METAL COMPLEXES OF SOME CONJUGATED β-KETOANILIDES

Thesis submitted to the Faculty of Science,
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requirements for the Degree of ***Doctor of Philosophy*** *in Chemistry*

By

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DECLARATION

I hereby declare that the Thesis bound herewith is an authentic record of the research work carried out by me under the supervision of Dr. K. Krishnankutty, Professor, Department of Chemistry, University of Calicut, in the partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry of the University of Calicut and further that, no part thereof has been presented before for any other Degree.

Muhammed Basheer Ummathur

CERTIFICATE

This is to certify that the thesis bound herewith is an authentic record of the research work carried out by Mr. Muhammed Basheer Ummathur, under my supervision in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry of the University of Calicut, and further that no part thereof has been presented before for any other degree.

Dr. K. Krishnankutty
(Supervising Teacher)

ACKNOWLEDGEMENT

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PREFACE

The variety of applications of metal complexes of organic compounds has become so wide that even in a quite arbitrarily restricted field, an abundance of research in being done. Among such compounds the β-dicarbonyls have a pride of place. The β-dicarbonyls and their metal complexes still serve as the starting material for the design and synthesis of new compounds with interesting structural features and having diverse types of uses particularly in bioinorganic chemistry. Majority of such studies are based on β-diketones. However β-ketoanilides, an important class of β-dicarbonyls, and their metal complexes have not received as much attention as they deserve. Thus unlike β-diketones reports on the synthesis and characterisation of novel structural types of β-ketoanilides and their coordination characteristics are scanty. The present investigation, therefore, has been so designed as to provide ample opportunity for the synthesis and structural investigations of certain new classes of β-ketoanilides and their metal chelates.

The term "conjugated β-ketoanilides" in the title of the Thesis has been used in a broad sense to embrace conjugated diketoanilides and allied derivatives, and the possible tantomaric forms of these types of compounds.

PART I is a general introduction which highlights briefly some of the salient structural features of β-dicarbonyl compounds such as β-diketones, β-ketoanilides, etc. and their metal complexes. Importance of the present investigation has been interspearsed at appropriate places.

PART II is a critical review on metal complexes of β-ketoanilides that appeared in the general literature.

Results of the present investigation are presented in **PART III**.

Mechanistic aspects on the formulation of the different conjugated ketoanilides from the reaction between aromatic aldehydes and acetoacetanilide based on the nature of the aryl groups, the electronic and steric effects of the aryl substitutes are briefly discussed. That the nature of the aryl substituent has considerable influence on the reaction product has been clearly indicated. Thus the products formed are highly dependent on the nature of the aromatic aldehydes employed.

Two types of conjugated ketoanilides and their metal complexes have been synthesised and characterised. The results are discussed in five chapters.

In **Chapter 1, Section 1**, details on the synthesis of the conjugated diketoanilides obtained from the condensation of benzaldehyde and substituted benzaldehydes with acetoacetanilide are given. That the compounds exist in the diketo tautomaric form has been well illuminated using UV, IR, NMR and mass spectral data. The behaviour of these diketoanilides as neutral ligands in 1:1 complexes of Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+} and Cd^{2+} are clearly indicated. The spectral data unequivocally showed that only the diketo function is involved in bonding with the metal ion and the enolised cinnamoyl carbonyl remains unaffected in complexes. In **Section 2** details on the synthesis and characterisation of conjugated β-ketoanilides are discussed. Spectral data clearly indicated the existence of the compound in the intramolecularly hydrogen bonded enol tautomeric form. The monobasic bidentate nature of compounds in Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+} and Cd^{2+} complexes are clearly evident from their physical, analytical and spectral data.

In **Chapter 2 Section I** details on the synthesis and characterisation of the β-ketoanilides derived from naphthaldelyde and 2-hydroxy-1-naphthaldehyde, and their metal complexes are presented. The corresponding conjugated diketoanilides and their metal complexes are discussed in **Section 2**

Chapter 3 is mainly on the synthesis and characterisation of a highly conjugated β-ketoanilide formed by the condensation of cinnamaldehyde and acetoacetanilide. Another interstring product fromed during the reaction has been characterised as a Schiff base of the β-ketoanilide with n-butylamine, the condensing agent used in the reaction. That the β-ketoanilides exist in the intramolecularly hydrogen bonded enol from is clearly indicated from various spectral data. Spectral and analytical data of the complexes conform to the replacement of enol proton by metal ion with the formation of a 6-membered chelate ring. In the metal complexes of the Schiff base the azomethine nitrogen and carbonyl oxygen are involved in the formation of the chelate ring.

Conjugated ketoanilides containing heteroaryl groups (furyl and pyridyl) are considered in **Chapter 4**. The structure and tautomric nature of the compounds and nature of bonding of their typical metal complexes are discussed on the basis of IR, NMR and mass spectral data.

Results obtained from antifungal studies of some of the conjugated ketoanilides and their metal complexes are also included.

Synthesis and characterisation of three unsaturated β-ketoesters and their copper complexes are discussed in **Chapter 5**.

In **PART IV** references are given in serial order.

NOMENCLATURE AND ABBREVIATIONS

The β-ketoanilide, acetoacetanilide, is systematically named as 3-oxo(N-phenyl)butanamide. Many of the unsaturated β-ketoanilides considered in the present investigation contain two carbonyl groups apart from the anilide carbonyl. Therefore, the compounds have been named as triketones. Thus, the conjugated β-ketoanilides are systematically named by considering them as diketones and the conjugated diketoanilides as triketones. Systematic names of all the compounds have been provided at appropriate positions in the Thesis. However, for brevity and better readability, trivial names of the compounds, rather than their polysyllabic systematic names, have also been used freely wherever necessary. Important abbreviations used in the Thesis are

acac	Acetylacetonato
acacH	Acetylacetone
acan	Acetoacetanilido
Ar	Aryl group
BM	Bohr Magneton
DMF	Dimethylformamide
DMSO	Dimethyl sulphoxide
Et	Ethyl
FAB	Fast atom bombardment
Fig.	Figure(s)

h	Hour
H_z	Hertz
J	Coupling constant
L	Deprotonated ligand
M.P	Melting point
OAc	Acetate
OPr^i	Isopropyl
Ph	Phenyl group
ppm	parts per million
tlc	thin layer chromatography
$\in$	molar extinction coefficient
μ_{eff}	effective magnetic moment in Bohr magnetons

UV-visible absorption maxima (λ_{max}) are given in nm/cm^{-1} as indicated. The infrared bands are given in cm^{-1}.

Chemical shifts in ^{1}H NMR spectra are expressed as δ values (ppm downfield from tetramethylsilane, TMS).

While reporting mass spectral data, P^+ represents the parent ion (molecular ion). In the case of metal complexes, the m/z of P^+ correspond to the most abundant isotope of the concerned metal atoms.

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CHAPTER 1

Section 1

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CHAPTER 2

Section 1

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PART I

GENERAL INTRODUCTION

GENERAL INTRODUCTION

Coordination chemistry of β-dicarbonyl compounds

The progress in studies of coordination compounds was rapid, perhaps partly because of the utility and economic importance of metal chemistry, but also because of the intrinsic interest of many of the compounds and the intellectual challenge of the structural problems to be solved[1,2]. There has been a great deal of growth in the field of coordination chemistry during the last few decades which has not only led to fuller understanding of the nature of many complex entities, but also has been instrumental in bringing the various branches of chemistry closer to one another[3,4].

The properties and structure of a metal complex are dependent on the nature of the metal ion and also of the ligands[5-11]. The variations in metal ions are considerable, on the other hand, the variations in ligands are virtually limitless because of the extent of organic chemistry available for the synthesis of suitable molecules. One of the fascinating area of modern coordination chemistry is the ever increasing academic, industrial and biological interest exhibited by metal complexes of organic ligand systems. Thus design and synthesis of polydentate ligand systems have become an interesting and useful activity in recent years.

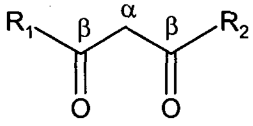
The variety of applications of metal complexes of organic compounds have become so wide that even in a quite arbitrarily restricted field, an abundance of research is being done. The story of metal complexes of β-dicarbonyl compounds provides a typical example for this[12-18]. The β-dicarbonyl compounds have over the years been of considerable interest to organic, inorganic, physical and analytical chemists.

The organic chemists have use of them chiefly as β-ketoesters in such reactions as the malonic ester synthesis, the Knoevenagel condensation, the Michael addition, the reverse Claisen condensation, etc. The inorganic chemists have found β-dicarbonyls to be useful chelating ligands and have often been fascinated by the variety of ways in which these can bond to metallic or metalloidal atoms to give varied molecular strucutres[19]. The analytical chemists have developed several indigenous methods for the qualitative and quantitative determination of metal ions from diverse matrices by exploiting the complexing ability of different β-dicarbonyl compounds[20-30]. The physical and theoretical chemists have used them mainly to study the various aspects of keto-enol tautomeric equilibrium.

It is now well established that proton transfer and hydrogen bonding are two important aspects of chemistry that are also necessary for the maintenance of life itself[31-44]. The β-dicarbonyl compounds exhibit both these features and have singled them out for the detailed study for many years. Literature reveals that ligand systems based on β-dicarbonyl type compounds have proliferated much during recent years. This trend is evident from the reports of numerous ligand systems based on β-dicarbonyl compounds[19,60,65-77]. This is not unexpected of these types of compounds because of the vast potential of their structures that permit the design and synthesis of compounds having wide applications in diverse fields. **The present investigation is mainly on the synthesis and characterisation of a new series of β-dicarbonyl compounds and their typical metal complexes.** Therefore, some of the salient structural features of 1,3-dicarbonyl compounds particularly the keto-enol tautomerism and coordination behaviour that are useful to the present study are briefly discussed below.

