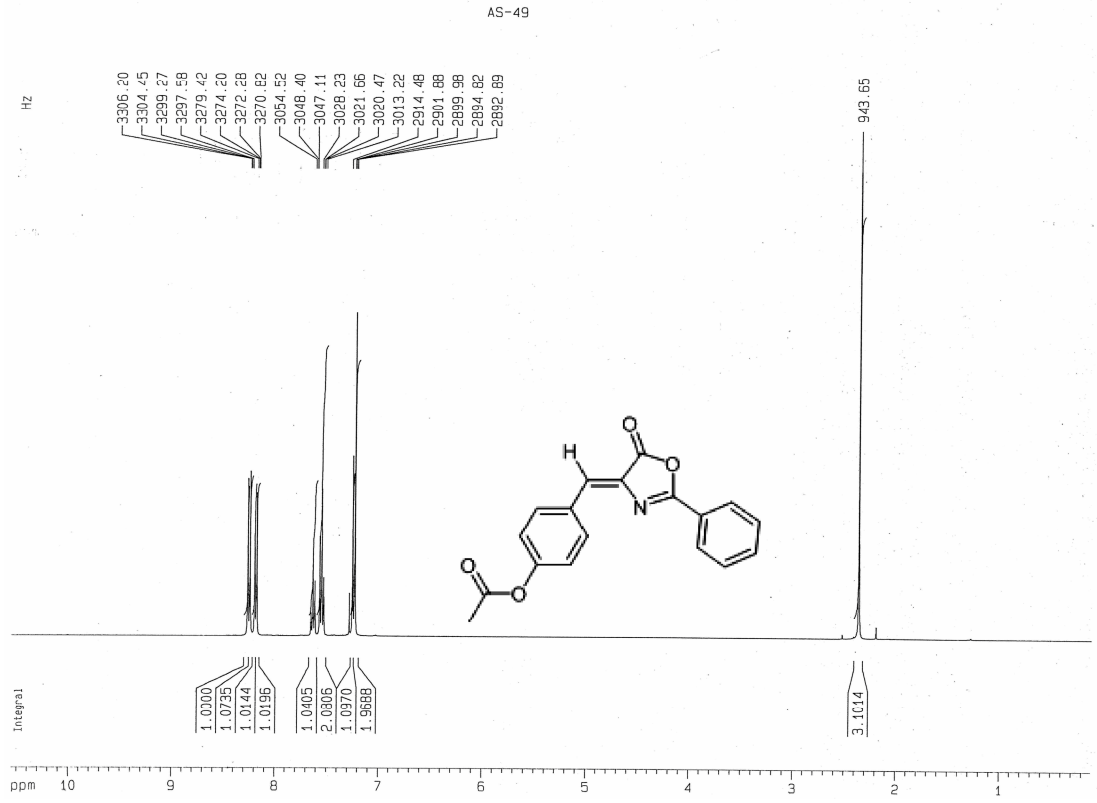

Figure 4. 20 ^{1}H NMR Spectrum of **70m**

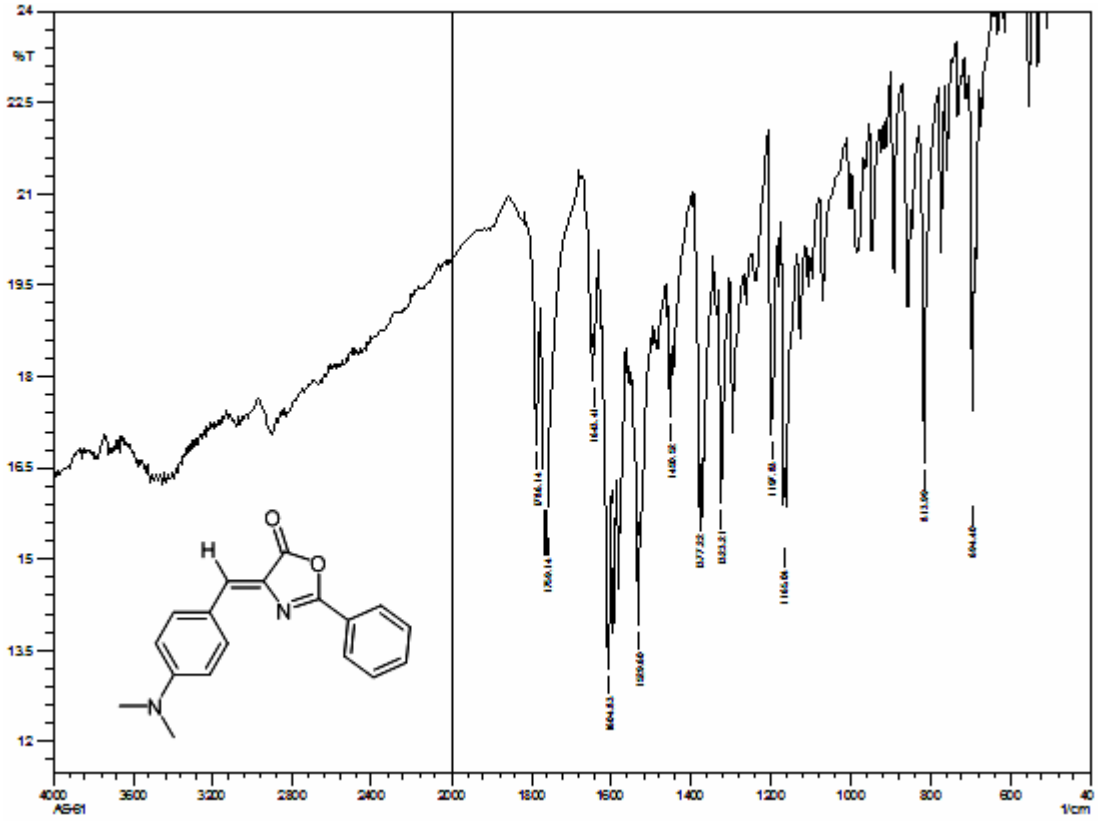

Figure 4. 21 IR Spectrum of **70n**

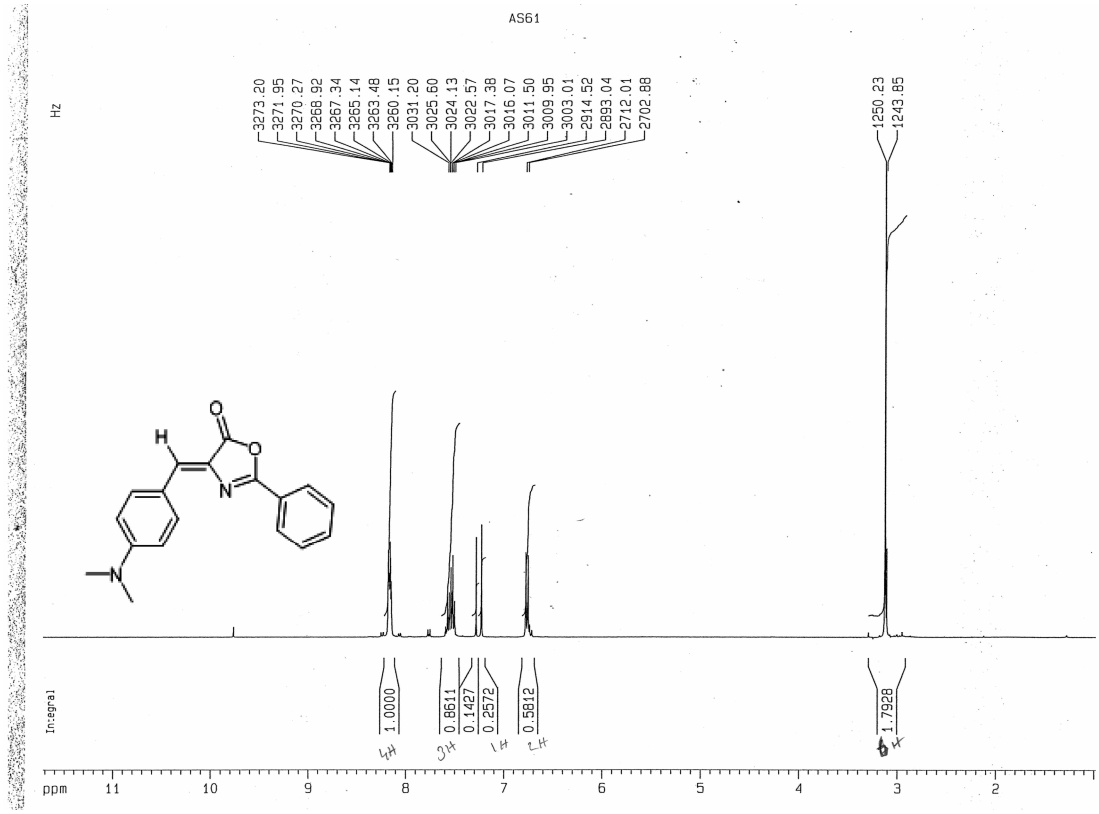

Figure 4. 22 ^{1}H NMR Spectrum of **70n**

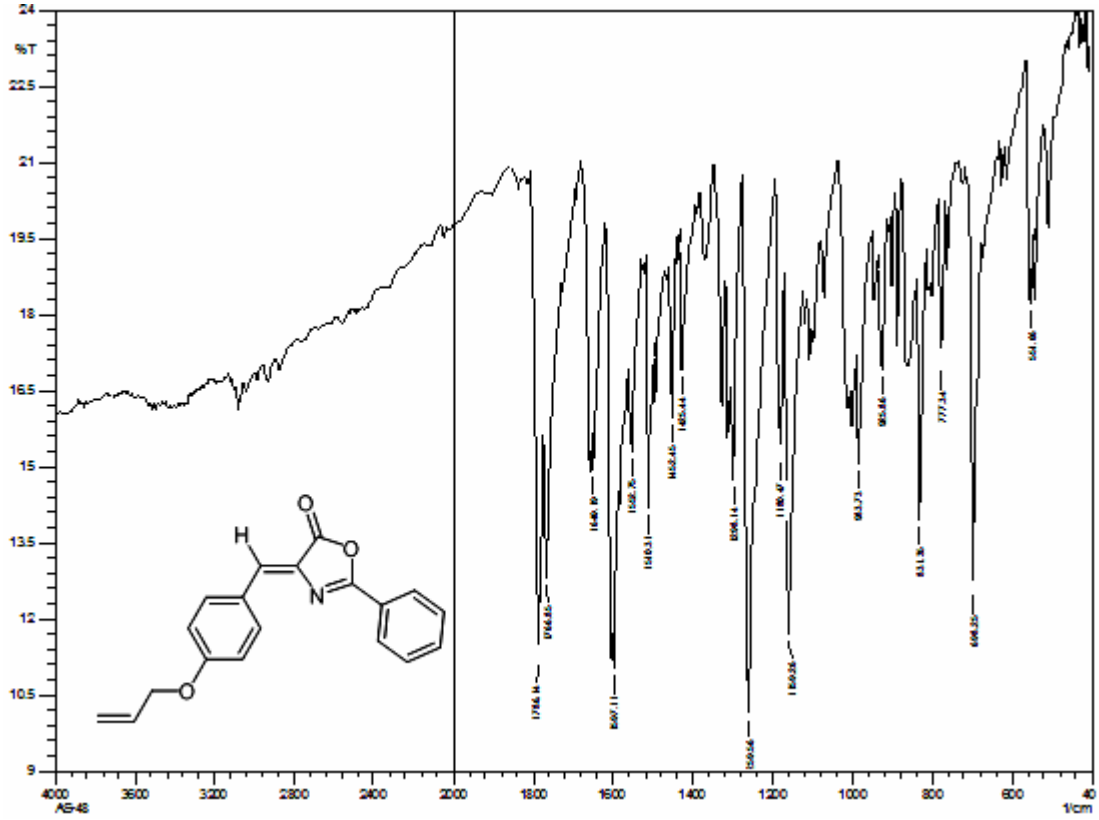

Figure 4. 23 IR Spectrum of **70p**

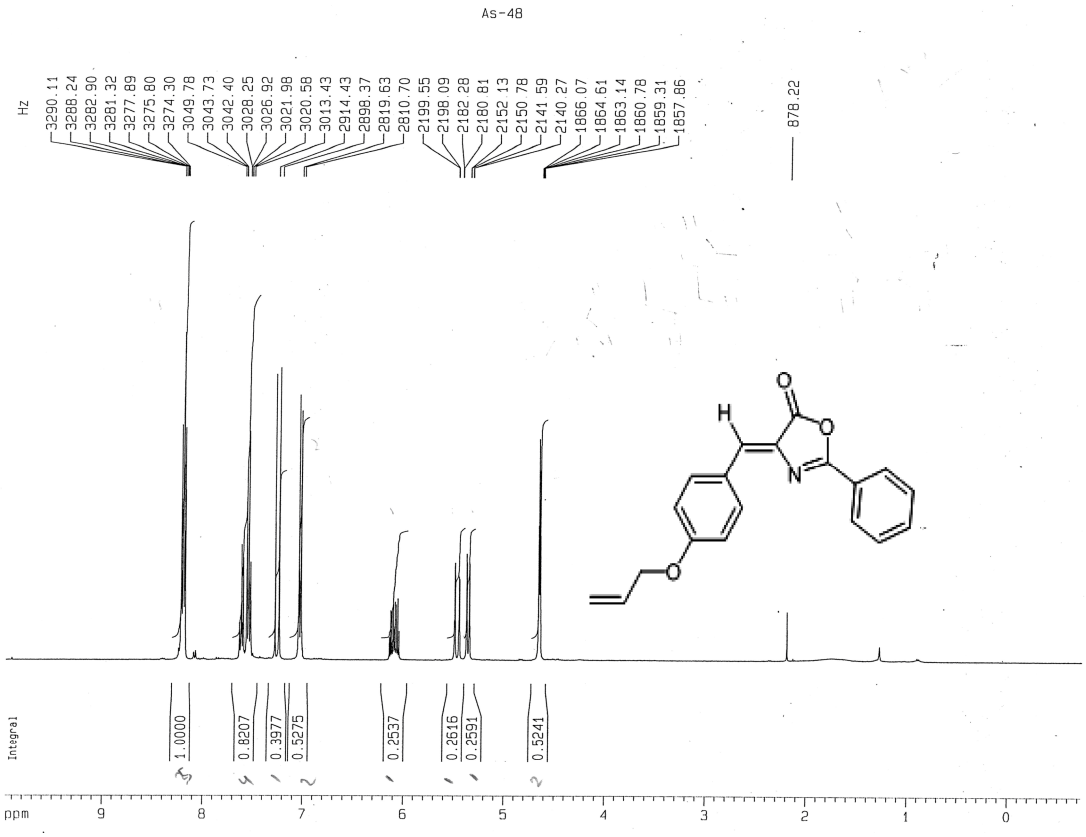

Figure 4. 24 ^{1}H NMR Spectrum of **70p**

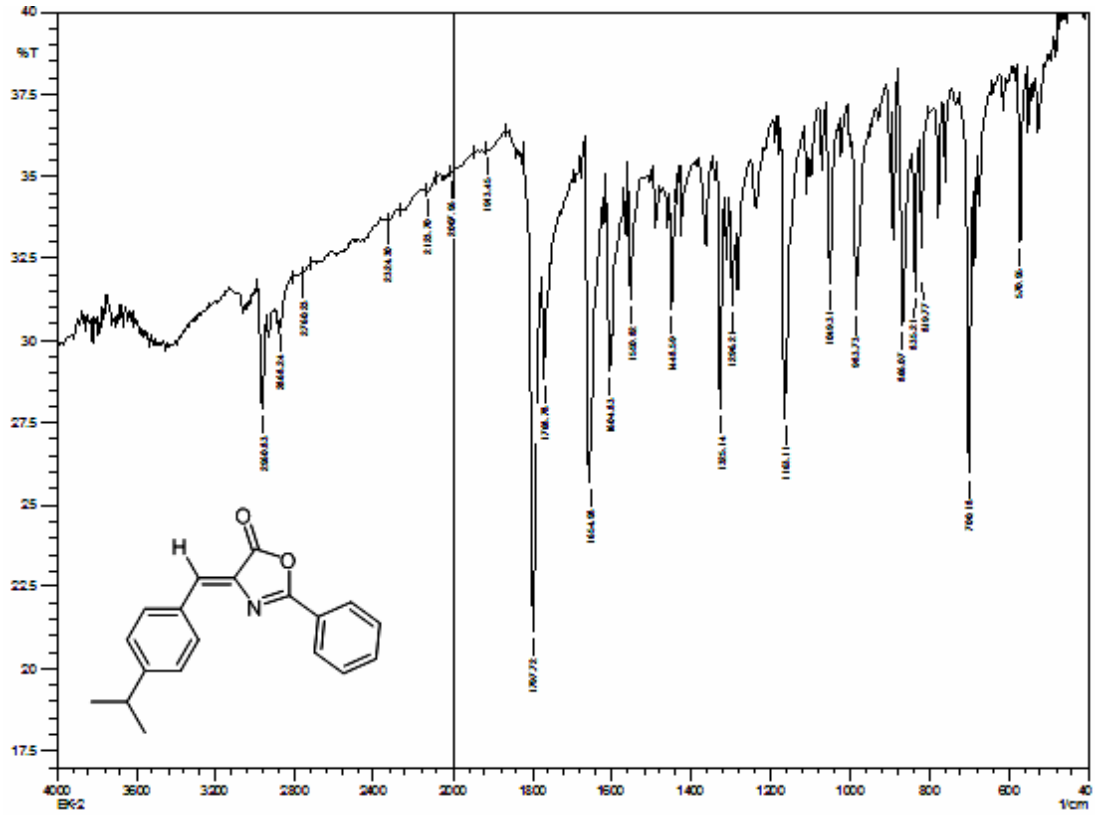

Figure 4. 25 IR Spectrum of **70r**

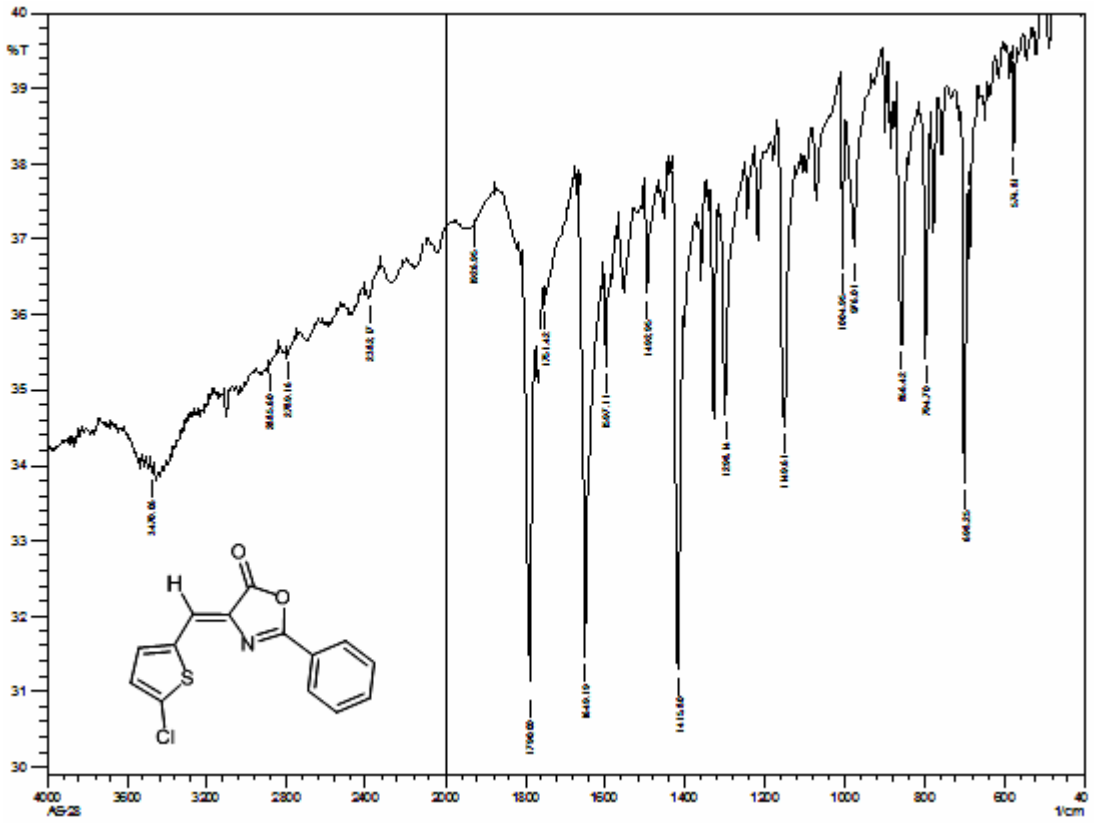

Figure 4. 26 IR Spectrum of **70s**

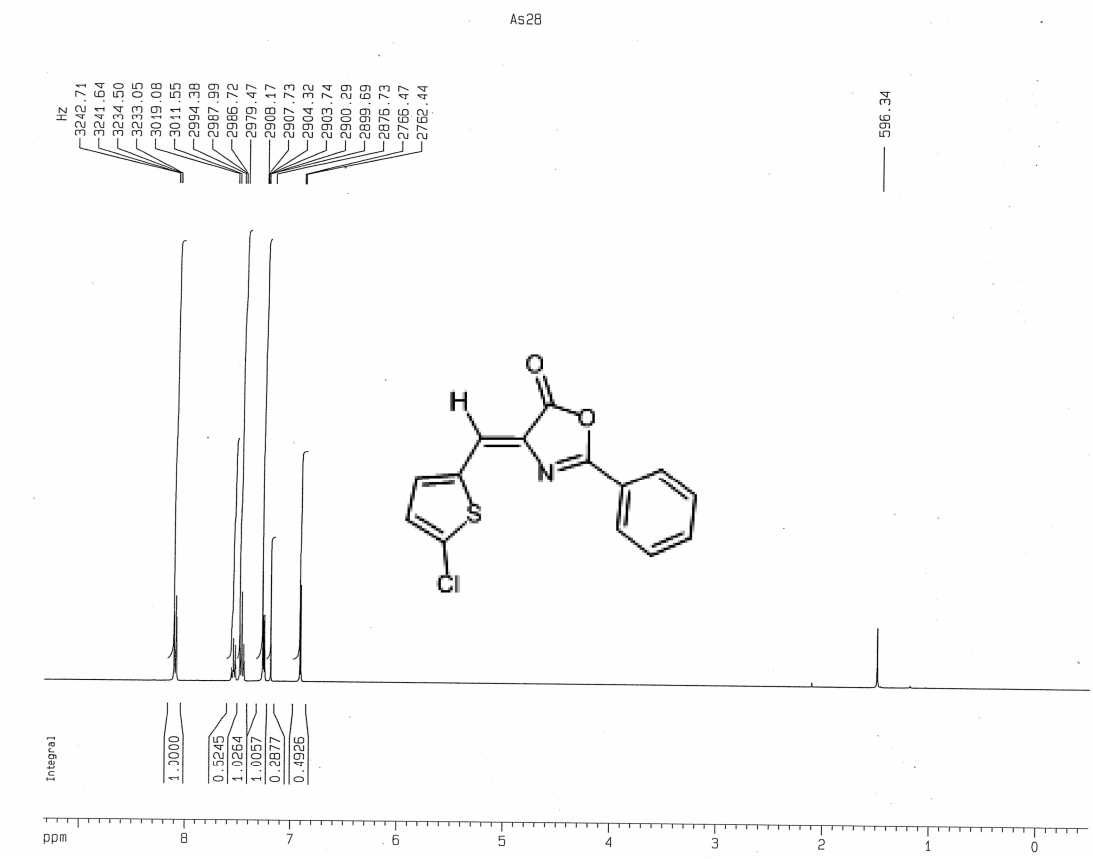

Figure 4. 27 ^{1}H NMR Spectrum of **70s**

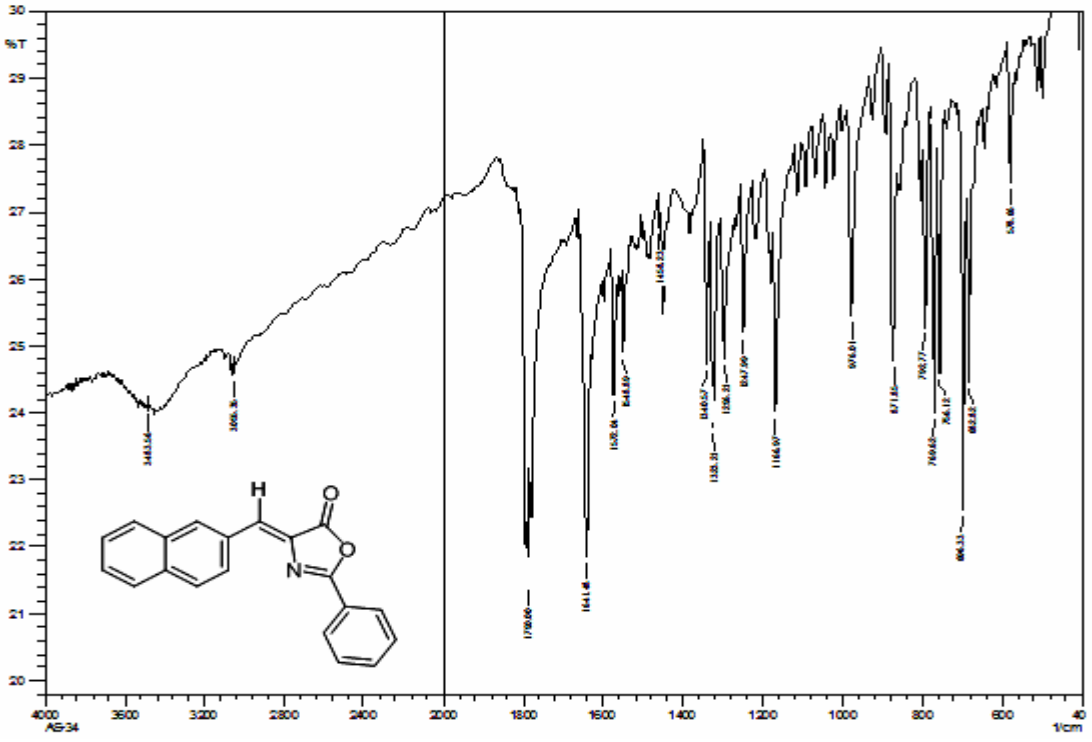

Figure 4. 28 IR Spectrum of **70t**

Figure 4. 29 ^{1}H NMR Spectrum of **70t**

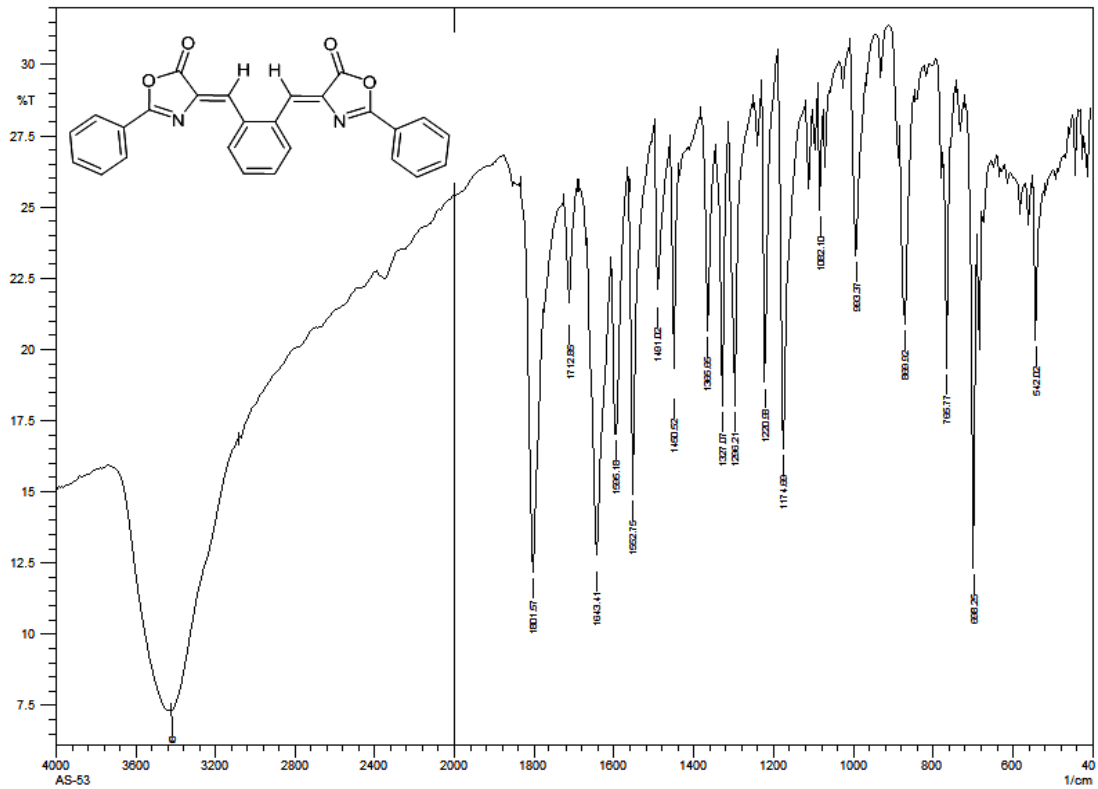

Figure 4. 30 IR Spectrum of **70u**

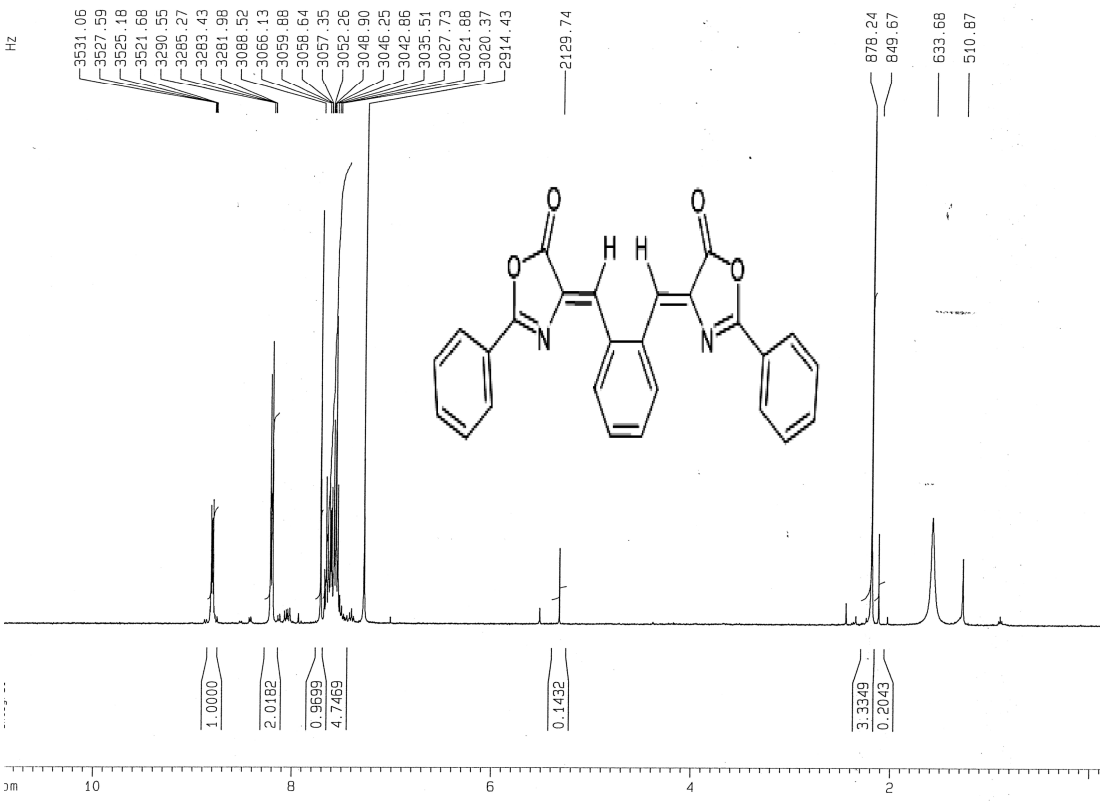

Figure 4. 31 ^{1}H NMR Spectrum of **70u**

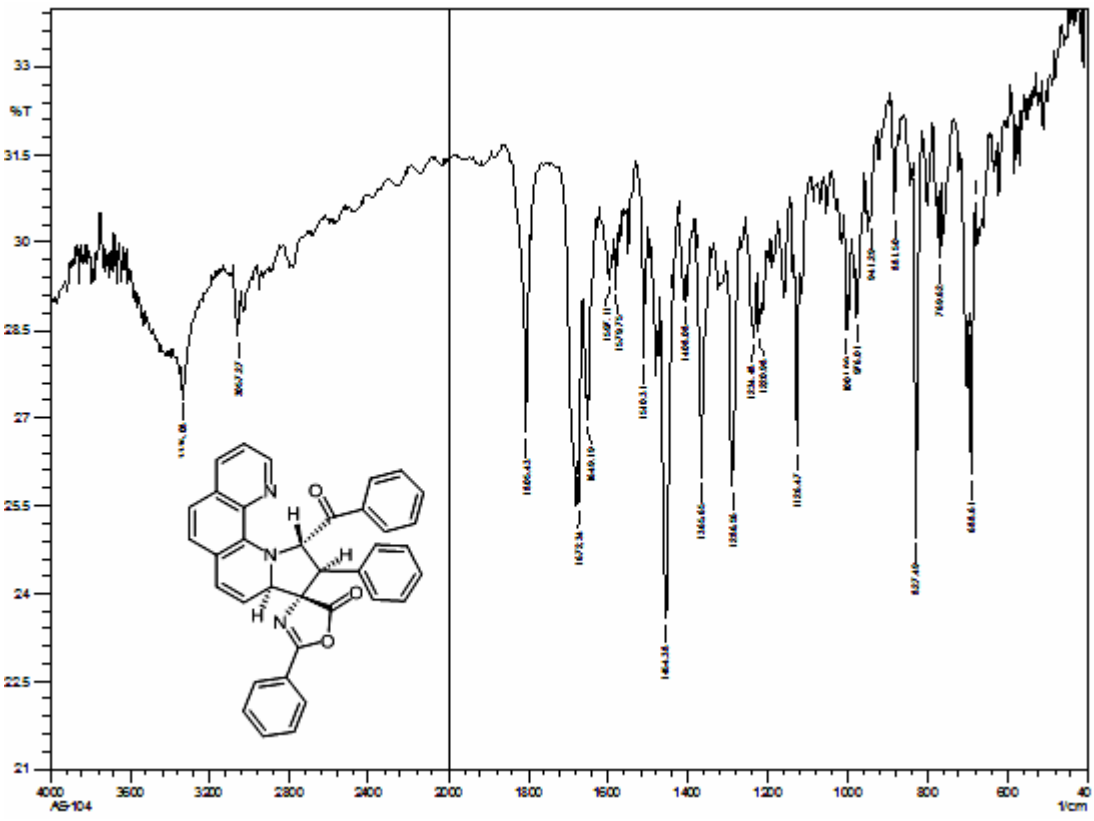

Figure 4. 32 IR Spectrum of **91a**

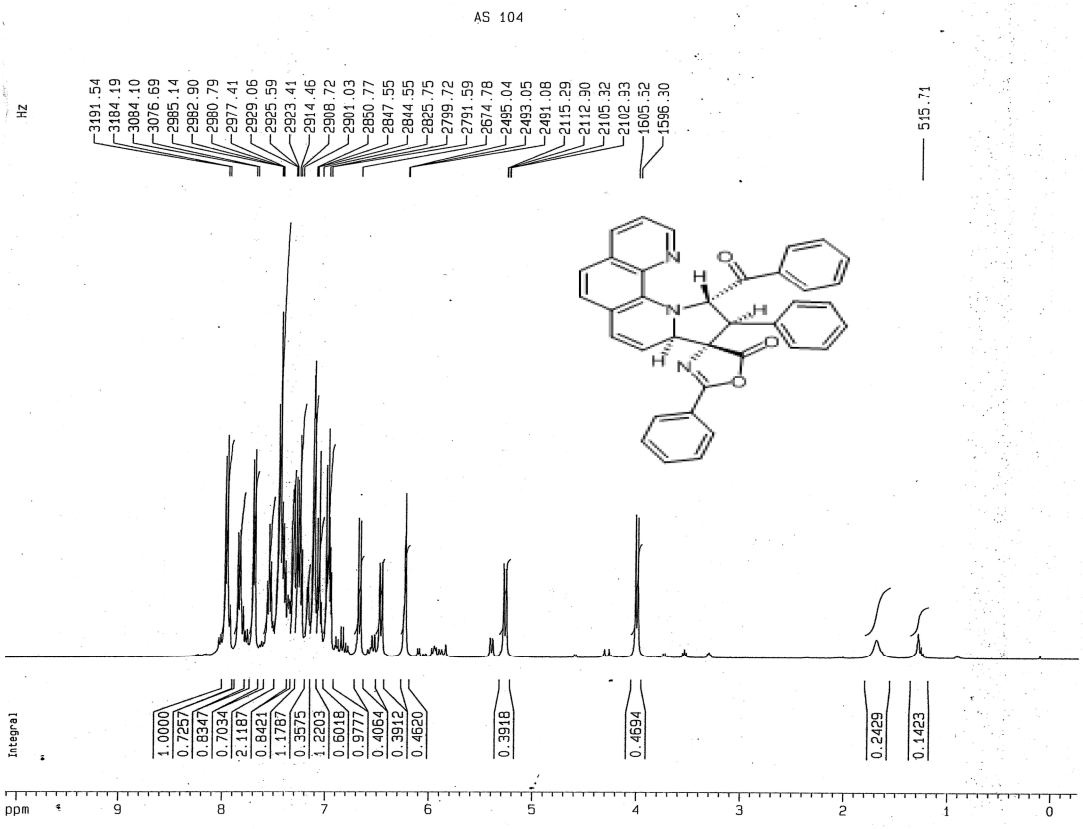

Figure 4. 33 ^{1}H NMR Spectrum of **91a**

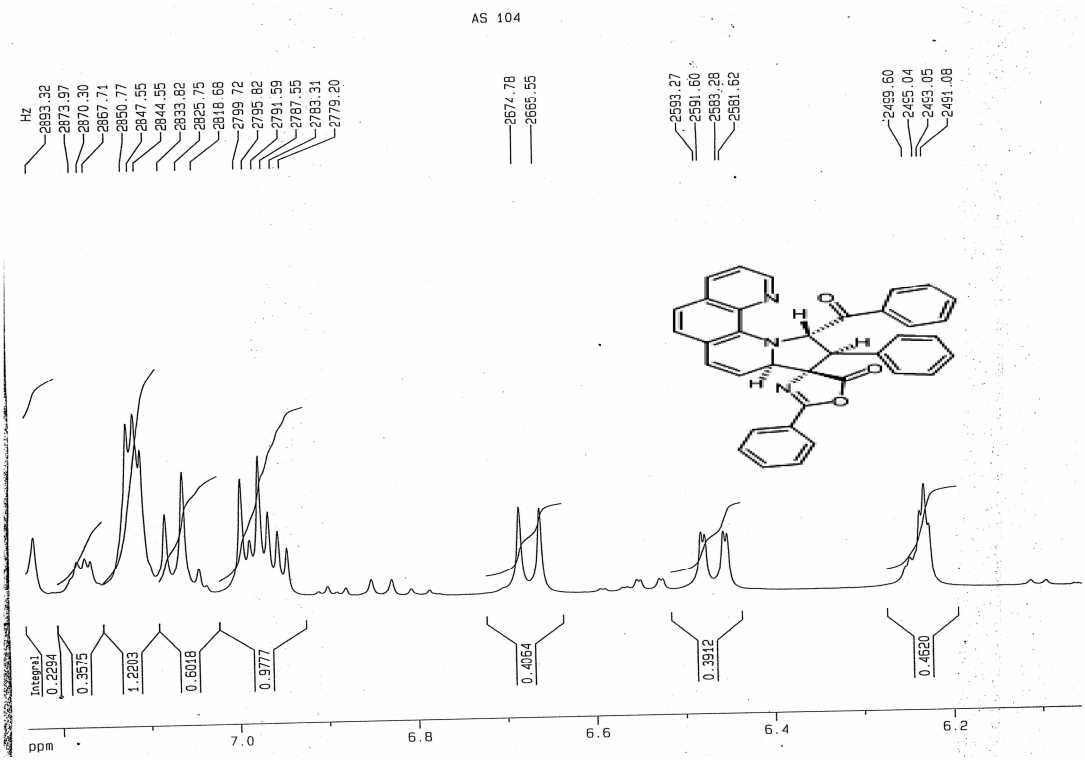

Figure 4. 34 Expanded (7.2-6.2 ppm) ^{1}H NMR Spectrum of **91a**

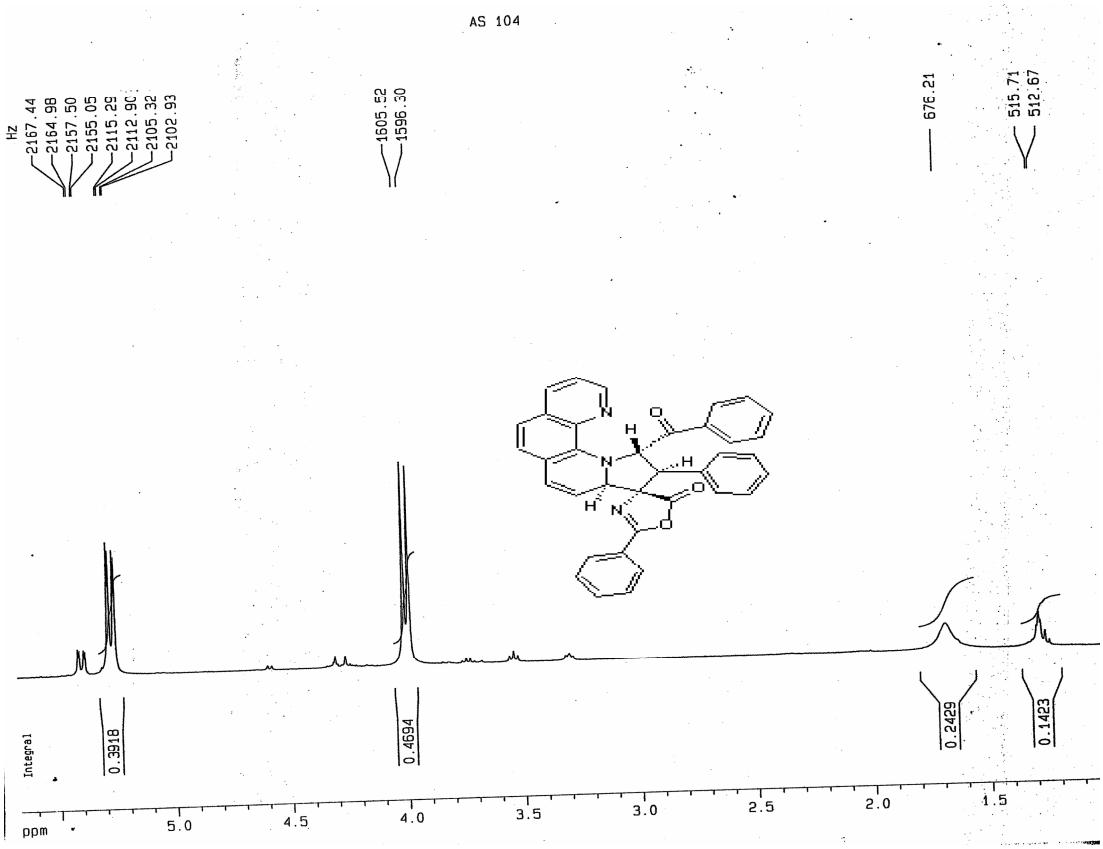

Figure 4. 35 Expanded (5.5-1.5 ppm) ^{1}H NMR Spectrum of **91a**

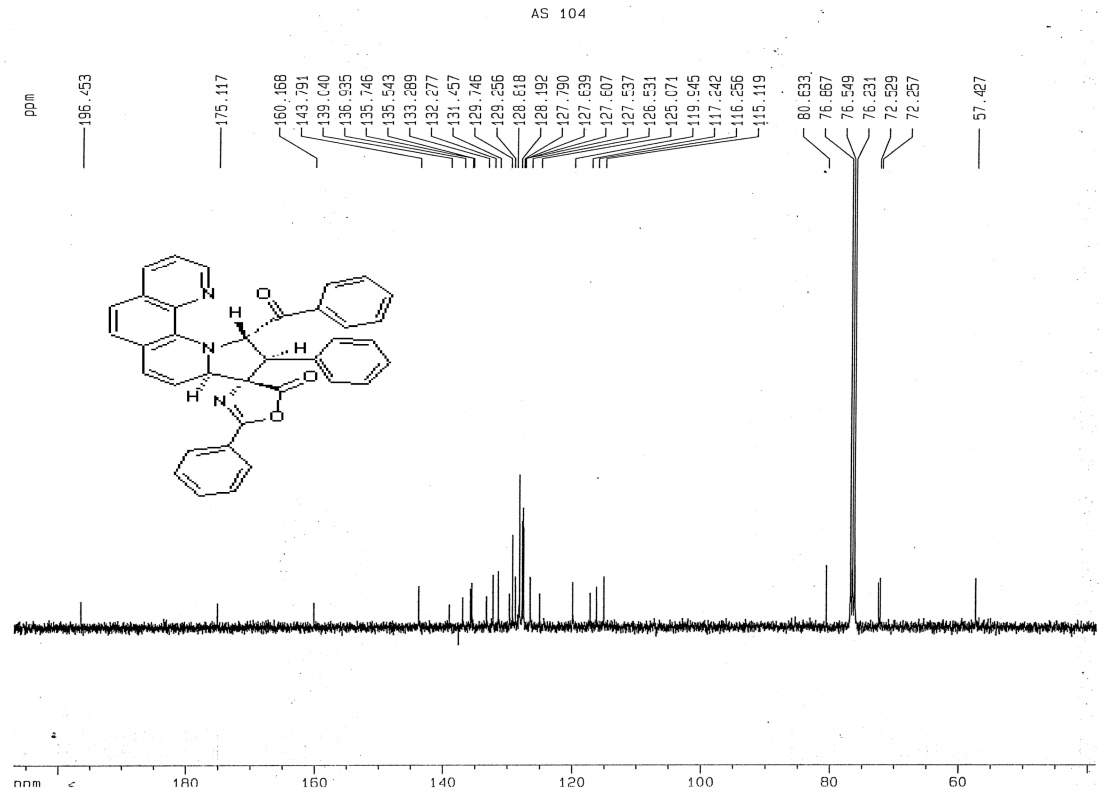

Figure 4. 36 ^{13}C NMR Spectrum of **91a**

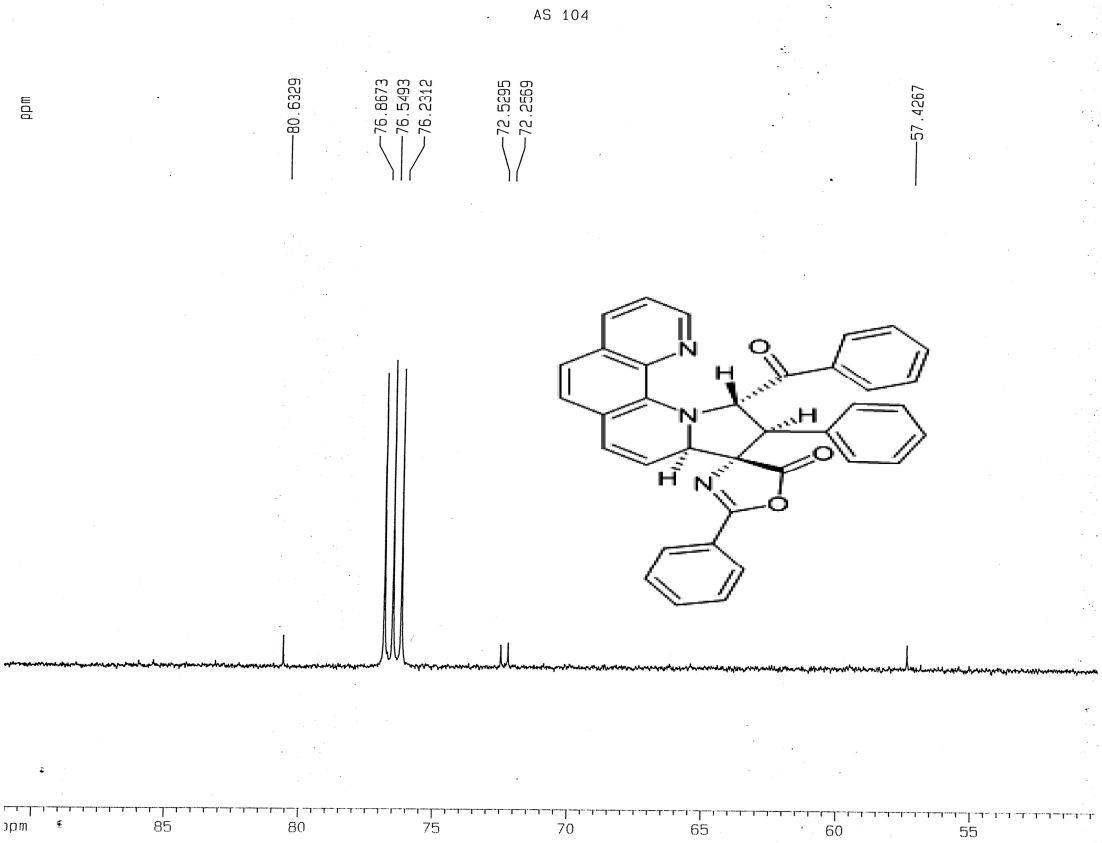

Figure 4. 37 Expanded (85-55 ppm) ^{13}C NMR Spectrum of **91a**

