# SYNTHESIS, CHARACTERISATION AND BIOLOGICAL STUDIES OF SOME UNSATURATED 1,3-DIKETONES AND THEIR METAL COMPLEXES

**Thesis submitted to the University of Calicut**
**in partial fulfilment of the requirements**
**for the degree of**
**DOCTOR OF PHILOSOPHY**
**in Chemistry**

***By***

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**SEPTEMBER 2013**

# DECLARATION

I hereby declare that the thesis bound herewith is an authentic record of the research work on "**SYNTHESIS, CHARACTERISATION AND BIOLOGICAL STUDIES OF SOME UNSATURATED 1,3-DIKETONES AND THEIR METAL COMPLEXES"** carried out by me under the supervision of Dr. K. Krishnankutty, Professor, Department of Chemistry, University of Calicut, in partial fulfillment of the requirements for the award of the degree Doctor of Philosophy in Chemistry of the University of Calicut, and further that this work or part thereof has not been presented before for the award of any other degree.

**Saifunneesa T.K**

# CERTIFICATE

This is to certify that the thesis entitled "**SYNTHESIS, CHARACTERISATION AND BIOLOGICAL STUDIES OF SOME UNSATURATED 1,3- DIKETONES AND THEIR METAL COMPLEXES"** is an authentic record of research work carried out by **Smt. Saifunneesa T.K**, under my supervision in partial fulfillment of the requirements for the award of the degree Doctor of Philosophy in Chemistry of the University of Calicut. This work or part thereof has not been presented before for the award of any other degree.

**Dr. K. Krishnankutty**
( Supervising Teacher)

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***Saifunneesa TK***

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# Preface

In recent years metal complexes of organic compounds have gained tremendous importance mainly because of their numerous applications in industrial and biological field apart from their academic interest. Thus an abundance of research is being done in these areas. This is particularly true in the case of certain organic ligand systems. The best known example is studies on various aspects of 1,3-dicarbonyl compounds and their metal complexes. Studies on 1,3-dicarbonyls and related polycarbonyl compounds and their metal complexes have gathered considerable importance mainly because of the fact that active chemical components of several medicinal plants contain diverse types of dicarbonyl functions. The best known example is curcuminoids, the active chemical entities present in the traditional Indian medicinal plant *Curcuma longa Linn*. (turmeric) and several other related spices.

Structurally curcuminoids are 1, 3-diketones in which the diketo group is directly linked to olefinic linkage. (1,7-diarylhepta 1,6-diene-3,5-diones). Numerous reports on the medicinal properties of curcuminoids such as antifungal, anti-oxidant, antitumour, anti-inflammatory,etc. have been well documented. Several synthetic curcuminoid analogues and similar unsaturated β-dicarbonyl compounds and their metal complexes have been reported to exhibit enhanced biological properties compared to natural curcuminoids and

their metal complexes. Therefore studies on such unsaturated 1,3-dicarbonyls compounds have considerable importance. The present study is also an attempt in this direction. The work comprises synthesis, characterization and biological studies of some new unsaturated β- diketones, β- ketoesters and tetraketones and their typical metal complexes.

The thesis is divided to seven chapters.

**Chapter 1** is a General Introduction which highlights briefly some of the salient features of β-dicarbonyl compounds and their metal complexes. A brief account on reported studies of 'unsaturated' 1,3-dicarbonyls and their metal complexes appeared in general literature have also been included. Importance of the present investigation has been interspersed at appropriate places.

**Chapter 2** is general description on various chemicals, methods employed, instruments used and techniques adopted for the synthesis and characterization of the unsaturated β-dicarbonyls and their metal complexes.

In **Chapter 3**, synthesis and characterization of some unsaturated β-ketoesters and their Cu(II) complexes are discussed. The best known method for the synthesis of curcuminoids and similar 'unsaturated' 1,3-dicarbonyls involve the Claisen-Schmidt condensation of aromatic aldehydes with 1,3-dicarbonyl compounds containing atleast one alkyl group attached to the dicarbonyl function. The same method was adopted for the synthesis of the

unsaturated 1,3-diketones considered in the present investigation. Experimental details for the synthesis of a series of unsaturated β- ketoesters that contain aryl groups such as phenyl, substituted phenyl, indole and naphthyl rings by the Claisen-Schmidt condensation starting from of various aromatic aldehydes and methyl acetoacetate are discussed in this chapter. The IR, NMR and mass spectral data clearly illuminated that the compounds exists in the keto-enol tautomeric form. The compounds formed well-defined complexes of stochiometry $[CuL_2]$ with Cu(II) ions. The spectral data suggest the formation of 6-membered $C_3O_2M$ chelate ring in their Copper(II) complexes.

When the Claisen-Schmidt condensation was carried out with 1,4-phthaldehyde and the 1,3-dicarbonyl compounds; acetylacetone, benzoylacetone, acetoacetatanilide and methylacetoacetate resulted in the formation of four new tetraketones in which the keto groups are directly linked to olefinic functions. Details on their synthesis and characterization are presented in **chapter 4**. The IR, NMR and mass spectral data showed that the compounds exist predominantly in the intramolecularly hydrogen bonded enol form. All the compounds formed stable 1:1 complexes with Cu(II), Ni(II) and Co(II) ions. Spectral data unequivocally support the dibasic tetradentate coordination of the tetraketones in their metal complexes.

The Claisen-Schmidt condensation of benzaldehyde with 2-acetylcyclopentanone and 2-acetylcyclohexanone yielded two novel unsaturated 1,3-diketones containing alicyclic ring. Based on IR, NMR and mass spectral data the pentanone derivative has been shown to exist entirely in the keto form and the hexanone derivative in the slightly enolised form. Both the compounds formed stable complexes of stochiometry $[ML_2]$ with Cu(II) and Ni(II) ions. The IR, NMR and mass spectral data of the complexes also support the formulation of the complexes. These details are presented in **Chapter 5**.

**Chapter 6** is mainly on the biological properties such as antifungal and antioxidant activities of the unsaturated 1,3-dicarbonyls and their metal complexes. The results of antifungal activity of the unsaturated dicarbonyl compounds and their Cu(II) complexes toward *Aspergillus niger*, *Penicillium* and *Fusarium* are presented in **section A**. The data revealed enhanced activity for the Cu(II) complexes. Procedural details adopted for the determination of antioxidant activity of the compounds by the DPPH method are presented in **section B**. The Ec 50 value, ARP and NRD data obtained for typical compounds and their Cu(II) complexes considered in chapter 3 are also discussed. The Ec10 values were calculated for compounds with lesser antioxidant activity. The observed results clearly demonstrated the antioxidant property of these compounds.

Since the biochemical properties of these compounds are mainly dependent on their electron transfer abilities, the redox behavior of these compounds considered in chapter 3 and 4 and their Cu(II) complexes were determined by cyclic voltammetry. The data obtained are compared with typical curcuminoid analogues and the results are presented in **chapter 7**.

Finally references are given at the end of the thesis in the chronological order.

The work described in the thesis has partially been published/ accepted/communicated for publication.

1. Synthesis and characterization of two unsaturated tetraketones and their metal complexes, *Inorganic Chemistry – An Indian Journal*, 199, **7(5)**, 2012.

2. Synthesis, characterization, antioxidant and redox behavior of some unsaturated β-ketoesters and their Cu(II) complexes. *J. Serb. Chem. Soc*., (accepted).

3. Metal complexes of new unsaturated tetraketones and their antifungal, antioxidant and redox activities. *J. Ind. Chem. Soc*. (accepted).

4. Synthesis and characterization of synthetic analogues of curcuminoids containing alicyclic rings and their metal complexes. *J. Serb. Chem. Soc*. (communicated).

# Nomenclature and Abbreviations

## Nomenclature

In the present study both the systematic and trivial names are used wherever necessary. Curcuminoids is a general term used to designate unsaturated 1,3-dicarbonyls, because such compounds were first isolated from the yellow pigment of the rhizomes of the plant Curcuma longa (turmeric). In the present investigation the term curcuminoid is used in a broader sense to include related unsaturated 1,3-dicarbonyls also.

## Abbreviations

| | | |
|---|---|---|
| Ar | – | aryl group |
| $E_{pa}$ | – | Anodic electrode potential |
| $I_{pa}$ | – | Anodic peak current |
| ARP | - | Anti radical power |
| $E_{pc}$ | – | Cathodic electrode potential |
| $I_{pc}$ | – | Cathodic peak current |
| CV | - | Cyclic voltammetry |
| DPPH | - | Diphenyl picryl hydrazyl |
| DMSO | – | Dimethyl sulphoxide |
| EI | – | Electron ionization |
| FAB | – | Fast atom bombardment |
| GCMS | – | Gas chromatography - Mass spectrometry |
| NRD | – | Number of reduced DPPH |
| Ph | – | Phenyl |
| SV | – | Stochiometric value |
| TBAI | – | Tetrabutyl ammonium iodide |

# CHAPTER 1
# GENERAL INTRODUCTION

## Coordination chemistry of 1, 3-dicaybonyl compounds

Design and synthesis of polydentate and macrocyclic ligand systems have become a fascinating area of modern coordination chemistry mainly because of the increasing academic, industrial and biological interest exhibited by metal complexes of these types of compounds [1-5]. This is particularly true in bioinorganic studies and in medicine. The ability of metal ions to influence many of the complex reaction upon which the vital processes of living organisms depends has been well established. Several synthetic metal complexes that mimic the behaviour of complicated biomolecules are known and at present, the studies of such compounds are of considerable importance.

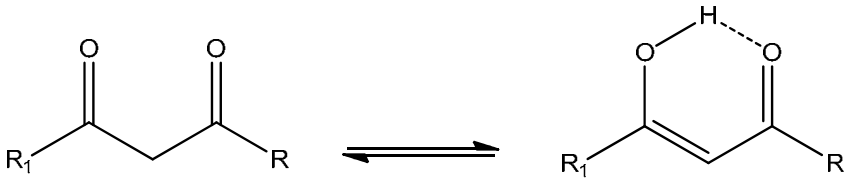
The properties and structure of metal complexes are dependent on the nature of the metal ion and the structure, conformation, etc., of the ligands attached to it[6-12]. That the variations in metal ions are considerable, on the other hand the variations in ligands are virtually limitless mainly because of the numerous methods developed by the modern synthetics organic chemists.

Literature reveals that metal complexes of organic compounds that contain carbonyl function(s) have proliferated much during recent years. This

trend is evident from the numerous reports of ligand systems based on β-dicarbonyl and related polycarbonyl compounds [13-45]. In general these type of compounds act as the starting materials for the design and synthesis of large number of compounds having wide application in many fields particularly in bioinorganic studies. This is not unexpected of these types of compounds because of the fact that proton transfer and hydrogen bonding are two important factors that governs the structure and functions of many molecules starting from water to DNA[45-55]. These properties are the characteristic features of β-dicarbonyl compounds. Two most important properties of β-dicarbonyl compounds are their ability to exhibit keto-enol tautomerism and formation of diverse types of coordination compounds with almost all the metal and metalloid elements present in the periodic table[56,59,88-93]. These aspects of β-dicarbonyls are briefly outlined below, because the present study is also on a new series of β-dicarbonyl compounds and their metal complexes.

**Keto-enol tautomerism of β-dicarbonyl compounds**

The β-dicarbonyls are compounds in which a methylene group is flanked by two carbonyl groups. The methylene hydrogen(s) are activated by the adjacent carbonyl groups and a conjugated system can arise by a prototropic shift as in structures **1** and **2**.




**1** **2**

| **R** | **$R_1$** |
|---|---|
| Alkyl | Alkyl |
| Alkyl | Alkyl |
| Aryl | Aryl |
| alkyl/aryl | alkoxy/aryloxy |
| alkyl/aryl | ArNH |

The existence of keto-enol tautomerism in β-dicarbonyls was confirmed by various analytical and spectroscopic techniques[60-70]. The extent of enolisation depends on various factors such as solvent, temperature, substituents at α-and β-position and presence of other functions that are capable of H-bonding, etc. In general bulky alkyl substituents present on the α-carbon leads to decreased amount of the enol tautomer while Cl, Br, CN, $COOCH_3$, $SCH_3$, etc., groups leads to almost hundred percentage of enol form[54-58, 71-73]. Electron withdrawing groups such as $CF_3$, $C_4H_3S$ (thienyl), $C_6H_5$, etc., shift the equilibrium in favour of the enol tautomer[71-73]. The

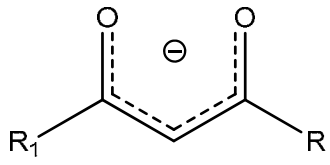
percentage of enolisation is very low when the R or $R_1$ are replaced by electron donating groups like -$OCH_3$, -$OC_2H_5$, -NHPh, -$NH_2$, etc[74-76].

In unsymmetrically substituted β-dicarbonyl compounds, the direction of enolisation mainly depends on the electron demand on the carbonyl carbons. For example in benzoylacetone, the benzoyl carbonyl undergoes enolisation[77]. In phenyl substituted β-dicarbonyls the phenyl groups bearing an electron releasing substituent such as –$OCH_3$ do not undergo enolisation[77]. In β-ketoesters and β-ketoanilides, the enolisation occur mainly at the acetyl carbonyl. In cinnamoyl benzoylmethane where the dicarbonyl function is attached to olefinic groups, the direction of enolisation occur at the cinnamoyl carbonyl[78].

**Metal complexes of β-dicarbonyl compounds**

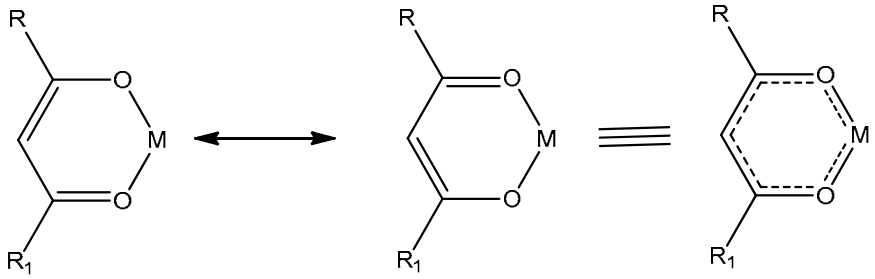
The coordination ability of β-dicarbonyl compounds was recognised as early as in 1887 when Combes[79-82] reported the synthesis of beryllium acetylacetonate. This was followed by pioneering works of Werner[83], Morgan[84-85] and Sidgewick[86] who confirmed their bifunctional chelating character. Being powerful complexing agents, β-dicarbonyl compounds forms complexes with virtually all the transition and main group metal and metalloid elements in the periodic table. The methine proton in the keto form

and –OH proton in the enol form of these β-dicarbonyls are acidic and their removal generates the 1,3-deketonate anion **3**



**3**

This anion can form bond with metal ions and they constitute an extremely broad class of coordination compounds generally known as metal 1, 3-diketonates. The high stability of these compounds is mainly due to the six membered $C_3O_2M$ ring structure of the chelate and delocalisation involving the metal ion (Strcture **4-6).**

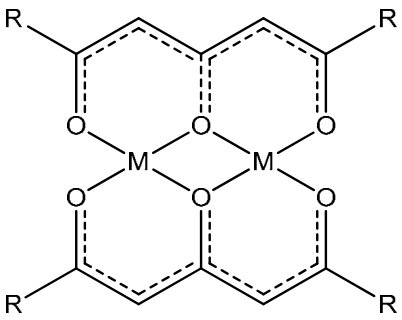


**4** **5** **6**

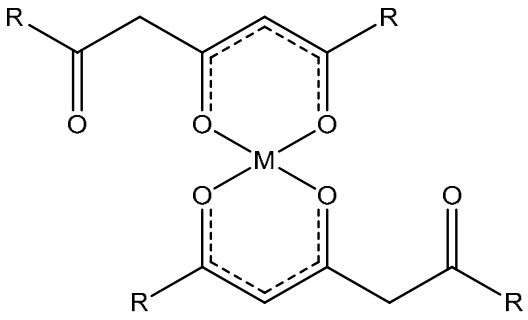
Although the most familiar mode of coordination of β-dicarbonyls is as monobasic bidentate as in structures 4-6, several other interesting modes of bonding involving even the alkyl, methylene and olefinic carbons are also known[15-29,45-46].

**Polyketons and their metal complexes**

Numerous higher homologoues of 1,3-diketones such as 1,3,5-triketones, 1,3,5,7-tetraketones have been reported[15-44]. These polyketones exist predominantly in the highly conjugated enol tautomer and are known to form diverse types of metal complexes as illustrated in structure **7-12**. Many of these complexes show interesting structures and unique spectral and magnetic properties that are of interest in bioinorganic studies. This is mainly due to their ability to form complexes with various biologically important metal ions[54-58, 87-93]. Therefore studies on the coordination behaviour of polyketones have tremendous importance.



**7**



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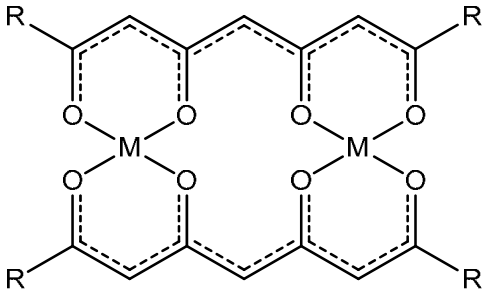

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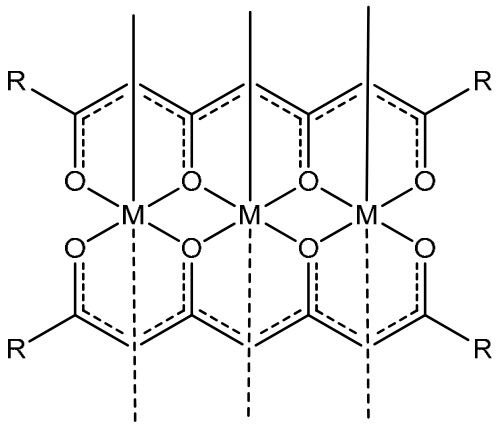

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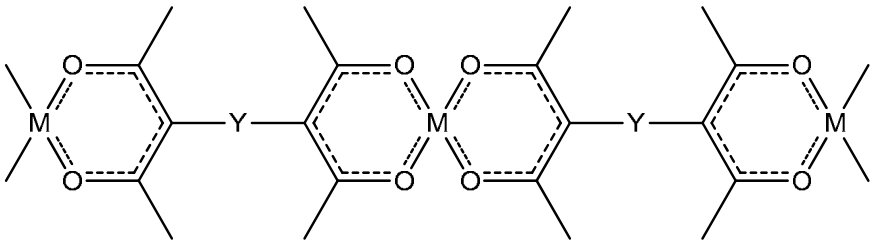

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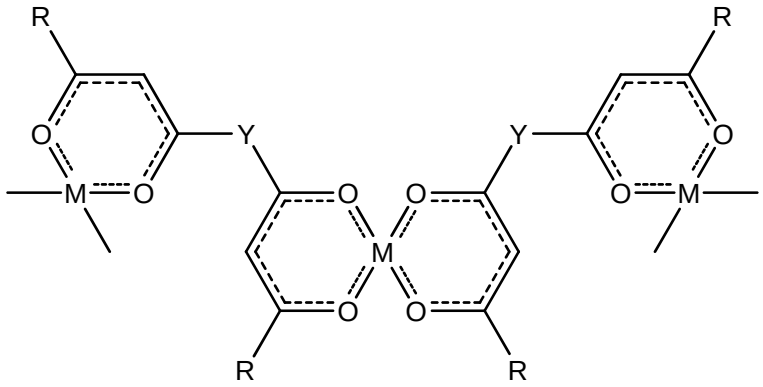


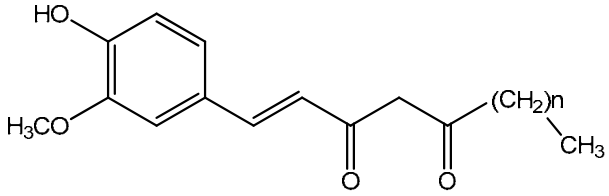
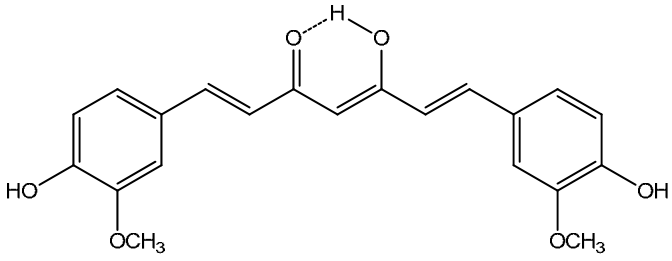
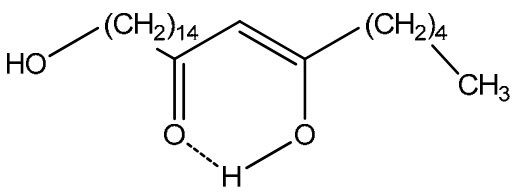
**12**

**Naturally occuring β-dicarbonyl compounds**

It has been well established that the active chemical constituents of several medicinal plants contain 1,3-dicarbonyl compounds in which the dicarbonyl function directly linked to olefinic bonds. Typical examples are given in **Table 1.1.** Among these, the best known example is curcuminoids, the most active chemical constituent present in the roots and shoots of the herbaceous Indian medicinal plant *Curcuma Longa* (turmeric) and several other related curcuma species of the family *Zingiberaceae*. Chemically curcuminoids are 1,7-diarylhepta-1,6-diene 3,5-diones (1,7-diarylheptanoids) which comprise a distinct class of natural products of wide pharmacological interest.[94]

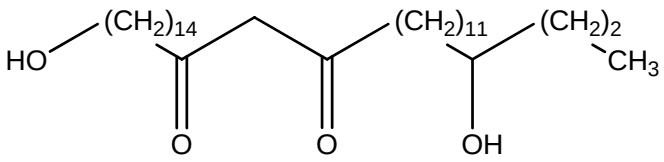
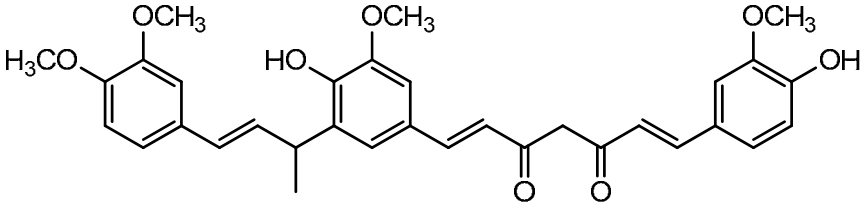
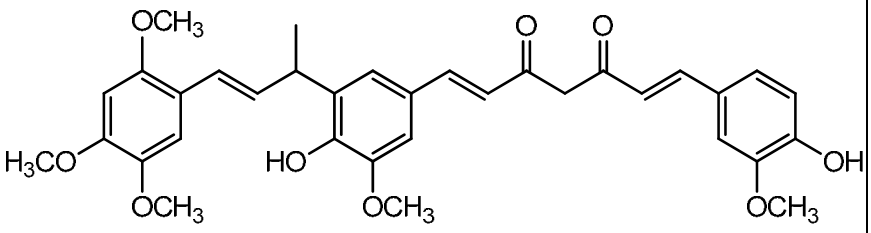
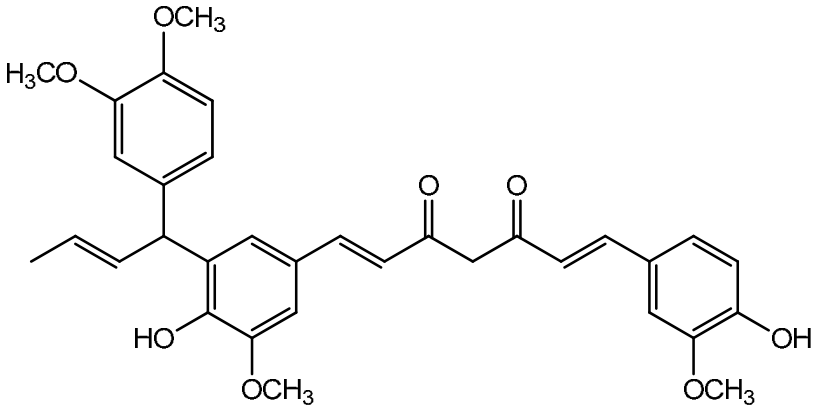
Turmeric occupies an important role in various food preparations, rituals and ceremonies of the Indian subcontinent. Due to its strong antiseptic properties, it has been used as a common remedy for all kinds of poisonous effects. The traditional Indian systems of medicine such as Ayurveda, Unani, Siddha, etc., involve the use of turmeric against biliary disorders, rheumatism, sinusitis and several other ailments.[95-101] Apart from the religious and medicinal uses, turmeric has also been used for dyeing fabrics and as a colouring agent in food and drugs[102].

**Table 1.1: 1,3-dicarbonyls as active chemical constituent present in selected medicinal plants**

| Spice (Plant species) Active Compound | Structure |
|---|---|
| Ginger (Zingiber officinale) Gingerols |  |
| Turmeric (Curcuma Longa) Curcumin I. |  |
| Eucalyptus (Eucalyptus globulus) n-Tritriacontan 16, 18-dione. |  |

Contd……

Table 1.1 contd……..

| | |
|---|---|
| 4-hydroxytritriaco - ntan 16, 8-dione. |  |
| Indonesian medicinal ginger (zingiber Cassumunar) Cassumumin A |  |
| Cassumumin B |  |
| Cassumumin C |  |

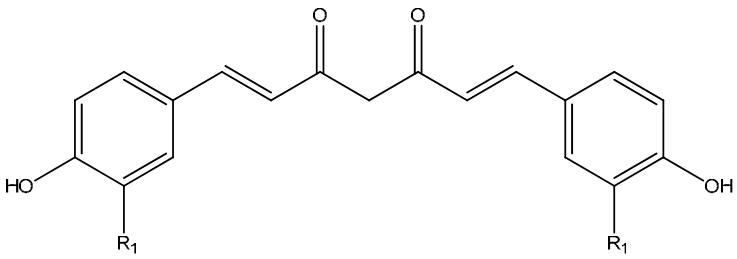
The composition of turmeric consists of various percentages of protein, fat, minerals, moisture and carbohydrate[103]. The important commercial products derived from raw turmeric are turmeric powder, turmeric oleoresin, turmeric oil and curcuminoids[95,104]. Aroma of turmeric, caused by the steam volatile oil fraction ranges from 2.5 – 7.2% of the spice[95,105,106].

**Constitution of curcuminoids**

The earliest report on the constitution of 'turmeric yellow' is by Vogel and Pelletier[107] in 1815, who reported the isolation of the colouring matter in a crude form by the partial evaporation of turmeric extracts and named the pigments as curcumin. In 1870, Daube[108] isolated curcumin in the crystalline form. Later Jackson[109] and Perkin and Phillips[110] obtained curcumin by precipitating through its lead salt form an alcoholic extract of turmeric. The molecular formula $C_{12}H_{20}O_6$ was first suggested by Ciamicin and Sibler[111] and the structure was elucidated by Lampe et al[112] in 1910 who later reported its synthesis.[113]

In 1953, Srinivasan[114] (using column chromatography over silica gel) showed the presence of three well defined yellow compounds along with other resinous materials in the crude pigment extracted from turmeric. These three compounds were tentatively identified on the basis of elemental analysis and methoxyl values as curcumin I (deferuloylmethane) or curcumin, curcumin II (feryloyl-p-hydroxycinnamoylmethane) and curcumin (III) (bis-

4-hydroxycinnamoylmethane) (3)[107,114] as in structures **13** Curcumin I which eluted first from the column was the major component (~40%) followed by curcumin II (~16%) and curcumin (III) (~10%). The structure of the compounds were later confirmed by chemical degradation studies.[115]




(1) $R_1 = OCH_3$ $R_2 = OCH_3$ Curcumin I

(2) $R_1 = OCH_3$ $R_2 = H$ Curcumin II

(3) $R_1 = H$ $R_2 = H$ Curcumin III

**13**

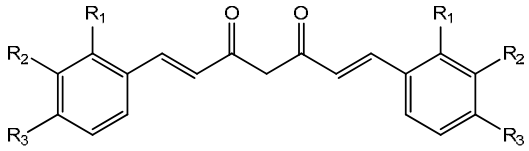
**Synthesis of Curcuminoids**

The first reported synthesis of curcumin was in 1913 by Lampe and Milobedzka[116] through the condensation of carbomethoxyferuloyl chloride and acetoacetic ester. Pavoloni *et al.*,[117] were reported an improved synthetic method which involves the condensation of vanillin with acetylacetone in presence of boric oxide at elevated temperature. It was then modified by Pabon[118] who obtained curcumin I in ~80% yield by condensing vanillin with acehylacetone at room temperature using n-butylamine as the condusing agent. The procedure of Pabon has been developed as a general route to synthesis curcuminoids and other 1, 7-diarylheptanoids from acetylacetone and suitable aromatic aldehydes.[119]

**Synthetic analogues of natural curcumioids and their metal complexes**

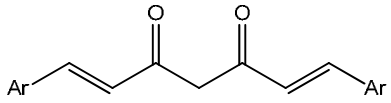
In recent years a number of synthetic amalogues of the natural curcuminoids have been prepared and studied their physicochemical and biological properties. These include typical unsaturated 1, 3-diketones such as *1,7-diarylhepta-1,6-diene-3,4-diones, 6-arylhexanoids, pentanoids, esters and anilides.* Some of the representative examples of the above mentioned compounds are given in **Table1.2-1.8**. Almost all of these compounds form stable complexes with various transition and non-transition metal ions. Reported metal complexes of these compounds are also summerised in **Tables 1.2 – 1.8.** In almost these cases the compounds functioned as monobasic bidentate ligand during complexation.

**Table 1.2: 1, 7-diarylhepta-1,6-diene-3,4-diones(Curcuminoid analogues) and their metal complexes**



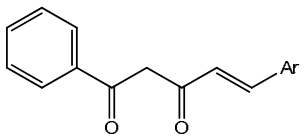

| $R_1$ | $R_2$ | $R_3$ | Complexes reported | References |
|---|---|---|---|---|
| H | H | H | | |
| H | H | $OCH_3$ | $Cu^{2+}$, $Ni^{2+}$, $Co^{2+}$ | |
| H | H | OH | $Zn^{2+}$, $Pd^{2+}$ | |
| H | $OCH_3$ | OH | $VO^{2+}$, $Al^{3+}$ | |
| H | $OCH_3$ | $OCH_3$ | $Fe^{3+}$, $Mn^{2+}$ | 119 – 134, |
| H | OH | OH | $Ga^{3+}$, $In^{3+}$, $UO_2^{2+}$ | 138 |
| Cl | H | H | $Cd^{2+}$, $Hg^{2+}$, $Pb^{2+}$ | 142, 143, |
| OH | H | H | | |

**Table 1.3: Unsaturated 1, 7-diarylheptanoids and their metal complexes.**



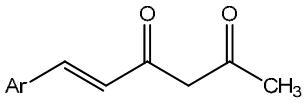

| Ar | Complex reported | References |
|---|---|---|
| 2-naphthyl<br>2-hydroxynaphthyl<br>cinnamyl<br>piperonyl<br>9-anthryl<br>2-furyl<br>3-indolyl | $Cu^{2+}$, $Al^{3+}$ ,$Cu^{2+}$, $Zn^{2+}$ ,$Al^{3}$, $Mn^{2+}$,$Ni^{2+}$,$Co^{2+}$ | 123-126<br>135-137<br>150, 151 |

**Table 1.4: 5-Aryl-1-Phenyl-4-Pentene-1, 3-diones and their metal complexes**



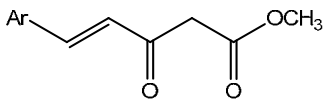

| Ar | Complex reported | References |
|---|---|---|
| Cinnamyl<br>2-naphthyl<br>3-pyridyl<br>2-furyl<br>2-hydroxyphenyl<br>3-indoly | $Cu^{2+}$, $Ni^{2+}$, $Co^{2+}$, $Zn^{2+}$, $Vo^{2+}$ | 139 – 141,<br>147 |

**Table 1.5: 6-Arylhex-5-ene-2,4-diones and their metal complexes**



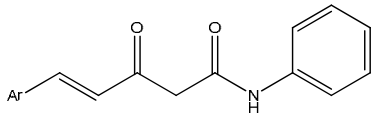

| Ar | Complex reported | References |
|---|---|---|
| Phenyl<br>4-Methoxyphenyl<br>4-Hydroxyphenyl<br>4-Hydroxy-3-methoxyphenyl<br>3,4-Dimethoxyphenyl<br>2 – Furyl<br>2-Hydroxyphenyl<br>2-Hydroxy-l-naphthyl | $Cu^{2+}$, $Ni^{2+}$<br>$Co^{2+}$,$Zn^{2+}$ | 138, 148 |

**Table 1.6: Methyl- 5-aryl-3-oxopent-4-enoate and their metal complexes**




| Ar | Complex reported | References |
|---|---|---|
| Phenyl<br>4-Hydroxyphenyl<br>4-N,N-Dimethylphenyl<br>4-Hydroxy-3-methoxyphenyl<br>2-Naphthyl<br>2-Hydroxynaphthyl | $Cu^{2+}$, $Ni^{2+}$,$Zn^{2+}$ | 144 |

**Table 1.7: 5-aryl-3-oxo-N-phenylpent-4-enamide and their metal complexes.**




| Ar | Complex reported | References |
|---|---|---|
| 2, 4-dimethoxyphenyl<br>3, 4-dimethexyphenyl<br>3, 4-methylene dioxyphenyl<br>4-methoxyphenyl<br>4-ethoxyphenyl<br>4-dimethylaminophenyl<br>4-nitrophenyl<br>3-hydroxyphenyl<br>3-methoxyphenyl<br>3-chlorophenyl<br>Phenyl<br>1-naphthyl<br>2-furyl<br>2-hydroxy phenyl<br>2-hydroxy-1-naphthyl | $Cu^{2+}$, $Ni^{2+}$, $Zn^{2+}$ | 145, 146, 149 |

**Biological and medicinal properties of curcuminoids**

In the indigenous systems of medicine of the orient, *Curcuma Longa* L. has been employed since time immemorial as remedy for several ailments. Turmeric acts as an anti-inflammatory agent, as a carminative, diuretic and blood purifier as well as a remedy against jaundice[152-155]. It is also recommended for use against common cold, cough, leprosy, affections of the

liver and in the treatment of various ulcers. These effects are ascribed to the yellow pigment curcumin isolated from the turmeric[95-97,101,156-159].

The interest in natural[160-163] and synthetic curcuminoids[164-169] particularly as a choleretic, hypocholestermic and antihepatotoxic agent is increasing and they now being regarded as a potential drug for many diseases due to several reasons[155]. Although the chemical structure of curcumin has known way back in 1913, the biochemical and medicinal properties of curcuminoids have received due attention only in 1970's[170-173]. The actual place of curcumin research as anticancer agent has picked up in 1990's after recognition of its ability to suppress activation of transcription factor, nuclear factor NF-kB[155,174]. Curcumin exhibits potential therapeutic application against several chronic diseases including cancer, inflammatory, neurological, cardio-vascular and skin diseases[175-183]. Now a days curcumin used as a clinical trials for the treatment of variety of cancers and also for Alzheimer's disease[170].

The antitumour activity of natural curcuminoids were compared by A.J Ruby and coworkers[162] and curcumin III was found to be more active. Their synthetic analogues and their metal complexes were also checked for antitumour activities and were found to behave similar to natural curcuminoids[121-126]. Natural curcuminoids showed cytotoxic activity against leukemia, colon, CNS, melanoma, renal and breast cancer cell lines[163,176].

Natural curcuminoids are best free radical scavengers and thus act as antioxidants[154,162,163]. They scavenge hydroxide, superoxide and peroxide radicals[129,162,164,167,184-186]. The metal complexes of these curcuminoids act as SOD mimics and this property of binding of curcumin to metals is considered as one of the useful requirements for the treatments of Alzhiemer,s disease, because of the correlation between the drugs of Alzhiemer's disease and the SOD mimics[129,187-188].

Several synthetic analogues of natural curcuminoids have been subjected to various biochemical properties. Thus several new synthetic compounds in which the dicarbonyl function directly linked to olefinic linkages were reported to exhibit interesting biological properties compared to natural curcuminoids. A number of these synthetic curcuminoids have been reported to possess many fold increased antifungal, antibacterial, antioxidant, antitumour etc. activities compared to natural curcuminoids[119-127,129162, 167-168]. This has been possible mainly because of varying the functional groups attached to the unsaturated dicarbonyl function. Therefore design and synthesis of novel β-dicarbonyls in which the dicarbonyl functions directly attached to olefinic linkages have considerable importance. Since these compounds are structurally related to typical 1,3-diketones, they can form stable metal complexes and can alter their biological properties. Thus studies on the complexes of these types of compounds will be interesting. The present study is an attempt in this direction.

## The present investigation

The physico-chemical properties, structural features, biological properties,etc of these unsaturated 1,3-dicarbonyl compounds are dependent on several factors. The most important factors are the nature of the aryl substituents type of the aryl groups and the groups attached to the olefinic functions. Similarly metal complexation can modify their beneficial properties. Depending on the nature of the metal ions the properties of these unsaturated 1,3-dicarbonyls can be tuned. Therefore synthesis, characterization and studies on biological properties of these types of unsaturated 1, 3-dicarbonyl compounds having different structural features are of considerable importance. Thus in this investigation a series of novel unsaturated 1, 3-dicarbonyl compounds and their typical metal complexes were synthesized and characterized. Important biological and redox properties were also studied. Results obtained are presented in **chapters 3-7**.

In **chapter 3** details on the synthesis and characterization of a series of unsaturated β-ketoesters and their Cu(II) complexes are discussed. A new series of unsaturated tetraketones in which the carbonyl function attached to olefinic linkages are considered in **chapter 4**. Synthetic details and their characterization using different spectral techniques are also included in this chapter. **Chapter 5** is mainly on the synthesis and characterization of two new unsaturated 1,3-diketones that contain cycloakanone ring systems and

their metal complexes. The biological properties such as the antifungal and antioxidant activity of the compounds considered in chapters 3 and 4 are discussed in **chapter 6**. Many of the compounds considered in chapters 3-5 are dependent on their electron transfer abilities. Therefore the redox behaviors of these compounds are examined by cyclic voltammetry. The results are given in **chapter 7**.

# CHAPTER 2

# MATERIALS, INSTRUMENTS AND METHODS

## Materials

Chemicals used for synthesis were of C.P.grade. For analytical purposes 'Analar R' grade chemicals were employed. Commercial solvents were distilled and used for synthesis. Solvents purified by methods recommended by Wiessberger[189] were employed for physico-chemical measurments.

The following metal salts were used for the synthesis of metal complexes. Cobalt(II) acetate tetrahydrate, nickel(II) acetate tetrahydrate, copper(II) acetate monohydrate.

Only compounds isolated analytically pure are reported in the thesis. The complexes reported here are stable and has good keeping qualities. Compounds for recording spectra were recrystallised from proper solvents several times till chromatographically pure (tlc-Silica gel) samples were obtained.

## INSTRUMENTS AND METHODS

*Elemental analysis:* The ligands-and metal complexes were analysed by standard methods. Carbon, hydrogen and nitrogen percentages were

determined by micro-analysis using HERAEUS CHNO rapid analyser. The metal percentages were determined using PERKIN ELMER 2380, atomic absorption spectrophotometer, after decomposing with concentrated sulphuric acid and nitric acid mixture.

*UV-Visible spectra* were recorded from JASCO V-550 UV-visible spectrophotometer, using a $10^{-6}$ M solution of the compounds in methanol unless otherwise mentioned.

*Infrared spectra* were recorded using JASCO FT/IR 4100 instrument. The spectra were recorded from disc with KBr. Bands were calibrated using the nearest polystyrene bands.

*$^{1}H$ nmr spectra*: The instrument used was JEOL JMS 6011 nmr spectrometer (NIIST, Thiruvananthapuram) , Bruker 500 MHz nmr spectrometer (IISER, Thiruvananthapuram), JEOL 400 nmr spectrometer (RSIC, IIT, Bombay) The spectra were recorded using $CDCl_3$/DMSO-$d_6$ as solvents and TMS as internal reference.

*FAB mass spectra* were obtained from NIIST, Thiruvananthapuram. The spectra were recorded at room temperature using argon (6KV, 10mA) as the FAB gas and meta-nitrobenzyl alcohol (NBA) as the matrix. The probable Matrix peaks are located at m/z 136, 137, 154, 289 and 307. The instrument used was JEOL JMS 600H.

*GCMS* were obtained from IISER, Thiruvananthapuram.

*EI mass spectra* were obtained from SAIF, ISISM, SRM University and they were recorded by imparting vapourised samples with a beam of electron at 7-10 ev.

*Biological studies*: Solvents and chemicals used for biological studies were analytical grade. Fungi used for antifungal activity were cultured in situ. The AR grade DPPH used for antioxidant activity was purchased from Sigma-Aldrich. Materials, chemicals, techniques and instruments employed for various biological studies are given in the chapter 6.

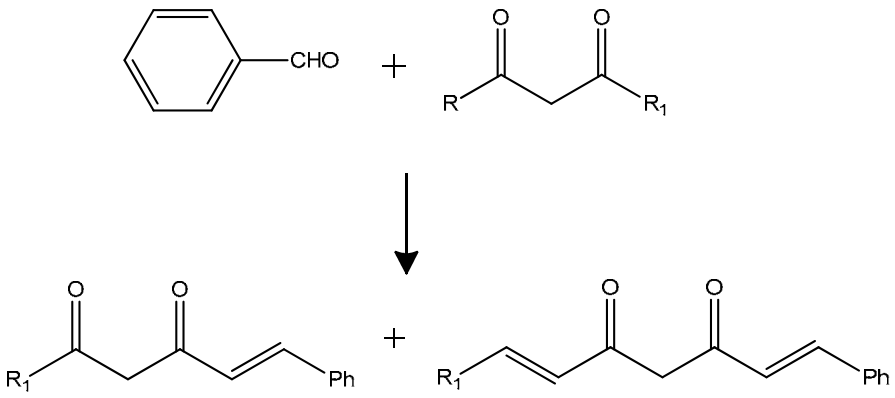
*Electrochemical studies*: Chemicals and solvents used for cyclic voltammetry were analytical grade and were purchased from Merck, India Ltd. The instrument used was SP-50 Biologic analyzer. Materials, chemicals and techniques employed for cyclic voltammetric measurements are given in chapter 7.

# CHAPTER 3

# SYNTHESIS AND CHARACTERISATION OF SOME UNSATURATED β-KETOESTERS AND THEIR Cu(II) COMPLEXES

## Introduction

The Claisen-Schmidt condensation of an aromatic aldehyde and 1,3-dicarbonyl compounds having atleast one acetyl function usually result in the formation of both mono- and bis condensation products[119,190] as given in the reaction **scheme 3.1**.




R and $R_1$ = alkyl

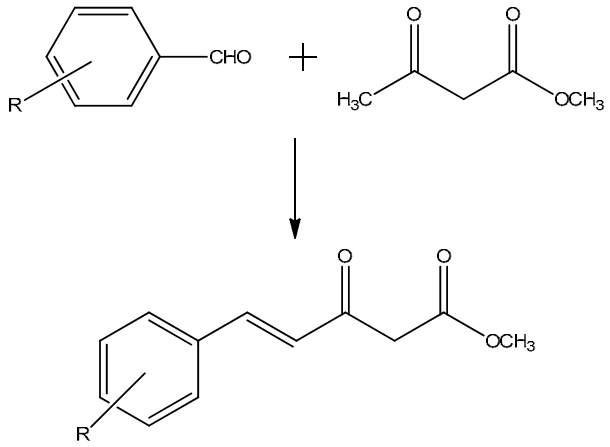
R = alkyl; $R_1$ = aryl

R = alkyl; $R_1$ = –OR, –NHPh, etc.

**Scheme 3.1**

Since β-ketoesters such as methylacetoacetate has only one acetyl group, the Claisen-Schmidt condensation reaction between aroamtic

aldehydes can only form a single product as in **scheme 3.2.** These unsaturated β-ketoesters can also form stable metal complexes similar to the β-ketoesters. The synthetic details and characterisation of these unsaturated β-ketoesters and their typical metal complexes are discussed in this chapter.




**Scheme 3.2**

## Experimental

### Synthesis of the unsaturated β-ketoesters

The condensation of various aldehydes with methylacetoacetate was carried out in presence of boric oxide and tri-butyl borate using n-butylamine as the condensing agent. Boric oxide was used to prevent the Knovenagal condensation. Procedural details are given below.

Methylaceoacetate (0.01 mol) and boric oxide (0.01 mol) were mixed thoroughly to get a pasty mass. The mixture was stirred on a magnetic stirrer at room temperature for ~ 1 h after adding 5 ml of dry ethyl acetate. To this

mixture a solution of the aromatic aldehyde (0.01 mol) and tri(sec-butyl) borate (0.04 mol) dissolved in dry ethylacetoacetate (~5 ml) were added and stirring was continued for ~ 6 h with the slow addition of n-butylamine (0.5 ml in 5 ml dry ethylacetate). The mixture was kept overnight. To this 10 ml HCl (0.01 M) was added and again stirred for ~1 h and extracted several times with ethylacetate. The combined extracts were evaporated to dryness on a water bath. The pasty mass obtained was stirred with methanol (15 ml) for ~ 2 h and was kept in an ice bath with constant stirring for ~ 3 h. The precipitated product was filtered and recrystallised from hot benzene. The purity of the product was checked by tlc (silica gel) and revealed the presence of only one well defined spot in all the cases. The synthetic details of the compounds are given in **table 3.1.**

**Synthesis of Cu(II) complexes**

To a refluxing solution of the compound (0.002 mole) in methanol (20 ml), a methanolic solution of copper(II) acetate (0.001 mole, 15 ml) was added drop by drop. The pH of the solution was adjusted around 6 using sodium acetate and refluxing was continued for ~ 6 h. The solution was concentrated to half of the volume. The precipitated complex on cooling to room temperature was filtered, washed with water, then with methanol and dried in vacuum.

**Table3.1: Synthetic details of the unsaturated β-ketoesters**

| Compounds | Aldehydes used for synthesis | Systematic name / Trivial name | Yield (%) |
|---|---|---|---|
| **3a** | Benzaldehyde | Methyl 3-oxo-5-phenyl pent-4-enoate | 55 |
| **3b** | 3,4-dihydroxybenzaldehyde | Methyl 5-(3,4-dihydroxyphenyl)-3-oxopent-4-enoate | 62 |
| **3c** | Vanillin | Methyl 5-(4-hydroxy-3-methoxyphenyl) -3-oxopent-4-enoate | 65 |
| **3d** | 4-nitrobenzaldehyde | Methyl 5-(4-nitrophenyl)-3-oxopent-4-enoate | 45 |
| **3e** | 4-methoxybenzaldehyde | Methyl 5-4-methoxyphenyl) -3-oxopent-4-enoate | 49 |
| **3f** | 4-hydroxybenzaldehyde | Methyl 5-(4-hydroxy phenyl) -3-oxopent-4-enoate | 86 |
| **3g** | 3,4-dimethoxy benzaldehyde | Methyl 5-(3,4-dimethoxyphenyl) -3-onepent-4-enoate | 61 |
| **3h** | 2-hydroxynaphthaldehyde | Methyl 5-(2-hydroxy naphthalene-1yl) -3oxopent-4-enoate | 60 |
| **3i** | Indole-3-carbaldehyde | Methyl 5-(1H-indol-3-yl)-3oxopent-4-enoate | 87 |

## Results and discussion

### Characterisation of the unsaturated β-ketoesters

The physical and analytical data of the compounds are given in **table 3.2**. All the compounds were crystalline in nature with low melting points and are soluble in common organic solvents. The observed C, H percentages of the compounds suggest that the condensation of the aldehyde has occurred only at the acetyl methyl group of the ester.

Though some of the compounds given in the table have been reported earlier[144], for comparison these compounds are also included. The compounds were characterised mainly using their IR, NMR and mass spectral data. The spectral details are discussed below.