Keto-enol tautomerism of β-dicarbonyl compounds

The class of β-dicarbonyl compounds include both cyclic and acyclic compounds and the basic structural unit is of the type–CO-X-CO- where X can be hetero atoms such as O (acid anhydride), NH (imide), etc. or carbon atoms. Since the present investigation is mainly on β-dicarbonyls in which the two carbonyl groups are interposed between a carbon or substituted carbon atom, the discussion is restricted to such compounds. That is the β-dicarbonyl compounds discussed here are of the structural type **1** where a methylene or a substituted methylene group is flanked by two carbonyl groups.



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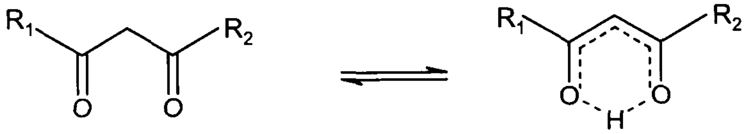
Depending up on the nature of R_1 and R_2 groups, the compounds are named accordingly. Some of the important and most familier β-dicarbonyl compounds are given in table 1.1. Structurally these 1,3-dicarbonyl compounds exist in solution as mixtures of keto **1** and enol **2** forms related by a 1,3-hydrogen shift.



1 **2**

Table 1.1

Common types of β- dicarbonyl compounds, $R_1–CO–CH_2–CO–R_2$

R_1	R_2	Type	Typical Example
Alkyl	Alkyl	β-diketone	Acetylacetone
Alkyl	Aryl		Benzoylacetone
Aryl	Aryl		Dibenzoyl methane
Hetero aryl	Alkyl		Thenoyl trifluoroacetone
Alkyl	Hydroxy	β-keto acid	Acetoacetic acid
Aryl	Hydroxy		Benzoylacetic acid
Hydroxy	Hydroxy		Malonic acid
Alkyl	Alkoxy	β-ketoester	Methylaceto acetate
Alkoxy	Alkoxy		Malonicester
Alkyl	Amino	β- ketoamide	Acetoacetamide
Aryl	Amino		Benzoylacetamide
Alkyl	Arylamino	β- ketoanilide	Acetoacetanilide
Aryl	Arylamino		Benzoylacetanilide

A variety of factors such as solvent, temperature, α-substituent, β-substituent and the presence of other species that are capable of hydrogen bonding influence the relative amount of the enol and keto forms present. In general bulky alkyl substituents present on the α-carbon leads to decreased amount of enol tautomer while Cl, Br, CN, CO_2CH_3, SCH_3 etc. groups lead to almost 100% enol from[45-50]. Replacement of the terminal methyl groups of acetylacetone by an electron withdrawing or aromatic groups such as CF_3, C_4H_3S (2-thienyl), C_6H_5, etc. shift the equilibrium in favour of the enol tautomer. Thus hexafluoroacetylacetone in CS_2 and dibenzoylmethane in CCl_4 exist entirely in the enol form[51]. Among the unsubstituted β-dicarbonyls also the percentage of enol form depends on the nature of the R_1 and R_2 groups[51-52] as is evident from table 1. 2.

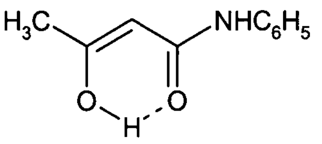
Table 1.2

Enol content of some common β-dicarbonyl compounds

Compound	Enol content (%)
CH_3– CO–CH_2– CHO	98
CH_3–CO–CH_2–CO–CH_3	76
C_6H_5–CO–CH_2–CO–CH_3	100
C_6H_5–CO–CH_2–CO–C_6H_5	100
CH_3–CO–CH_2–CO–NH–C_6H_5	13
CH_3–CO–CH_2–COOEt	7
EtOOC–CH_2–COOEt	<1%
CH_3–CO–CH_2–CO–NH_2	<1%

The reason for the low enol contents of acetoacetanilide and ethyl acetoacetate is due to the involvement of N and O lone pair in diminishing the electron deficiency on the carbonyl carbon[53]. It may be noted in this context that diethyl malonate in which both the carbonyl groups are connected to oxygen is negligibly enolised[54]. β-Ketoamines do not enolise and their deprotonation is extremely difficult[55].

In unsymmetrically substituted β-dicarbonyl compounds the direction of enolisation mainly depend on the electron demand on the carbonyl carbons. In benzoylacetone the benzoyl carbonyl undergo enolisation[56]. In phenyl substituted β-dicarbonyls such as dibenzoylmethane the phenyl groups bearing an electron releasing substituent such as -OCH_3 do not undergo enolisation[56]. Thus it is obvious that in acetoacetanilide and in ethylacetoacetate the enolisation will be mainly through acetyl carbonyl, though the enol content is very low as indicated by structures **3** and **4**.



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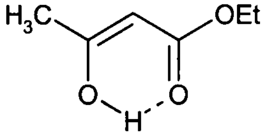

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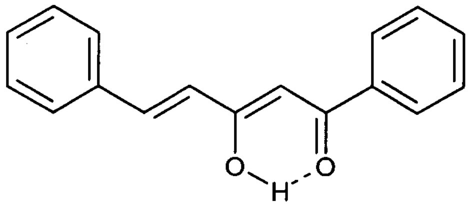
In cinnamoylbenzoylmethane, the direction of enolisation is towards the cinnamoyl carbonyl[57] which clearly reveal the increase in enolisation due to conjugation **5**. The rate of enolisation also depend on the electronic environment of the α-carbon substituent. Thus α-chloroacetoacetanilide[52] and α-benzoylacetoacetanilide[58] are 27% and 85% enolised respectively while α-alkylacetoacetanilide[59] exist entirely in the keto form.



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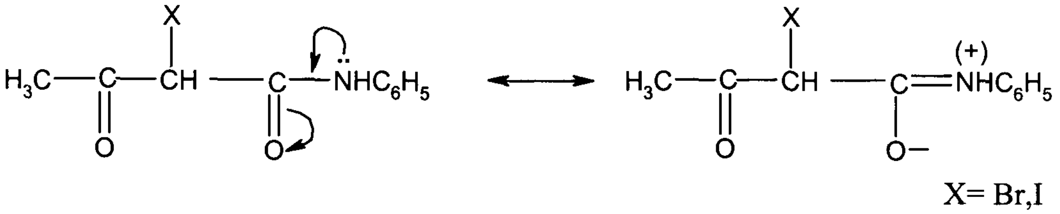
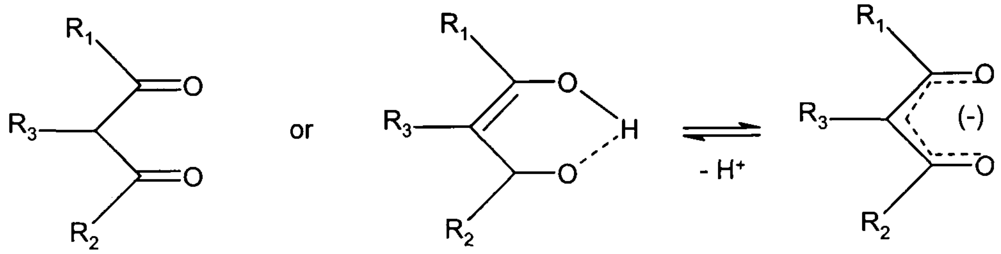
Since the resonance forms of the chelate ring of acetoacetanilide are not equivalent as in acetylacetone and dibenzoylmethane, the resonance energy of the former is very low. In contrary to the above observed factors of enolisation, the enol contents of α-bromo and α-iodoacetoacetanilides[52] are lower than that of acetoacetanilide itself. This is due to the greater stablilisation of the diketo form through amide resonance compared to the resonace stablilisation of the enol form as indicated below.



Metal complexes of β-dicarbonyl compounds

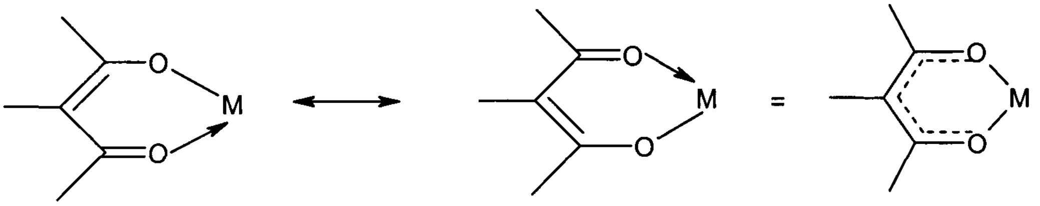
The coordinating ability of β-dicarbonyl compounds was recognised as early as in 1887 when Combes reported[60] the synthesis of berylliumacetylacetonate. This was followed by the pioneering works of Werner[61], Morgan[62,63] and Sidgwick[64] who confirmed the bifunctional chelating character of β-dicarbonyl compounds. Being powerful complexing agents, many types of β-dicarbonyl compounds form complexes with virtually all the transition and main group elements. Although the most familiar mode of coordination of β-dicarbonyls is as monobasic bidentate, several other interesting mode of bonding involving even the alkyl carbons are also known. Different types of bonding modes reported of β-dicarbonyl compounds are given below.

1. ***β-Dicarbonyls as a monobasic bidentate chelating ligand*:** The methylene proton in the keto form **6** and OH proton in the enol form **7** of 1,3-dicarbonyl compounds are acidic and their removal generates the 1,3-dicarbonyl anion **8**. This ion can form bond with metal ions and they constitute to an extremely broad class of coordination compounds.