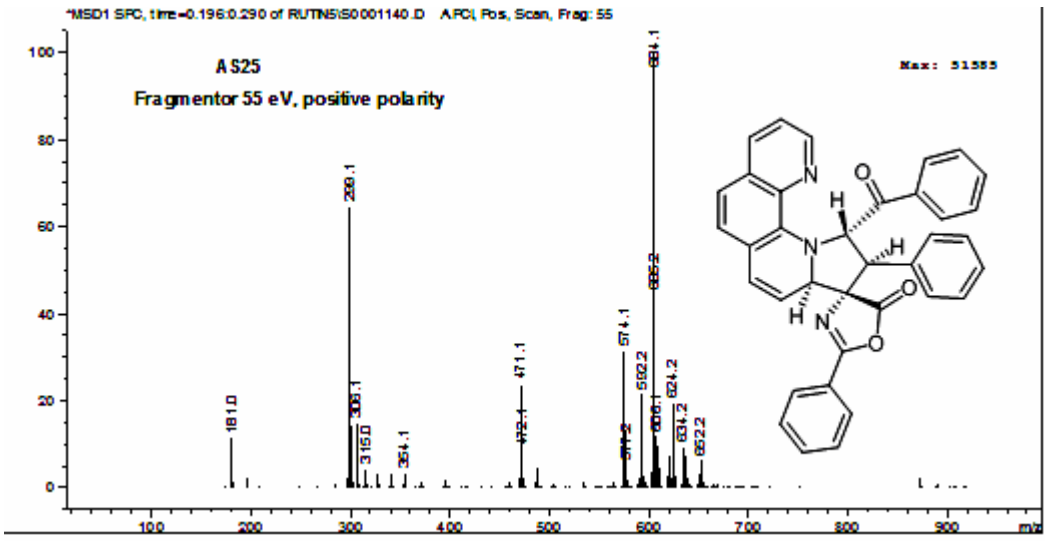

Figure 4. 38 MASS Spectrum of **91a**

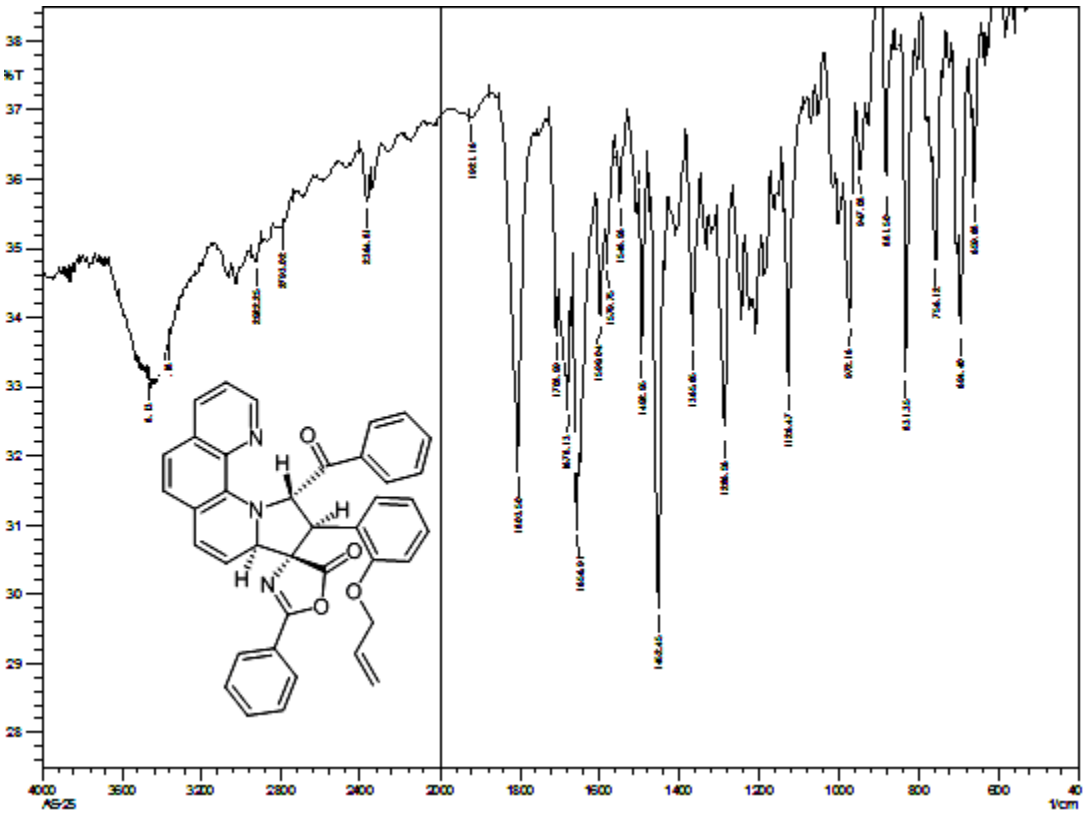

Figure 4. 39 IR Spectrum of **91b**

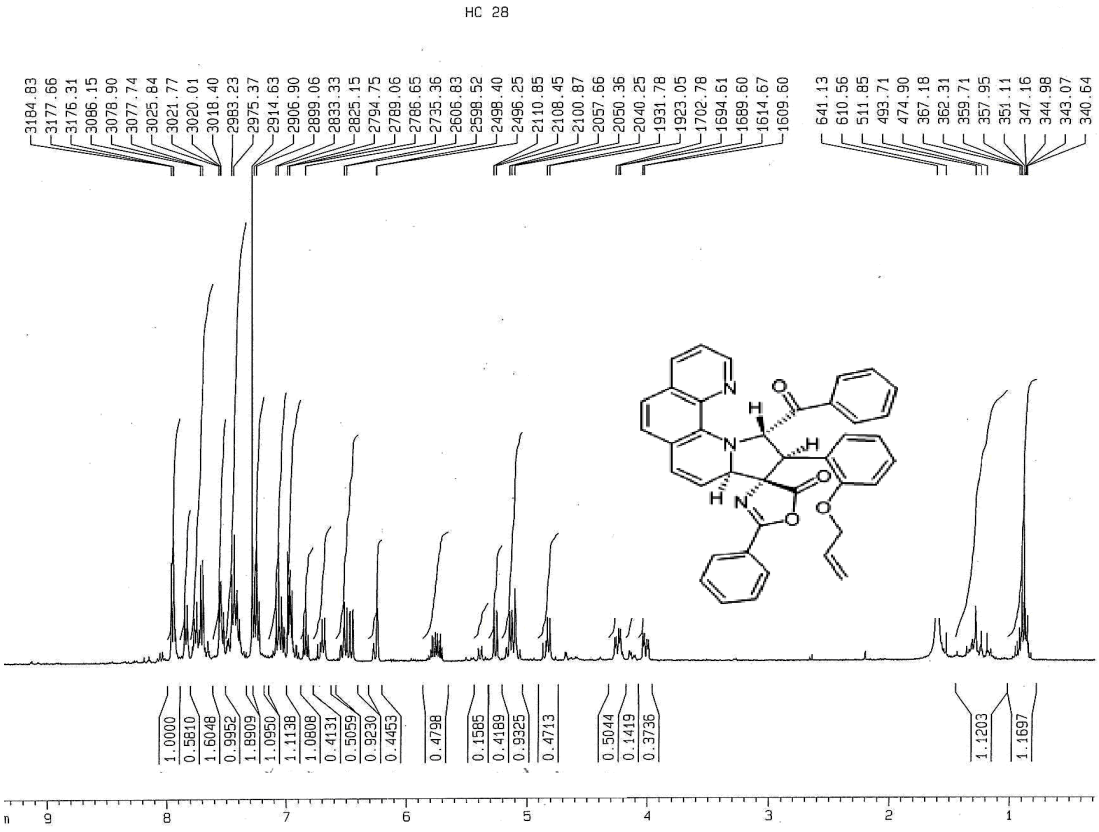

Figure 4. 40 ^{1}H NMR Spectrum of **91b**

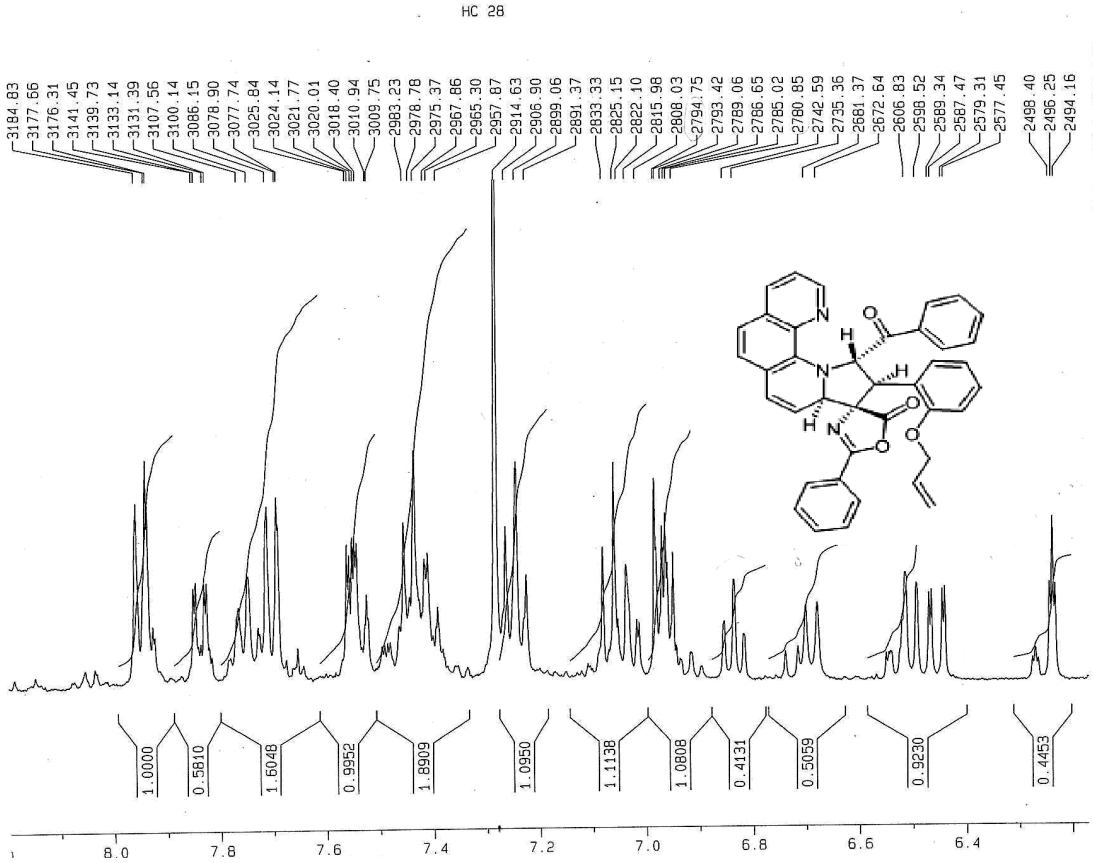

Figure 4. 41 Expanded (8.0-6.3 ppm) ^{1}H NMR Spectrum of **91b**

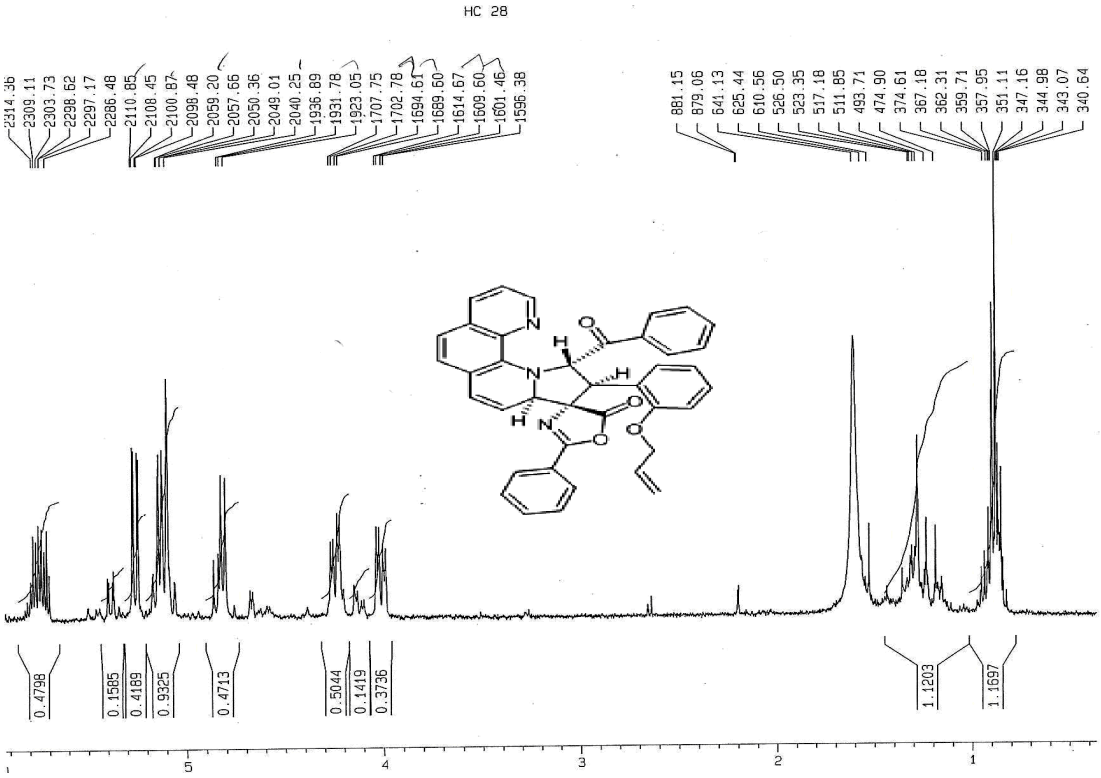

Figure 4. 42 Expanded (6.3-1.0 ppm) ^{1}H NMR Spectrum of **91b**

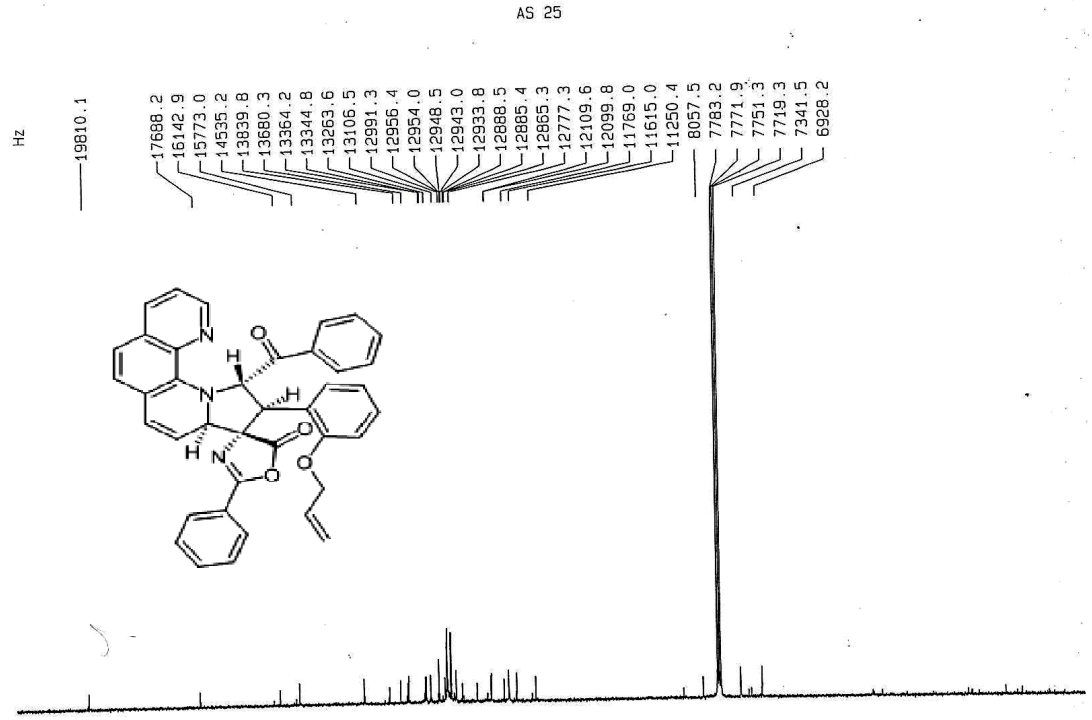

Figure 4. 43 ^{13}C NMR Spectrum of **91b**

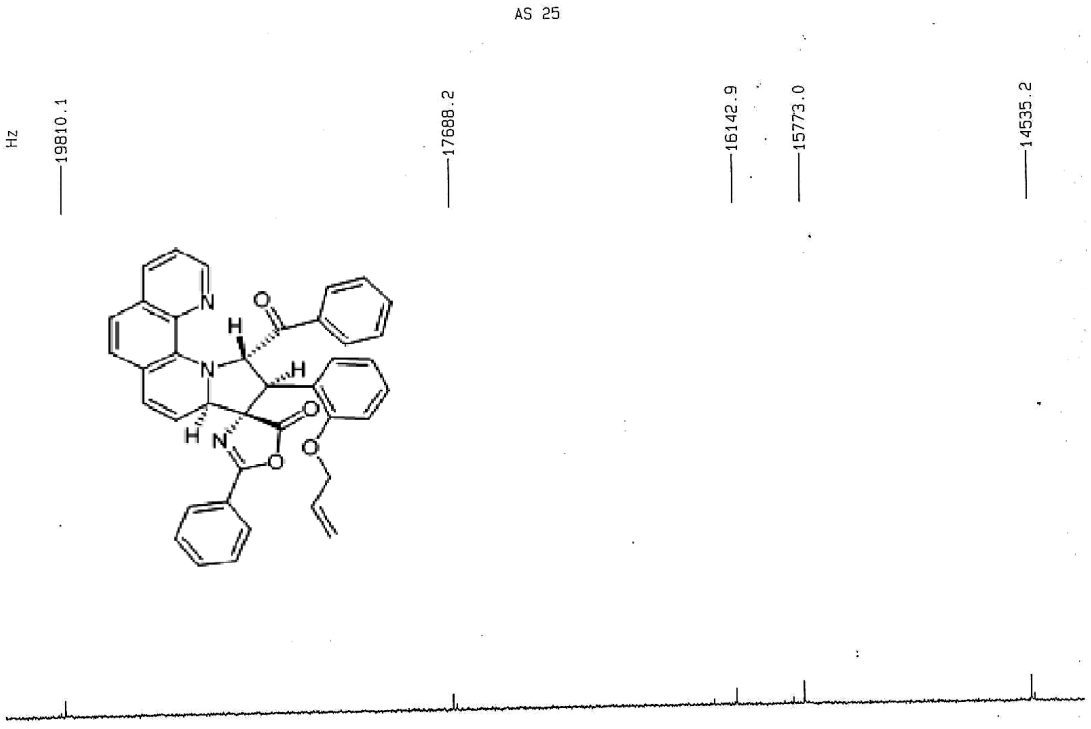

Figure 4. 44 Expanded (200-140 ppm) ^{13}C NMR Spectrum of **91b**

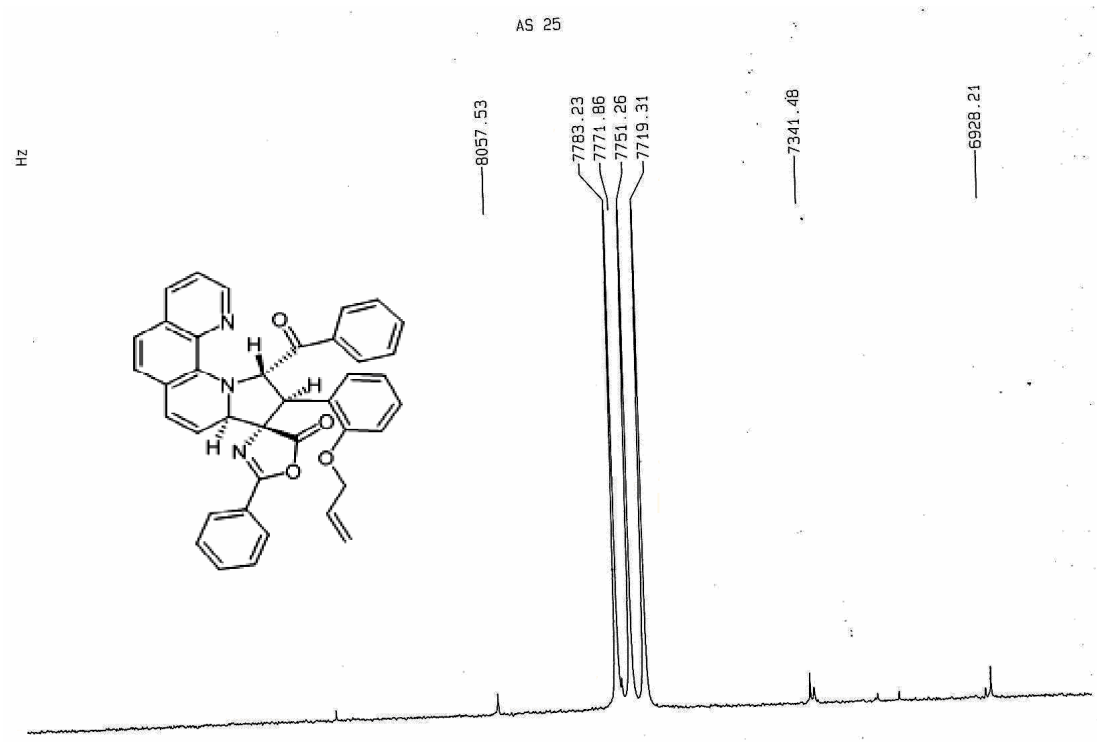

Figure 4. 45 Expanded (87.5-67.5 ppm) ^{13}C NMR Spectrum of **91b**

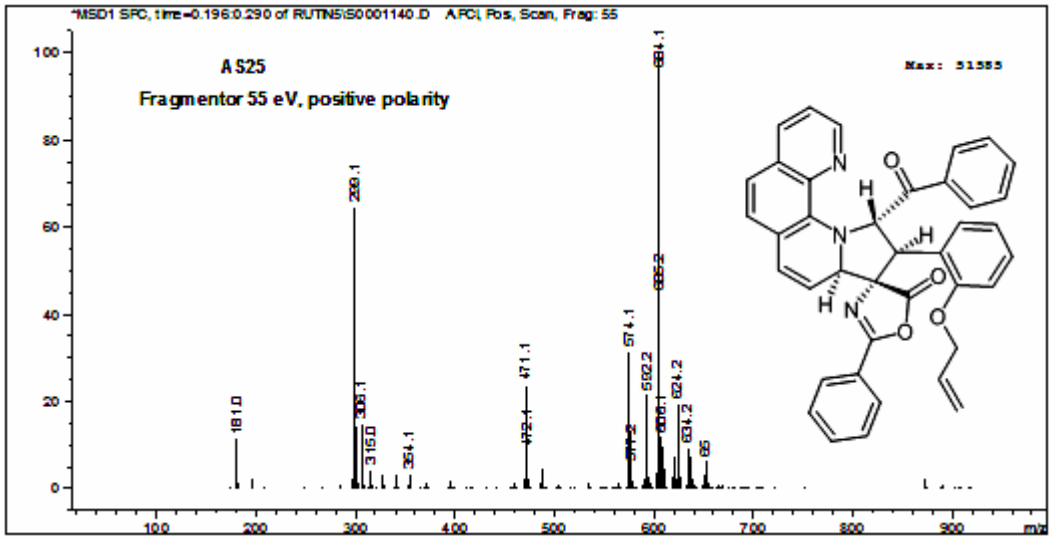

Figure 4. 46 MASS Spectrum of **91b**

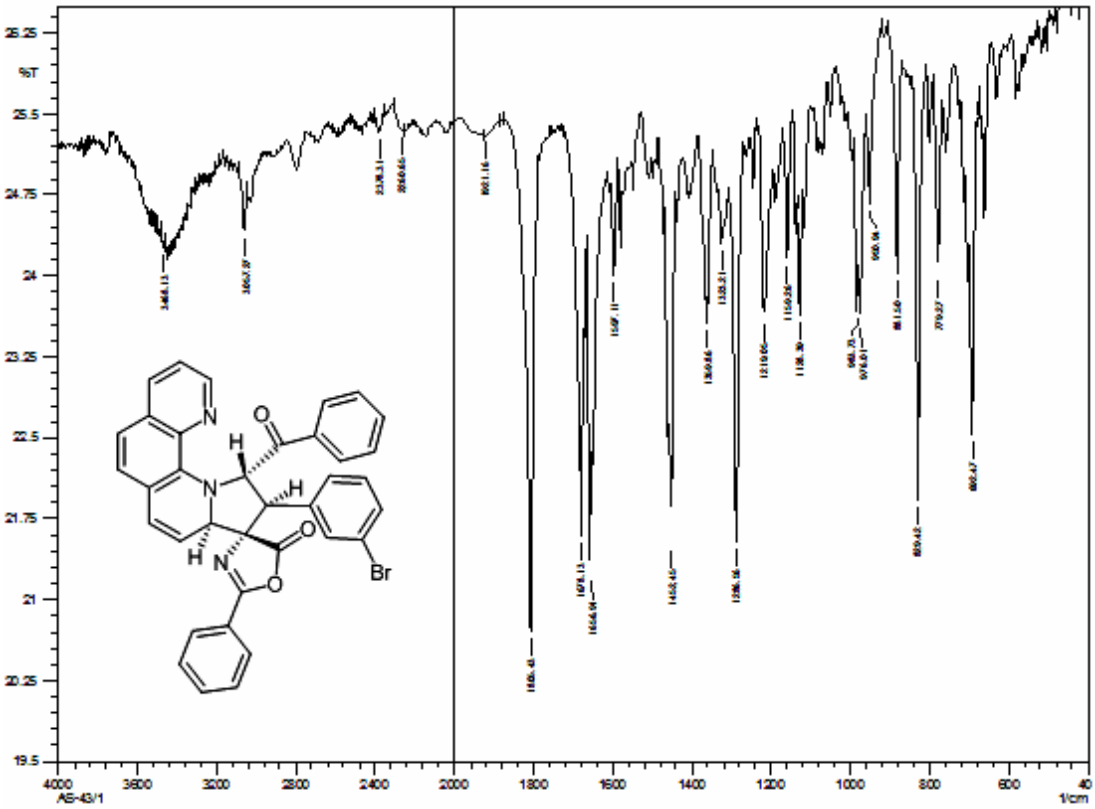

Figure 4. 47 IR Spectrum of **91d**

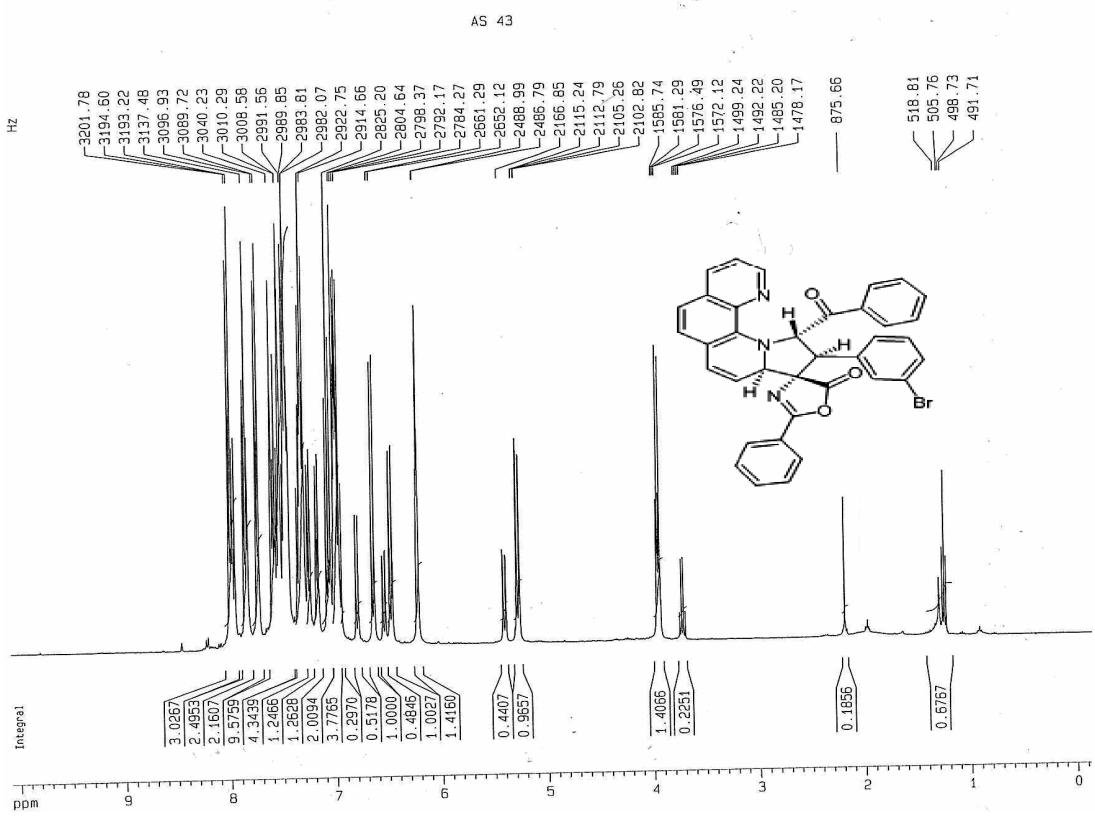

Figure 4. 48 ^{1}H NMR Spectrum of **91d**

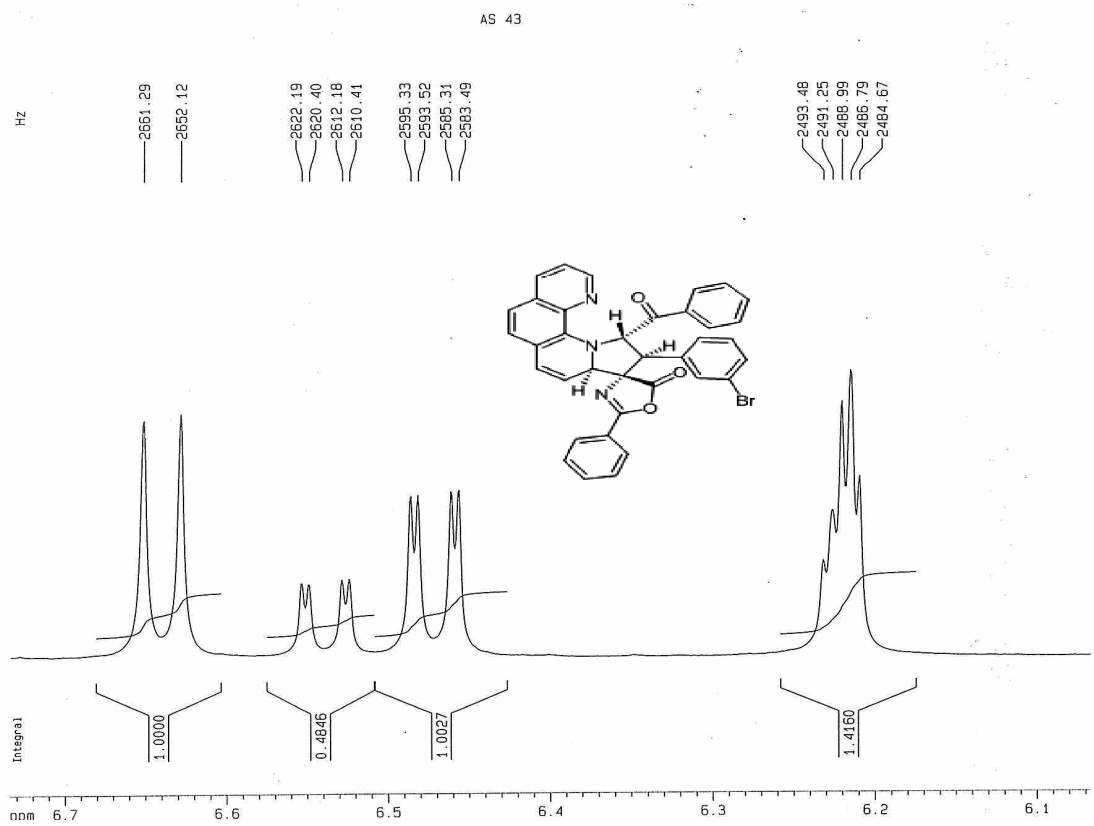

Figure 4. 49 Expanded (6.7-6.1 ppm) ^{1}H NMR Spectrum of **91d**

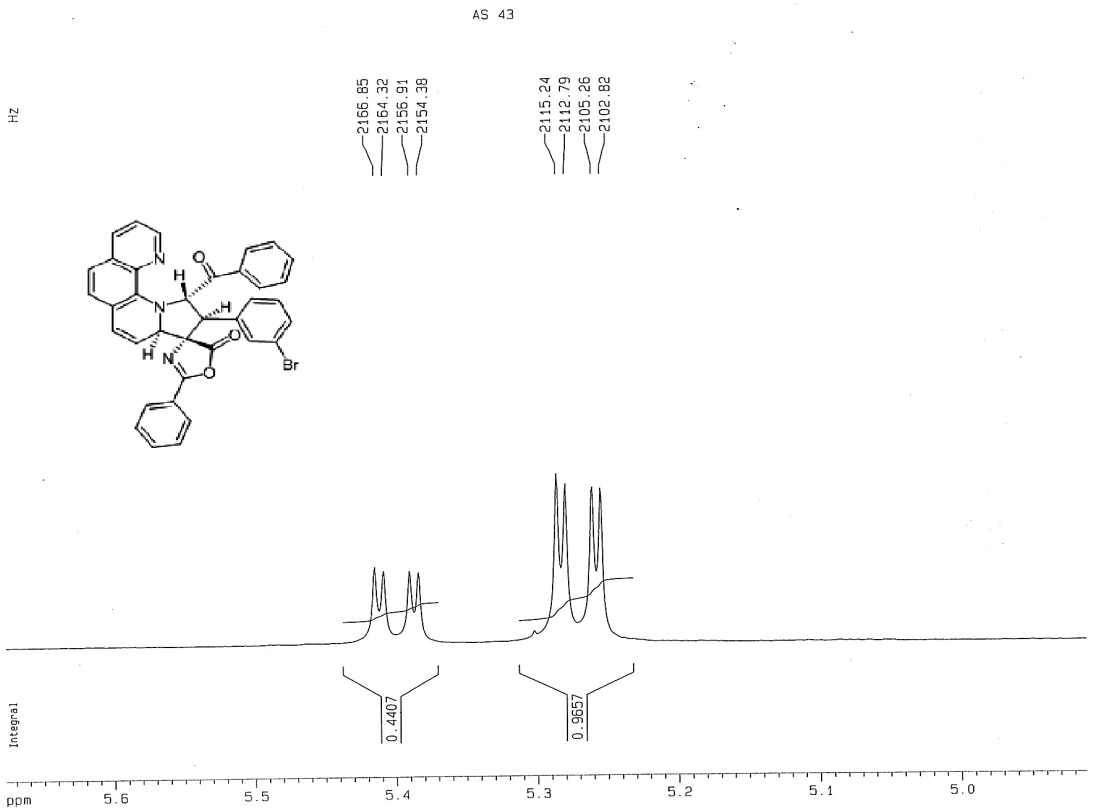

Figure 4. 50 Expanded (5.6-5.0 ppm) ^{1}H NMR Spectrum of **91d**

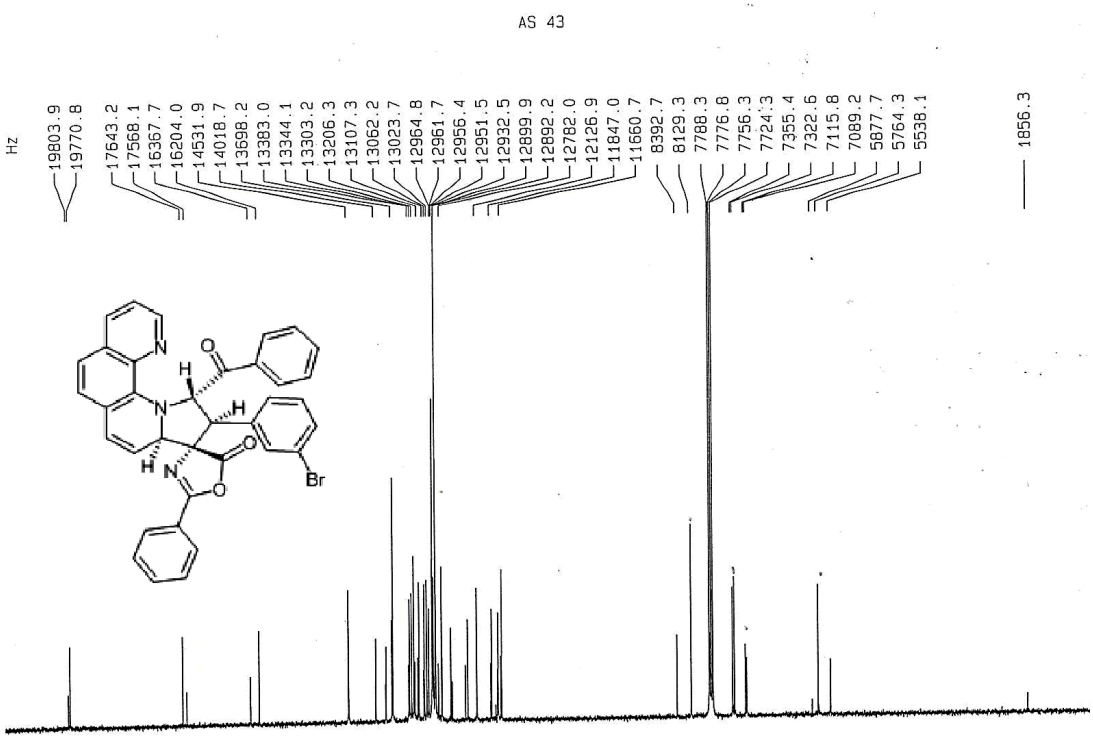

Figure 4. 51 ^{13}C NMR Spectrum of **91d**

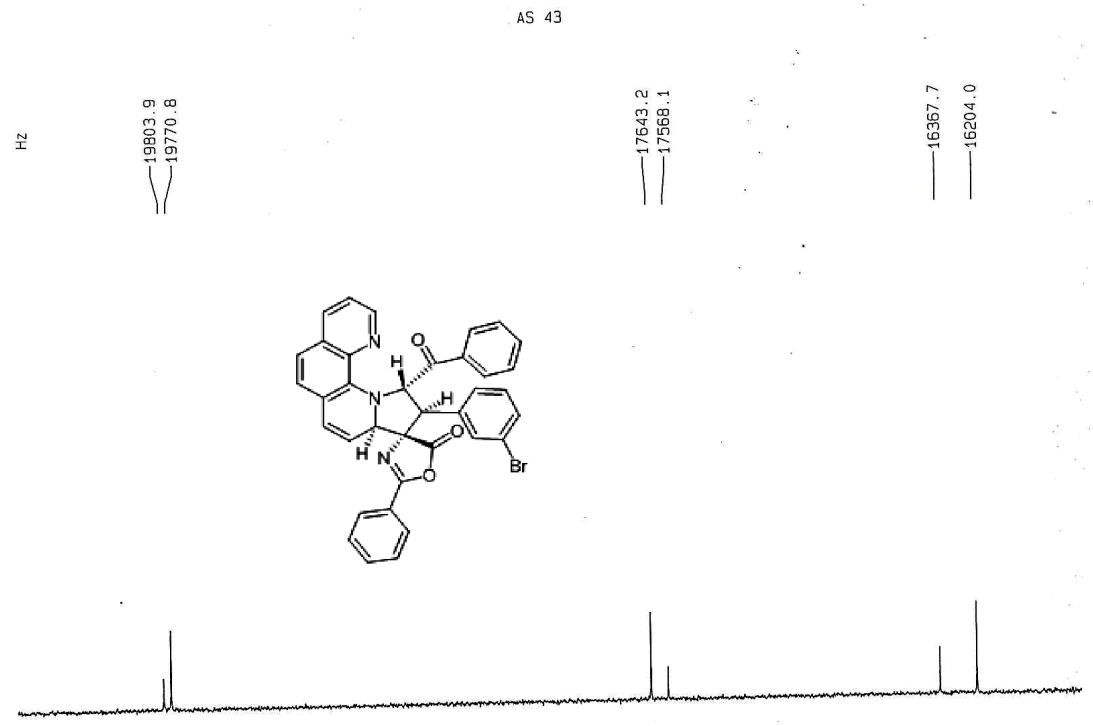

Figure 4. 52 Expanded (200-160 ppm) ^{13}C NMR Spectrum of **91d**

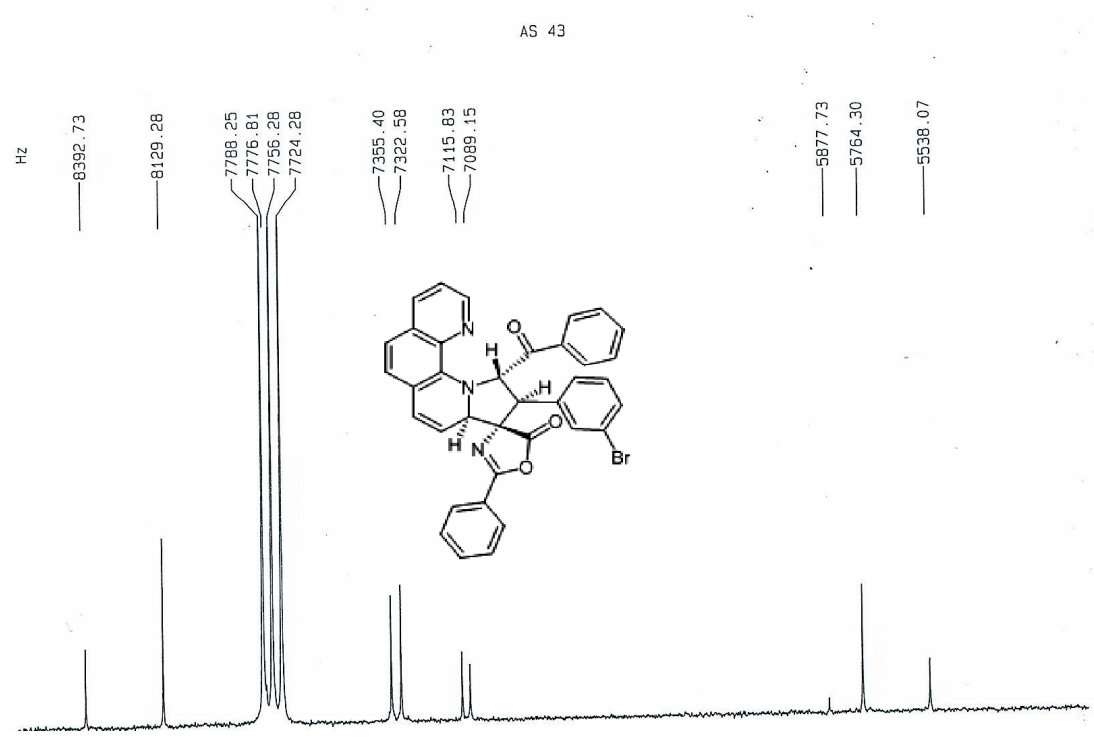