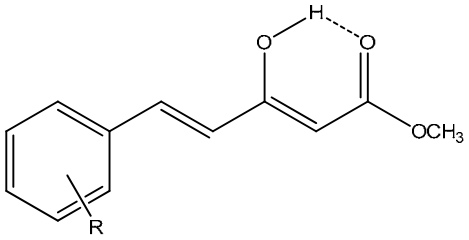
### Infrared spectra

Infrared spectra of all the compounds show three strong bands in the region 1600-1800 $cm^{-1}$ at ~1720, ~1670 and at ~1610 $cm^{-1}$. The ester carbonyl of methylacetoacetate shows the carbonyl stretching band at ~ 1750 $cm^{-1}$ and the acetyl carbonyl at ~1720 $cm^{-1}$. Two weak bands at ~ 1660 $cm^{-1}$ and 1630 $cm^{-1}$ have been attributed to the carbonyl functions of ester and acetyl groups respectively of the enol form of the compound. Thus the bands observed at ~ 1720 $cm^{-1}$ and ~ 1680 $cm^{-1}$ of the unsaturated β-ketoesters considered here **(Table 3.3)** can safely be assigned respectively to

**Table 3.2: Physical and analytical data of the unsaturated β-ketoesters**

| Compound | M.P. $^0$C | Elemental analysis (%) Calcd. (found) | | | $\lambda_{max}$ |
|---|---|---|---|---|---|
| | | C | H | N | |
| **3a** | 55 | 70.49 (70.59) | 5.92 (5.88) | -- | 392<br>276 |
| **3b** | 84 | 60.55 (61.01) | 4.96 (6.08) | -- | 390<br>276 |
| **3c** | 62 | 62.48 (62.40) | 4.64 (5.60) | -- | 397<br>288 |
| **3d** | 54 | 57.78 (57.83) | 5.48 (55.34) | 5.79 (5.62) | 372<br>266 |
| **3e** | 49 | 65.46 (66.10) | 6.62 (5.93) | -- | 386<br>280 |
| **3f** | 86 | 65.50 (65.45) | 5.44 (5.45) | -- | 390<br>270 |
| **3g** | 61 | 63.05 (63.63) | 6.53 (6.06) | -- | 384<br>272 |
| **3h** | 60 | 71.18 (71.11) | 5.14 (5.19) | -- | 393<br>270 |
| **3i** | 87 | 68.82 (69.13) | 5.68 (5.34) | 5.79 (5.76) | 389<br>278 |

the stretching of the ester carbonyl and the cinnamoyl carbonyl of the compounds. The band at ~ 1640 $cm^{-1}$ can arise as due to the carbonyl stretching of the enol tautomer. Other bands observed in the region are due to various C=C stretching vibrations. The broad peak in the region 2500-3500 $cm^{-1}$ suggest the intramolecularly hydrogen bonded enol form of the compounds as in structure **3.1.** However the spectral data of **3d** suggest the existence of the compound predominantly in the keto form presumably due to the electron withdrawing effect of the nitro group. Typical spectra were reproduced in **figures 3.1-3.4.**




**3.1**

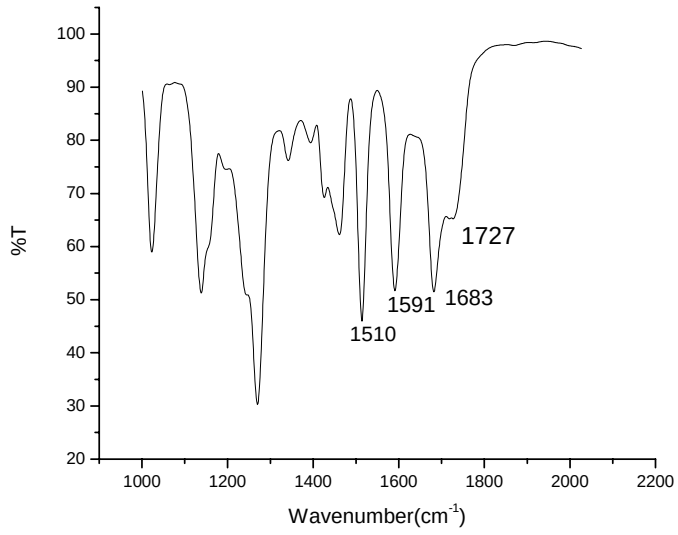



**Fig.3.1 IR spectrum of 3b**

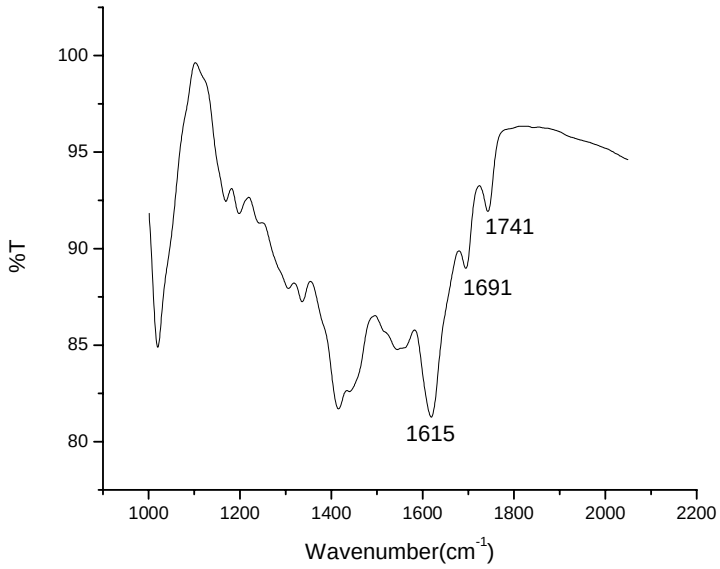



**Fig.3.2 IR spectrum of 3d**

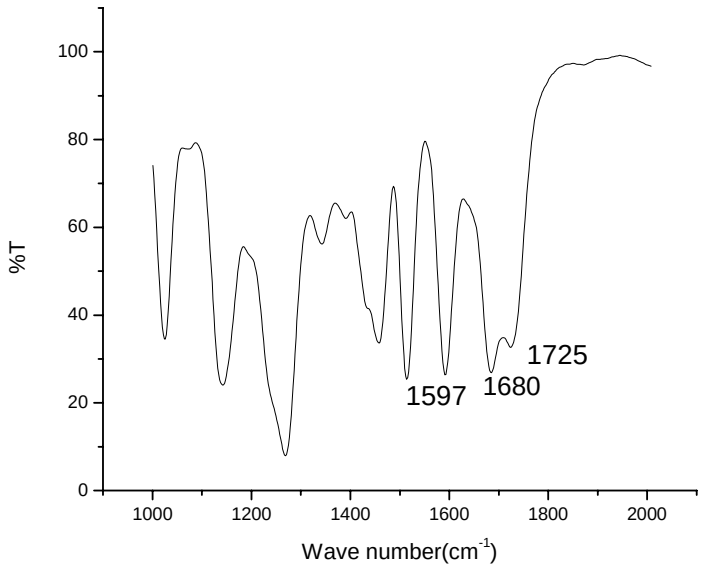



**Fig. 3.3 IR spectrum of 3e**

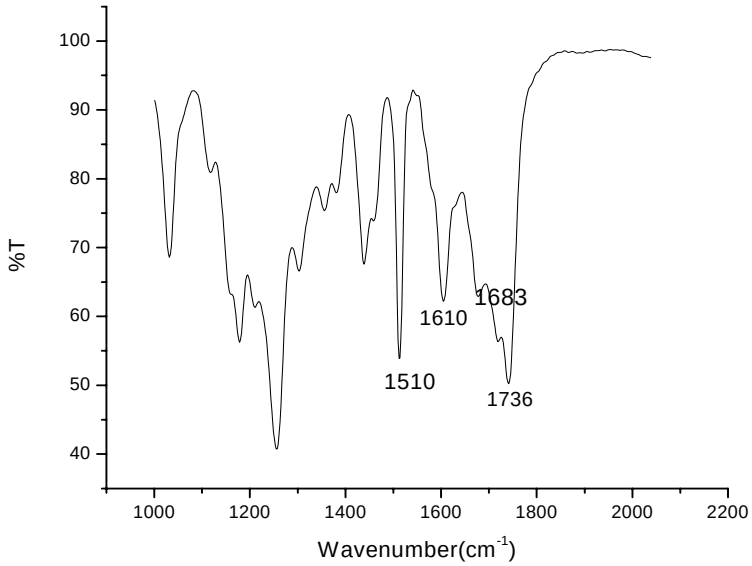



**Fig.3.4 IR spectrum of 3i**

**Table 3.3: Characteristic IR specral data of the unsaturated β- ketoesters**

| Compounds | IR stretching bands in $cm^{-1}$ | | |
|---|---|---|---|
| | Ester C=O | Cinnamoyl C=O | Olefinic / Phenyl C=C |
| **3a** | 1728 | 1678 | 1592, 1512 |
| **3b** | 1727 | 1683 | 1591, 1516 |
| **3c** | 1730 | 1678 | 1594, 1511 |
| **3d** | 1741 | 1690 | 1615, 1594, 1519 |
| **3e** | 1725 | 1680 | 1597, 1515 |
| **3f** | 1722 | 1681 | 1591, 1513 |
| **3g** | 1724 | 1685 | 1597, 1513 |
| **3h** | 1720 | 1681 | 1590, 1518 |
| **3i** | 1736 | 1683 | 1610, 1510 |

**$^1$H NMR spectra**

The proton NMR spectra of all the compounds except that of 3d are characterised by the presence of a slightly broadened one proton signal in the range δ 13-14 ppm. Based on earlier reports[144,191,192] the signal can be assigned to the intramolecularly H-bonded enol proton of **structure 3.1**. Similarly all the compounds show a three proton signal in the range δ 3-4 ppm due to the $OCH_3$ group. The observed aromatic, olefinic and aryl substituent proton chemical shifts are as expected and of **structure 3.1** and typical spectra are given in **figures 3.5-3.9.**

**Mass spectra**

Mass spectra of all the compounds show either molecular ion $P^+$ or $P^+$+1/$P^+$ -1 peak. The observed fragmentation patterns are clearly in agreement with the structure of the compounds. Typical spectra are reproduced in **figures 3.10-3.14**. Other major peaks are due to the elimination of -$OCH_3$, -$COCH_3$, etc from the parent ion. The probable fragmentation pattern of the compounds based on the various mass spectral peaks are given in **scheme 3.3**

**Characterisation of Cu(II) chelates**

Physical and analytical data of Cu(II) chelates of these unsaturated β-ketoesters are given in **Table 3.4**. Elemental, analytical data suggest [$ML_2$] stoichiometry, for all the compounds except that of **3d**. In the case of **3d** the

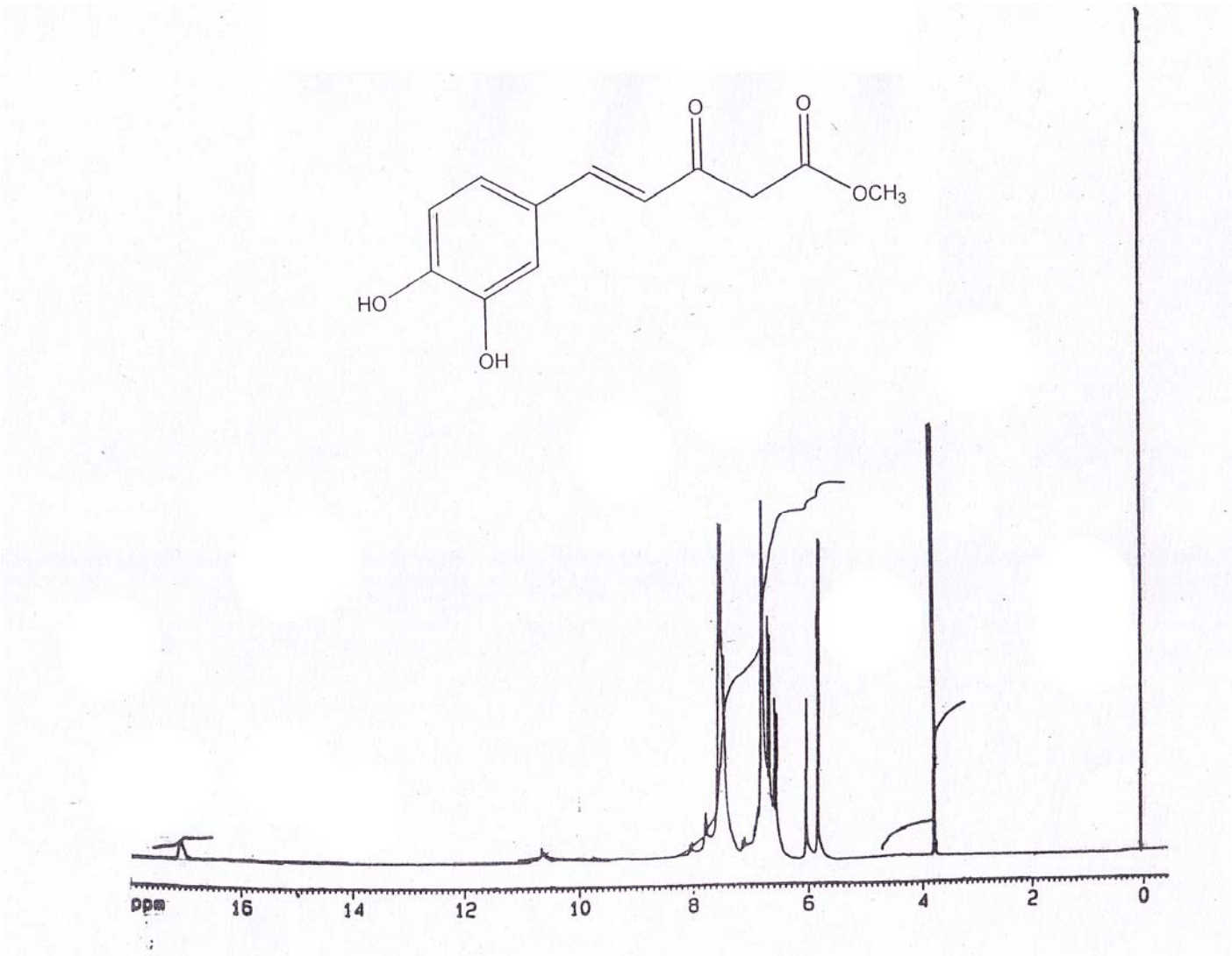



Fig. 3.5 $^{1}$H NMR spectrum of 3b

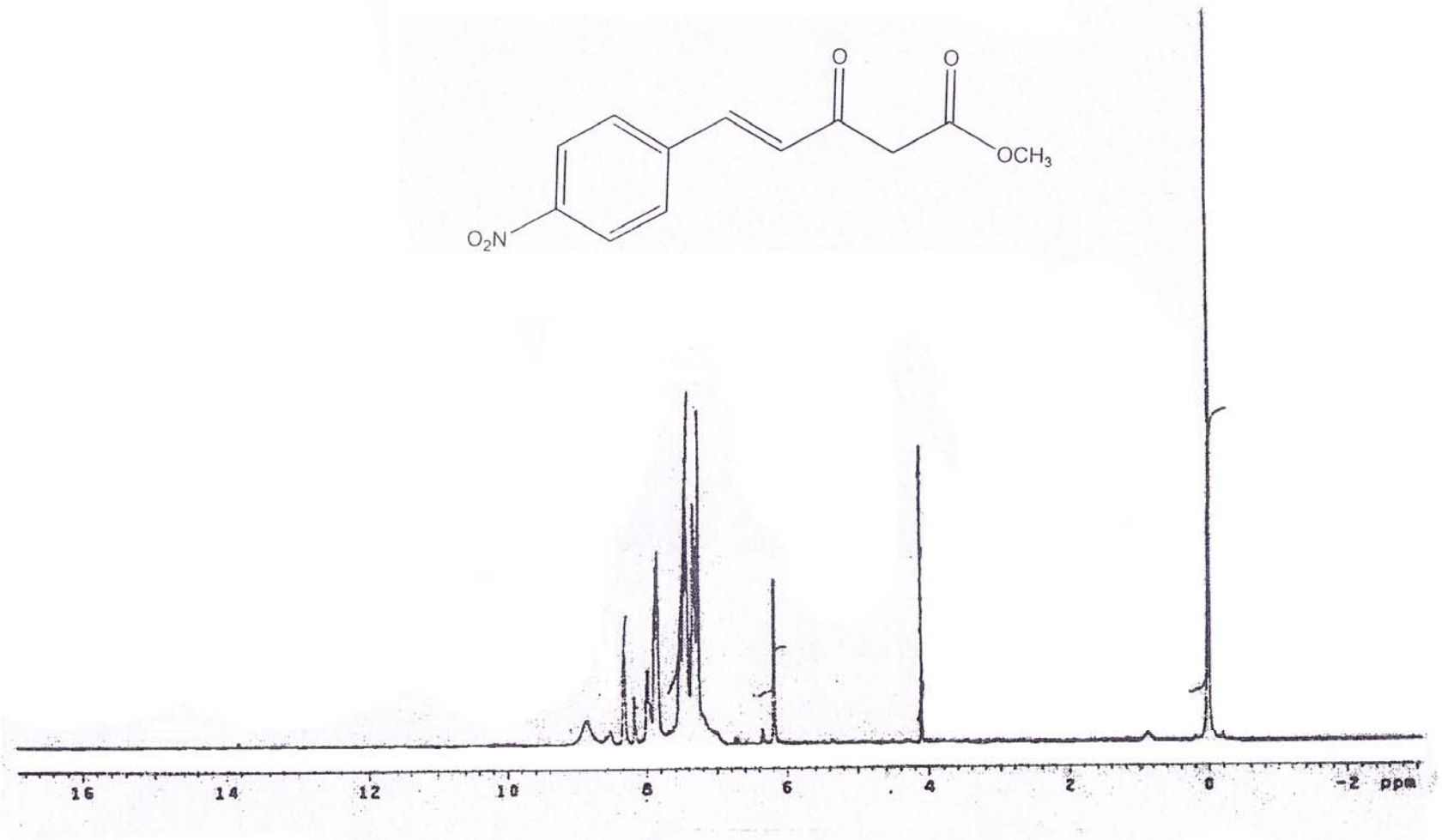



Fig. 3.6 $^{1}$H NMR spectrum of 3d

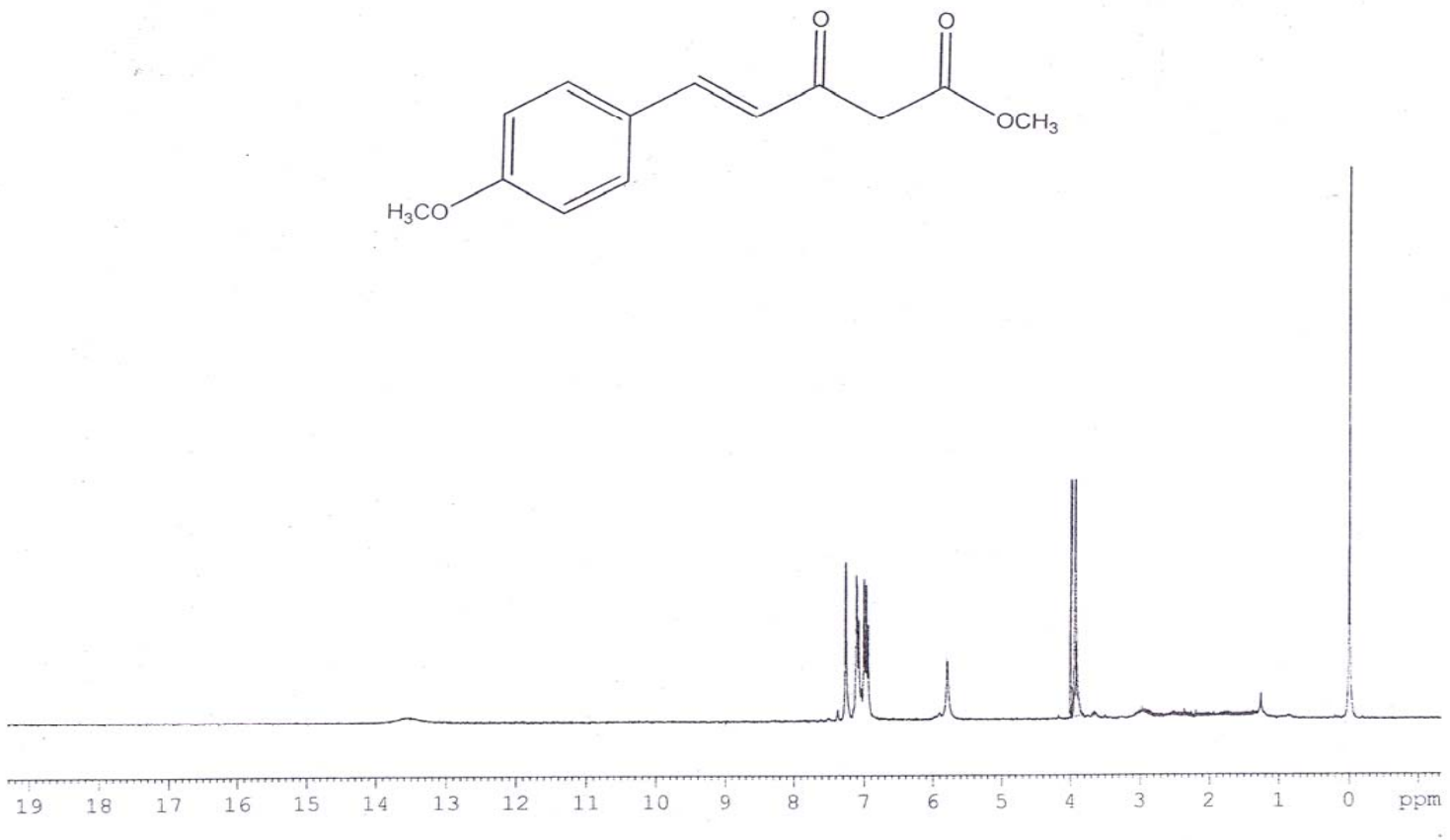



**Fig. 3.7 $^{1}$H NMR spectrum of 3e**

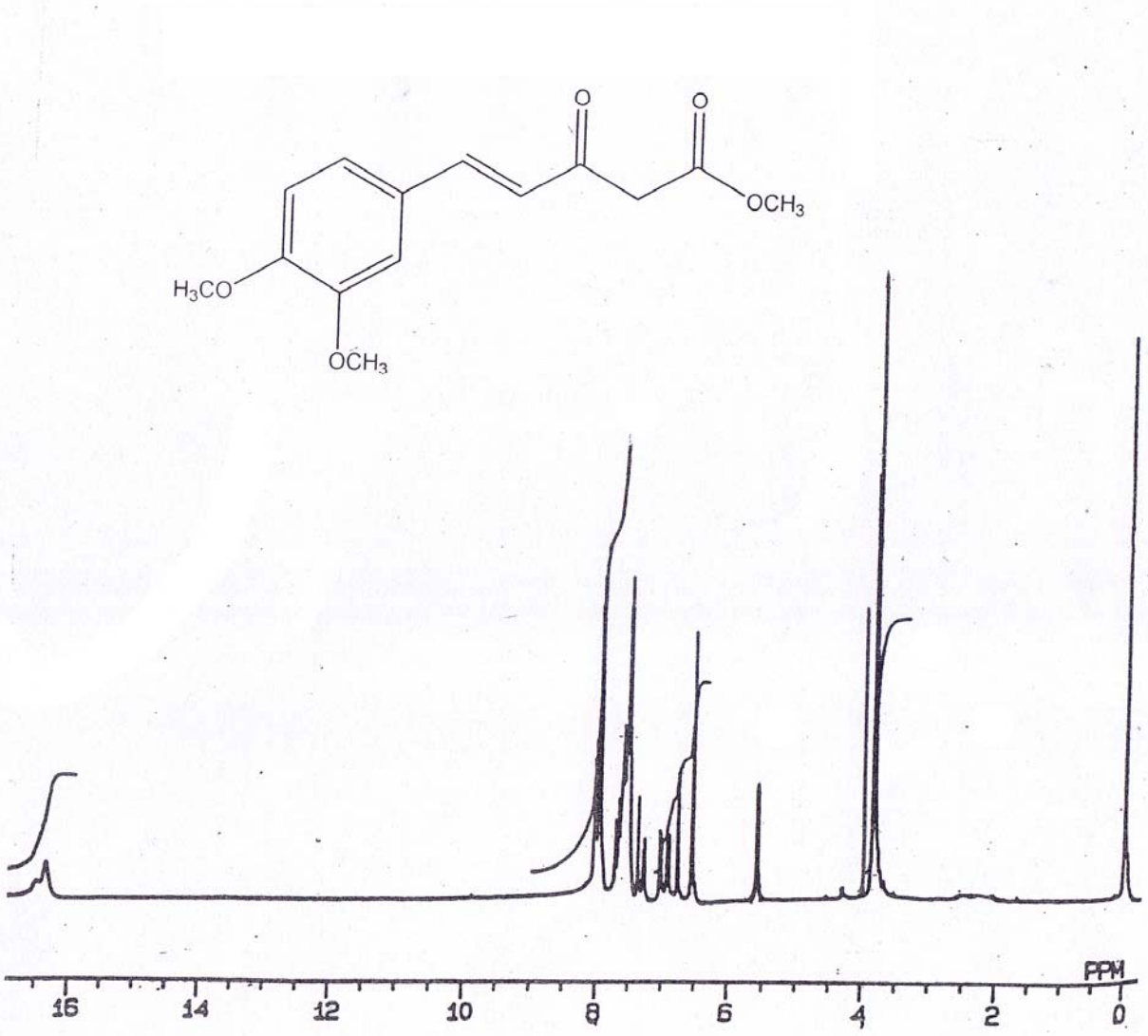



**Fig. 3.8 $^{1}$H NMR spectrum of 3g**

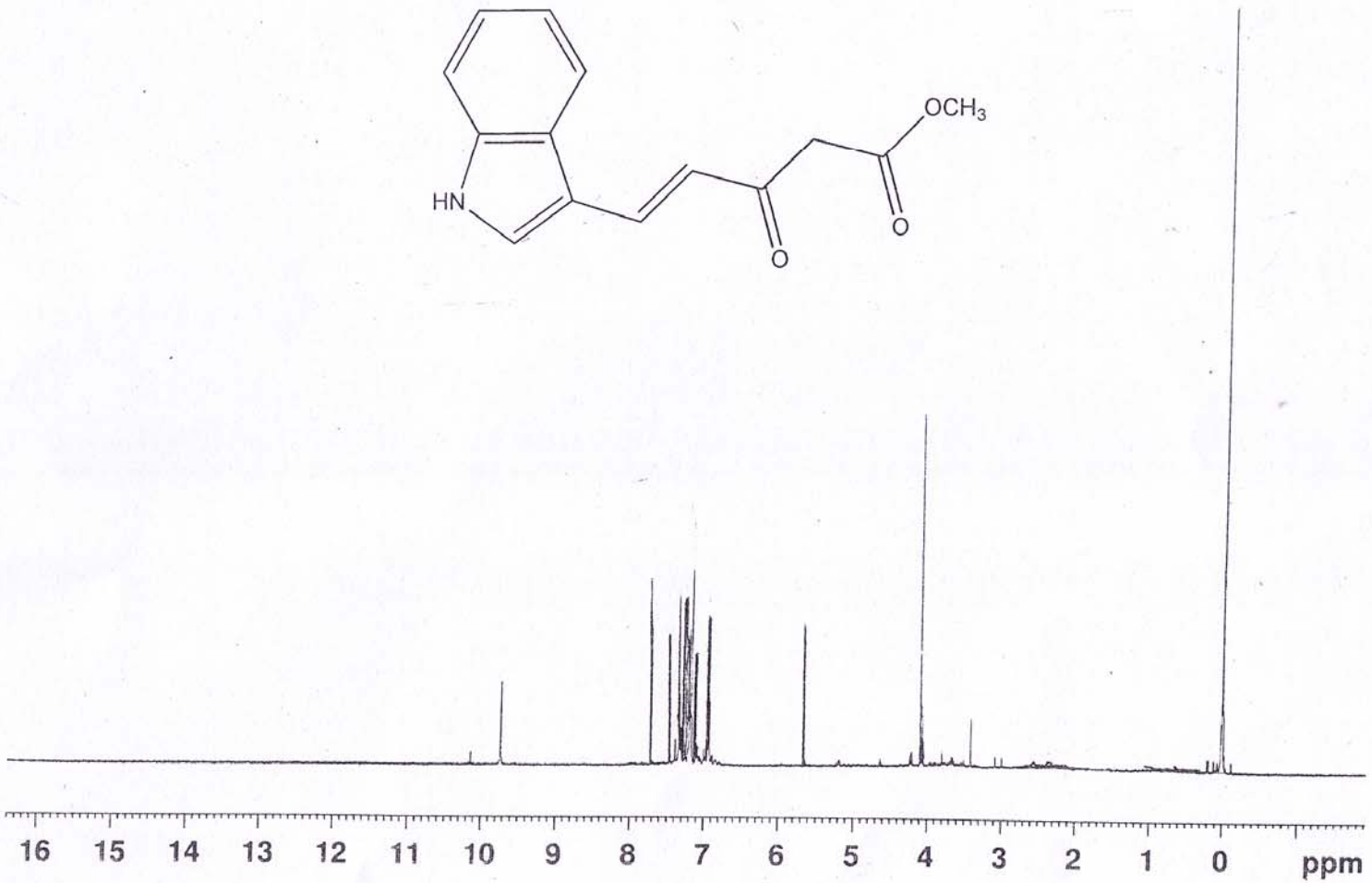
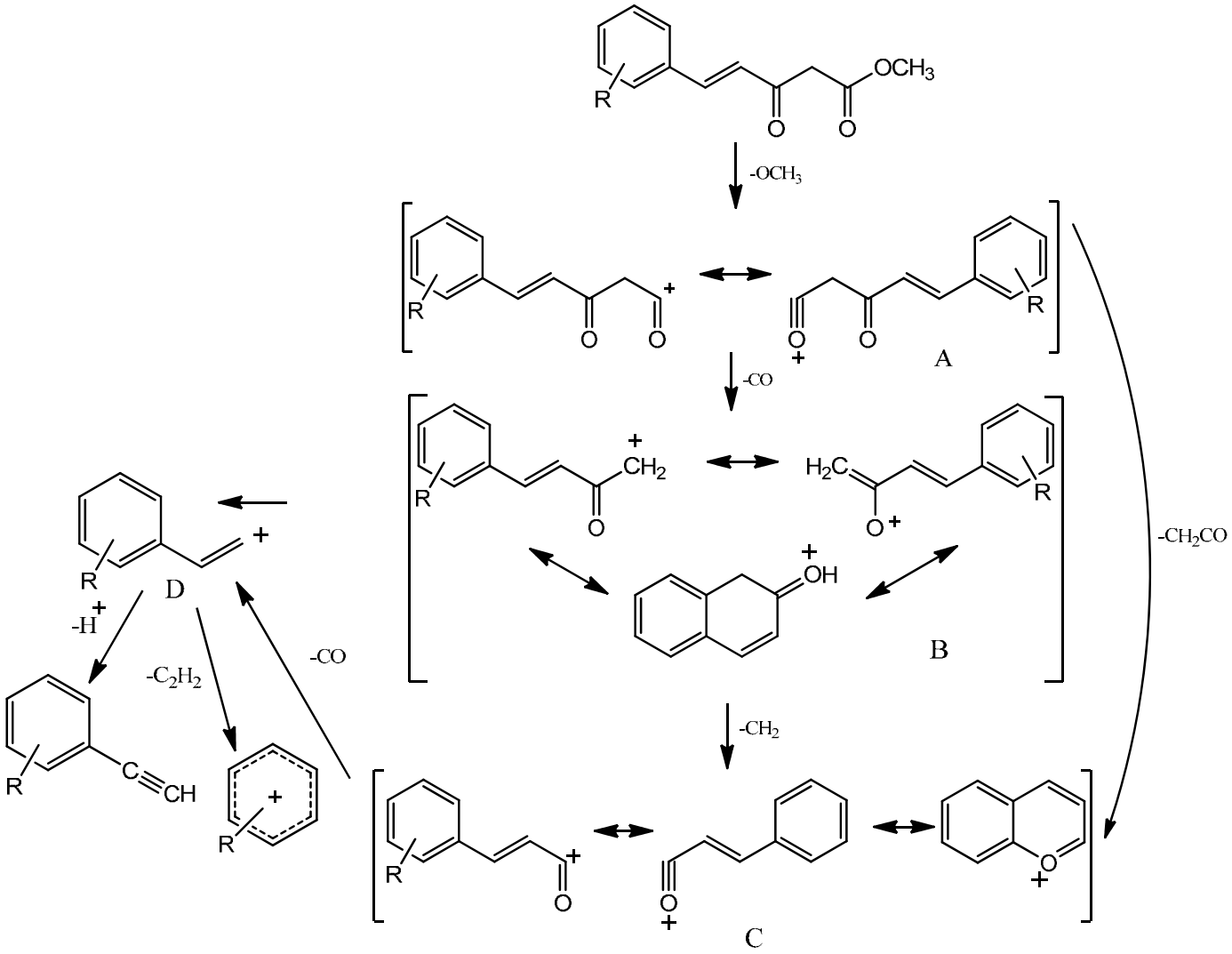



Fig. 3.9 $^{1}$H NMR spectrum of 3i




**Scheme 3.3. Mass spectral fragmentation pattern of compounds 3a-3i.**

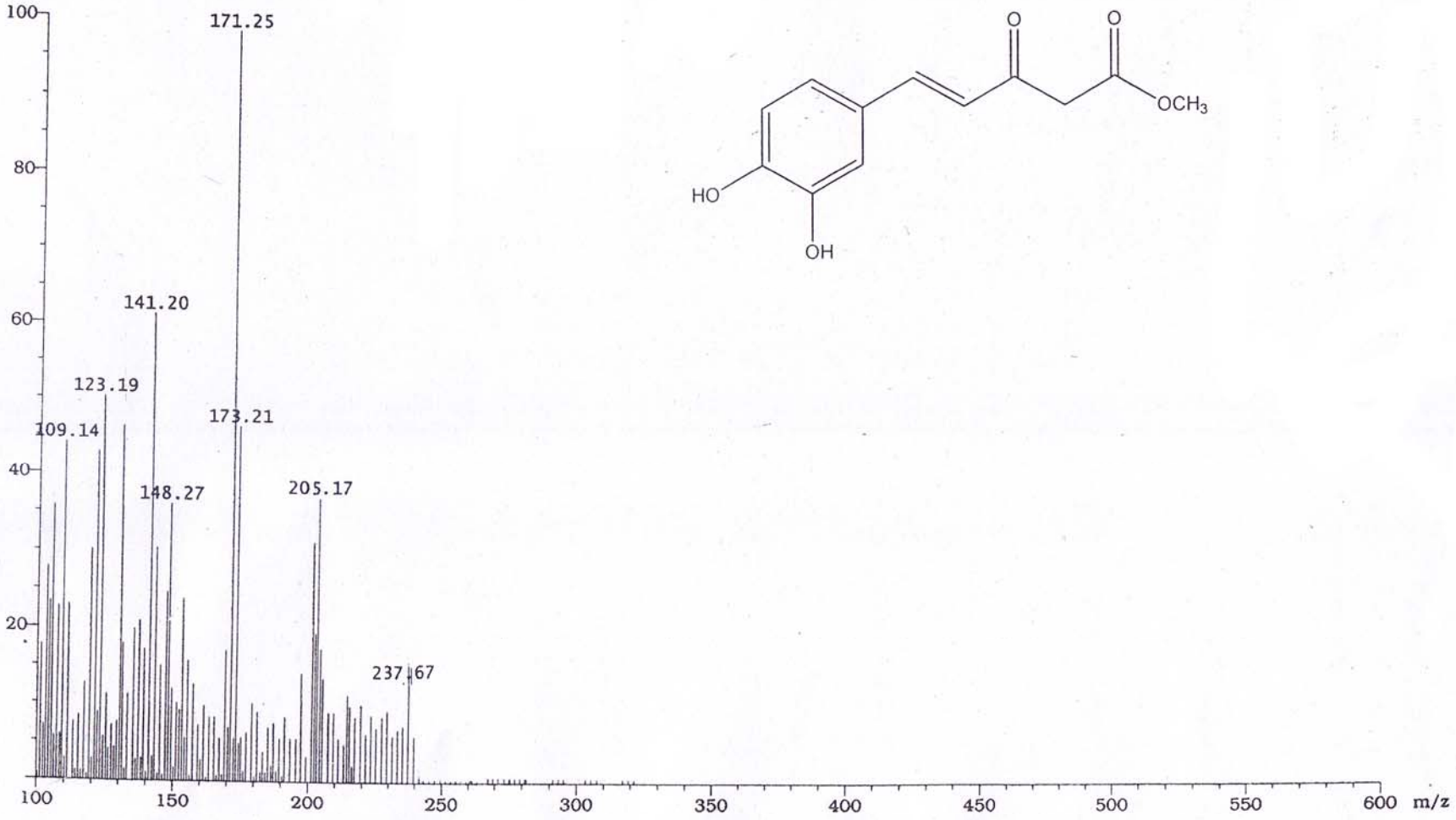



**Fig. 3.10 Mass spectrum of 3b**

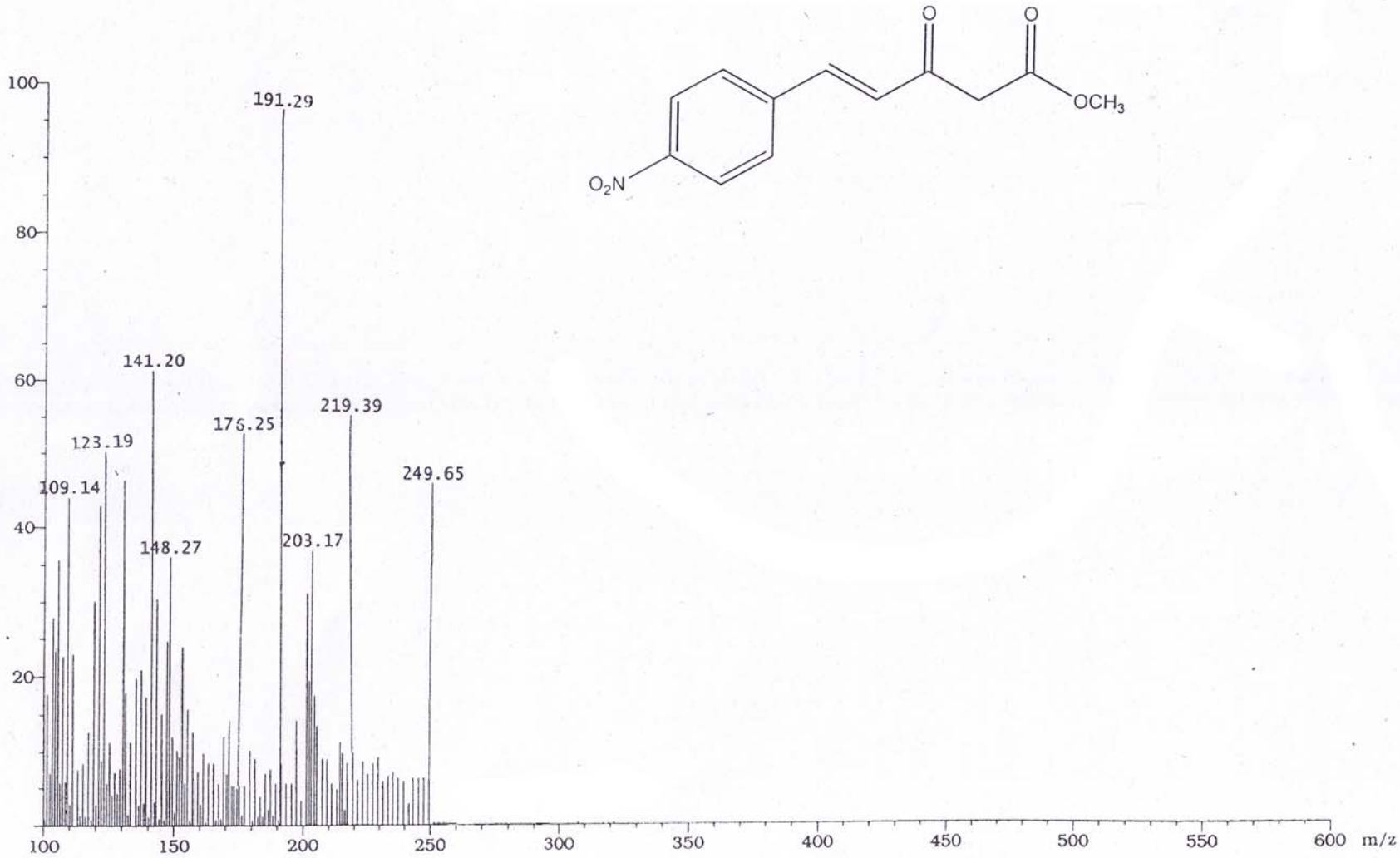



**Fig. 3.11 Mass spectrum of 3d**

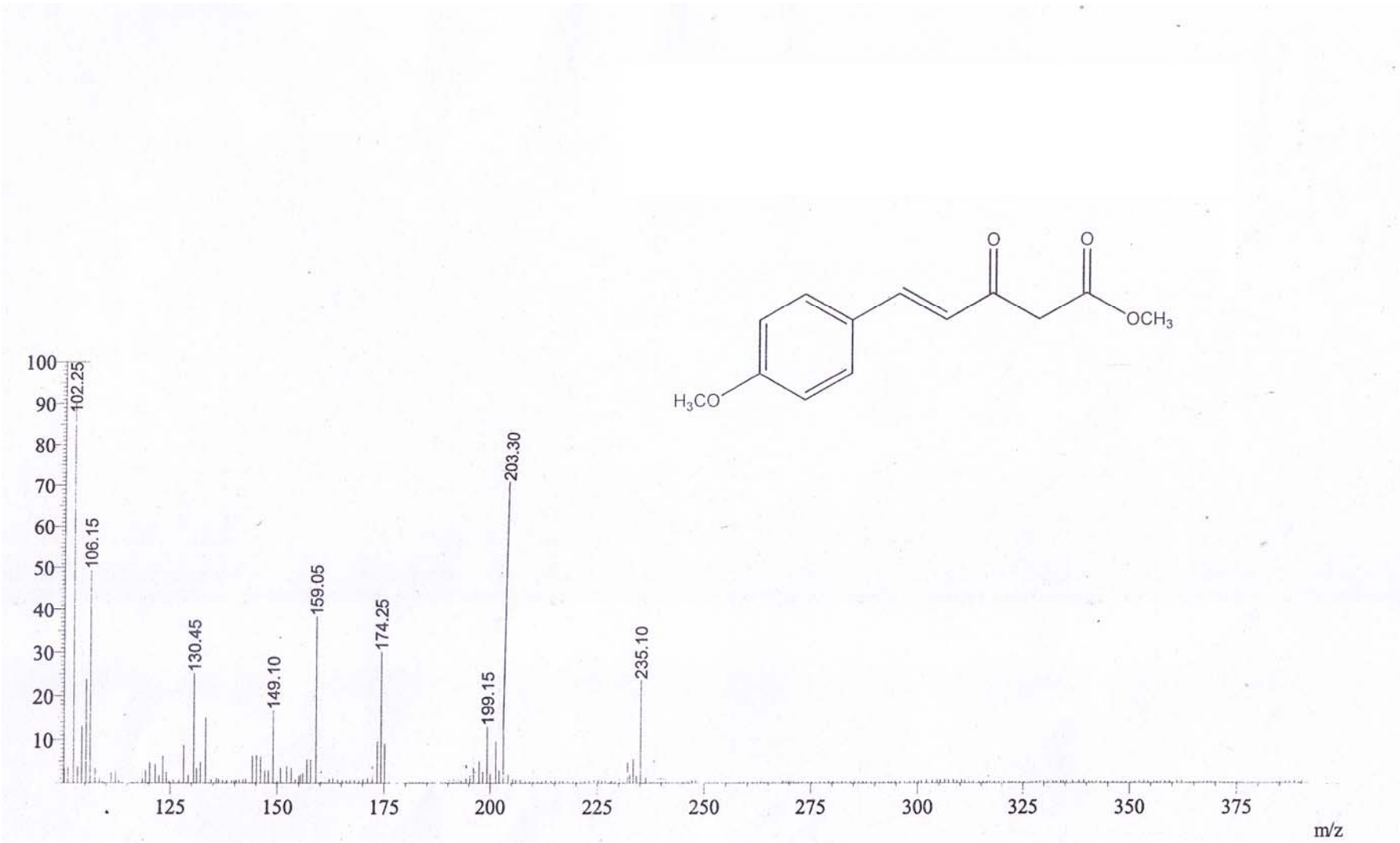



**Fig. 3.12 Mass spectrum of 3e**

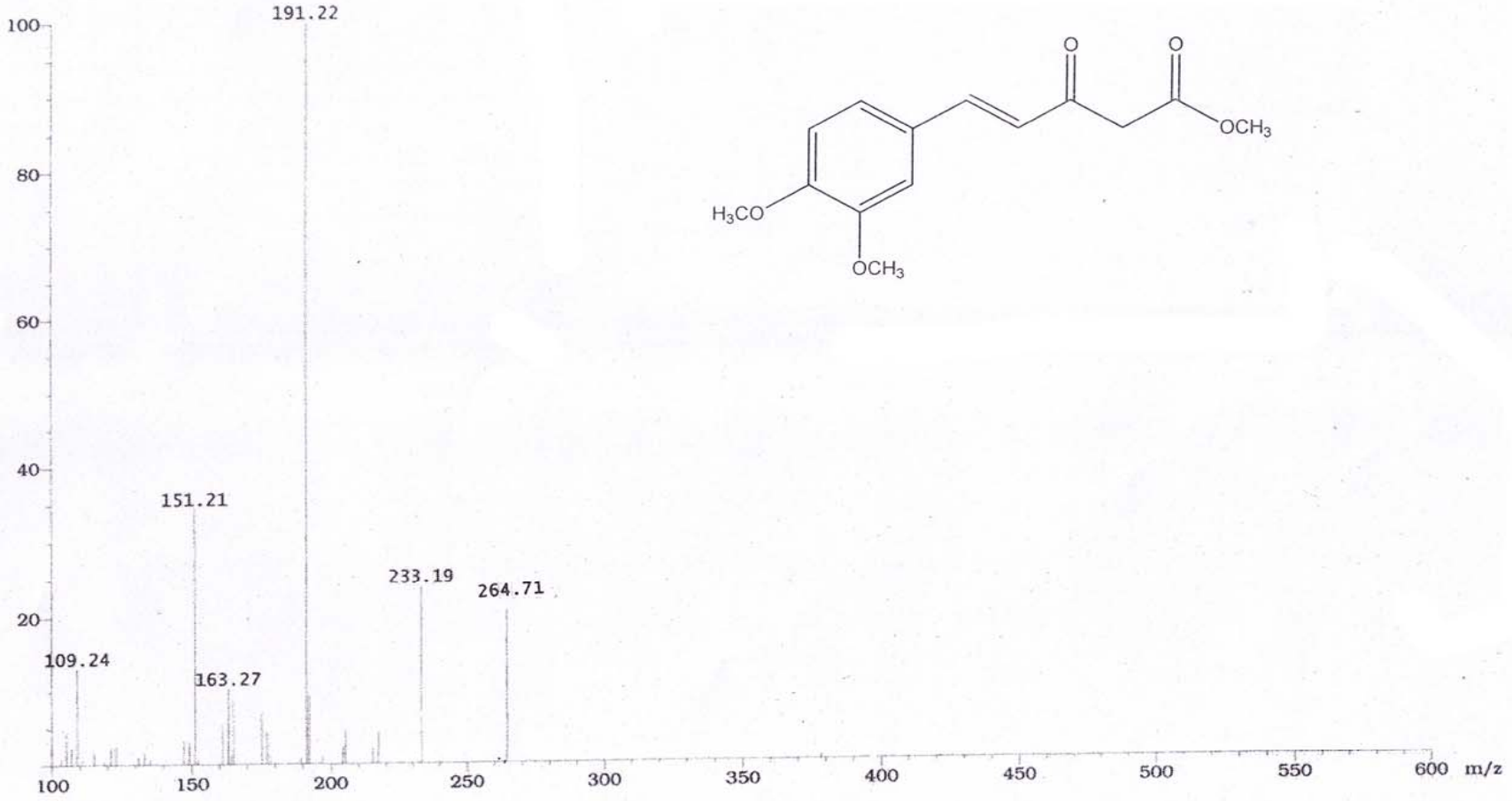



**Fig. 3.13 Mass spectrum of 3g**

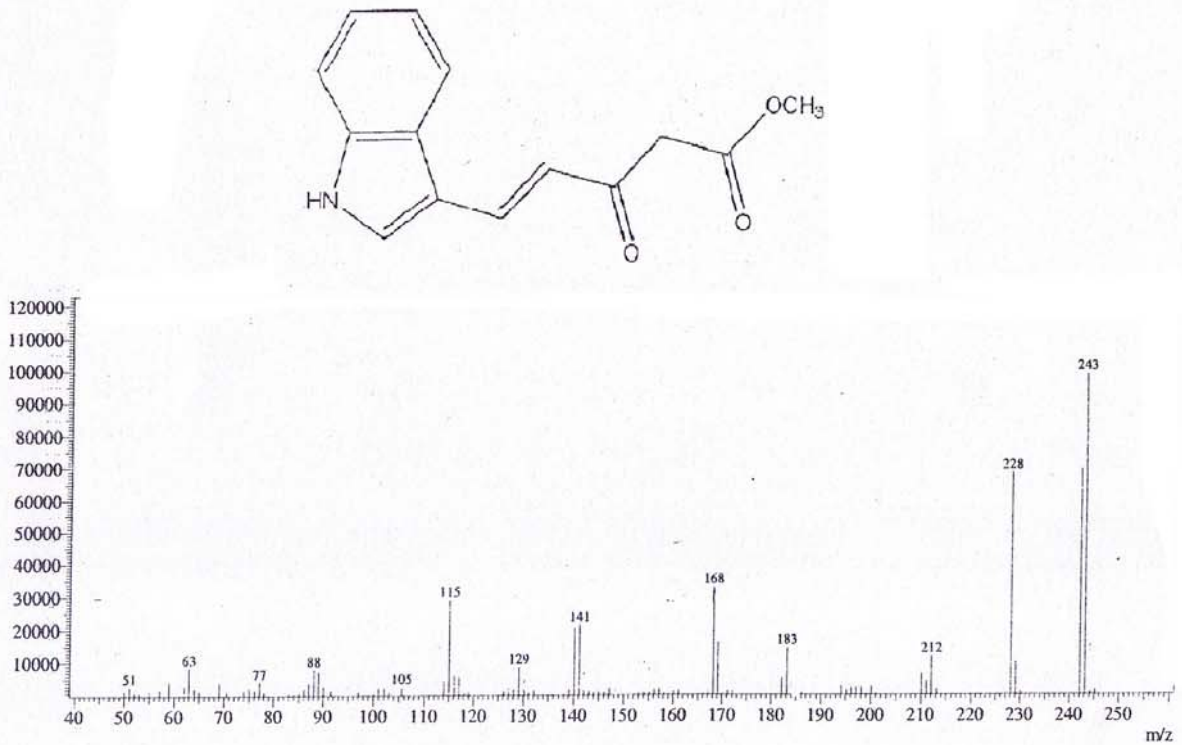
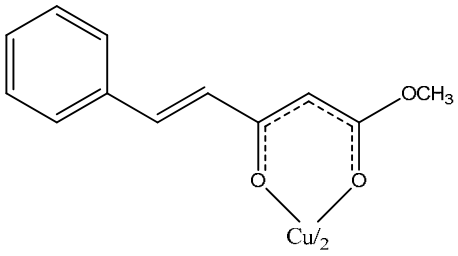



**Fig. 3.14 Mass spectrum of 3i**

data agree with the composition $[CuL(OAc)_2]$ . The IR and mass spectral data are in agreement with the **structure 3.2** of the complexes.