6 **7** **8**

The anion form stable chelates with almost all metals and metalloid elements in the periodic table. The high stability is due to quasiaromatic six membered ring structure of the chelate and delocalisation involving metal ion of the C_3O_2M ring system as in structure **9-11**.



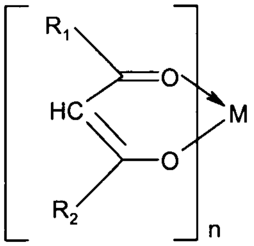
9 **10** **11**

Since the enolate ion carries a single negative charge metal atoms can react with one or more enolate ions to give either neutral molecules or charged molecules depending on the coordination number(m) and valency (n) of the central metal atom. Thus three cases may arise in this bonding mode.

a) When m = 2n: The complex behaves as an inner complex of the structure 12.

b) When m>2n: The complex formed behaves as a lewis acid and achieves the desired coordination either by polymerisation or by adduct formation **13**.

c) When m<2n: Complex of the type **14** is typical of this mode of bonding.



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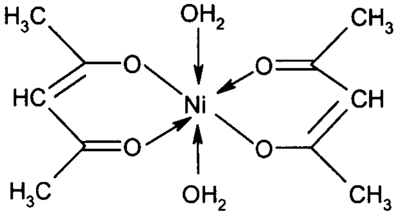

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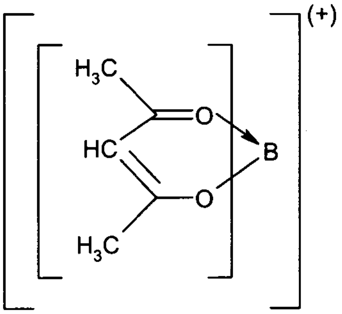

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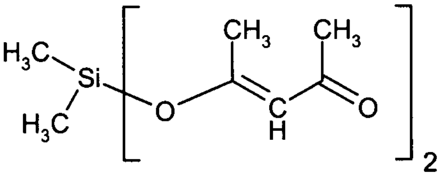
2. ***Coordination of the enol form*:** A typical example of this type of bonding mode is the silicon complex[60] **15**.



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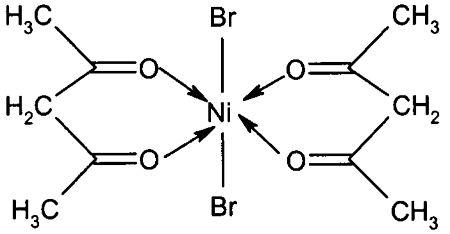
3. ***β-Dicarbonyl as neutral ligand*** **:** Bidentate coordination of the neutral diketo form[65-68] lead to the formation of complexes of the type **16** and **17**.



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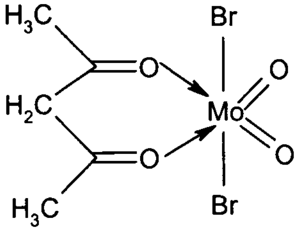

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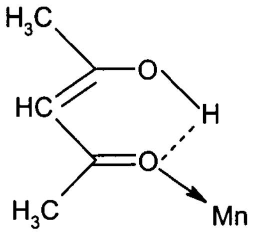
Examples are also known for the neutral monodentate coordination of the enol form[66] as in structure **18**.



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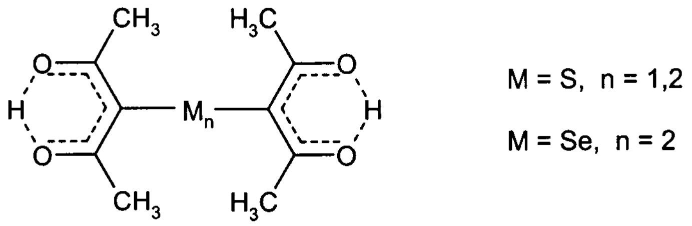
4. ***Carbon bonded β-diketonate complexes***: Interesting complexes of the type **19-23** where the methylene carbon is involved in bonding with metal, excluding the carbonyl groups from coordination[69-71] are well known.



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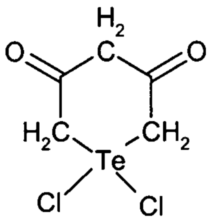

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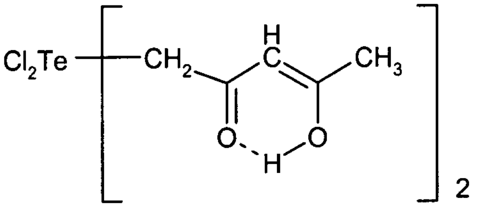

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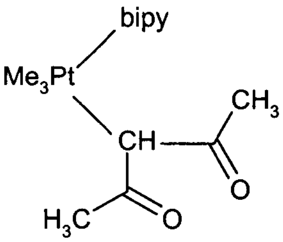

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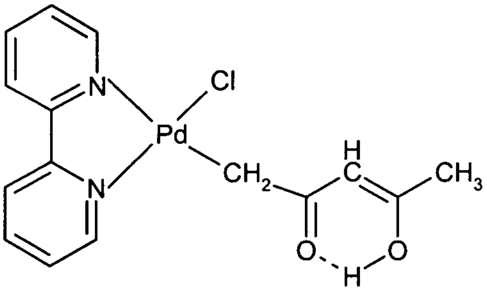

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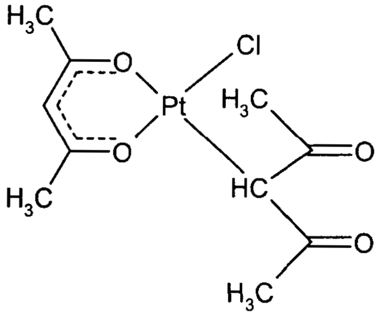
5. ***Both carbon bonded and oxygen bonded complexes*:** Metal β-dicarbonyls in which the metal atom is bonded to one ligand moiety *via* two carbonyl oxygen while the other through the methylene carbon atom are also quite common[69-71]. A typical example is given in structure **24**.



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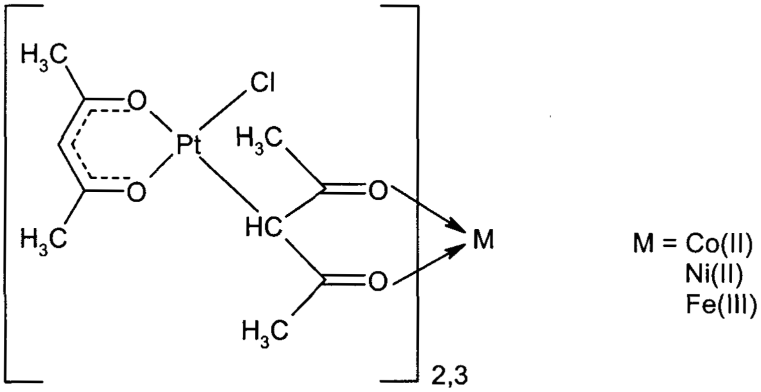
6. ***Carbon bonded β-dicarbonyl group chelating through its carbonyl group of the keto form*:** That the two oxygen atoms of the carbon bonded acetylacetone group retain their ability to coordinate to a metal through the diketo groups was first demonstrated by Lewis and Oldham[72] by preparing complexes of the type **25.**



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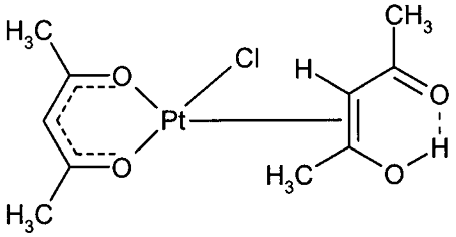
7. ***As a π donar ligand*** **:** The complex [Pt(acac)$_2$Cl] (one acac normal and other carbon bonded) on acidification forms [Pt(acac)(acacH)Cl] in which

acacH (previously carbon bonded acac) become bonded to the metal through only its C=C bond[19,73,74] as in structure **26**.



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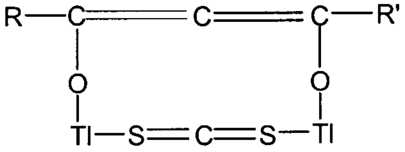
8. ***As a bridging ligand*****:** In presence of CS_2 β-dicarbonyl compounds attach to Tl as bridging dienolate anion[75] and form complex of the type **27**.



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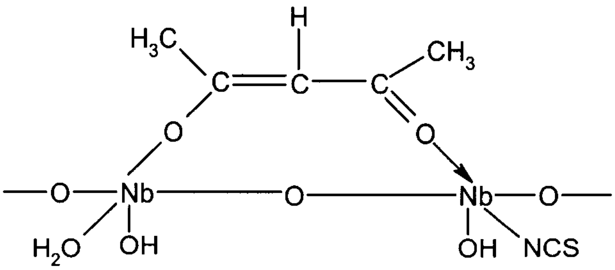
Bridging complexes of the structural type **28** have also been reported for certain metal acetylacetonates[76,77].