Figure 4. 53 Expanded (200-160 ppm) ^{13}C NMR Spectrum of **91d**

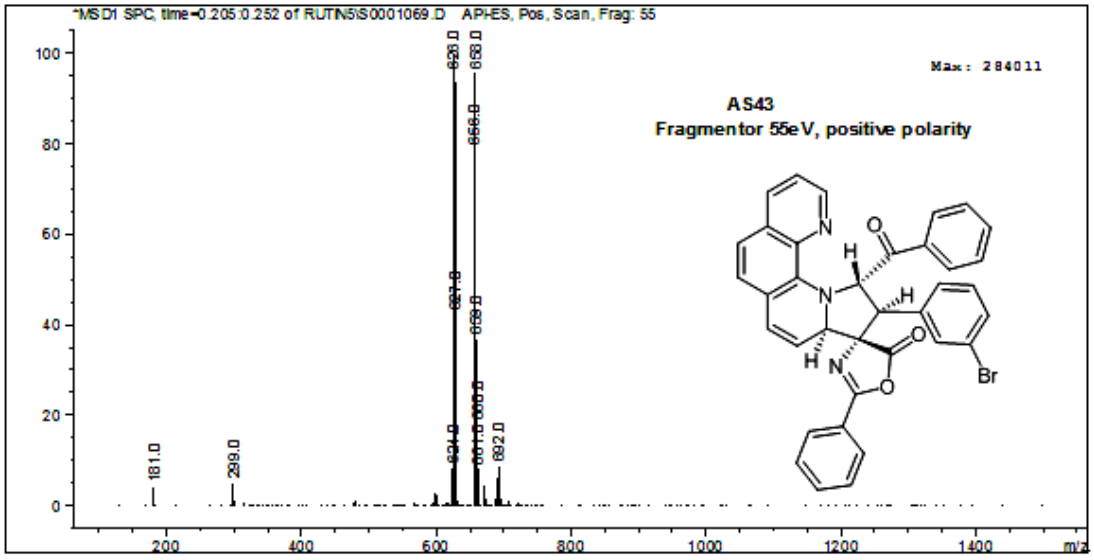

Figure 4. 54 MASS spectra of **91d**

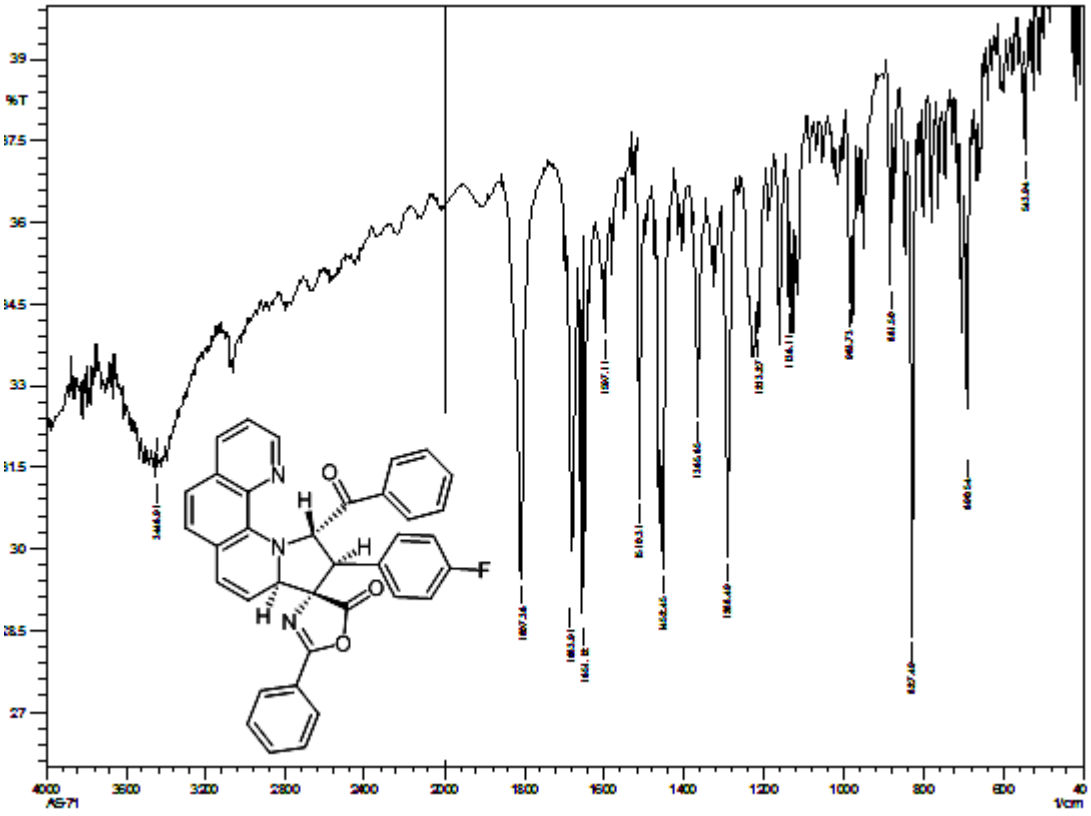

Figure 4. 55 IR Spectrum of **91e**

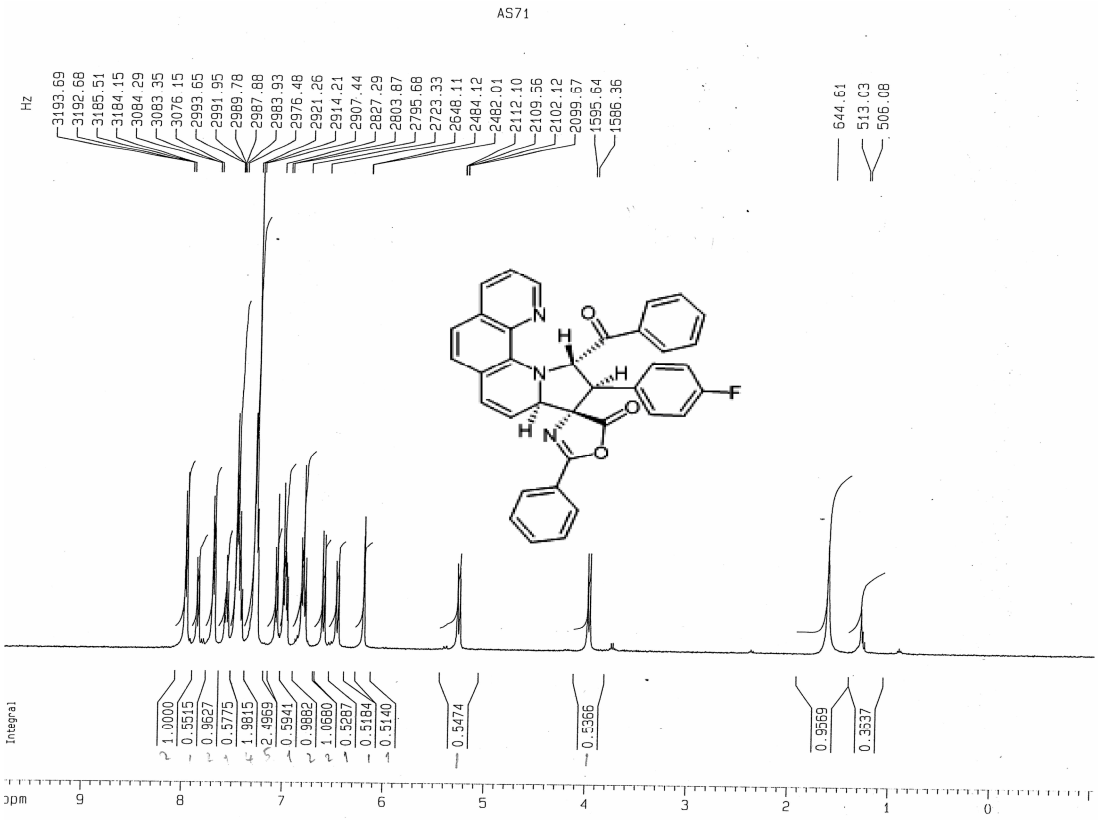

Figure 4. 56 ^{1}H NMR Spectrum of **91e**

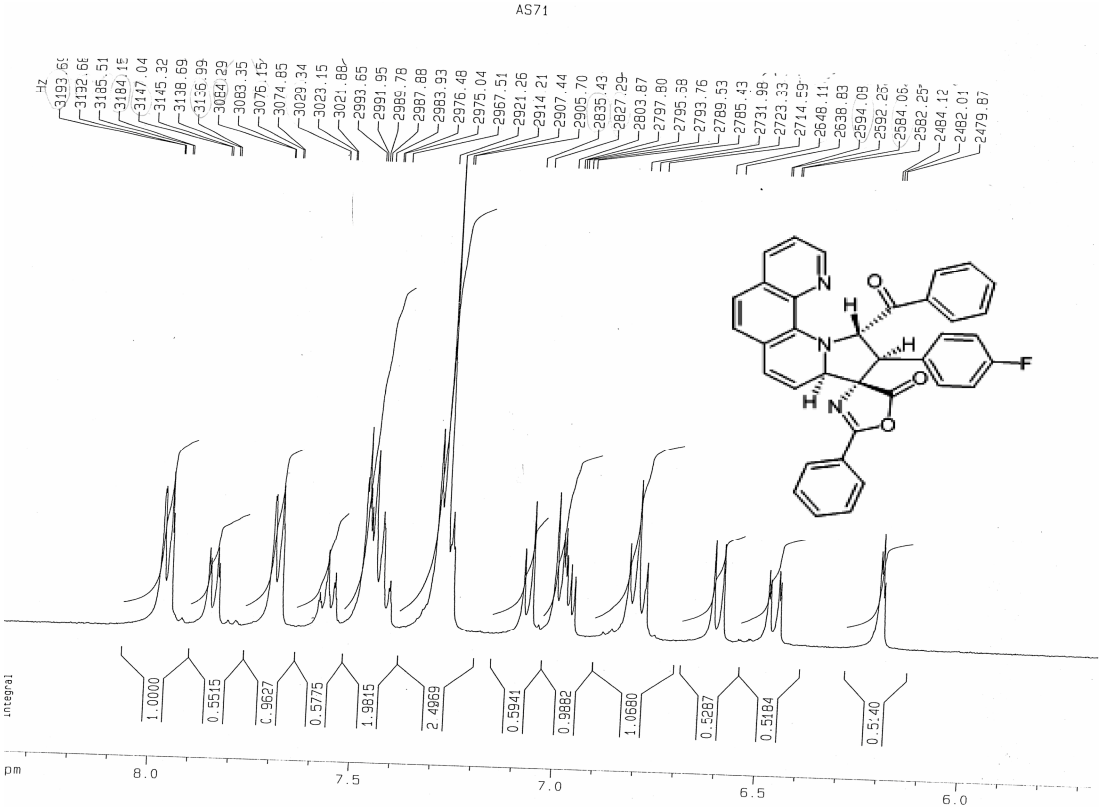

Figure 4. 57 Expanded (8-6 ppm) ^{1}H NMR Spectrum of **91e**

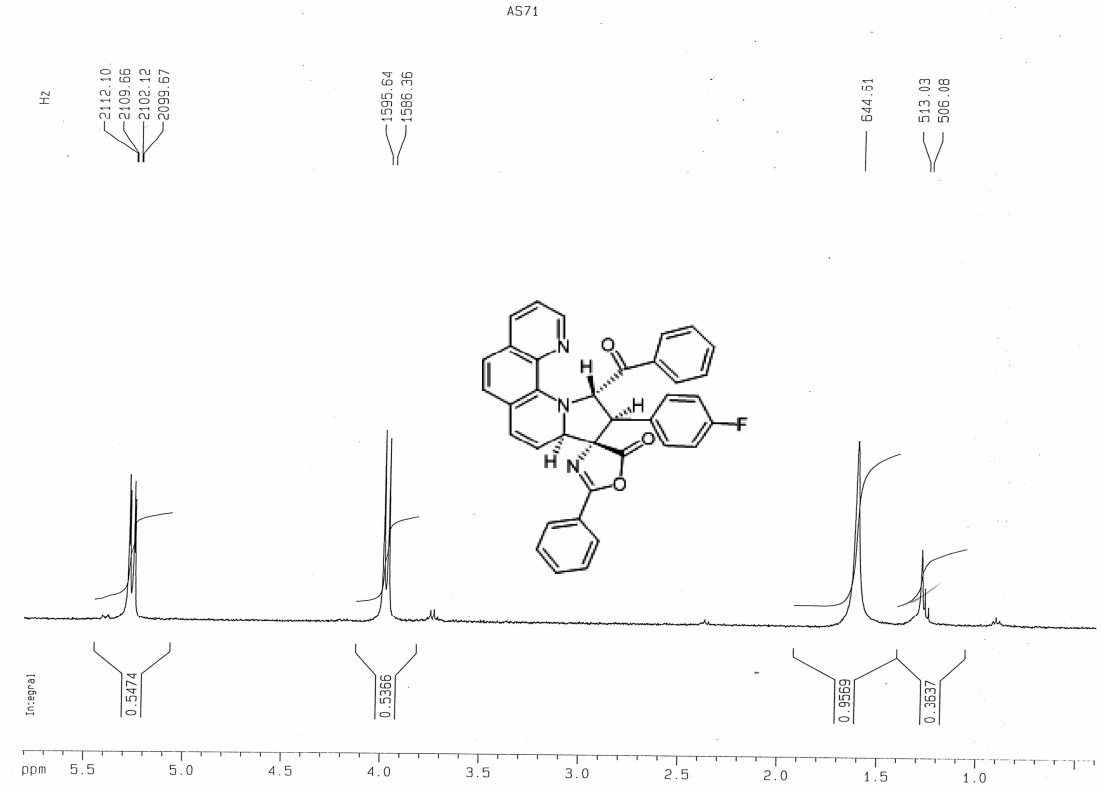

Figure 4. 58 Expanded (5.5-1.0 ppm) ^{1}H NMR Spectrum of **91e**

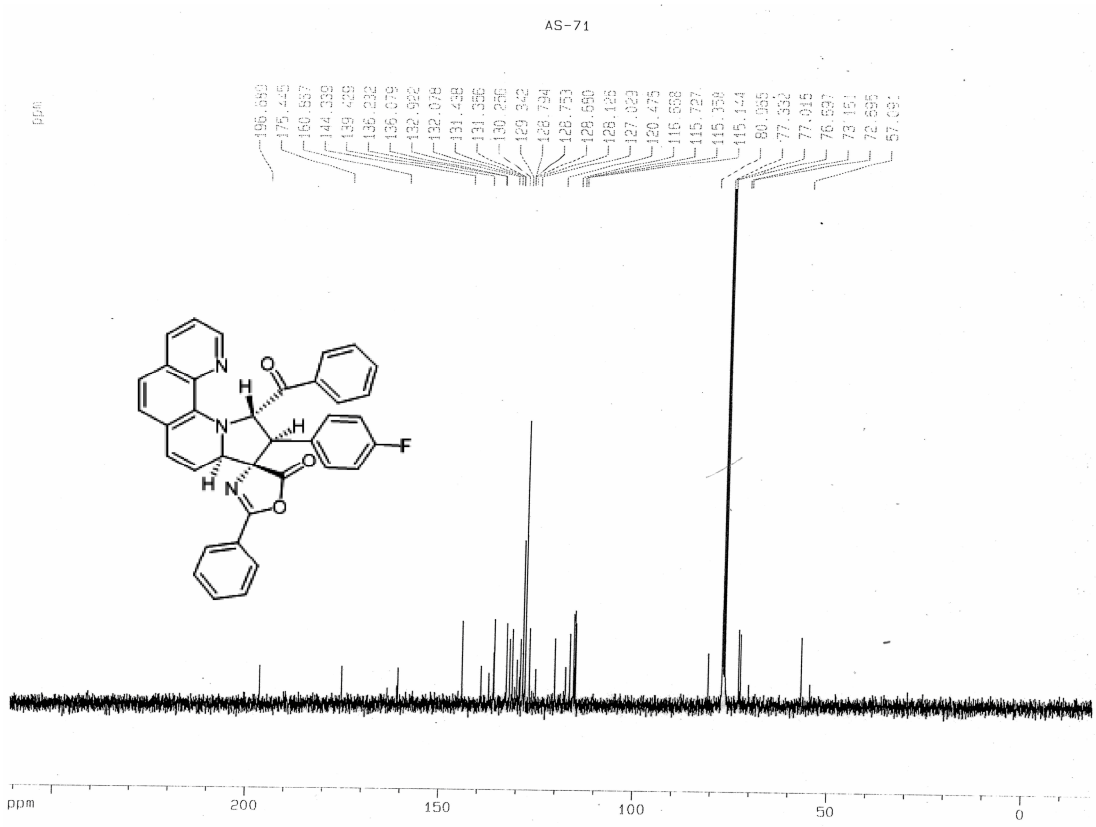

Figure 4. 59 ^{13}C NMR Spectrum of **91e**

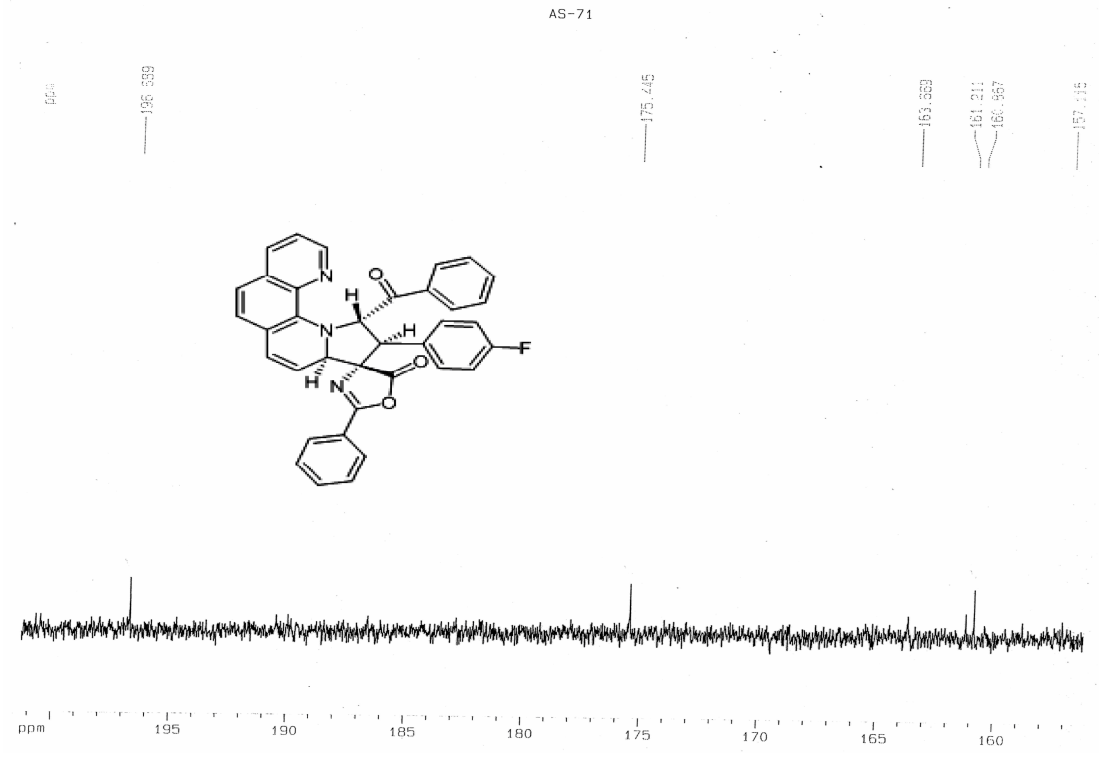

Figure 4. 60 Expanded (200-160 ppm) ^{13}C NMR Spectrum of **91e**

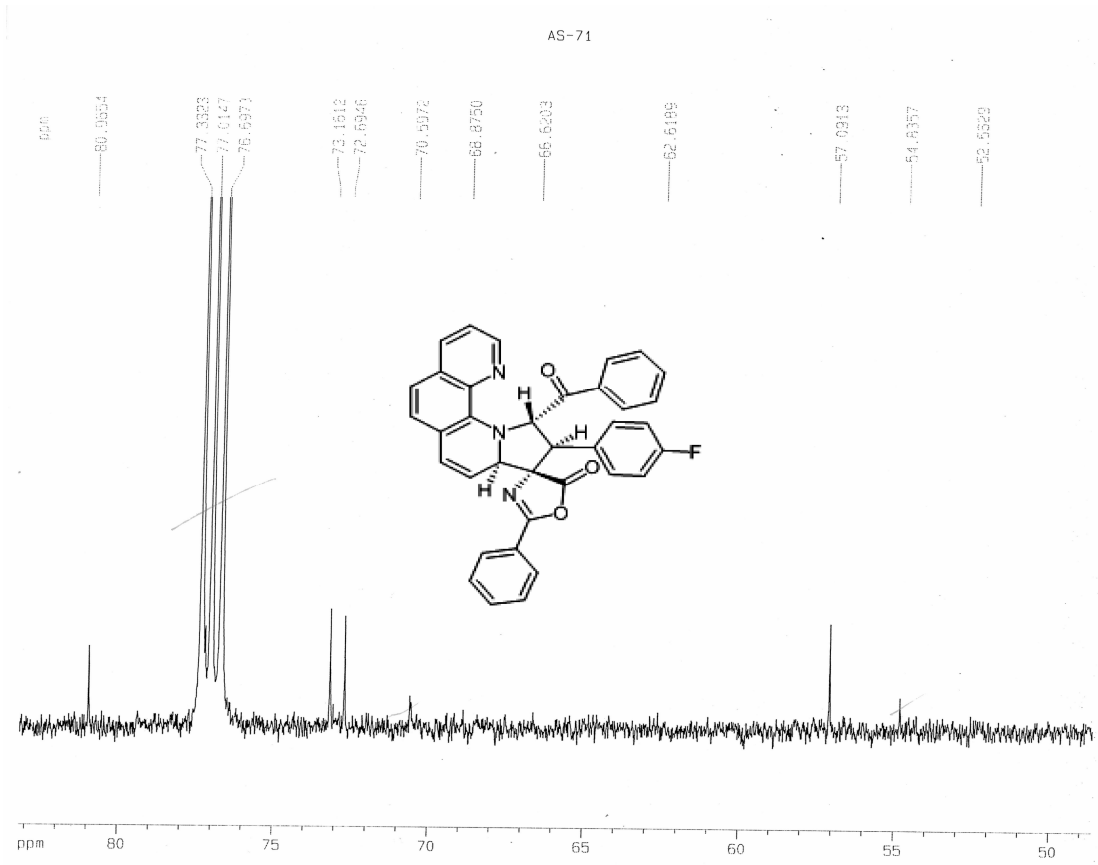

Figure 4. 61 Expanded (200-160 ppm) ^{13}C NMR Spectrum of **91e**

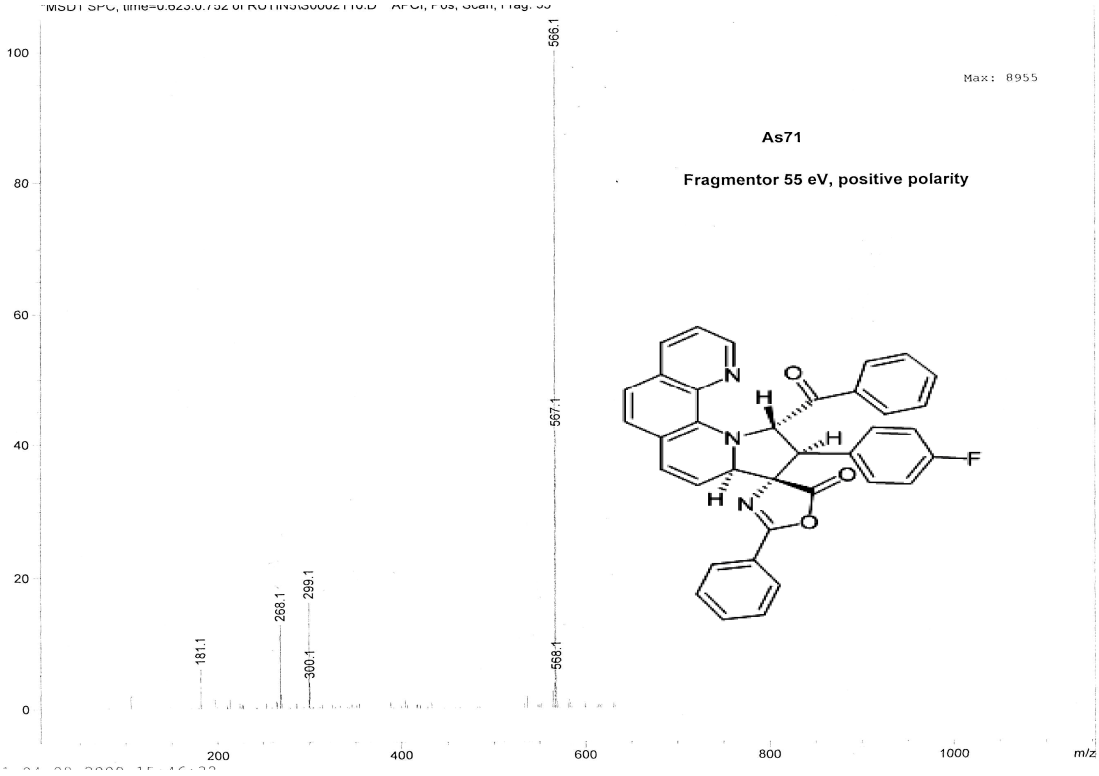

Figure 4. 62 MASS Spectrum of **91e**

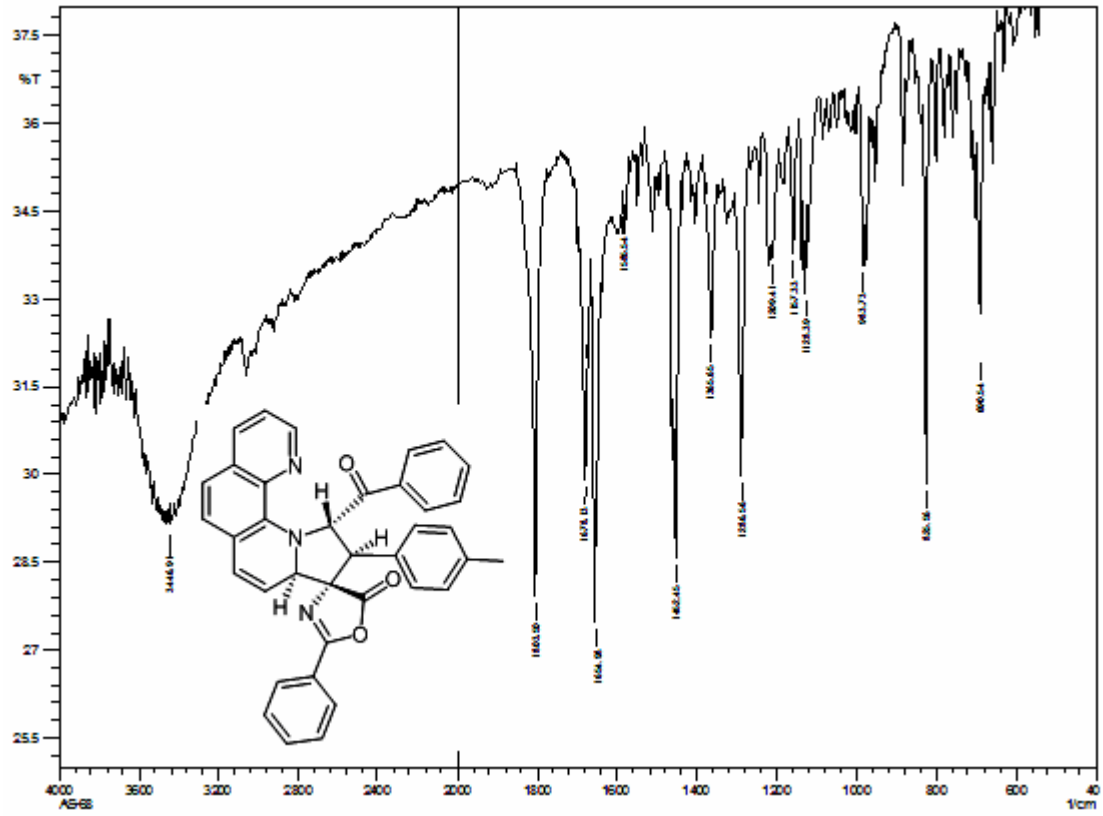

Figure 4. 63 IR Spectrum of **91f**

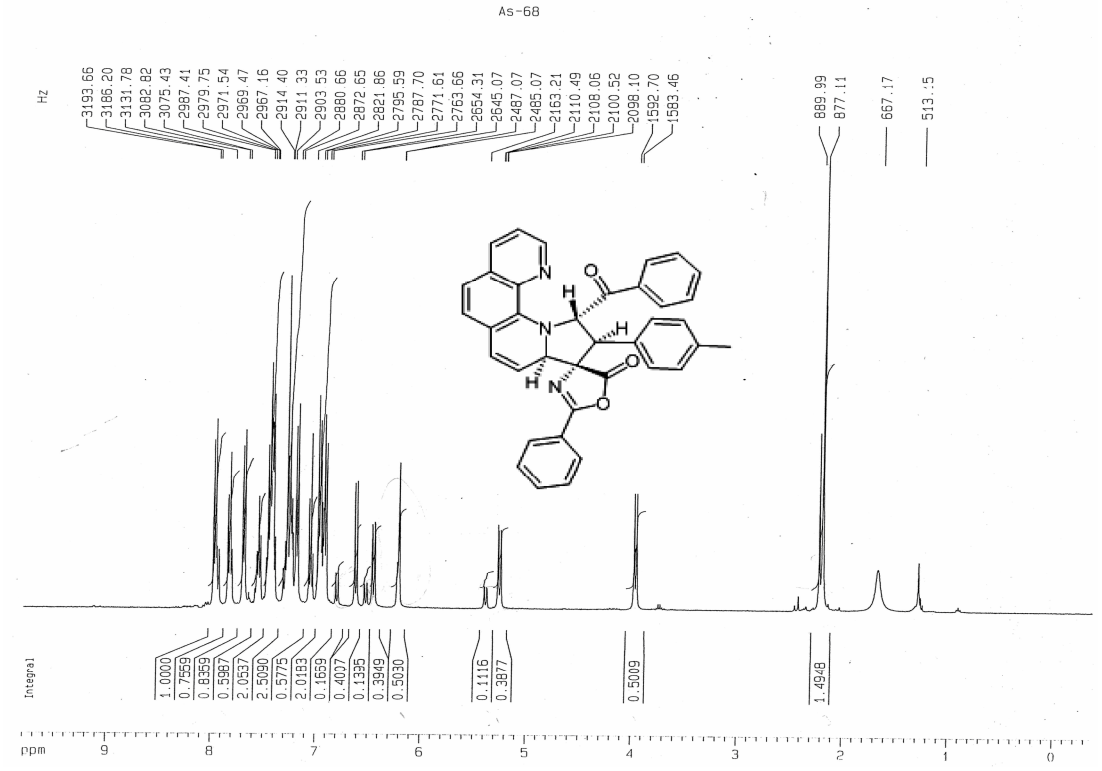

Figure 4. 64 ^{1}H NMR Spectrum of **91f**

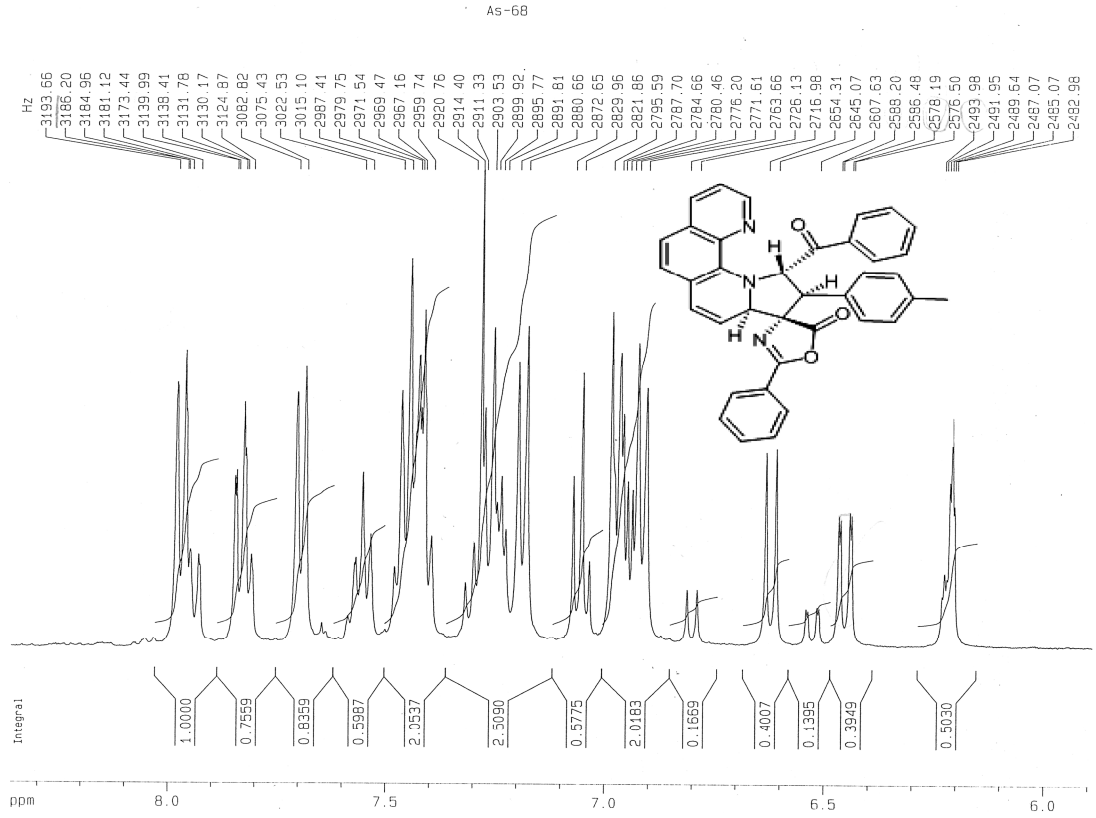

Figure 4. 65 Expanded (8.0-6.0 ppm) ^{1}H NMR Spectrum of **91f**

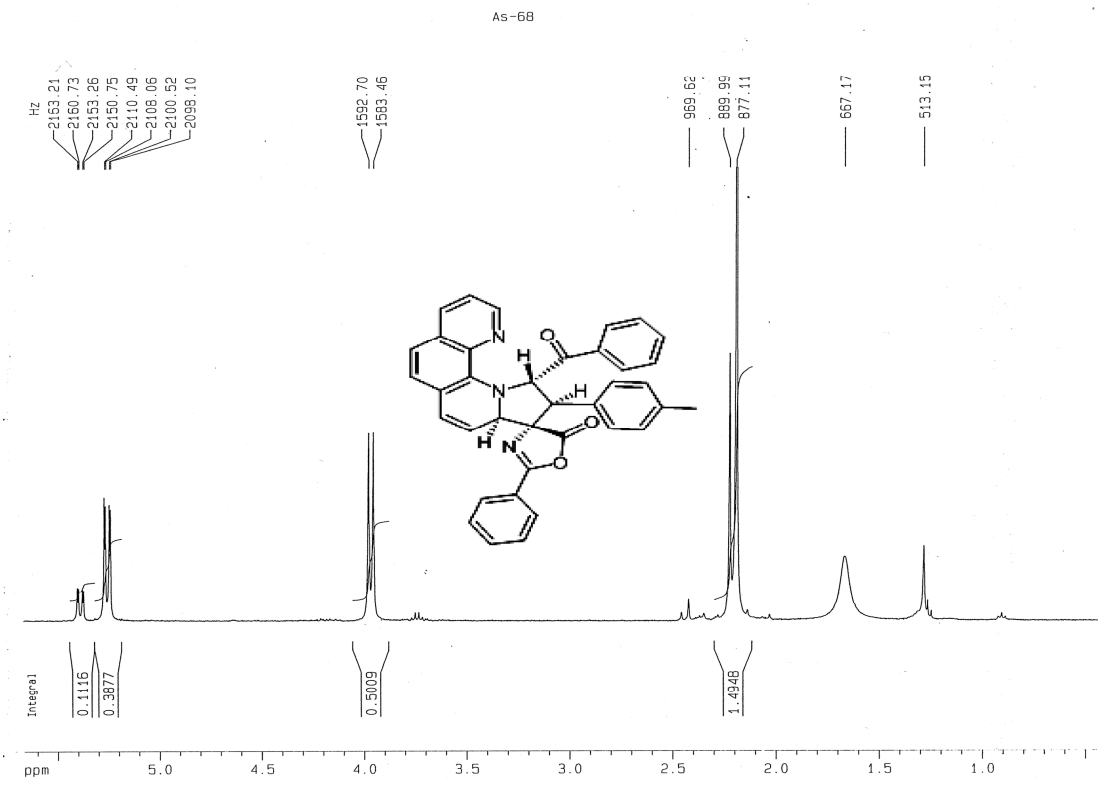

Figure 4. 66 Expanded (5.5-1.0 ppm) ^{1}H NMR Spectrum of **91f**

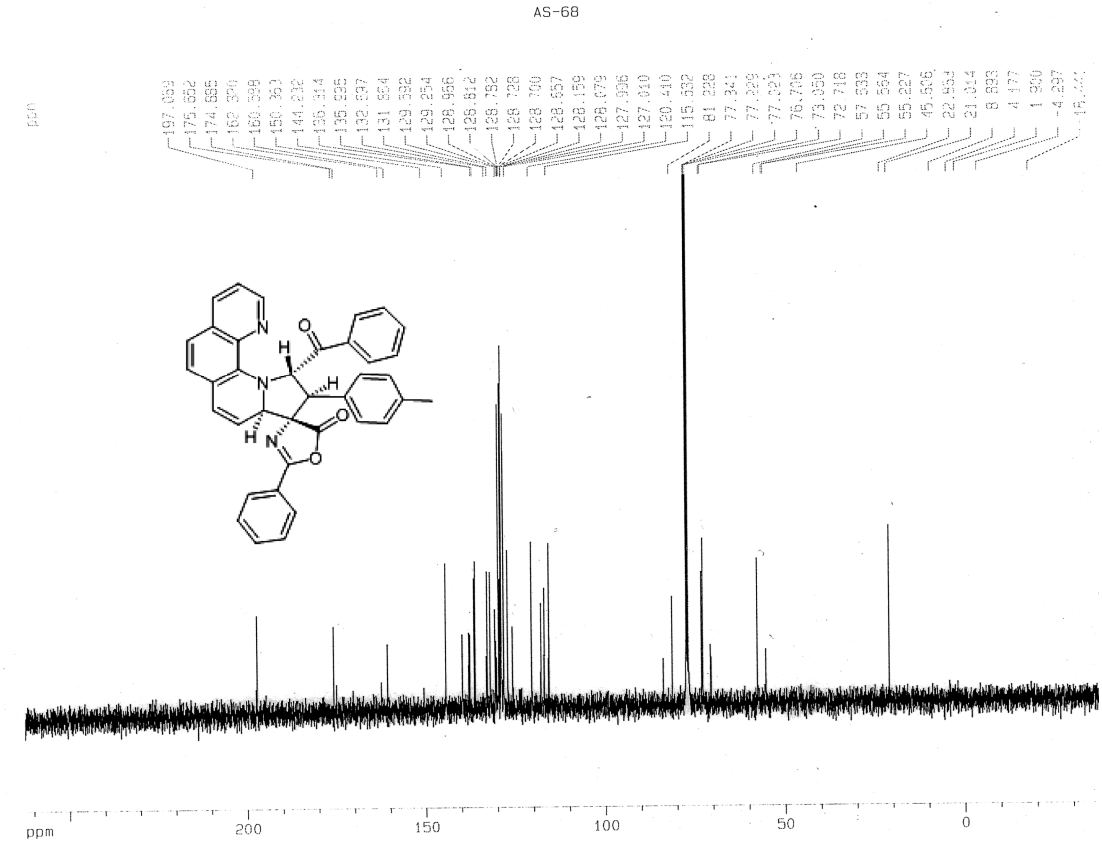

Figure 4. 67 ^{13}C NMR Spectrum of **91f**

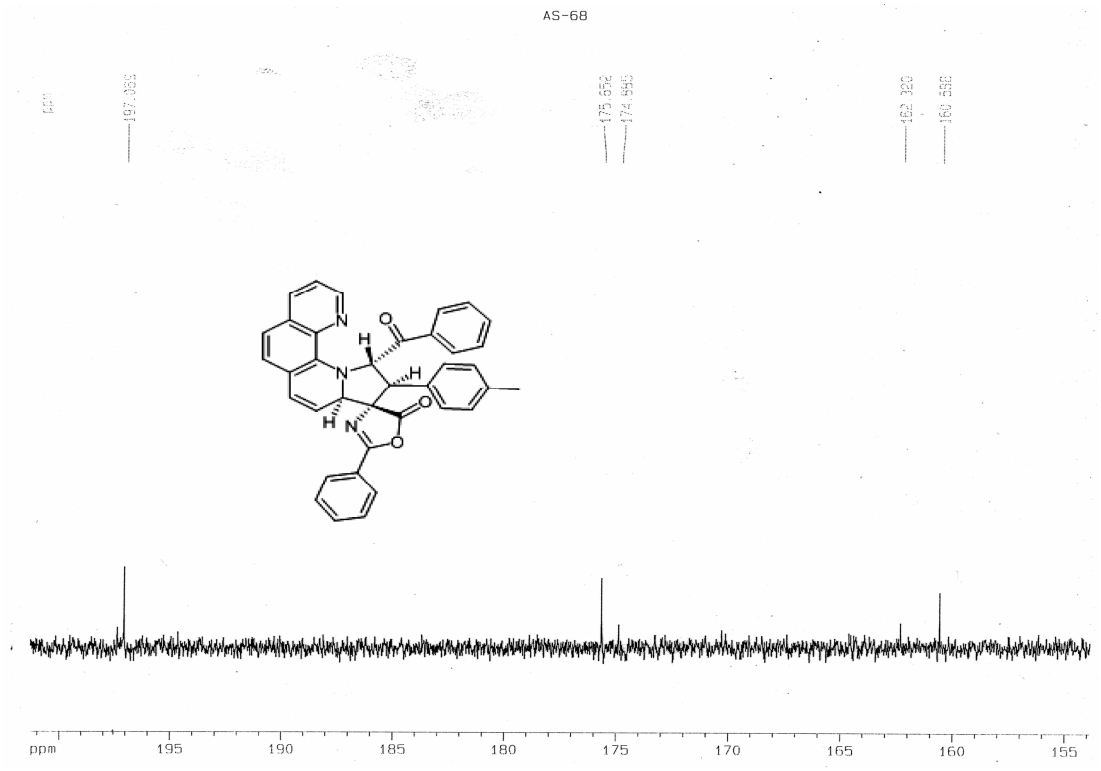

Figure 4. 68 Expanded (200-155 ppm) ^{13}C NMR Spectrum of **91f**

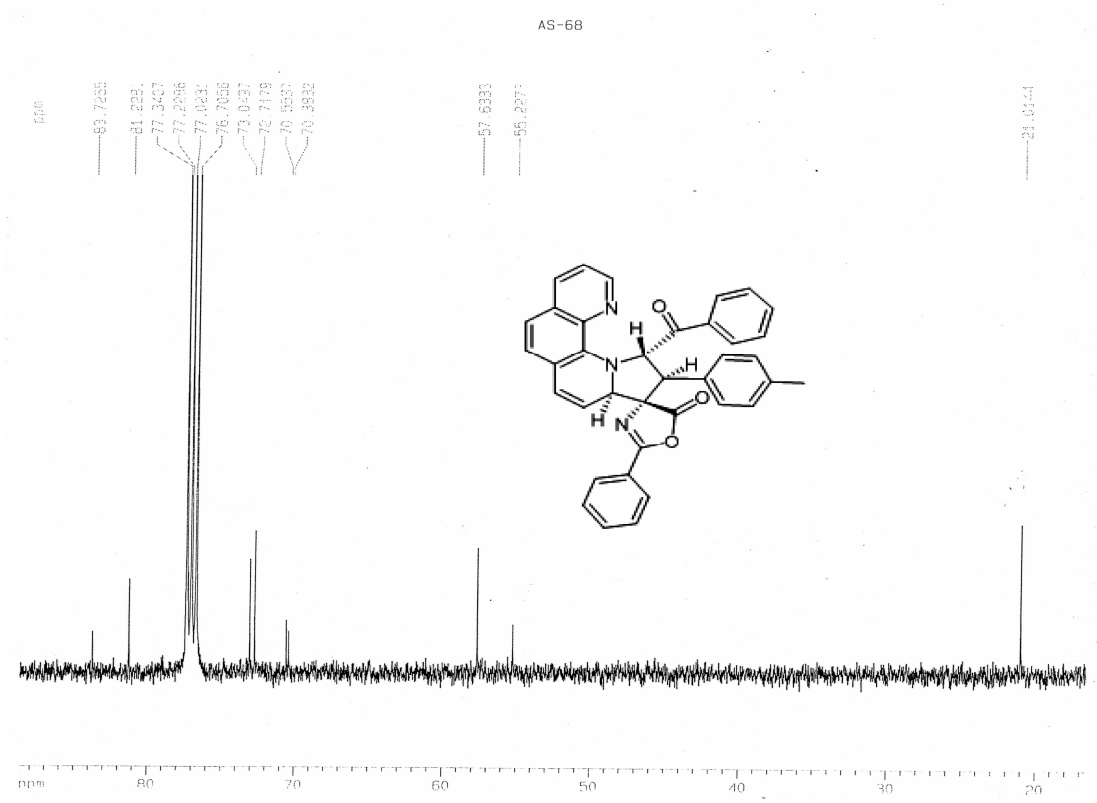