**3.2**

**Table 3.5: Elemental analytical data of Cu(II) complexes of the unsaturated β-ketoesters**

| Cu complexes of | Elemental analysis(found/calcd) | | |
|---|---|---|---|
| | C | H | M |
| **3a** | 61.28 (61.34) | 4.84 (4.74) | 13.44 (13.53) |
| **3b** | 53.87 (54.03) | 4.25 (4.12) | 11.84 (11.90) |
| **3c** | 55.48 (55.55) | 4.74 (4.63) | 11.33 (11.31) |
| **3d** | 44.57 (44.65) | 4.17 (3.95) | 14.70 (14.75) |
| **3e** | 58.82 (58.91) | 5.15 (4.91) | 11.92 (11.99) |
| **3f** | 57.35 (57.42) | 4.56 (4.39) | 12.74 (12.67) |
| **3g** | 54.12 (54.23) | 4.99 (4.84) | 10.13 (10.25) |
| **3h** | 63.78 (63.84) | 4.50 (4.33) | 10.60 (10.56) |
| **3i** | 61.14 (61.36) | 4.74 (4.49) | 11.39 (11.60) |

## Infrared spectra

In the IR spectra of the complexes, the free ligand bands at ~ 1740 $cm^{-1}$ and ~1640 $cm^{-1}$ disappeared. Instead two new bands appeared at ~ 1680 $cm^{-1}$ and ~1590 $cm^{-1}$. Based on earlier reports the former band can be assigned to the metal coordinated ester carbonyl and the later to the coordinated cinnamoyl carbonyl. The band due to hydrogen bonded dicarbonyl function of the free ligands indicating the replacement of the enolic hydrogen by metal ion as in **structure 3.2**. Spectrum of copper (II) complex of 3d contains two additional bands at ~ 1699 $cm^{-1}$ and 1654 $cm^{-1}$ assignable to the stretching of the coordinated acetate function and ester carbonyl function respectively. All the spectra show additional bands at ~ 425 $cm^{-1}$ and ~ 460 $cm^{-1}$ assignable to $\nu_{M-O}$ vibrations.

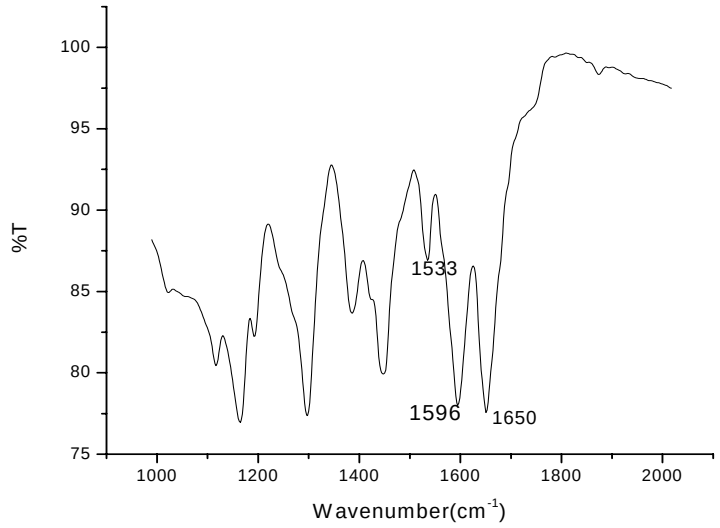



**Fig. 3.15: IR spectrum of Cu(II) complex of 3b**

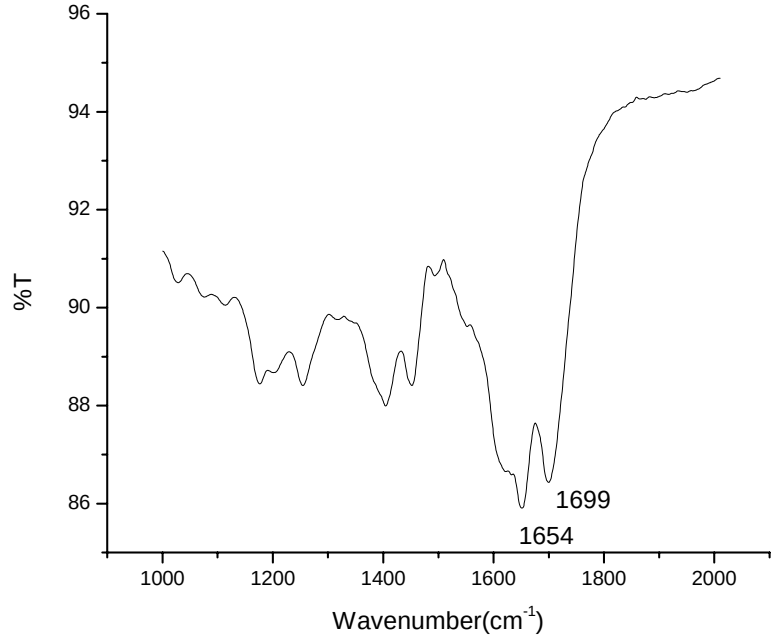



**Fig. 3.16 IR spectrum of Cu(II) complex of 3d**

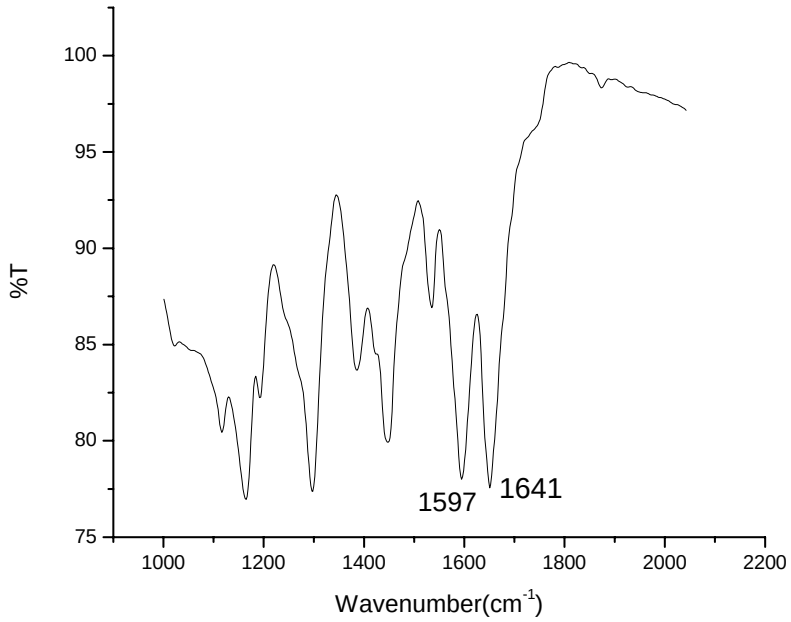



**Fig. 3.17 IR spectrum of Cu(II) complex of 3e**

**Table 3.4: Characteristic IR spectral data of Cu(II) complexes of the unsaturated β-ketoesters**

| Cu complexes of | IR stretching bands in $cm^{-1}$ | | | |
|---|---|---|---|---|
| | C=O ester | C=O cinnamoyl | C=C aryl/alkenyl | M–O |
| **3a** | 1648 | 1595 | 1536, 1580 | 428, 470 |
| **3b** | 1650 | 1596 | 1533, 1579 | 431, 460 |
| **3c** | 1640 | 1585 | 1554, 1587 | 416, 487 |
| **3d** | 1654 | 1618 | 1541, 1558 | 418, 463 |
| **3e** | 1641 | 1597 | 1533 | 435, 469 |
| **3f** | 1638 | 1590 | 1539, 1560 | 420, 470 |
| **3g** | 1635 | 1577 | 1532, 1565 | 426, 475 |
| **3h** | 1635 | 1590 | 1540, 1570 | 425, 476 |
| **3i** | 1636 | 1589 | 1535,1578 | 424, 461 |

**Mass spectra**

All the complexes show a relatively intense molecular ion peaks. The base peaks in all spectra are due to the ligand moiety and peaks due to $[CuL]^+$, $L^+$ and fragments of $L^+$. Typical spectra are reproduced in **figures 3.18-3.22.**

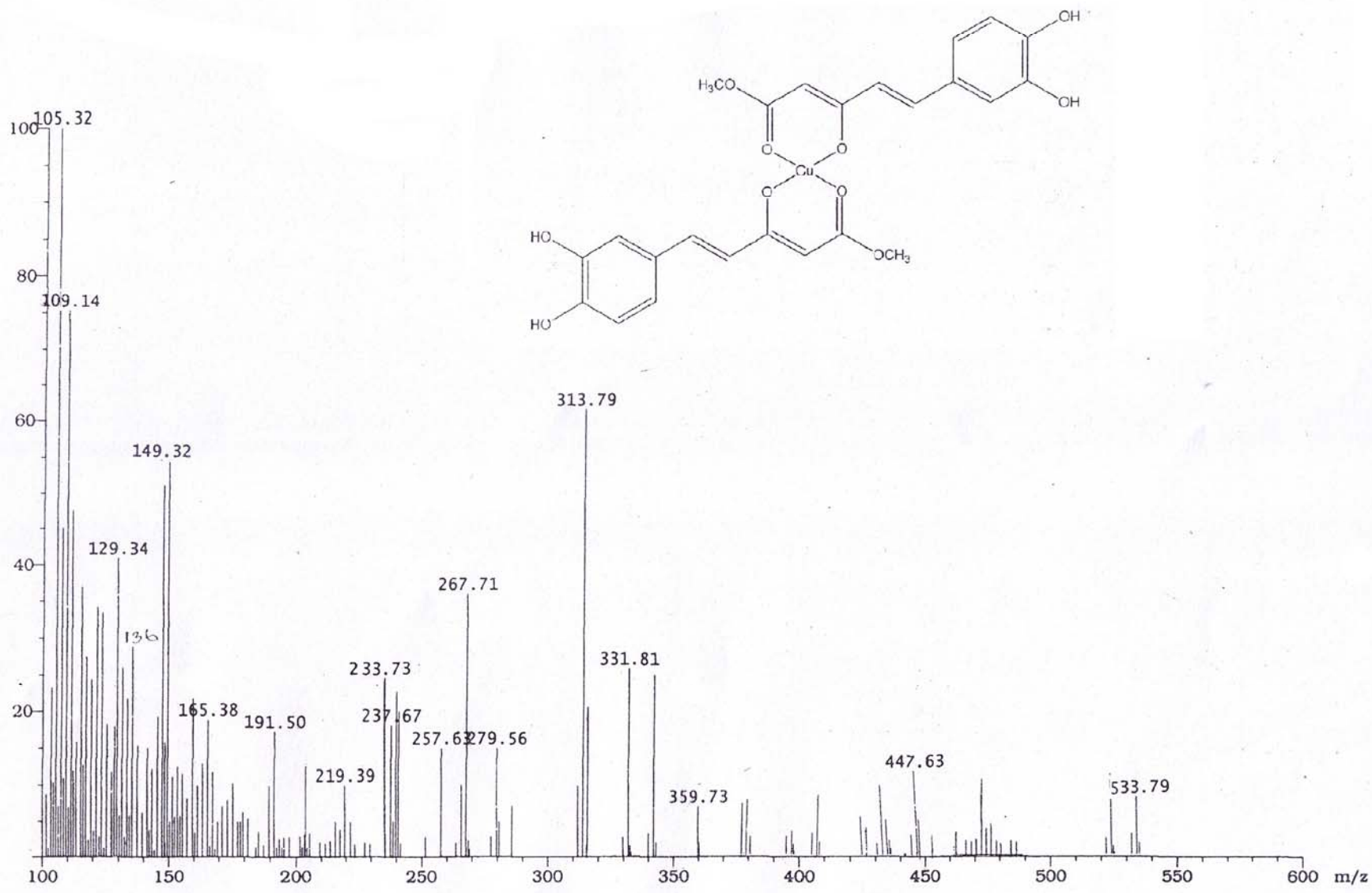



**Fig. 3.18 Mass spectrum of Cu(II) complex of 3b**

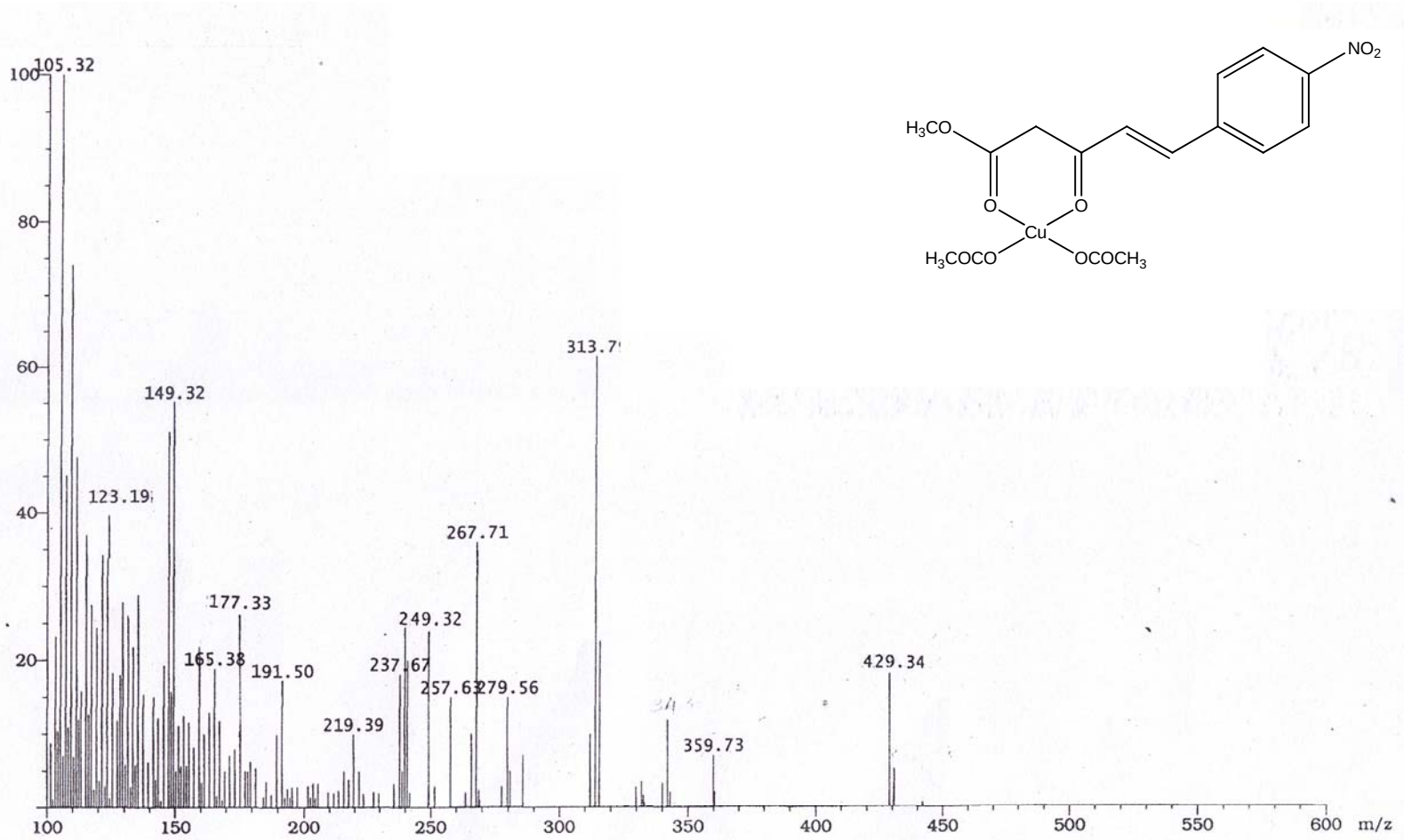



**Fig. 3.19 Mass spectrum of Cu(II) complex of 3d**

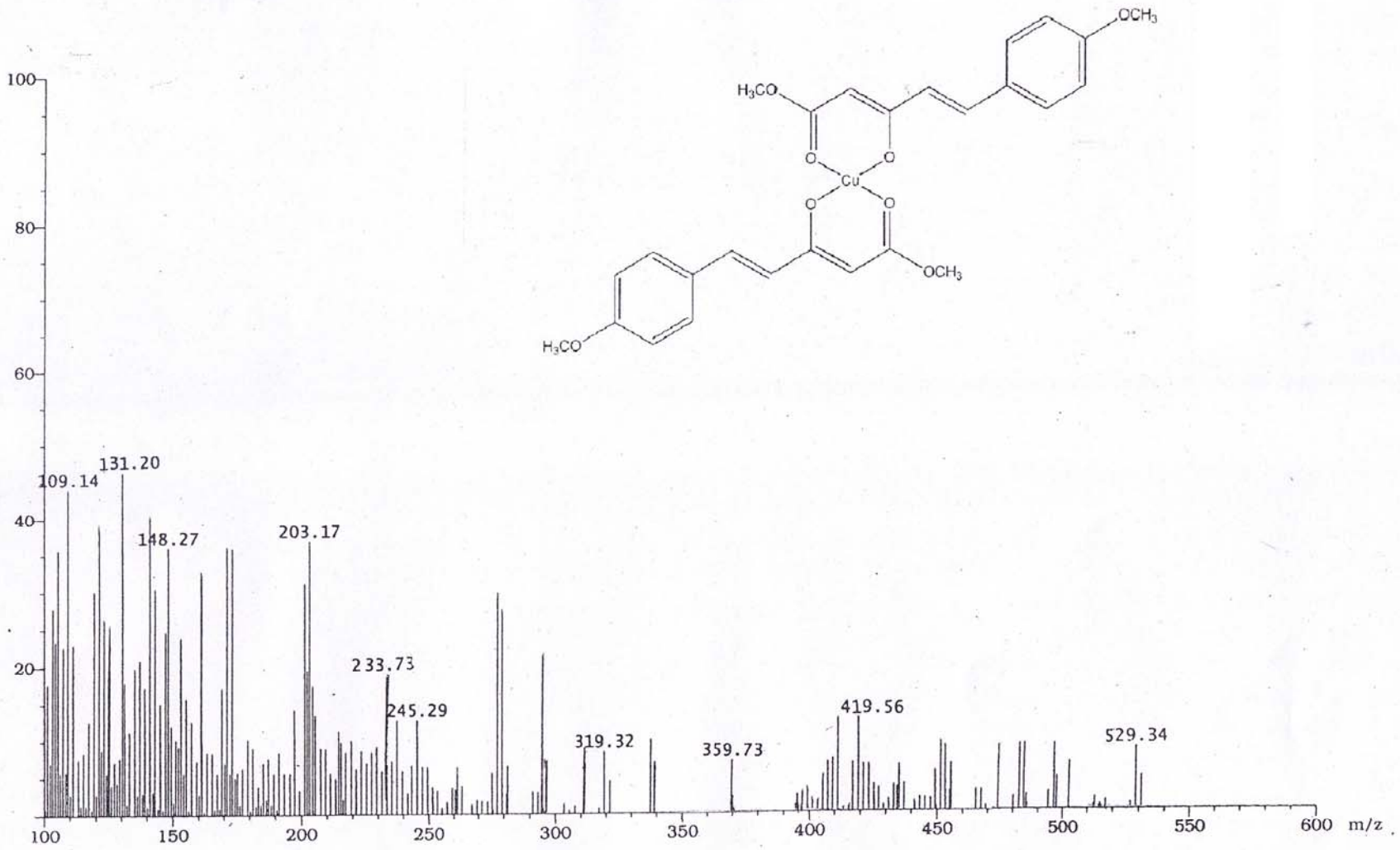



**Fig. 3.20 Mass spectrum of Cu(II) complex of 3e**

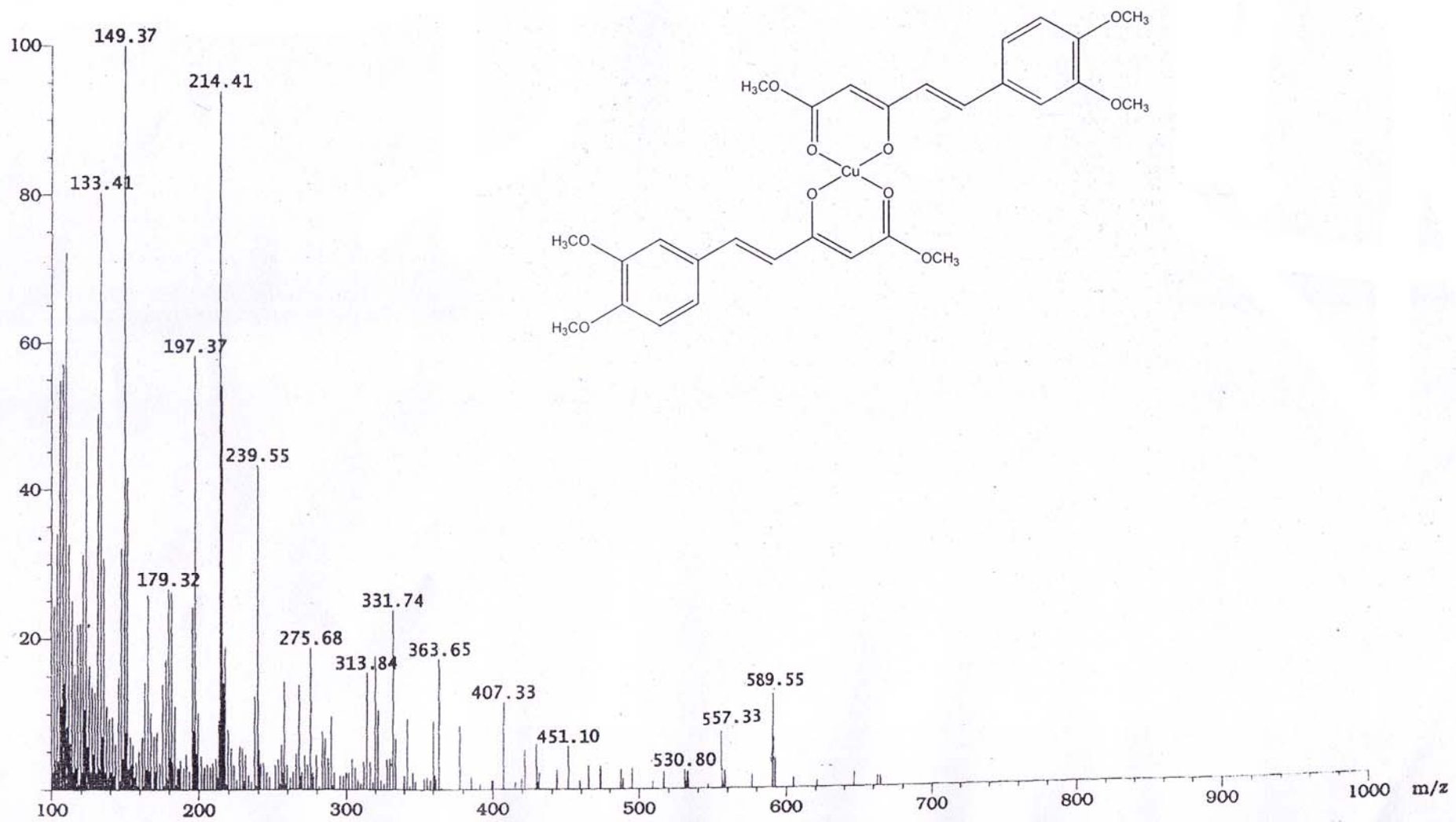



**Fig. 3.21 Mass spectrum of Cu(II) complex of 3g**

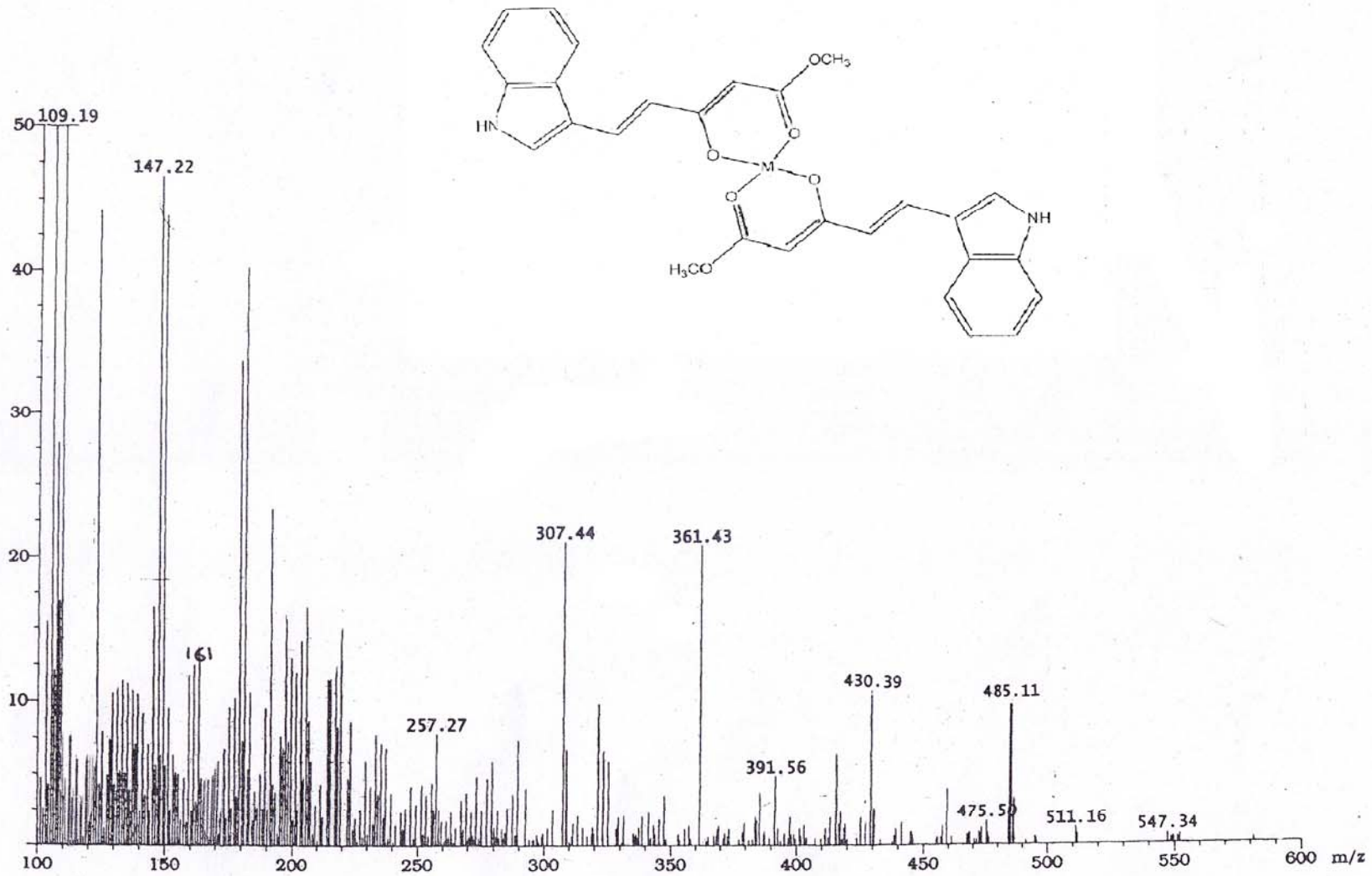



**Fig. 3.22 Mass spectrum of Cu(II) complex of 3i**

**Summary**

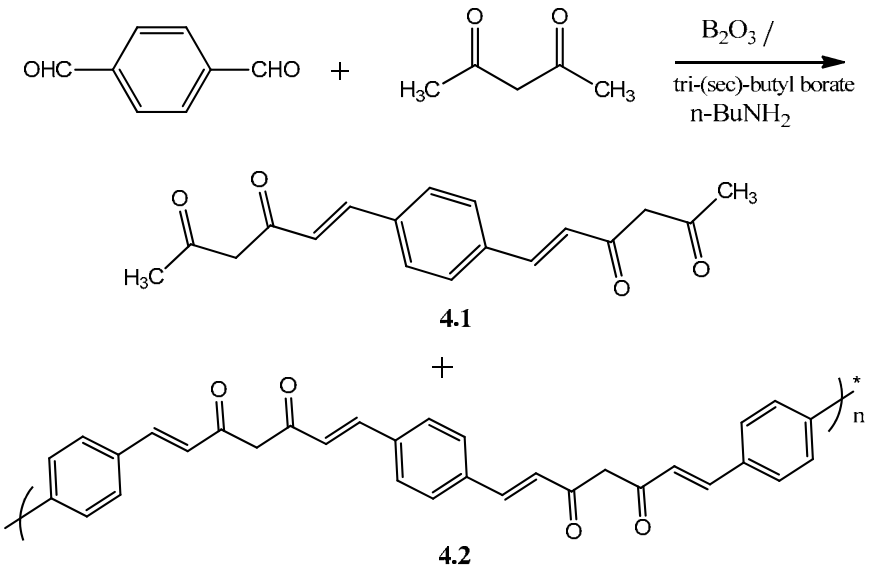
A series of β-ketoesters in which the keto group is directly linked to olefinic functions were synthesized through the Claisen-Schmidt condensation of aromatic aldehydes with methyl acetoacetate. From spectral data it has been shown that the compound in the keto/enol tautomeric forms dependent on the nature of the substituents on the aryl ring. Thus electron withdrawing groups in the aryl ring increases the percentage of keto form while electron donating groups increases the percentage of enol form. These unsaturated β-ketoesters formed well defined complexes of $[CuL_2]$ stoichiometry. Physical, analytical and spectral data of the complexes are in conformity with the monobasic bidentate nature of the unsaturated β-ketoesters. Spectral data clearly indicated the formation of stable $C_3O_2Cu$ ring system in these complexes.

# CHAPTER 4

# SYNTHESIS AND CHARACTERISATION OF NEW UNSATURATED TETRAKETONES AND THEIR METAL COMPLEXES

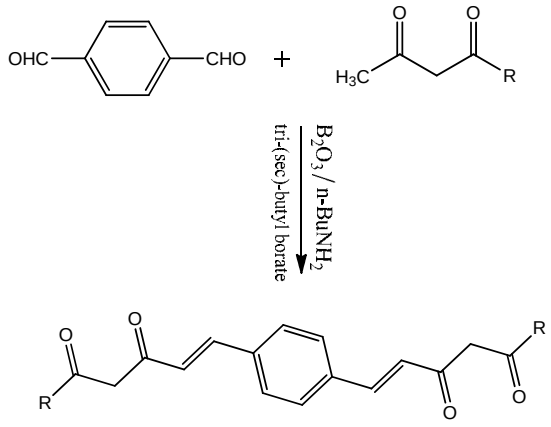
## Introduction

The Claisen-Schmidt condensation of aromatic aldehydes such as benzaldehyde with acetylacetone usually results in the formation of both mono and biscondensation products[119]. At low temperature (<10$^{o}$C) the formation of monocondensation product is favoured and at elevated temperature (50-80$^{0}$C) the formation of the bis condensation product is preferred. Since 1,4-phthalaldehyde contains two aldehydic groups, its claisen condensation reaction with acetylacetone will be more complex and the major products expected are given in **scheme 4.1**.




**Scheme 4.1**

The present study also revealed that the relative percentages of these two products are dependent on the reaction temperature. At low temperature (< 5 $^{o}$C) the mono condensation product **4.1** is favoured while at temperature above 60 $^{o}$C the bis condensation product **4.2** predominates. However isolation and the purification of the polycondensation product appeared to be very difficult. Therefore synthesis and characterization of the mono condensation product is only considered in this chapter. However when the Claisen-Schmidt condensation reaction of 1,4-phthalaldehyde with 1,3-diketones such as benzolylacetone, methylacetoacetate and acetoacetanilide which contains only one acetyl group result in the formation of only the monocondensation product **4.3** as shown below. Synthetic details of these unsaturated tetraketones and their typical metal complexes are discussed below.




**4.3**

R = $-C_6H_5$, $-OCH_3$, $-NHC_6H_5$

**Scheme 4.2**

## Experimental

### a) Synthesis of the unsaturated tetraketone from acetylacetone, ($H_2$aa)

Acetylacetone (0.5 ml, 0.01 mol) was mixed with $B_2O_3$ (0.7 g, 0.01 mol) in 5 ml dry ethylacetate and stirred for ~ 1 h at room temperature. The mixture was then cooled to ~ 0 $^oC$ and a solution of 1, 4-phthalaldehyde (0.67 g, 0.005 mol) in 10 ml dry ethylacetate was added slowly followed by tributylborate (5.3 ml, 0.01 mol) drop by drop and stirred for ~ 10 minutes. To this mixture n-butylamine (0.2 ml) was added slowly during half an hour, stirred for about 4 h and kept overnight. To this a solution of 0.4 M HCl (7.5 ml) was added and stirred for ~ 1 h. The product formed was extracted using ethylacetate several times and the combined extracts were evaporated to a pasty mass and stirred well with 2 M HCl (10 ml) for about half an hour. The solid product separated was collected, washed with water and then with ethanol and dried in vacuum. From tlc , the product obtained revealed the presence of two compounds and therefore subjected to column chromatography as illustrated below.

The crude product obtained was dissolved in minimum amount of acetone and little amount of silica gel were added and dried. It was then placed over a column packed with silica gel (mesh 60-120) using 1:1 v/v chloroform : toluene mixture and eluted with the same solvent system at a uniform flow rate of 2ml/minute. As the elution proceeds, two bands were

developed in the column, a lower yellow band and an upper red band. The lower yellow band was collected in aliquots of 10 ml in separate test tubes, and checked by tlc. The combined extracts were distilled off to recover the solvent and then evaporated to dryness. The product obtained were washed with ethanol and then with benzene and dried in vacuum. It was recrystallised from ethanol to yield tlc pure product. ( Melting point 145$^{o}$C).

The upper band was eluted with 1:5 acetone : chloroform mixture. The collected eluates were distilled off and then evaporated to dryness. The pasty mass obtained was not pure and therefore not subjected to further studies.

**b) Synthesis of tetraketone from methylacetoacetate, ($H_2$ma)**

Methylacetoacetate (0.01 mol) and boric oxide (0.01 mol) were mixed thoroughly to get a pasty mass. It was then stirred magnetically for 1 ~ h at room temperature. To this mixture a solution of 1,4-phthalaldehyde (0.005 mol) and tri-(sec-butyl) borate (0.04 mol) dissolved in dry ethylacetate were added and stirred for ~ 6 h with slow addition of n-butylamine (0.2 ml). After keeping the mixture overnight 10 ml HCl (0.01 M) was added and again stirred for ~1 and extracted with ethylacetate and dried over a water bath. The pasty mass obtained was stirred with 15 ml methanol for ~ 2 h and then kept in an ice bath with constant stirring for ~ 3 h. The precipitated product was filtered and recrystallised from hot benzene. The purity of the product was

checked by tlc (silica gel) and revealed the presence of impurities and hence it was purified by column chromatography as outlines below.

The product was dissolved in minimum amount of acetone and a pinch of silica gel and dried. It was then placed over a column (2x50 cm) densely packed with silica gel (mesh 60-120) and eluted with 1:5 v/v toluene: chloroform mixture at a uniform flow rate of about 2ml/minute. As the elution proceeded two bands were developed in the column, an yellow lower band and orange upper band. The lower yellow lower band was collected, checked for purity and discarded because of its impure nature. The upper orange band was eluted using 5:1 chloroform-acetone mixture (v/v). The eluate coming first were discarded and that came later were collected in aliquots of 10 ml in separate test tubes, checked by tlc and the combined extracts were distilled to recover the solvent and then evaporated to dryness. The product obtained was washed thoroughly with ethanol and dried in vacuum. The product obtained was tlc pure orange crystals with melting point 110$^{o}$C.

**c) Synthesis of the unsaturated tetraketone from benzolylacetone, ($H_2$ba)**

A mixture of 1.62 g (0.01 mol) of benzoylacetone and 0.7g (0.01 mol) of boric oxide and 5 ml dry ethyl acetate were stirred for about one hour. To this mixture, a solution of 0.67 g (0.005 mol) of 1, 4-phthalaldehyde in 5 ml dry ethyl acetate was added slowly followed by 2.3 ml (0.01 mol) of

tributylborate drop by drop. The mixture was warmed to about 60$^{o}$C for ~ 10 min. n-Butylamine (0.2 ml) was added drop by drop and then stirred for ~ 4 h, and kept overnight. The mixture was stirred for ~ 1 h after adding a hot solution of 0.4 M HCl (10 ml). The product was extracted using ethylacetate several times and the combined extract were evaporated to a pasty mass which was stirred well with 2 M HCl (10 ml) for half an hour, washed with water and then with ethanol and dried in vaccum. Tlc of the material indicated the presence of impurities and therefore subjected to column chromatography as given below.

The benzene solution of the product was placed over a column (2x50 cm) densely packed with silica gel (mesh 60-120) and eluted with 1:8 v/v acetone – petroleum ether mixture at a uniform flow rate of about 2 ml per minute. As the elution proceeded two bands developed in the column, a yellow lower band and red orange upper band. The eluate of the lower band on evaporation yielded golden yellow crystals of melting point 230$^{0}$C. The upper orange band was collected by eluting with 1:2 v/v acetone-petroleum ether mixture and on evaporation yielded orange crystals. Though the compound was identified as a Knoevenagal condensation product, no further studies were carried out because of its very low yield.

**d) Synthesis of the unsaturated tetraketone from acetoacetanilide,($H_2$an)**

Acetoacetanilide (1.77 g, 0.01 mol) and boric oxide 0.7g (0.01 mol)

were mixed and made into a paste with dry ethylacetate and stirred for ~ 1 h at room temperature. To this a solution of 1,4-phthalaldehyde (0.67 g, 0.005 mol) and tri (sec-butyl) borate (0.02 mol) dissolved in dry ethylacetate was added and stirred for ~ 5 h with the slow addition of ~ n-butylamine (0.5 ml) and the mixture was kept overnight. To this hot HCl (0.4 M, 7.5 ml) was added and again stirred for ~ 1 h. It was then extracted with ethylacetate and dried to yield a pasty mass. To this 10 ml of 2 M HCl was added and kept for ~ 24 h. The solution was stirred well and the precipitate formed was filtered and dried. The purity was checked by tlc and revealed the presence of two compounds and they were separated by column chromatography as outlined below.

The crude product was dissolved in minimum quantity of dry ethylacetate and placed over a column densely packed with silica gel (mesh 60-120) and eluted with 5:1 chloroform-acetone mixture at a uniform flow rate of 2 ml per minute. As the elution proceeds, two bands were developed in the column, a lower yellow band and an upper orange band. The lower portion was collected as 10 ml aliquots in separate tubes and combined eluates on evaporation yielded solid yellow product which on recrystallisation from hot benzene gave golden yellow crystals with sharp melting point. The orange band was discarded because of its impure nature. The systematic name and other details of the tetraketones are given in **Table 4.1.**

**Synthesis of metal complexes**

A solution of the unsaturated tetraketones (0.005 mol) in 30 ml ethylacetate-methanol (1:1 v/v) mixture was refluxed on a boiling water bath for half an hour. To this metal(II) acetate (0.005 mol) in 20 ml methanol was added drop by drop and again refluxed for ~ 6 h. It was the concentrated to half the volume, cooled to room temperature and the complex precipitated was filtered washed several times with ethylacetate, then with methanol following water and recrystallised from hot ethanol to get the pure compounds.

**Table 4.1: Systematic name and other details of the unsaturated tetraketones**

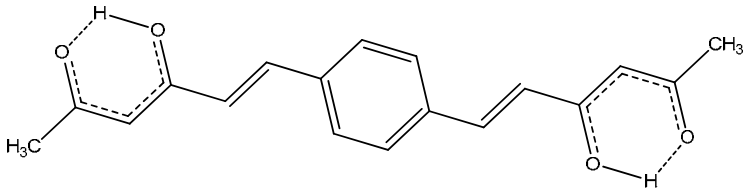
| Compounds | 1,3- diketones used | Systematic name | % yield | M.P $^0C$ |
|---|---|---|---|---|
| $H_2$aa | Acetylacetone | 6,6'-(1,4-Phenylene) bis (hex-5-ene-2,4-dione) | 85 | 145 |
| $H_2$ma | Methylacetoacetate | Dimethyl [5,5' –(1,4-phenylene) bis (3-oxopent-4-enoate)] | 67 | 110 |
| $H_2$ba | Benzoyl acetone | 5,5' (1,4- Phenylene) bis (1-phenyl pent-4-ene-1,3-dione) | 62 | 230 |
| $H_2$an | Acetoacetanilide | 5,5' (1,4- Phenylene) bis (3-oxo-N-phenyl pent-4-eneamide) | 58 | 240 |

## Results and Discussion

### Characterization of the unsaturated tetraketones and their metal complexes

### Characterization of $H_2$aa

The observed carbon, hydrogen percentages (**Table 4.2**) clearly suggest that one equivalent of the aldehyde condensed with two equivalents of acetylacetone. The observed IR, NMR and mass spectral data are in conformity with **structure 4.4** of the compound. The spectral data are discussed below.




**4.4**

**Table 4.2: Physical and analytical data of $H_2$aa and its metal complexes**

| Compounds | Elemental analysis (found/calcd) | | |
|---|---|---|---|
| | C | H | M |
| $H_2$ aa | 72.40 (72.48) | 6.02 (6.04) | - |
| [Cu(aa)] | 59.94 (60.08) | 4.42 (4.45) | 17.62 (17.67) |
| [Ni (aa)] | 60.96 (60.89) | 4.50 (4.51) | 16.62 (16.55) |
| [Co(aa)($H_2O$)] | 55.96 (56.10) | 4.28 (4.15) | 15.26 (15.31) |

**Infrared spectrum**

The problem of assigning the correct structure of these type compounds can be done with the help of IR spectra. In these compounds the carbonyl groups are the most useful functions available for charaterisation and structure elucidation. The position and intensity of the carbonyl stretching band is determined by the molecular structure in its immediate vicinity, and is therefore very valuable for characterising the type of carbonyl function.

Normal acetyl carbonyl gives[56,95,193] stretching band at ~1720 $cm^{-1}$. Hydrogen bonding, conjugation and enolisation decrease the carbonyl stretching frequency considerably. The IR spectrum of **$H_2$aa** (**Table 4.3**) does not contain any band assignable to free acetyl carbonyl groups. Instead a strong band observed at 1636 $cm^{-1}$ can be assigned to the stretching of the conjugated and enolised acetyl carbonyl functions of **structure 4.4** . Another strong band appeared at 1615 $cm^{-1}$ can safely be assigned to the intramolecularly H-bonded cinnamoyl carbonyl function of the compound. The olefinic and aryl $\nu_{C=C}$ appeared in the range 1580-1600 $cm^{-1}$ of the spectrum. In the X-H region show a broad band ranging from 2500-3500 $cm^{-1}$ typical of hydrogen bonded enol form of the compound as in **structure 4.4**. Infrared spectrum of the compound is reproduced in **figure 4.1.**

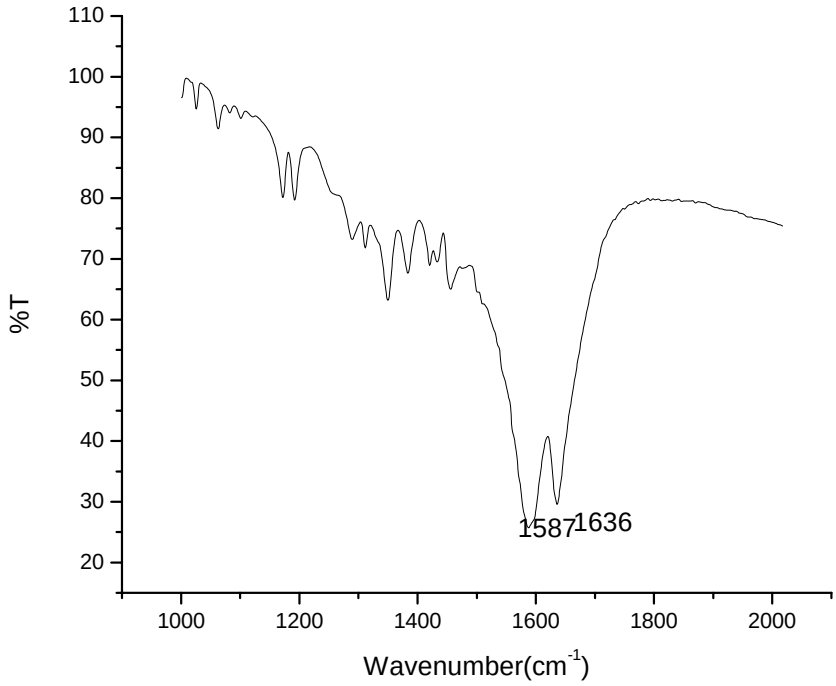



**Fig. 4.1. IR spectrum of $H_2$aa**

**Table 4.3: IR Spectral data of $H_2$aa and its metal complexes**

| Compounds | IR stretching bands in $cm^{-1}$ | | | | |
|---|---|---|---|---|---|
| | C=O acetyl | C=O Cinnamoyl | C=C Phenyl/alkenyl | CH=CH trans | M-O |
| H2aa | 1636 | 1615 | 1588, 1520 | 964 | - |
| [Cu(aa)] | 1573 | 1525 | 1525, 1485 | 982 | 487,429 |
| [Ni(aa)] | 1576 | 1528 | 1528, 1480 | 980 | 483,431 |
| [Co(aa)$(H_2O)_2$] | 1578 | 1522 | 1522, 1490 | 976 | 470,428 |

## $^1$H NMR spectrum

Proton NMR spectroscopy is one of the most useful technique in structure determination and in the study of keto-enol tautomerism of dicarbonyl compounds. In the case of enol tautomer having strong intramolecular H-bonding, the resonance signal of the proton generally appears in the downfield (δ >14 ppm) region of the nmr spectrum and is characteristically broad. Thus it has been shown that the chemical shift of the enolic proton in $^1$H NMR spectra of 1,3-diketones is a measure of the strength of the intramolecular hydrogen bond. Further the integrated intensity of the enolic proton signal is a measure of the percentage of the enol tautomer[56].