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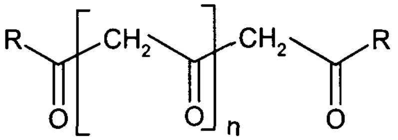
Polyketones and their metal complexes

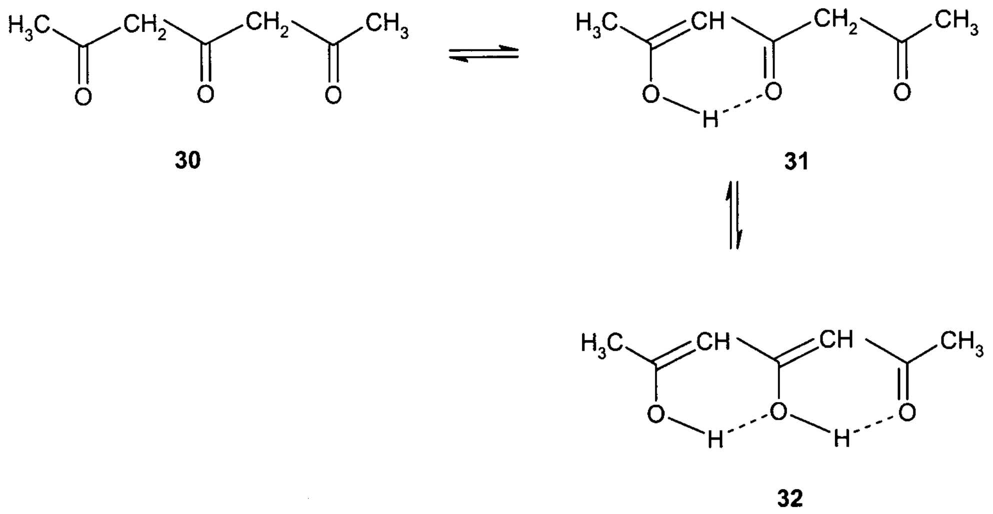
The higher homologues of 1,3-dicarbonyl compounds of the type **29** have considerable importance in the design and synthesis of multidentate ligand systems that can function as model compounds in various bioinorganic studies. Thus a large number of 1,3,5-tricarbonyls, 1,3,5,7-tetracarbonyls, etc. compounds and their derivatives have been synthesised and characterised. Many of these compounds are known to exhibit certain important biological functions exhibited by living system[103]. Their biological functions are mainly due to their ability to form complexes with various biologically important metal ions. Therefore, studies on the coordination behaviour of polyketones have tremendous importance in modern coordination chemistry. The ligand properties of polyketones are so vast. Some of the well studied complexes of tri and tetracarbonyl compounds are briefly cited here.

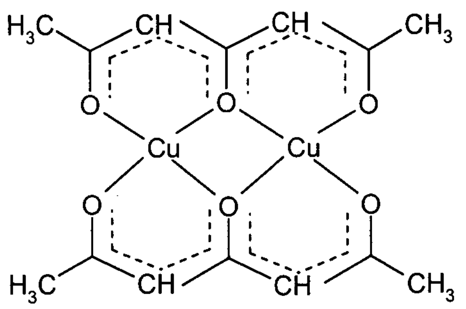


29

n = 0; 1,3-diketone
n = 1; 1,3,5-triketone

The simplest polyketone is the triketone, 1,3,5-heptanetrione[78]. The compound can form different types of tautomeric forms[79] such as in structure **30-32**. These types of polyketones can exhibit a great versatility of structure depending on the nature of the substituent groups present on the various carbon atoms. 2,4,6-Heptanetrione were reported to from 1:1 **33** and 1:2 **34** complexes with Cu(II)[79].





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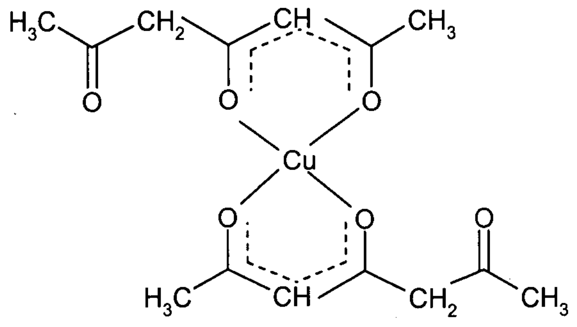
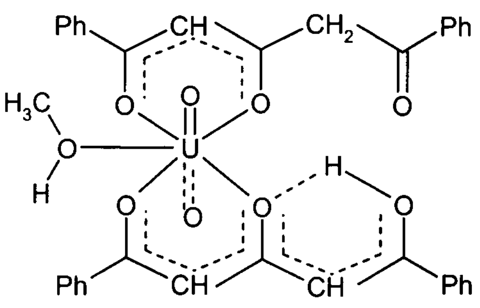


34

1,5-Diphenyl-1,3,5-pentanetrione form complex with UO_2^{2+} of the type **35**. The two terminal noncoordinated oxygens are used to bind a second metal ion to form complex **36**[77].



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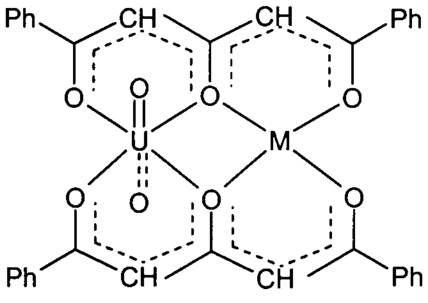
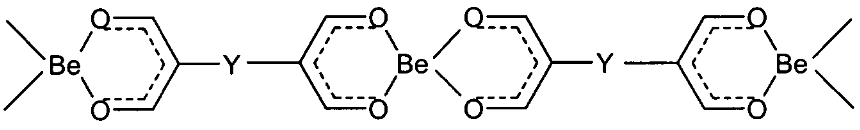


36

Coordination polymers of structure **37** and **38** with oligomeric 1,3-diketonate ligands have also been reported[78-80].



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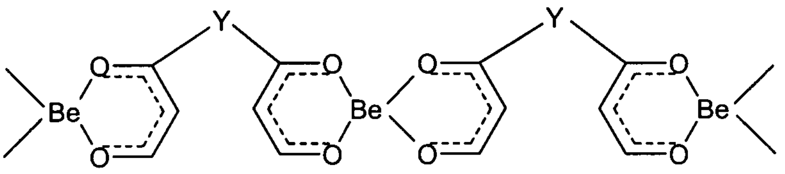
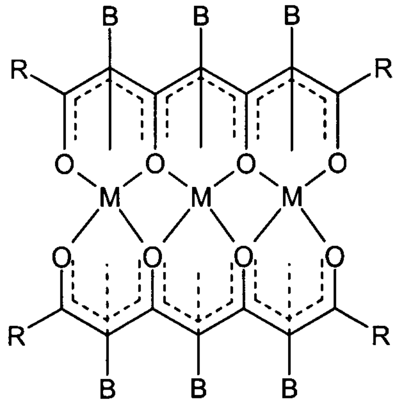


Y = CH_2SCH_2 or CH_2

38

Tetraketone such as 1,7-diphenyl-1,3,5,7-heptanetrione can form complex of the type **39** with different metal ions[79,80,83,84]. Complexes of these polyketones of the type **40-42** with two or more metal ions have also reported[83].



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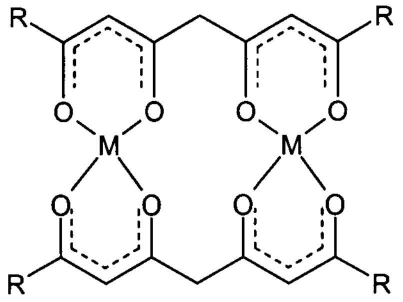

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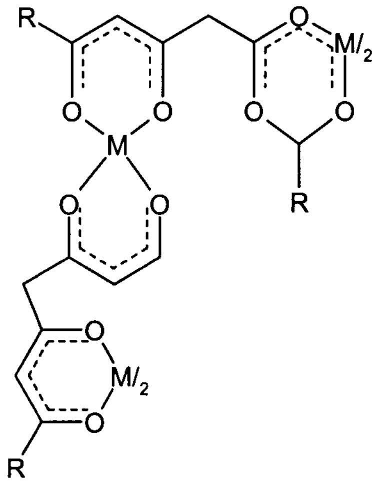

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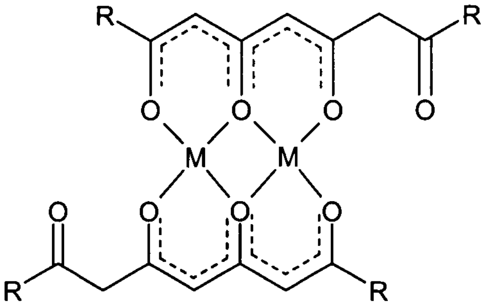
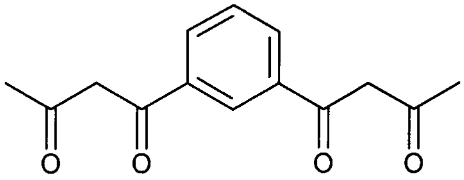


42

Tetraketone of the structure **43** and **44** are well characterised[85]. Their metal complexes have also been studied in view of their importance as model compounds in bioinorganic chemistry.



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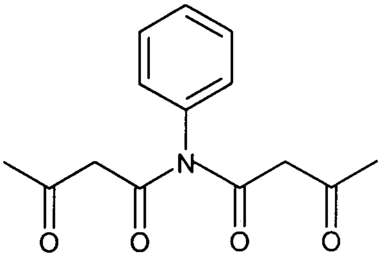
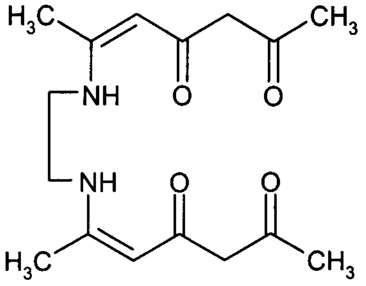


44

Similarly metal complexes of several schiff's base derivatives of polyketones of the type **45** and **46** have studied in detail[86] in view of their importance as model compounds.