Figure 4. 69 Expanded (90-20 ppm) ^{13}C NMR Spectrum of **91f**

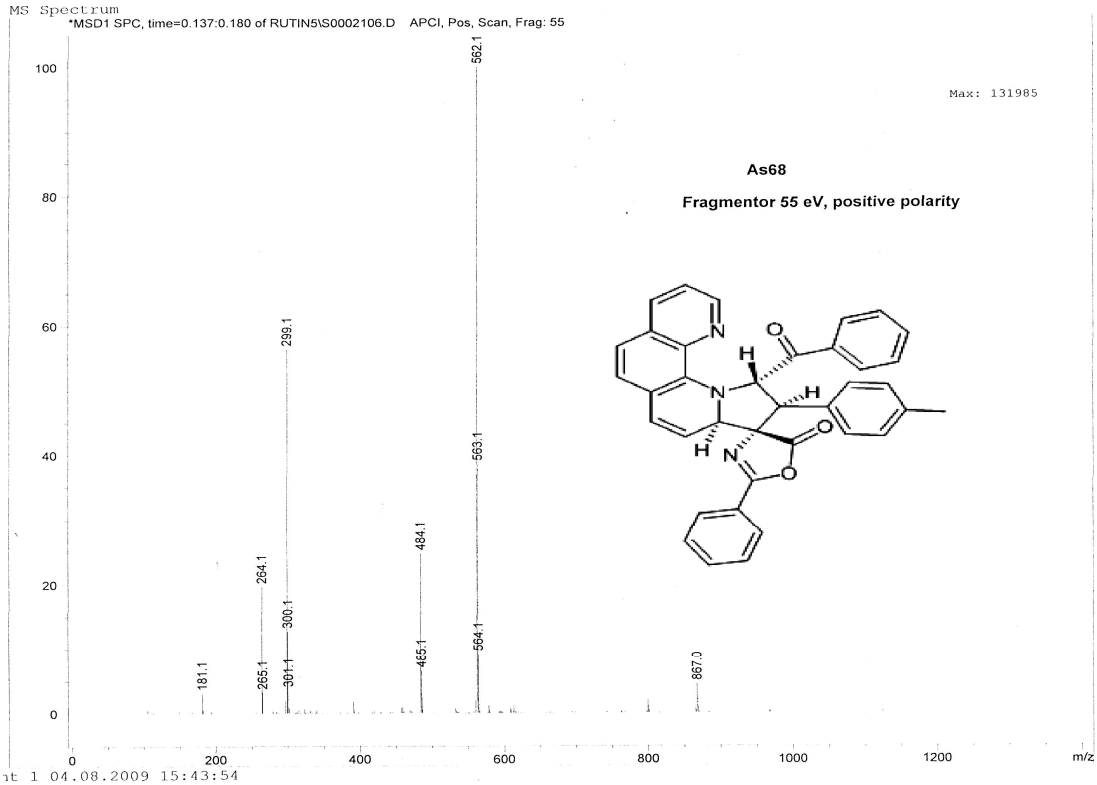

Figure 4. 70 MASS spectra of **91f**

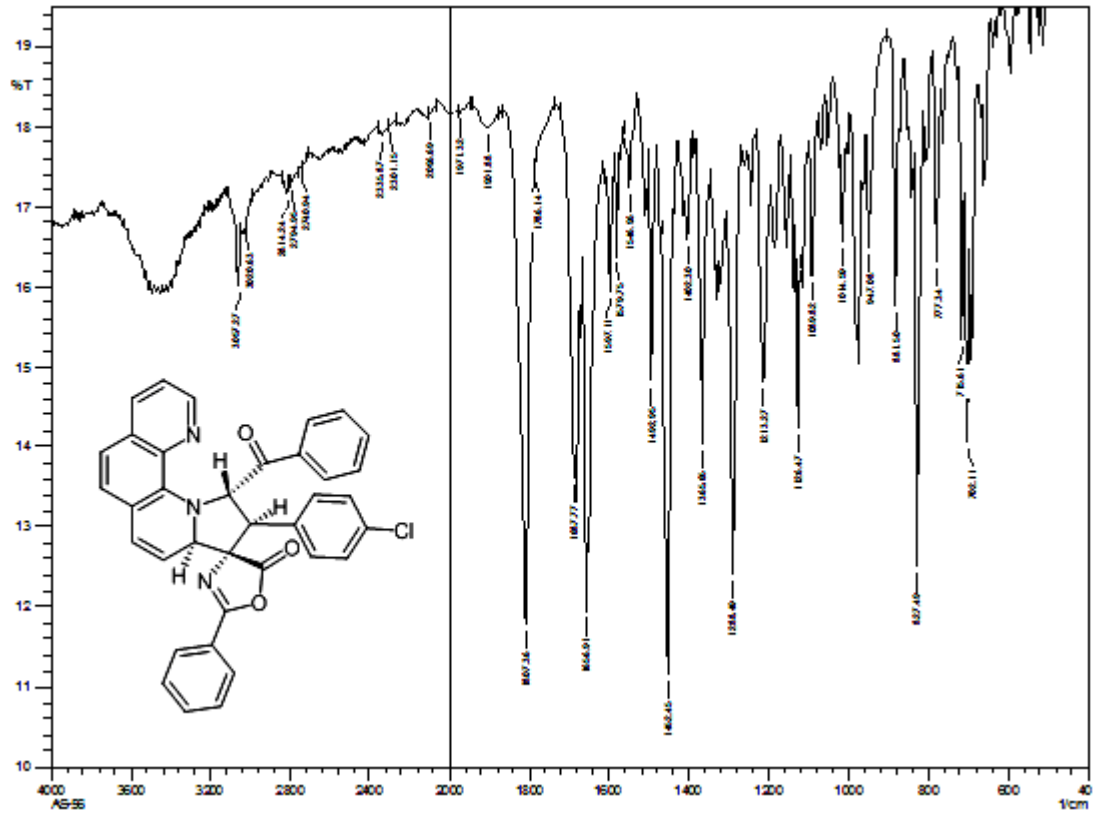

Figure 4. 71 IR Spectrum of **91g**

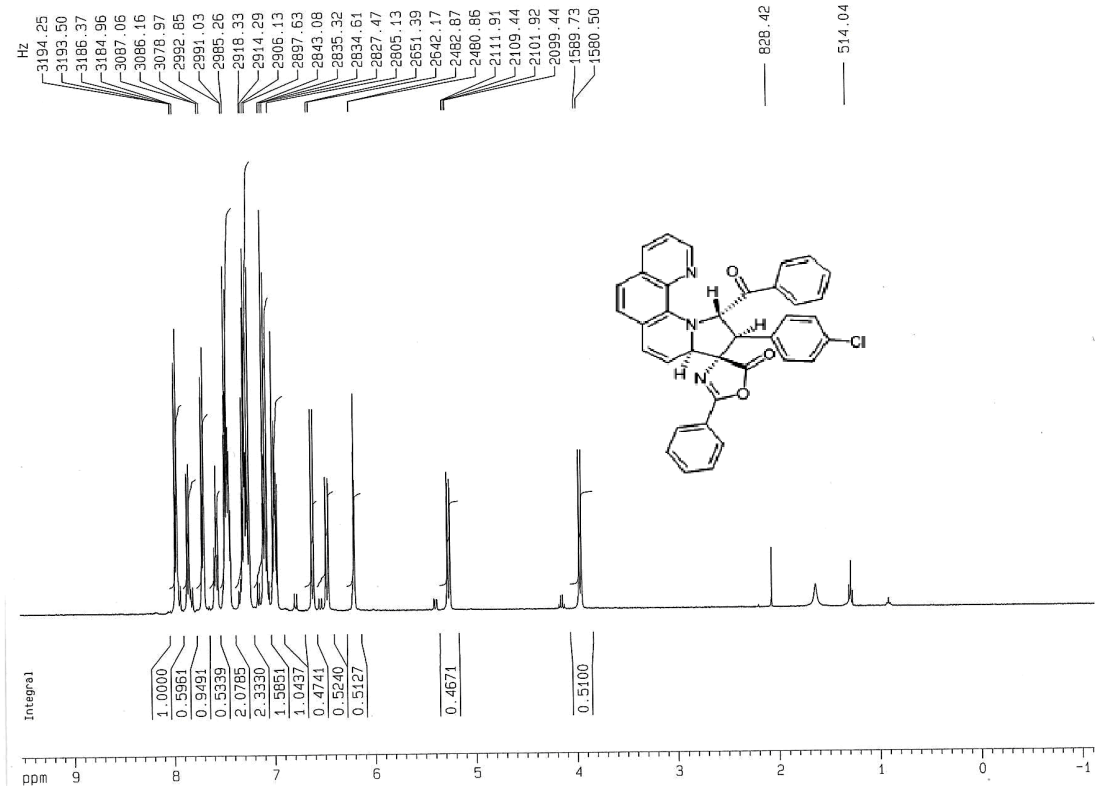

Figure 4. 72 ^{1}H NMR Spectrum of **91g**

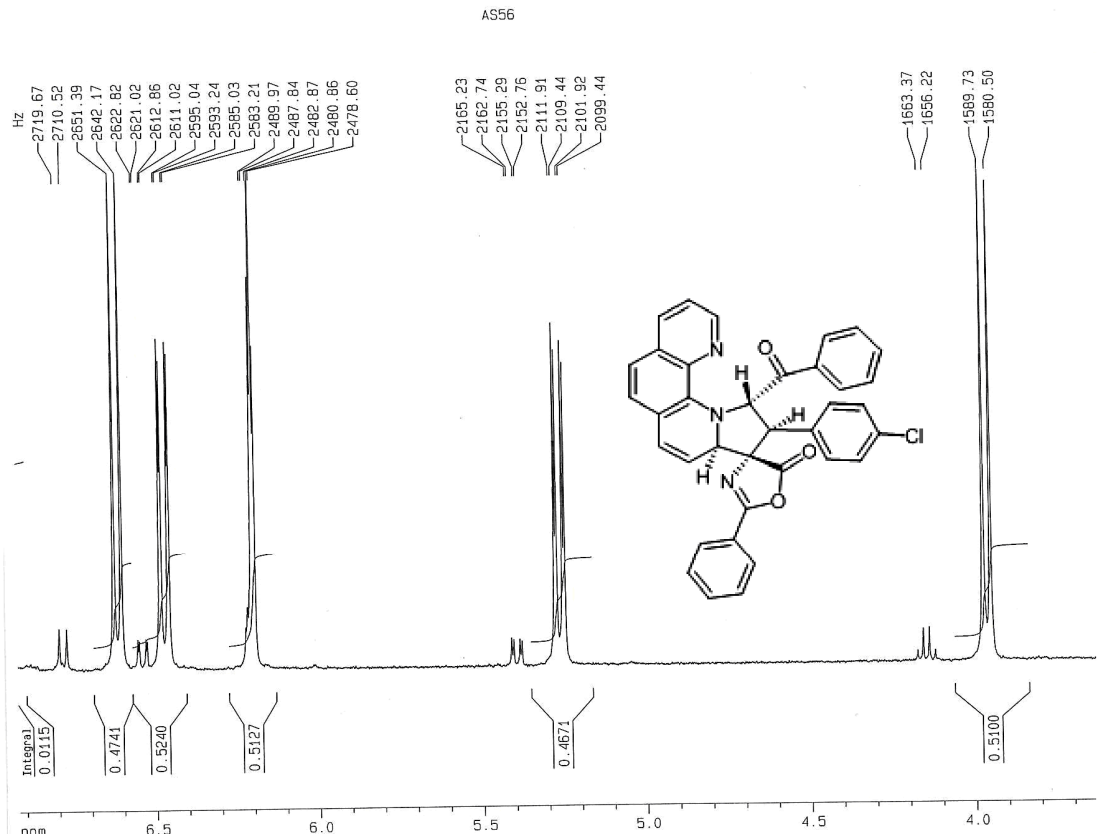

Figure 4. 73 Expanded (6.9-3.7 ppm) ^{1}H NMR Spectrum of **91g**

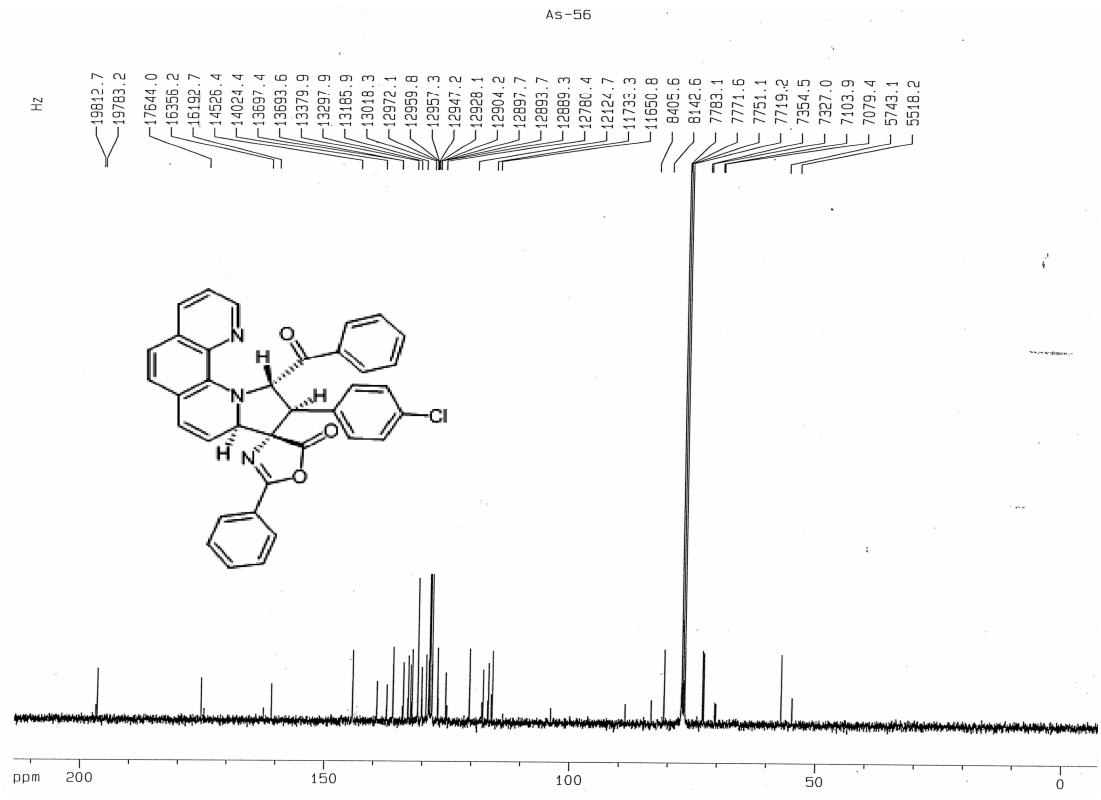

Figure 4. 74 ^{13}C NMR Spectrum of **91g**

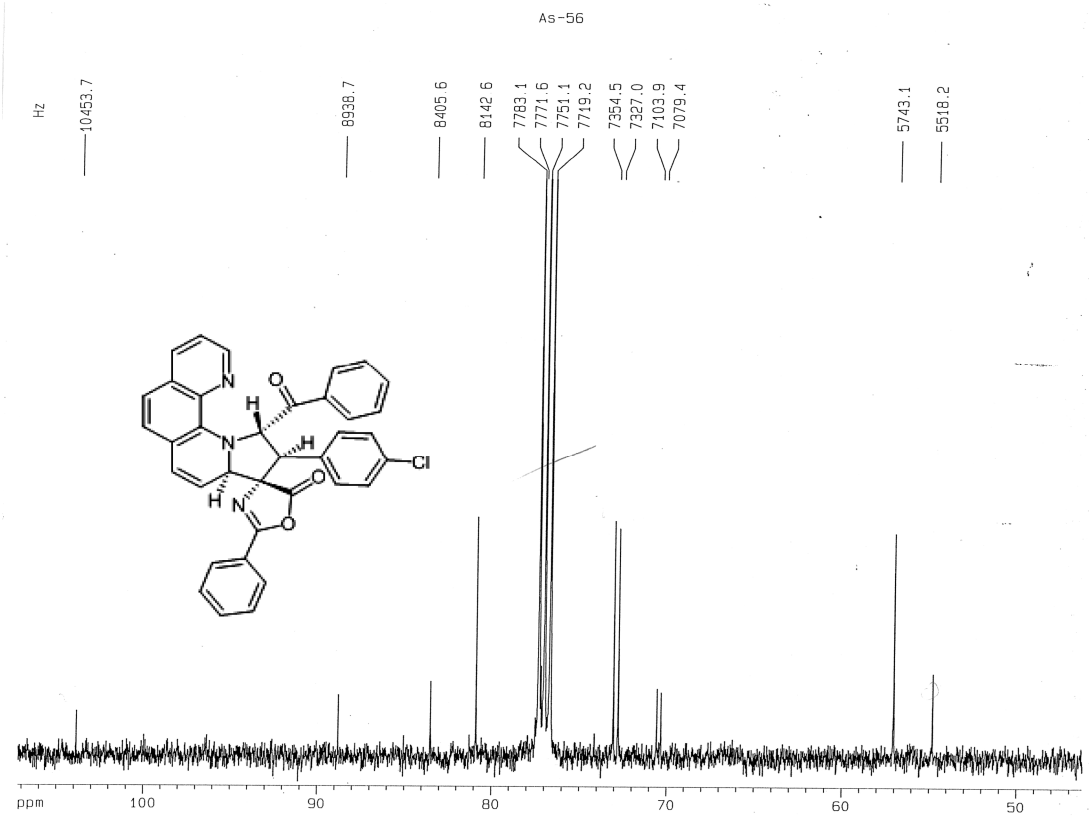

Figure 4. 75 Expanded (110-50 ppm) ^{13}C NMR Spectrum of **91g**

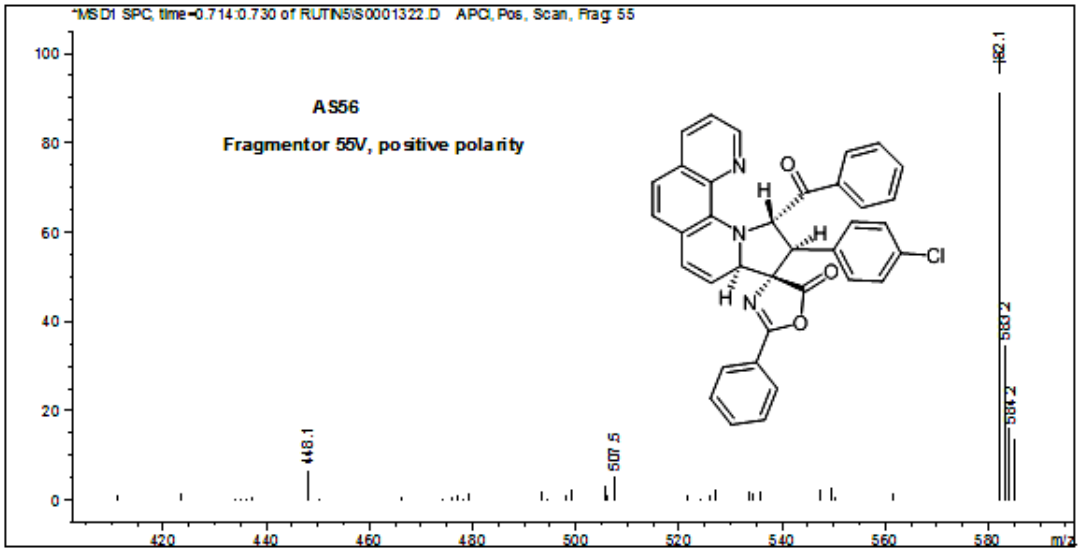

Figure 4. 76 MASS spectrum of **91g**

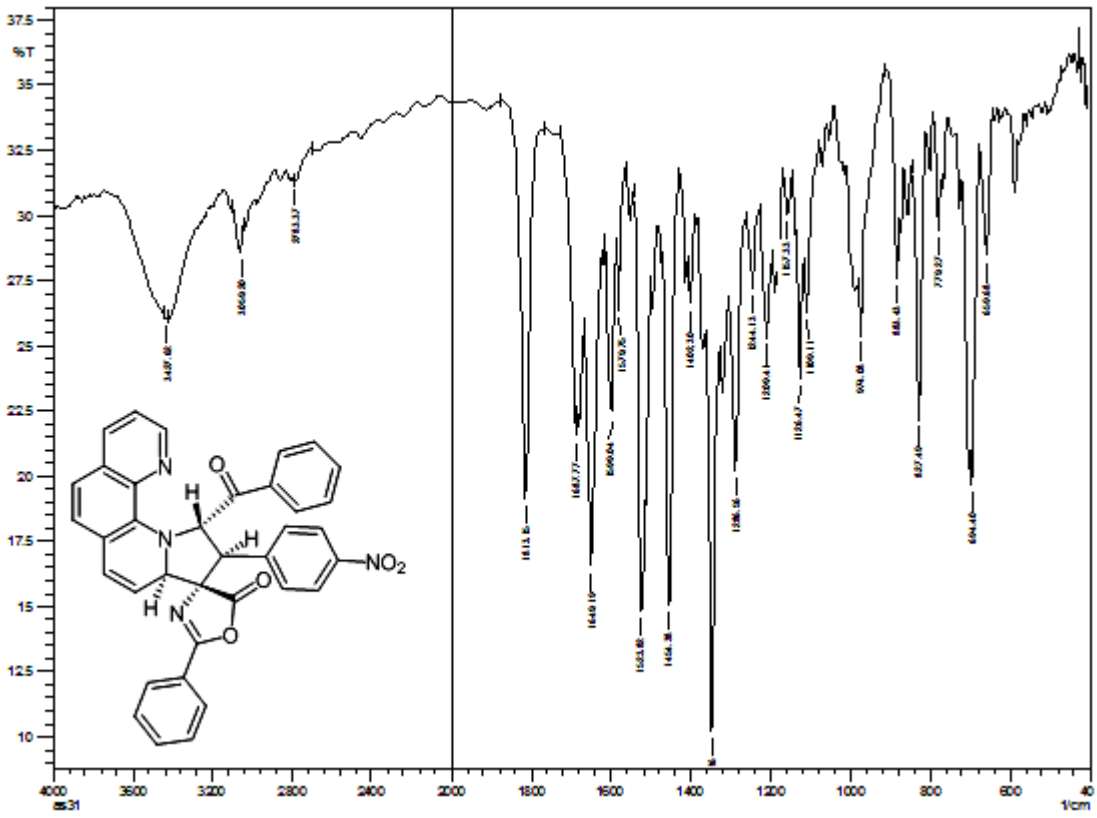

Figure 4. 77 IR Spectrum of **91h**

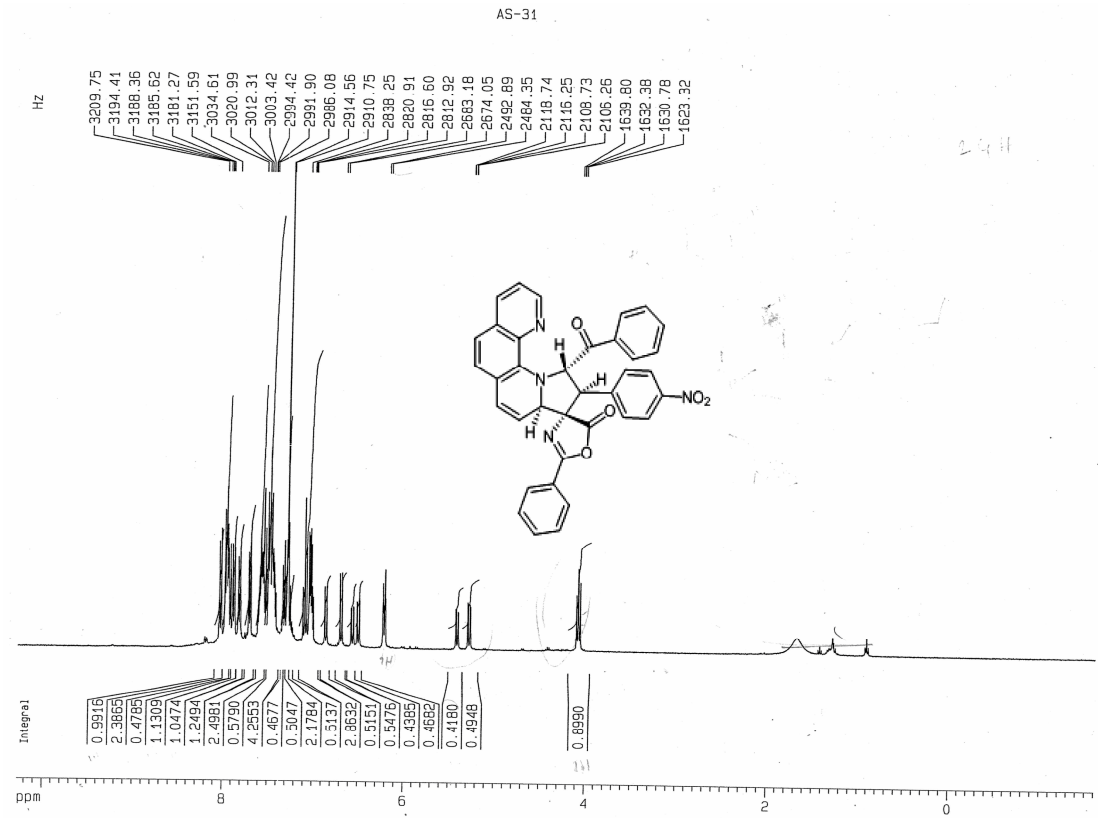

Figure 4. 78 ^{1}H NMR Spectrum of **91h**

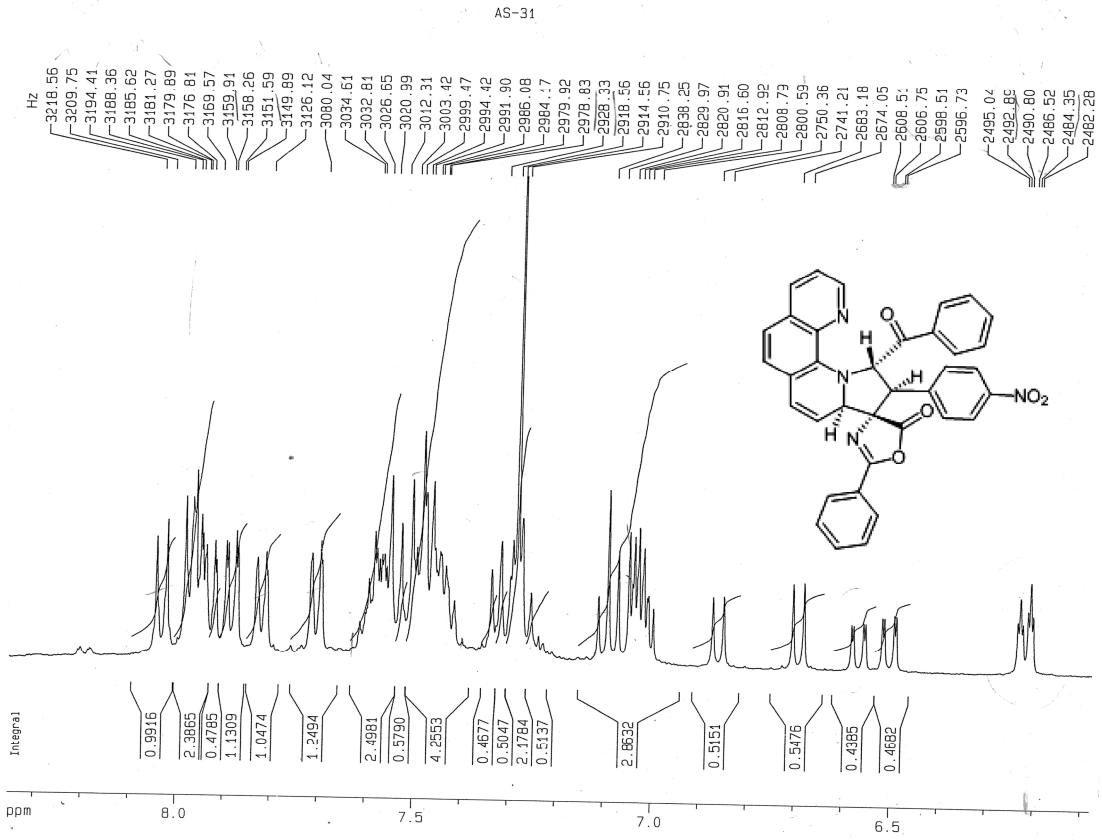

Figure 4. 79 Expanded (8.1-6.2 ppm) ^{1}H NMR Spectrum of **91h**

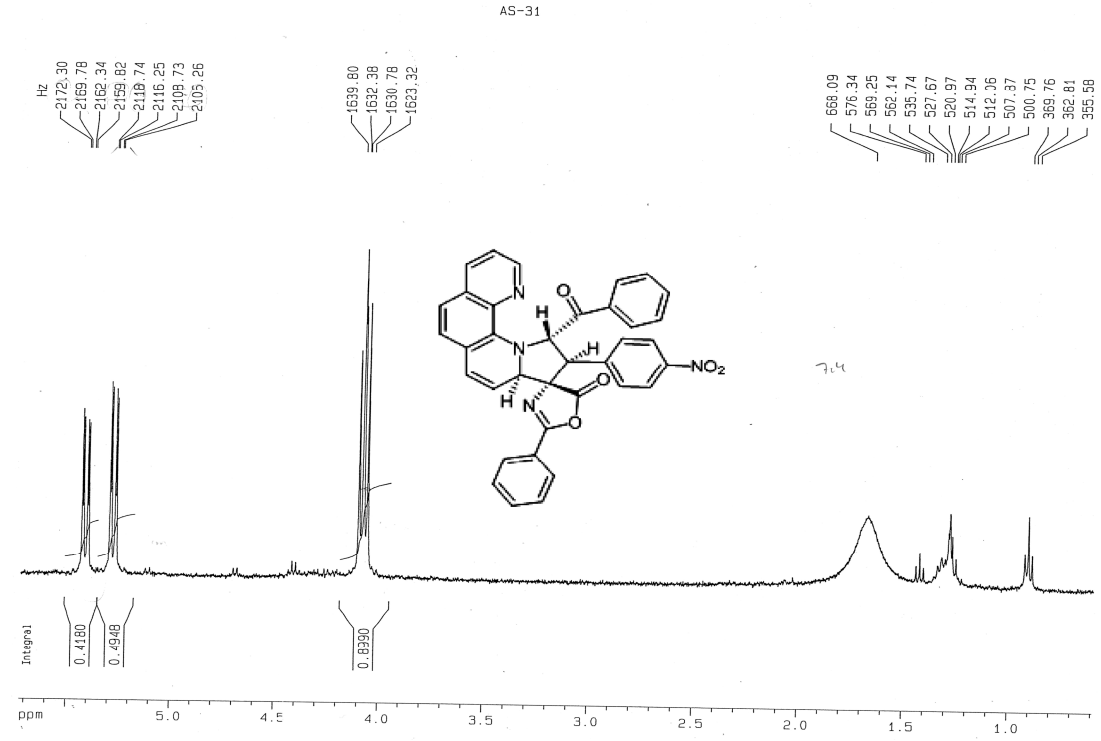

Figure 4. 80 Expanded (8.1-6.2 ppm) ^{1}H NMR Spectrum of **91h**

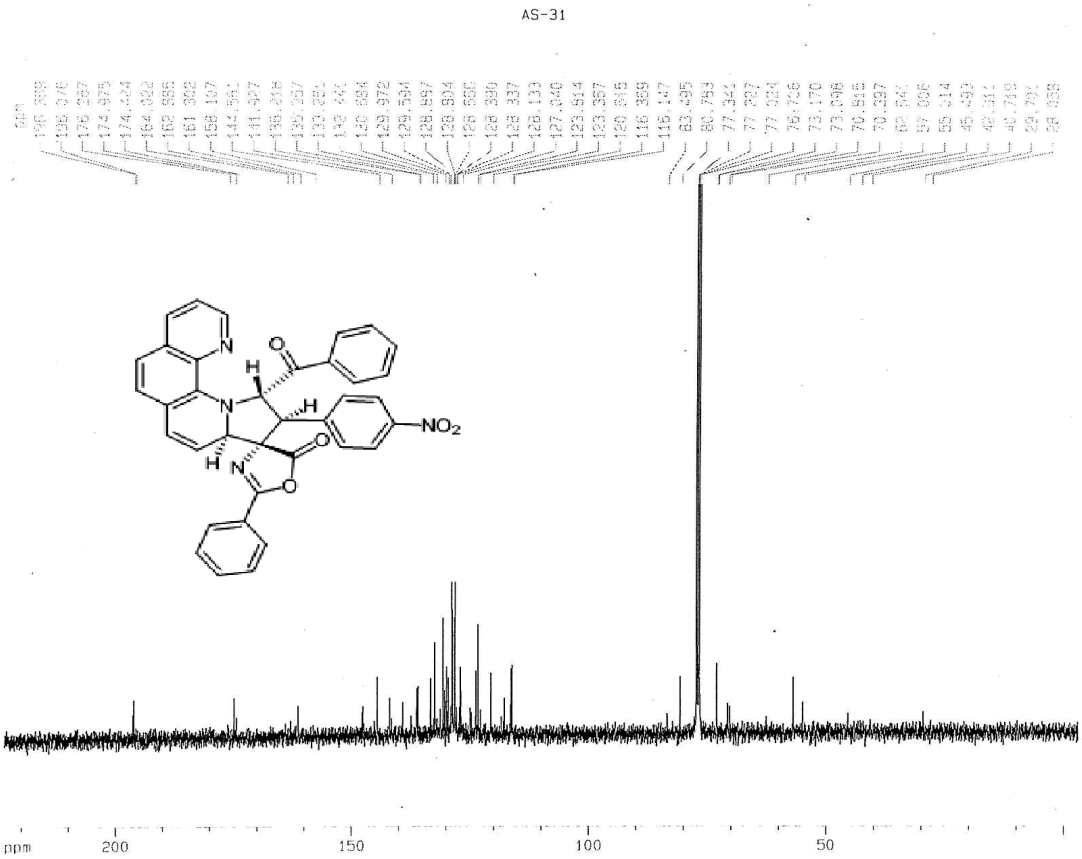

Figure 4. 81 ^{13}C NMR Spectrum of **91h**

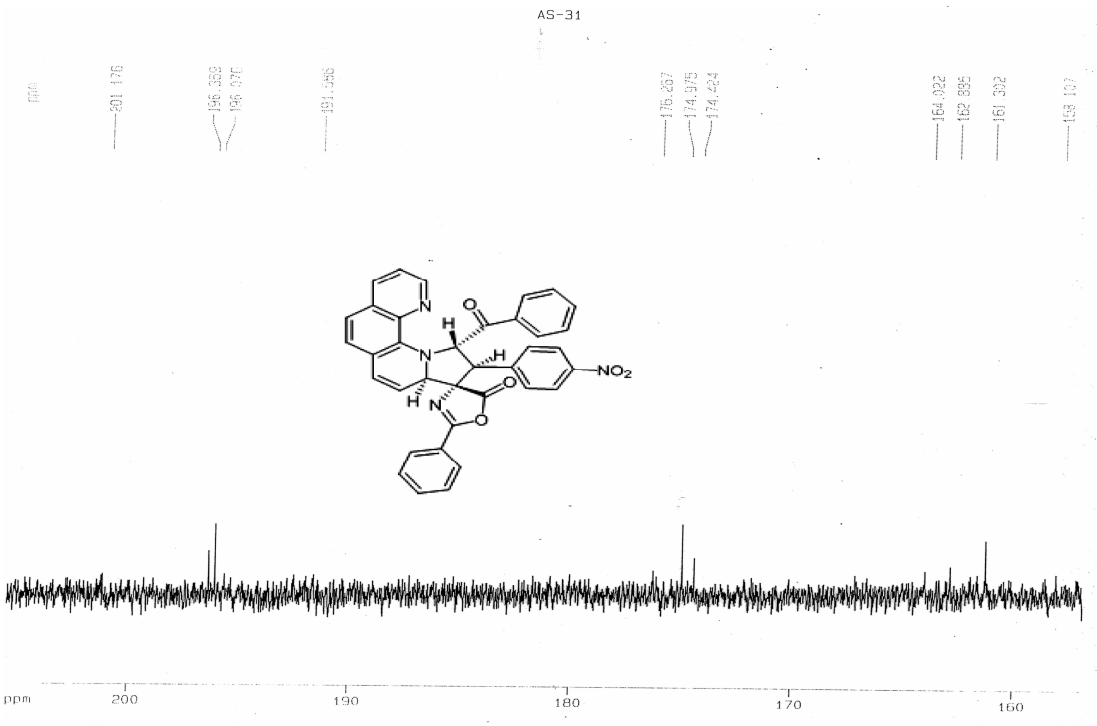

Figure 4. 82 Expanded (200-160 ppm) ^{13}C NMR Spectrum of **91h**

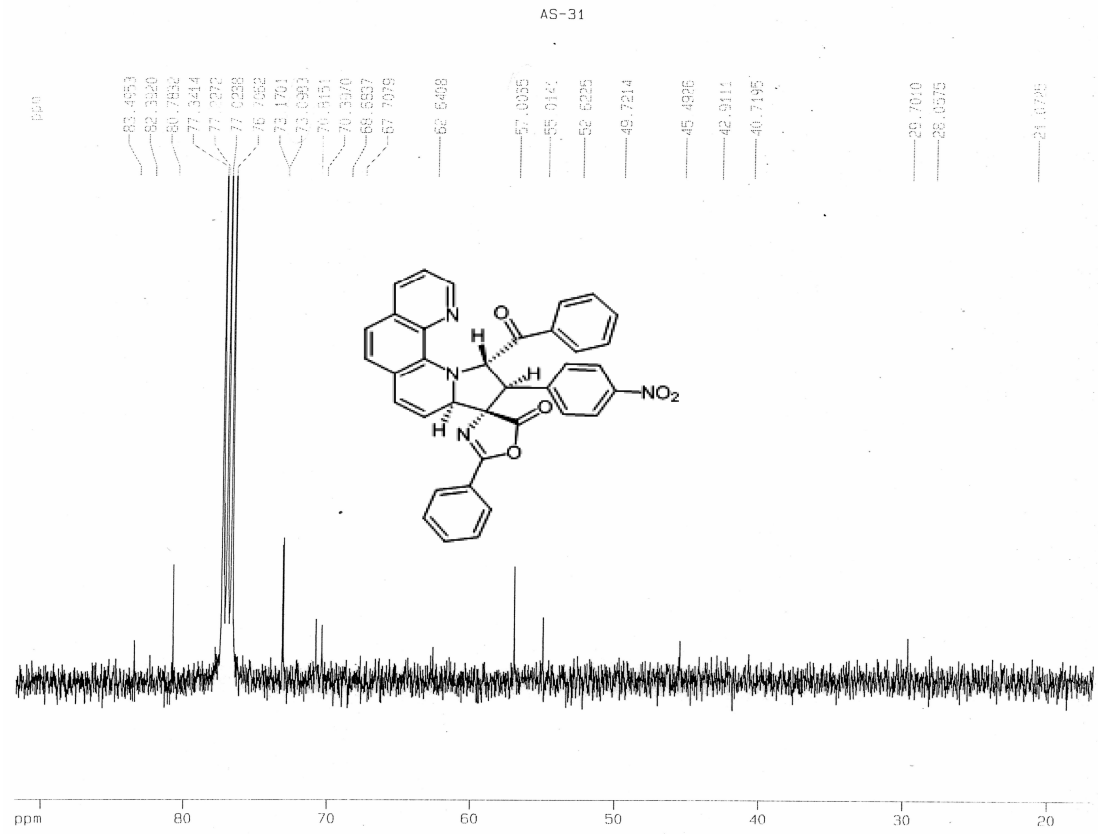

Figure 4. 83 Expanded (90-20 ppm) ^{13}C NMR Spectrum of **91h**

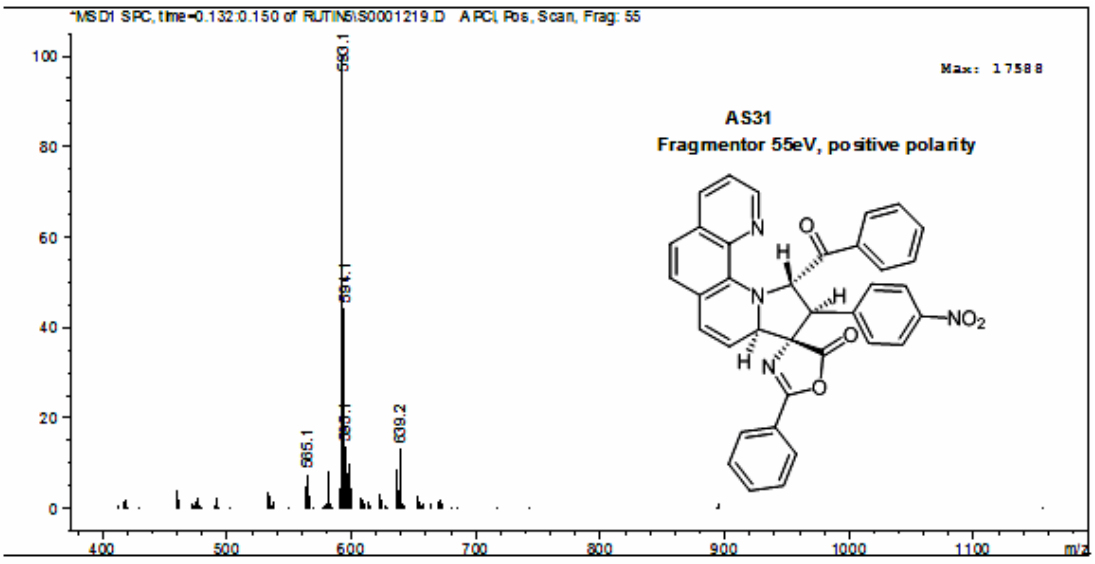

Figure 4. 84 MASS spectra of **91h**

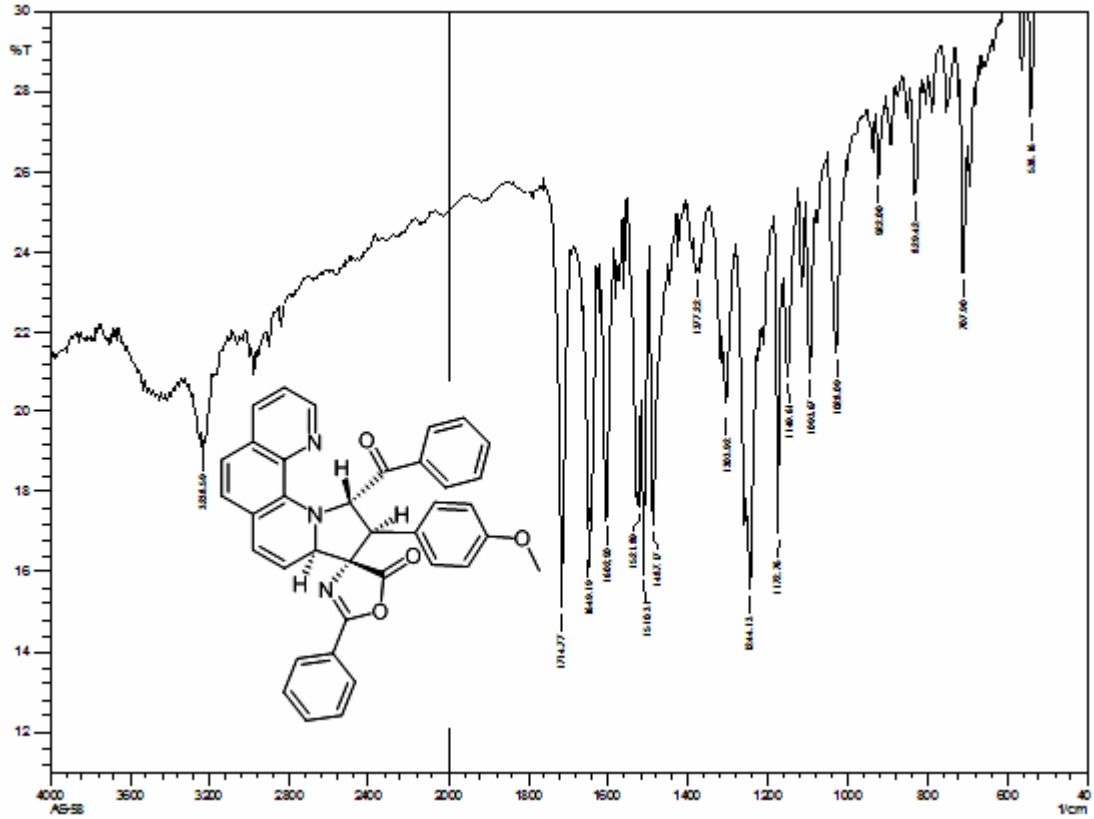