The observed $^1$H NMR spectrum of **$H_2$aa** shown in **figure 4.2**. is characterised by the presence of a two proton signal at δ 15.95 ppm assignable to the intramolecularly hydrogen bonded enol protons of the compound. The methine proton signals are observed at δ 5.95 ppm. The integrated intensities of all the protons agree well with **structure 4.4** of the compound.

## Mass Spectrum

The mass spectrum of the compound shows the parent ion peak ($P^+$) at m/z 298. Other prominent peaks are due to the elimination of –$CH_3$, -$COCH_3$ -CH=CH-, -$CH_2$=C=O, etc from the molecular ion. Thus all

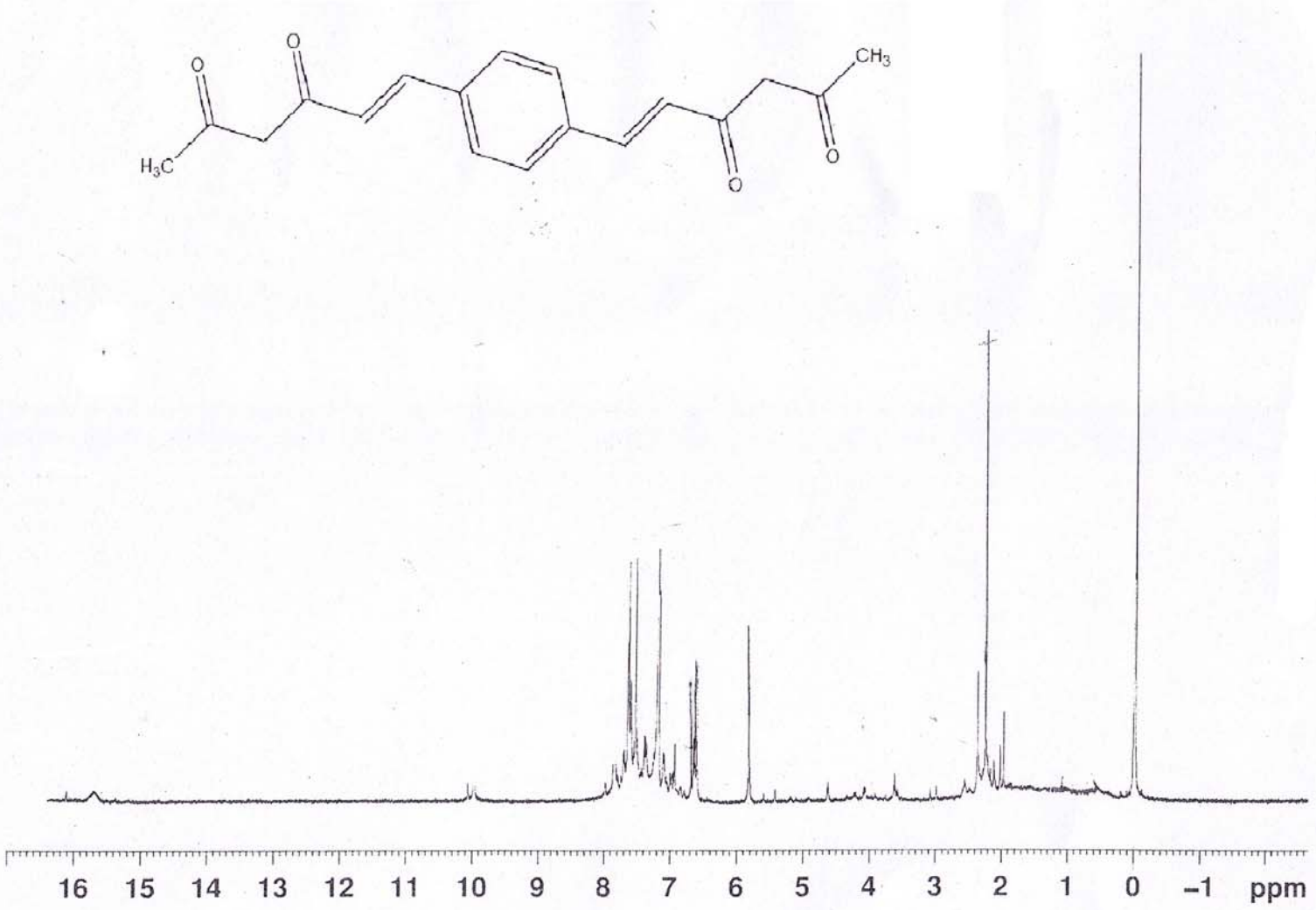



**Figure 4.2 $^{1}$H NMR spectrum of $H_2$aa**

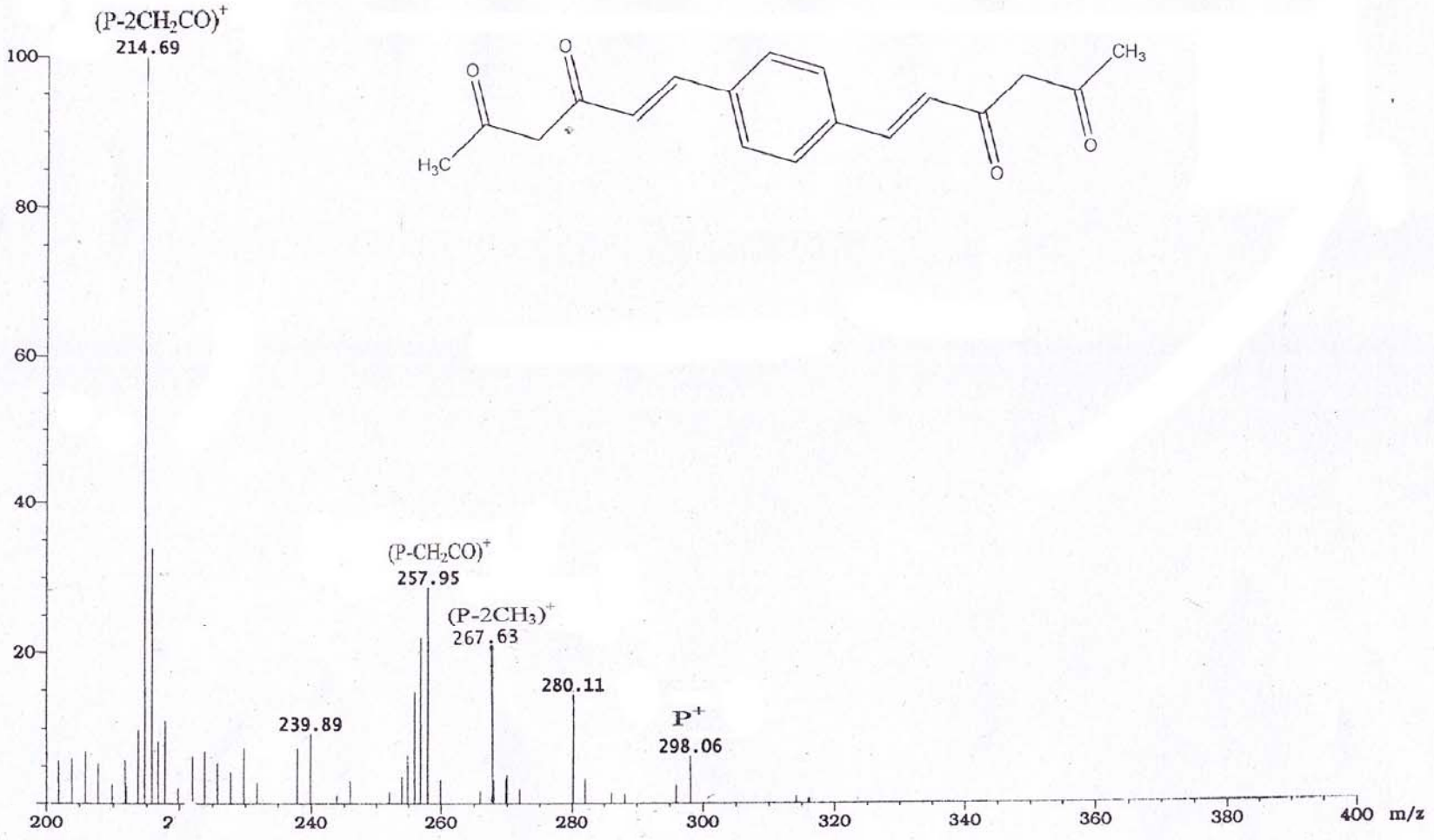
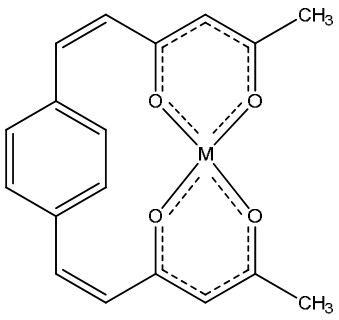



**Figure 4.3 FAB Mass spectrum of $H_2$aa**

available evidences suggest **structure 4.4** of the compound. The spectrum is reproduced in **figure 4.3.**

**Characterisation of metal complexes of $H_2$aa**

The compound formed well defined complexes with Cu(II), Co(II) and Ni(II) ions. Elemental analysis and physical data of the complexes are given in **Table 4.2**. The analytical data suggest a 1:1 metal ligand stochiometry for all complexes. The copper(II) and cobalt(II) complexes are paramagnetic, while nickel(II) complex is diamagnetic. The observed IR, NMR and mass spectral data are in agreement with the **structure 4.5** of the complexes. The spectral data are discussed below.




**4.5**

In the IR spectra of all the complexes of **$H_2$aa**, the free ligand band due to the stretching of intramolecularly H-bonded carbonyl functions disappeared and no band assignable to free or enolised carbonyl groups present in the region 1600-1800 $cm^{-1}$. This clearly suggested that both the dicarbonyl functions are involved in bonding with metal ion. A new band appeared at

~1570 $cm^{-1}$ in the spectra of the complexes can be assigned to metal bonded carbonyl groups**(Table 4.3)**. Further the broad free ligand band in the region 2800-3500 $cm^{-1}$ due to intramolecualrly hydrogen bonded enol form cleared up in the spectra of complexes. This indicates the replacements of the enol protons by metal ions as in **structure 4.5**. The presence of two medium intensity bands in the region 420-470 $cm^{-1}$ which are assignable to $\nu_{M-O}$ vibrations also supported the structure of the complexes. The specrum of **[Cu(aa)]** are reproduced in **figure 4.4.**

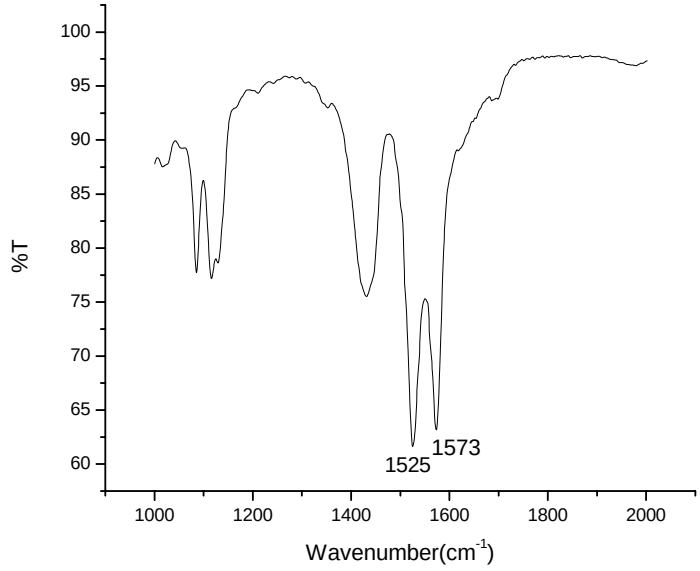



**Fig. 4.4. IR spectrum of [Cu (aa)]**

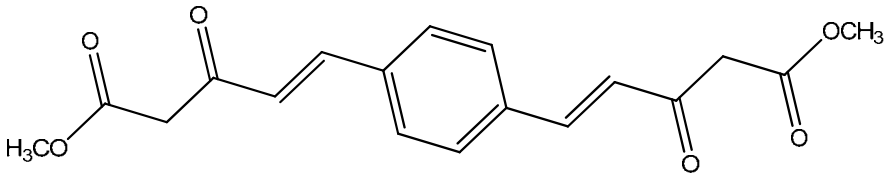
The $^1H$ NMR spectrum of the diamagnetic Ni(II) complex of **$H_2$aa** is shown in **figure 4.5.** In the spectrum, the low field signal of the free ligand due to the hydrogen bonded enol disappeared which indicated that the metal ion replaced the enolic proton during complexation. The methine proton and

aromatic proton signals shifted slightly to downfield. Thus the NMR spectrum strongly support the bonding mode of the ligands as in **structure 4.5**. The integrated intensities of all protons agree well with the formulation of the complexes.

The mass spectrum (**Figure 4.6**) of the Cu(II) complex show the molecular ion peak at m/z 359 of moderate intensity. The intense peaks present in the spectrum are due to ligand and its different fragments.

**Characterisation of $H_2$ma**

The observed C, H percentages of **$H_2$ma** (**Table 4.5**) clearly suggest that both aldehydic group of 1,4-phthalaldehyde condensed with methylacetoacetate. The observed IR, NMR and mass spectral data suggest the structure **4.6** of the compound. The spectral data are discussed below.




**4.6**

**Table 4.5: Elemental analytical data of $H_2$ma and its copper complexes**

| Compounds | Elemental analysis (found/calcd) | | |
|---|---|---|---|
| | C | H | M |
| $H_2$ ma | 63.13 (63.45) | 5.73 (5.45) | - |
| [Cu(ma)] | 54.99 (55.25) | 5.10 (4.09) | 16.01 (15.22) |

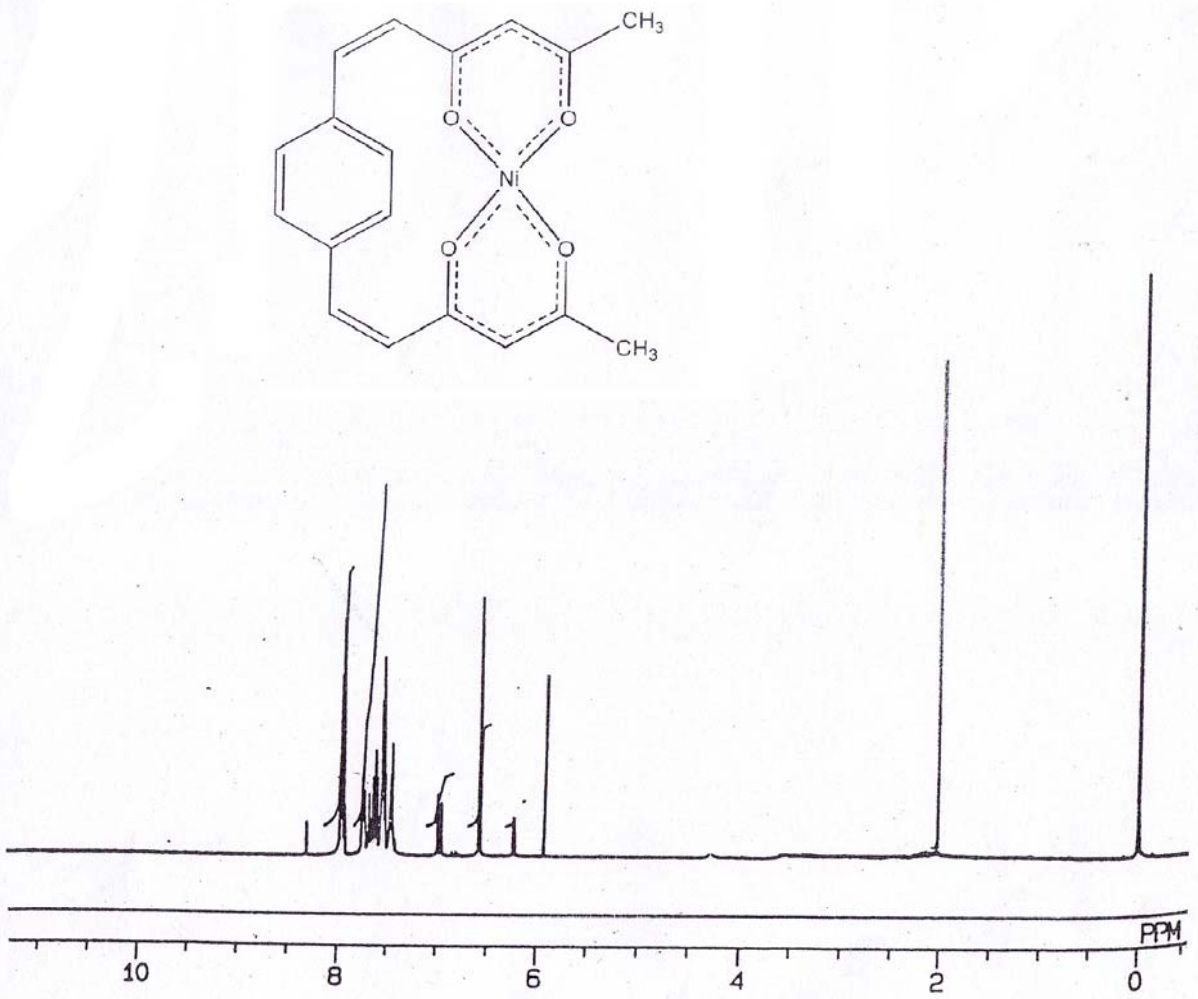



**Figure 4.5 $^{1}$H NMR spectrum of [Ni(aa)]**

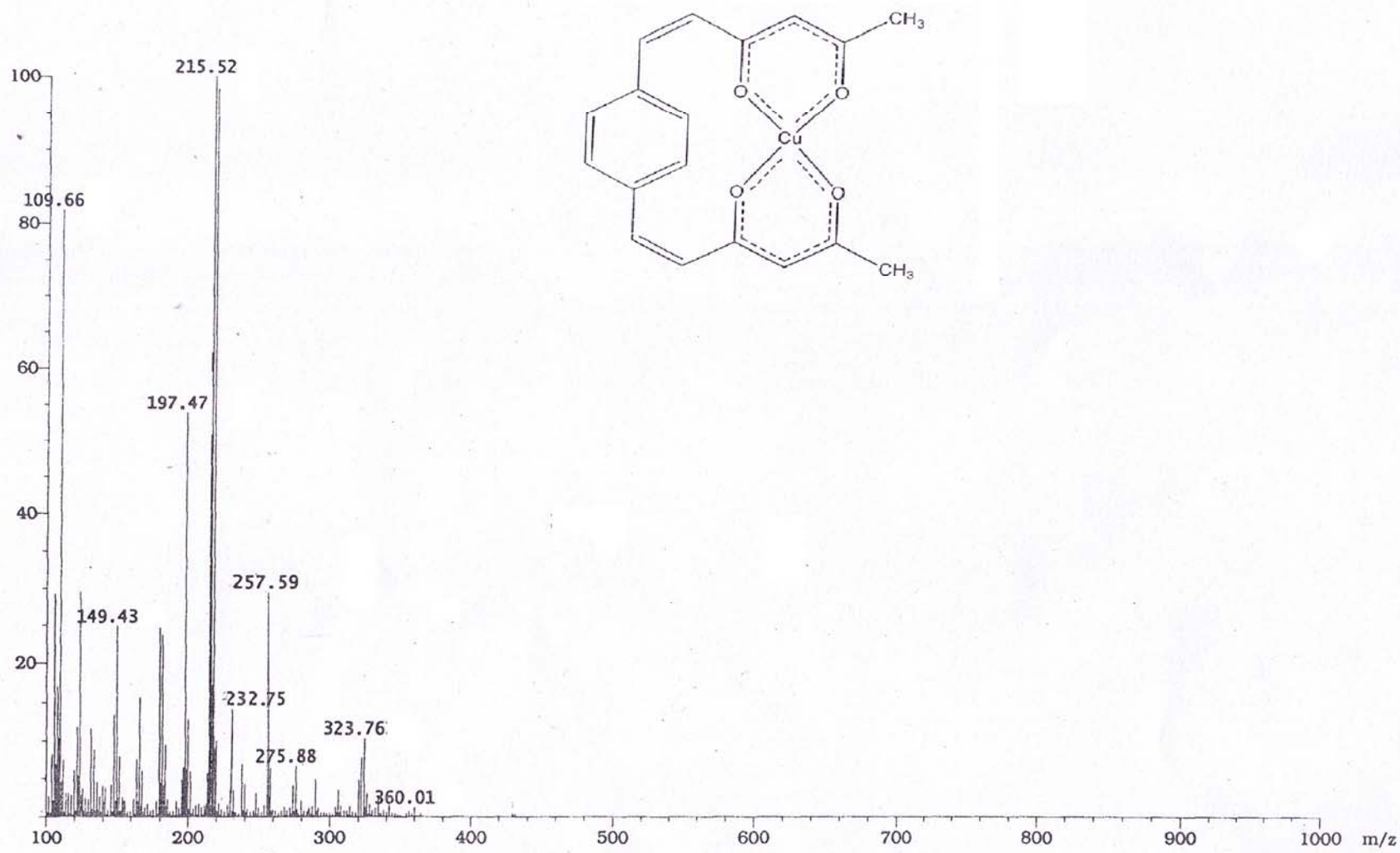



**Figure 4.6 FAB Mass spectrum of [Cu(aa)]**

**Infrared spectrum**

The IR spectrum of the compound shows three strong bands at 1605, 1654 and 1725 $cm^{-1}$ in the region 1600-1800$cm^{-1}$**(figure 4.7.)** which are assignable to specific functional groups. The ester carbonyl of methylacetoacetate shows the carbonyl stretching band at ~ 1750$cm^{-1}$ and the acetyl carbonyl at ~ 1720 $cm^{-1}$. The enolisation and H-bonding decreases these stretching frequencies. Therefore the two strong bands appeared in the spectrum of the compound at 1725 $cm^{-1}$ and 1654 $cm^{-1}$ can safely be assigned to the stretching of the ester carbonyl and the cinnamoyl carbonyl respectively. The weak band at 1605 $cm^{-1}$ present in the spectrum can arise as due to the stretching of olefinic and C=C vibrations.The slightly broad peak present in the region 2500-3500 $cm^{-1}$ indicate the low percentage of the enol tautomer of the compound.

**Table 4.6: IR spectral data of $H_2$ma and its copper complexes**

| Compounds | IR stretching bands $cm^{-1}$ | | | | |
|---|---|---|---|---|---|
| | C=O ester | C=O cinnamoyl | C=C phenyl/alkenyl | CH=CH trans | M-O |
| $H_2$ma | 1729 | 1654 | 1605, 1565 | 970 | - |
| [Cu(ma)] | 1690 | 1627 | 1601 | 964 | 417, 459 |

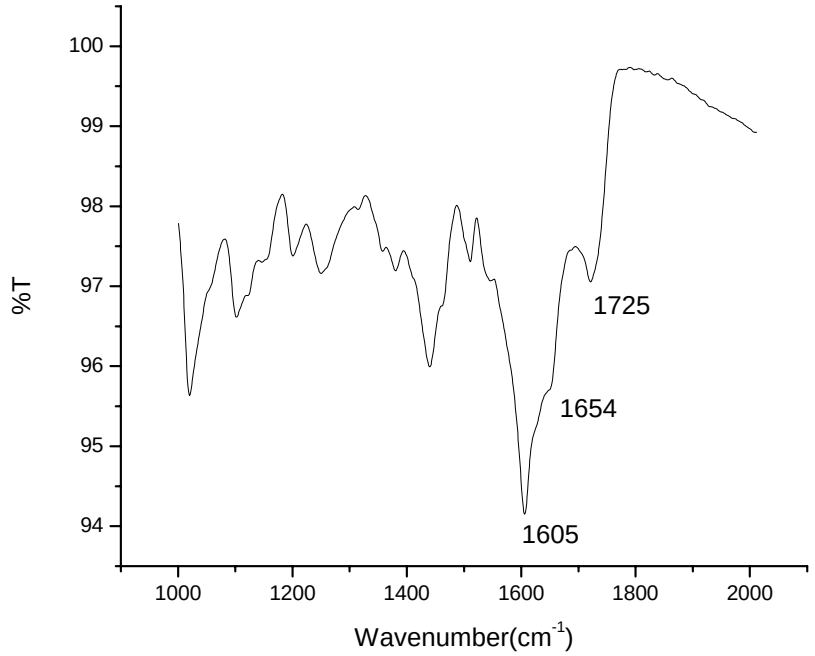



**Fig.4.7 IR spectrum of $H_2$ma**

## $^1$H NMR spectrum

The compound show a three proton signal at ~ δ 3.9 ppm due to the -$OCH_3$ protons. Aromatic protons show peaks in the range ~ 7-8 ppm. There is no peak in the low field region above 12 ppm **(Figure 4.8)** in the proton nmr spectrum of the compound which suggest the existence of the compound predominantly in the keto form. Integrated intensities of the -$OCH_3$, –CH=CH– and aryl protons agree well with the formulation of the compound as in **structure 4.6.**

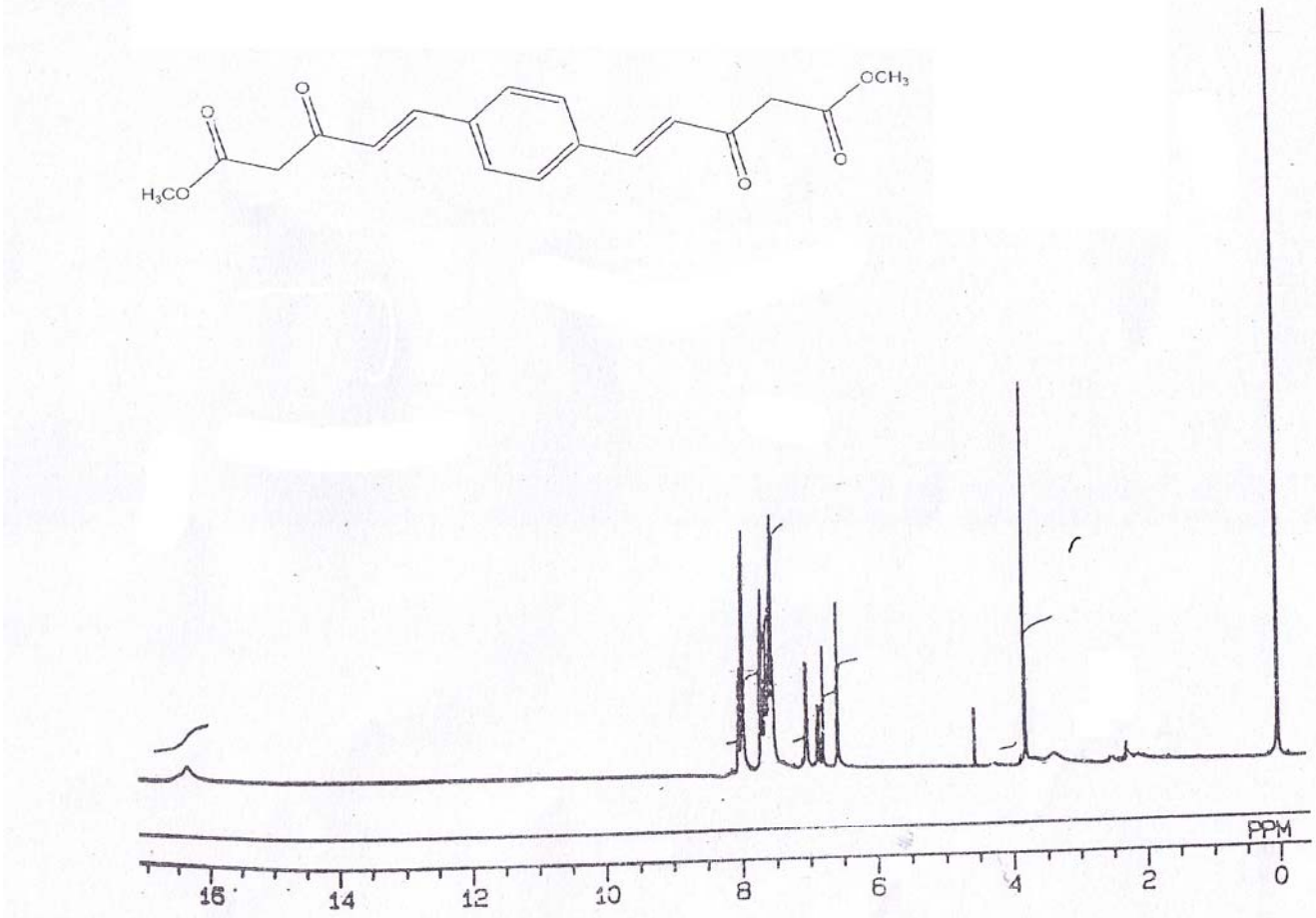


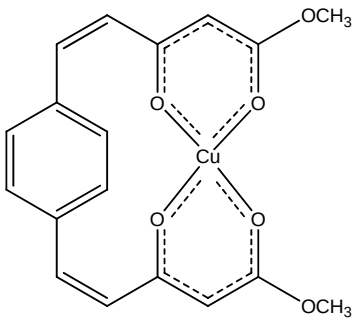

**Figure 4.8 $^1$H NMR spectrum of $H_2$ma**

## Mass Spectrum

Mass spectrum of the compound shows molecular ion ($P^+$) peak at m/z 330 **(Figure 4.9)**. Other prominent peaks are due to the fragmentation of the molecular ion with elimination of -$CH_3$, -$OCH_3$, -$CH_2CO$, etc.

## Characterization of metal complex of $H_2$ma

Physical and analytical data of the Cu(II) complex of $H_2$ma is given in **Table 4.5**. Elemental analytical data suggest [CuL] stochiometry for the complex as shown in structure **4.7**.




**4.7**

The IR spectrum of the complex displayed three bands at ~1605, 1627 and 1690 $cm^{-1}$ in the region 1600-1800 $cm^{-1}$ instead the free ligand bands at 1725$cm^{-1}$ and 1654 $cm^{-1}$ due to the cinnamoyl and ester carbonyl function. From the spectra it is clear that, the band at 1690$cm^{-1}$ and 1627 $cm^{-1}$ can safely be assigned to the stretching of the metal bonded ester and cinnamoyl carbonyl function respectievely. The spectrum is reproduced in **figure 4.10.**

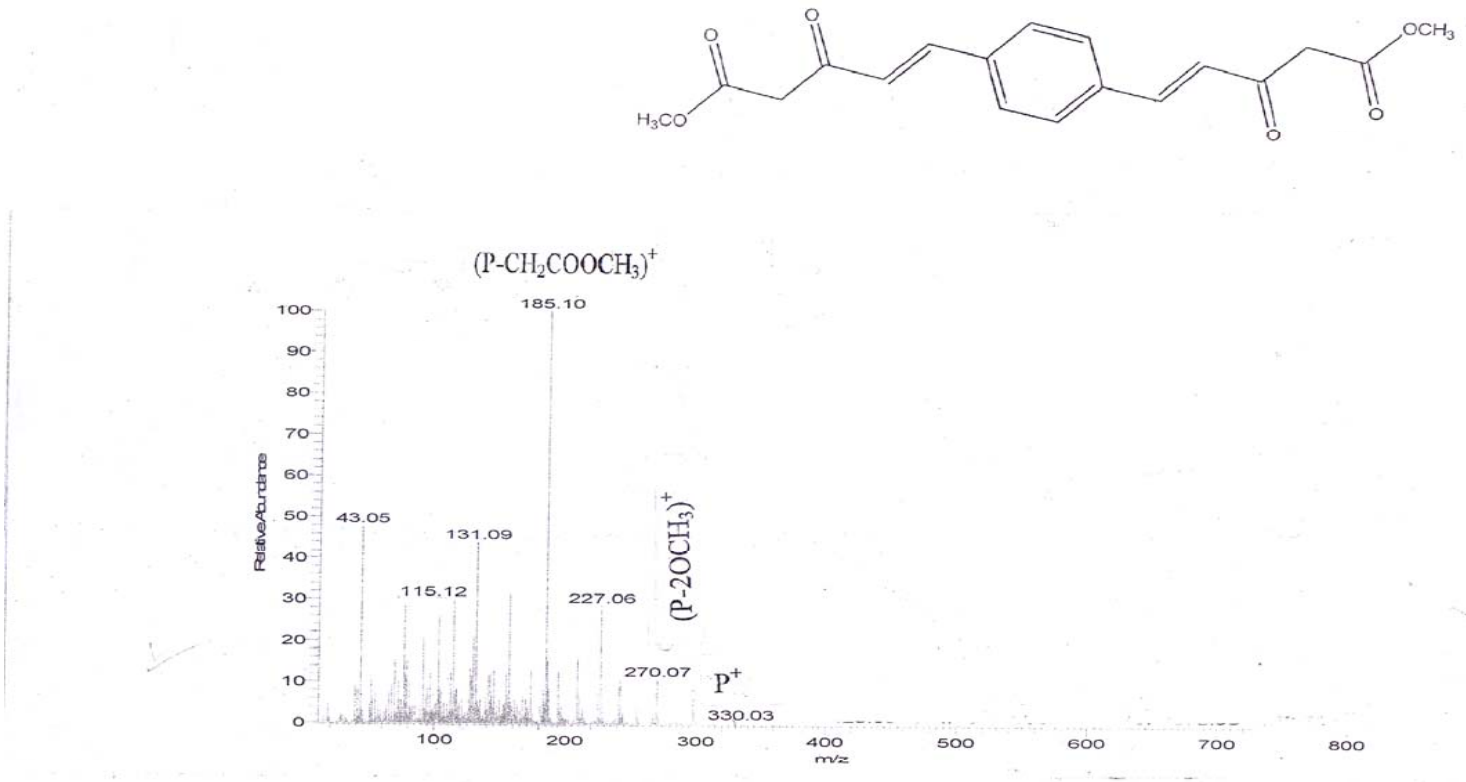



**Figure 4.9 FAB Mass spectrum of $H_2$ma**

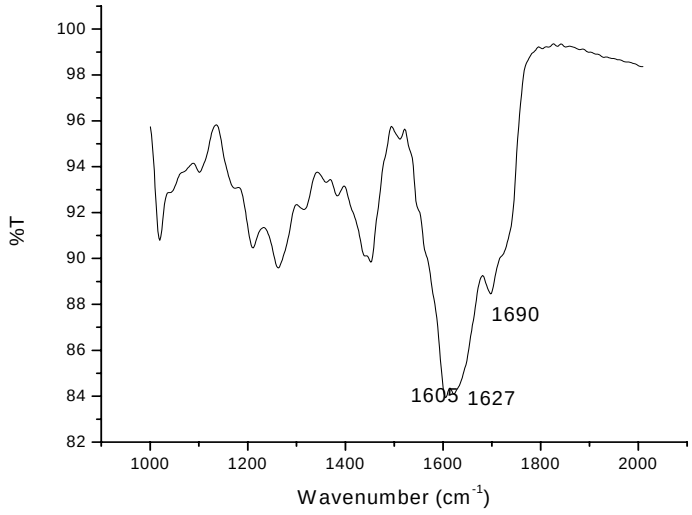
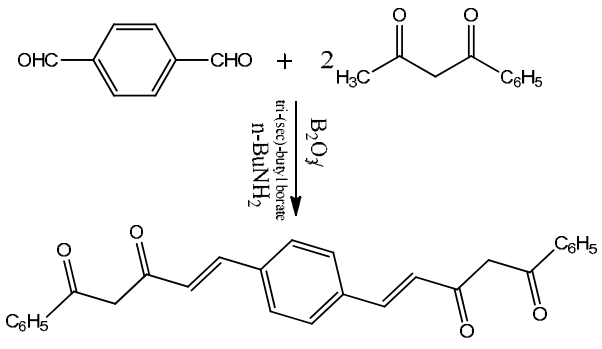



**Fig.4.10 IR Spectrum of [Cu(ma)]**

The mass spectra of the Cu(II) complex is in full agreement with the **structure 4.7** of the complex **(Figure 4.11).** It shows a moderately intense molecular ion peak at 391. The base peaks are due to the ligand moeity and its different fragments.

## Characterisation of $H_2ba$

The expected product of the Claisen-Schmidt reaction between 1,4-phthalaldehyde and benzoylacetone can be written as given below.




**Scheme 4.3**

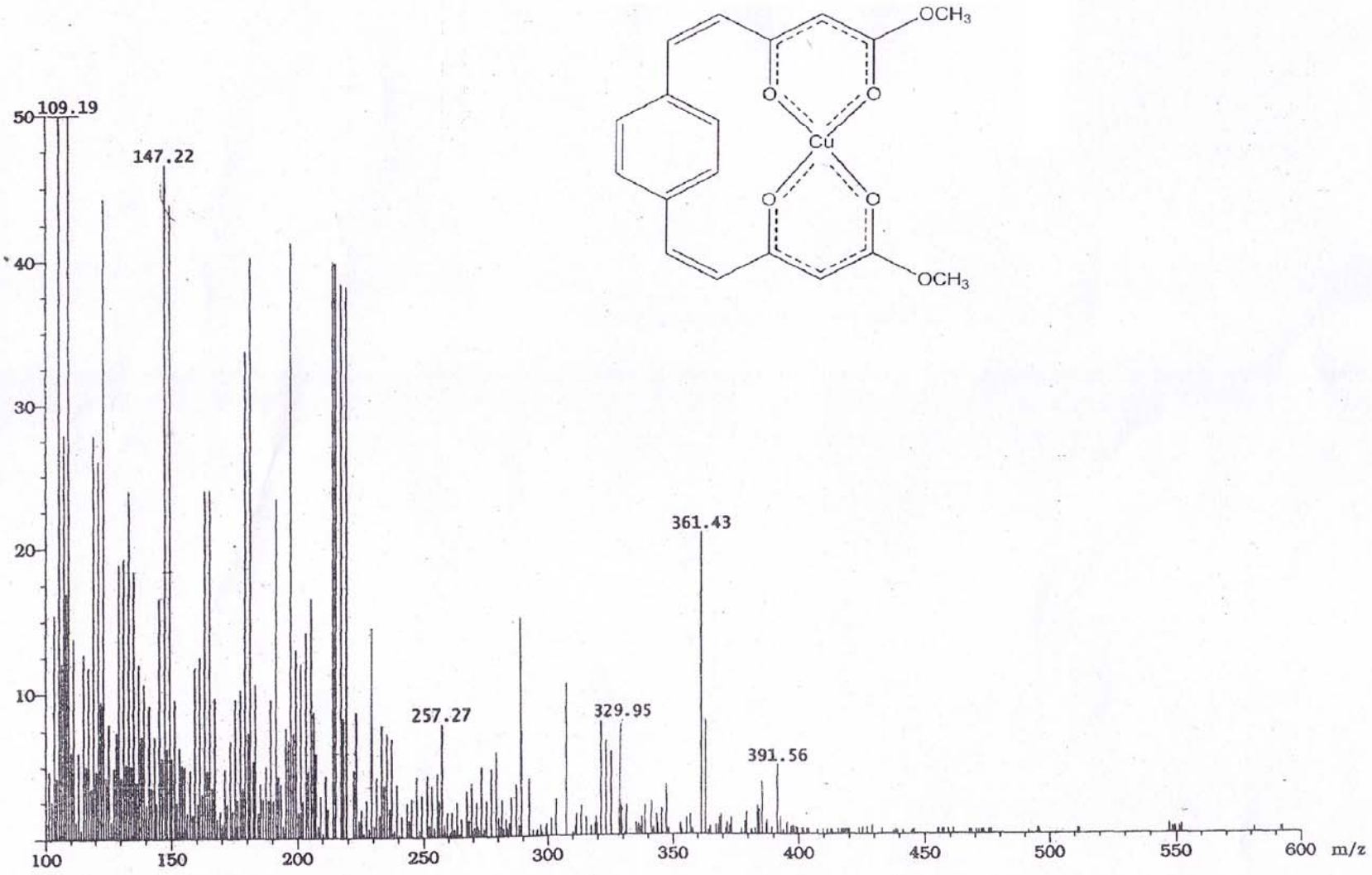
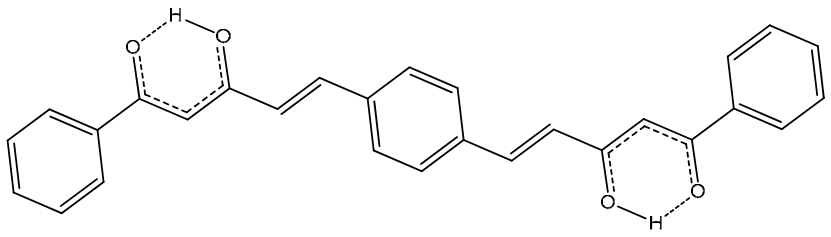



**Figure 4.11 FAB Mass spectrum of [Cu(ma)]**

The observed C, H percentages and the IR, NMR and mass spectral data of the reaction product are well in agreement with the structure **4.8** of the compound. The spectral data are discussed below.



**4.8**

**Table 4.7: Elemental analytical data of $H_2$ba and its metal complexes**

| Compounds | Elemental analysis (found/calcd) | | |
|---|---|---|---|
| | C | H | M |
| $H_2$ ba | 79.18 (79.60) | 4.8 (5.20) | - |
| [Cu(ba)] | 69.07 (69.48) | 4.52 (4.13) | 13.45 (13.14) |
| [Ni(ba)] | 69.75 (70.19) | 4.47 (4.18) | 12.54 (12.25) |
| [Co(ba)$(H_2O)_2$] | 63.32 (63.51) | 3.93 (3.78) | 11.42 (11.13) |

**Infrared spectrum**

The IR spectrum of **$H_2$ba** in the 1600-1700 $cm^{-1}$ region shows two strong bands at 1636$cm^{-1}$ and 1601 $cm^{-1}$ **(Figure 4.12)**. Based on earlier reports[193-195] the band at 1636$cm^{-1}$ can confidently be assigned to intramolecularly hydrogen bonded enolic form of the compound as shown in structure **4.8**. Further the presence of a broad band in the 2500-3500$cm^{-1}$ region of the spectrum also support the intramolecularly H-bonded the enolic

form of the compound. The band at 1601 $cm^{-1}$ is due to $\nu_{C=C}$ stretching frequencies of aryl/alkenyl groups.

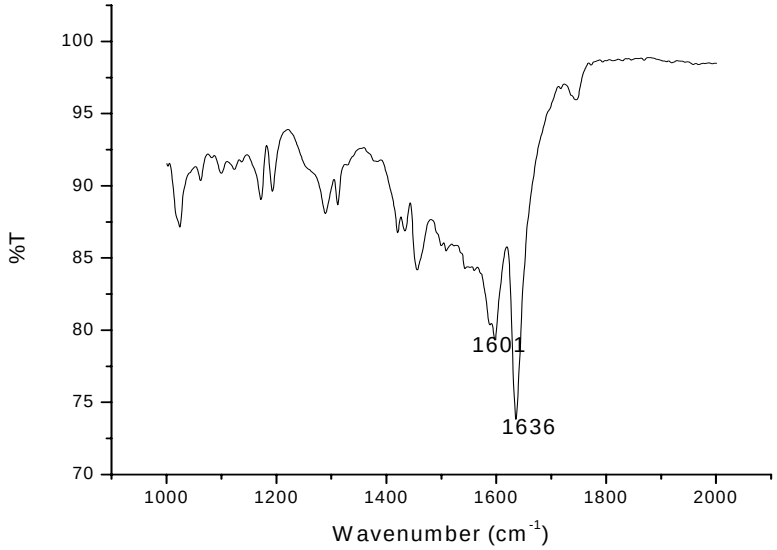



**Figure 4.12 IR spectrum of $H_2$ba**

**Table 4.8: IR spectral data of $H_2$ba and its metal complexes**

| Compounds | IR bands $cm^{-1}$ | | | |
|---|---|---|---|---|
| | C=O aroyl/ Cinnamoyl | C=C Phenyl/alkenyl | CH=CH trans | M-O |
| $H_2$ba | 1636 | 1601, 1570 | 982 | - |
| [Cu(ba)] | 1582 | 1582, 1533 | 972 | 411, 458 |
| [Ni(ba)] | 1580 | 1578, 1547 | 985 | 418, 462 |
| [Co(ba)$(H_2O)_2$] | 1575 | 1584, 1538 | 969 | 420, 461 |

**$^1$H NMR spectrum**

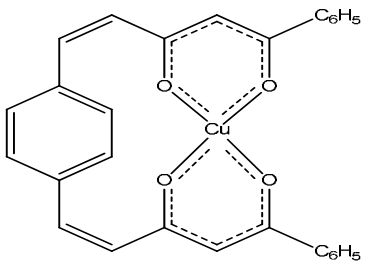
The $^1$H NMR spectrum of **$H_2$ba** shows a low field signal at δ 15 ppm assignable to the enol protons. The alkenyl protons of the conjugated structure appeared in the region δ 6.54- 6.80 ppm and the aryl protons in the range δ 7.08 – 8.03 ppm **(Figure 4.13).** The absence of methyl protons signals clearly suggest that the methyl groups of benzoyl acetone has condensed with 1,4-phthalaldehyde.

**Mass spectrum**

The FAB mass spectrum of $H_2$ba **(Figure 4.14)** shows a moderately intense molecular ion peaks at m/z and several intense peaks due to successive removal of groups like -$C_6H_5$, -$C_6H_5CO$, -$OCH_3$ ,-CH=CH-, etc from the molecular ion.

**Characterisation of metal complexes of $H_2$ba**

Carbon, hydrogen and metal percentages of the complexes are given in **Table 4.7**. The elemental analysis gives a [ML] stochiometry for the complexes. The IR, NMR and mass spectral data of the complexes are in full agreement with the **structure 4.9** of the complexes.