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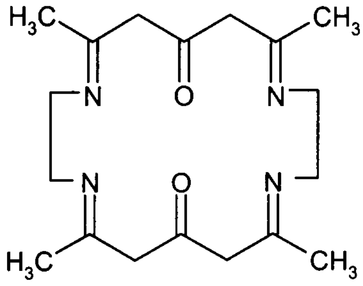


46

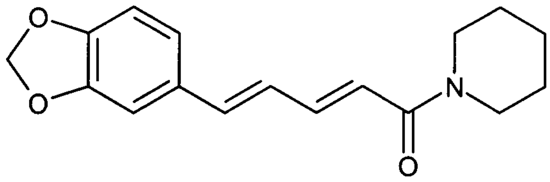
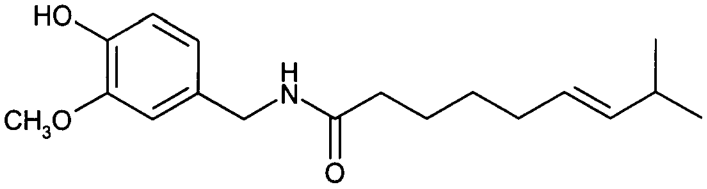
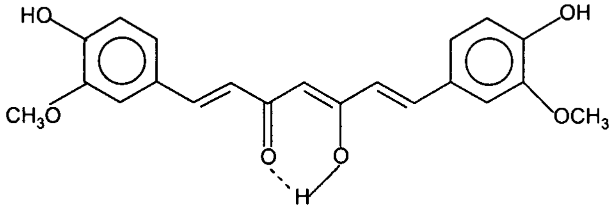
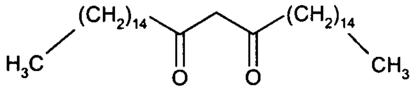
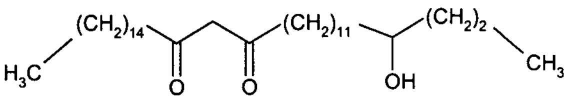
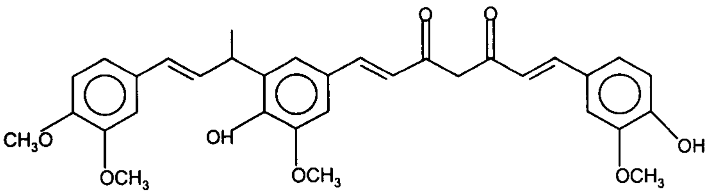
Applications of metal complexes of β-dicarbonyl compounds

Metal complexes of 1,3-dicarbonyls and allied derivatives have a number of practical applications in addition to those mentioned earlier. Some of the well established uses of these types of compounds are mentioned below.

Partially fluorinated 1,3-diketones can from complexes with lanthanide cations and due to the presence of vacant coordination sites they are used as NMR shift reagents[87-90]. These lanthanide complexes are volatile and hence act as precursors for the synthesis of lanthanide containing superconductors by vapour deposition. This procedure is popularly known as chemical vapour deposition (CVD)[91]. The chromium acetylacetonate [Cr(acac)$_3$] in appropriate molar ratio can be used for the measurement of carbon-13 NMR spectra in reducing the normally long longitudinal relaxation times[92-94]. Rare earth metal diketonates are used as potential laser materials[95,96]. Fluorinated β-diketone ligands are used in quantitative analysis especially in the gas chromatographic separation of various metals[97,98]. For instance the measurement of the ultra trace levels of beryllium in polluted air can be carried out with trifluoroacetylacetone. 1,3-Diketones and their complexes are widely used in solvent extraction procedures in qualitative and quantitative analysis[99,100].

Extensive literature is available on the chemical and structural aspects and diverse type of synthesis and other applications of various types of 1,3-dicarbonyl compounds. However, it is to be pointed out that with very few exceptions[15,18-19] all of the reported works contain alkyl/ aryl substituents attached to the carbonyl group. Only very few reports[101,102] are available on 1,3-dicarbonyl compounds in which the carbonyl groups are directly attached to olefinic linkages. Such unsaturated carbonyl compounds are of considerable importance in view of the fact that several biologically important medicinal plants contain compounds having these types of olefinic linkages attached to the carbonyl groups[103]. One of the best known examples is curcuminoids, the active chemical constituent of the herbaceous Indian medicinal plant turmeric (*Curcuma longa,* Linn, *Zingiberacea* family) and related species. Similarly there are several other plant species especially spices which contain carbonyl groups directly linked to olefinic group that constitute the major chemical principle responsible for their biological activity. Typical examples for these types of compounds of plant origin are brought out in table 1.3.

Table 1.3
Active constituents of some common spices and medicinal plants

Spice (Plant species)/ Active principle	Structure
Black pepper (*Piper nigrum*) Piperine	
Red pepper (*Capsicum annum*) Capsaicin	
Turmeric (*Curcuma longa*) Curcumin I	
Eucalyptus (*Eucalyptus globulus)* n-Tritri acontan-16,18-dione	
4-Hydroxy-tritri acontan-16,18-dione	
Indonesian medical ginger (*Zingiber cassumunar*) Cassumunin A	

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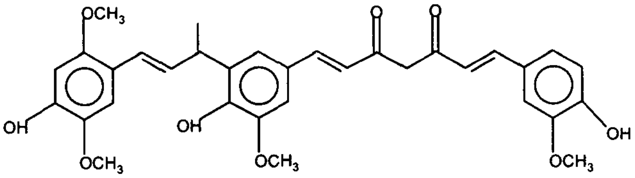
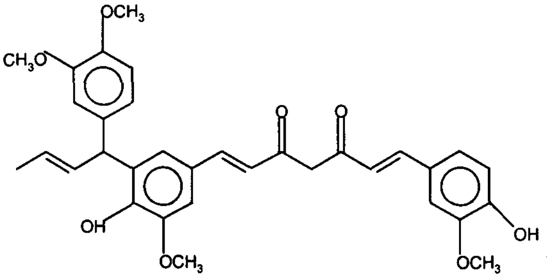
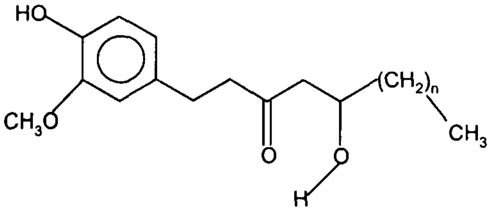
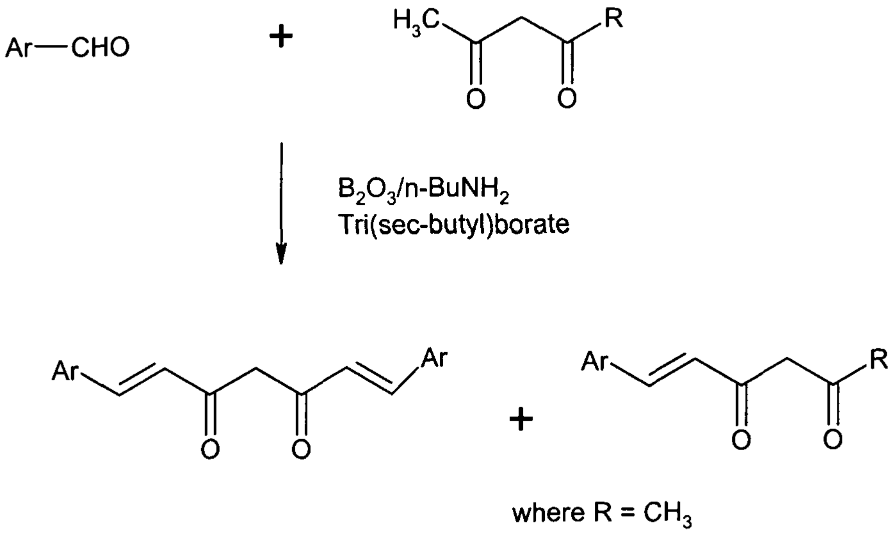
Spice (Plant species)/ Active principle	Structure
Cassumunin B	
Cassumunin C	
Ginger (*Zingiber officinale*) Gingerols	 n = 2, 4, 6 and 8

The table reveals that unsaturated carbonyl compounds in which carbonyl groups attached to nitrogen or substituted nitrogen are also dominant in medicinal plant chemistry. Thus studies on 1,3-dicarbonyl compounds containing nitrogen groups attached to the carbonyl functions have considerable significance. In recent years numerous reports appeared on the synthesis, characterisation and biological applications of compounds structurally related to curcuminoids (1,7-diarylheptanoids) and their metal complexes[104,105]. However, reports on 1,3-dicarbonyl compounds of the types β-ketoanilides and β-ketoesters, in which the carbonyl groups directly attached to olefinic groups are scanty. These unsaturated β-ketoanilides and β-ketoesters and their metal complexes may also have several interesting applications in addition to their structural and coordination behaviour. **The present investigation has been so designed as to provide some insight in this direction on β-ketoanilides and β-ketoesters in which keto group is directly linked to an olefinic group**.