Figure 4. 85 IR Spectrum of **91j**

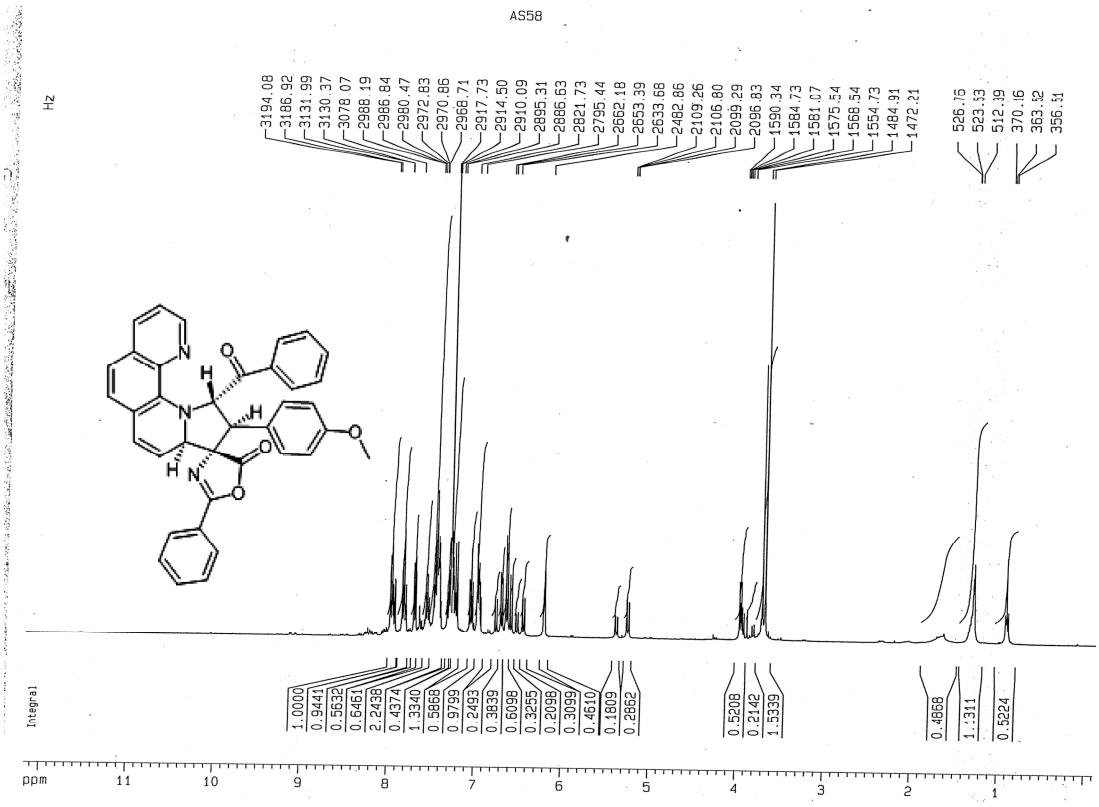

Figure 4. 86 ^{1}H NMR Spectrum of **91j**

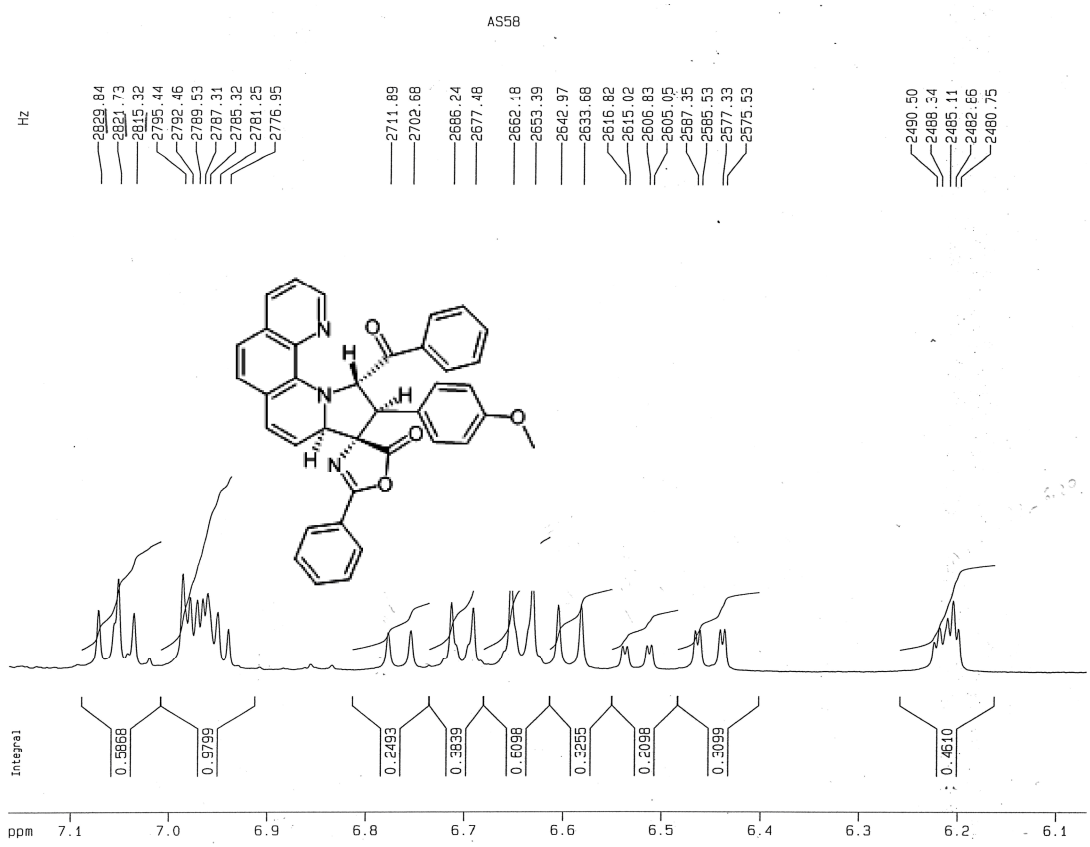

Figure 4. 87 Expanded (7.1-6.1 ppm) ^{1}H NMR Spectrum of **91j**

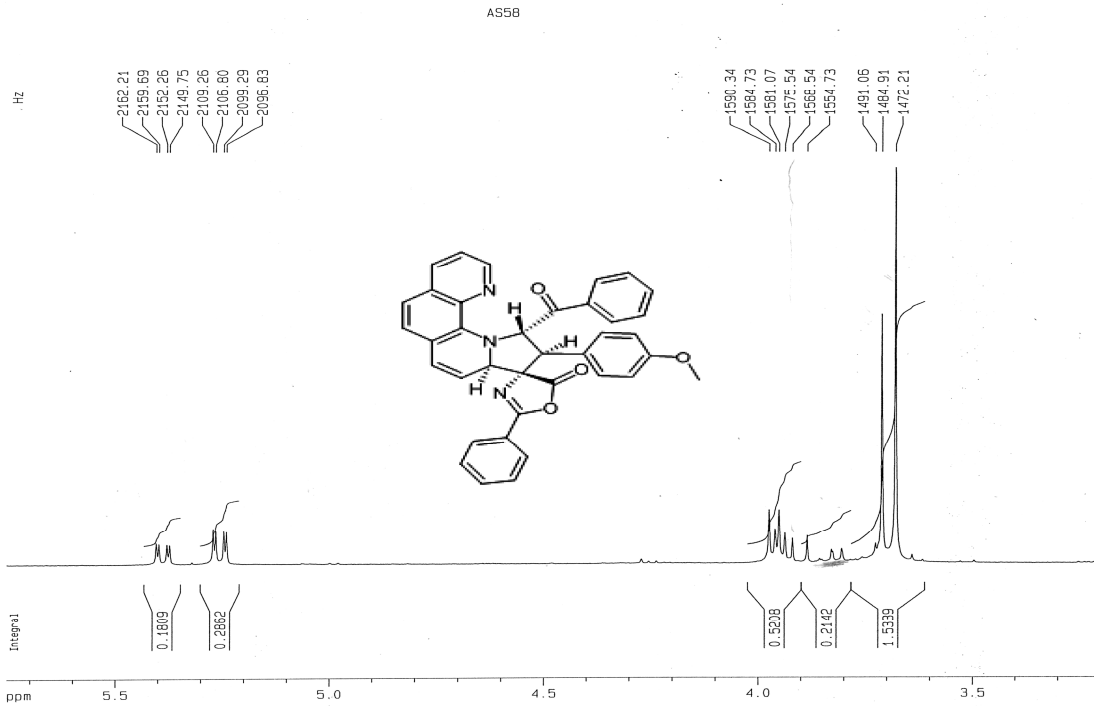

Figure 4. 88 Expanded (5.5-3.5 ppm) ^{1}H NMR Spectrum of **91j**

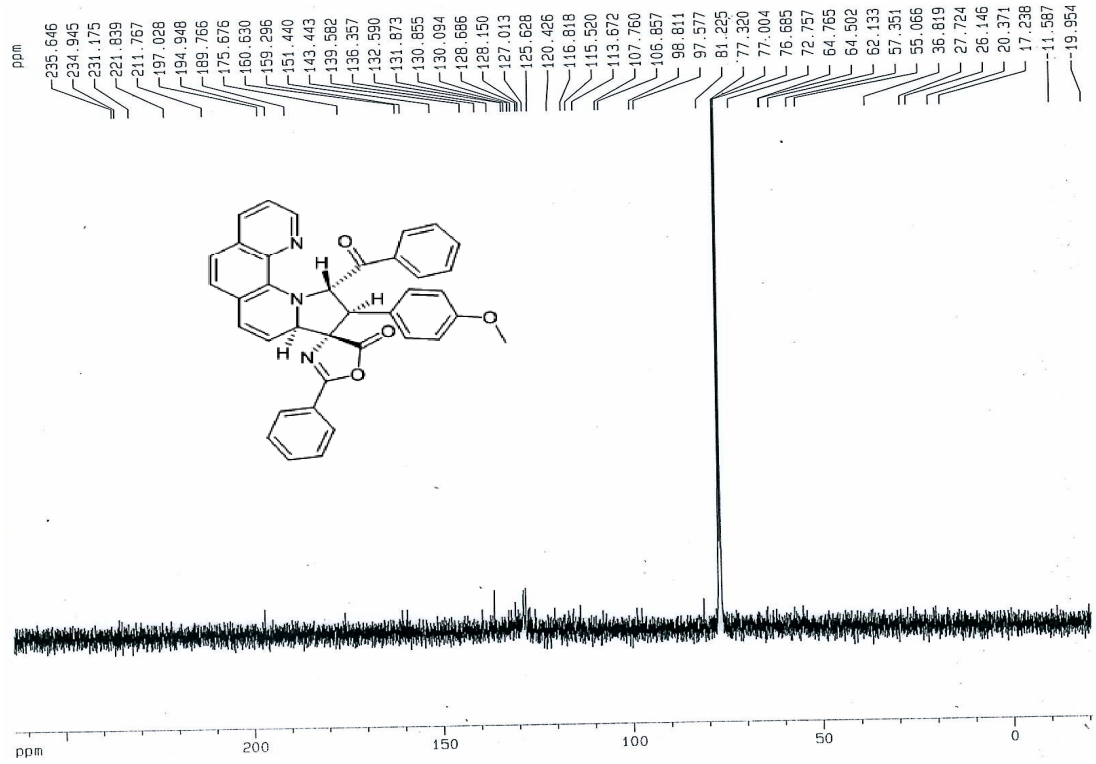

Figure 4. 89 ^{13}C NMR Spectrum of **91j**

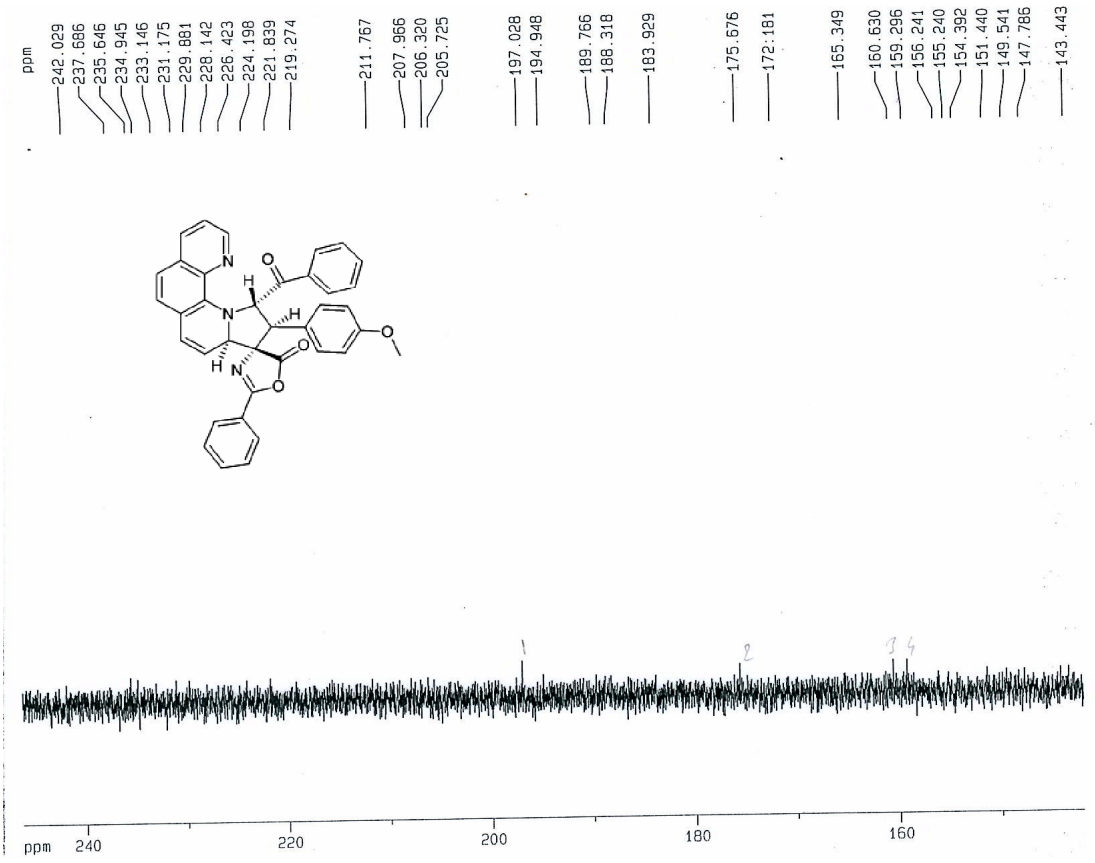

Figure 4. 90 Expanded (200-150 ppm) ^{13}C NMR Spectrum of **91j**

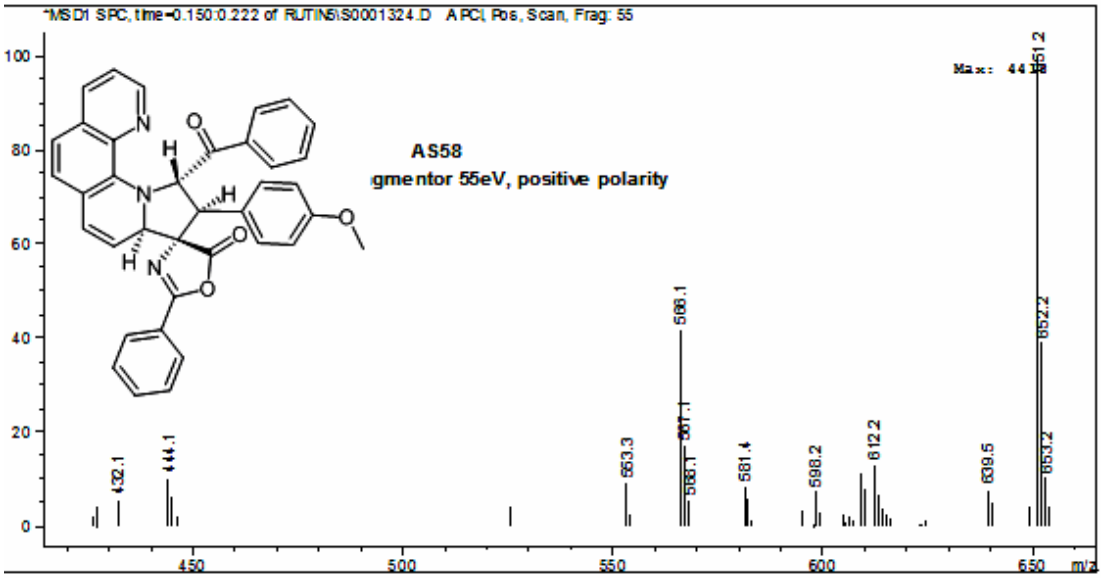

Figure 4. 91 MASS spectra of **91j**

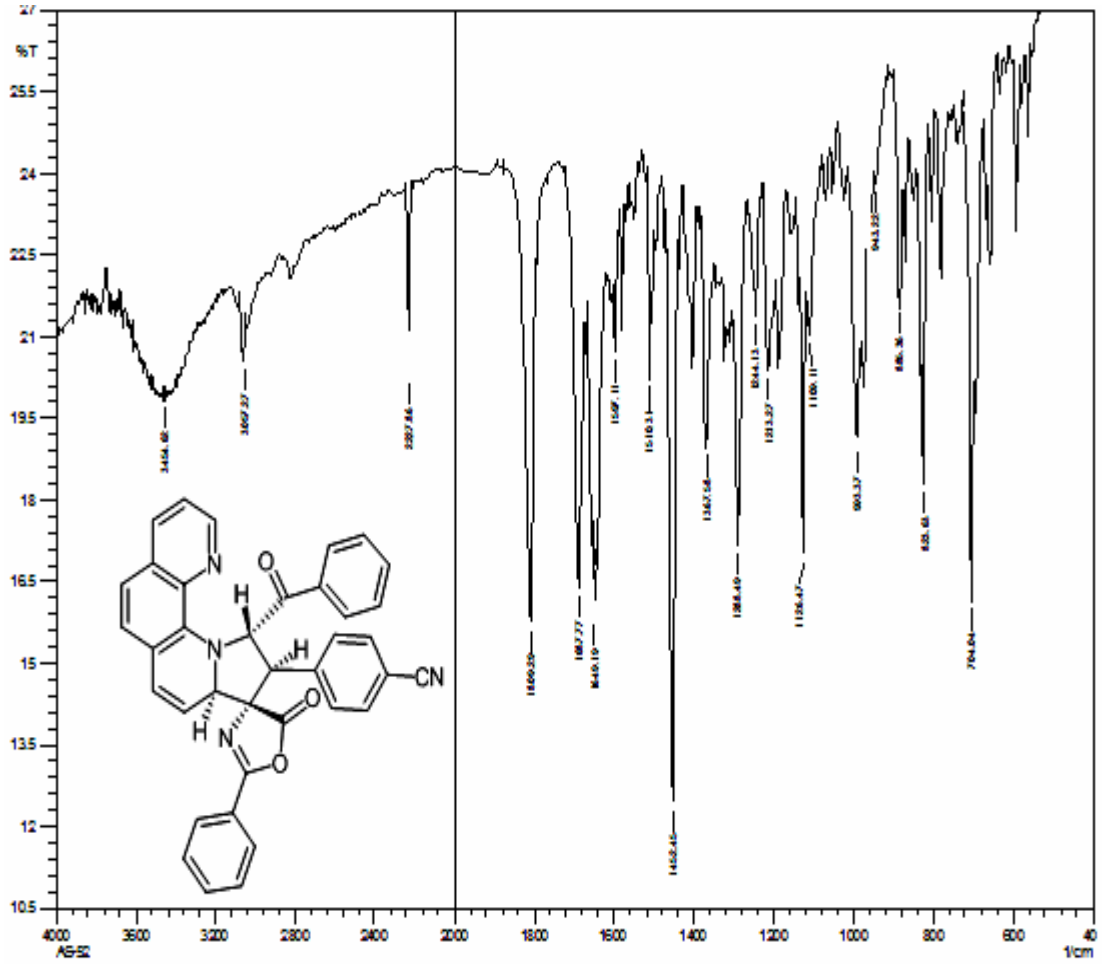

Figure 4. 92 IR Spectrum of **91k**

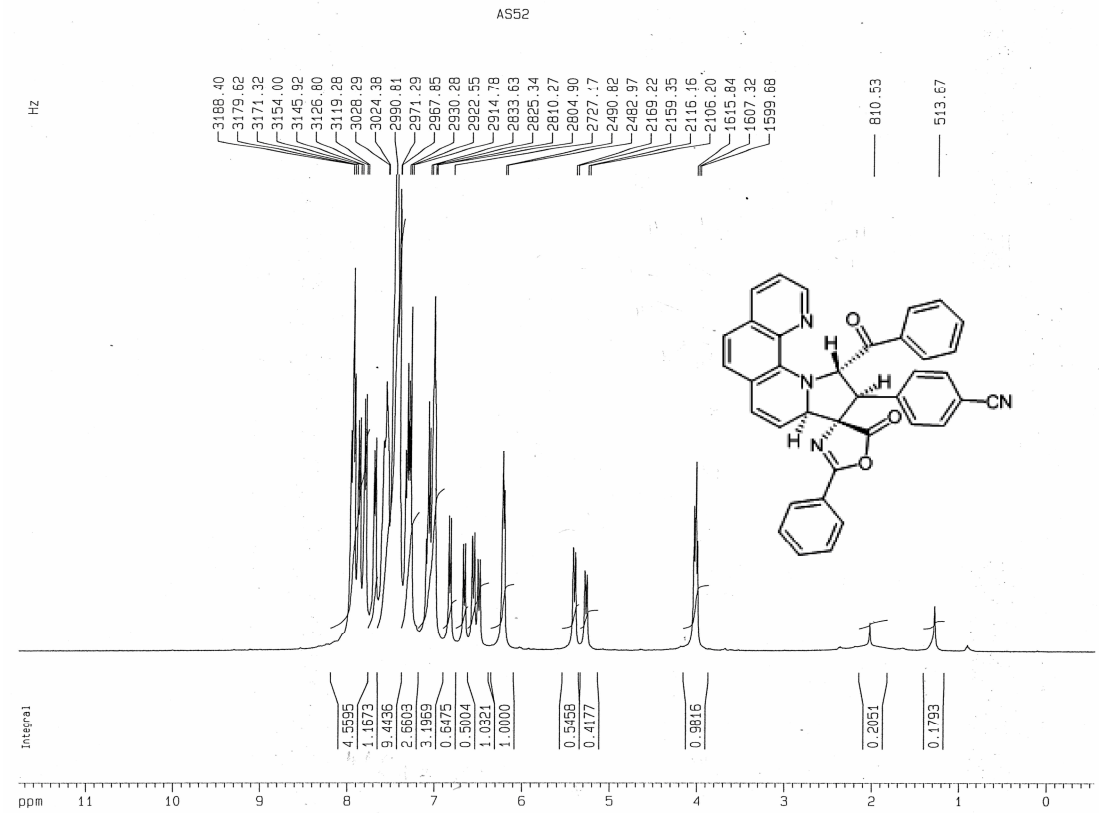

Figure 4. 93 ^{1}H NMR Spectrum of **91k**

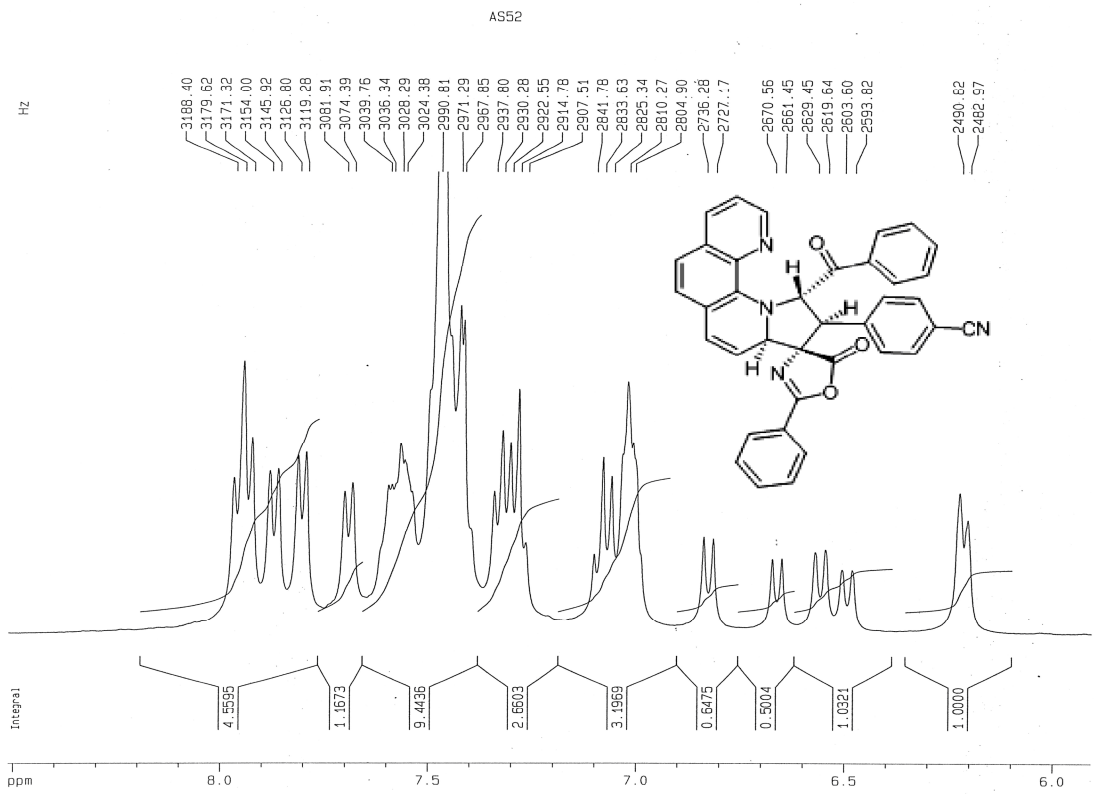

Figure 4. 94 Expanded (8.0-6.0 ppm) ^{1}H NMR Spectrum of **91k**

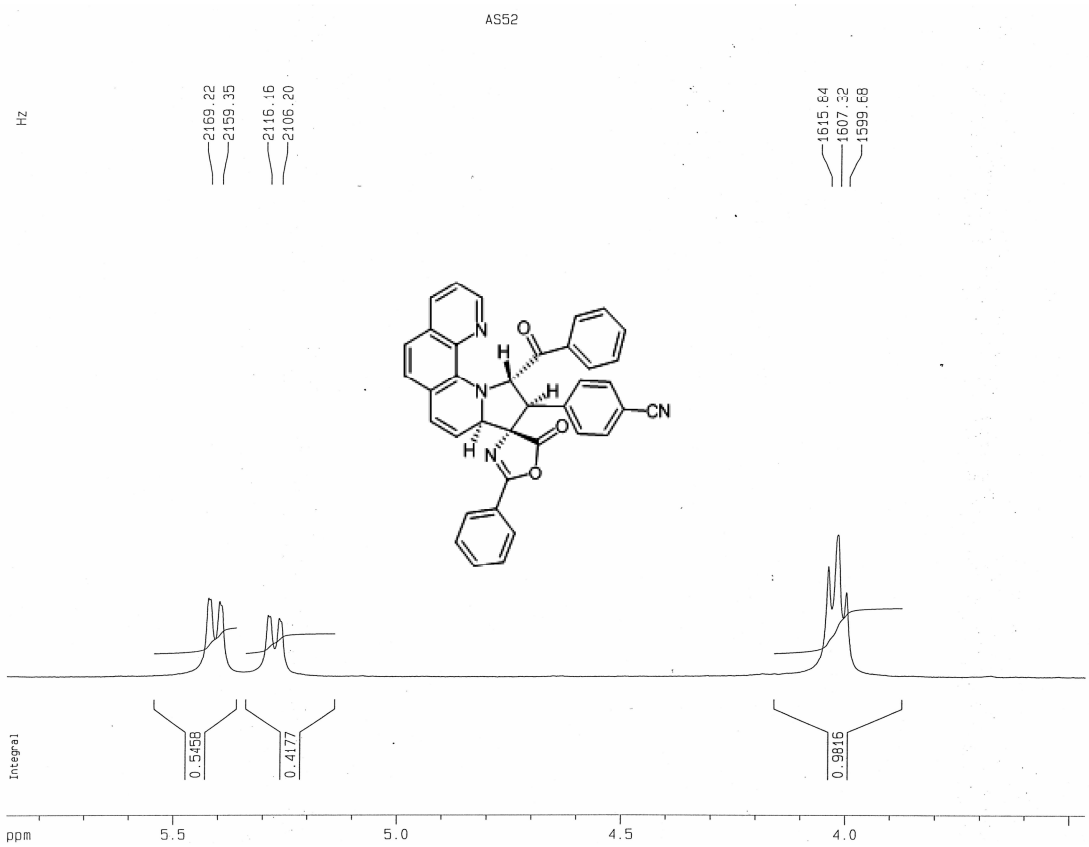

Figure 4. 95 Expanded (5.5-4.0 ppm) ^{1}H NMR Spectrum of **91k**

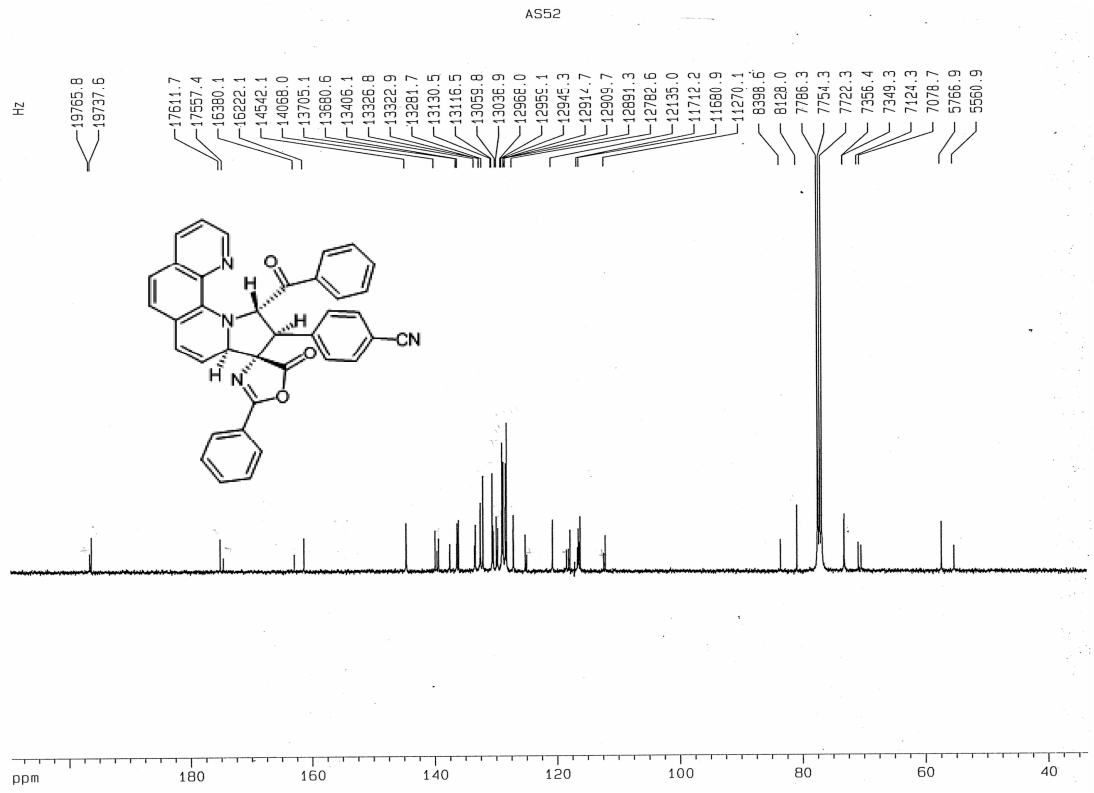

Figure 4. 96 ^{13}C NMR Spectrum of **91k**

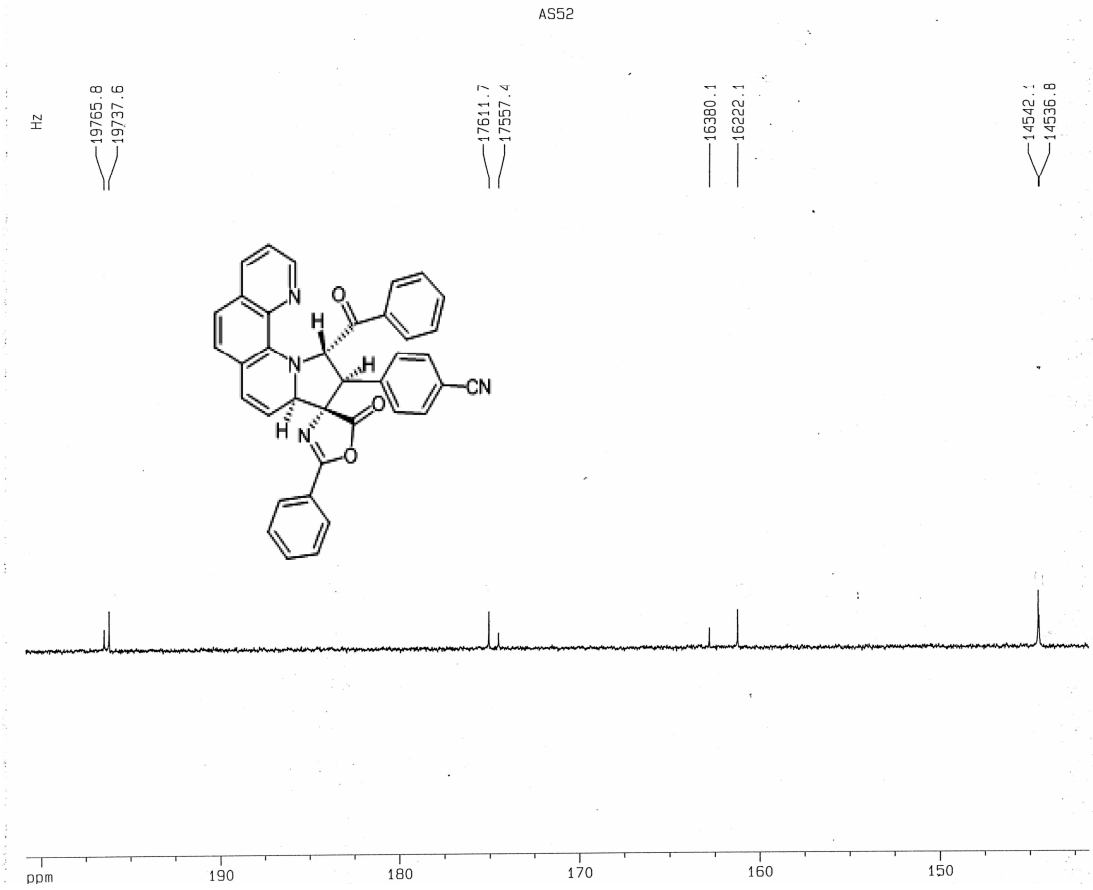

Figure 4. 97 Expanded (200-135 ppm) ^{13}C NMR Spectrum of **91k**

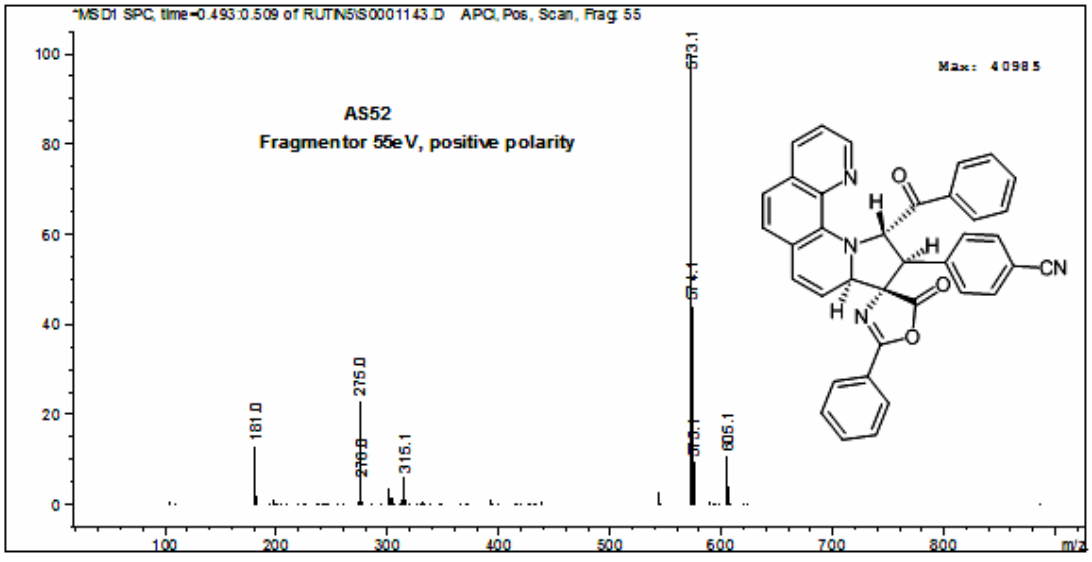

Figure 4. 98 MASS spectra of **91k**

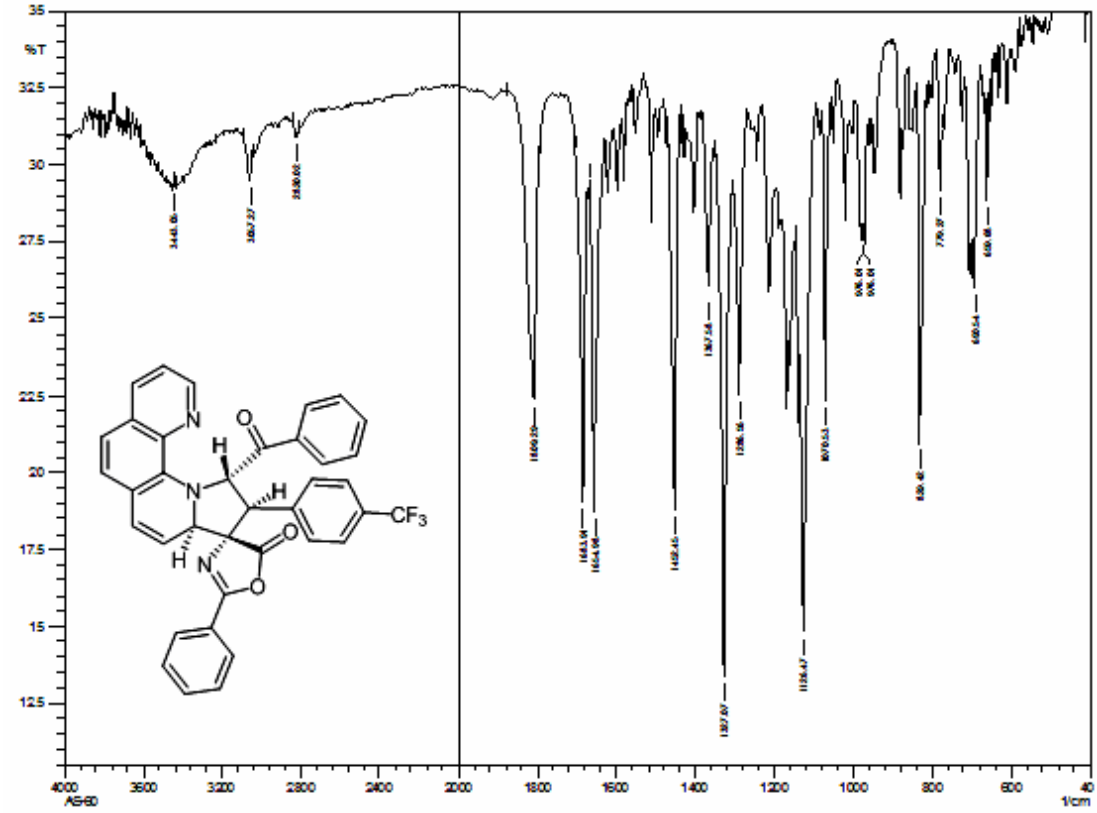

Figure 4. 99 IR Spectrum of **91l**

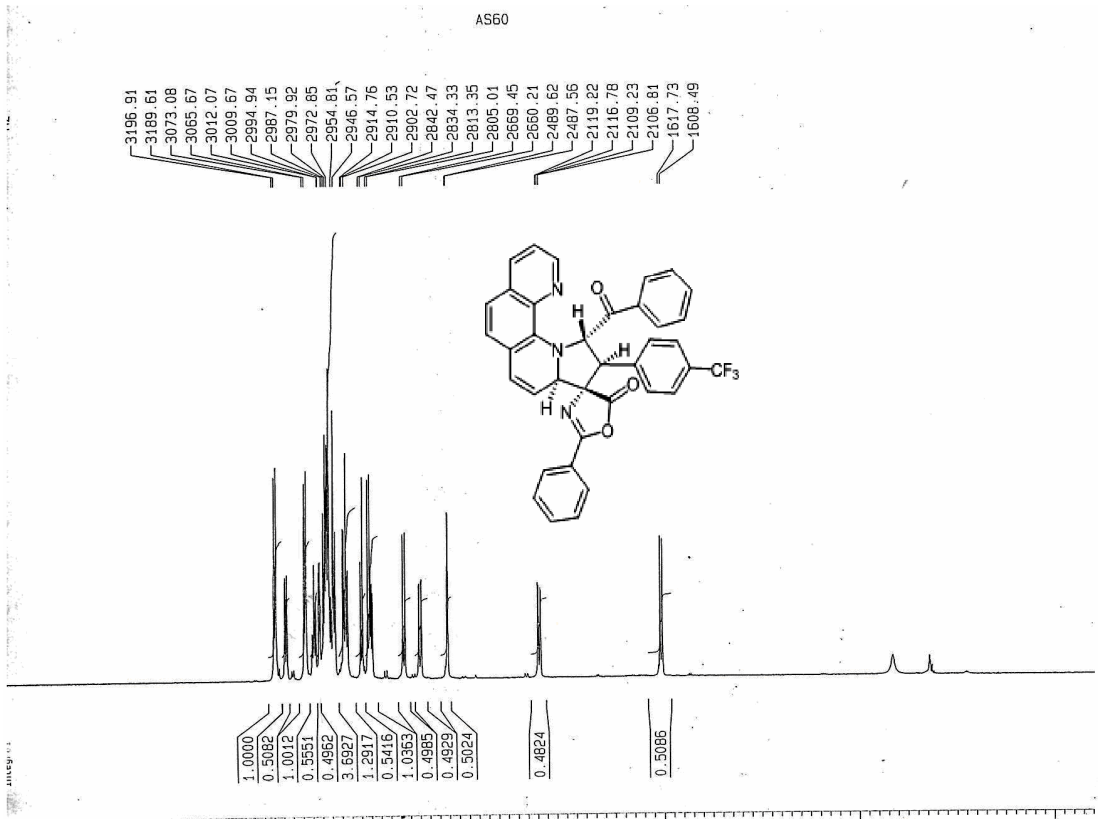

Figure 4. 100 ^{1}H NMR Spectrum of **91l**

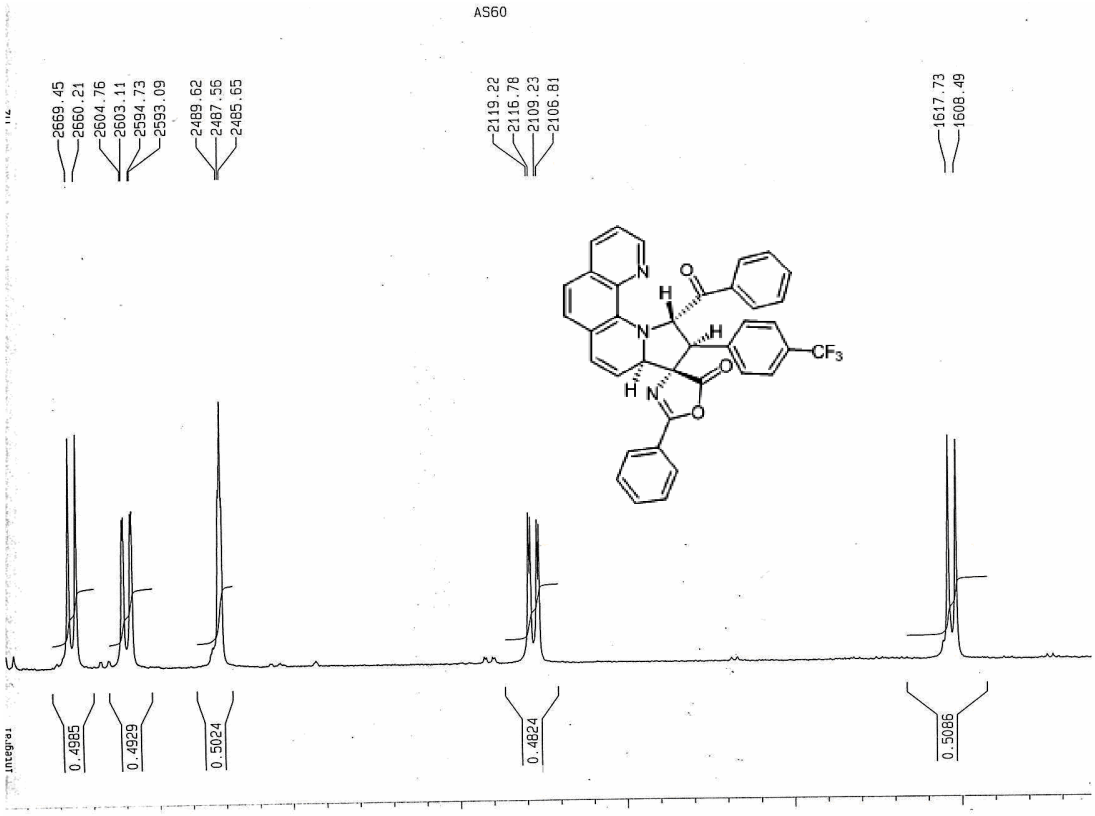