**4.9**

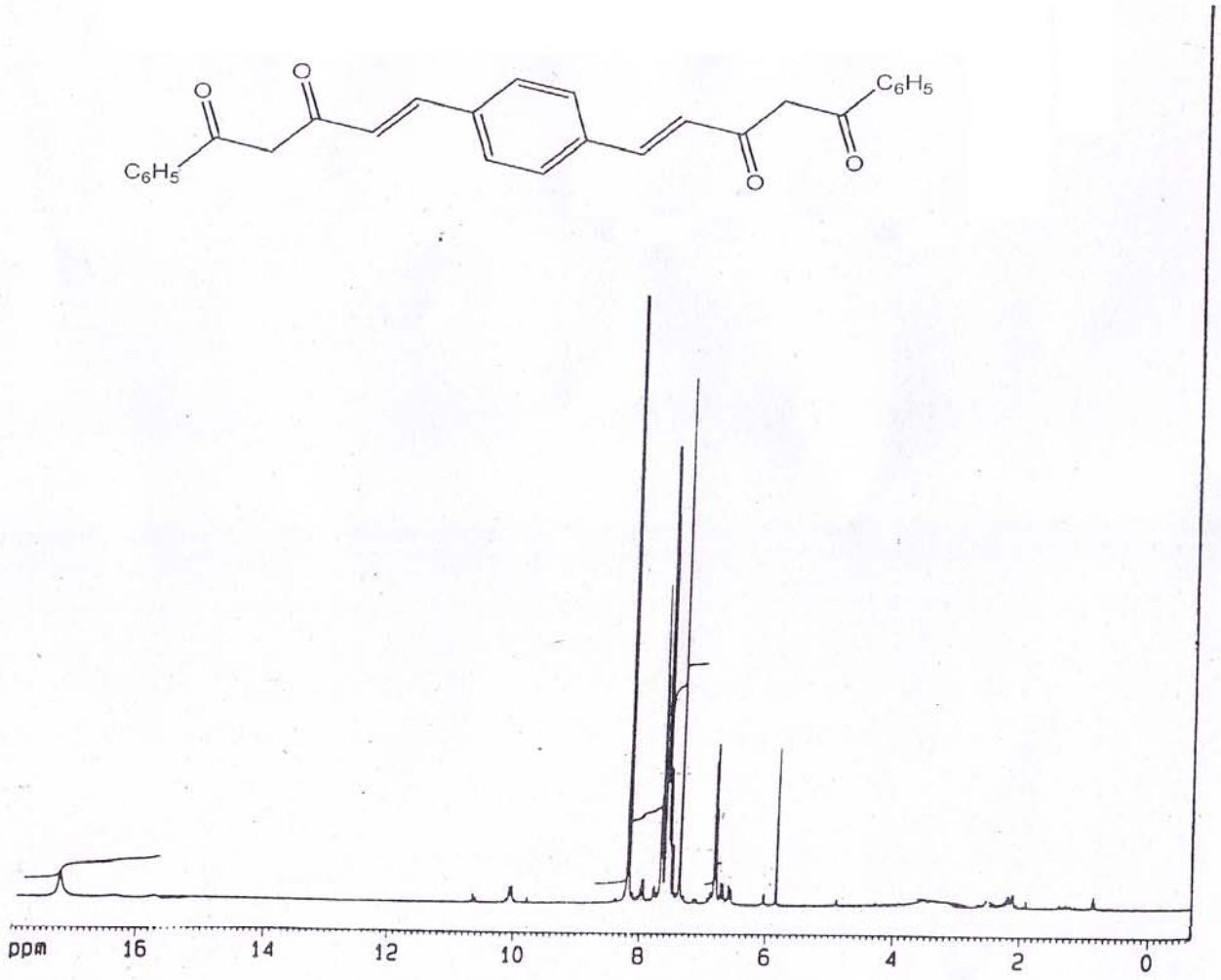



**Figure 4.13 $^{1}$H NMR spectrum of $H_2$ba**

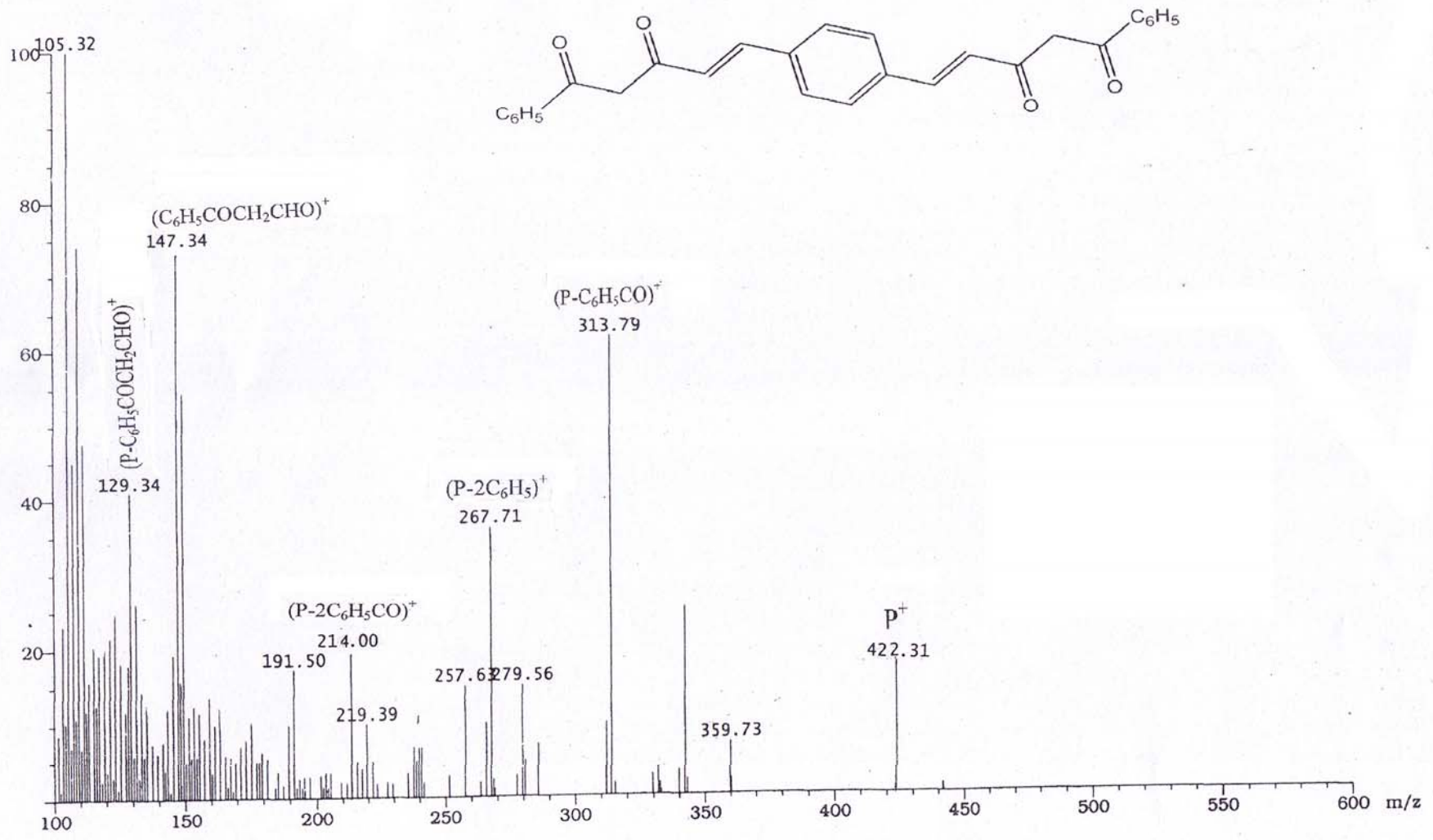



**Figure 4.14 FAB Mass spectrum of $H_2ba$**

In the IR spectra of the complexes the band at 1636cm$^{-1}$ due to H-bonded carbonyl groups disappeared and instead a new band observed at ~1580 cm$^{-1}$ assignable to metal bonded carbonyl function as in **structure 4.9.** Further two new bands at 411cm$^{-1}$ and 458 cm$^{-1}$are observed due to $\nu_{M-O}$ stretching vibrations. The broad band due to intramolecularly H-bonded diketo functions in the region 2800-3500cm$^{-1}$ also disappeared in the spectra of the complexes which confirms the complexation as shown in structure **4.9**.

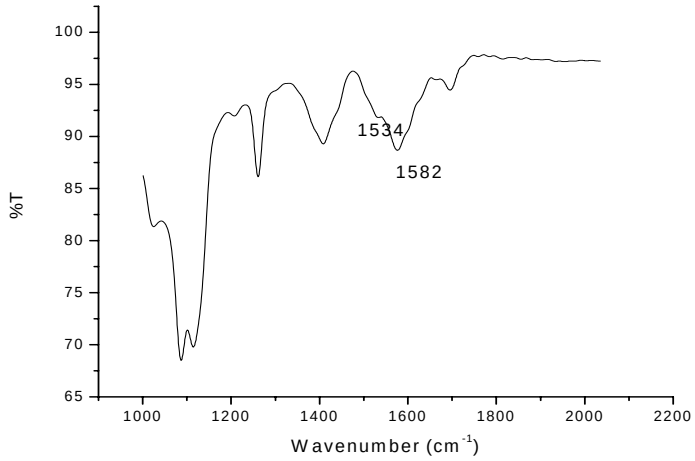



**Fig.4.15 IR Spectrum of [Cu(ba)]**

$^1$H NMR spectra of the Ni(II) complex of **$H_2$ba** is shown in **Figure 4.16.** In the spectrum, the downfield signal near ~15 ppm due to intramolecularly H - bonded enol protons disappeared which confirms the metal complexation as in structure **4.9.** The olefinic and aryl protons slightly shifted to downfield due to the metal complexation of the diketone moeity.

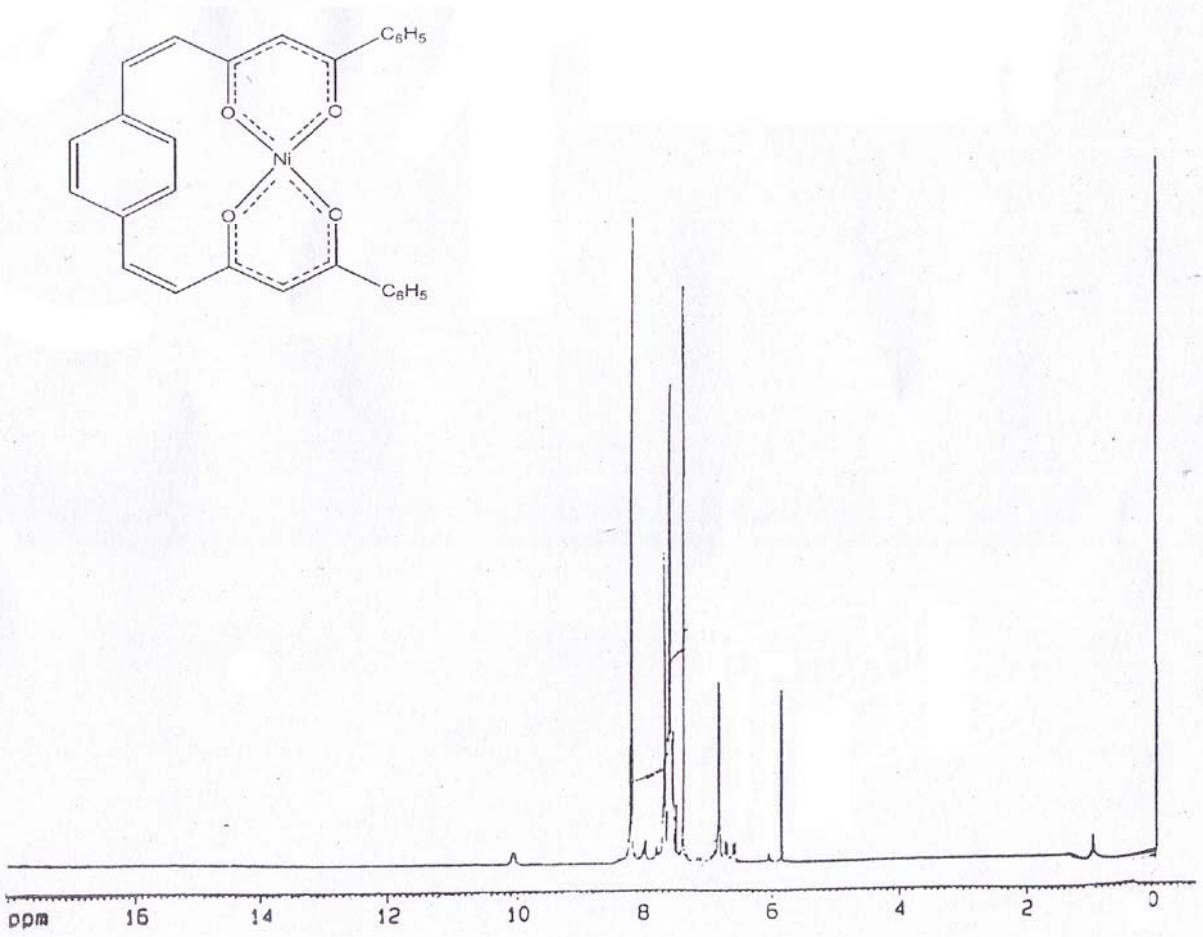
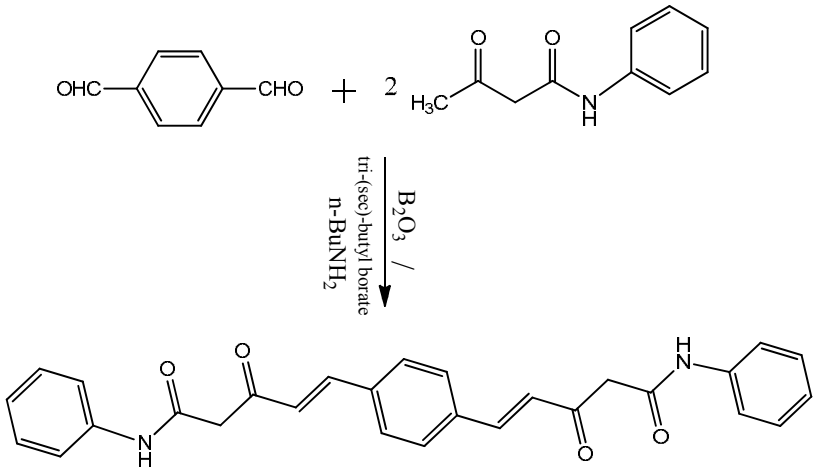



**Figure 4.16 $^{1}$H NMR spectrum of [Ni(ba)]**

The FAB mass spectrum of the Cu(II) complex is shown in **Figure 4.17.** The spectrum clearly suggest 1:1 metal-ligand stochiometry because of the presence of the peak at m/z 483 due to the molecular ion as shown in **structure 4.9.** Other prominent peaks are due to ligand and its fragments.

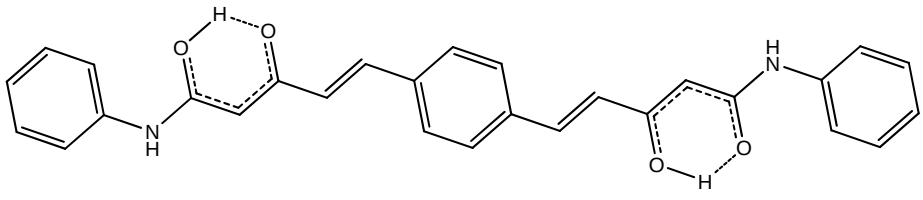
**Characterisation of $H_2$an**

The expected Claisen-Schmidt condensation product of acetoacetanilide and 1,4-phthalaldehyde, can be summarised as shown below.




**Scheme 4.4**

The physical and analytical data of the product are given in **Table 4.9**. The observed C, H, N, percentages and the IR, NMR and mass spectral data of the reaction product are fully justified the formation of the compound **4.10.**




**4.10**

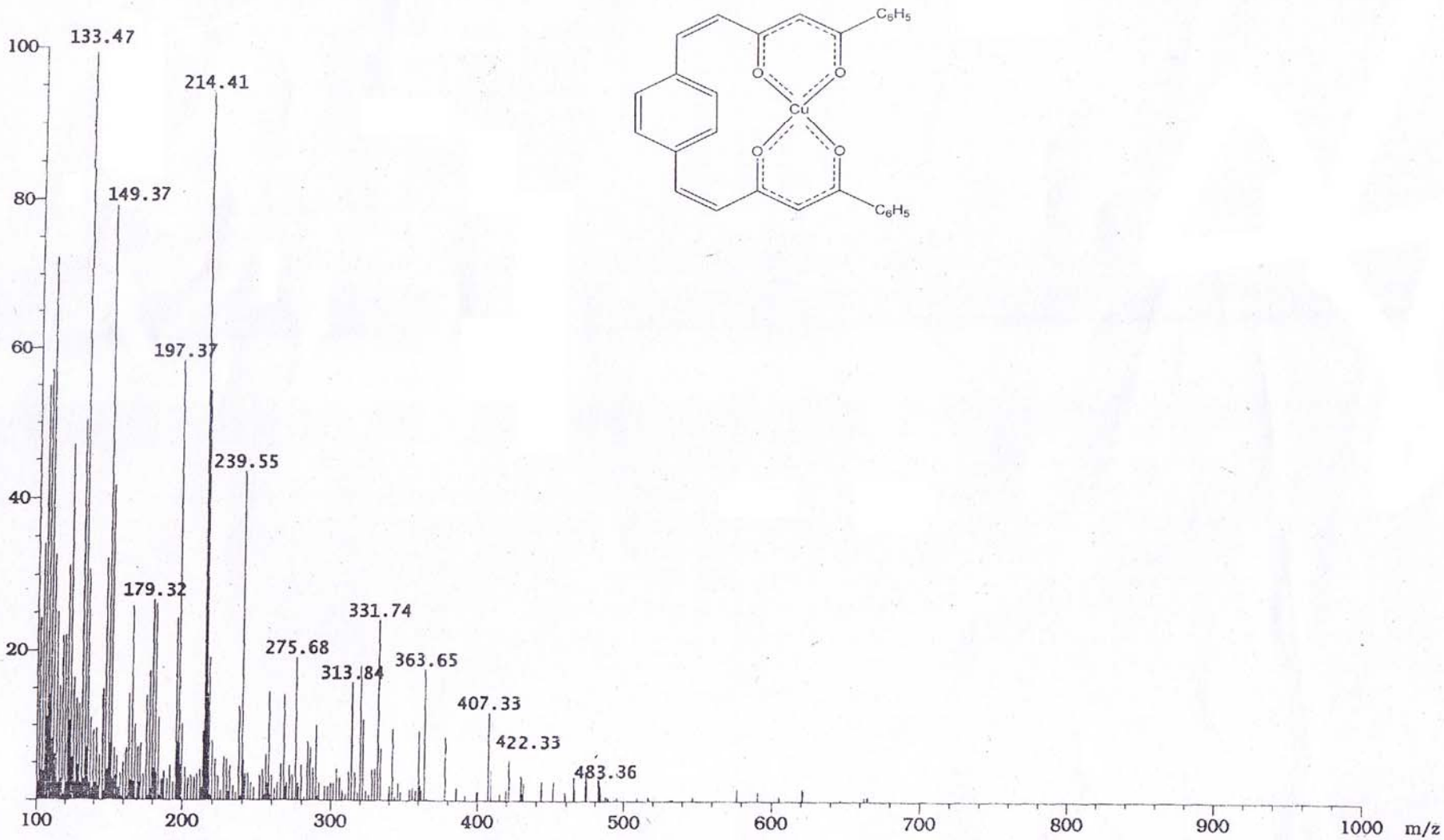



**Figure 4.17 FAB Mass spectrum of [Cu(ba)]**

**Table 4.9: Physical and analytical data of $H_2$an and its metal complexes**

| Compounds | Elemental analysis (found/calcol) | | | |
|---|---|---|---|---|
| | C | H | N | M |
| $H_2$an | 74.41 (74.33) | 5.48 (5.30) | 6.25 (6.19) | - |
| [Cu(an)] | 65.13 (65.42) | 4.57 (4.28) | 5.29 (5.45) | 12.51 (12.37) |
| [Co(an)($H_2O$)] | 61.07 (61.20) | 4.24 (4.00) | 5.02 (5.13) | 10.99 (10.82) |
| [Ni(an)] | 65.89 (66.05) | 5.58 (4.34) | 5.34 (5.50) | 11.65 (11.53) |

**Infrared Spectrum**

The IR spectrum of the compound can easily be interpreted by comparing with the spectrum of acetoacetanilide. Acetoacetanilide exist predominantly in the keto form with very small percentage of the enol form. Therefore the most characteristic bands in the IR spectrum of acetoacetanilide is due to the amide carbonyl and acetyl carbonyl which occur at ~1667 $cm^{-1}$ and ~1720 $cm^{-1}$ respectively[196,197]. When the acetyl group is replaced by cinnamoyl group , stretching frequency of the acetyl carbonyl function will decrease due to conjugation. Enolisation of the diketo function further decreases the stretching frequency.

The spectrum of the compound shows only two prominent bands at 1663 $cm^{-1}$ and 1654$cm^{-1}$ in the region 1650-1800 $cm^{-1}$. These bands cannot assigned to a free cinnamoyl carbonyl stretching because such conjugated carbonyl groups usually absorb below 1650 $cm^{-1}$. Therefore the band at 1663 $cm^{-1}$ of the compound is due to the amide carbonyl stretching and the band at

1654cm$^{-1}$ assignable to partially enolised cinnamoyl carbonyl function. Further the enolisation is supported by the presence of a broad band in the region 2800-3500 cm$^{-1}$. The band at 1601 cm$^{-1}$ is due to $\nu_{C=C}$ stretching vibrations and the spectrum is reproduced in **Figure 4.18.**

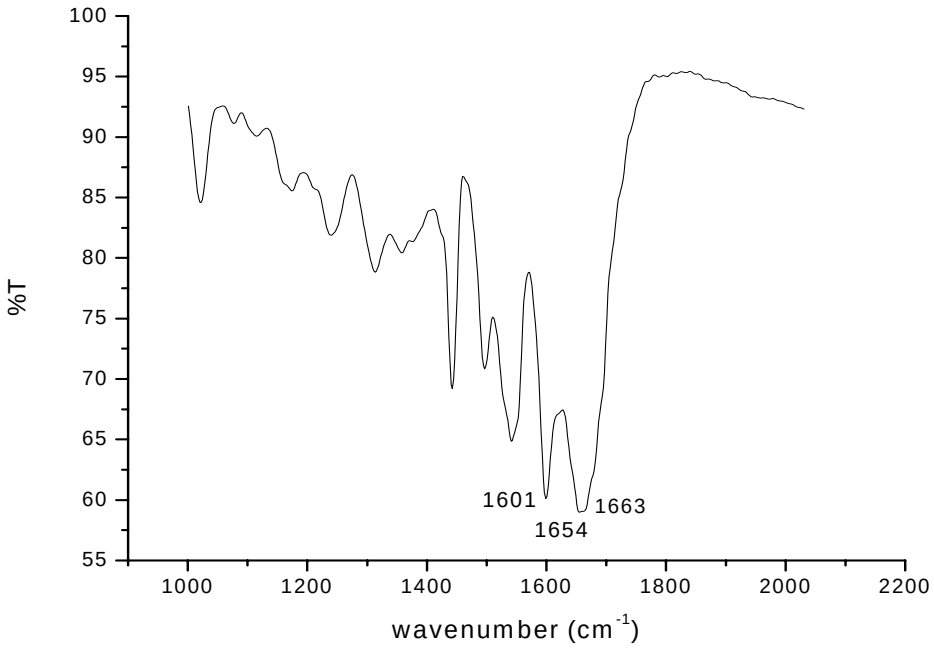



**Fig. 4.18 IR spectrum of$H_2$an**

**Table 4.10**: **IR spectral data of $H_2$an and its metal complexes**

| Compounds | IR bands cm$^{-1}$ | | | | |
|---|---|---|---|---|---|
| | C=O amide | C=O Cinnamoyl | C=C Phenyl/alkenyl | CH=CH trans | M-O |
| $H_2$an | 1663 | 1654 | 1601, 1540 | 962 | - |
| [Cu(an)] | 1629 | 1629 | 1567, 1537 | 946 | 413, 452 |
| [Co(an)($H_2O$)] | 1623 | 1623 | 1564, 1544 | 967 | 414, 472 |
| [Ni(an) | 1618 | 1618 | 1568, 1549 | 974 | 418. 466 |

**$^1$H NMR Spectrum**

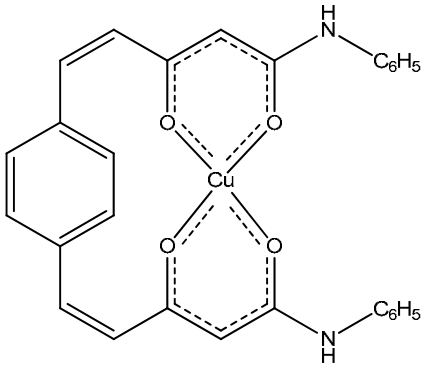
The $^1$H NMR spectrum of the compound shows a one proton signal in the region δ 9-10 ppm and another one proton signal between δ 12-13 ppm **(Figure.4.19)**. The former signal is undoubtedly due to NH proton and the later due to the enol protons. Aryl protons show signals at ~ 6.7-7.8 ppm. The position and integrated intensities of the various proton signals agree well with the **structure 4.10** of the compound.

**Mass spectrum**

Mass spectrum of the compounds showed intense molecular ion peak $P^+$ at m/z which confirms the formation of the reaction product as in **structure 4.10.** Other prominent peaks in the spectra are due to $(P\text{-}C_6H_5)^+$, $(P\text{-}C_6H_5NH)^+$, $(P\text{-}C_6H_5NHCO)^+$ etc. The FAB mass spectrum of the compound is reproduced in **Figure 4.20**.

**Characterisation of metal complexes of $H_2$an**

From the elemental analysis of the metal complexes given in **Table 4.9**. It is clear that the complexes formed are of [ML] stochiometry. Further the IR and mass spectral data of the complex supports the **structure 4.11** .




**4.11**

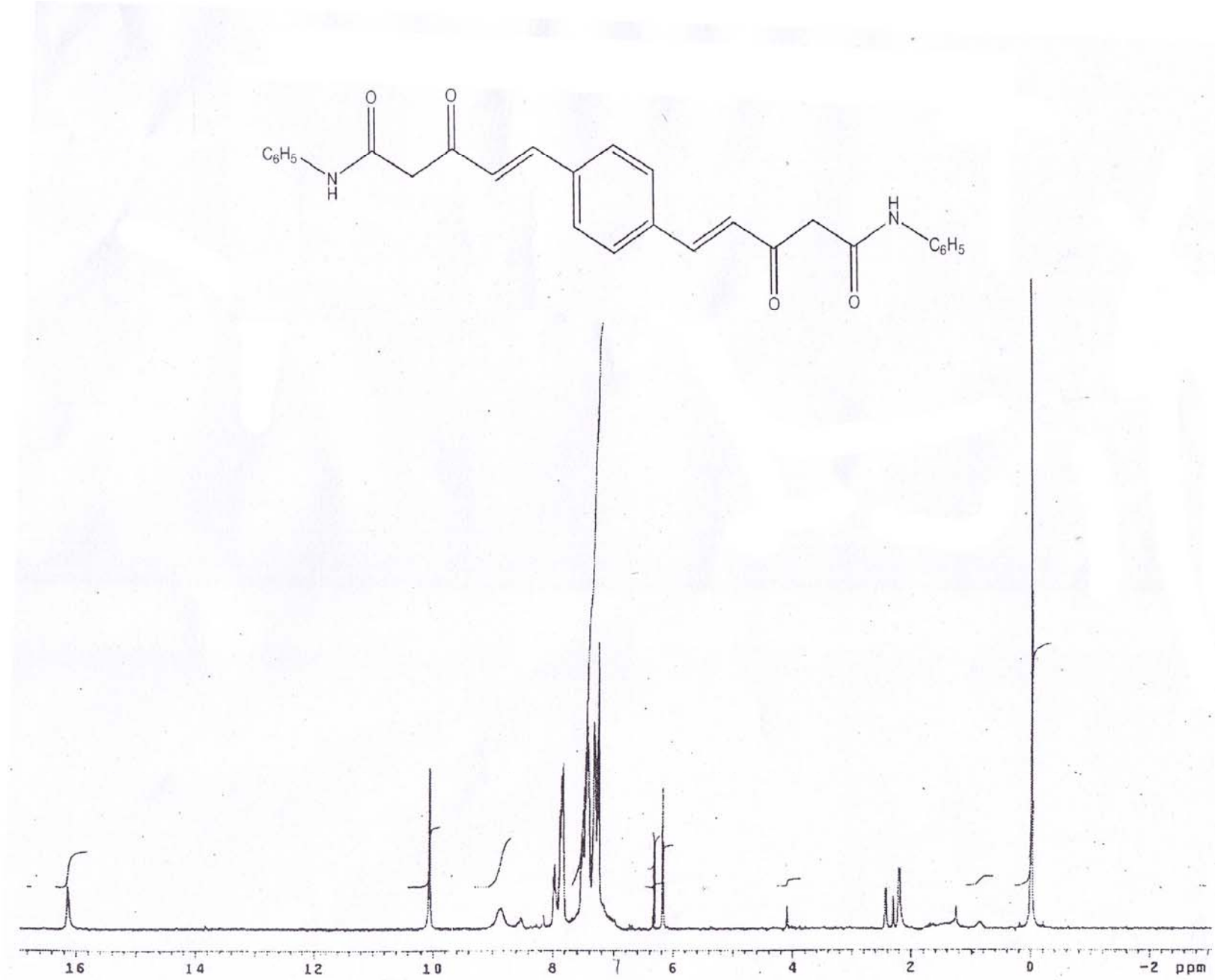



**Figure 4.19 $^{1}$H NMR spectrum of $H_2$an**

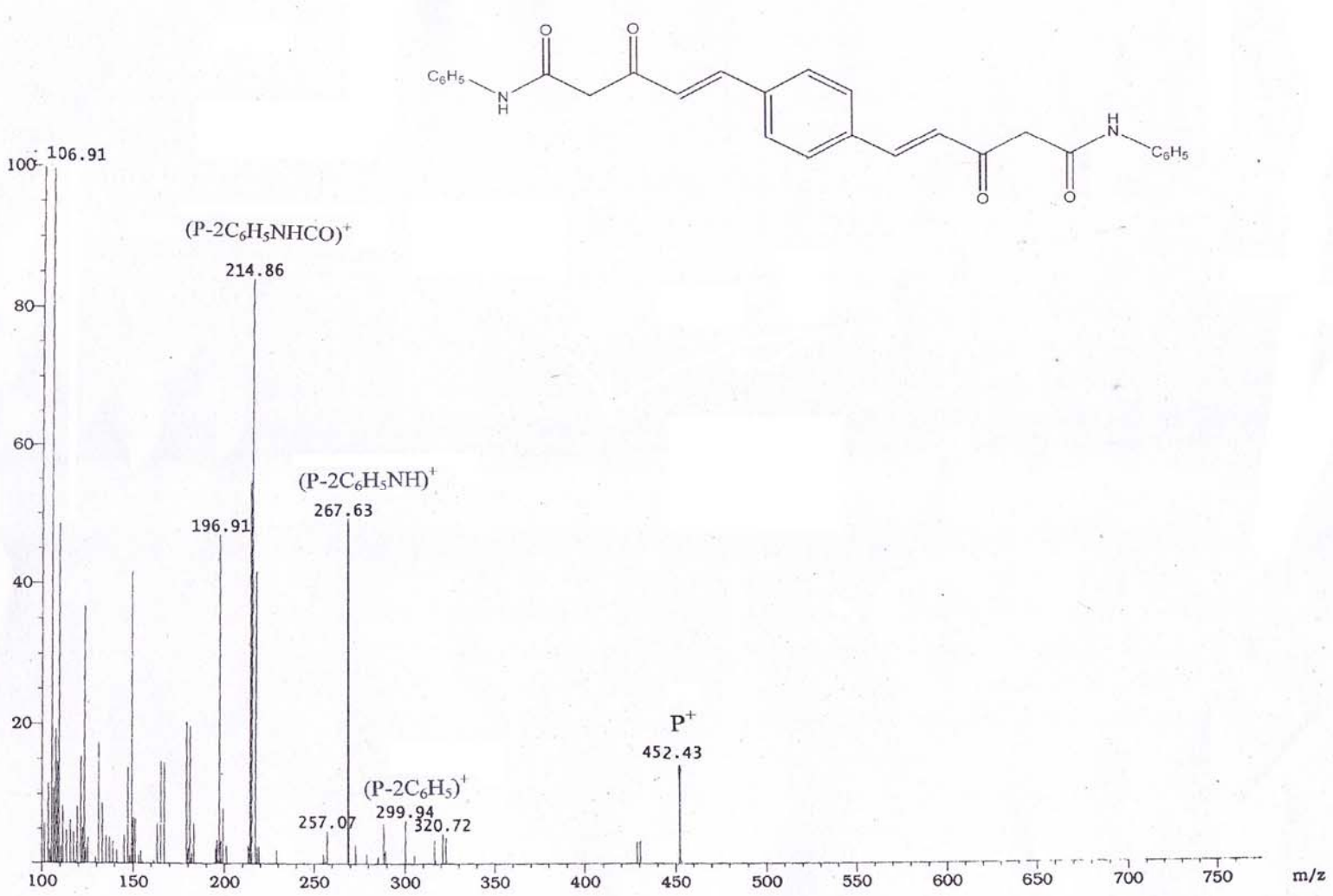



**Figure 4.20 FAB Mass spectrum of $H_2$an**

In the IR spectrum (**Figure 4.21**) of the complexes the band at ~ 1660 $cm^{-1}$ and ~ 1640 $cm^{-1}$ of amide carbonyl and cimmamoyl carbonyl of the free ligand disappeared and instead a new band appeared at ~ 1600 $cm^{-1}$ assignable to metal bonded diketo function as in **structure 4.11**. Further the broad band due to intramolecularly H-bonded diketo function in the region 2800-3500 $cm^{-1}$ also disappeared in the spectrum which confirms the metal complexation.

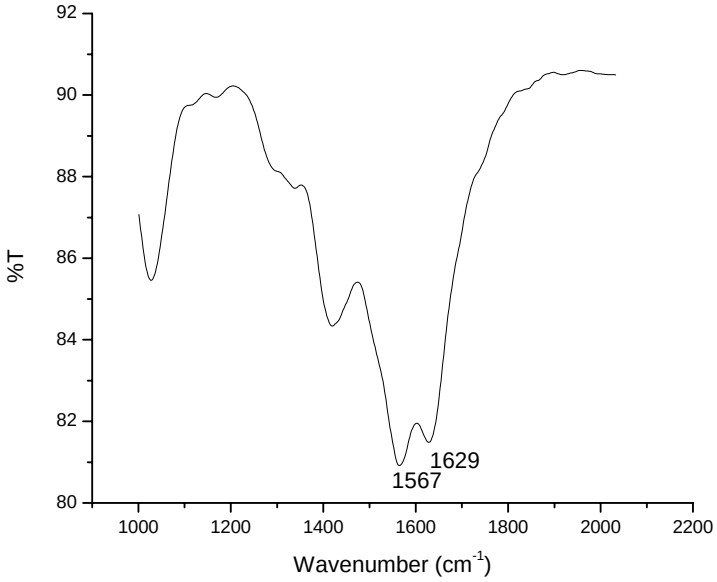



**Fig. 4.21 IR Spectrum of [Cu(an)]**

In the $^1H$ NMR spectrum of the Ni(II) complex of the $H_2$an, the enolic proton singlet of the free ligand disappeared. The position of NH proton signalis only marginally altered in the complexes. Integrated intensities of the various proton signals agree well with the [ML] stochiometry of the complexes. The spectrum is reproduced in **Figure 4.22**

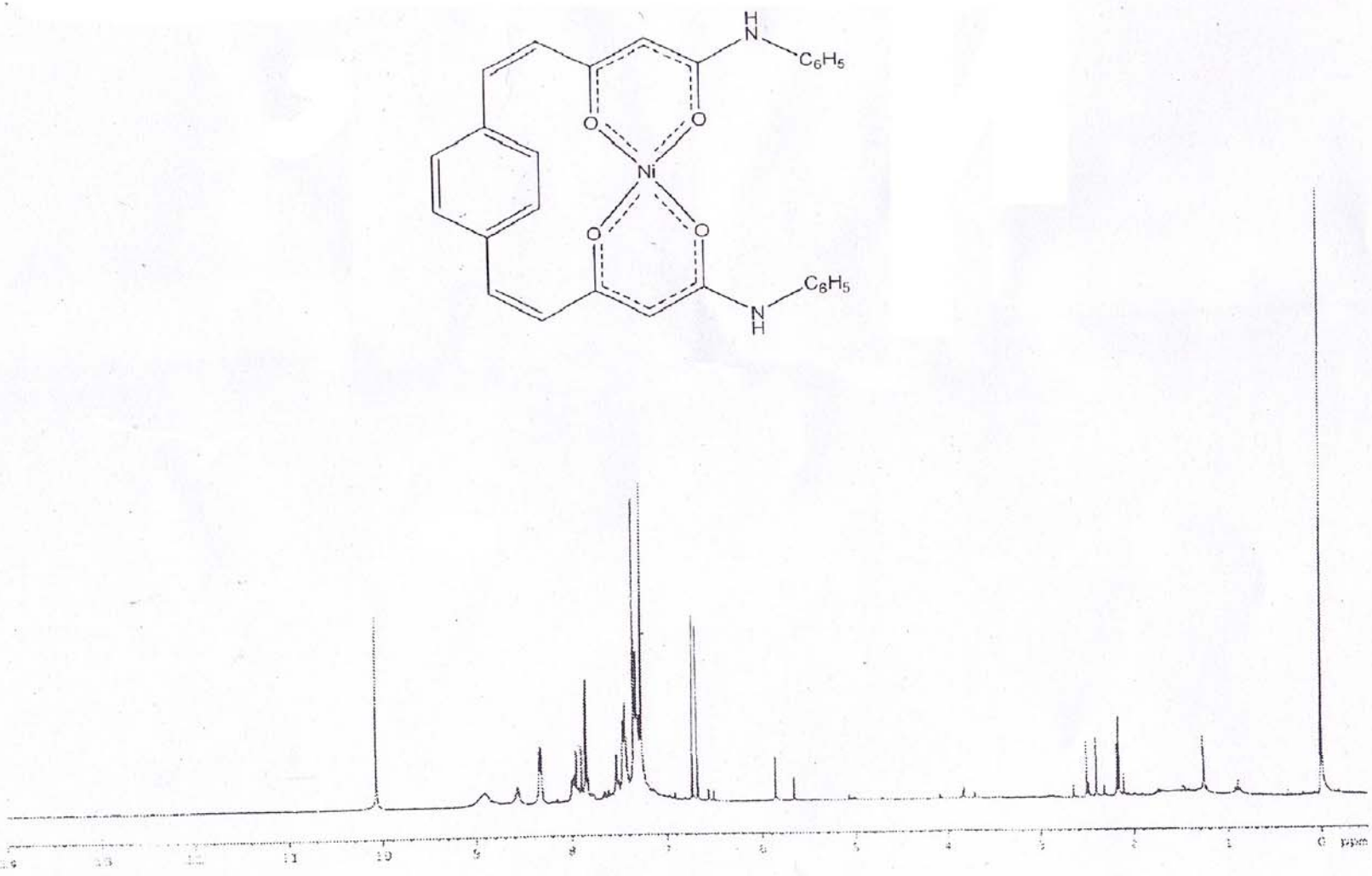



**Figure 4.22 $^{1}$H NMR spectrum of [Ni(an)]**

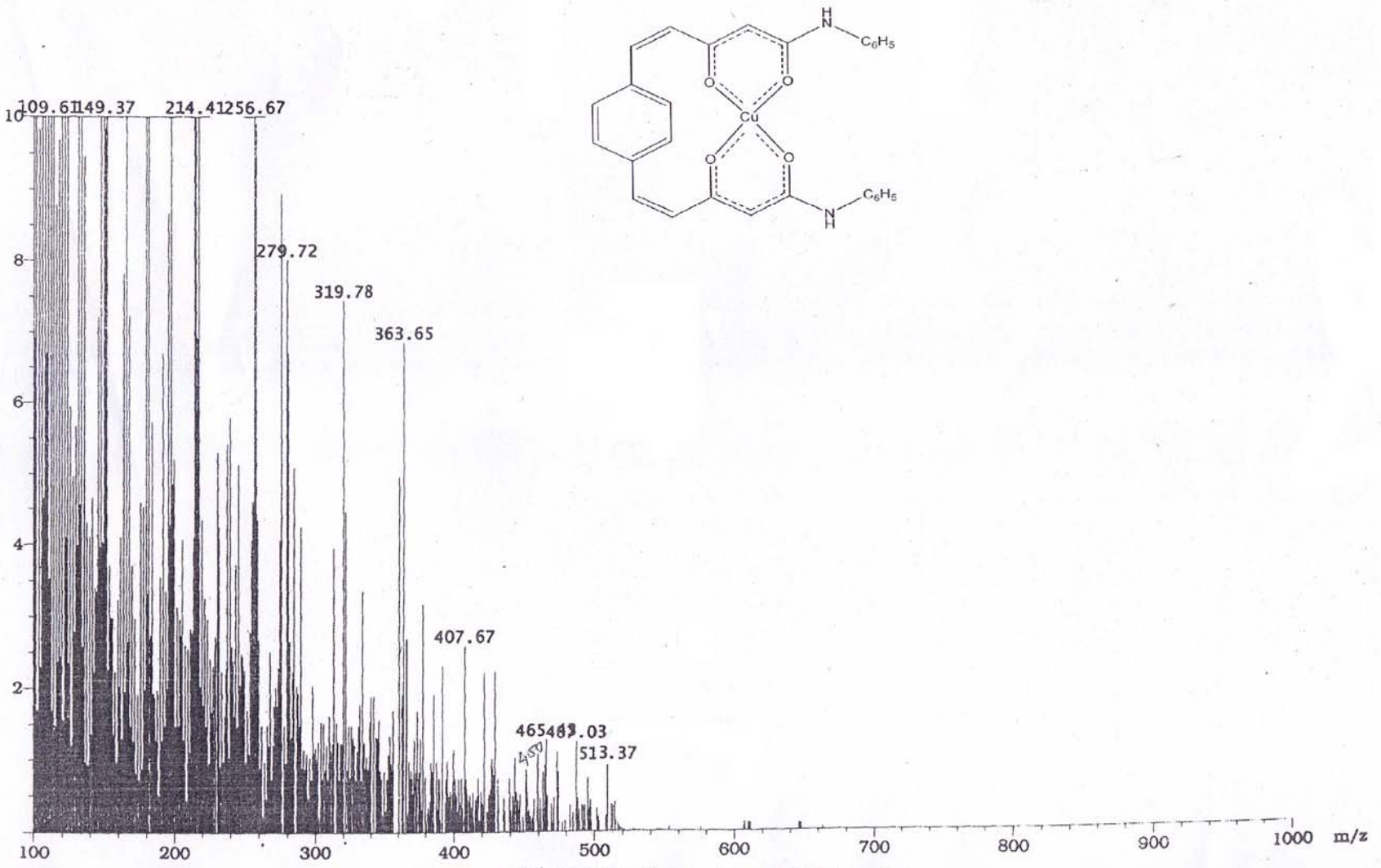



Figure 4.23 FAB Mass spectrum of [Cu(an)]

The FAB mass spectrum (**Figure4.23**) of the Cu(II) complex of a $H_2$an shows a moderately intense molecular ion peak at m/z. Another important peak is due to P-$NHC_6H_5$ with 3:1 ratio. The prominent peaks are due to ligand and its fragments.

**Summary**

A new series of polycarbonyl compounds where two dicarbonyl functions attached to the para positions (1,4-positions) of a phenyl ring were synthesized by the Claisen-Schmidt condensation of 1,4- phthalaldehyde and four different β-dicarbonyl compounds namely acetylacetone, benzoylacetone, methylacetoacetate and acetoacetanilide. Spectral data unequivocally confirmed that the keto-enol tautomeric forms of these tetraketones strongly dependent on the type of the 1,3-diketones used. Thus the condensation product of methylacetoacetate with 1,4-phthalaldehyde exist predominantly in the keto form while all other compounds preferred the enol form.

All the tetraketones formed stable complexes of 1:1 stochiometry with Cu(II), Ni(II) and Co(II) ions. The observed analytical and spectral data suggested that the unsaturated tetracarbonyl compounds functioned as dibasic tetradentate ligands in their complexes.

# CHAPTER-5

# SYNTHESIS AND CHARACTERISATION OF UNSATURATED 1, 3-DIKETONES CONTAINING ALICYCLIC RINGS AND THEIR METAL COMPLEXES

## Introduction

Majority of the work reported on unsaturated β-dicarbonyls are on compounds in which the olefinic diketo function attached to either alkyl/aryl functions (that is linear 1,3-dicarbonyls) . Only very few reports appeared in the general literature on unsaturated β- diketones containing cycloalkanone functions. In the present study two unsaturated 1,3-diketones containing cycloalkanone ring were synthesized starting from 2-acetylcyclopentanone and 2-acetylcyclohexanone. These 2-acetylcycloalkanones are interesting because they may exist simultaneously in endo- and exocyclic enol forms[198]. The keto-enol tautomers of the compounds have also attracted theoretical[199]Further these compounds are intermediates in the preparation of HIV inhibitors[200] and have several industrial applications[201]. Typical metal complexes of these compounds were also studied[202].

## Experimental

To a well stirred solution of 2-acetylcyclopentanone/2-acetyl cyclohexanone (0.01 mol) in dry ethylacetate (5 ml), a solution of

benzaldehyde (0.01 mol) in dry ethylacetate (10 ml) was added slowly with stirring. To this mixture, a solution of n-bulylamine (0.2 ml) in dry ethyl acetate was added dropwise and stirring was continued for ~ 4 h and kept overnight. The product formed was extracted several times with ethylacetate and the combined extracts were evaporated to a pasty mass. Tlc of the product revealed the presence of two compounds and they were separated by column chromatography as detailed below.

The crude product obtained was dissolved in minimum amount of acetone, a little amount of silica gel was added and dried. It was then placed over a column packed with silica gel (mesh 60-120) using toluene as the solvent and then eluted with the same solvent system at a uniform flow rate of 2 ml/min. As the elution proceeds two bands were developed in the column, a lower yellow band and an upper red band. The lower yellow band was collected in aliquots of 10 ml in separate test tubes, checked for purity and evaporated to yield yellow crystals having chromatographic purity with sharp melting point. The upper red band was eluted with 5:1 toluene: chloroform (v/v) mixture and the collected eluate was checked for purity. It was not pure and hence not subjected to further studies.

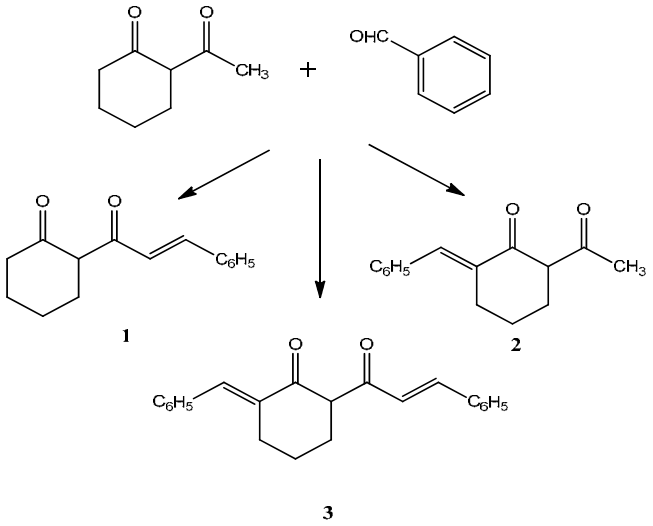
**Synthesis of metal complexes**

To a methanolic solution (20 ml) of the diketone (0.01 mol) a solution of metal(II)acetate was added with stirring and refluxed for ~ 30 min.

Sodium acetate was added to maintain the pH of the medium around 7 and refluxed for about ~ 6 h, concentrated to half the volume and cooled to room temperature. The complex formed was filtered, washed several times with methanol and then with water. The solid product was dried in vacuum.

**Results and Discussion**

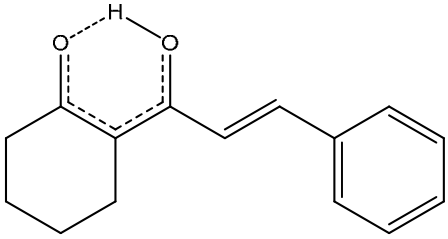
An important reaction of aromatic aldehydes with 1,3-dicarbonyls containing at least one acetyl groups is the Claisen-Schmidt condensation. For this reaction to occur, the active methylene hydrogen has to be protected, usually by complexation with $B_2O_3$ in order to prevent the Knoevenagal reaction. Thus the possible reaction that can occur between benzaldehyde and the alicyclic 1, 3 diketones under the experimental conditions employed can be represented as shown below (**scheme 5.1**) in the case of 2-acetylcyclohexanone. 2-Acetylcyclopentanone may also undergo the same reaction.



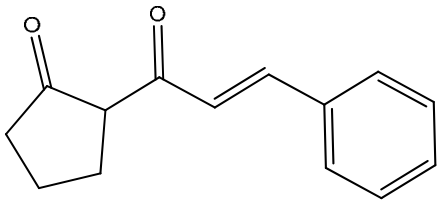

**Scheme 5.1**

Steric effects and loss of coplanarity of the alicyclic ring will prevent the formation of **2** and **3** and the major product will be **1**. This observation is fully justified from the analytical and spectral data of the compounds. These data are discussed below.

The compounds are crystalline in nature with sharp melting point and are soluble in all common organic solvents. The C, H percentages of the compounds given in **Table 5.1** suggest that one equivalent of the diketones reacted with one equivalent of the aldehyde. The observed IR, NMR and mass spectral data of the condensation product obtained using 2-acetylcyclohexanone is in agreement with **structure 5.1** and that of 2-acetylcyclopentanone with **structure 5.2.**




**5.1**




**5.2**

**Infrared Spectra**

It has been reported that 2-acetylcyclopentanone exist in the keto form with only very small percentage of enolisation[202-204,207]. Thus the IR spectrum of the compound consist of two strong band at 1740 $cm^{-1}$ and 1720 $cm^{-1}$

**Table 5.1: Physical and analytical data of Hcch and Hccp and thier Metal Complexes**

| Compounds | Elemental analysis (found/ calcd) | | | M.P $^0$C |
|---|---|---|---|---|
| | C | H | M | |
| Hcch | 78.85 (78.94) | 6.88 (7.01) | - | 155 |
| [Cu(cch)$_2$] | 69.18 (69.29) | 5.89 (5.77) | 12.34 (12.33) | 249 |
| [Ni (cch)$_2$] | 70.28 (70.21) | 5.82 (5.85) | 11.35 (11.44) | 243 |
| Hccp | 77.30 (77.07) | 6.38 (6.59) | - | 126 |
| [Cu(ccp)(OAc)] | 54.83 (54.68) | 4.68 (4.81) | 15.89 (16.08) | 232 |
| [Ni(ccp)(OAc)] | 54.75 (54.96) | 4.72 (4.83) | 14.72 (14.93) | 245 |

respectively due to the stretching of the ring carbonyl and the acetyl carbonyl functions[207]. Whereas 2-acetylcyclohexanone exist predominantly in the enol form with appreciable percentage of the keto form[202,204-206]. The keto-enol percentage depends on the nature of the solvent. The IR spectrum of the compound contains a band at 1700 cm$^{-1}$ due to the intramolecularly H-bonded dicarbonyl function of the enol tautomer. Presence of weak bands assignable to both cyclic carbonyl and acetyl carbonyl of the diketo form 1715 cm$^{-1}$ were also reported in spectrum of the compound.