An efficient synthetic route for the formation of unsaturated 1,3-dicarbonyl compounds such as the curcuminoids is the reaction between suitable aromatic aldehydes and 1,3-diketones such as acetylacetone, benzoylacetone, etc. under specified conditions[53,104,226,227]. Usually the condensing agents for an efficient synthesis are B_2O_3, tri(sec-butyl)borate and n-butylamine as illustrated in the reaction scheme 1.1

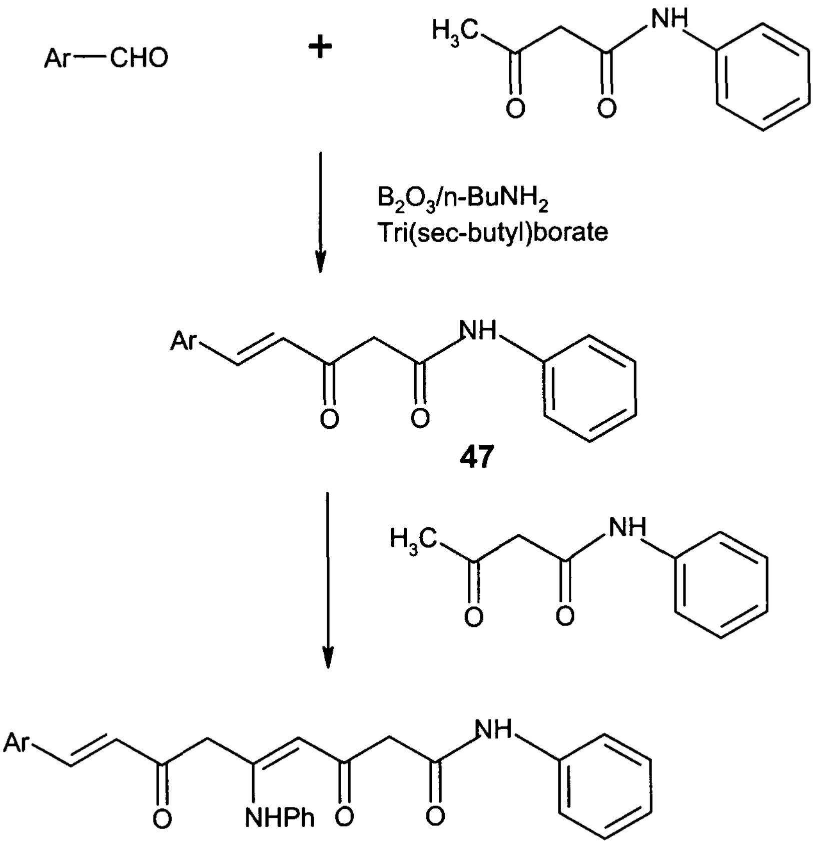


Scheme 1.1

The monocondensation product (6-arylhexanoids) can be separated from the biscondensation product (1,7-diarylheptanoids) by column chromatography. This is a well established method for the synthesis of unsaturated β-dicarbonyl compounds starting from β-diketones that contain at least one methyl group capable of forming a carbanion under the experimental conditions so that only the Claisen type condensation will take place. The Knoevenagel condensation possible in this reaction is effectively prevented by B_2O_3 and tri(sec-butyl)borate. A boron complex that formed protects the methylene carbon from undergoing the Knoevenagel type condensation. This reaction has been well studied for the synthesis of a number of α,β-unsaturated diketones and the products obtained possess number of biological applications especially antitumour activity[255-258].

The present investigation

In the present study, the reaction in Scheme 1.1 of Pabon[227] was adopted with suitable modifications for the synthesis of a new series of unsaturated β-ketoanilides and β-ketoesters. However, it is to be expected that β-ketoanilides such as acetoacetanilide and β-ketoesters like methylacetoacetate may exhibit significant deviation in reactivity towards araldehydes compared to 1,3-diketones such as acetylacetone and benzoylacetone. This is mainly because of the presence of amide and ester carbonyl groups in the former type of compounds. Because of the electronic effects of amide and ester carbonyl groups in acetoacetanilide and methylacetoacetate, reactions other than the normal Claisen condensation can occur as illustrated in the reaction scheme 1.2.



Scheme 1.2 **48**

From the above reaction scheme, it is quite evident that β-ketoanilides such as acetoacetanilide can be utilised as a highly useful starting material for the synthesis of not only the unsaturated β-ketoanilide of type **47**, but also unsaturated diketoanilide of the type **48**. Thus under appropriate conditions β-ketoanilides are good synthetic reagents for the design and fabrication of polyketones having interesting properties and applications. This potential of acetoacetanilide has been properly exploited in the present investigation. Thus the synthesis and characterisation of certain novel derivatives of β-ketoanilides and their coordination behaviour are studied in this investigation. To get a clear understanding on the need of further studies in this field has clearly been brought out in the form of a review on the scanty data available on β-ketoanilides and their metal complexes in **Part II** of the Thesis.

METAL COMPLEXES OF SOME CONJUGATED β-KETOANILIDES

Thesis submitted to the Faculty of Science,
University of Calicut in partial fulfilment of the
requirements for the Degree of ***Doctor of Philosophy*** *in Chemistry*

By

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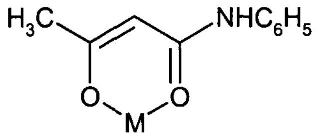
PART II

METAL COMPLEXES OF β-KETOANILIDES – A REVIEW

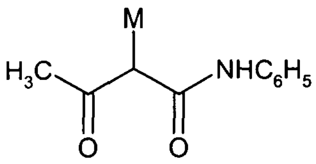
METAL COMPLEXES OF β-KETOANILIDES – A REVIEW

Introduction

Like β-diketones, β-ketoanilides, are known to form diverse types of complexes with various transition and non-transition elements. However, majority of the reported complexes of β-ketoanilides are based on acetoacetanilide and their derivatives. Therefore, metal complexes of acetoacetanilides are mainly considered in this critical review. In the case of 1,3-diketones a variety of coordination modes exist as mentioned in **Part I** of the Thesis. Many of these coordination modes are also exhibited by acetoacetanilides. However, the most important mode of coordination of acetoacetanilides is through the carbonyl oxygens of the monoenol form as in structure **1**. In this structure acetoacetanilide functions as a monobasic bidentate ligand. Other important coordination modes reported are represented in structures **2** to **4**.



1



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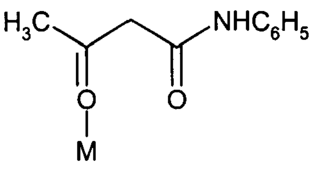

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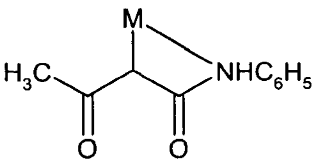

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Metal complexes of acetoacetanilides

As early as in 1886, Knorr[105a] reported the formation of a copper(II) complex of acetoacetanilide, the β-ketoanilide. Later Chaplin and Hunter[105b] prepared the complex in pure state during their studies on the associating effect of the enolisable hydrogen of acetoacetanilide and this second report in this field appeared only after 50 years, around 1940[105b]. Since then numerous reports exist on the synthesis, characterisation and applications of metal complexes of acetoacetanilides and allied derivatives. Majority of these complexes are O,O-bonded. Isolated reports exist on complexes containing other bonding modes also. For brevity and better readability reported metal complexes of acetoacetanilides and allied derivatives that appeared in the general literature have been briefly discussed below under several headings.

Metal complexes of O,O-bonded acetoacetanilides

Stable metal complexes containing only acetoacetanilide ligand are limited. However mixed ligand complexes of acetoacetanilide with other donar ligands are more abundant. Well characterised complexes of acetoacetanilide and substituted acetoacetanilides are brought out in table 2.1.

Table 2.1
Metal chelates of acetoacetanilides CH_3-CO-CH_2-CO-NH-R*

R	Metal ions (Numbers shown are references)													
	Be^{2+}	Al^{3+}	VO^{2+}	Sb^{3+}	Cr^{3+}	Fe^{3+}	Co^{2+}	Ni^{2+}	Cu^{2+}	MoO_2^{2+}	Eu^{3+}	Ln^{3+}	Hg^{2+}	UO_2^{2+}
Phenyl	106	106	107, 108	159	106, 109, 110	106	118	119	111,112,113	114		115, 116	116	67.117
2-Methylphenyl			108		109		118	119	106.113.120, 121			122	116	117
3-Methylphenyl									106					
4-Methylphenyl									106,111					
2-Methoxyphenyl	123		108		109	124			111,113,120, 121				116	117
3-Methoxyphenyl								119	113					
2-Methoxyphenyl	123								112,113					
2-Halophenyl	125				109	124	118	119	111,112,120		126	122	116	117
3-Halophenyl	127								112					
4-Halophenyl	123								111,113					
2-Nitrophenyl									113					
3-Nitrophenyl									113					
4-Nitrophenyl									113					
4-acetylphenyl									112					
2,4-Dichlorophenyl	123								111					
2,5-Dichlorophenyl	123													
2,4-Dimethylphenyl					109	124			111,128				116	128
2,5-Dimethylphenyl	123													
2,5-Dimethoxy-4-halophenyl	123,125													

Ln = La,Pr,Nd,Sm,Gd &Y R* = Phenyl/ substituted phenyl group

These complexes were characterised mainly on the basis of their elemental analysis, molar conductance, magnetic moment and electronic and IR spectral data[107-109,111,119,120,124]. In some cases proton NMR[123-127] and mass spectral data were also reported[123,125,129,130].

The mode of bonding in these complexes were established mainly on the basis of IR data. In the IR spectra of acetoacetanilide complexes, both the acetyl carbonyl and amide carbonyl frequencies are shifted to lower wave numbers justifying their involvement in coordination[106,111,116,122,131-133]. If coordination occurred through the nitrogen, the amide carbonyl stretching frequency would have been considerably raised. The N-H stretching frequency of the complexes increased compared to the spectra of the free ligand in accordance with the non involvement of the amide nitrogen in bonding with the metal ion.

That only the carbonyl groups are involved in bonding with the metal ion were observed in the ^{1}H NMR spectra of certain complexes where the enolic OH peak has disappeared and the N-H proton signal remained unaffected which supplement the absence of nitrogen coordination. From the absence of nitrogen hyperfine splitting in the reported ESR spectral data of Cu(II) complex of acetoacetanilide confirmed that the amide nitrogen is excluded from bonding with the metal ion[134].