Figure 4. 101 Expanded (7.5-3.0 ppm) ^{1}H NMR Spectrum of **91l**

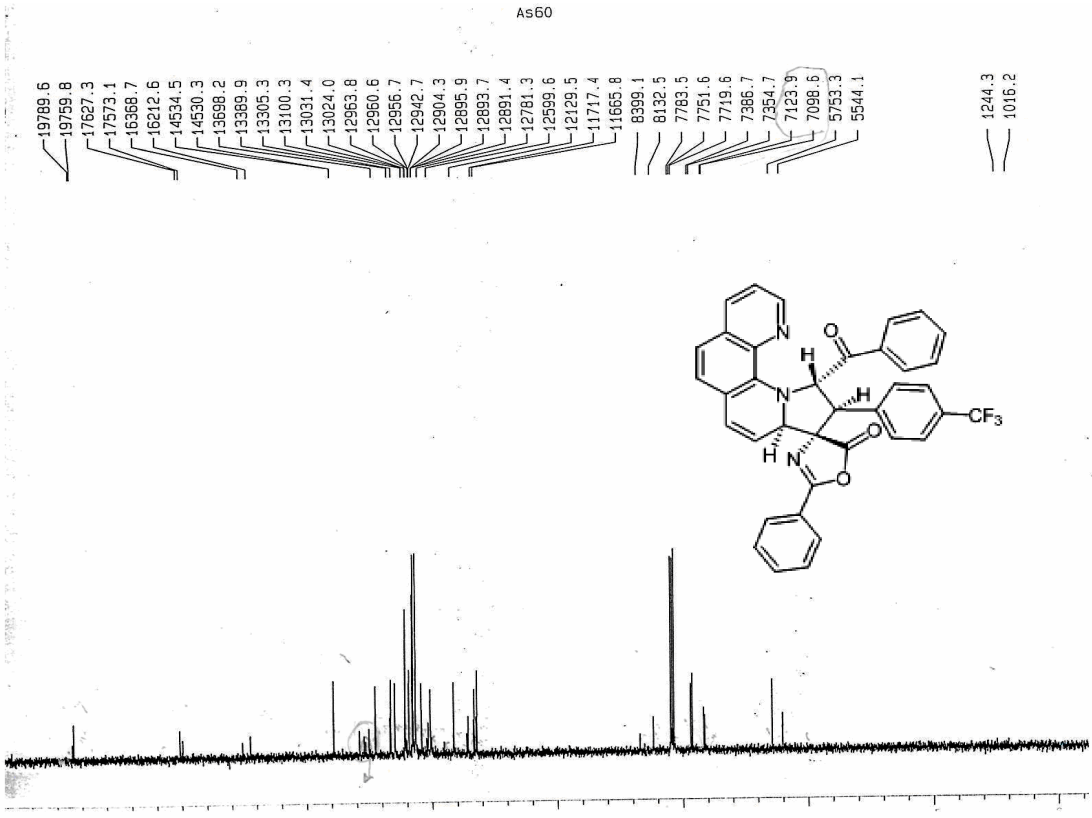

Figure 4. 102 ^{13}C NMR Spectrum of **91l**

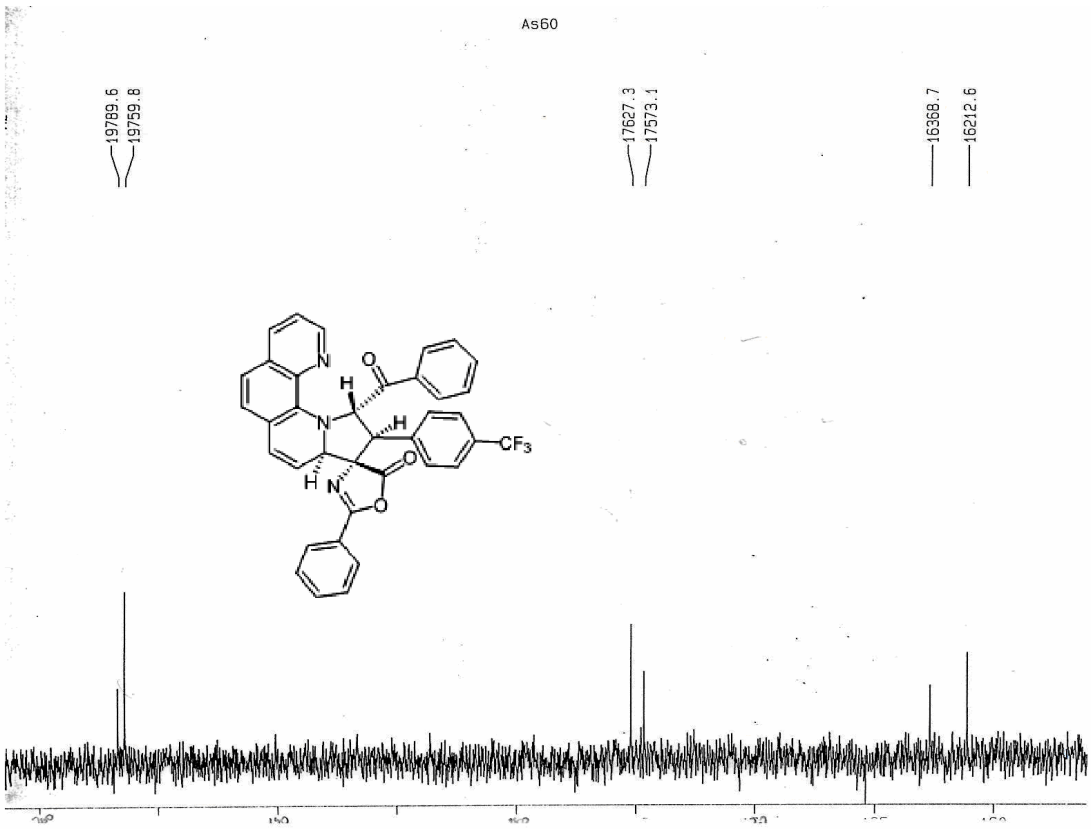

Figure 4. 103 Expanded (200-160 ppm) ^{13}C NMR Spectrum of **91l**

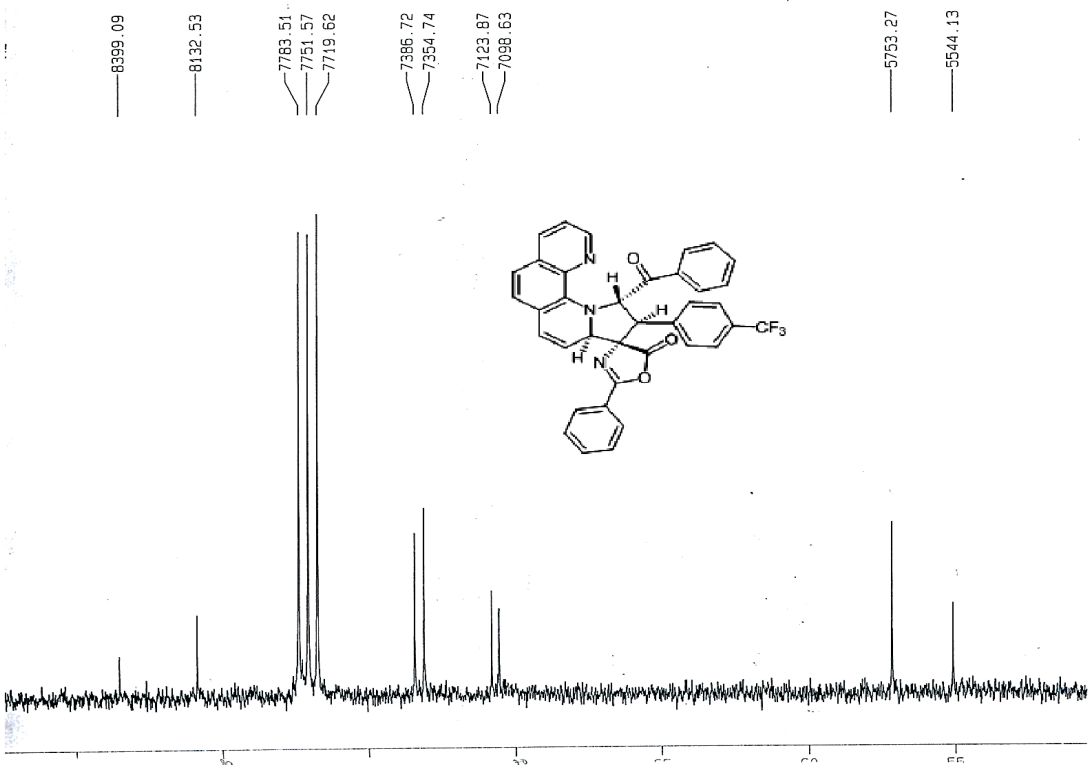

Figure 4. 104 Expanded (85-55 ppm) ^{13}C NMR Spectrum of **91l**

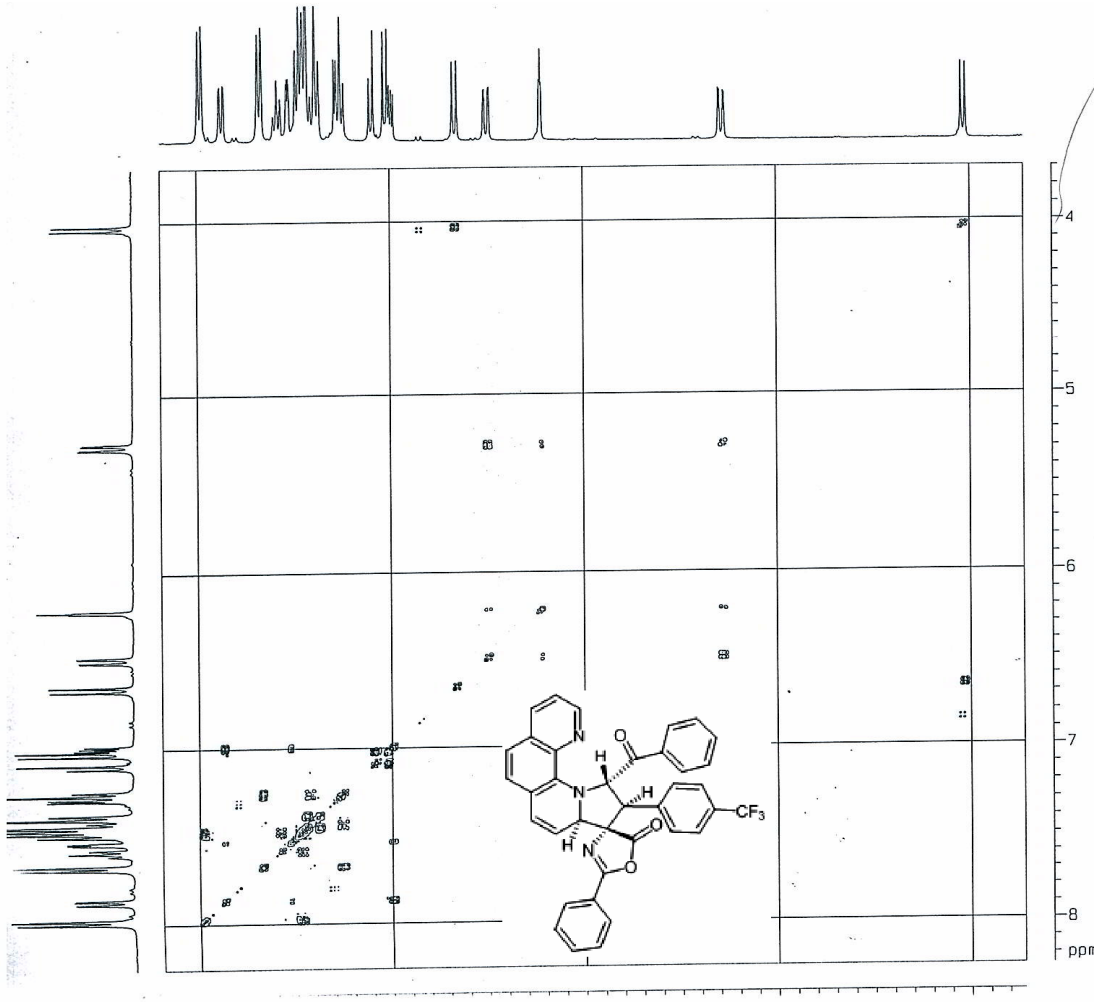

Figure 4. 105 COSY NMR Spectrum of **91l**

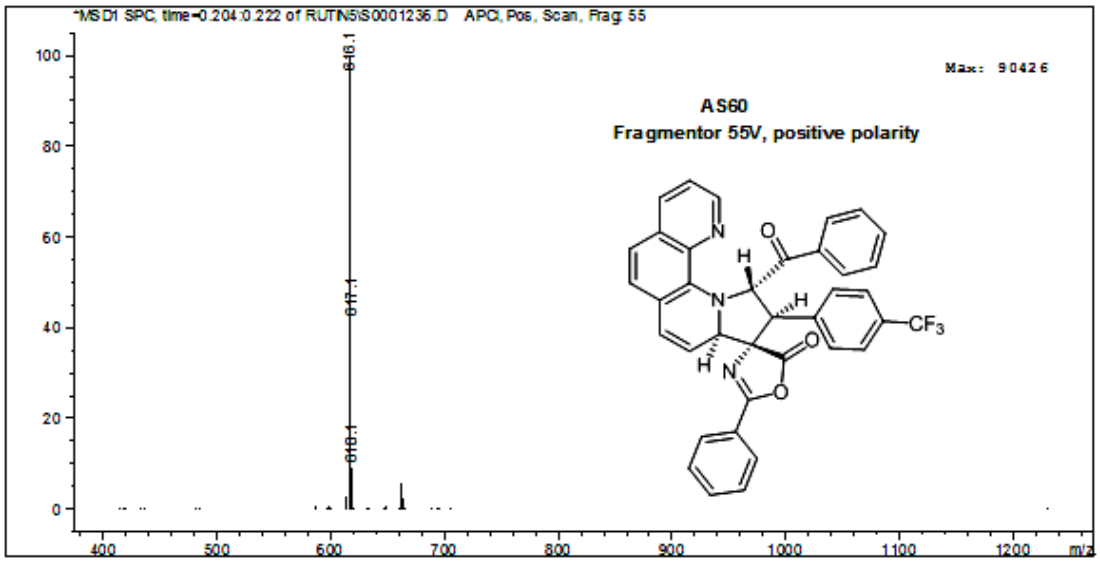

Figure 4. 106 MASS spectra of **91l**

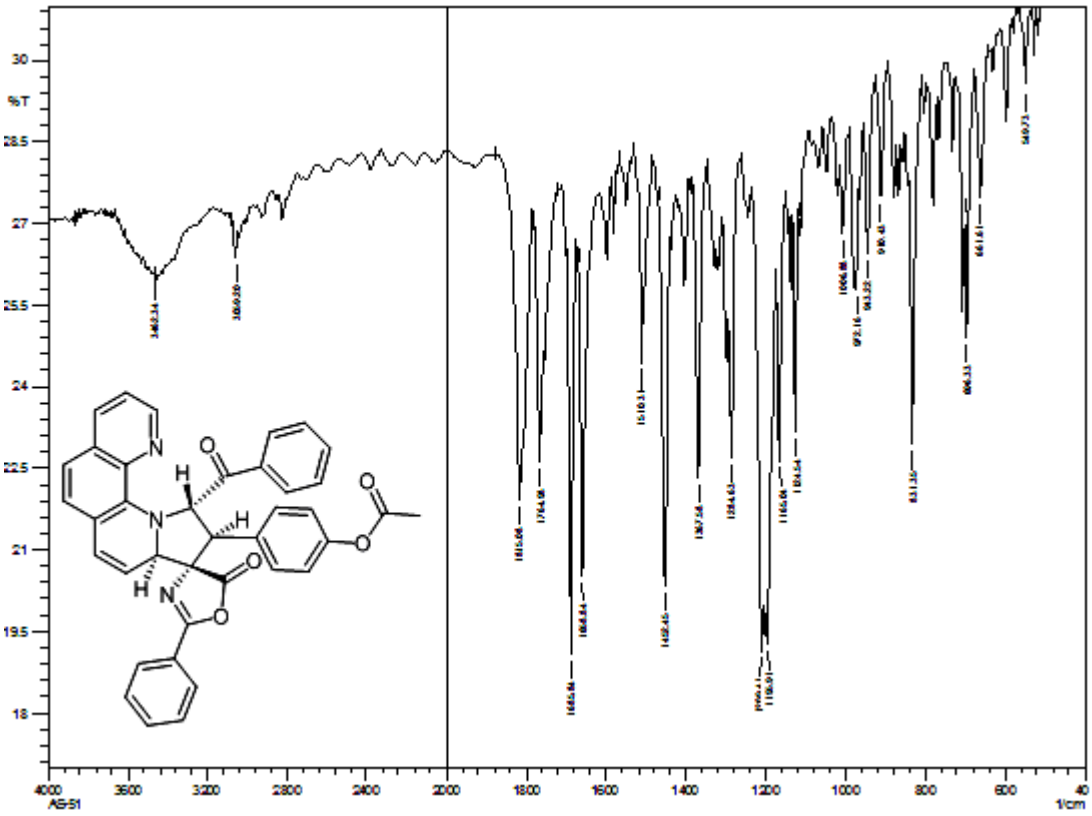

Figure 4. 107 IR Spectrum of **91m**

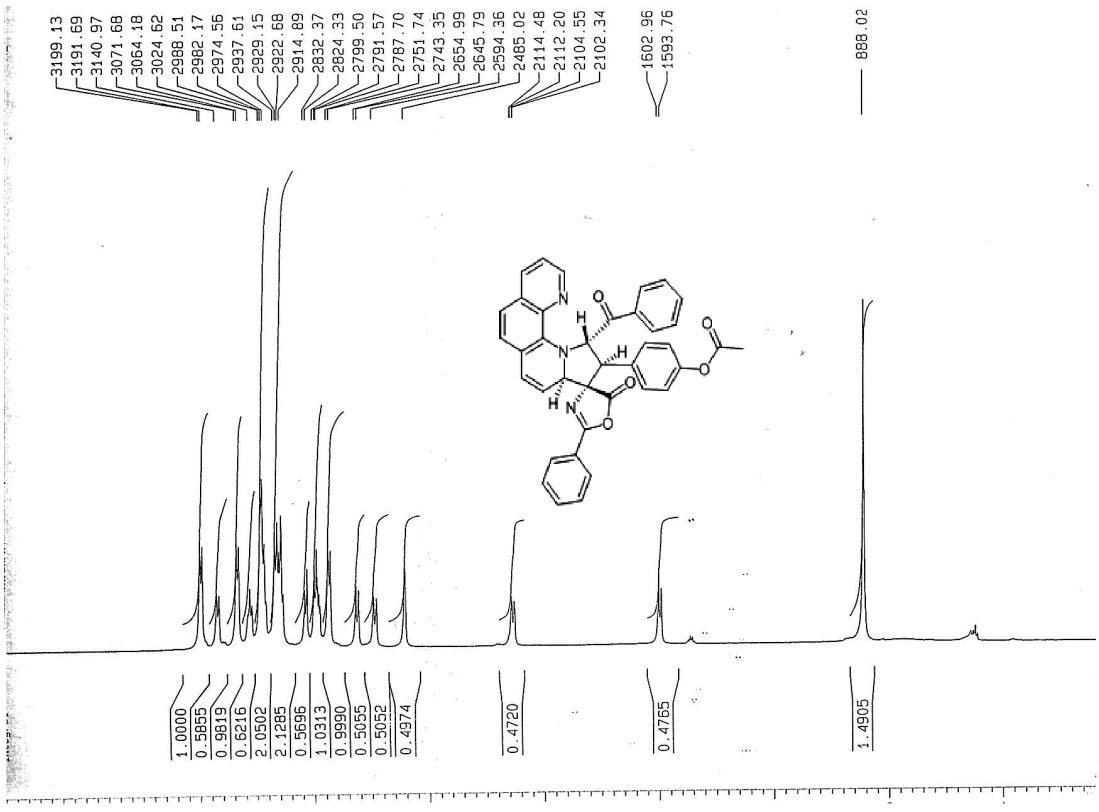

Figure 4. 108 ^{1}H NMR Spectrum of **91m**

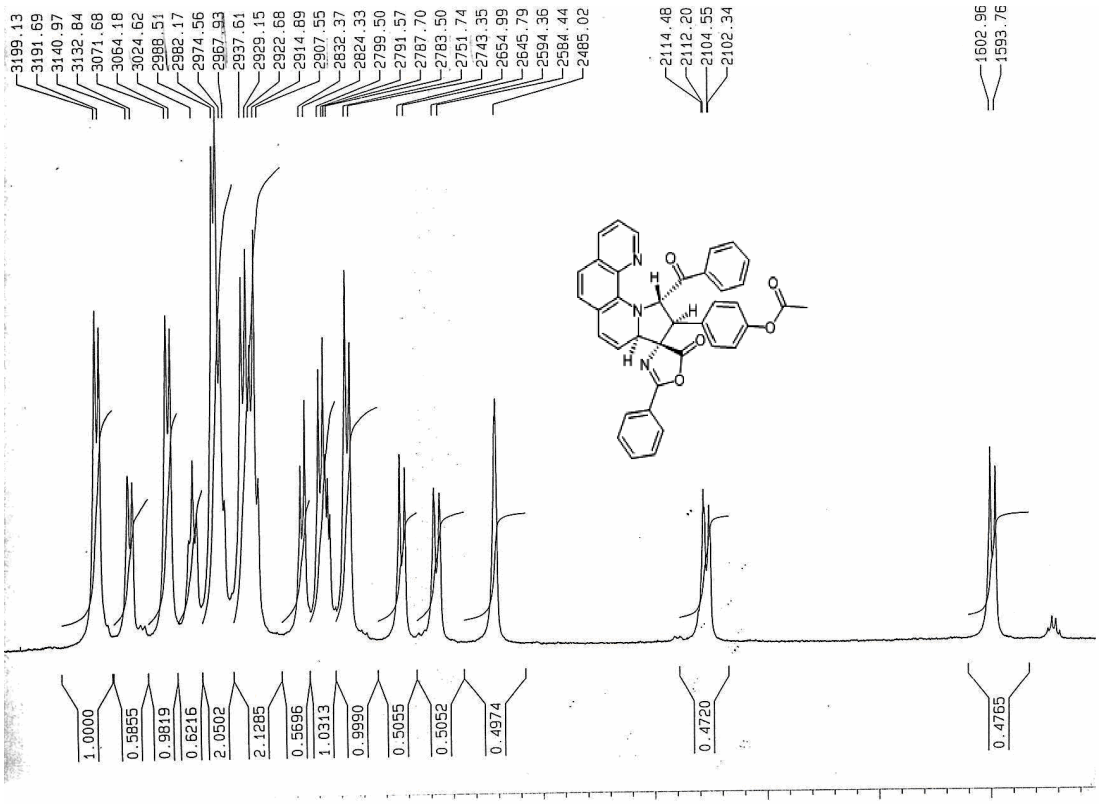

Figure 4. 109 Expanded (8.0-4.0 ppm) ^{1}H NMR Spectrum of **91m**

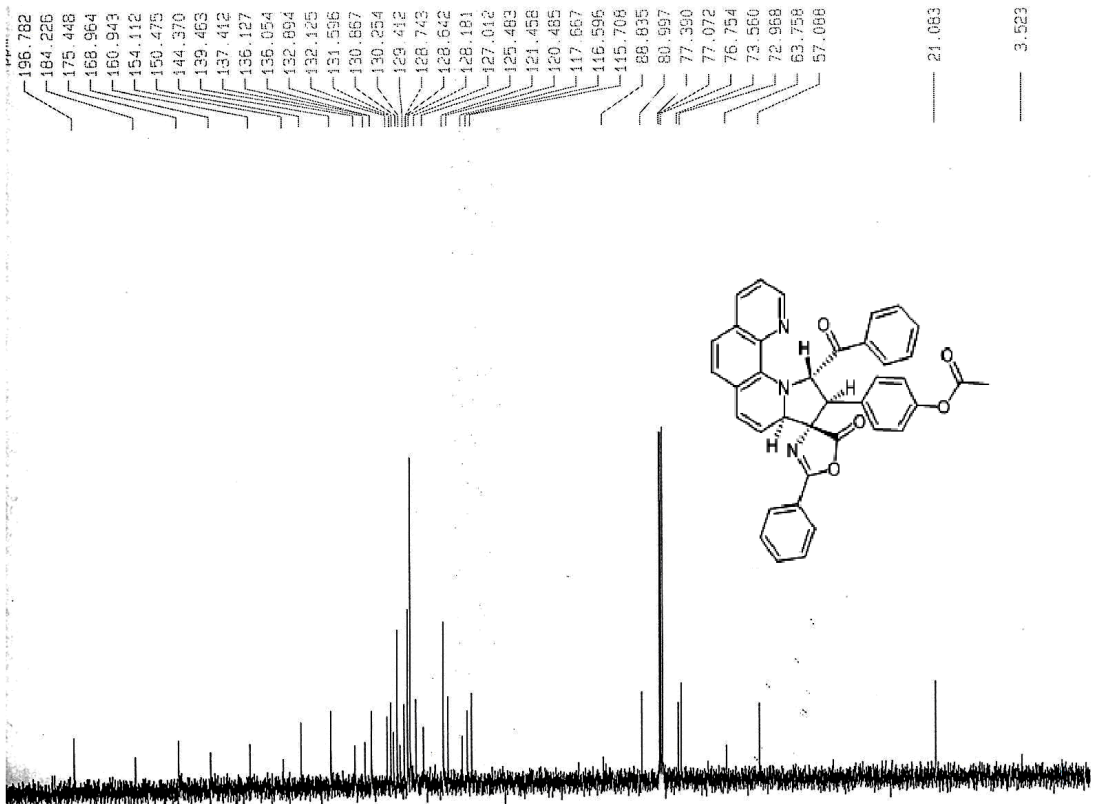

Figure 4. 110 ^{13}C NMR Spectrum of **91m**

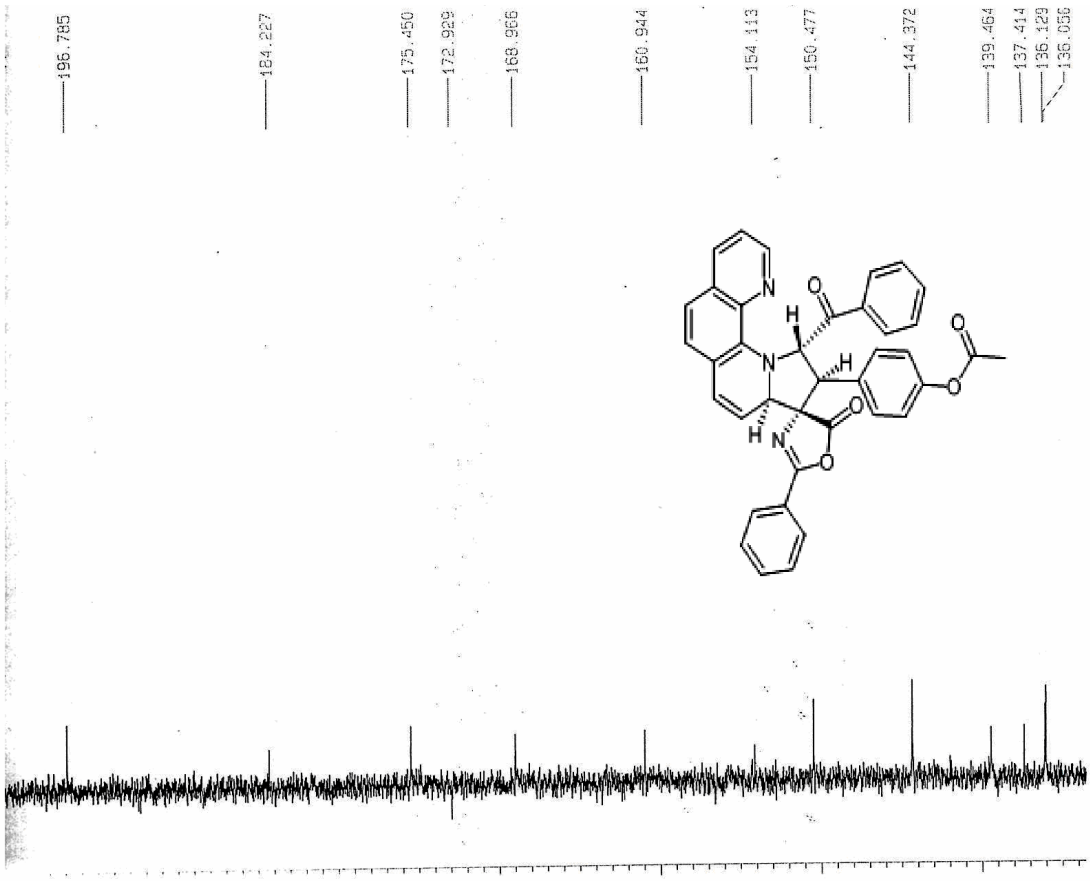

Figure 4. 111 Expanded (200-135 ppm) ^{13}C NMR Spectrum of **91m**

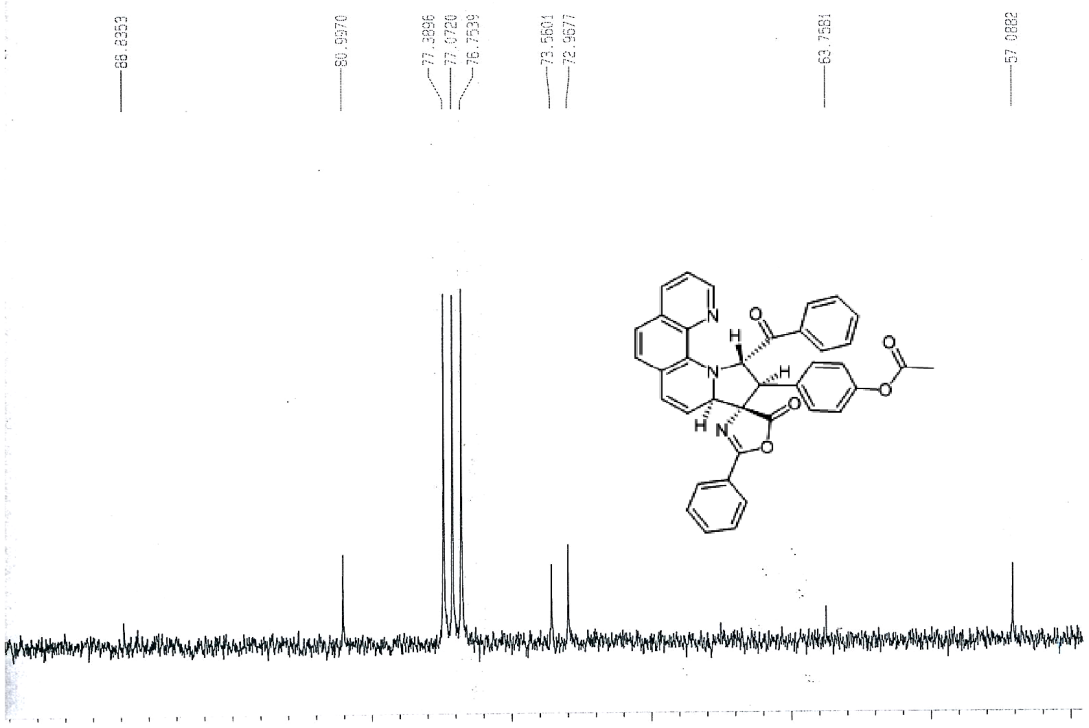

Figure 4. 112 Expanded (90-55 ppm) ^{13}C NMR Spectrum of **91m**

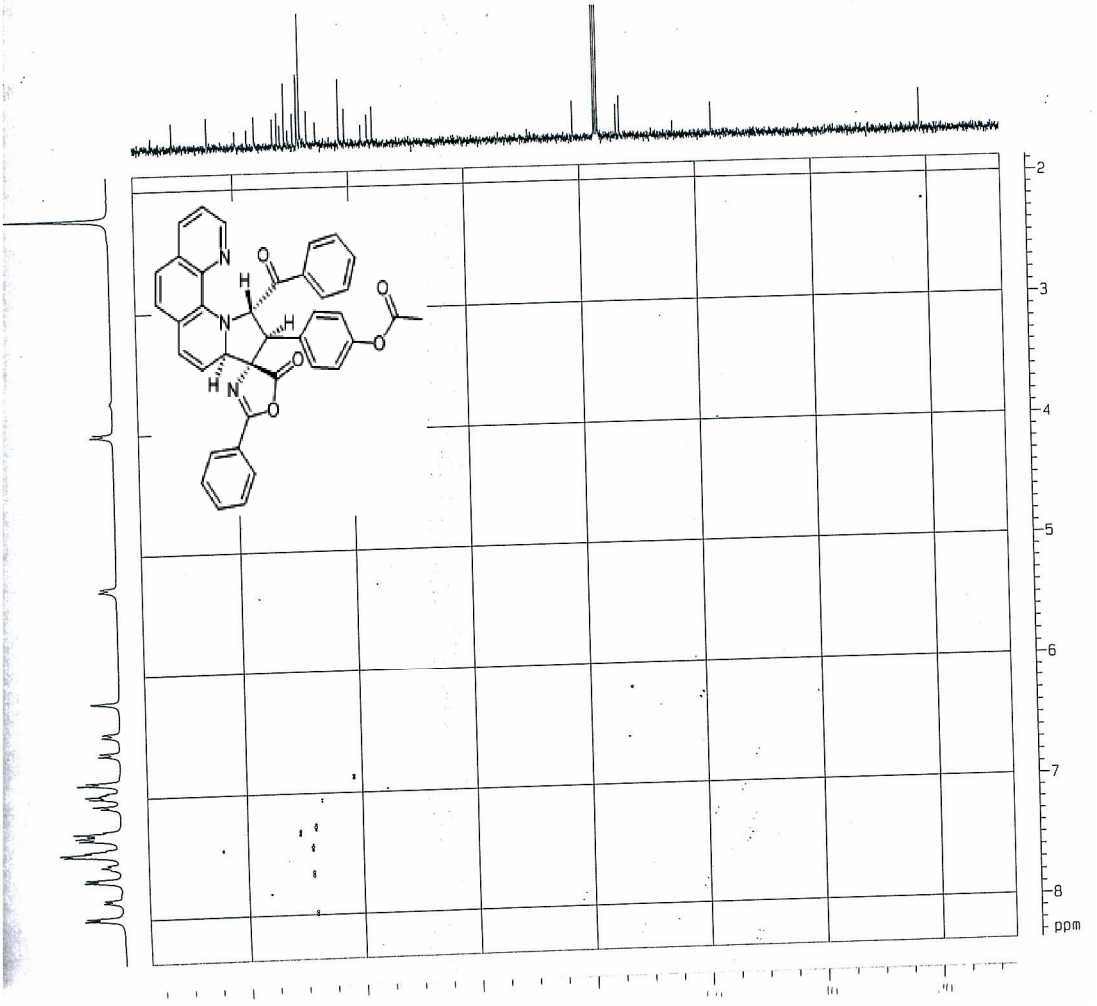

Figure 4. 113 COSY NMR Spectrum of **91m**

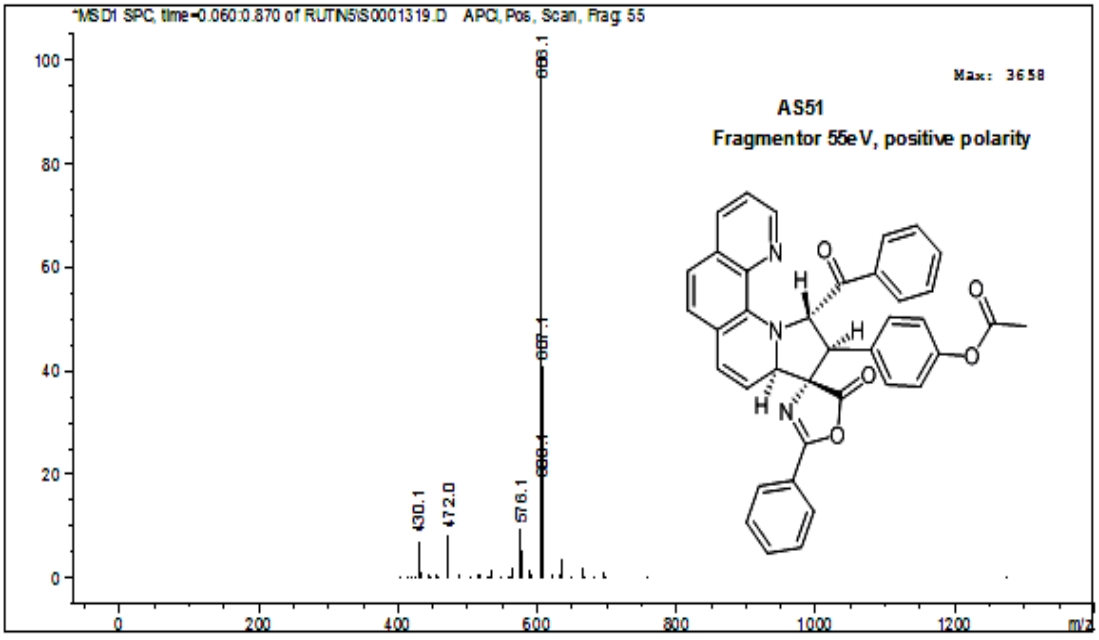

Figure 4. 114 MASS spectra of **91m**

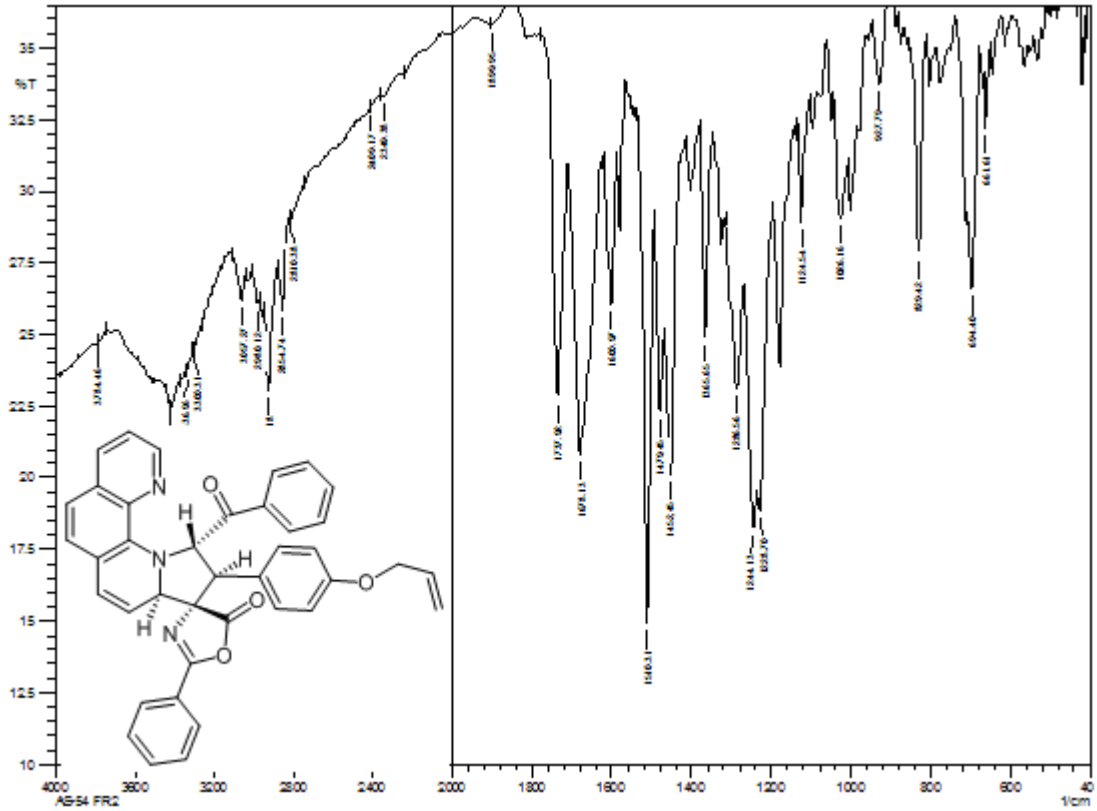

Figure 4. 115 IR Spectrum of **91p**

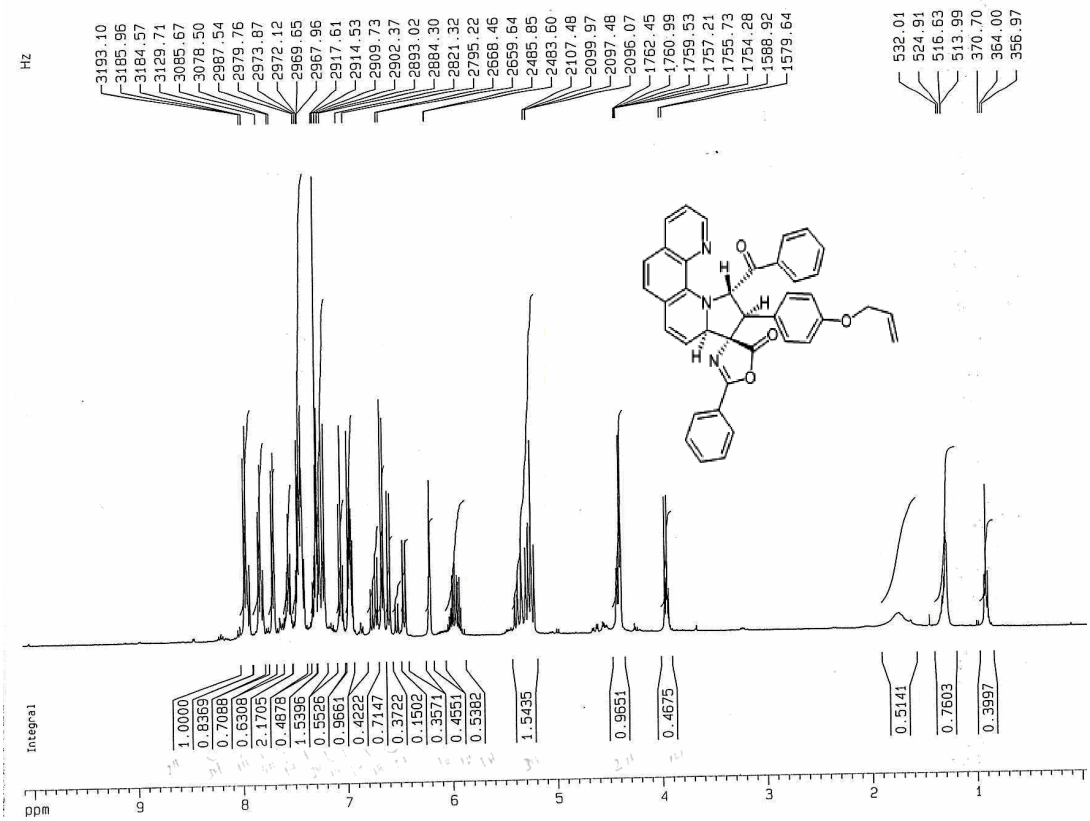

Figure 4. 116 ^{1}H NMR Spectrum of **91p**

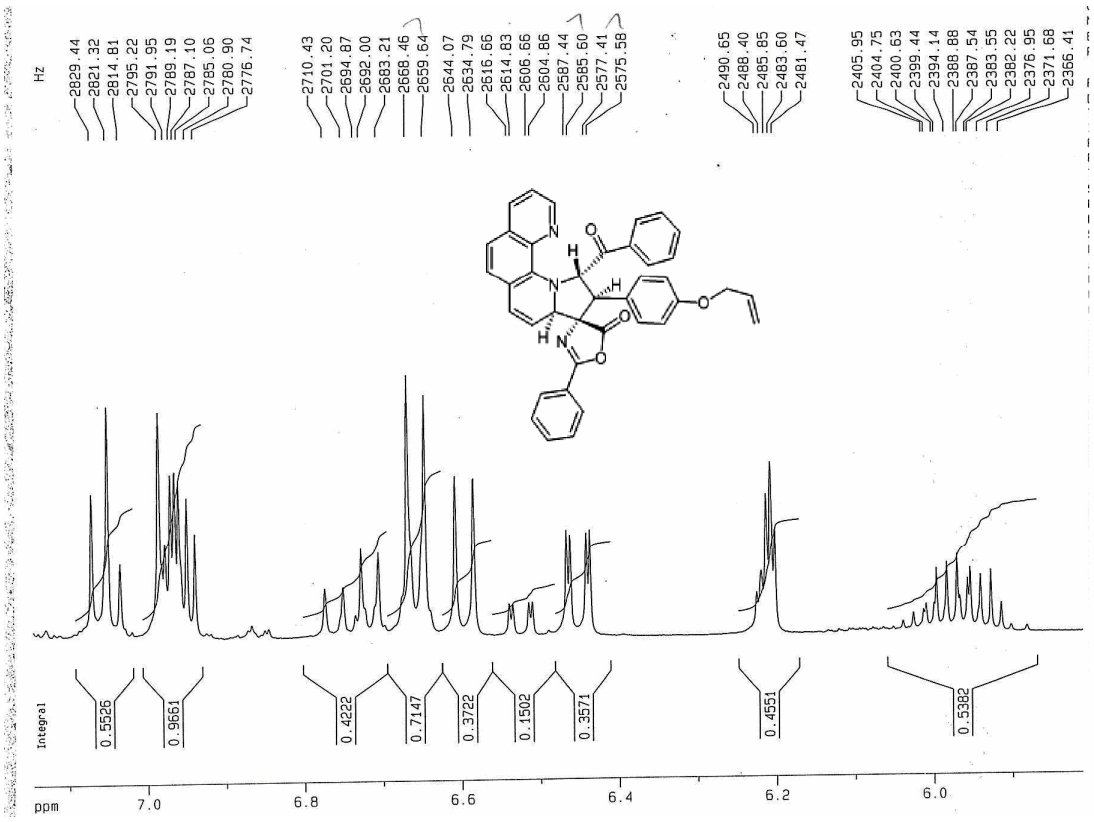

Figure 4. 117 Expanded (7.5-5.8 ppm) ^{1}H NMR Spectrum of **91p**