The IR spectrum of **Hcch** shows two intense bands at 1699 $cm^{-1}$ and 1654 $cm^{-1}$ in the 1600-1800 region, which can confidently be assigned to the intramolecularly H-bonded carbonyl function attached to the alicyclic ring and to the conjugated cinnamoyl carbon of function respectively. There is a broad band in the range 2800-3500 $cm^{-1}$ due to intramolecularly hydrogen bonded enol form. The observed position and intensity of these bands indicate that the compound exist predominantly in the enolic form as shown in **structure 5.1.** The spectrum of the compound is presented in **figure 5.1.**

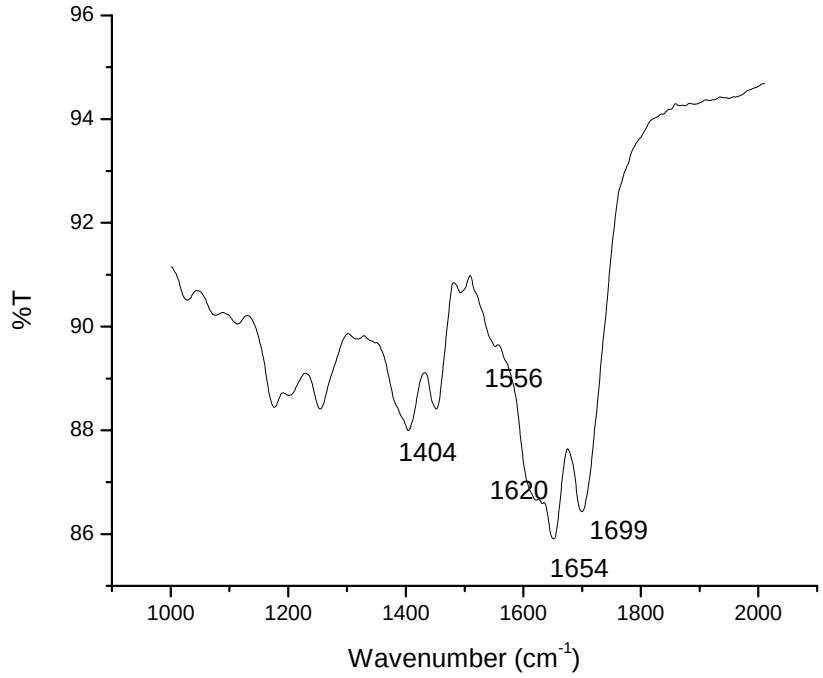



**Fig. 5.1 IR Spectrum of Hcch**

The IR spectrum of the Claisen-Shmidt condensation product of 2-acetylcyclopentanone with benzaldehyde **(Hccp)** shows two intense bands at

1740cm$^{-1}$ and 1690cm$^{-1}$.These bands can be assigned to a free carbonyl functions attached to the alicylic ring and to the conjugated cinnamoyl carbonyl function respectively[207]. There is no broad band in the region 2800-3500 cm$^{-1}$ due to H-bonded enol form which supports the keto form of **Hccp** as shown in **structure 5.2.**

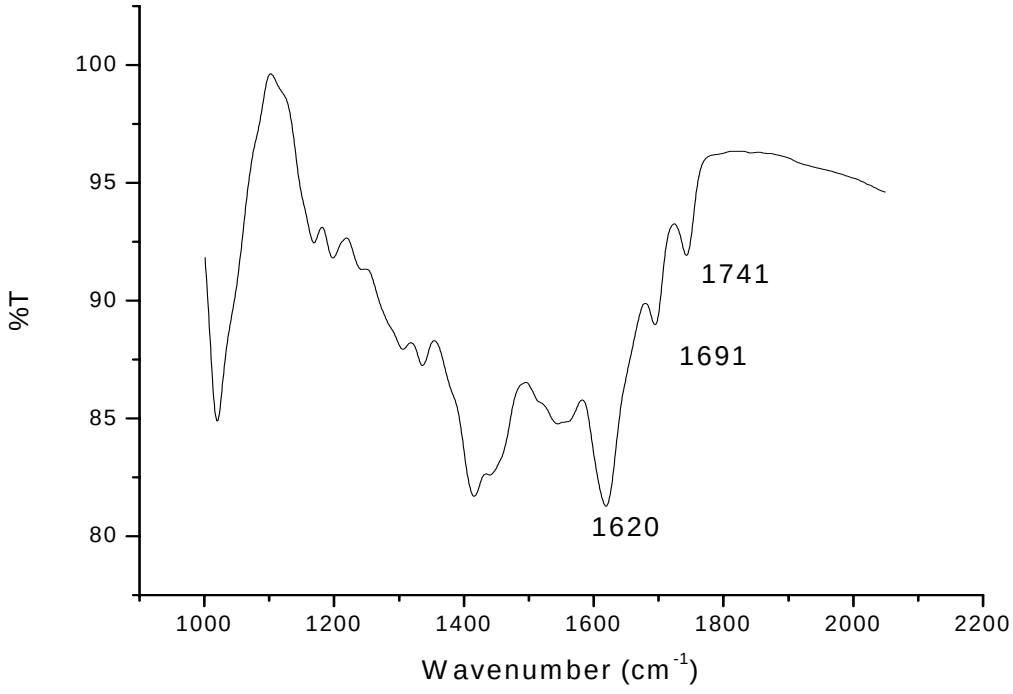



**Fig. 5.2 IR Spectrum of Hccp**

## $^{1}$H NMR spectra

The compound **Hcch** exist predominantly in the intramolecularly H-bonded enol form and **Hccp** in the keto form is fully justified from the

**Table5.2: IR spectral data of Hcch, Hccp and their metal complexes**

| Compound | IR stretching bands ($cm^{-1}$) | | | | |
|---|---|---|---|---|---|
| | Rnig C=O | Cinnamoyl C=O | C=C phenyl/alkenyl | CH=CH Trans | M-O |
| Hcch | 1699 | 1651 | 1620,1556 | 984 | - |
| $[Cu(cch)_2]$ | 1631 | 1594 | 1569 | 963 | 478,418 |
| $[Ni\ (cch)_2]$ | 1649 | 1583 | 1573 | 974 | 469,424 |
| Hccp | 1741 | 1691 | 1620, 1551 | 968 | - |
| [Cu(ccp)(OAc)] | 1690 | 1605 | 1578 | 979 | 464,412 |
| [Ni(ccp)(OAc)] | 1688 | 1602 | 1577 | 974 | 475,421 |

recorded $^1$H NMR spectra of the compounds. Thus the $^1$H NMR spectrum of **Hcch** shows a one proton signal at δ 15.85 ppm due to the intramolecularly hydrogen bonded enolic proton(**Fig 5.3**). Whereas the $^1$H NMR spectrum (**Fig 5.4**) of **Hccp** does not show any signal above δ10 ppm which clearly indicates that the compound exist entirely in the diketo form. Spectra of both the compounds displayed signals in the region 7-8 ppm due to aryl protons. Cycloalkyl protons show signals in the region 1.8-2.5 ppm as expected. The spectra of the compounds are given in **figures 5.3** and **5.4.**

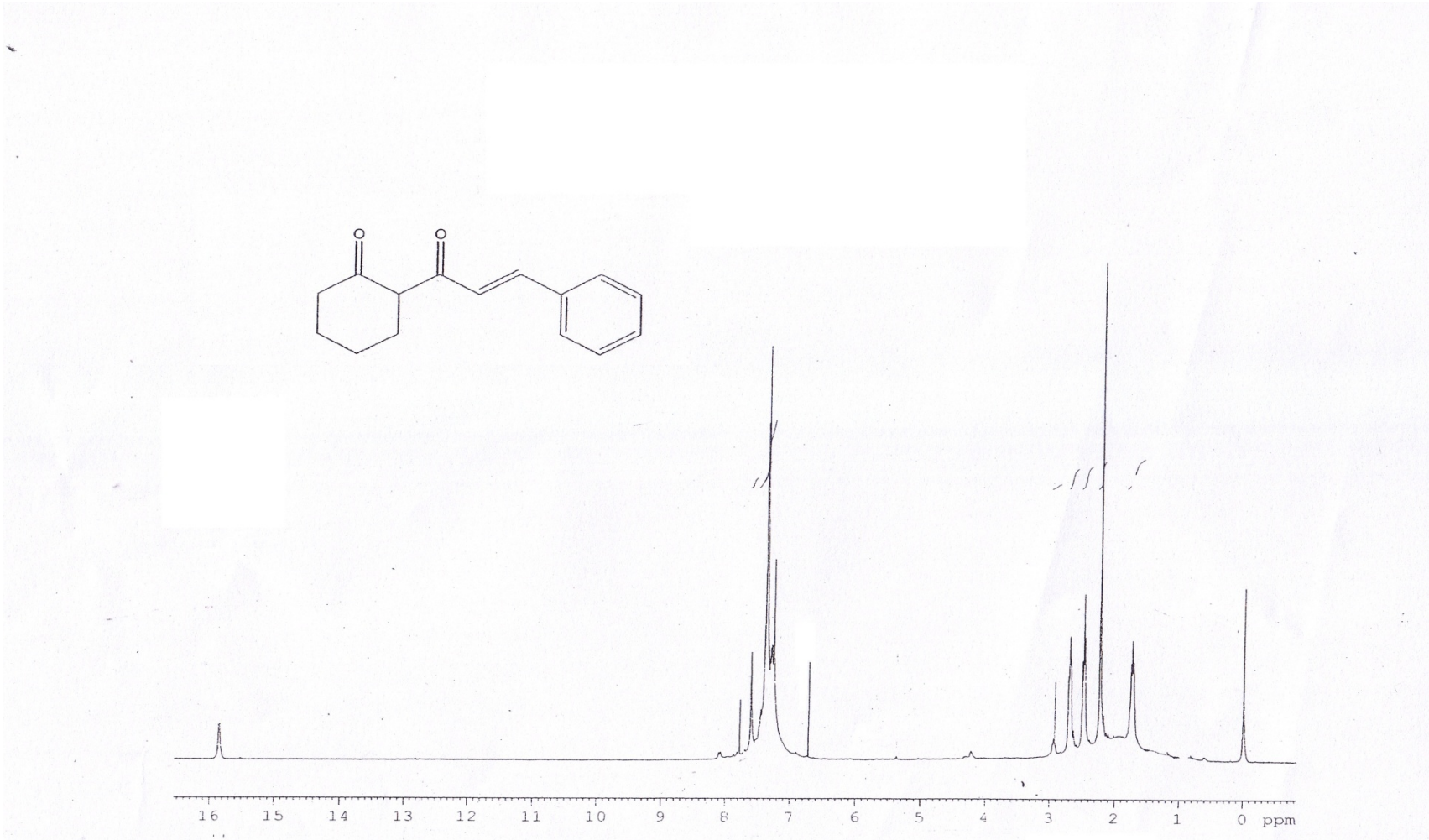



**Fig. 5.3 $^{1}$H NMR spectrum of Hcch**

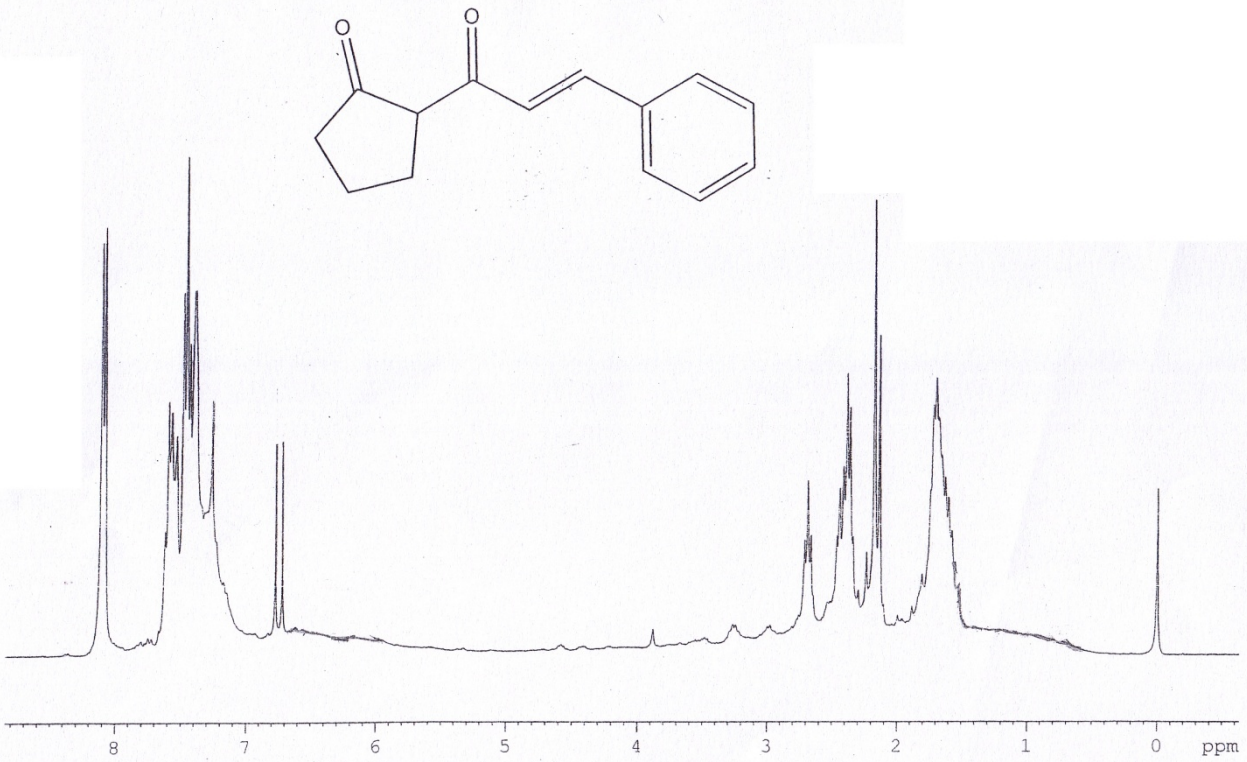


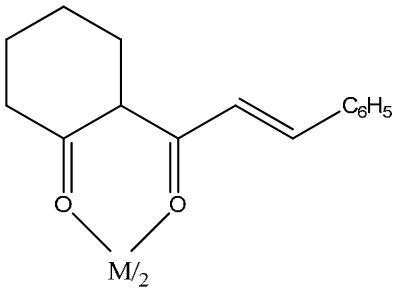

**Fig. 5.4 $^{1}$H NMR spectrum of Hccp**

## Mass Spectra

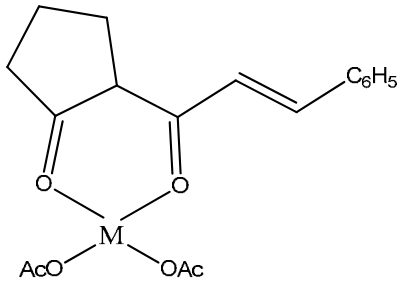
The mass spectra of the compounds considered in the present study show parent ion peak as expected, at m/z 214 and 228 for **Hccp** and **Hcch** respectievely. The other intense peaks are due to elimination of -$CH_2CO$, -Ar, -CO, etc. from the molecular ions. The spectra are reproduced in **figures 5.5** and **5.6**. The observed peaks can be accounted from the fragmentation pattern given in scheme **5.2.**

## Characterization of metal complexes

The 1, 3-diketones formed well defined complexes with Cu(II) and Ni(II) ions. The observed carbon, hydrogen and metal content of the complexes revealed the formation of [$ML_2$) type complexes in the case of **Hcch** and [$ML(OAc)_2$] in the case of **Hccp.** All the complexes behave as non electrotype in DMF solution and do not contain the anion of the metal salt used for their preparation. The observed electronic and IR spectra are in agreement with the **structures 5.3** and **5.4** of the complexes.




**5.3**




**5.4**

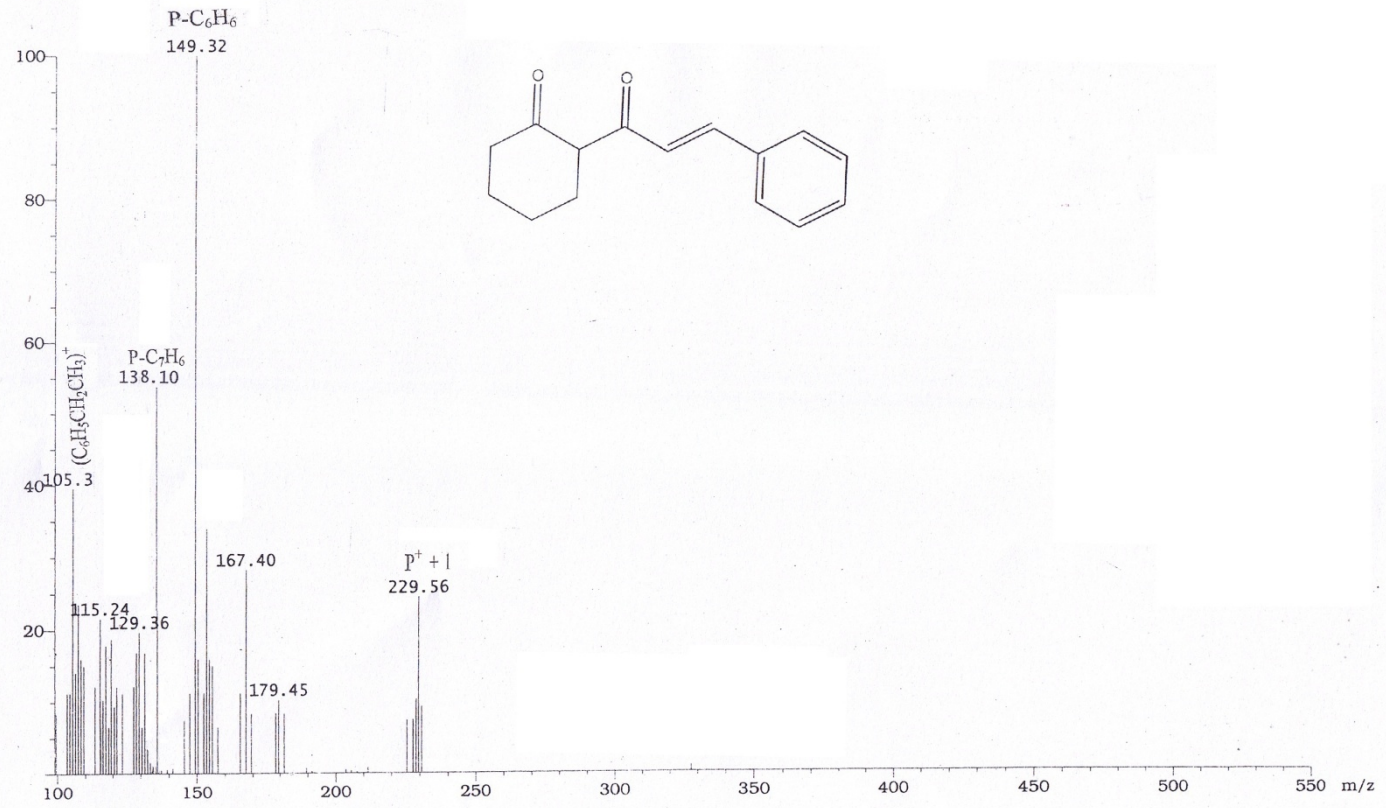



**Fig. 5.5 Mass spectrum of Hcch**

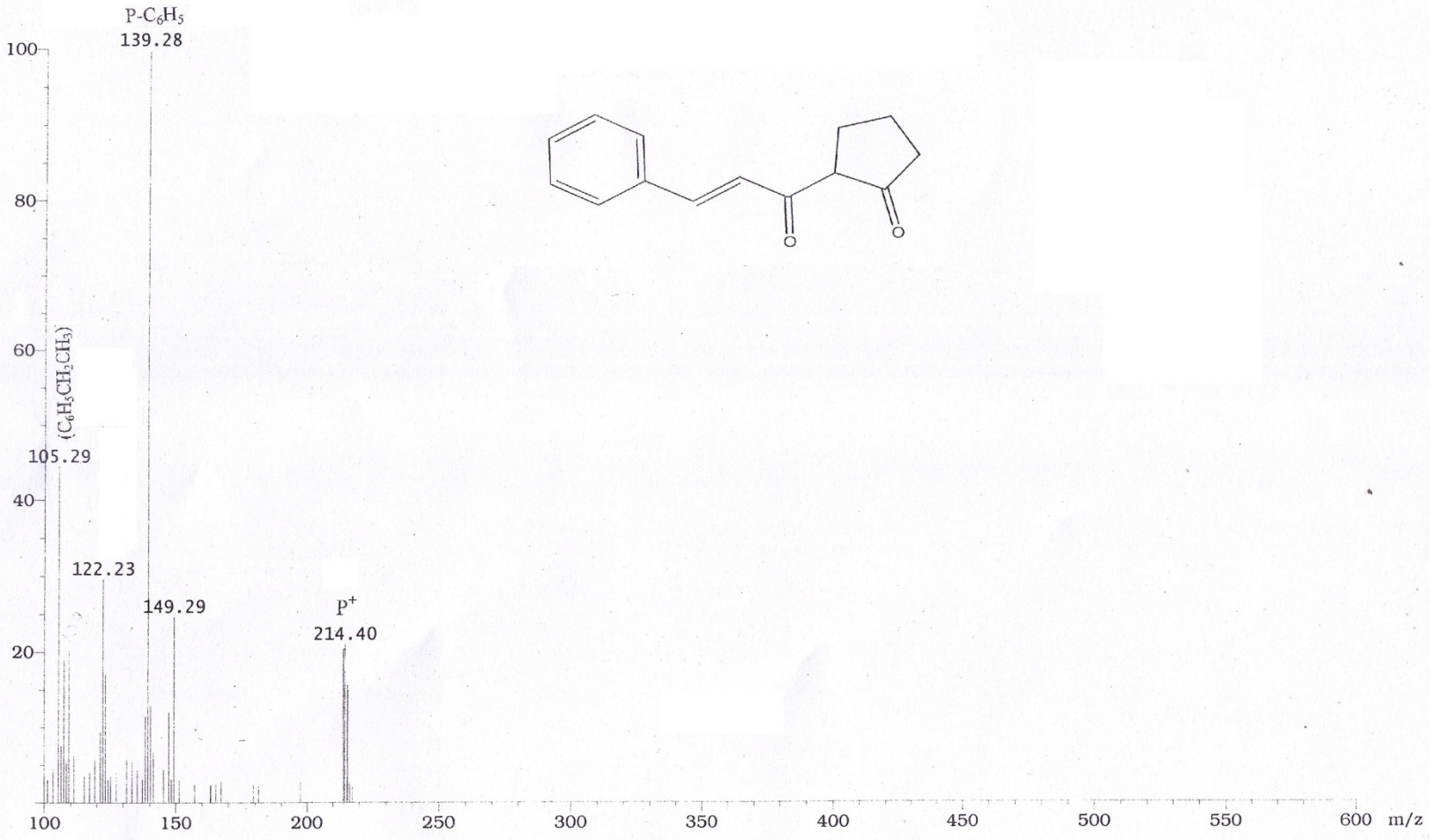



**Fig. 5.6 Mass spectrum of Hccp**

**Infrared Spectra**

A comparison of the spectra of metal complexes with that of the corresponding ligands revealed that the band due to carbonyl stretching of **Hcch** at 1690 and 1654 $cm^{-1}$ totally disappeared in the spectra of the complexes. Instead a slightly broadened band with maximum at ~1634 $cm^{-1}$ appeared in the spectra of the complexes. This band can confidently be assigned to the carbonyl stretching of metal bonded diketo function. In the low frequency region of the spectra of complexes two new bands observed at ~ 520 and ~ 420 $cm^{-1}$ can be assigned to the stretching of M-O vibrations. Thus the IR spectra strongly support the structure **5.3** of the complexes of **Hcch**. The spectrum of **$[Cu(cch)_2]$** is given in **figure 5.7.**

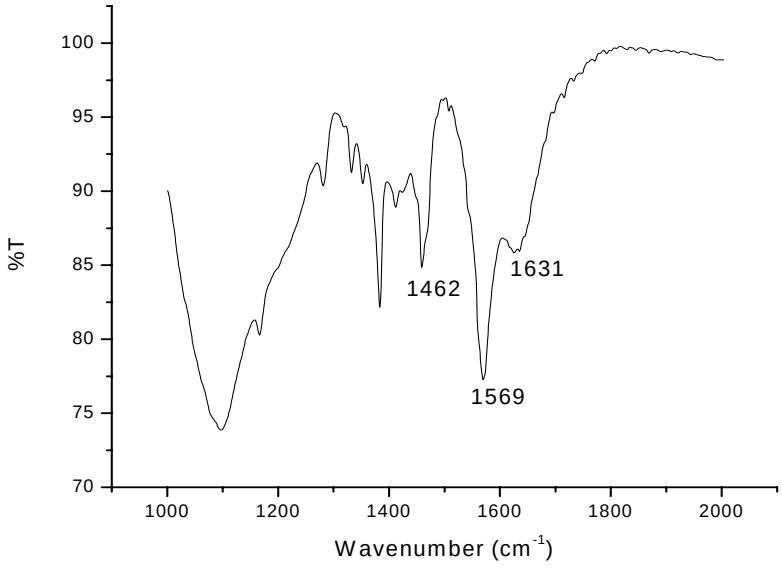



**Fig. 5.7: IR Spectrum of $[Cu(cch)_2]$**

The spectra of the complexes of **Hccp** consists of strong broad bands at ~ 1660 $cm^{-1}$, 1630 $cm^{-1}$ and a band at ~ 1610 $cm^{-1}$ instead of the carbonyl bands of the free ligand in the region 1600-1800 $cm^{-1}$. The former band at 1690 $cm^{-1}$ and 1630 $cm^{-1}$can safely be assigned to the stretching of the metal bonded cyclic carbonyl and cinnamoyl carbonyl as in structure **5.4** and the latter to the antisymmetric stretching of the acetyl carbonyl groups. The $\nu_{M-O}$ vibrations are appeared at ~ 510 and 415 $cm^{-1}$.

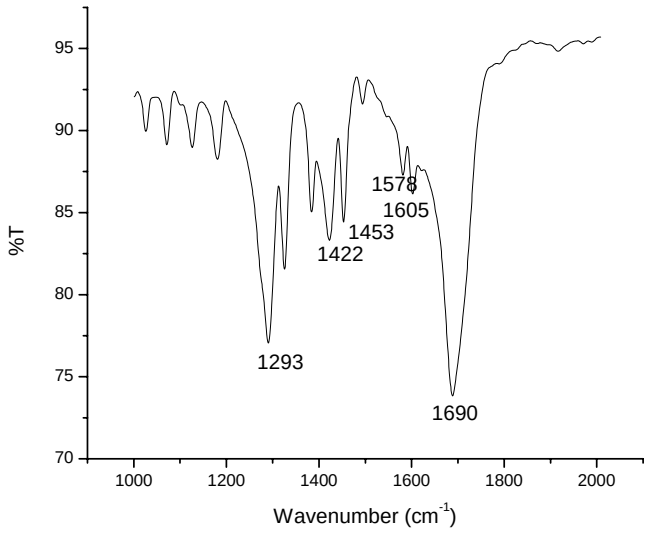



**Figure 5.8: IR Spectrum of $[Cu(hcp)(OAc)_2$**

**Mass Spectra**

The FAB mass spectrum of the Cu(II) complex of **Hcch** showed molecular ion peak corresponding to [Cu $L_2$] stochiometry **(Figure 5.9**). The base peaks in the spectra of the complexes are mainly due to ligand moity and peaks due to $[CuL]^+$, $L^+$ and fragments $L^+$ are also present. The observed mass spectrum of the Cu(II) complex of **Hccp** (**Figure 5.10**)support the

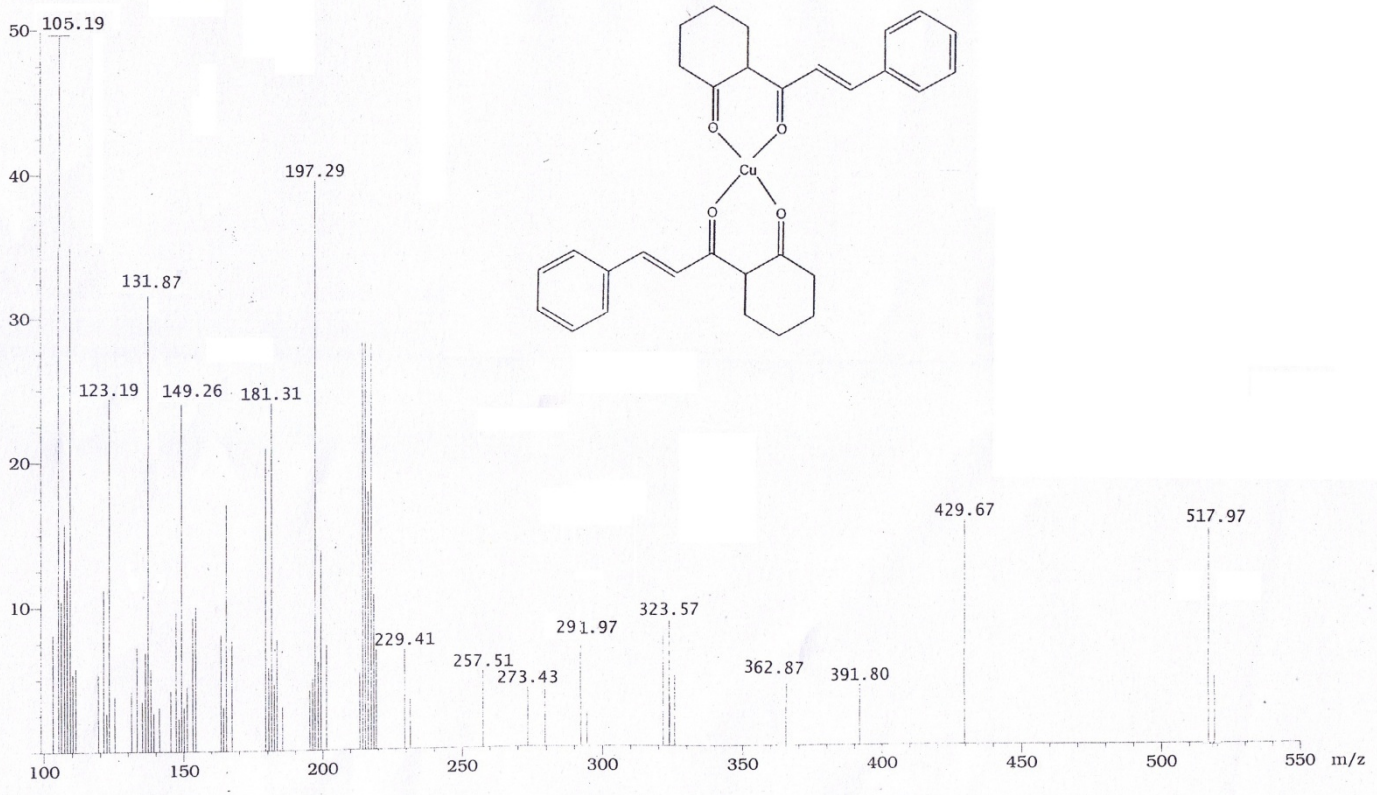



**Fig. 5.9 Mass spectrum of $[Cu(cch)_2]$**

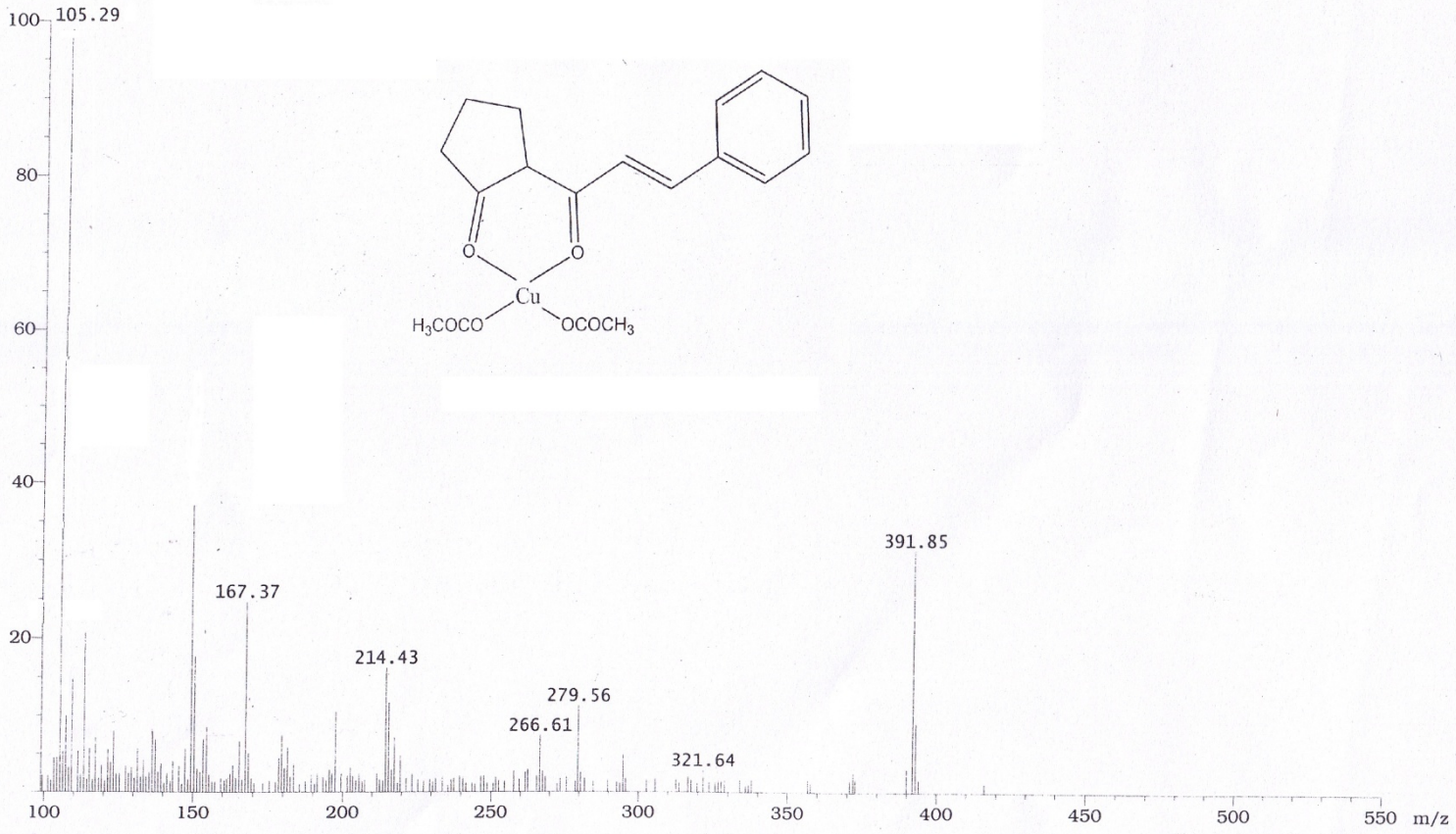
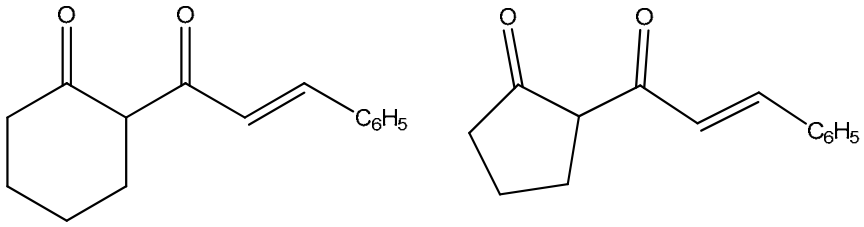



**Fig. 5.10 Mass spectrum of $[Cu(ccp)(OAc)_2]$**

formulation of the complex as in structure **5.4.** Thus the molecular ion peak correspond to the stochiometry $[Cu(Hccp)(OAc)_2]$ clearly appeared in the spectrum at m/z 395 and m/z 397 in the 3:1 ratio corresponds to the isotopic percentage of $^{63}Cu$ and $^{65}Cu$. Similarly several metal containing fragments can be identified in the 3:1 isotopic ratio of the metal.

**Summary**

The Claisen- Schmidt condensation of benzaldehyde with 2-acetylcyclopentanone and 2-acetylcyclohexanone yielded two new unsaturated 1,3-diketones containing alicyclic rings as given below.




The observed IR, NMR and mass spectral data clearly revealed the cyclopentanone derivative exist predominantly in the keto form and the cyclohexanone derivative in the enol form. From spectral and analytical data it has been conclude that Hcch functioned as a monobasic bidentate ligand in the formation of $[M(cch)_2]$ complex where as Hccp behaved as a neutral bidentate ligand and formed complexes of the type $[M(hccp)(OAC)_2]$

# CHAPTER 6

# BIOLOGICAL STUDIES

## Introduction

Unsaturated β-dicarbonyl compounds such as curcuminoids, their synthetic analogues and metal complexes posseses a number of beneficial biological activities as mentioned in chapter 1. These activities have been attributed as mainly due to the presence of phenolic groups, olefinic groups, and substituents such as $–OCH_3$, $-CH_3$, etc on the aryl ring(s) of these compounds. Since no definite conclusion has been reported regarding these factors further studies are essential in this direction. Therefore in order to correlate the biochemical properties to the structural features of these curcuminoids, In the present study, the antifungal and antioxidant activities of the unsaturated 1,3-dicarbonyls and their metal complexes considered in the previous chapters were determined and the results are presented here.

## Section A: Antifungal activity.

## Experimental

Antifungal activities of the compounds were determined by the disc diffusion method[208]. The principle behind the technique is that when an antibiotic impregnated disk placed on an agar medium previously inoculated with the test organism, the antibiotic diffuses rapidly outwards through the

agar producing an antibiotic concentration gradient. A well defined inhibition zone or ring will be formed around the disc if the agent inhibits antimicrobial growth. The effectiveness of the substance is determined by measuring the diameter of the inhibited zone. The detailed procedure is given below.

The different fungal stains used were *Fursarium, Aspergillus* and *Penicillium*, and were maintained in subourands' dextrose agar media which was prepared by dissolving peptone (1 g), D-glucose (4 g) and agar (2.5 g) in distilled water (100 ml) and adjusting the pH of the medium about 5.6 – 6.0 using 10% HCl. Normal saline was used as a suspension of fungal spore for lawning. It was prepared by dissolving NaCl (0.95 g) in distilled water (100 ml). Solutions of the test compounds were prepared in DMSO and for sterilizing, all the media used were autoclaved at 120$^{o}$C for 30 minutes.

The spore suspension of all fungi was prepared in normal saline. For this each fungus were grown on sabourands' dextrose agar (SDA) till they get sporulated. Sterile filter paper disc of 6 mm diameter were impregnated with varying concentrations (250µg/disc, 500µg/disc, 1000 µg/disc) of the test samples dissolved in DMSO and placed on the surface of SDA plates at a distance of 2cm using a sterile forceps. A disc with DMSO was used as control. The plates were incubated at room temperature for 2 days and inhibition zone diameter were measured.

**Results and Discussion**

Average diameter of the zone of inhibition observed for the unsaturated β-dicarbonyls and their Cu(II) complexes are given in **Table 6.1** and **6.2**. In all the cases the complexes showed increased antifungal activity than the free compounds. Some of the unsaturated β-diketones show little activity for specified concentration of different fungi but their metal complex showed better activity for the same concentration of the same fungus.

All the β-ketoesters show low activity towards *Fursarium* and higher activity towards *Penicillium* among the three different fungi. As the concentration increases, the antifungal activity increases. Eventhough all β-ketoesters show comparable activity, there is a slight difference in the activity due to the presence of various substituents on phenyl ring. Electron donating groups like –OH, $–OCH_3$, etc increases the activity while $–NO_2$ decreases the activity.

Among the four different unsaturated tetraketones and their Cu(II) complexes, Cu(II) complexes show more activity than the ligands. Both ligands and complexes show more activity towards *penicillium* and less a activity towards *fusarium.*

**Table6.1: Antifungal activity of the unsaturated β-ketoesters and their Cu(II) complexes**

| Compound | Diameter of zone of inhibition in mm | | | | | |
|---|---|---|---|---|---|---|
| | Aspergillus | | Penicillium | | Fasarium | |
| | 500 µg/disc | 1000 µg/disc | 500 µg/disc | 1000 µg/disc | 500 µg/disc | 1000 µg/disc |
| **3b** | - | 9 | - | 9 | - | 10 |
| **Cu(II) complex** | 12 | 15 | 20 | 25 | - | 8 |
| **3c** | - | 10 | 0 | 11 | - | 9 |
| **Cu(II) Complex** | 14 | 17 | 19 | 22 | - | 10 |
| **3d** | - | 8 | 8 | 7 | - | - |
| **Cu(II) complex** | - | 11 | - | 10 | - | 8 |
| **3e** | - | 10 | 0 | 9 | - | 8 |
| **Cu(II) complex** | 12 | 16 | 15 | 19 | - | 8 |
| **3f** | - | 10 | - | 19 | - | 9 |
| **Cu(II) complex** | 13 | 17 | 14 | 19 | - | 10 |
| **3i** | 8 | 14 | - | 9 | - | 8 |
| **Cu(II) complex** | 12 | 16 | 14 | 18 | 10 | 12 |

**Table 6.2**: **Anti fungal activity of the unsaturated tetraketones and their metal complexes**

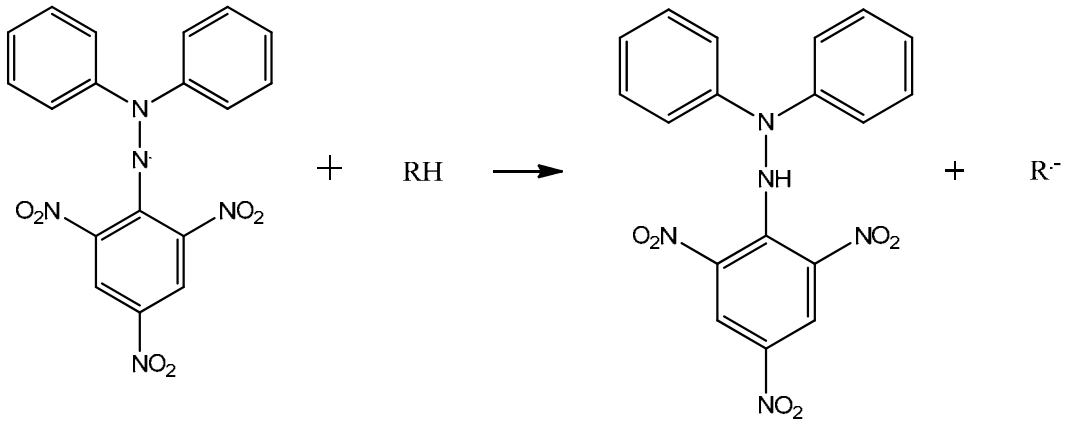
| Compounds | Diameter zone of inhibition in mm | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Aspergillus | | | Penicillium | | | Fusarium | | |
| | 250 µg/disc | 500 µg/disc | 1000 µg/disc | 250 µg/disc | 500 µg/disc | 1000 µg/disc | 250 µg/disc | 500 µg/disc | 1000 µg/disc |
| **$H_2$aa** | - | - | 8 | - | - | 9 | - | - | 10 |
| **[Cu(aa)]** | - | 9 | 12 | - | 19 | 24 | - | - | 9 |
| **$H_2$ma** | - | - | 12 | - | - | 14 | - | - | 10 |
| **[Cu(ma)]** | 8 | 12 | 19 | 9 | 15 | 20 | - | - | 12 |
| **$H_2$ba** | - | - | 10 | - | - | 9 | - | - | 9 |
| **[Cu(ba)]** | - | 11 | 18 | - | 20 | 25 | - | - | 10 |
| **$H_2$an** | - | - | 10 | - | - | 10 | - | - | 19 |
| **[Cu(an)]** | - | 12 | 19 | - | 19 | 23 | - | - | 10 |

**Section B: Antioxidant activity**

Several methods are available for the evaluation of the antioxidant activity of compounds[127,129,160-164,209-213]. The most widely used is the DPPH method[129,213-217]. It is rapid, simple and less expensive and involves the use of the free radical 1, 1-diphenyl-2-picrylhydrazyl (DPPH). The method can be used for solid or liquid samples and is not specific to any particular antioxidant compound, but applies to the overall antioxidant capacity of the sample.

In this method the antioxidant is allowed to react with DPPH radical in methanol solution at room temperature. The reduction of the DPPH radical is followed by monitoring the decrease of its optical absorbance. In the radical form DPPH gives a strong absorption at 515nm, but after the reaction, the absorption decreases. The steady decrease in absorption is a measure of the rate. Here the antioxidant activities are typically characterised by their $EC_{50}$ value, which is the amount of antioxidant necessary to decrease the initial DPPH concentration by 50 percentage, after a plateau has been reached for various antioxidant/DPPH molar ratios. The anti radical power (ARP) equal to $1/EC_{50}$ has also been measured. The larger the ARP, the more efficient the antioxidant activity. The time necessary to reach the plateau at a molar ratio corresponding to $EC_{50}$ (Time $EC_{50}$) is also important because this value

depends on the reaction rate between the antioxidant and the DPPH radical. The reaction can be represented as below.




**Experimental**

In this method a fixed concentration of the DPPH solution whose absorbance is less than one was mixed with different volume of the sample solution and decrease in the absorbance is noted at 516 nm. From the absorbance value, the percentage difference and percentage inhibition in each case can be calculated using the equations;

$$\text{Percentage difference} = \frac{\text{Sample absorbance}}{\text{DPPH absorbance (blank)}} \times 100$$

$$\text{Percentage inhibition} = 100 - (\text{percentage difference})$$

The details of procedure are given below.

A stock solution of DPPH of concentration $6x10^{-4}$ M in methanol was prepared and 2 ml of the solution was made up to 10 ml in methanol so as to get an absorbance of less than one. Similarly 2 ml of the stock DPPH solution were mixed with the sample solution of varying volumes, 100-1000 µl, (concentration varies from 1-200 µg/ml) and made up to 10 ml with methanol. This solution was kept in dark for 30 minutes and measured the absorbance 516nm. The absorbance of a blank solution, that is DPPH solution without the sample, was also noted which give the blank absorption.

From the absorbance of the blank, $EC_{50}$ values were calculated as given above. The absorption spectra at different time interval were also recorded at $EC_{50}$ concentration (2 minutes and 5 minutes). The reaction kinetics was plotted from the result and the percentage of DPPH remaining at steady state was determined from the graph. The time $EC_{50}$ was also calculated from this plot. For the less reactive compounds, the ratio antioxidant/DPPH was measured after 90% remaining DPPH concentration that is 10 % conversion. The $EC_{50}$ values were determined from the calibration curve in which the percentage inhibition is plotted against concentration. For comparison of various antioxidents it is then converted to molar ratio of concentration of sample required for 50 percent inhibition to concentration of DPPH.

$$\text{DPPH Concentration} = P\ \mu g/L \equiv \frac{P\ \text{in}\ g/L}{\text{Molecular weight}} = Q\ \text{moles}$$

Concentration of sample required for 50 % inhibition

$$= R\ \mu g/L \equiv \frac{R\ \text{in}\ g/L}{\text{Molecular weight}} = S\ \text{moles}$$

$$EC_{50} = \frac{\text{Concentration required for 50 \% inhibition}}{\text{Concentration of DPPH}} = \frac{S\ \text{moles}}{Q\ \text{mole}} = T$$

$$\text{Anti radical power} = 1/T = U$$

Stochimetric value (Hypothetical value for 100% inhibition) = 2xT = V

Number of reduced DPPH (NRD) = 1/V = W

**Results and discussion**

The antioxidant activities of both natural and synthetic curcuminoids and their metal complexes were reported earlier[129, 162-164,213-217.] The free radical scavenging activity of these compounds have been attributed as be due to the phenolic hydroxyl group and to the methylene group of the β-diketone moiety. The phenolic group appears to play the major role in the antioxidant activity of curcuminoids. According to Bondet et al[218] the mechanism involves first a reversible phenolic hydrogen abstraction by a DPPH radical to give a non sufficiently stabilized antiradical. The second reaction step concerns radicals obtained after delocalization of the latter on

the aromatic ring (ortho- or para position) lead to a monoquinonoid species by dimerisation.