Fay and Piper[135] isolated the different geometrical isomers of tris(acetoacetanilido)chromium(III) from aqueous alcoholic solution following the chromatographic technique. Thermogravimetric analysis of the complexes showed that the *trans* isomer is more stable than the *cis* isomer[110].

Mixed ligand complexes of acetoacetanilides

Mixed ligand complexes of acetoacetanilide with other donar ligands are more abundant than complexes containing acetoacetanilide alone. Most of the mixed ligand complexes contain water, halogen, acetate, sulphate, nitrate, heterocyclic bases, alkoxides, etc. as co-ligand(s). Typical examples of stable mixed ligand complexes of acetoacetanilide reported are brought out in table 2.2 and 2.3.

Table 2.2

Important mixed ligand complexes of acetoacetanilide (HL)

Complex	Co-ligand (X)	Ref.
$[TiL_2X_2]$	Br, I	136,137
$[TiL_3X]$	Br, I	137
$[TiLX_3]$	Cl	137
$[Ti(HL)_3X_4]$	Cl	137
$[TiL_2X]$	SO_4	138
$[TiL_2X]$	salicylaldazine dianion	139
$[TiL_2X_2]$ $[TiL_2X_3]$	Chlorophenoxide	140-143
$[CoL_2X_2]$	Pyridine, α-Picoline	118
$[CoL_2X]$, $[CoLX]$ $[CuLX]^+$	Dianion of N,N′-ethylenediamionobis(salicylideneimine)	144-147
$Na[CoL_2X_2]$	NO_2	148-151

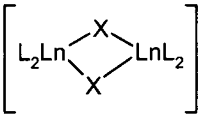
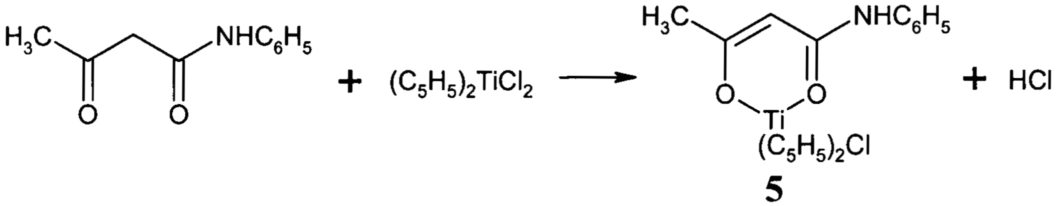
$[CoLX_2]^{2+}$	tn	152
$[CoLX]^{2+}$	trien	153
$[NiLX]$ $[CoLX]$ $[CuLX]$ $[CdLX]$ $[HgLX]$	Oxine, glycine and carbamates	154,155
$[CuL_2X]$	Pyridine	120
$[CuLX]$	Pyridine, ∝-picoline, Quinoline	118
	OH	156
$[BLX_2]$	CH_3-COO	131
$[SnL_2X_2]$	Cl	157
$[SnL_2X_2]$	n-Butyl	157
$[SnL_2X_2]$	Phenyl	157
$[SnL_2X_2]$	α-Thienyl	158
$[SbLX_4]$	Cl	159,170
$[SbL_2X_3]$	Phenyl	159,170
$[LnL_2X]$	OPr^i	171-174
$[LnLX_2]$	OPr^i	171-174
$[ZnL_2X]$	H_2O	167
$[ZnL_2X]^+$	N_3^-, SCN^-	213
$[ZnL_2X]$	2-(2′-Pyridyl)benzimidazole, 2-(2′-Pyridyl)imidazoline	190
$[ZnL_2X]$	5-Pyrazolones	214

Table 2.3

Complex	Co-ligands		Ref.
	X	Y	
$[TiLXY_2]$	Cl	$C_5H_5^-$	160
$[TiLXY_2]$, $[TiLX_2Y]$	Cl	Chlorophenoxide	140-143
$[CoLXY]$	Cl, Br, NO_3, ClO_4	Pyridine, ∝-Picoline Quinoline or Isoquinoline	118,160
$[CoLXY_2]$ $[NiLXY_2]$	H_2O	Oxine, glycine and carbamates	154,155
$[NbLX_2Y]$	Cl	OCH_3	161
$[TaLX_2Y_2]$	Cl	OCH_3	161
$[CoLXY]^{2+}$	pn	tn	162

These type of complexes of benzoylacetanilide were also reported in the literature[107-109,114,116,122,132,162-166], but not as much abundant as that of acetoacetanilide.

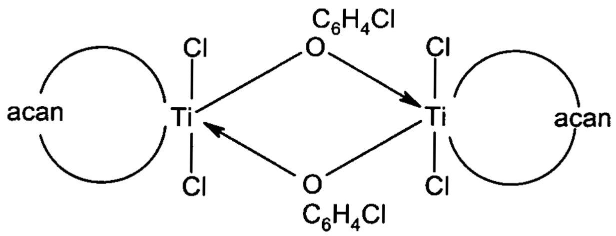
Synthesis of several interesting structural types of acetoacetanilide complexes were also reported. Some of them are mentioned below. The two chlorine atoms of $TiCl_4$ can be replaced by acetoacetanilide anion by refluxing in dry benzene. When $[Ti(acac)_2Cl_2]$ was refluxed with acetoacetanilide, complexe of the type $[Ti(acacn)_3Cl]$ was isolated[137]. Similarly reaction between bis(cyclopentadienyl)titanium(IV)dichloride and acetoacetanilide on distillation for an unusual period of about 380 h[160], gave the compound(5) **5**.



5

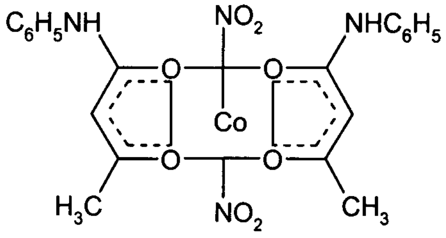
Most of the complexes reported are of either square planar or octahedral geometry as expected of the stoichiometry. Uranyl complex of the type [$UO_2L(HL)$] were shown to possess a coordination number of 7[67,117].

Chelated complexes of chlorophenoxides of Ti(IV) with acetoacetanilide of the composition [$Ti(OC_6H_4Cl)_2(acan)_2$], [$TiCl(OC_6H_4Cl)(acan)_2$], [$Ti(OC_6H_4Cl)_3(acan)$], [$TiCl(OC_6H_4Cl)_2(acan)$] and [$TiCl_2(OC_6H_4Cl)(acan)$] have been isolated by reacting monochloro, dichloro and trichlorotitanium(IV)chlorophenoxides with acetoacetanilide. A dimeric structure **6** was proposed for the complex of stoichiometry [$TiCl_2(OC_6H_4Cl)(acan)$][140-143].



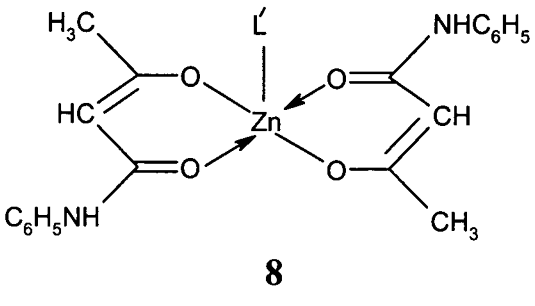
6

Based on IR data the *trans* orientation of the NO_2 group have been established in the case of the diamagnetic complex $Na[Co(NO_2)_2(acan)_2]$. The IR spectra of the complex showed only one band in the range 1290-1325 cm^{-1} and another in the range 790-825 cm^{-1} has been suggested as evidence for the *trans* structure **7**[148-45].



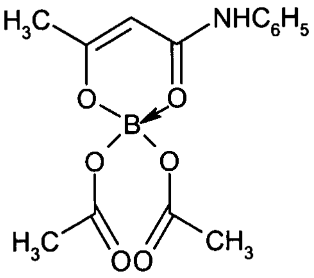
7

Several complexes of Zn(II) and Cu(II) were shown as pentacoordinated with the composition $Na[M(acan)_2L']$ where L′ = pseudo halides like N_3^-, SCN^-, heterocyclic donar ligands, etc, were shown[213] to be square pyramidal structure **8**.



8

In the moisture sensitive boron complex of acetoacetanilide prepared from boric acid dissolved in acetic anhydride, the boron atom has been shown to be in tetrahedral environment[131] of four oxygen donar atoms as in structure **9**.



9

The reactions of lanthanide isopropoxide (Pr, Nd, Sm, Dy and Ho) with acetoacetanilide in 1:1 and 1:2 molar ratios in refluxing benzene yielded products of the type $[Ln(OPr^i)_2(acan)]$ and $[Ln(OPr^i)(acan)_2]$[174]. All these complexes are microcrystalline solids with a colour characteristic of the trivalent oxidation state of the corresponding lanthanide ion[171-172].

$$Ln(OPr^i)_3 + n\ C_6H_5\text{–}NH\text{–}CO\text{–}CH_2\text{–}CO\text{–}CH_3 \rightarrow$$

$$Ln(OPr^i)_{3-n}(C_6H_5NHCOCHCOCH_3) + n\ Pr^iOH, \text{ where } n = 1 \text{ or } 2.$$

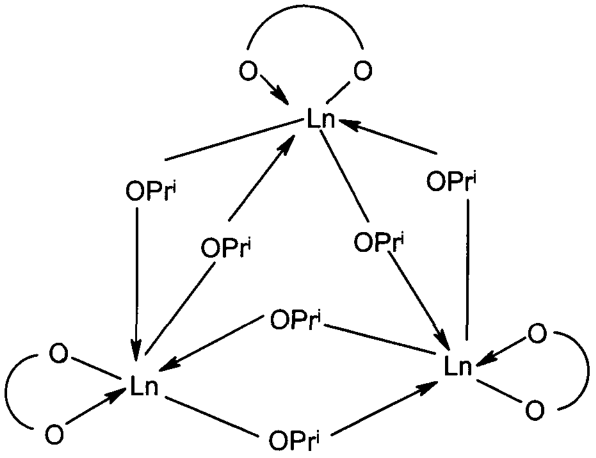
When the reaction was carried out in 1:3 molar ratio, the replacement of only two isopropoxide groups took place and the replacement of the third isopropoxy group was not possible even on prolonged refluxing with an excess of acetoacetanilide. The failure to get tris(acetoacetanilide) chelate have been suggested as due to the factors like proton–ligand stability, π electron delocalisation in the ring and steric hindrance[173].