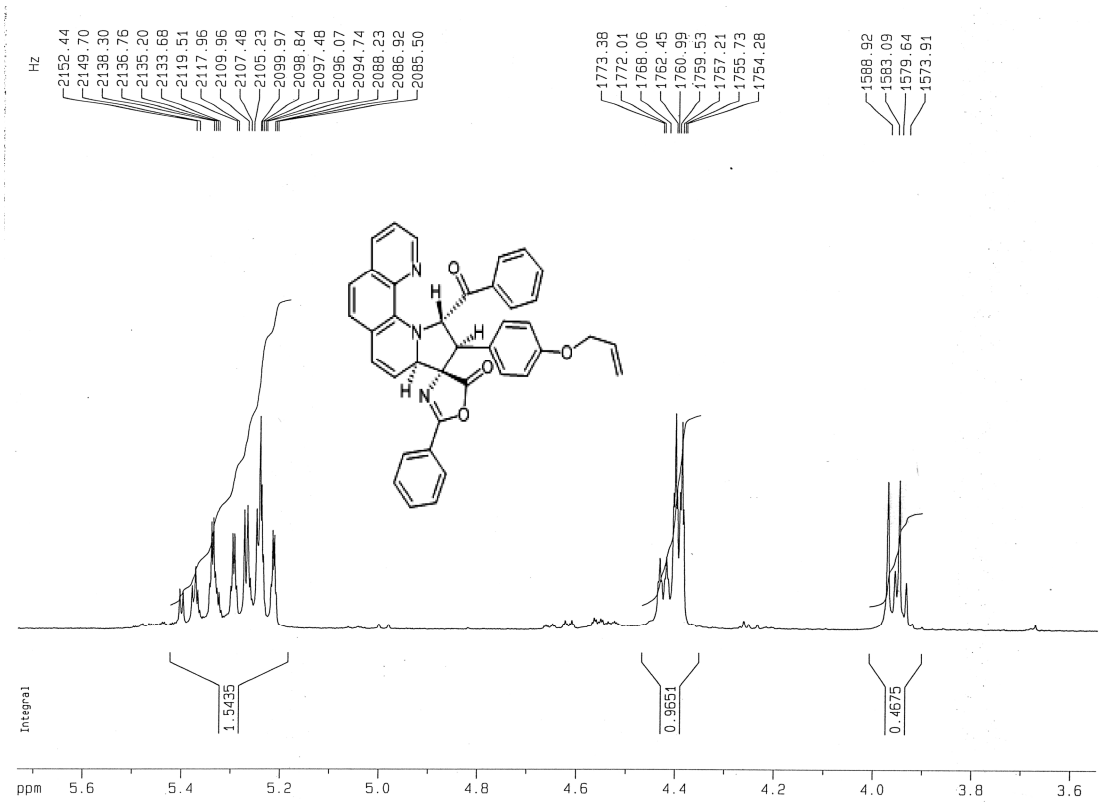

Figure 4.118 Expanded (5.6-3.6 ppm) ^{1}H NMR Spectrum of **91p**

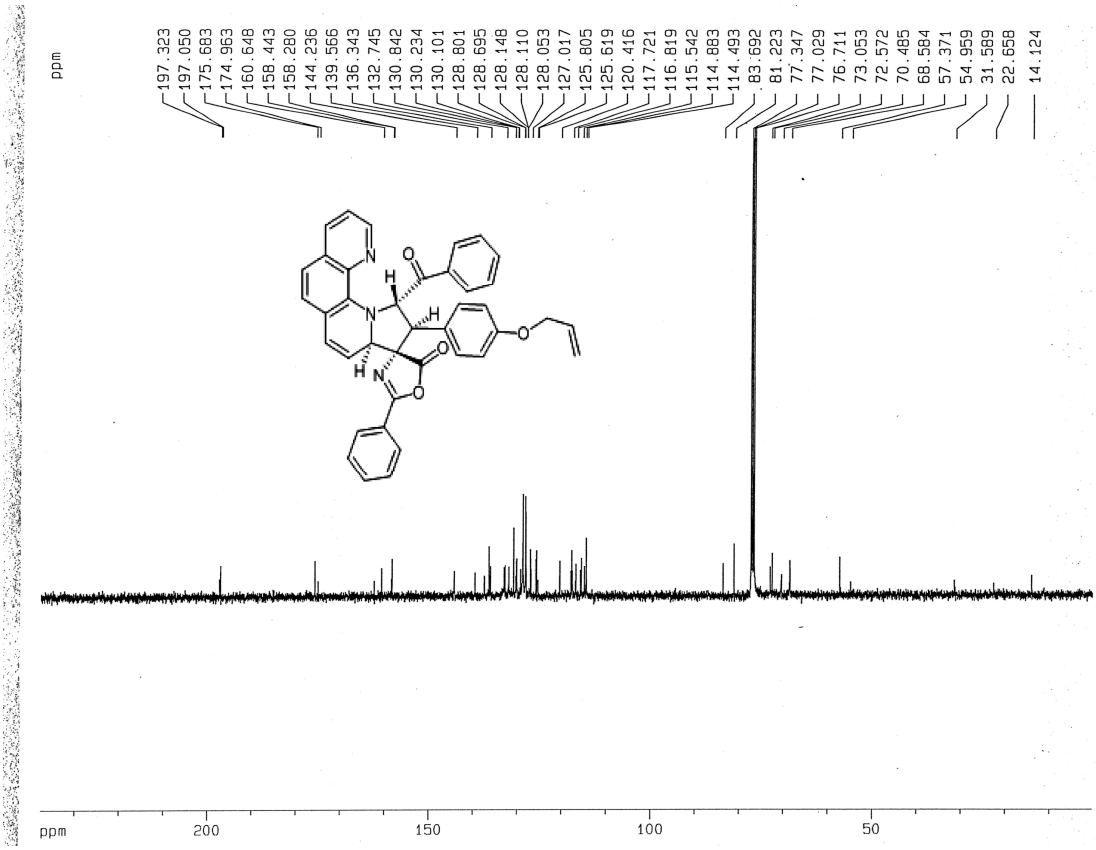

Figure 4. 119 ^{13}C NMR Spectrum of **91p**

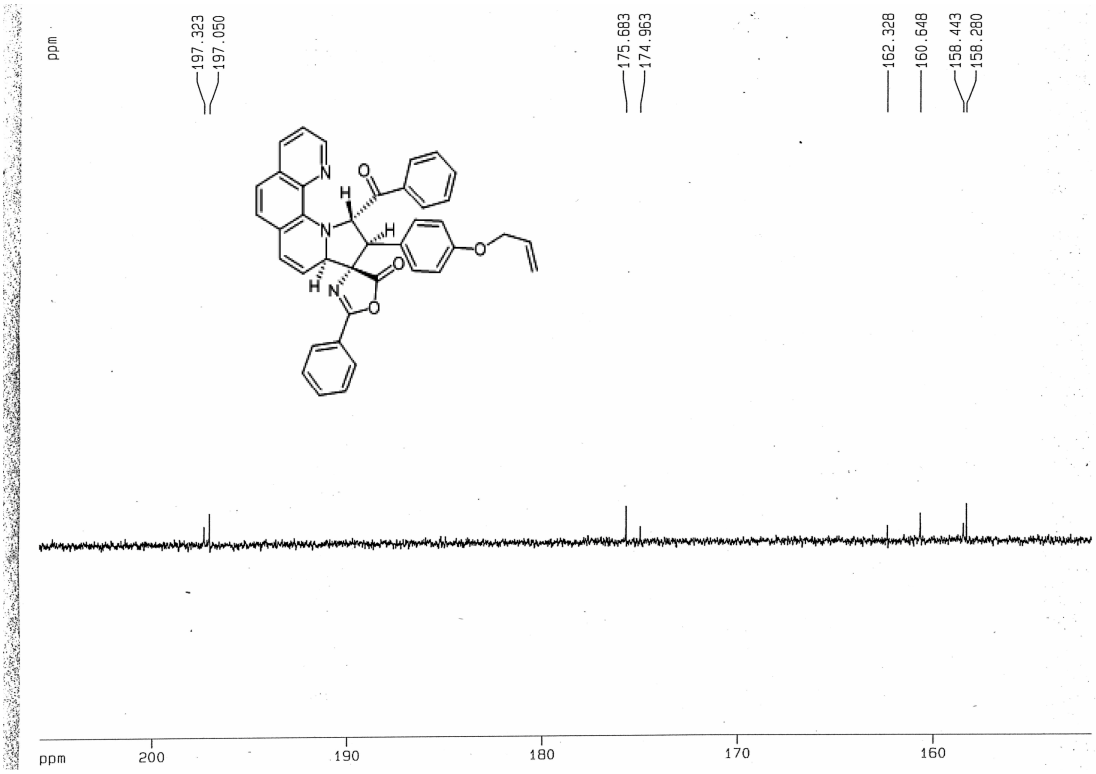

Figure 4. 120 Expanded (200-150 ppm) ^{13}C NMR Spectrum of **91p**

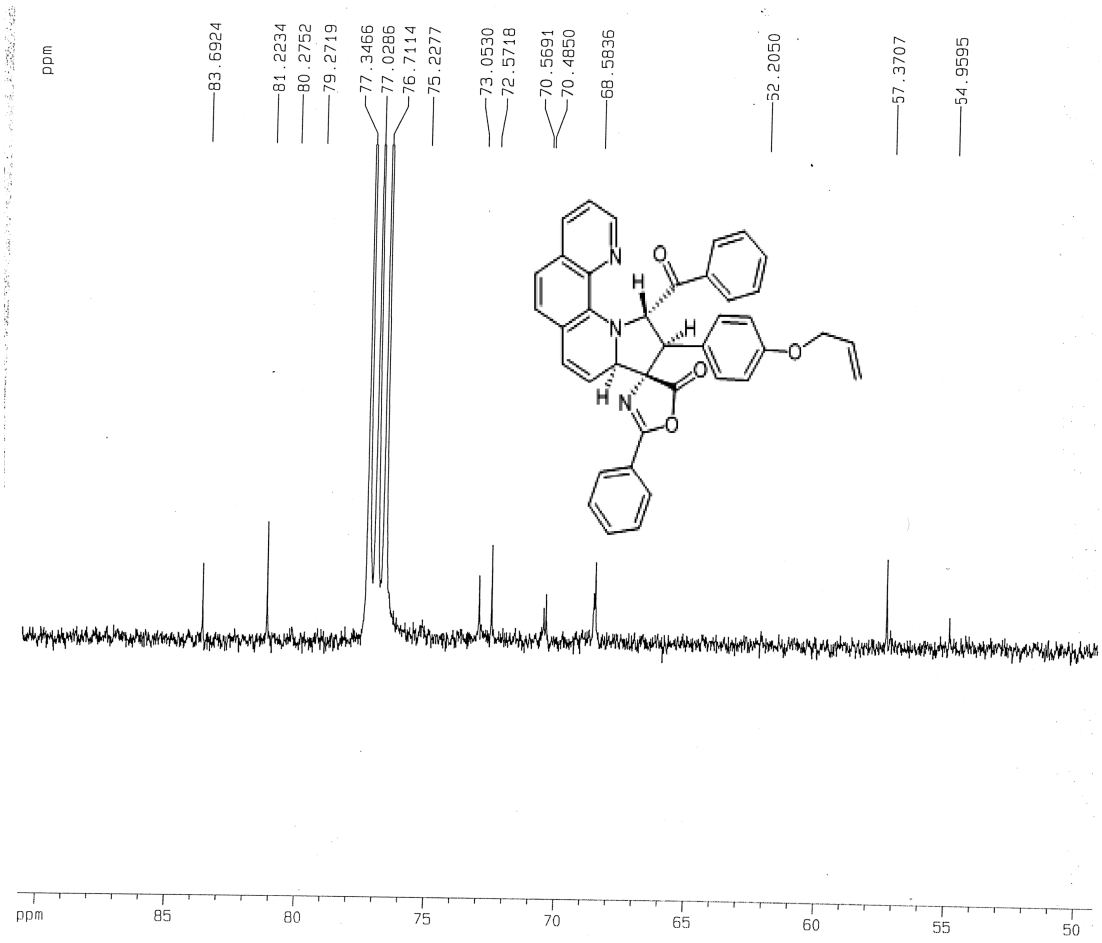

Figure 4. 121 Expanded (90-50 ppm) ^{13}C NMR Spectrum of **91p**

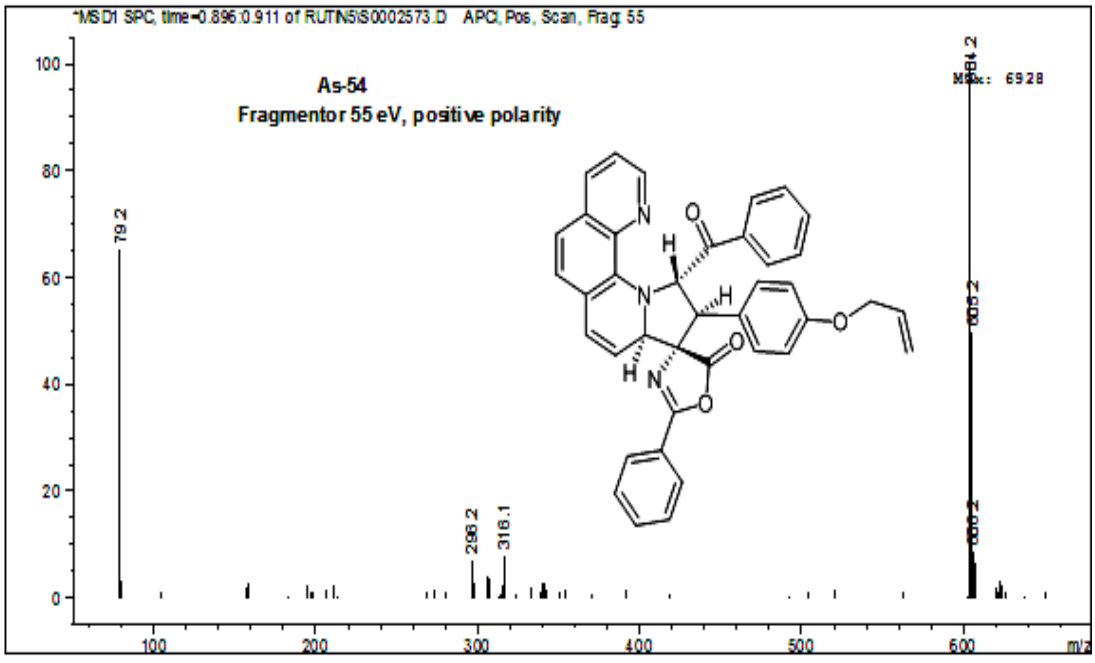

Figure 4. 122 MASS spectra of **91p**

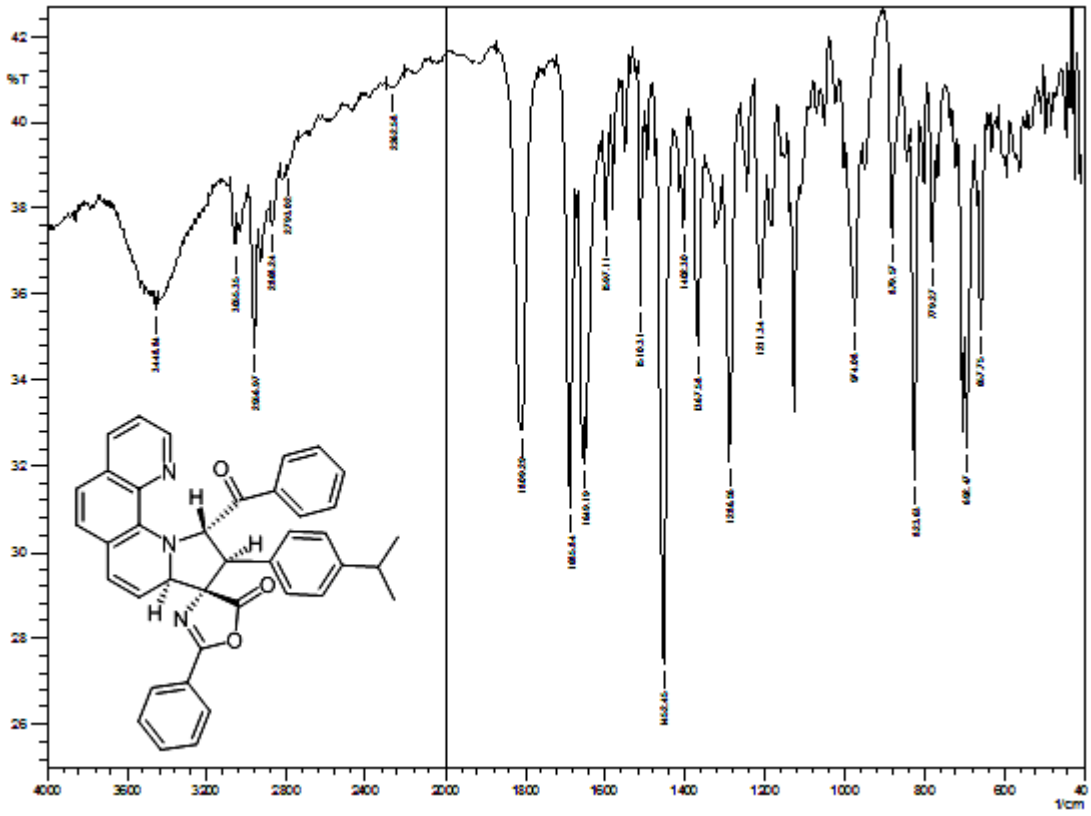

Figure 4. 123 IR Spectrum of **91r**

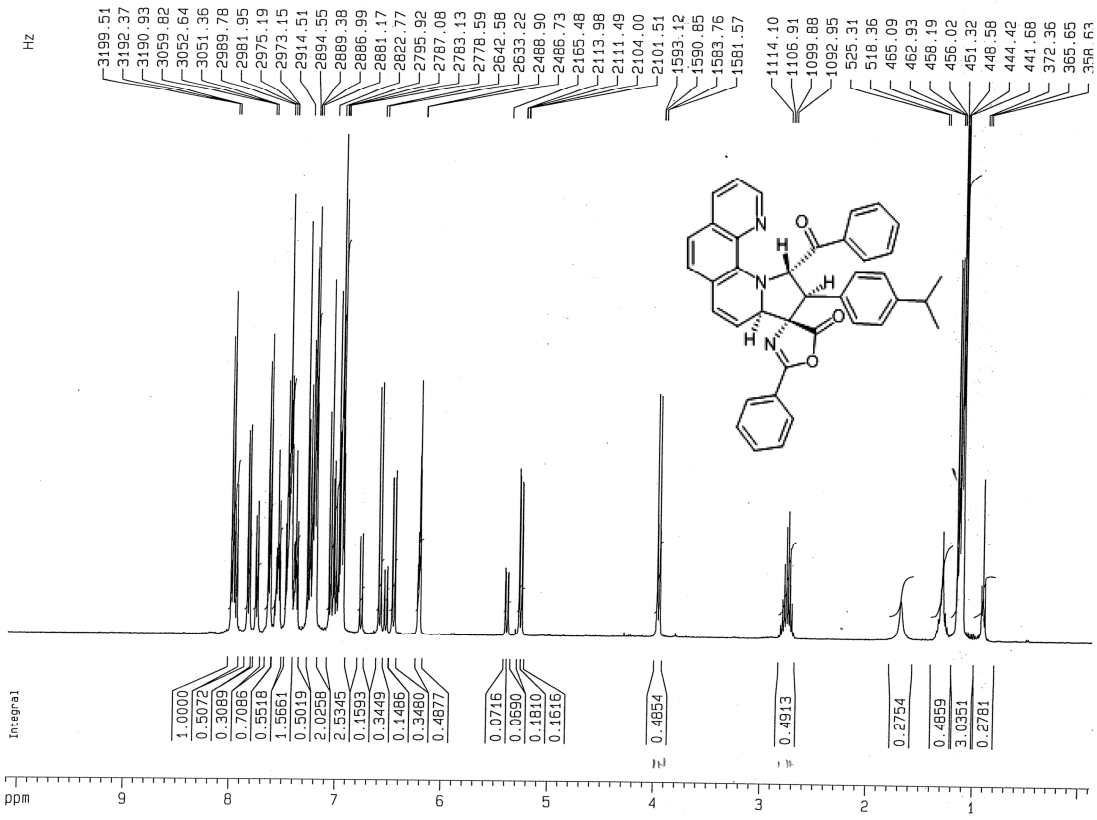

Figure 4. 124 ^{1}H NMR Spectrum of **91r**

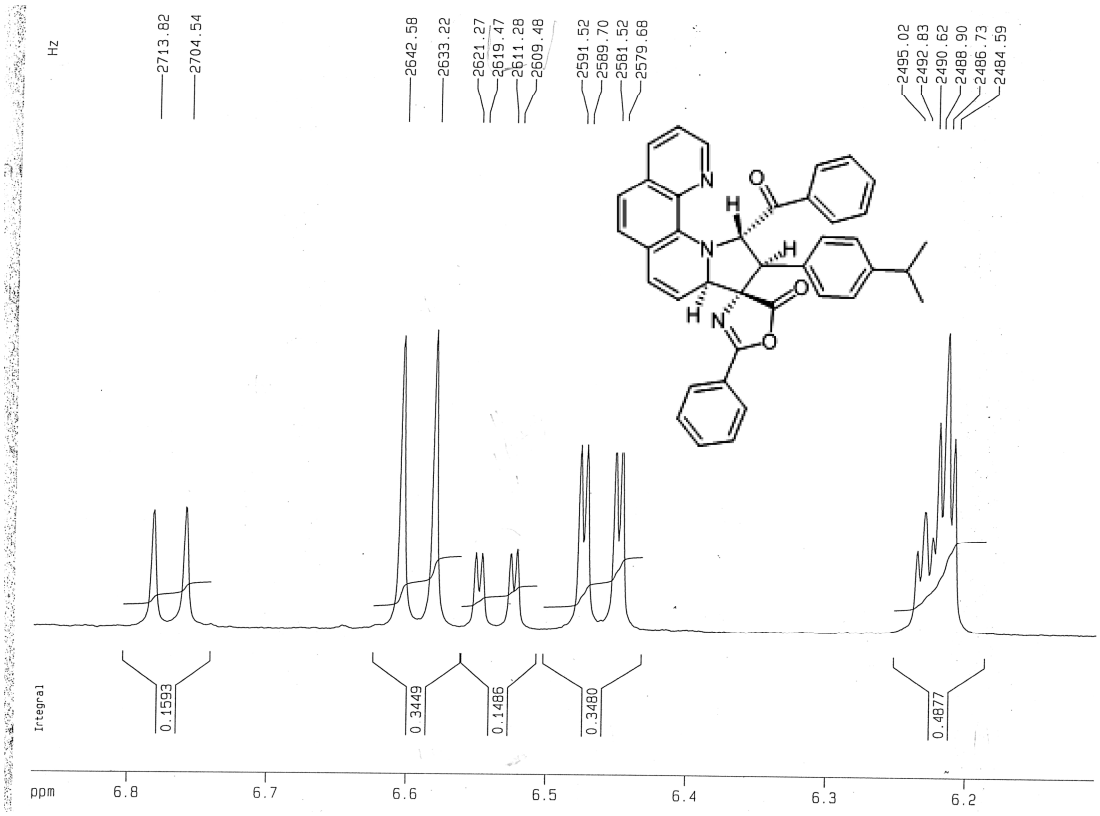

Figure 4. 125 Expanded (6.8-6.2 ppm) ^{1}H NMR Spectrum of **91r**

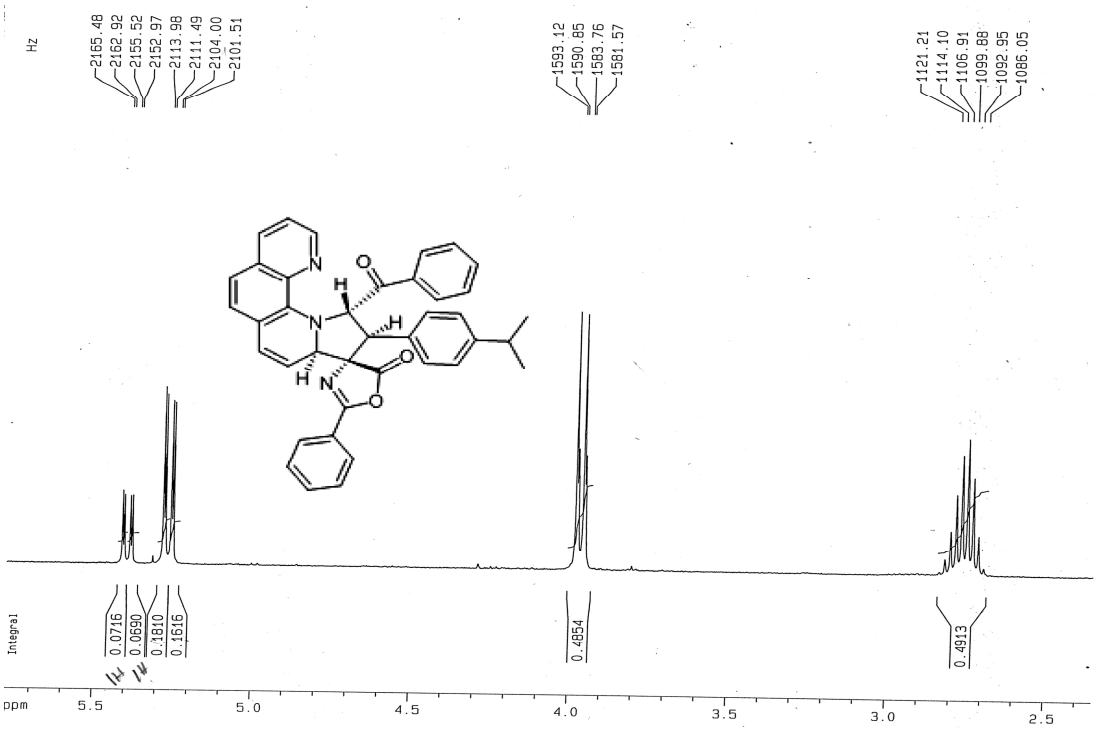

Figure 4. 126 Expanded (5.5-2.5 ppm) ^{1}H NMR Spectrum of **91r**

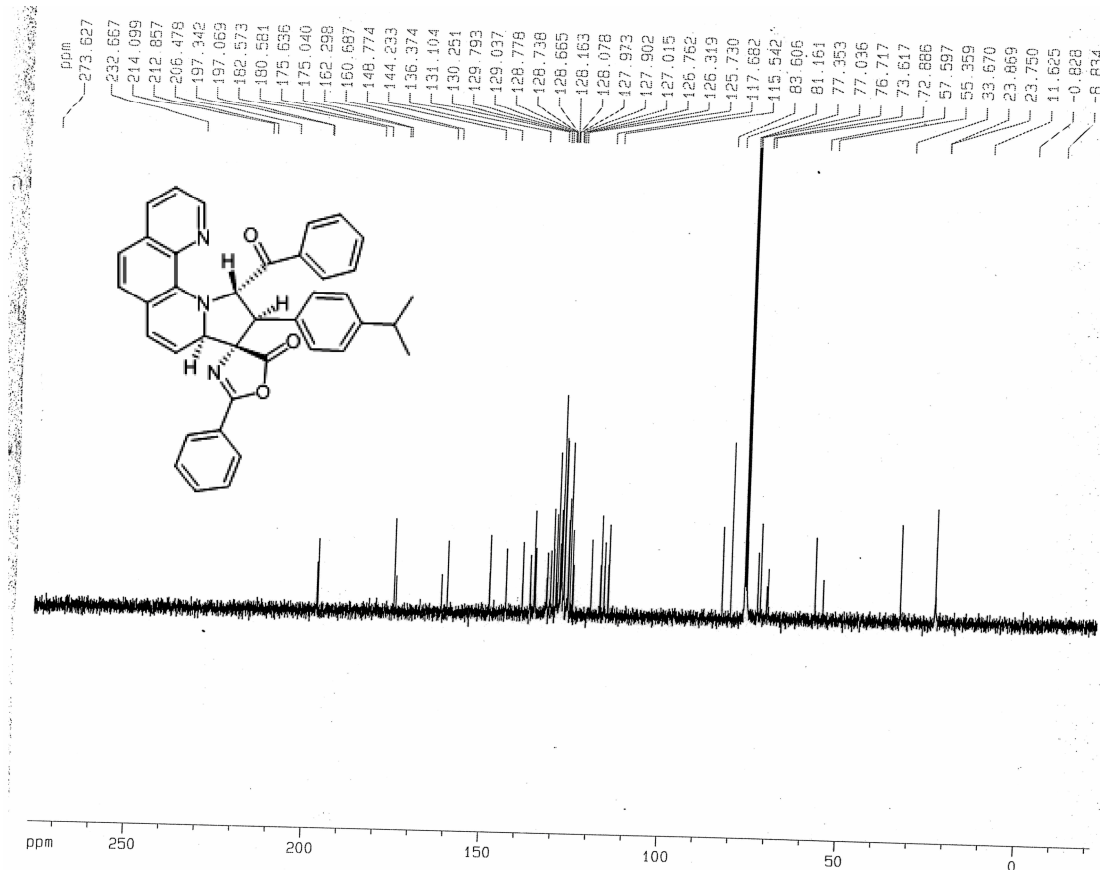

Figure 4. 127 ^{13}C NMR Spectrum of **91r**

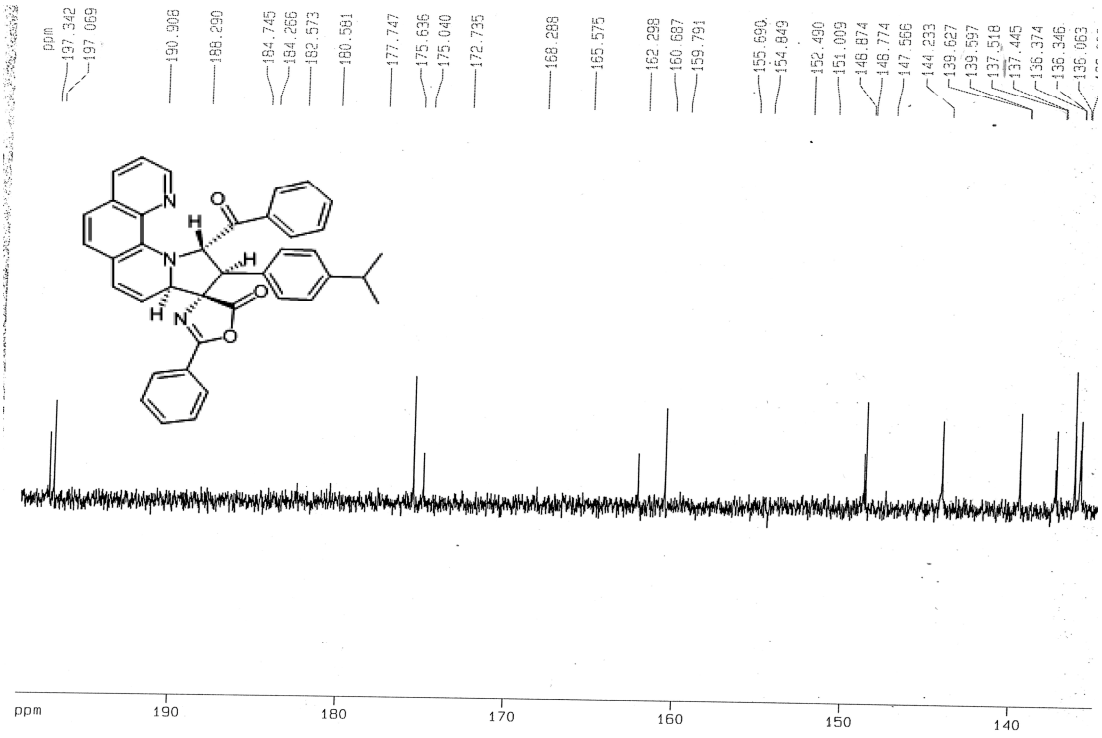

Figure 4. 128 Expanded (200-135 ppm) ^{13}C NMR Spectrum of **91r**

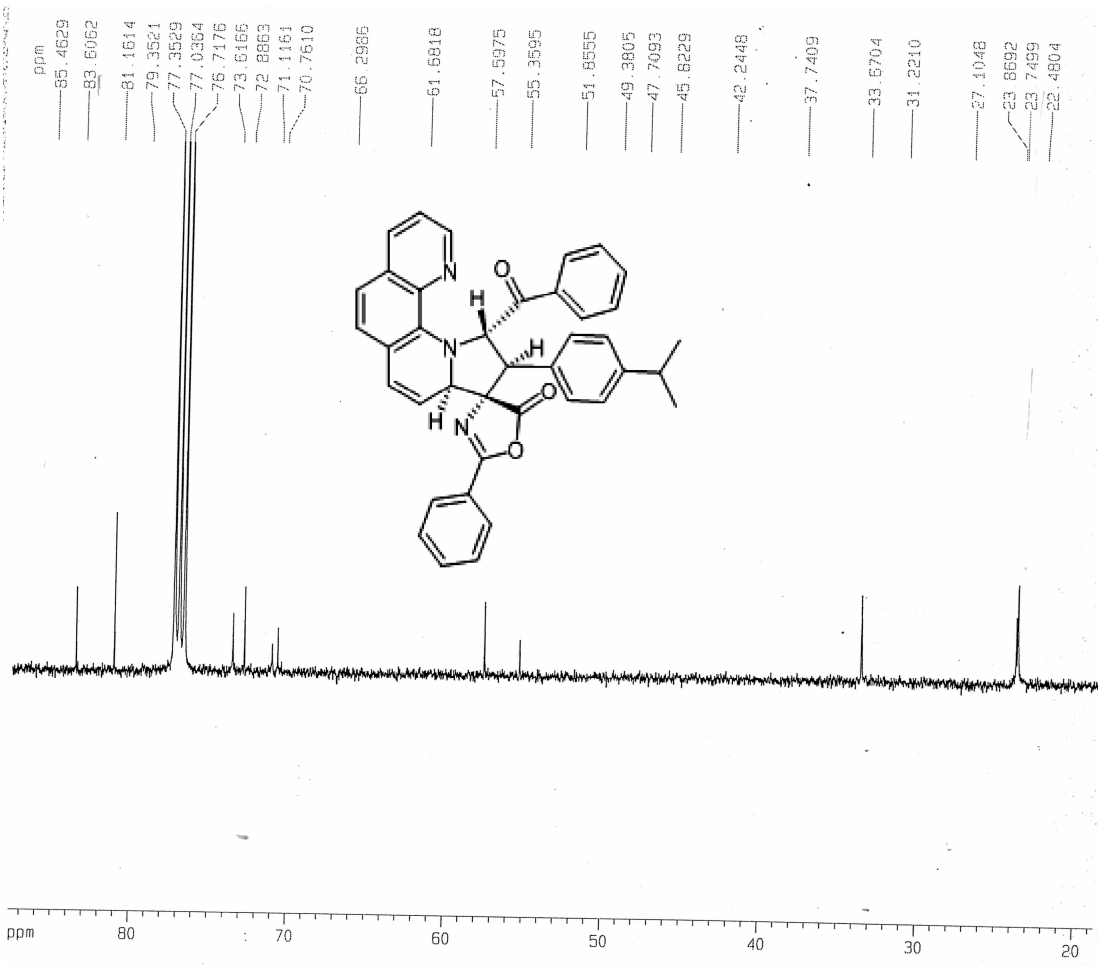

Figure 4. 129 Expanded (90-20 ppm) ^{13}C NMR Spectrum of **91r**

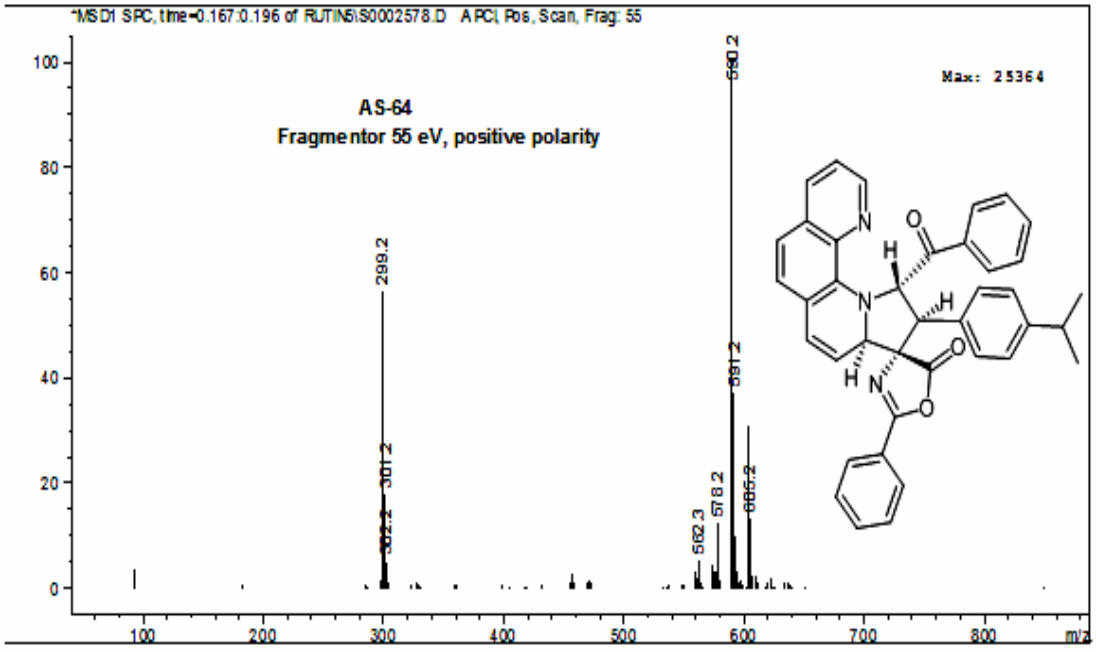

Figure 4. 130 MASS spectra of **91r**

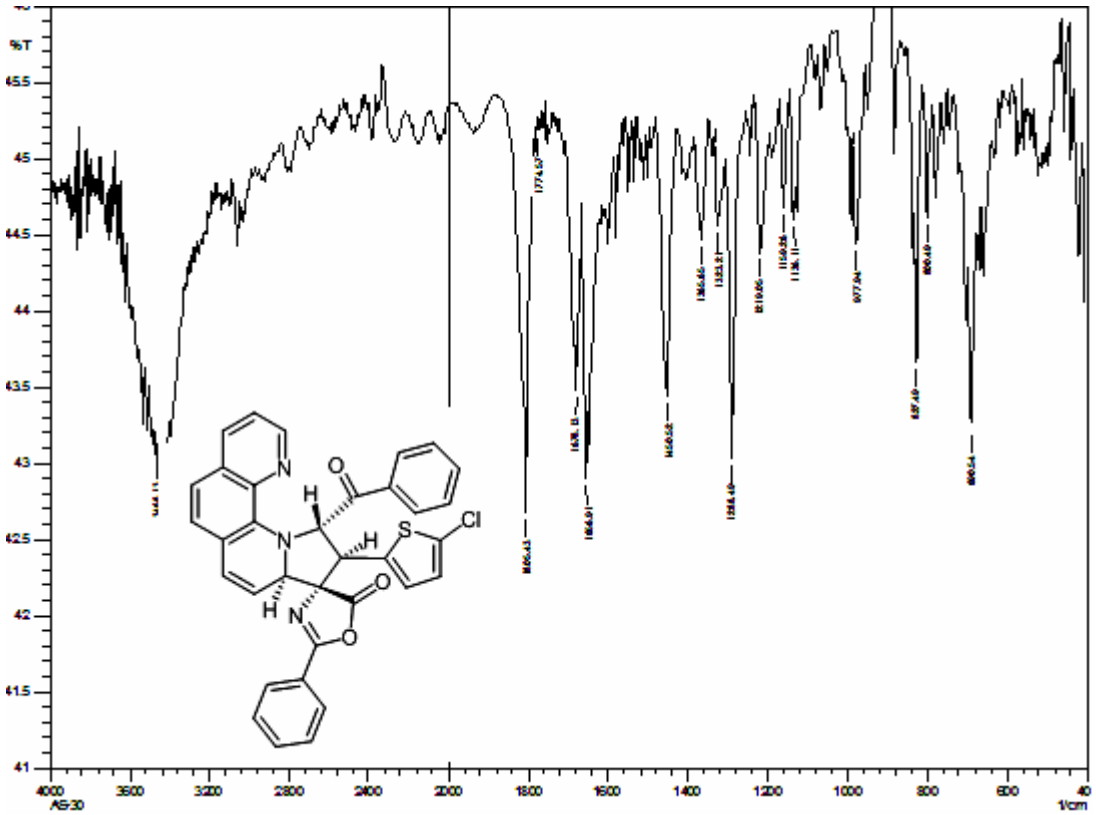

Figure 4. 131 IR Spectrum of **91s**

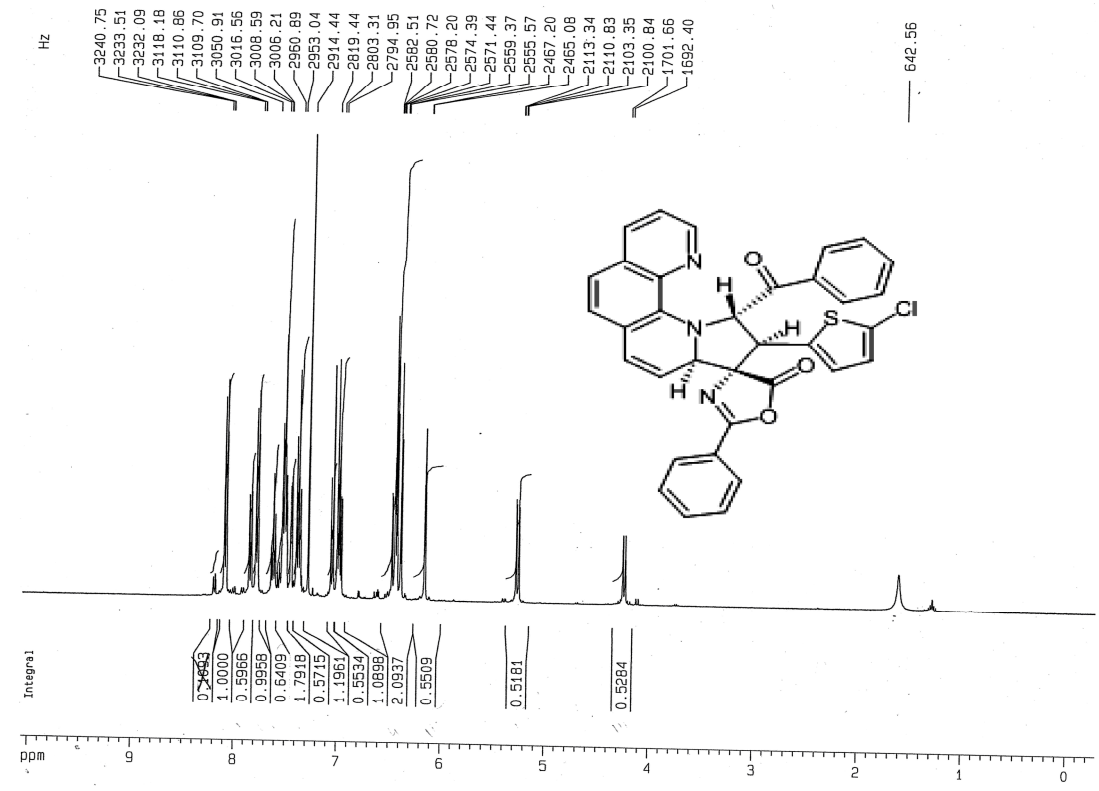

Figure 4. 132 ^{1}H NMR Spectrum of **91s**

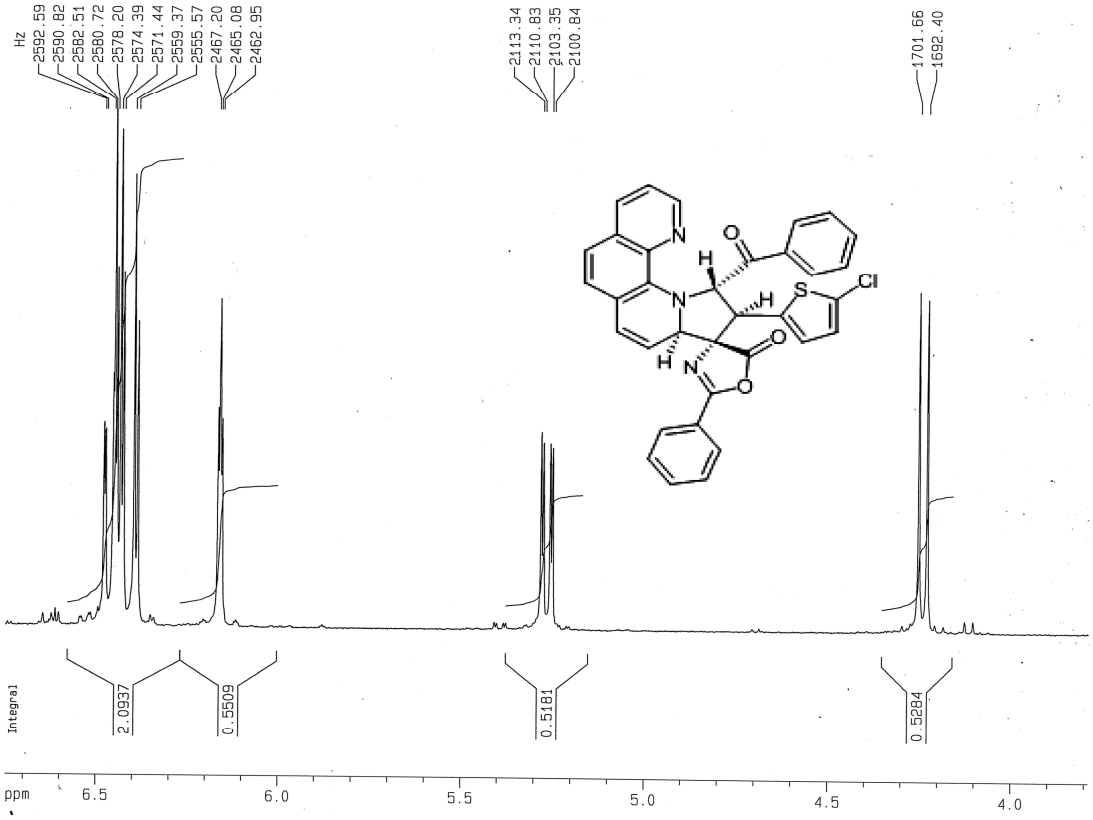