The compounds considered in chapter **3** and **4** also contain unsaturated β-diketone moiety with or without phenolic groups in the aryl rings which allows the delocalization of the radical formed by the hydrogen abstraction of DPPH. Therefore in the present study, a series of unsaturated β-ketoesters, their Cu(II) complexes considered in chapter **3** and unsaturated tetraketones discussed in chapter **4** were subjected to antioxidant assay by the DPPH method according to Brand Williams et al[216] and compared with the antioxidant activity of curcuminoids.

**Antioxidant activity of β-ketoesters and their Cu(II) complexes**.

The results obtained for these compounds are shown in **Tables 6.3-6.6** and **Figures 6.1-6.4.** Among the unsaturated β-ketoesters **3b, 3c, 3f** and **3h** show better antioxidant activity and the order is **3b > 3c > 3f >3h**. Their Cu(II) complexes follows the same order but lesser activity. All of the above compounds have a phenolic group and it is the reason for the greater activity in accordance with Priyadarsini et al[219]. But when comparing with the antioxidant activity of curcumionoids with the same aromatic group, the antioxidant activity is less because they are monocondensation product instead of biscondensation product as in curcuminoids.

**Table 6.3: Antioxidant assay of 3b**

| Concentration µg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 1.0628 | - | - |
| 14.64 | 0.8324 | 78.3 | 21.7 |
| 29.28 | 0.631 | 59.4 | 40.6 |
| 43.92 | 0.469 | 44.2 | 55.8 |
| 58.56 | 0.25 | 23.5 | 76.5 |
| 73.2 | 0.0958 | 9.1 | 90.9 |

$EC_{50}$ = 38.95 µg/ml

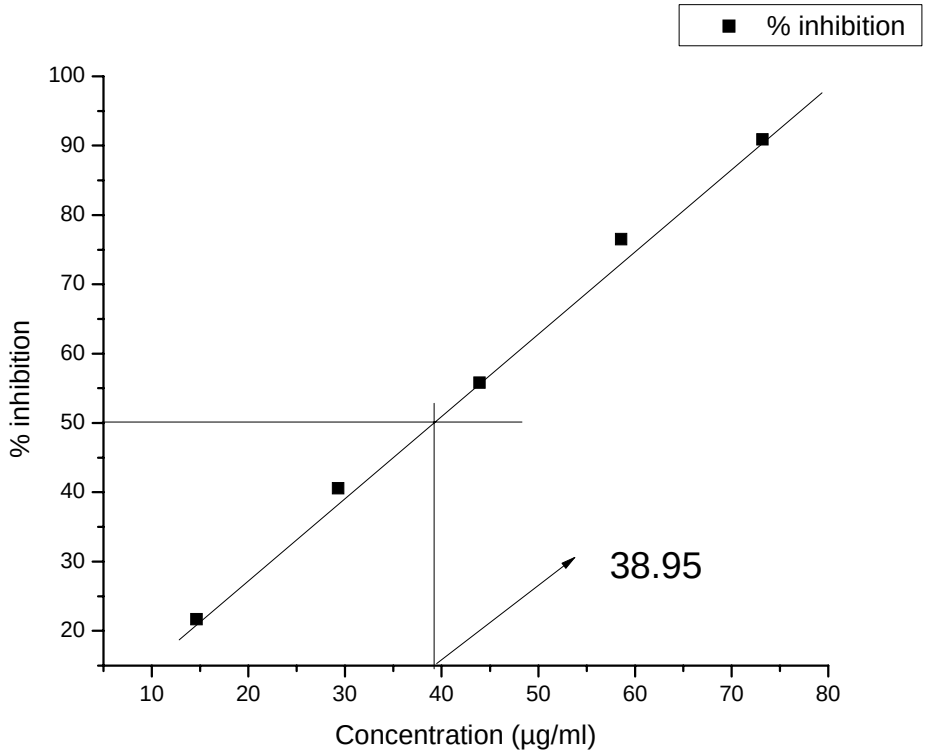



**Figure 6.1: Antioxidant assay of 3b**

**Table 6.4: Antioxidant Assay of 3c**

| Concentration µg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.695 | - | - |
| 31.2 | 0.673 | 96.8 | 3.2 |
| 46.8 | 0.549 | 79.0 | 21.0 |
| 62.4 | 0.423 | 60.9 | 39.1 |
| 78.0 | 0.325 | 46.8 | 53.2 |
| 93.6 | 0.235 | 33.8 | 66.2 |
| 109.2 | 0.107 | 15.5 | 84.5 |

$EC_{50}$ =75.17 µg/ml

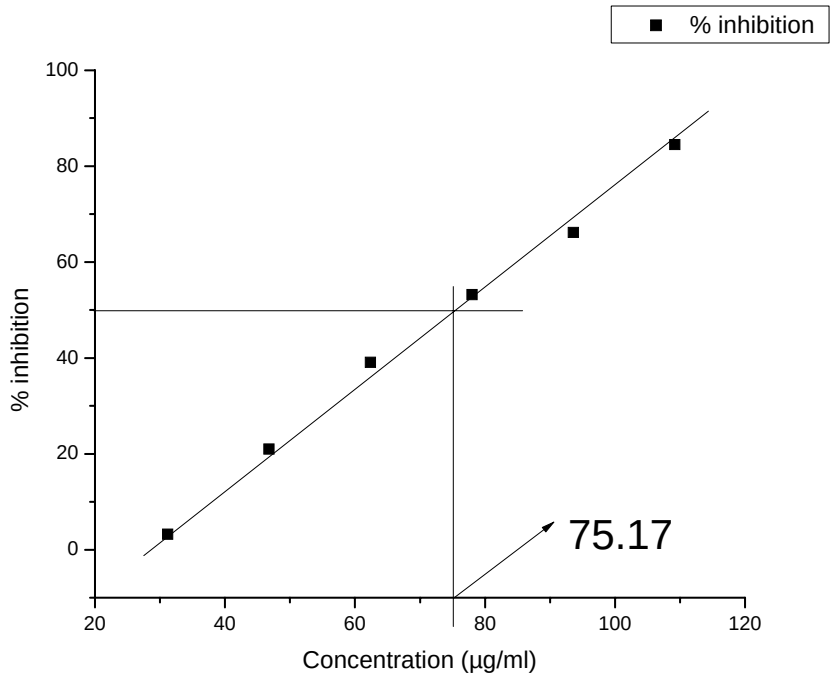



**Figure 6.2: Antioxidant assay of 3c**

**Table 6.5: Antioxidant Assay of 3f**

| Concentration µg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.689 | - | - |
| 39.9 | 0.568 | 82.35 | 17.65 |
| 79.8 | 0.445 | 64.63 | 35.37 |
| 119.7 | 0.328 | 47.6 | 52.4 |
| 159.6 | 0.204 | 29.6 | 70.4 |
| 199.5 | 0.124 | 15.06 | 81.9 |

$EC_{50}$ =114.89 µg/ml

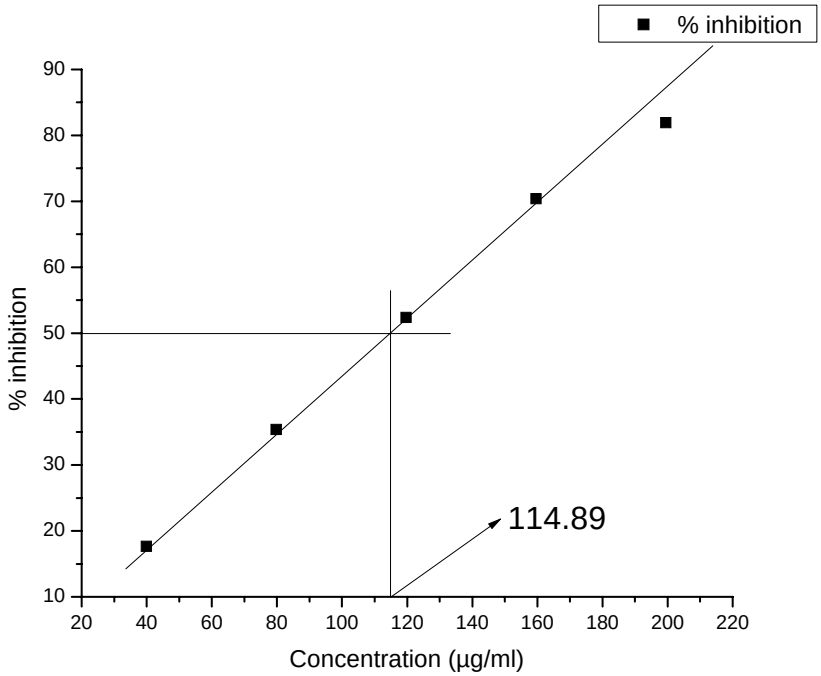



**Figure 6.3: Antioxidant assay of 3f**

**Table 6.6: Antioxidant Assay of 3h**

| Concentration µg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.697 | - | - |
| 51.2 | 0.603 | 86.5 | 13.5 |
| 102.4 | 0.5034 | 72.2 | 27.8 |
| 153.6 | 0.409 | 58.8 | 41.2 |
| 204.8 | 0.331 | 47.6 | 52.4 |
| 256.0 | 0.211 | 30.3 | 69.7 |

$EC_{50}$ = 190.37 µg/ml

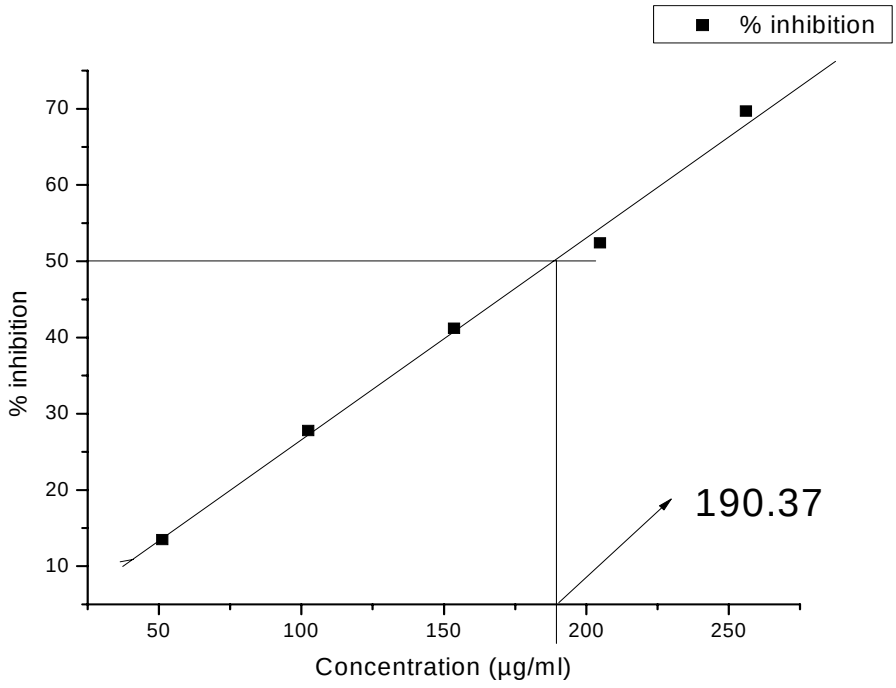



**Figure 6.4: Antioxidant assay of 3h**

The compound 3**b** contains two -OH groups, at the meta and para positions with respect to conjugated double bond. The –OH group at meta position activates the removal of hydrogen from the –OH group at the para position and stabilizes by delocalisation of the radical along with the extension of conjugation. Since both the -OH groups are adjascent position and stabilizes the radical formed by the mesomeric effect. This is the reason for the greater activity of **3b**. In the case of **3c**, an $–OCH_3$ group is present at meta position with respect to congated diketone moiety which is not a hydrogen donor itself but activates the hydrogen removal from the –OH group at position ortho to the $–OCH_3$ group and stabilizes the radical formed by the delocalistion of it. The compound **3f** contains an –OH group at para position of the conjugated diketone moity and no activating group is present in the phenyl ring. Thus the activity decreases as compared to **3b** and **3c**. In the case of **3h** , which contains a 2-hydroxy naphthalene group attached with respect to the conjugated diketo system show the least activity may be due to the presence of the bulky naphthalene ring.

The antioxidant properties of the Cu(II) complexes of **3b, 3c, 3f** and **3h** shows better activity than the respective ligands. It may be due to the presence of two equivalents of phenolic groups in one mole of the $[CuL_2]$complexes. The observed better activity of the complexes can also be attributed as due toCu(II) ↔ Cu(I) redox couple possible in these compounds. The results are given in **tables 6.7-6.10** and **figures 6.5-6.8**

**Table 6.7: Antioxidant Assay of Cu complex of 3b**

| Concentration µg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.6982 | - | - |
| 18.96 | 0.532 | 76.2 | 23.8 |
| 37.92 | 0.429 | 61.5 | 38.5 |
| 56.88 | 0.275 | 39.4 | 60.6 |
| 76. | 0.146 | 20.9 | 79.1 |
| 94.8 | 0.082 | 12.8 | 87.2 |

$EC_{50}$ = 46.37 µg/ml

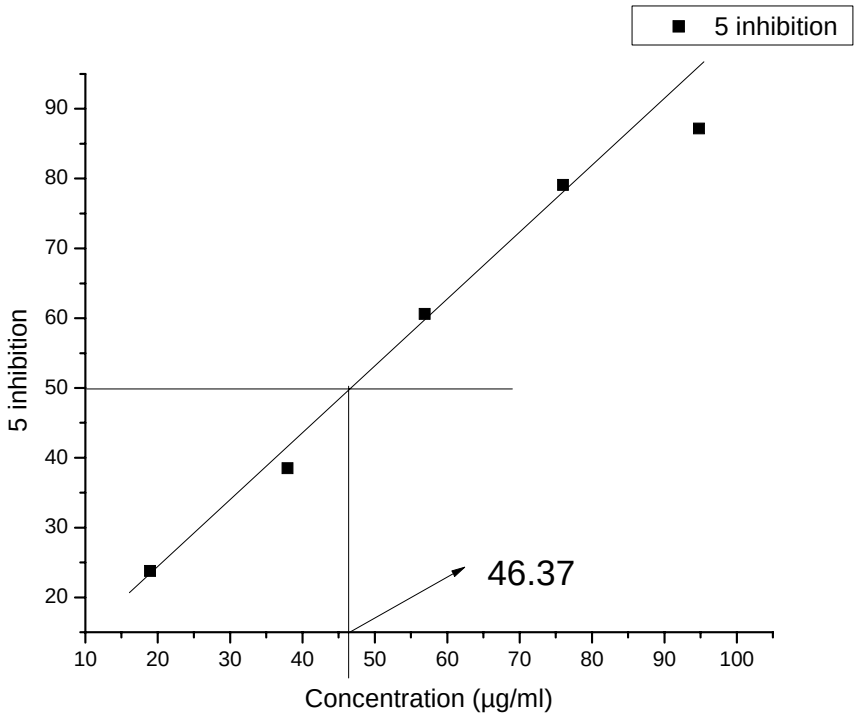



**Figure 6.5: Antioxidant assay of Cu(II) complex of 3b**

**Table 6.8: Antioxidant Assay of Cu(II) complex of 3c**

| Concentration µg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.698 | - | - |
| 33.6 | 0.528 | 75.64 | 24.36 |
| 67.2 | 0.471 | 59.74 | 40.26 |
| 100.8 | 0.285 | 40.8 | 59.11 |
| 134.4 | 0.175 | 21.07 | 4.93 |
| 168 | 0.091 | 13.2 | 86.8 |

$EC_{50}$ = 85.37 µg/ml

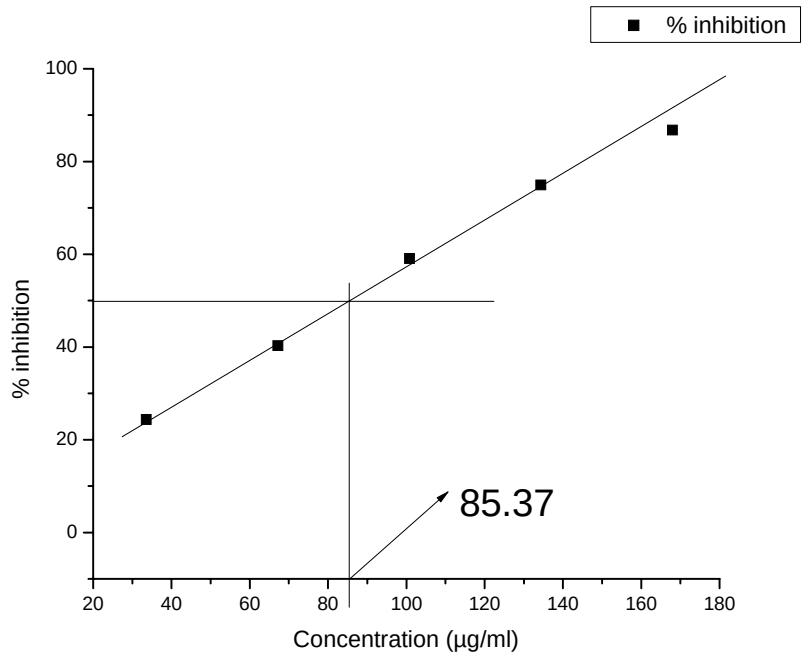



**Figure 6.6: Antioxidant assay of Cu(II) complex of 3c**

**Table 6.9: Antioxidant assay of Cu(II) complex of 3f**

| Concentration µg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.698 | - | - |
| 42.5 | 0.539 | 77.3 | 22.7 |
| 85 | 0.411 | 58.9 | 41.1 |
| 127.5 | 0.268 | 38.4 | 61.6 |
| 170 | 0.162 | 23.3 | 76.7 |
| 212.5 | 0.092 | 13.2 | 86.8 |

$EC_{50}$ = 108.16 µg/ml

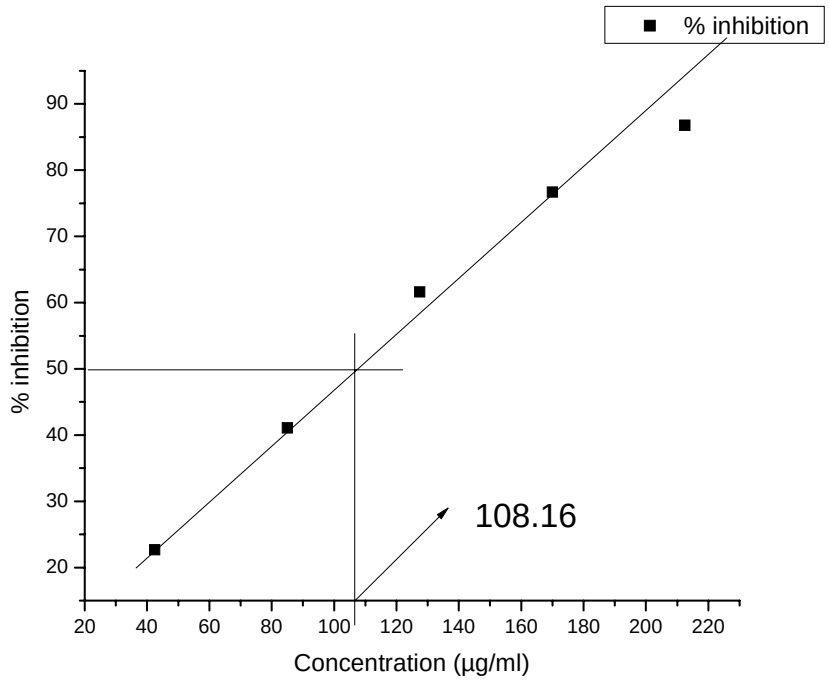



**Figure 6.7: Antioxidant assay of Cu(II) complex of 3f**

**Table 6.10: Antioxidant Assay of Cu(II) complex of 3h**

| Concentration µg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.683 | - | - |
| 61.2 | 0.592 | 86.67 | 13.33 |
| 120.4 | 0.438 | 64.13 | 35.87 |
| 180.36 | 0.314 | 45.97 | 54.07 |
| 240.48 | 0.197 | 28.84 | 71.16 |
| 300.06 | 0.075 | 10.98 | 89.02 |

$EC_{50}$ = 171.7 µg/ml

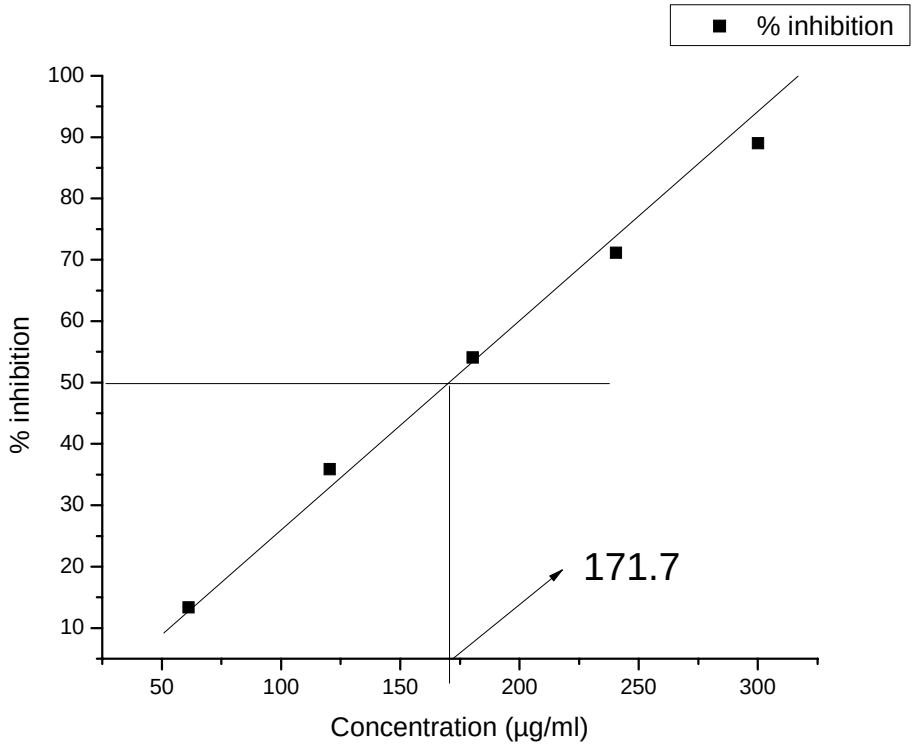



**Figure 6.8: Antioxidant assay of Cu(II) complex of 3h**

The antioxidant activity of the unsaturated β-ketoesters that do not contain phenolic groups, **3a, 3e, 3g** and **3i** are very low. This is in accordance with Priyadarsini et al. conclusions that despite the energy to remove hydrogen from both phenolic –OH and $–CH_2$ group of the β-diketone structure (or enol –OH) are very close, the phenolic hydroxyl groups play a major role in the antioxidant activity of curcuminoid analogues[186]. They follows the order **3i > 3g > 3e > 3a**, but they are comparable except **3i**. It shows a better activity than expected and the reason may be due to the presence of the –NH group of the indolyl function. The compound **3d** does not show any activity. The Cu(II) complex of these ligands are almost inactive.

**Table 6.11: Antioxidant Assay of 3a**

| Concentration mg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.689 | - | - |
| 10.2 | 0.674 | 97.8 | 2.2 |
| 20.4 | 0.658 | 95.5 | 4.5 |
| 30.6 | 0.635 | 92.1 | 7.9 |
| 40.8 | 0.617 | 89.5 | 10.5 |
| 51 | 0.601 | 87.2 | 12.8 |

$EC_{10}$ =39.7 mg/ml

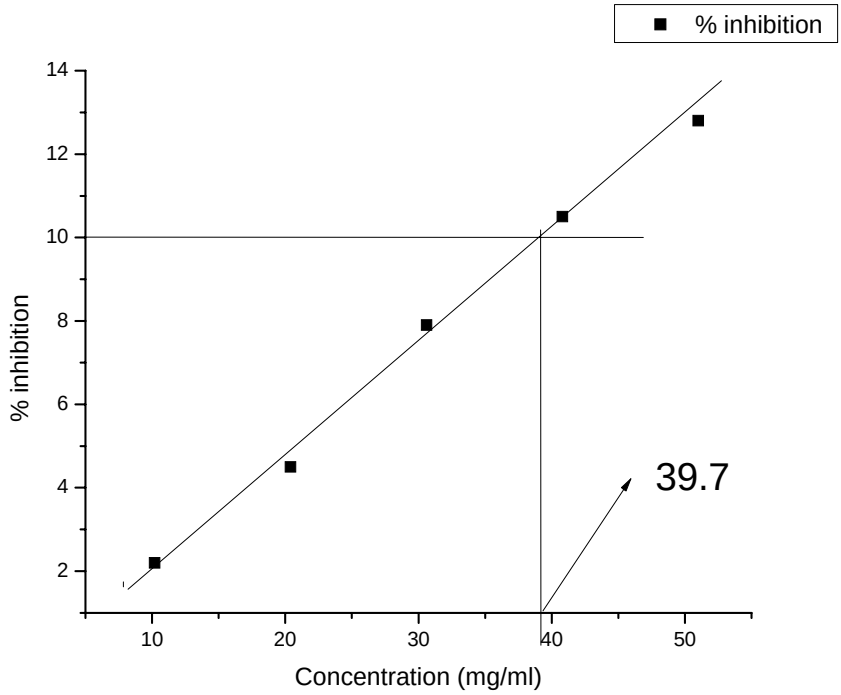



**Figure 6.9: Antioxident assay of 3a**

**Table 6.12:Antioxidant Assay of 3e**

| Concentration mg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.683 | - | - |
| 9.36 | 0.669 | 97.95 | 2.05 |
| 18.72 | 0.642 | 93.99 | 6.01 |
| 28.08 | 0.620 | 90.77 | 9.23 |
| 37.44 | 0.609 | 89.16 | 10.84 |
| 46.8 | 0.582 | 85.94 | 14.06 |

$EC_{10}$ =34.44 mg/ml

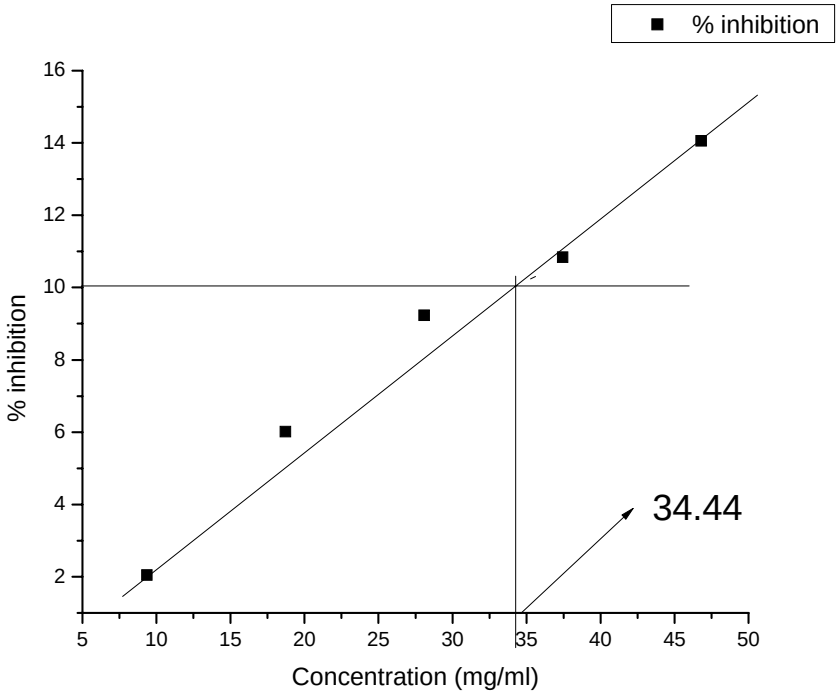



**Figure 6.10: Antioxidant assay of 3e**

**Table 6.13: Antioxidant Assay of 3g**

| Concentration mg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.689 | - | - |
| 5.4 | 0.671 | 97.3 | 2.7 |
| 10.8 | 0.662 | 96.08 | 3.92 |
| 21.6 | 0.649 | 94.19 | 5.81 |
| 32.4 | 0.624 | 90.56 | 9.44 |
| 43.2 | 0.609 | 88.38 | 11.62 |

$EC_{10}$ =35.07mg/ml

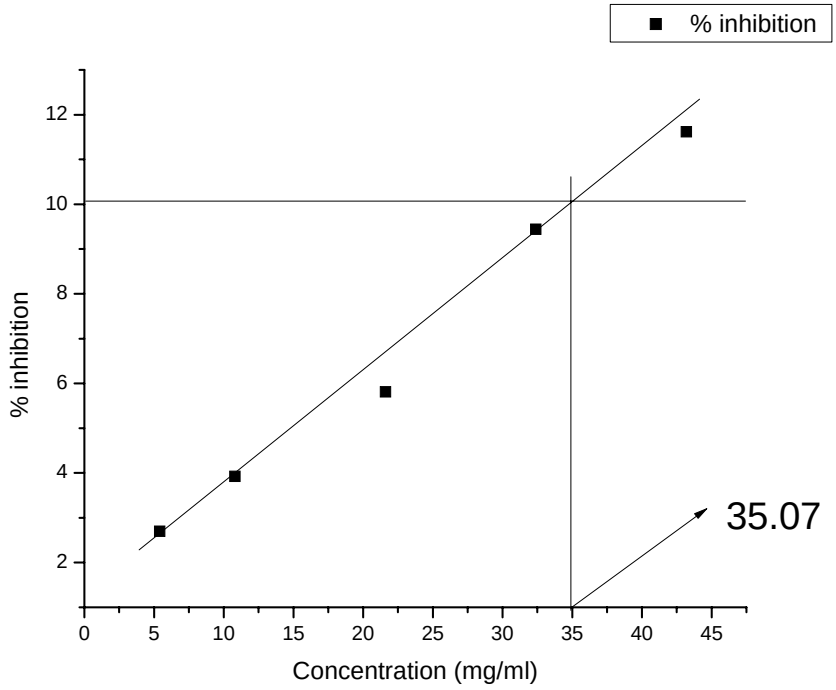



**Figure 6.11: Antioxidant assay of 3g**

**Table 6.14: Antioxidant Assay of 3i**

| Concentration mg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.683 | - | - |
| 2.43 | 0.671 | 98.3 | 1.7 |
| 4.86 | 0.661 | 96.79 | 3.29 |
| 7.29 | 0.647 | 94.78 | 5.22 |
| 9.72 | 0.623 | 91.22 | 8.78 |
| 12.15 | 0.602 | 88.11 | 11.89 |

$EC_{10}$ =10.96 mg/ml

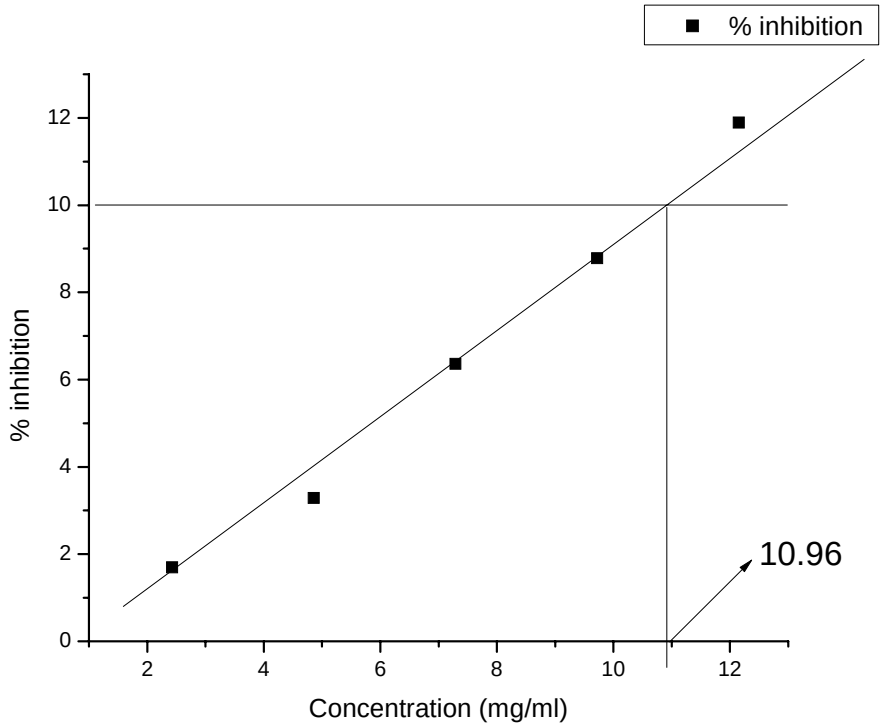



**Figure 6.12: Antioxidant assay of 3i**

**Antioxidant activities of the unsaturated tetraketones**

Unsaturated tetraketones considered in chapter 4 also show very little antioxidant activity . This may be due to the absence of phenolic groups in these compounds. The Cu(II) complexes of these unsaturated tetraketones does not show any activity. From all of these results, it can be concluded that that the role of phenolic groups to the antioxidant actity is major and the involvement of β-diketone moiety to their antioxidant properties as it is reported by Sugiyama *et al.* should be minor[220].

**Table 6.15: Antioxidant Assay of $H_2$aa**

| Concentration mg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.689 | - | - |
| 14.9 | 0.672 | 97.5 | 2.5 |
| 29.8 | 0.653 | 94.7 | 5.3 |
| 44.7 | 0.639 | 92.7 | 7.3 |
| 59.6 | 0.627 | 90.00 | 9.0 |
| 74.5 | 0.608 | 88.2 | 11.8 |

$EC_{10}$ =63.48 mg/ml

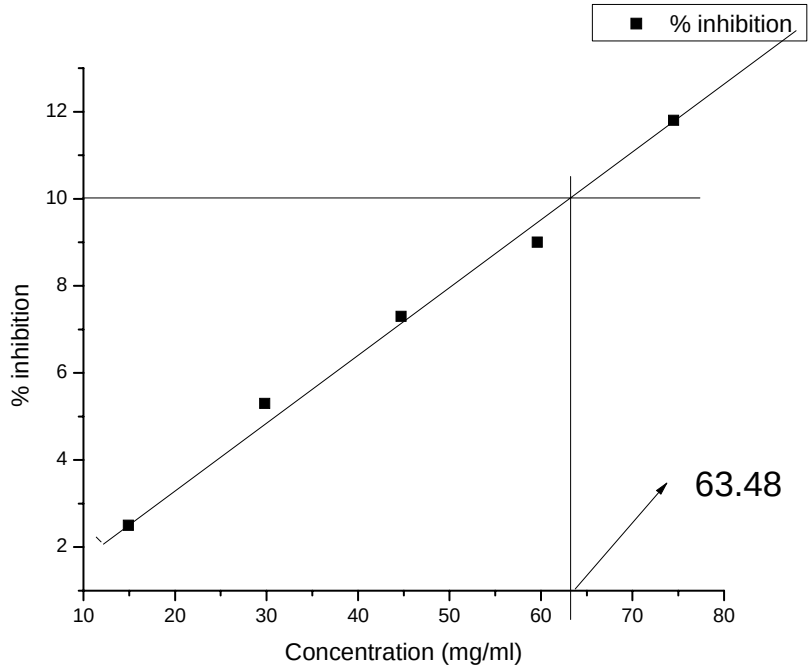



**Figure 6.13: Antioxidant assay of $H_2$aa**

**Table 6.16: Antioxidant Assay of $H_2$ma**

| Concentration mg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.689 | - | - |
| 16.5 | 0.673 | 97.6 | 2.4 |
| 33 | 0.659 | 95.6 | 4.4 |
| 49.5 | 0.641 | 93 | 7 |
| 66 | 0.625 | 90.7 | 9.3 |
| 82.5 | 0.612 | 88.8 | 11.2 |

$EC_{10}$ = 71.73 mg/ml

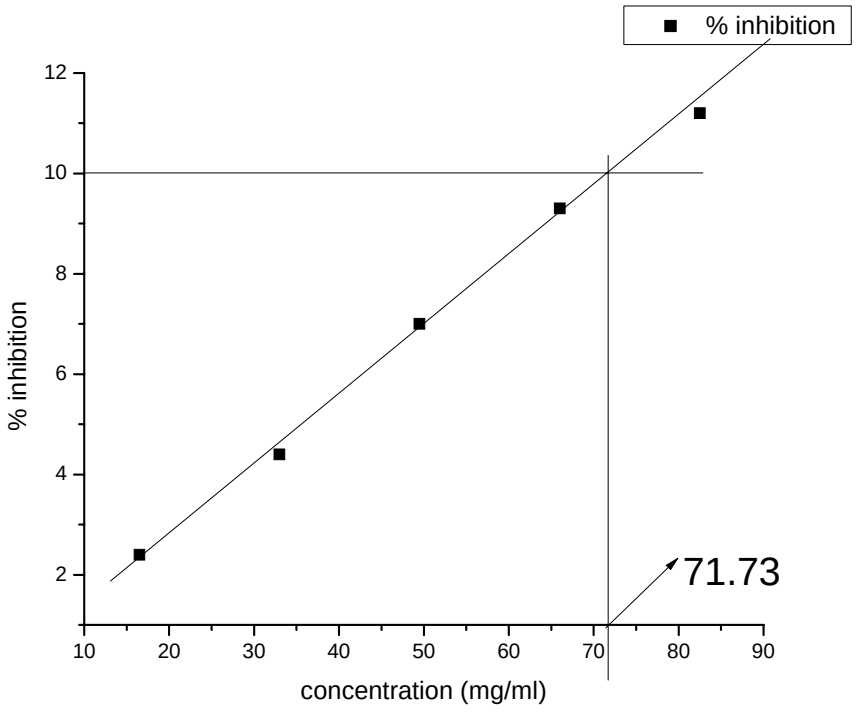



**Figure 6.14: Antioxidant assay of $H_2$ma**

**Table 6.17: Antioxidant Assay of $H_2$ba**

| Concentration mg/ml | Absorbance | % Difference | % inhibition |
|---|---|---|---|
| 0 | 0.683 | - | - |
| 21.1 | 0.669 | 97.9 | 2.1 |
| 42.2 | 0.651 | 95.3 | 4.7 |
| 63.3 | 0.632 | 92.5 | 7.5 |
| 84.4 | 0.617 | 90.7 | 9.3 |
| 105 | 0.596 | 87.2 | 12.8 |

$EC_{10}$ = 83.59 mg/ml

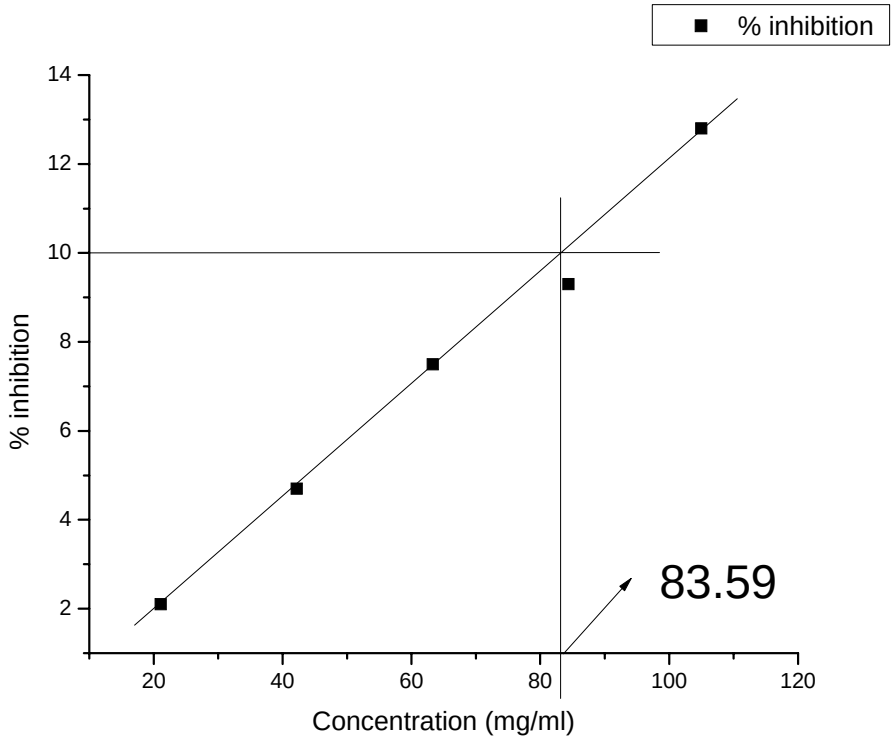



**Figure 6.15: Antioxidant assay of $H_2$ba**

The ARP at $EC_{50}$ , Stochiometric value ie, theoretical concentration for 100% reduction of DPPH , NRD ( number of DPPH moles reduced by one mole of antioxidant), and time $EC_{50}$ of the unsaturated β-ketoesters , their Cu(II) complexes and unsaturated tetraketones are tabulated in Tables 6.18-6.19 for the easy comparison of the antioxidant properties of these compounds.

**Table 6.18**: **Antioxidant assay of β-Ketoesters and their Cu(II) complexes**

| Compound | $EC_{50}$ | ARP | SV | NRD | Time $EC_{50}$ (minutes) |
|---|---|---|---|---|---|
| 3b | 0.14 | 7.1 | 0.28 | 3.57 | 45 |
| 3c | 0.25 | 4 | 0.5 | 2 | 60 |
| 3f | 0.43 | 2.3 | 0.86 | 1.16 | 60 |
| 3h | 0.58 | 1.72 | 1.16 | 0.86 | - |
| Cu comlex of 3b | 0.07 | 14.28 | 0.14 | 7.14 | 80 |
| Cu complex of 3c | 0.15 | 6.66 | 0.30 | 3.33 | 90 |
| Cu complex of 3f | 0.18 | 5.55 | 0.36 | 2.77 | - |
| Cu complex of 3h | 0.24 | 4.16 | 0.48 | 2.08 | 100 |

**Table 6.19: Antioxidant Assay of β -keto esters with lesser activity**

| Compound | $Ec_{10}$ | ARP |
|---|---|---|
| 3a | 2.11 | 0.47 |
| 3e | 1.63 | 0.63 |
| 3g | 1.52 | 0.65 |
| 3i | 0.49 | 2.04 |
| $H_2$aa | 2.38 | 0.42 |
| $H_2$ma | 2.46 | 0.40 |
| $H_2$ba | 2.2 | 0.45 |

**Summary**

Biochemical properties such as antifungal and antioxidant activities of unsaturated β-ketoesters and unsaturated tetraketones and their Cu(II) complexes were carried out. The results obtained showed that the Cu(II) complexes exhibit more antifungal activity compared to the free ligands. Electron donating groups on the aryl ring enhances the antifungal activity. Whereas the antioxidant activity decreases during complexation. Compounds containing –OH groups on the aryl ring showed maximum activity. When electron donating groups like $–OCH_3$ are present, further enhanced the antioxidant activity.

# CHAPTER 7
# ELECTROCHEMICAL STUDIES

## Introduction

Cyclic voltammetry is one of the most widely used voltammetric technique for studying redox reactions of both organic and inorganic compounds. This is mainly because of its ability to provide informations on the various steps involved in electrochemical processes. Further CV requires only simple instrumentation and is rapid in acquisition and interpretation of data.

An electrochemical process occurs generally through a series of steps such as (a) the transfer of both reactant from bulk of the solution to the electrode surface and the product in the opposite direction, (b) charge transfer reaction and (c) structural rearrangements and other electrode surface reactions. These processes are mainly dependent on the time scale of the experiment, that is the scan rate adopted. Depending on the nature of the electrochemical reactions that may occur during the experimental conditions the processes may be reversible, quasireversible or totally irreversible. In CV these electrode processes mainly dependent on the scan rate ν employed which determines the time scale available for the electrode solution interphase to attain equilibrium condition governed by the Nernst equation such as

dependence is usually rationalized by a dimensionless parameter ψ which is for oxidation process.

$$\Psi = \gamma^{\alpha} k_{sh} / (\pi a D_O)^{1/2}$$

Where $\gamma = (D_O/D_R)^{1/2}$ [ $D_O$ and $D_R$ are diffusion coefficiants of the oxidized and reduced species respectively], α = the charge transfer coefficient, $a = nF\nu/RT$ where n is the number of electrons involved and $k_{sh}$ is the standard heterogeneous rate constant. It can be shown that a particular redox system may display a reversible behavior for high ψ value that low value of ν which it may become totally irreversible for high scan rates when $\psi < 10^{-3}$ .

Important parameters in cyclic voltammogram are the cathode peak potential $E_{pc}$, the anodic peak potential $E_{pa}$, the cathodic current $i_{pc}$ and anodic peak current $i_{pa}$ at different scan rates ν. For a reversible electrode process, the anodic and cathodic peak currents are approximately equal but opposite in sign. In the case of a reversible electrode reaction at $25^{0C}$ the difference in peak potentials $\Delta E_p$ is expected to be

$\Delta E_p = E_{pa} - E_{pc} = 0.059/n$ V where n is the number of electrons involved in the half reaction. For an irreversible process $\Delta E_p$ exceeds the expected value because of slow electron transfer reaction kinetics[221-224]. Though the electron transfer reaction may appear reversible at slow scan rates , increasing scan rates may lead to increase in the value of $\Delta E_p$ , a sure indication of irreversibility[221-224]. Therefore it is necessary to record the

voltammogram at different scan rates inorder to determine the nature of the electron transfer kinetics.

The major use of CV is to provide qualitative information about electrochemical process under various conditions and is widely employed in organic and inorganic chemists.

In the present study the redox behavior of the unsaturated 1,3-dicarbonyl compounds considered in chapter 3 and chapter 4 and their Cu(II) complexes were examined using cyclic voltammetry. For comparison a series of synthetic analogues of natural curcuminiods (1, 7-diarylhepta-1,6-diene-2,3-diones) and their Cu(II) complexes were also investigated.

**Experimental**

The curcuminoids (7.1-7.4) were synthesized according to the reported procedures[119]. That is, the acetylacetone-boron complex is reacted with various aromatic aldehydes in presence of tributylborate and n-butyl amine as the condensing agent followed by acidification. Their Cu(II) complexes were also synthesized as reported earlier[120-126]. The synthetic details of unsaturated β-ketoesters, unsaturated tetraketones and their Cu(II) complexes were as given in chapters 3 and 4.

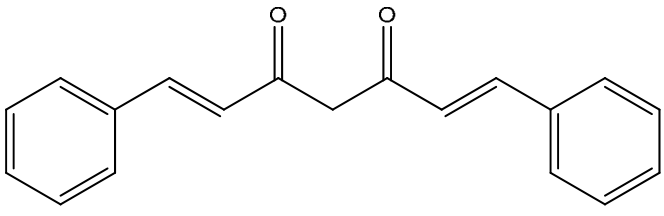
The cyclic voltammetric data were recorded on a SP-50 Biologic analyser. The three electrode cell contains areference Ag/AgCl electrode, Pt wire auxillary electrode and glassy carbon working electrode.

Tetrabutylammoniumiodide was used as supporting electrolyte. For CV measurements 0.01 moles of samples were mixed with 0.1M tetrabutylammoniumiodide in methanol. The sample solutions were poured to the electrolytic cell, the electrodes were connected with proper wires and the cyclic voltammogram were recorded from -3 to 3 potential range.

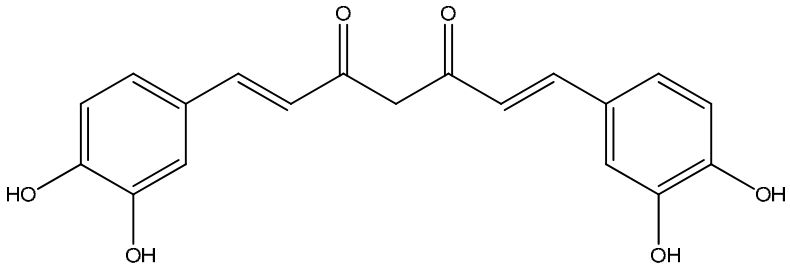
**Results and discussion**

Cyclic voltammetry provides a direct estimate of the electrode reversibility because the potential at which the oxidation and reduction occur are directly observed. For example at low frequencies it may be possible for a given system that electrochemical equilibrium always is maintained at the electrode surface. Under these conditions the separation of anodic and cathodic peak potential is about 60/n mv and the reaction is reversible[224-228]. In this case no kinetic information about the electron transfer reaction can be obtained. However it is possible to get the kinetics by increasing the scan rate until the separation of the peak potentials become greater than 60/n mv.

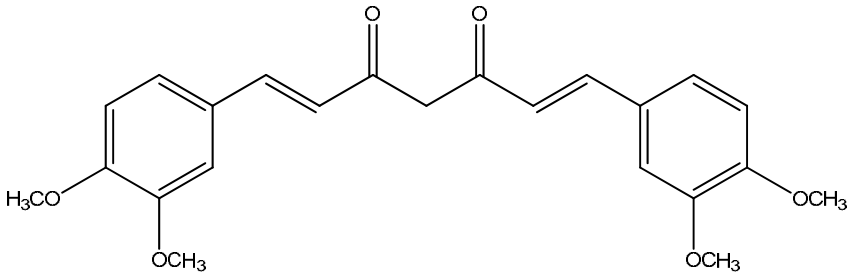
The cyclic voltammogram of the following synthetic analogues **7.1 – 7.4** of natural curcuminoids were recorded at different scan rates (20, 50, and 100).



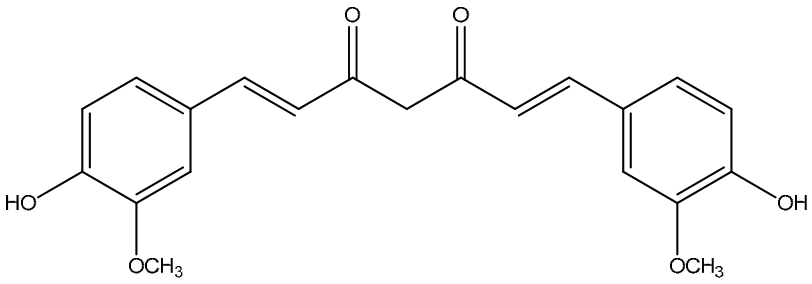
**7.1**




**7.2**




**7.3**




**7.4**

The electrochemical data are given in **Table 7.1** and typical voltammograms are reproduced in **Figure 7.1.** All the compounds showed one well defined redox couple. Both the anodic and cathodic peaks appeared in the positive potential range. The $\Delta E_p$ and $I_{pa}/I_{pc}$ values are almost constant for various scan rates for all compounds and the value of $\Delta E_p$ is in the range 0.05-0.07 V

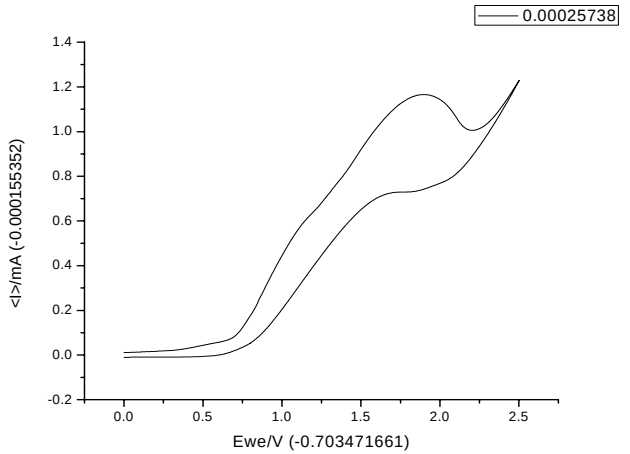
which clearly suggests the reversible process and $I_{pa}/I_{pc}$ is almost equal to unity (0.9-1.1) which clearly suggest indicates the simple one electron electrode process. The cathodic and anodic peak potentials are highly dependent on the nature of the substituents present in the aromatic ring.

It can be seen that when electron donating groups are present on the aryl ring the cathodic and anodic potentials become more positive compared to unsubstituted phenyl rings. Upon complexation both the anodic and cathodic potentials due to the ligand shifted to more positive values. The trend of various curcuminoids is of the order **7.2 > 7.4 > 7.3 > 7.1.** The cathodic and anodic peak potentials are in the range 1.8-2.05 and 1.9-2.1 V respectively.

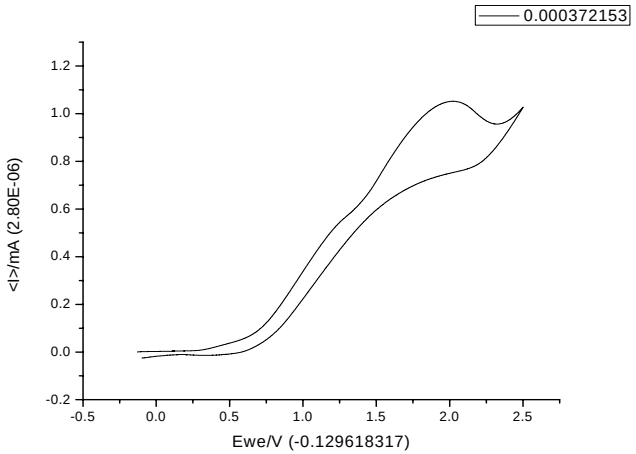
The voltammograms of the Cu(II) complexes of the curcuminoids displayed two well defined redox couples **(Figure 7.2)**. The Epa, Epc, Ipa, and Ipc values are given in **table7.2 and 7.3.** Both redox process occur in the positive potential range. From a comparison of the voltammograms of the free ligands with that of complexes, it can be presumed that tha cathodic peak appeared in the range 1.9 to 2.1 and the corresponding anodic peak in the range 1.97-2.15 V is due to the redox reactions of the complexed ligand moiety. These values shifted to more positive potentials compared to the free ligand redox couple. The value of $\Delta E_p$ falls in the range 0.05-0.07 V and independent on the scan rates which clearly indicates the reversible redox couple. But the peak current ratio is less than one (~ 0.5) upon complexation.

**Table 7.1 Cyclic voltammetric data of curcuminoids 7.1-7.4**

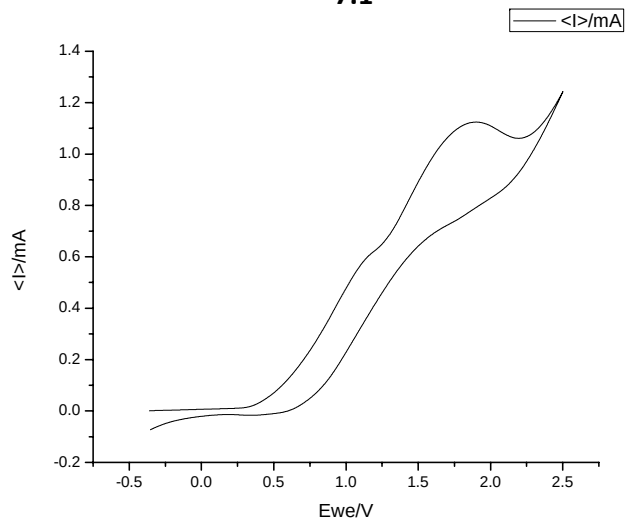
| Compounds | Scan rate | $E_{pc}$ | $E_{pa}$ | $\Delta E_p$ | $I_{pc}$ | $I_{pa}$ | $I_{pa}/I_{pc}$ |
|---|---|---|---|---|---|---|---|
| **7.1** | 20 | 1.83 | 1.90 | 0.07 | 0.41 | 0.38 | 0.92 |
| | 50 | 1.87 | 1.92 | 0.05 | 0.43 | 0.41 | 0.95 |
| | 100 | 1.89 | 1.94 | 0.05 | 0.45 | 0.44 | 0.97 |
| **7.2** | 20 | 1.99 | 2.06 | 0.07 | 0.31 | 0.28 | 0.89 |
| | 50 | 2.01 | 2.07 | 0.06 | 0.32 | 0.29 | 0.90 |
| | 100 | 2.03 | 2.09 | 0.06 | 0.34 | 0.31 | 0.91 |
| **7.3** | 20 | 1.87 | 1.94 | 0.07 | 0.38 | 0.35 | 0.92 |
| | 50 | 1.88 | 1.94 | 0.06 | 0.40 | 0.37 | 0.92 |
| | 100 | 1.92 | 1.98 | 0.06 | 0.42 | 0.39 | 0.92 |
| **7.4** | 20 | 1.93 | 1.97 | 0.06 | 0.42 | 0.39 | 0.92 |
| | 50 | 1.96 | 2.02 | 0.06 | 0.45 | 0.40 | 0.88 |
| | 100 | 1.98 | 2.03 | 0.05 | 0.46 | 0.41 | 0.91 |



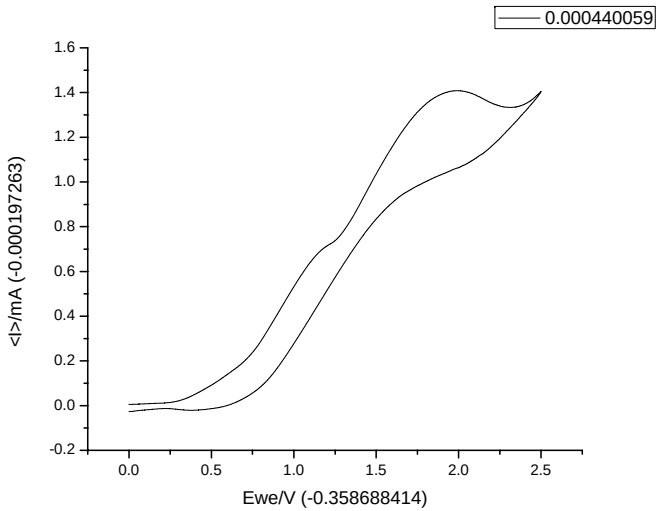

**7.1**




**7.2**




**7.3**




**7.4**

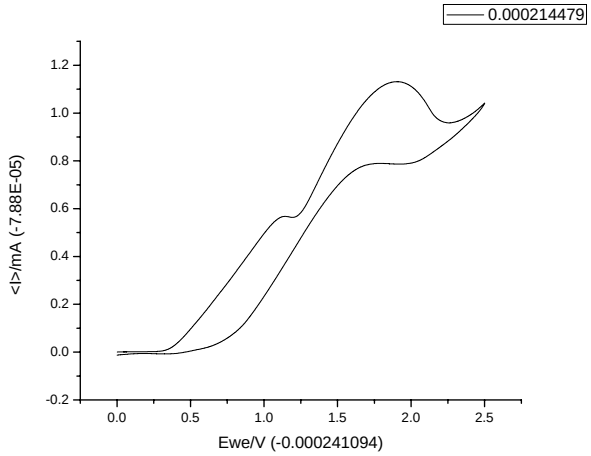
**Figure 7.1: Cyclic Voltammograms of Curcuminoids (7.1-7.4)**

**Table 7.2: Cyclic voltammetric data reversible redox process of Cu(II) complexes of the curcuminoids(HL), 7.1-7.4**

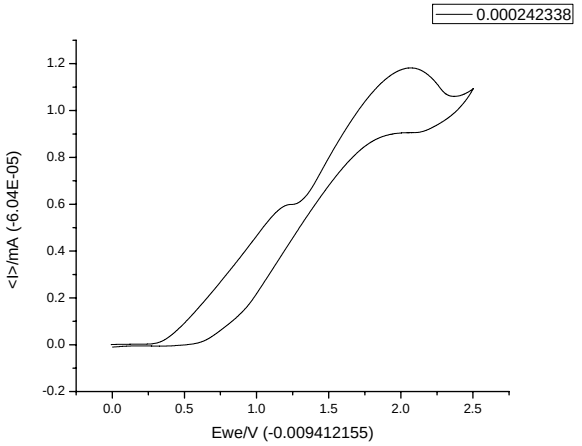
| $[CuL_2]$ complexes of | Scan rate | $E_{pc}$ | $E_{pa}$ | $\Delta E_p$ | $I_{pc}$ | $I_{pa}$ | $I_{pa}/I_{pc}$ |
|---|---|---|---|---|---|---|---|
| **7.1** | 20 | 1.83 | 1.77 | 0.06 | 0.62 | 0.23 | 0.37 |
| | 50 | 1.87 | 1.83 | 0.06 | 0.67 | 0.25 | 0.37 |
| | 100 | 1.91 | 1.97 | 0.06 | 0.71 | 0.29 | 0.41 |
| **7.2** | 20 | 2.03 | 1.98 | 0.05 | 0.42 | 0.17 | 0.40 |
| | 50 | 2.05 | 2.09 | 0.04 | 0.45 | 0.19 | 0.42 |
| | 100 | 2.08 | 2.13 | 0.05 | 0.49 | 0.22 | 0.44 |
| **7.3** | 20 | 1.95 | 2.01 | 0.06 | 0.42 | 0.15 | 0.35 |
| | 50 | 1.97 | 2.02 | 0.05 | 0.45 | 0.17 | 0.37 |
| | 100 | 2.00 | 2.05 | 0.05 | 0.47 | 0.19 | 0.40 |
| **7.4** | 20 | 1.99 | 2.06 | 0.07 | 0.52 | 0.21 | 0.40 |
| | 50 | 2.01 | 2.07 | 0.06 | 0.53 | 0.23 | 0.43 |
| | 100 | 2.03 | 2.09 | 0.06 | 0.55 | 0.25 | 0.45 |

**Table 7.3: Cyclic voltammetric data quasireversible redox process of Cu(II) complexes of curcuminoids**

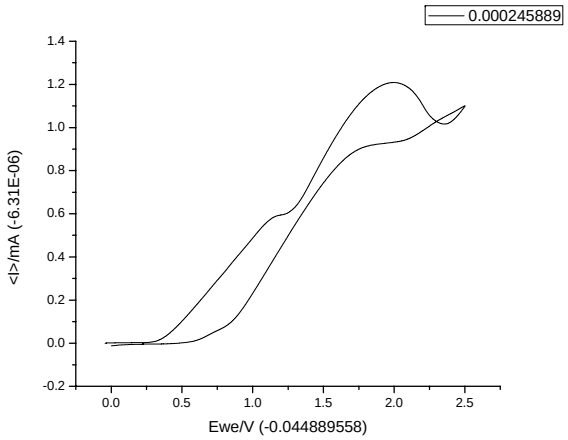
| $[CuL_2]$ complex of | Scan rate | $E_{pc}$ | $E_{pa}$ | $\Delta E_p$ | $I_{pc}$ | $I_{pa}$ | $I_{pa}/I_{pc}$ |
|---|---|---|---|---|---|---|---|
| **7.1** | 20 | 1.05 | 0.78 | 0.27 | 0.52 | 0.73 | 1.37 |
| | 50 | 1.09 | 0.81 | 0.28 | 0.51 | 0.72 | 1.38 |
| | 100 | 1.12 | 0.84 | 0.28 | 0.50 | 0.71 | 1.42 |
| **7.2** | 20 | 1.08 | 0.76 | 0.32 | 0.53 | 0.73 | 1.37 |
| | 50 | 1.12 | 0.79 | 0.33 | 0.52 | 0.74 | 1.42 |
| | 100 | 1.15 | 0.82 | 0.33 | 0.52 | 0.75 | 1.44 |
| **7.3** | 20 | 1.09 | 0.77 | 0.32 | 0.51 | 0.72 | 1.41 |
| | 50 | 1.11 | 0.81 | 0.30 | 0.50 | 0.72 | 1.44 |
| | 100 | 1.13 | 0.84 | 0.29 | 0.51 | 0.73 | 1.43 |
| **7.4** | 20 | 1.09 | 0.77 | 0.32 | 0.52 | 0.75 | 1.44 |
| | 50 | 1.12 | 0.78 | 0.34 | 0.54 | 0.78 | 1.44 |
| | 100 | 1.14 | 0.81 | 0.33 | 0.54 | 0.79 | 1.44 |



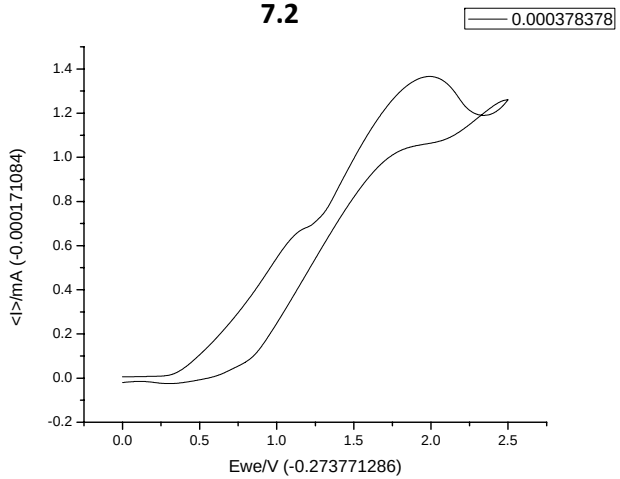

**7.1**




**7.2**




**7.3**




**7.4**

**Figure 7.2: Cyclic Voltammograms of Cu (II) Complexes of Curcuminoids (7.1-7.4)**

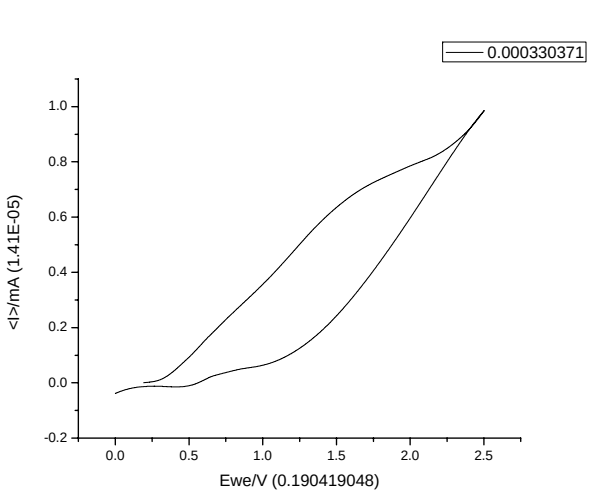
The cathodic peaks appeared in the range 1.1-1.5 V and the corresponding anodic peak in the range 0.8-0.9 V is undoubtedly due to the redox couple Cu(II)/Cu(I). Here the $\Delta E_p$ value exceeds the range 0.05-0.06 V and falls in the range 0.07-0.35 which is the condition for quasireversible process and the ratio of anodic current to cathodic current ($I_{pa}/I_{pc}$) is almost equal to one which confirms the one electron transfer.

The electrochemical data of the unsaturated β-ketoesters considered in chapter 3 are presented in **table7.4** and typical voltammogram are given in **figure 7.3** the voltammogram of all compounds consists of one well shaped redox couple in the positive potential. The cathodic peaks are in the range 1.5-1.8 V and the anodic peaks are in the range1.6-1.9 V. The ΔEp value in the range 0.05-0.07 V which is independent on scan rate clearly indicates the redox processes are reversible. The $I_{pa}/I_{pc}$ values fall in the range 0.9-1.1 confirms the one electron redox process. Compared to curcuminoids the peak potentials are shifted to less positive values. Among the β-ketoesters the observed order is **3b > 3c > 3f > 3i > 3a** which is of the same substituent effect of the aryl ring that observed for curcuminoids.

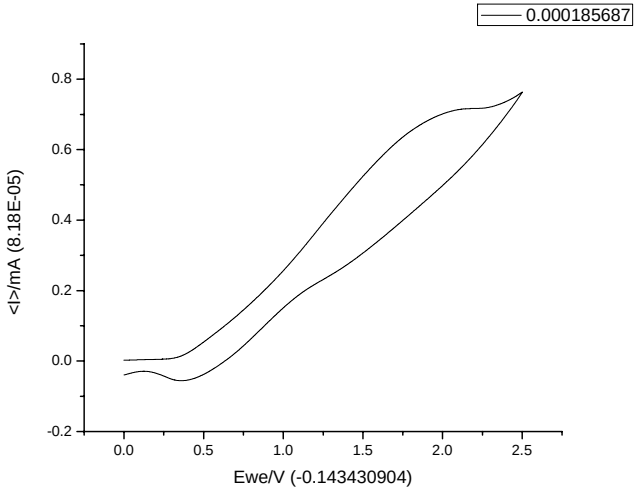
The voltammogram of Cu(II) complex of all unsaturated β-ketoesters contain two well defined redox couples both in the positive potential region **(Figure 7.4)**. The electrochemical data are presented in **table 7.5 and 7.6**. The anodic and cathodic peaks at the more positive potentials are due to the

**Table 7. 4: Cyclic voltammetric data of the unsaturated β-ketoesters**

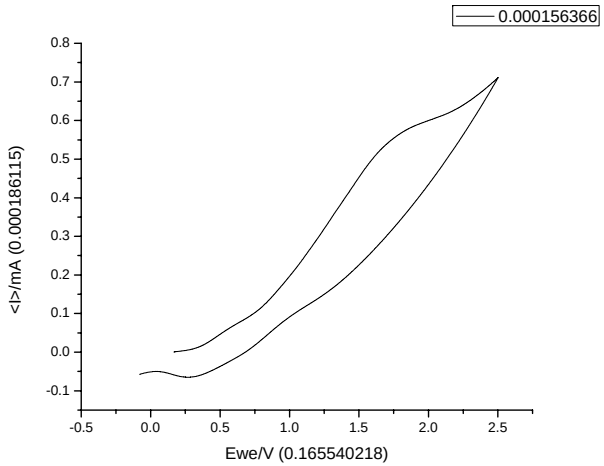
| Compounds | Scan rate | $E_{pc}$ | $E_{pa}$ | ΔEp | $Ip_c$ | $Ip_a$ | $Ip_a/Ip_c$ |
|---|---|---|---|---|---|---|---|
| | 20 | 1.99 | 2.06 | 0.07 | 0.62 | 0.61 | 0.98 |
| **3a** | 50 | 2.01 | 2.07 | 0.06 | 0.63 | 0.67 | 1.06 |
| | 100 | 1.55 | 1.49 | 0.06 | 0.61 | 0.66 | 1.08 |
| | 20 | 1.99 | 2.06 | 0.07 | 0.32 | 0.31 | 0.96 |
| **3b** | 50 | 2.01 | 2.07 | 0.06 | 0.30 | 0.30 | 1.00 |
| | 100 | 1.83 | 1.87 | 0.04 | 0.31 | 0.32 | 1.03 |
| | 20 | 1.95 | 2.01 | 0.06 | 0.35 | 0.35 | 1.00 |
| **3c** | 50 | 1.97 | 2.02 | 0.05 | 0.35 | 0.36 | 1.02 |
| | 100 | 1.73 | 1.79 | 0.06 | 0.35 | 0.37 | 1.05 |
| | 20 | 1.63 | 1.57 | 0.06 | 0.32 | 0.33 | 1.03 |
| **3f** | 50 | 1.67 | 1.63 | 0.06 | 0.35 | 0.34 | 0.97 |
| | 100 | 1.71 | 1.75 | 0.04 | 0.36 | 0.36 | 1.00 |
| | 20 | 1.63 | 1.68 | 0.05 | 0.45 | 0.47 | 1.04 |
| **3i** | 50 | 1.65 | 1.69 | 0.04 | 0.48 | 0.47 | 0.97 |
| | 100 | 1.66 | 1.71 | 0.05 | 0.50 | 0.48 | 0.96 |




**3a**




**3b**




**3c**

**Figure 7.3: Cyclic Voltammograms of Unsaturated β-ketoesters**

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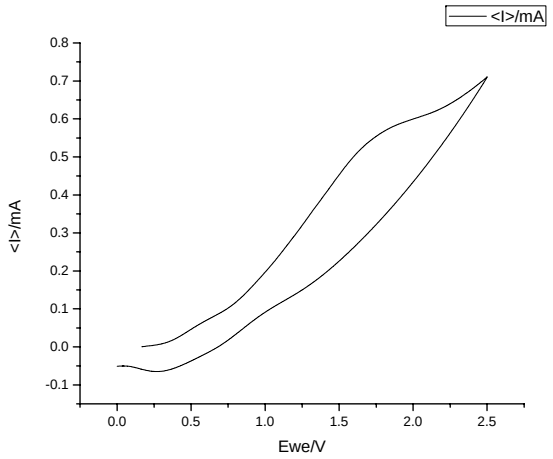
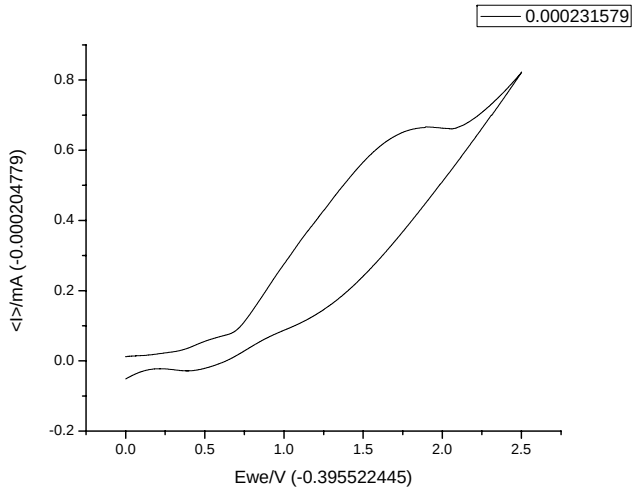
Fig. 7.3 contd…….




**3f**




**3i**

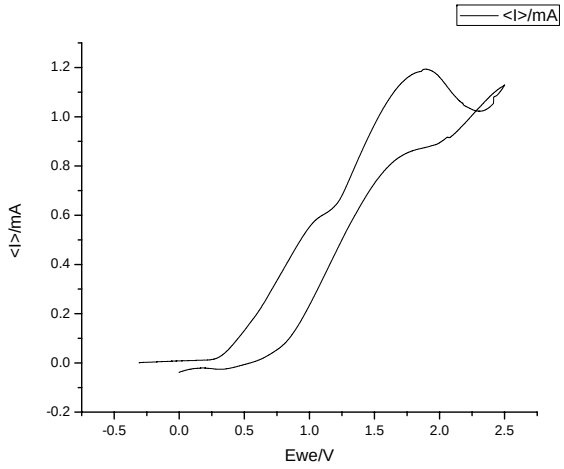
**Figure 7.3: Cyclic Voltammograms of Unsaturated β-ketoesters**

**Table 7.5: Cyclic voltammograms reversible redox process of Cu(II) complex of the unsaturated β-ketoesters,(HL)**

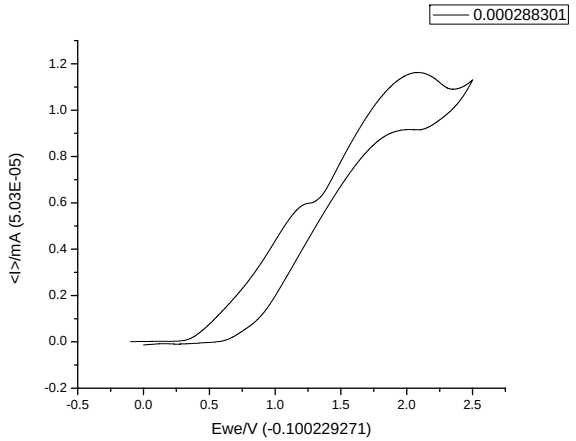
| $[CuL_2]$ complexes of | Scan rate | $E_{pc}$ | $E_{pa}$ | $\Delta E_p$ | $Ip_c$ | $Ip_a$ | $Ip_a/Ip_c$ |
|---|---|---|---|---|---|---|---|
| **3a** | 20 | 1.83 | 1.87 | 0.06 | 0.52 | 0.23 | 0.44 |
| | 50 | 1.87 | 1.93 | 0.06 | 0.54 | 0.24 | 0.44 |
| | 100 | 1.89 | 1.95 | 0.06 | 0.52 | 0.25 | 0.48 |
| **3b** | 20 | 1.02 | 2.09 | 0.07 | 0.54 | 0.22 | 0.40 |
| | 50 | 2.05 | 2.12 | 0.07 | 0.53 | 0.21 | 0.39 |
| | 100 | 2.08 | 2.13 | 0.05 | 0.53 | 0.21 | 0.39 |
| **3c** | 20 | 1.95 | 2.02 | 0.07 | 0.53 | 0.20 | 0.37 |
| | 50 | 1.99 | 2.06 | 0.07 | 0.54 | 0.21 | 0.38 |
| | 100 | 2.02 | 2.08 | 0.06 | 0.55 | 0.22 | 0.40 |
| **3f** | 20 | 1.99 | 2.06 | 0.07 | 0.52 | 0.21 | 0.40 |
| | 50 | 2.01 | 2.07 | 0.06 | 0.50 | 0.21 | 0.42 |
| | 100 | 2.01 | 2.07 | 0.06 | 0.51 | 0.22 | 0.43 |
| **3i** | 20 | 1.92 | 1.97 | 0.05 | 0.42 | 0.41 | 0.97 |
| | 50 | 1.94 | 1.99 | 0.05 | 0.43 | 0.42 | 0.97 |
| | 100 | 1.96 | 2.01 | 0.05 | 0.42 | 0.42 | 1.00 |

**Table 7.6: Cyclic voltammograms quasireversible redox process of Cu(II) complex of the unsaturated β-ketoesters,(HL)**

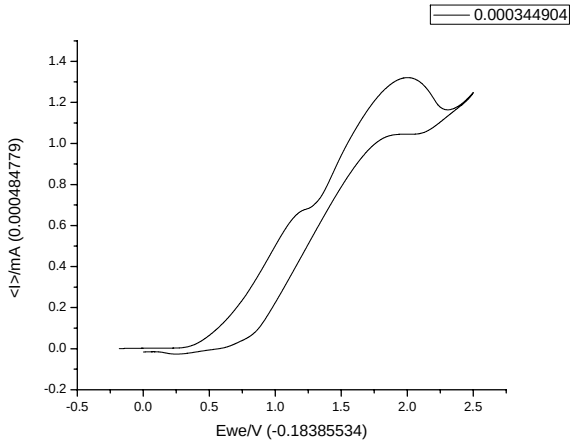
| Cu(II) complexes of | Scan rate | $E_{pc}$ | $E_{pa}$ | $\Delta E_p$ | $Ip_c$ | $Ip_a$ | $Ip_a/Ip_c$ |
|---|---|---|---|---|---|---|---|
| **3a** | 20 | 1.05 | 1.75 | 0.30 | 0.45 | 0.65 | 1.44 |
| | 50 | 1.07 | 1.78 | 0.29 | 0.48 | 0.67 | 1.39 |
| | 100 | 1.09 | 0.80 | 0.29 | 0.50 | 0.68 | 1.36 |
| **3b** | 20 | 1.95 | 2.02 | 0.07 | 0.53 | 0.71 | 1.33 |
| | 50 | 1.99 | 2.06 | 0.07 | 0.54 | 0.73 | 1.35 |
| | 100 | 1.21 | 0.90 | 0.31 | 0.55 | 0.75 | 1.36 |
| **3c** | 20 | 1.02 | 2.09 | 0.07 | 0.56 | 0.80 | 1.42 |
| | 50 | 2.05 | 2.12 | 0.07 | 0.58 | 0.81 | 1.39 |
| | 100 | 1.18 | 0.86 | 0.32 | 0.60 | 0.83 | 1.38 |
| **3f** | 20 | 1.99 | 2.06 | 0.07 | 0.52 | 0.70 | 1.34 |
| | 50 | 2.01 | 2.07 | 0.06 | 0.50 | 0.71 | 1.42 |
| | 100 | 1.16 | 0.83 | 0.33 | 0.52 | 0.73 | 1.40 |
| **3i** | 20 | 1.92 | 1.97 | 0.05 | 0.42 | 0.49 | 1.16 |
| | 50 | 1.94 | 1.99 | 0.05 | 0.43 | 0.49 | 1.13 |
| | 100 | 1.13 | 0.83 | 0.30 | 0.46 | 0.52 | 1.13 |




**3a**




**3b**




**3c**

**Figure 7.4. Cyclic Voltammograms of Cu(II) complexes of Unsaturated β-ketoesters**

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Figure 7.4 contd….

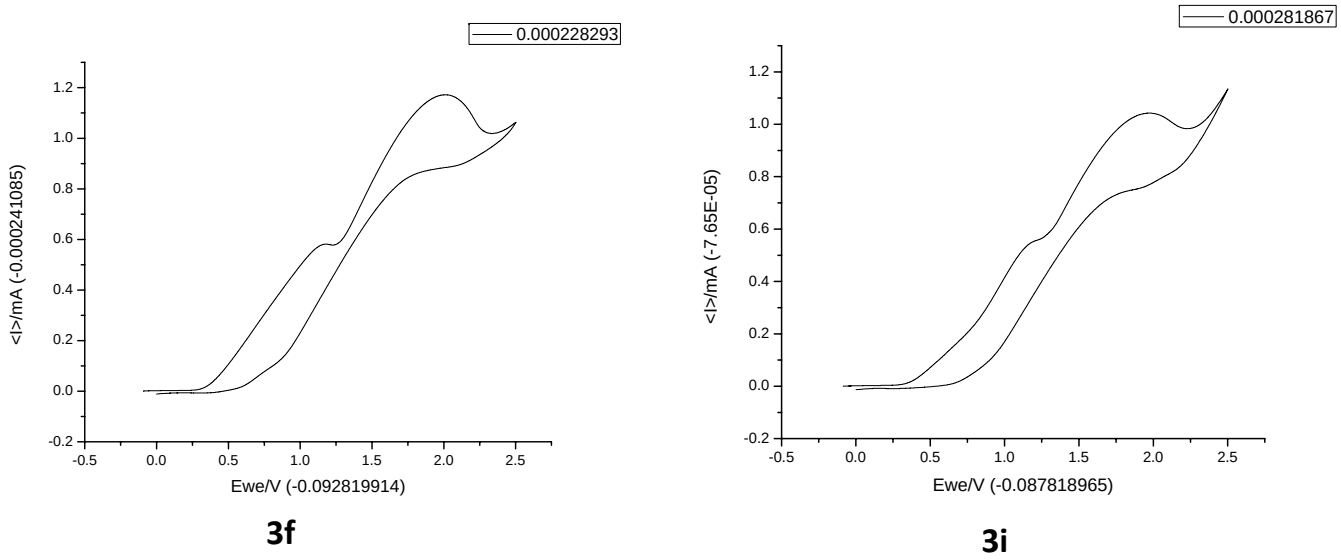



**Figure 7.4. Cyclic Voltammograms of Cu(II) complexes of Unsaturated β-ketoesters**

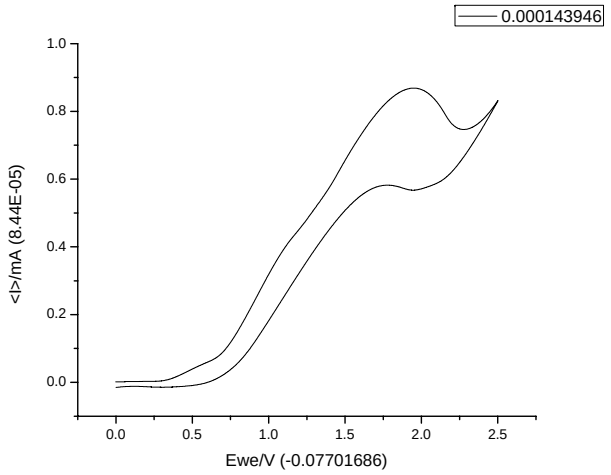
redox processes occur in the coordinated moiety and the peak potential range is 1.8-2.1. The $\Delta E_p$ value is in between 0.05-0.07 which suggests the reversible redox couple. The ratio of anodic peak current and cathodic peak current becomes less than one upon complexation as shown by Cu(II) complexes of curcuminoids. The peak potentials in the range 1.09-1.21 V and corresponding anodic peak potentials in the range 0.80-0.90 V is due to the Cu(II)/Cu(I) redox couple and the observed $\Delta E_p$ and $I_{pa}/I_{pc}$ values clearely indicates one electron quasireversible process.

The unsaturated tetraketones considered in the chapter 4 showed one well defined cathodic and anodic peaks in their cyclic voltammogram. Both the peaks are in the positive potential range. the relevant electrochemical data are given in **Table7.7** and voltammograms are given in **Figure 7.5.** The observed $\Delta E_p$ and $I_{pa}/I_{pc}$ values suggest that the redox processes are reversible in nature and one electron transfer reactions. The observed order of unsaturated tetraketones is **$H_2$ba > $H_2$aa > $H_2$an > $H_2$ma.** Except **$H_2$ma** all the tetraketones have almost similar peak potentials when compared to unsubstituted curcuminoid. **$H_2$ma** showed less positive peak potentials.

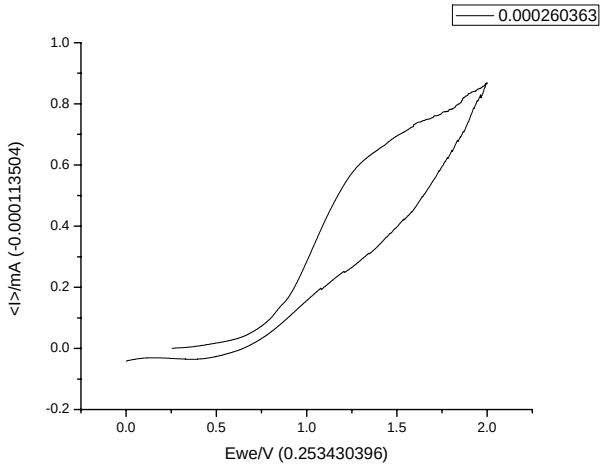
The voltammograms of the Cu(II) complexes of the tetraketones are characterized by the prior of two redox couple. The data are given in **Table7.8 and 7.9** and typical voltammograms are reproduced in **Figures 7.6.** The redox couple in the more positive region is due to the complexed ligand moiety and shifted to more positive region when compared to free ligands.

**Table 7.7: Cyclic voltammetric data of unsaturated tetraketones**

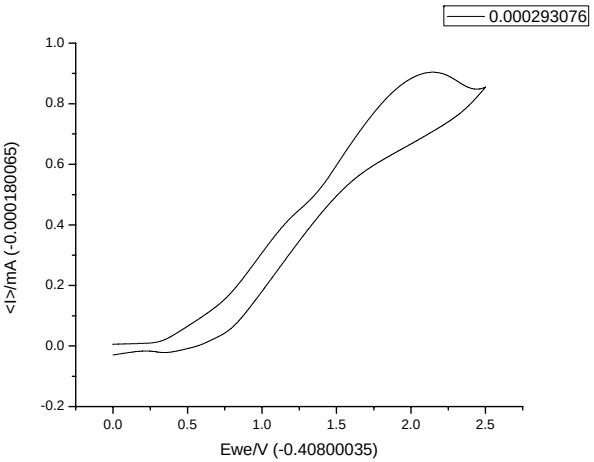
| Compounds | Scan rate | $E_{pc}$ | $E_{pa}$ | $\Delta E_p$ | $I_{pc}$ | $I_{pa}$ | $I_{pa}/I_{pc}$ |
|---|---|---|---|---|---|---|---|
| **$H_2$aa** | 20 | 1.89 | 1.93 | 0.04 | 0.32 | 0.30 | 0.94 |
| | 50 | 1.91 | 1.95 | 0.04 | 0.31 | 0.30 | 0.97 |
| | 100 | 1.94 | 1.97 | 0.03 | 0.30 | 0.29 | 0.96 |
| **$H_2$ma** | 20 | 1.25 | 1.44 | 0.19 | 0.39 | 0.36 | 0.92 |
| | 50 | 1.27 | 1.46 | 0.19 | 0.40 | 0.37 | 0.92 |
| | 100 | 1.29 | 1.49 | 0.20 | 0.40 | 0.38 | 0.95 |
| **$H_2$ba** | 20 | 2.05 | 2.09 | 0.06 | 0.30 | 0.28 | 0.93 |
| | 50 | 2.08 | 2.12 | 0.04 | 0.32 | 0.30 | 0.93 |
| | 100 | 2.10 | 2.13 | 0.03 | 0.33 | 0.30 | 0.91 |
| **$H_2$an** | 20 | 1.77 | 1.83 | 0.06 | 0.34 | 0.33 | 0.97 |
| | 50 | 1.78 | 2.84 | 0.06 | 0.35 | 0.35 | 1.00 |
| | 100 | 1.80 | 1.86 | 0.06 | 0.36 | 0.37 | 1.02 |



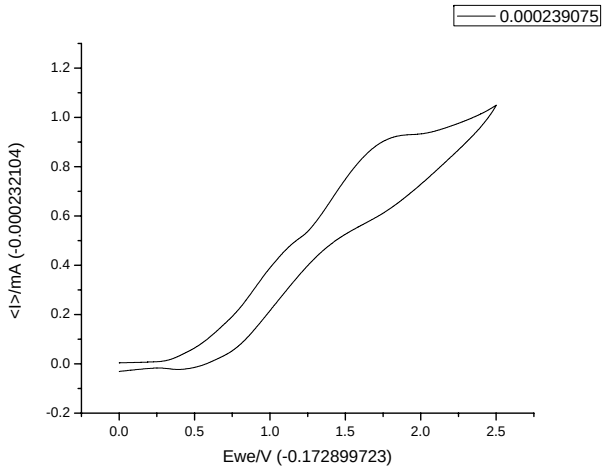

**$H_2$aa**




**$H_2$ma**




**$H_2$ba**




**$H_2$an**

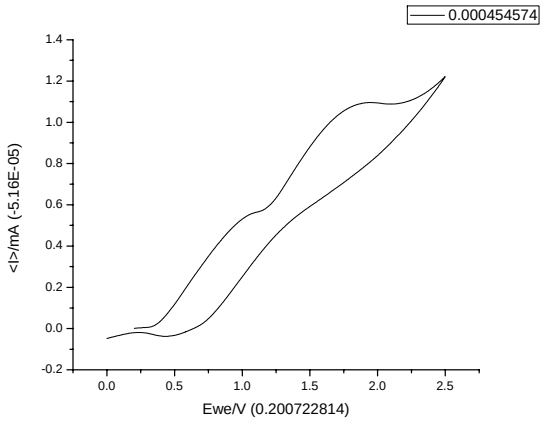
**Figure 7.5. Cyclic Voltammograms of Unsaturated tetraketones**

**Table 7. 8: Cyclic voltammetric data reversible redox process of Cu (II) complexes of the unsaturated tetraketones**

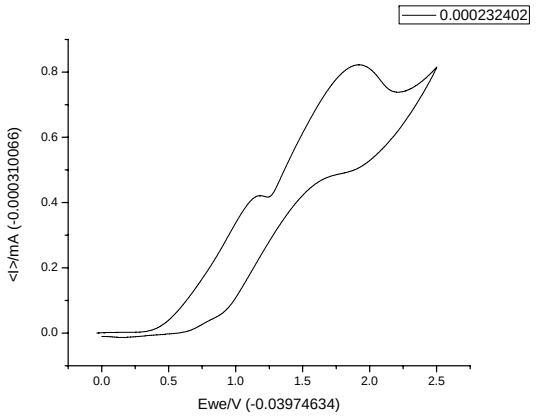
| Compounds | Scan rate | $E_{pc}$ | $E_{pa}$ | $\Delta E_p$ | $I_{pc}$ | $I_{pa}$ | $I_{pa}/I_{pc}$ |
|---|---|---|---|---|---|---|---|
| **[Cu(aa)]** | 20 | 1.98 | 1.93 | 0.05 | 0.40 | 0.38 | 0.95 |
| | 50 | 2.00 | 1.96 | 0.04 | 0.42 | 0.39 | 0.92 |
| | 100 | 2.01 | 1.98 | 0.03 | 0.43 | 0.40 | 0.93 |
| **[Cu(ma)]** | 20 | 1.87 | 1.83 | 0.06 | 0.44 | 0.43 | 0.97 |
| | 50 | 1.87 | 1.91 | 0.04 | 0.45 | 0.44 | 0.97 |
| | 100 | 1.88 | 1.93 | 0.05 | 0.46 | 0.45 | 0.98 |
| **[Cu(ba)]** | 20 | 2.01 | 2.04 | 0.03 | 0.54 | 0.49 | 0.90 |
| | 50 | 2.03 | 2.07 | 0.04 | 0.55 | 0.50 | 0.91 |
| | 100 | 2.05 | 2.08 | 0.03 | 0.57 | 0.52 | 0.91 |
| **[Cu(an)]** | 20 | 1.87 | 1.92 | 0.05 | 0.31 | 0.28 | 0.90 |
| | 50 | 1.89 | 1.95 | 0.06 | 0.33 | 0.30 | 0.91 |
| | 100 | 1.91 | 1.97 | 0.06 | 0.34 | 0.31 | 0.91 |

**Table 7. 9: Cyclic voltammetric data ( quasireversible) of Cu (II) complexes of unsaturated tetraketones**

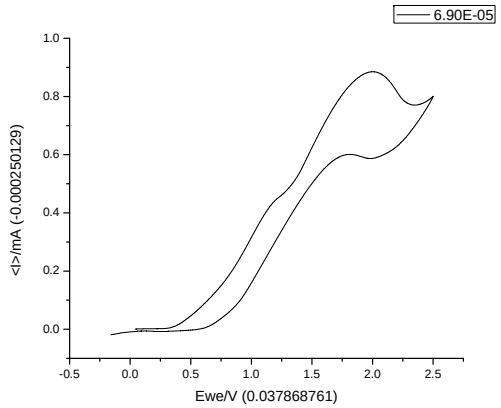
| Compounds | Scan rate | $E_{pc}$ | $E_{pa}$ | $\Delta E_p$ | $Ip_c$ | $Ip_a$ | $Ip_a/Ip_c$ |
|---|---|---|---|---|---|---|---|
| **[Cu(aa)]** | 20 | 1.11 | 0.93 | 0.18 | 0.35 | 0.33 | 0.94 |
| | 50 | 1.13 | 0.96 | 0.17 | 0.36 | 0.35 | 0.97 |
| | 100 | 1.15 | 0.94 | 0.19 | 0.37 | 0.36 | 0.97 |
| **[Cu(ma)]** | 20 | 0.99 | 0.70 | 0.29 | 0.46 | 0.48 | 1.04 |
| | 50 | 1.01 | 0.72 | 0.29 | 0.48 | 0.49 | 1.02 |
| | 100 | 1.02 | 0.74 | 0.28 | 0.49 | 0.49 | 1.00 |
| **[Cu(ba)]** | 20 | 1.18 | 0.85 | 0.33 | 0.58 | 0.73 | 1.25 |
| | 50 | 1.19 | 0.87 | 0.32 | 0.59 | 0.73 | 1.23 |
| | 100 | 1.21 | 0.88 | 0.33 | 0.61 | 0.74 | 1.21 |
| **[Cu(an)]** | 20 | 1.17 | 0.94 | 0.23 | 0.39 | 0.38 | 0.97 |
| | 50 | 1.17 | 0.95 | 0.22 | 0.42 | 0.40 | 0.95 |
| | 100 | 1.16 | 0.96 | 0.20 | 0.40 | 0.40 | 1.00 |



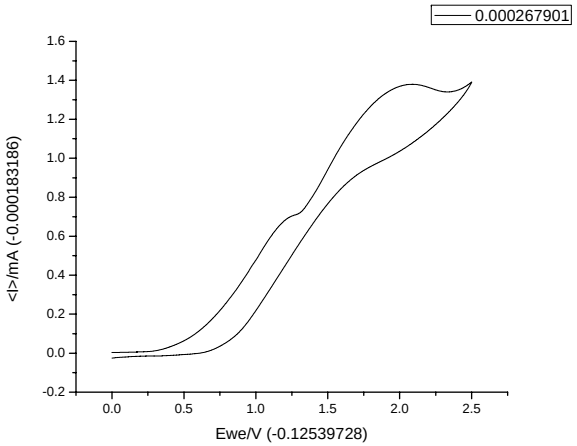

**[Cu(aa)]**




**[Cu(ma)]**




**[Cu(ba)]**




**[Cu(an)]**

**Figure 7.6. Cyclic Voltammograms of Cu(II) complexes of the unsaturated tetraketones**

The observed $\Delta E_p$ and $I_{pa}/I_{pc}$ values suggest the simple one electron reversible process. The cathodic peak potentials in the range 1.15-1.21 V and anodic peak potentials in the range 0.74-0.94 is due to the Cu(II)/Cu(I) redox couple and the observed $\Delta E_p$ and $I_{pa}/I_{pc}$ values suggests one electron quasireversible process.

**Summary**

Cyclic voltammograms of 1,7-diarylheptanoids (curcuminoids) showed one well defined diffusion controlled reversible one electron redox process where both anodic and cathodic potentials are in the positive region. Electron donating groups in the aryl ring shifts both the potentials to more positive region compared to unsubstituted curcuminoids. Two well defined redox couples are displayed upon complexation, one is of the coordinated ligand moiety and the other is due to Cu(II)/Cu(I) redox couple. Both the potentials are in the positive region and the redox couple due to ligand moiety is shifted to more positive values compared to the free ligands. A similar trend has also been observed by the unsaturated β-ketoesters, unsaturated tetraketones and their Cu(II) complexes. But the peak potentials are shifted to less positive values.

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