Figure 4. 133 Expanded (6.5-4.0 ppm) ^{1}H NMR Spectrum of **91s**

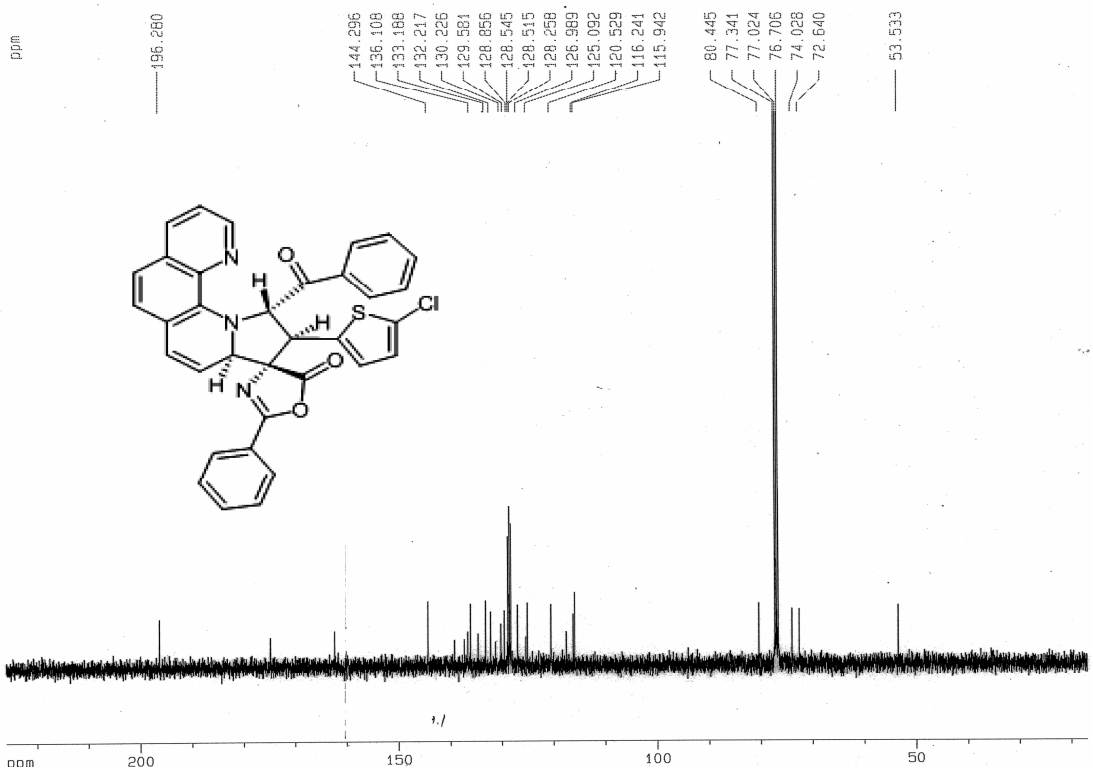

Figure 4. 134 ^{13}C NMR Spectrum of **91s**

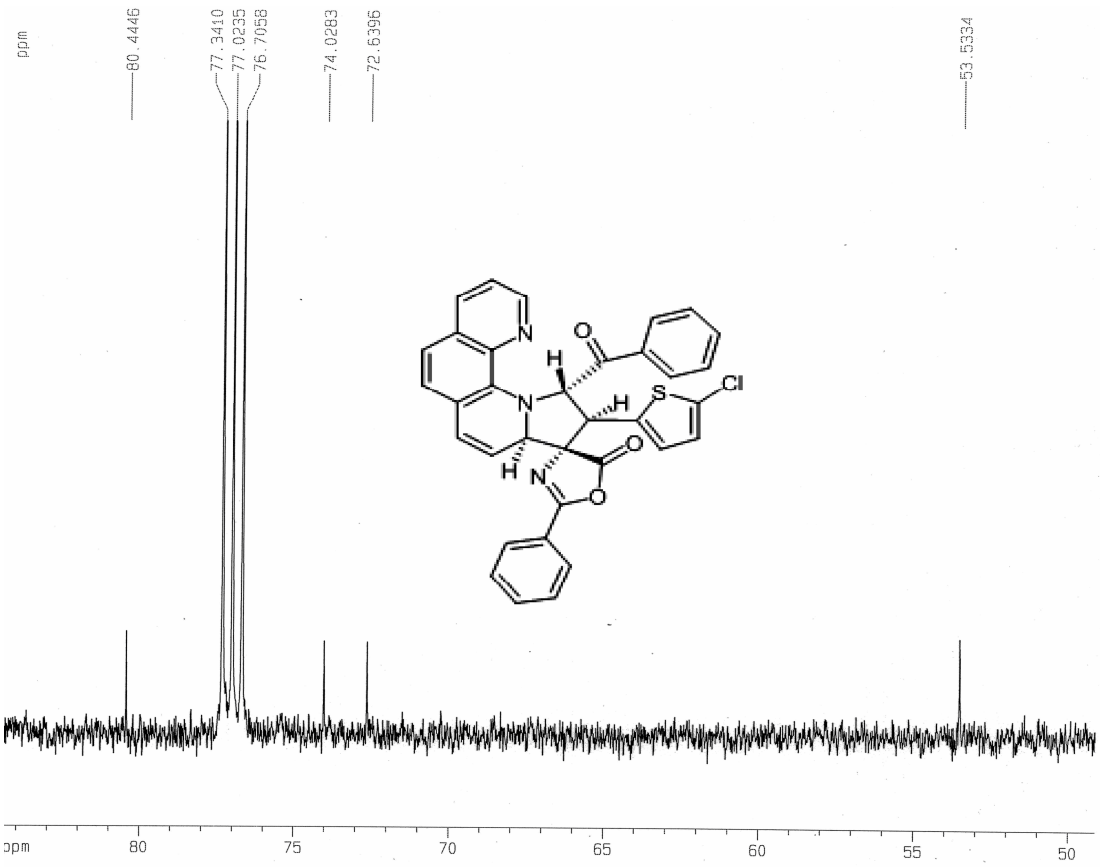

Figure 4. 135 Expanded (85-50 ppm) ^{13}C NMR Spectrum of **91s**

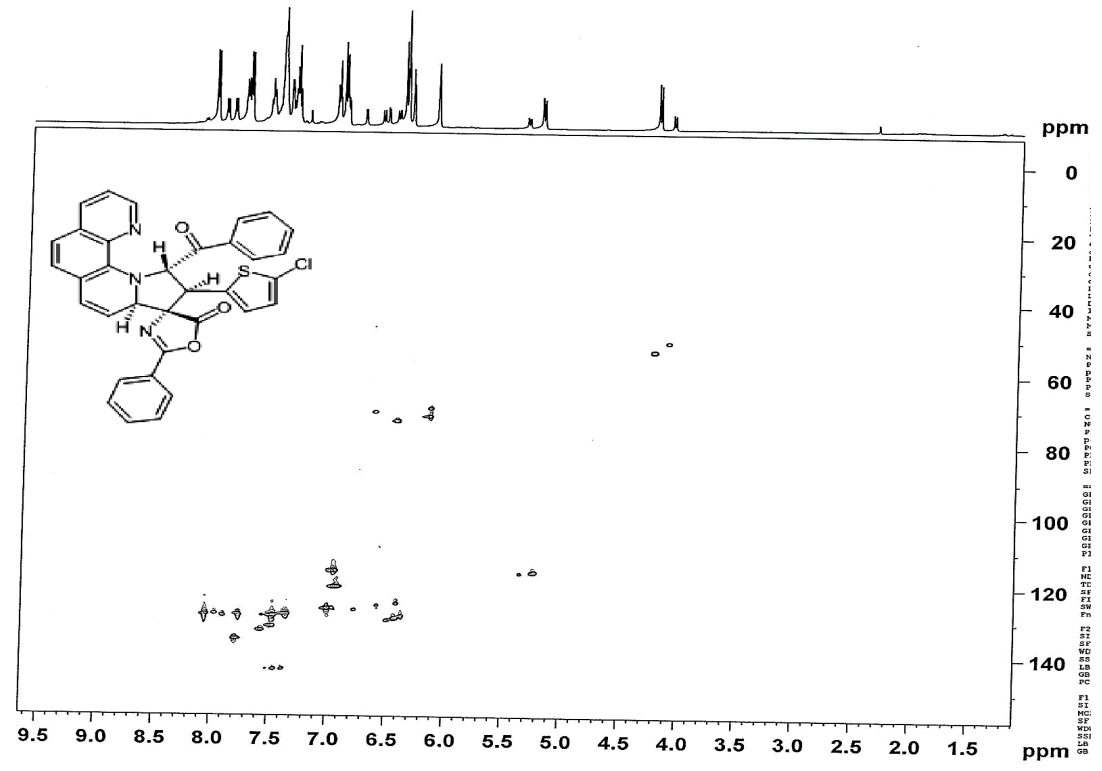

Figure 4. 136 HSQC NMR spectra of **91s**

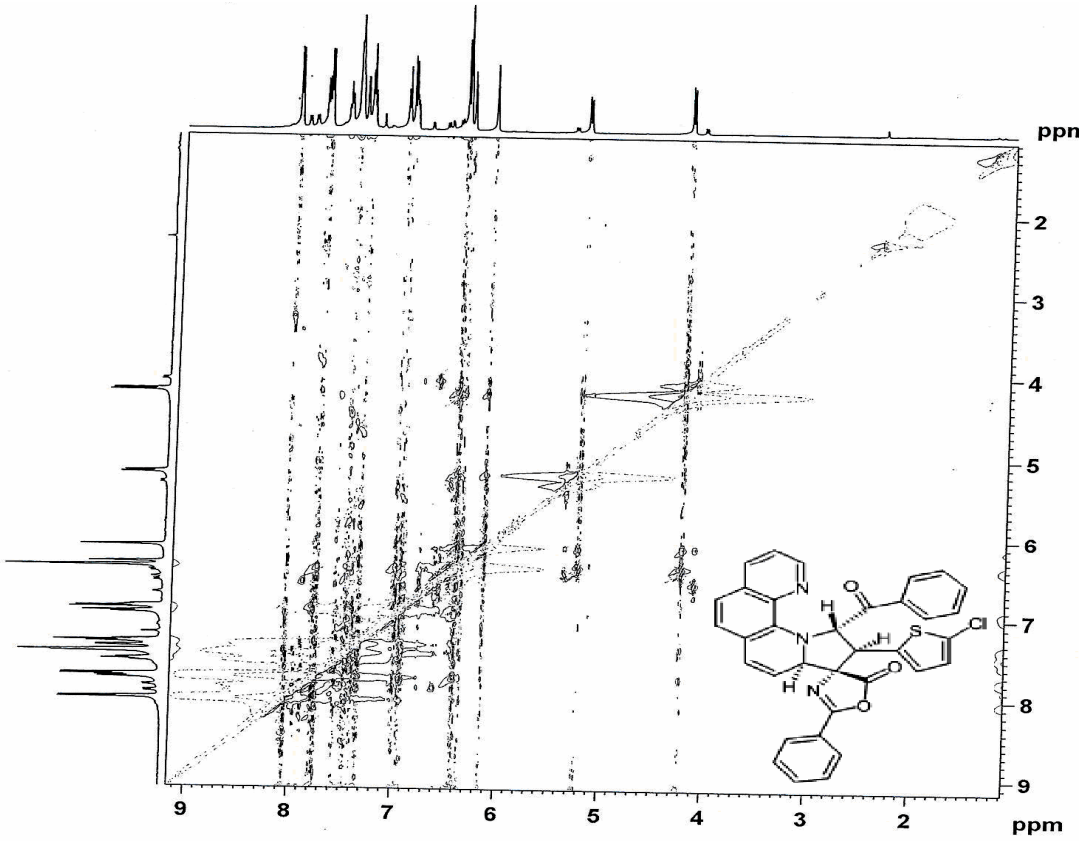

Figure 4. 137 NOESY NMR spectra of **91s**

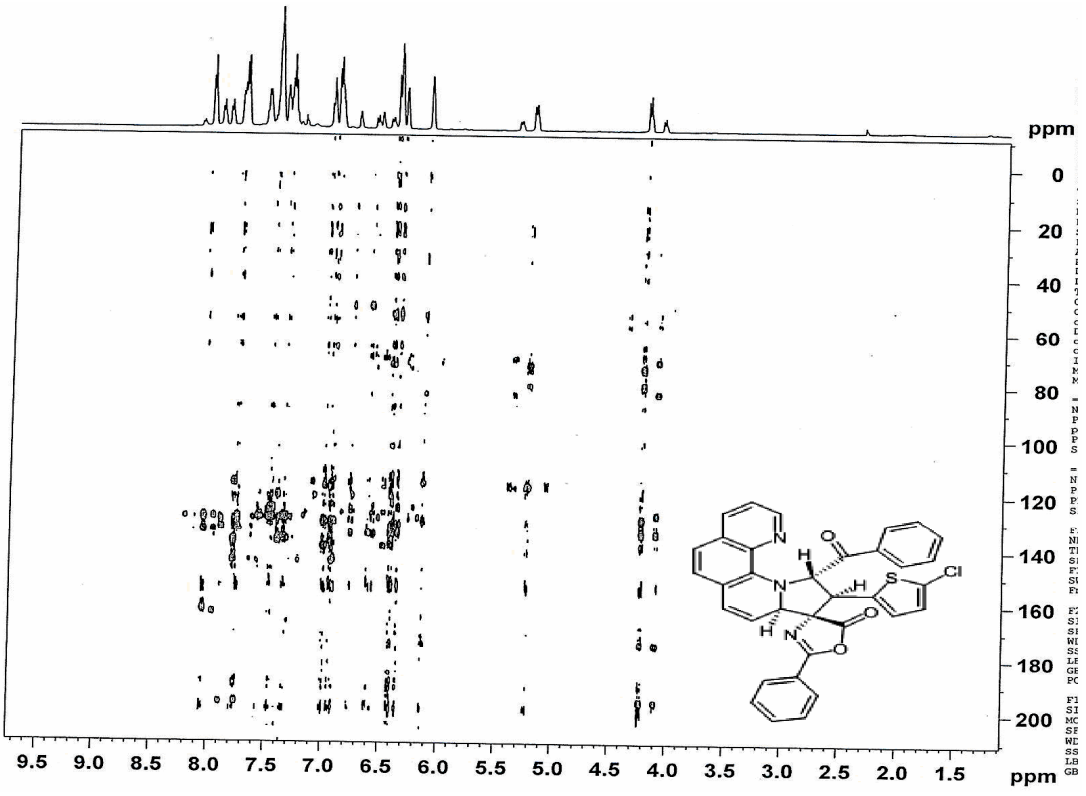

Figure 4. 138 HMBC NMR spectra of **91s**

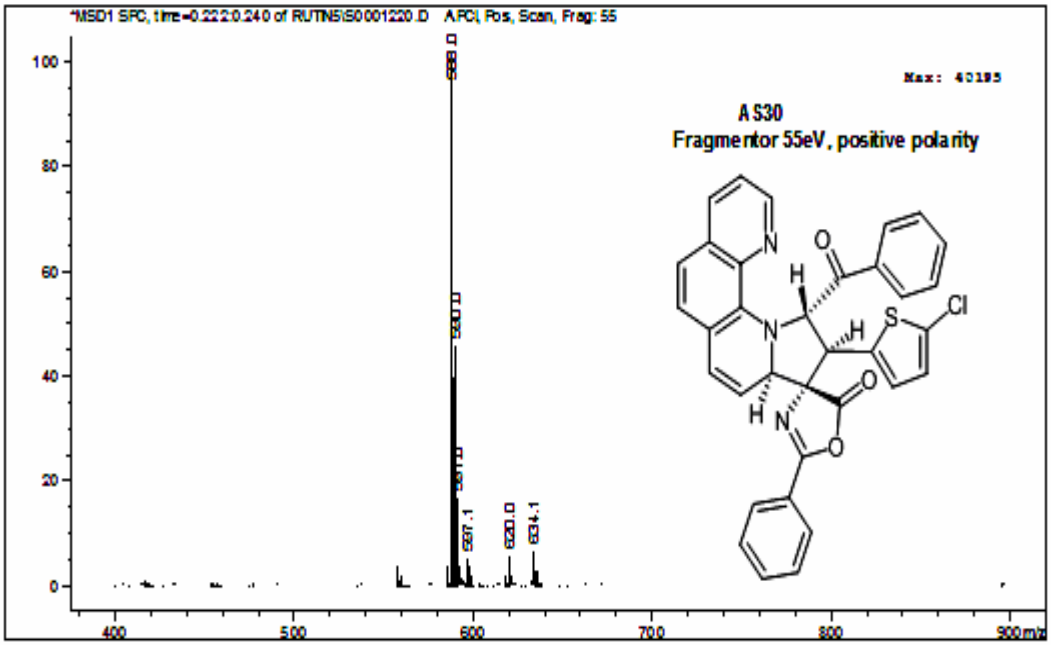

Figure 4. 139 MASS Spectrum of **91s**

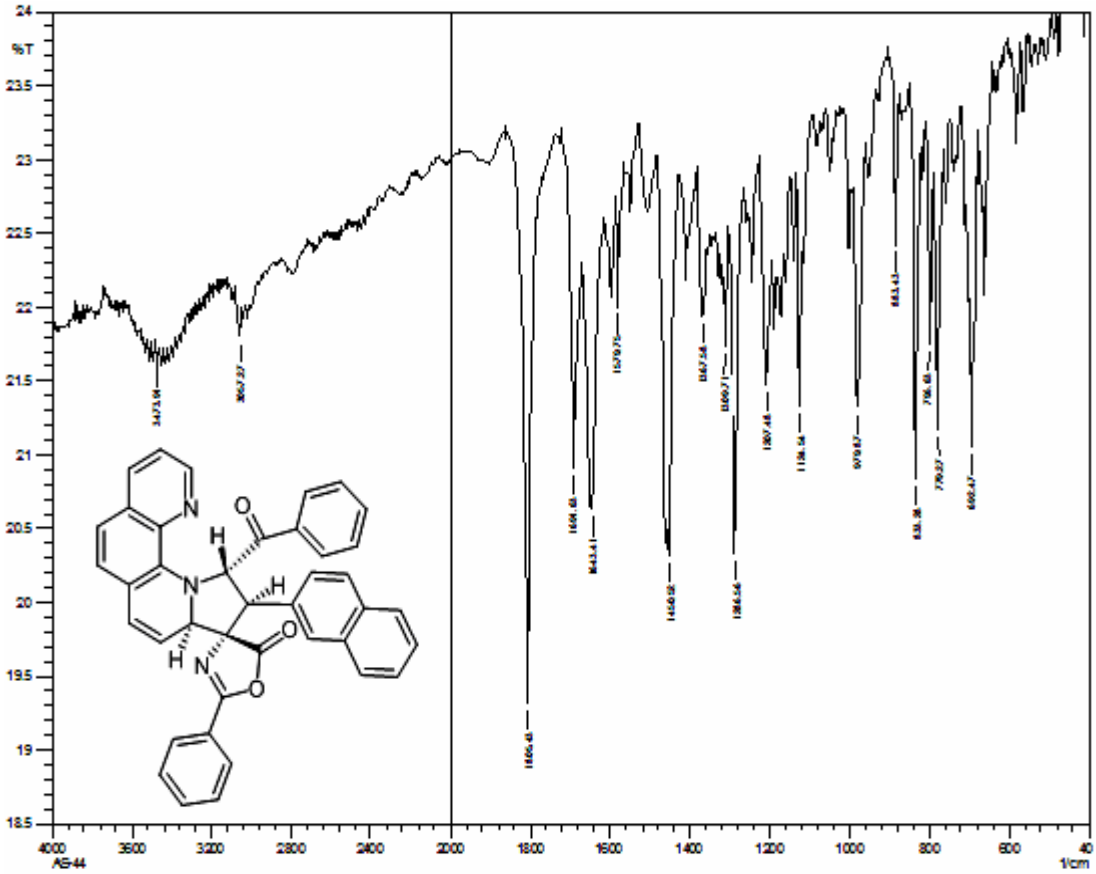

Figure 4. 140 IR Spectrum of **91t**

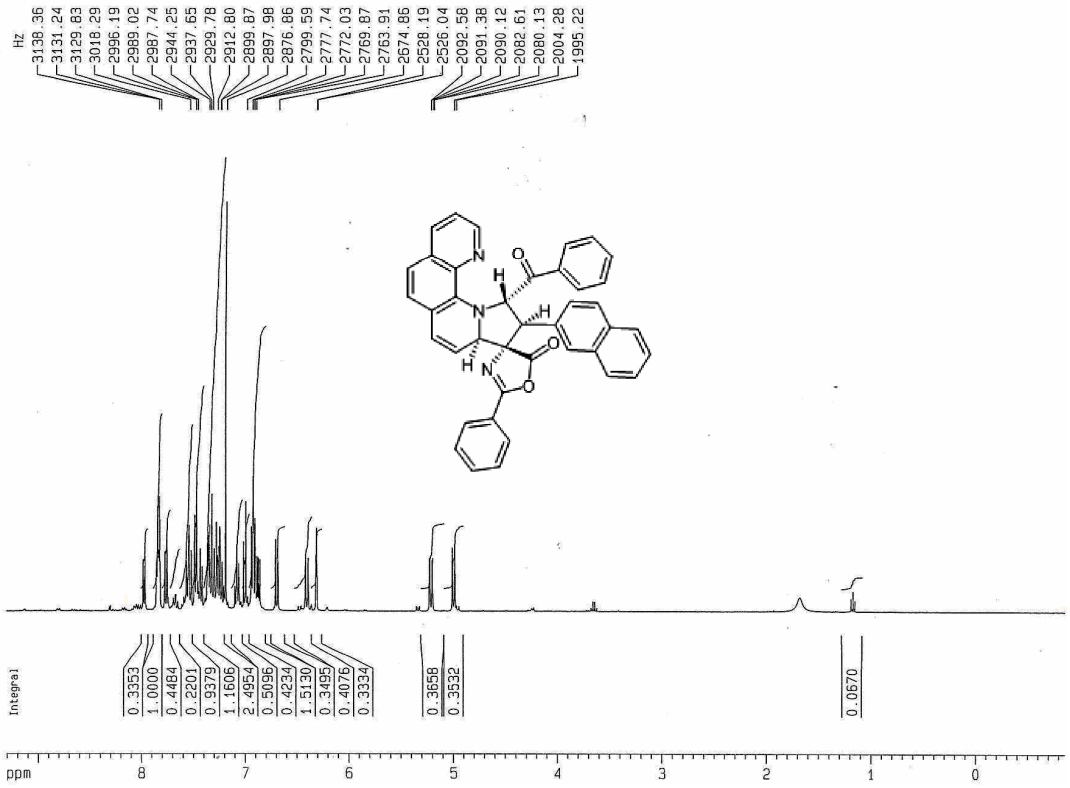

Figure 4. 141 ^{1}H NMR Spectrum of **91t**

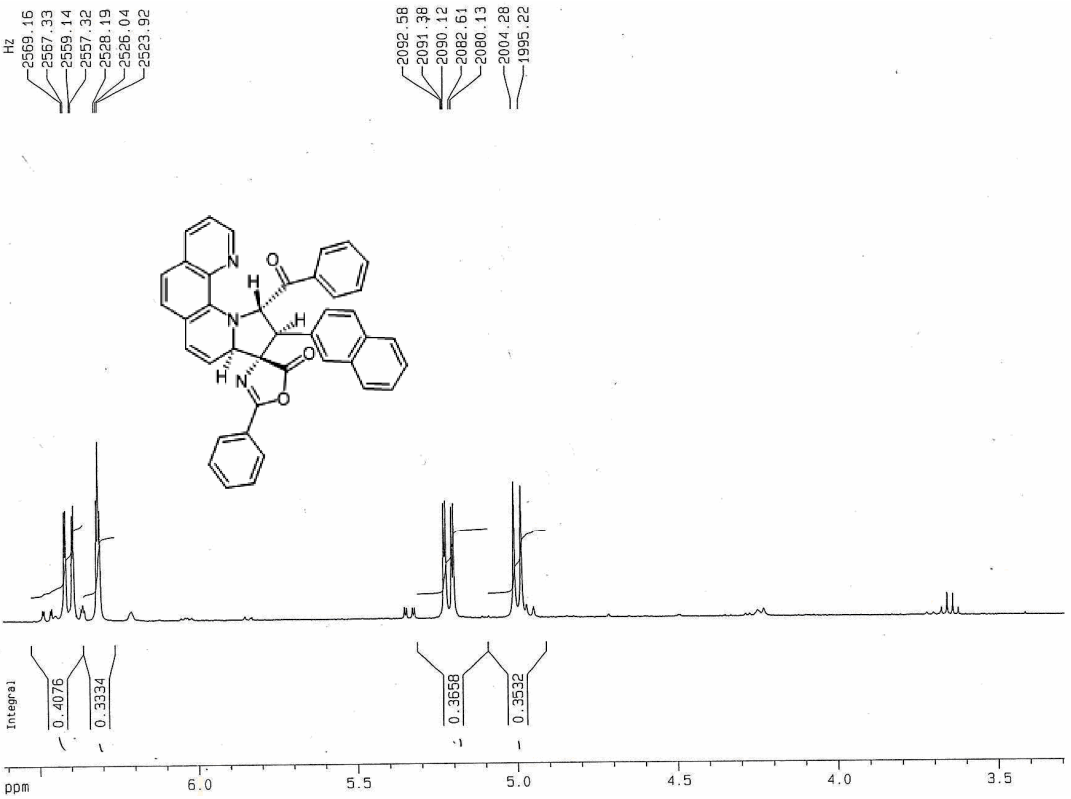

Figure 4. 142 Expanded (6.5-3.5 ppm) ^{1}H NMR Spectrum of **91t**

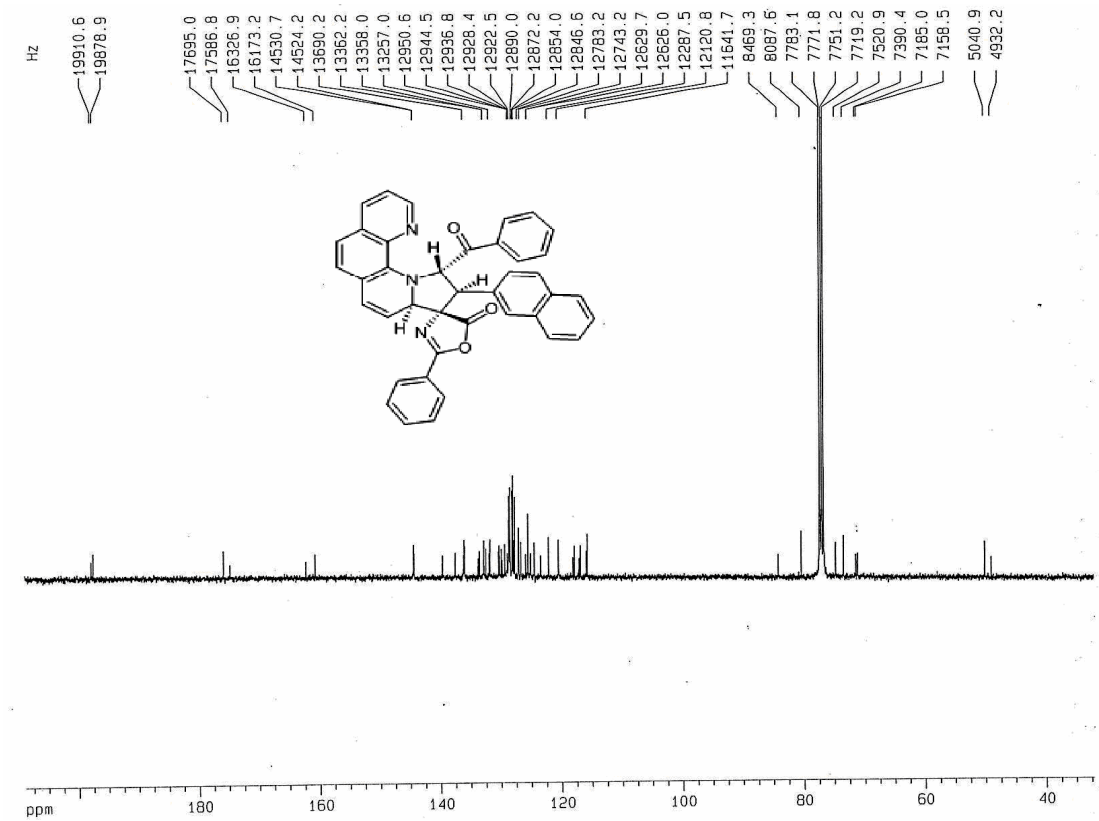

Figure 4. 143 ^{13}C NMR Spectrum of **91t**

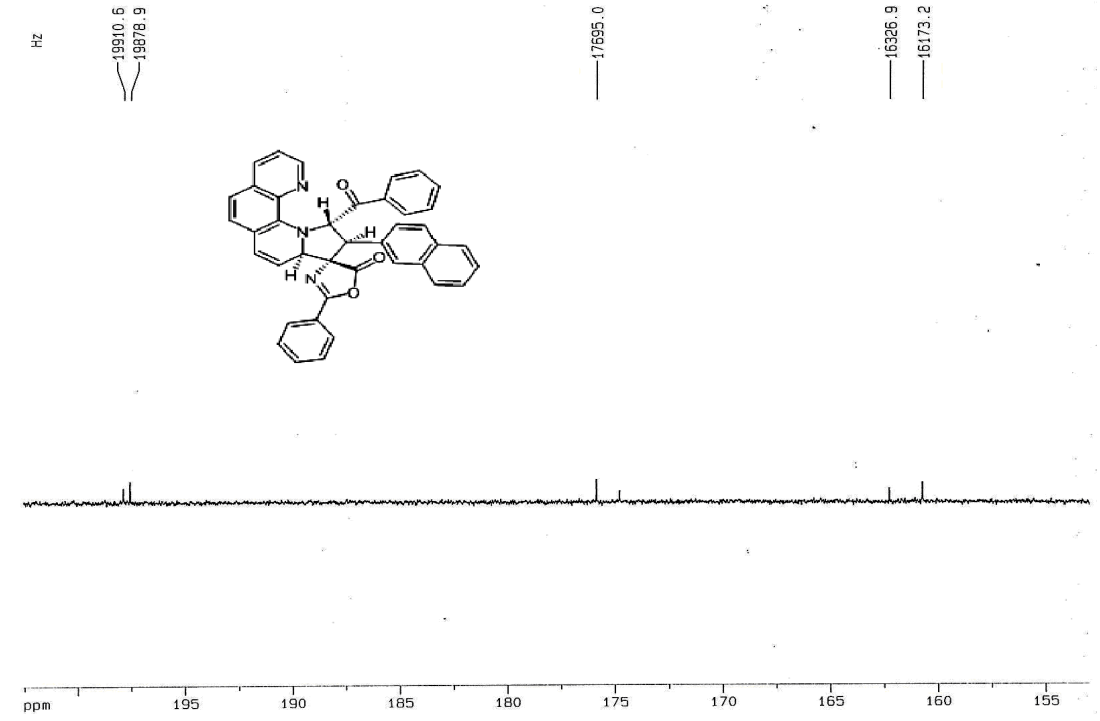

Figure 4. 144 Expanded (200-155 ppm) ^{13}C NMR Spectrum of **91t**

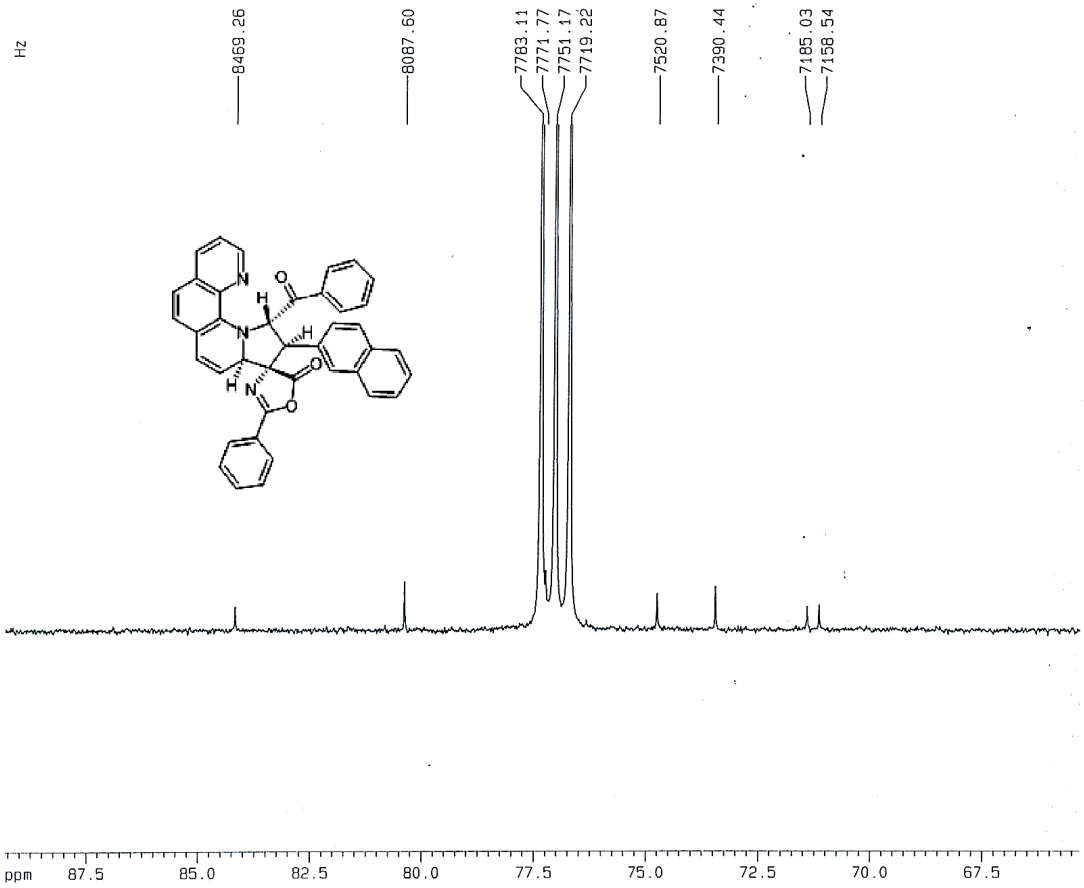

Figure 4. 145 Expanded (90-70 ppm) ^{13}C NMR Spectrum of **91t**

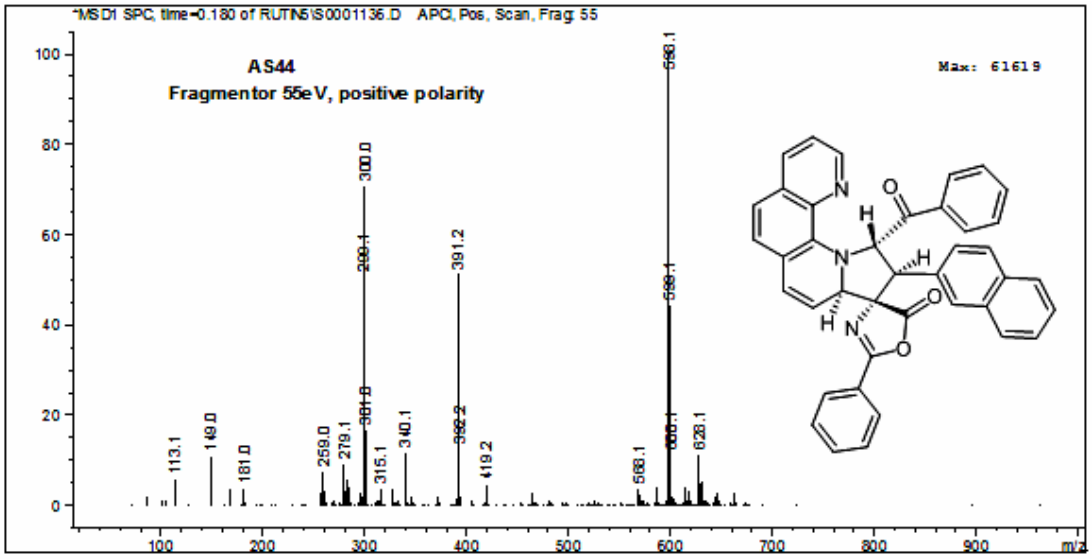

Figure 4. 146 MASS Spectrum of **91t**

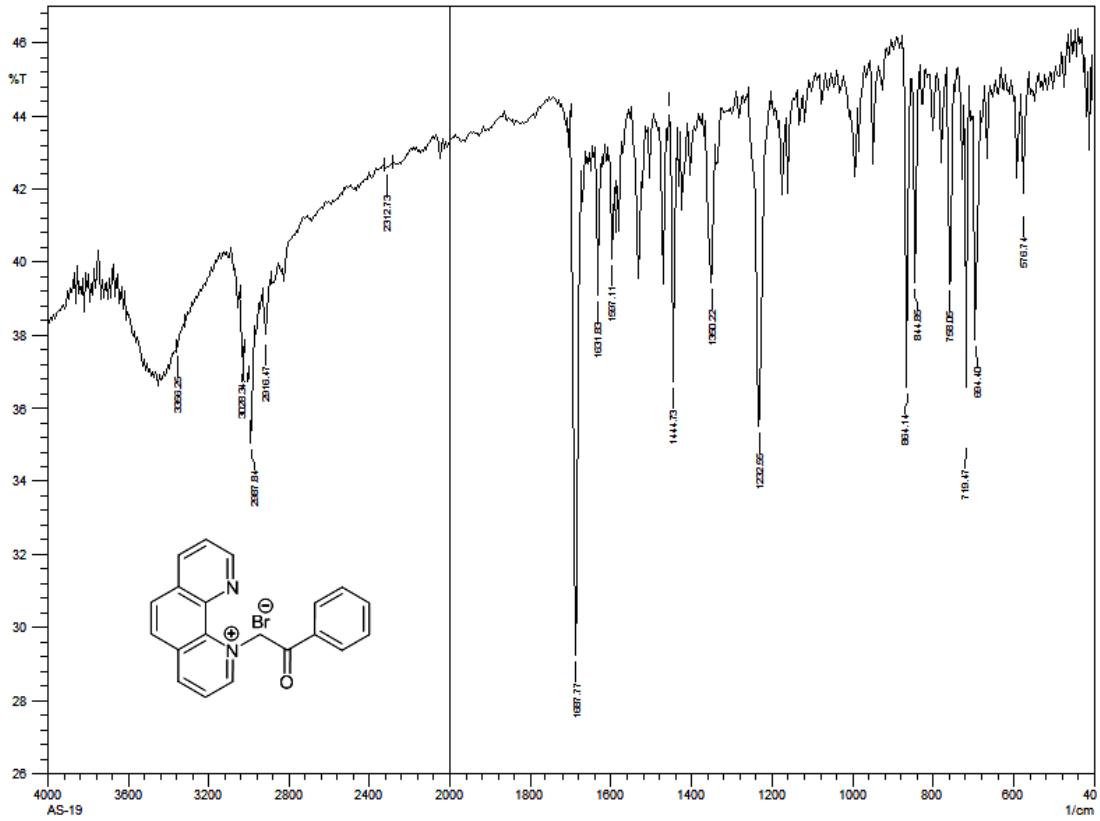

Figure 4. 147 IR Spectrum of **61**

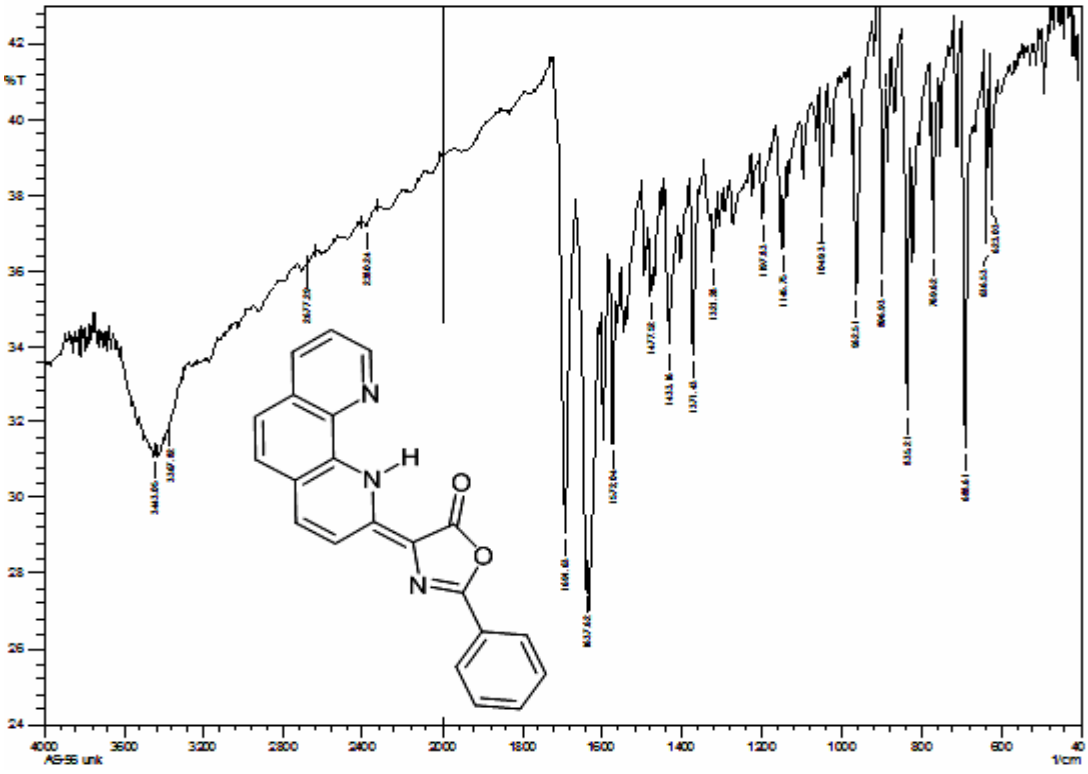

Figure 4. 148 IR Spectrum of **93**

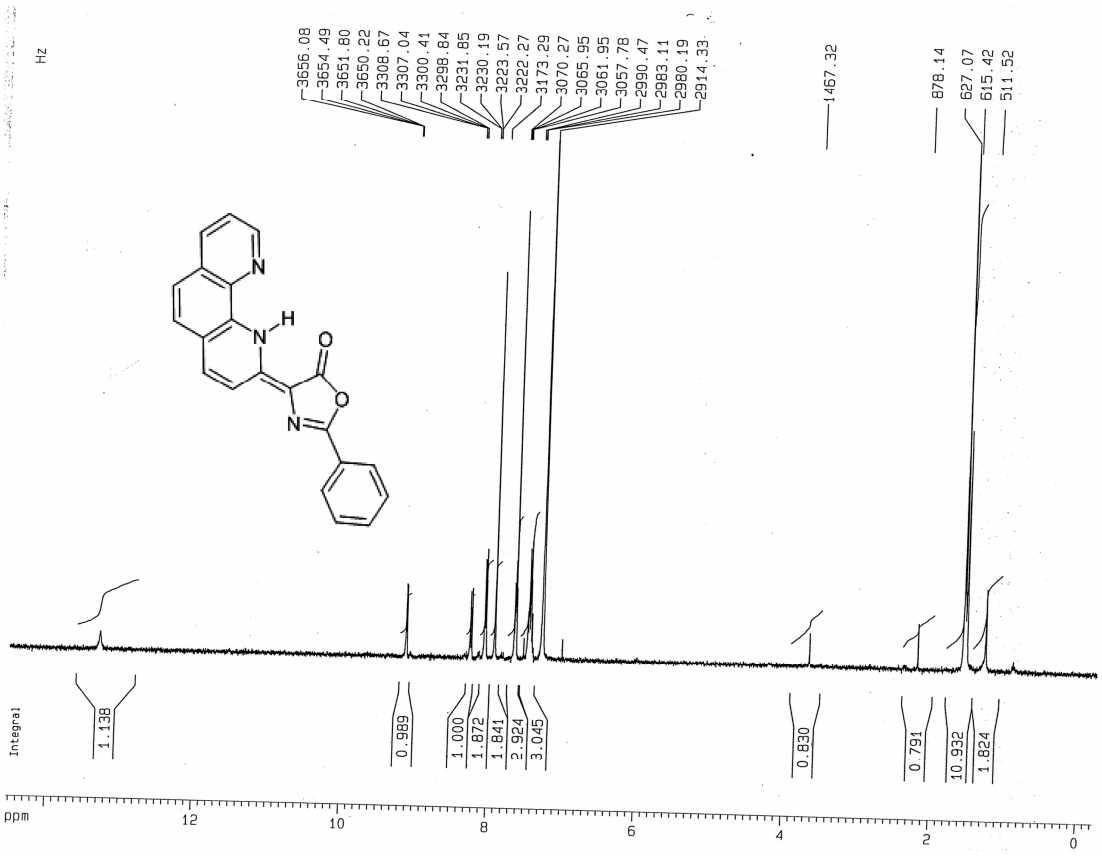

Figure 4. 149 ^{1}H NMR Spectrum of **93**