Monoisopropoxylanthanidebis(acetoacetanilide) derivatives have been found to undergo exchange reactions with an excess of *tert*-butyl alcohol in benzene[174].

$Ln(OPr^i)(C_6H_5–NH–CO–CH–CO–CH_3) + t–C_4H_9OH \rightarrow$

$Ln(O–\textit{t}–C_4H_9)(C_6H_5\text{-}NHCOCH–COCH_3)_2 + n\ Pr^iOH$

The 1:1 derivative was found to be a trimeric structure **10** where as the 1:2 derivatives were of dimeric type **11**.



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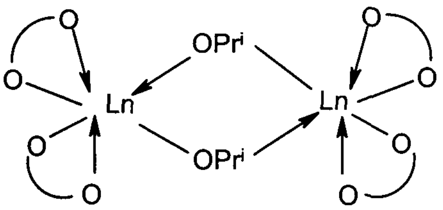
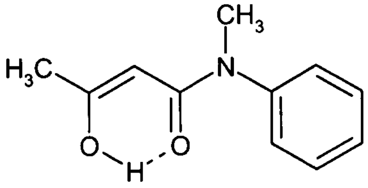


11

Complexes of N-substituted acetoacetanilides

Substituted acetoacetanilides like N-methyl and N-ethyl acetoacetanilide **12** and **13** form complexes analogous to unsubstituted acetoacetanilide (Table 2.4). The complexes[175-177] show close resemblance with the corresponding complexes of acetoacetanilide. In the IR spectra of N-alkylacetoacetanilides, the amide carbonyl frequency is lowered as expected due to the electron releasing effect of the alkyl groups.



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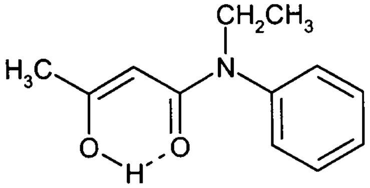

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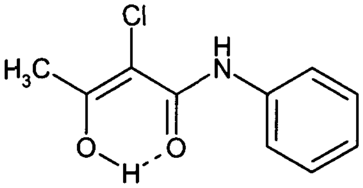
Table 2.4

Reported metal chelates of N-methyl and N-ethylacetoacetanilides

N-metylacetoacetanilide (HL)		N-ethylacetoacetanilide (HL)	
Complex	Ref.	Complex	Ref.
[BeL_2]	175,177	[BeL_2]	175,177
[CuL_2]	175,177	[CuL_2]	175,177
[FeL_3]	175,177	[CrL_3]	175,177
		[FeL_3]	175,177
		[$UO_2L_2(LH)$]	175,177

Complexes of α-substituted acetoacetanilides

The rate of enolisation and the percentage of enol content of acetoacetanilide can be drastically altered by substituents on the α-carbon. α-Chloroacetoacetanilide[182] **14** and some of its metal complexes were thoroughly investigated (Table 2.5)using various spectral techniques. In the IR spectra of the metal chelates of α-chloroacetoacetanilide, the overall intensity of the OH stretching band becomes less indicative of the replacement of enolic hydrogen by metal cations. The position of the NH stretching band is not much raised as in the free ligand. This has been explained as due to the intramolecular hydrogen bonding of the α-chlorine with the NH hydrogen both in the intramolecularly hydrogen bonded structure of ligand **15** and in the complex **16**. As expected the α-CH in plane bending vibration at about 1195 cm^{-1} of the free ligand disappeared in the metal complex.



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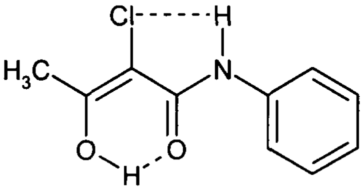

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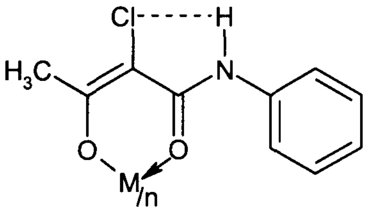
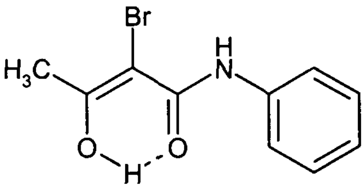


16

Table 2.5
Reported metal chelates of α-chloroacetoacetanilide (HL)

Complex	Ref.	Complex	Ref.
[BeL_2]	178	[FeL_3]	178
[CuL_2]	178	[$TiCl_2L_2$]	178
[AlL_3]	178	[VOL_2]$5H_2O$	178
[CrL_3]	178	[$UO_2L_2(H_2O)$]	178

Metal complexes of other α-haloacetoacetanilides like α-bromo acetoacetanilide **17**[177,183] and α-iodoacetoacetanilide **18**[184,177] have also been reported (Table 2.6). No conspicuous changes were observed in different spectral techniques of these complexes compared to that of α-chloroacetoacetanilide.



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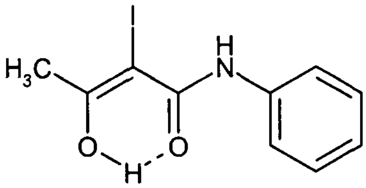

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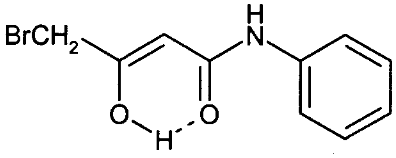
Table 2.6
Reported metal chelates of α-bromo and α-iodoacetoacetanilides

α-bromoacetoacetanilide (HL)		α-iodoacetoacetanilide (HL)	
Complex	Ref.	Complex	Ref.
$[BeL_2]$	179	$[BeL_2]$	180
$[CuL_2]$	179	$[CuL_2]$	180
$[CrL_3]$	179	$[CrL_3]$	180
$[FeL_3]$	179	$[FeL_3]$	180
$[VOL_2]4H_2O$	179		
$[UO_2L_2]H_2O$	179		

The involvement of OH proton in complexation has been confirmed from NMR spectra of the Be(II) and Al(III) chelates of α-chloroacetoacetanilide[177].

Complexes of γ-substituted acetoacetanilides

Certain metal complexes of γ-bromoacetoacetanilide **19**[177,185] were also reported and are given in table 2.7. The γ-phenylmercaptoacetoacetanilide **20** has been prepared by the addition of γ-bromoacetoacetanilide into thiophenol[186]. Cu(II) and Ni(II) chelates of the compound were reported with $[ML_2]$ stoichiometry[187,188].



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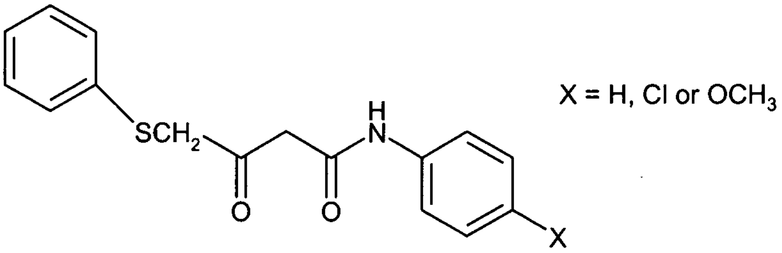


20

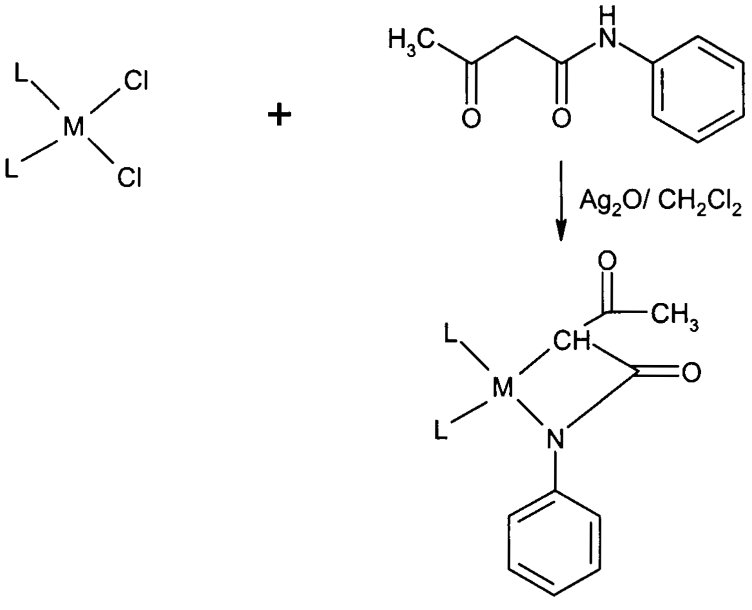
Table 2.7

Reported metal chelates of γ-bromoacetoacetanilide (HL)

Complex	Ref.	Complex	Ref.
$[BeL_2]$	181	$[FeL_3]$	181
$[CuL_2]$	181	$[TiCl_2L_2]$	181
$[AlL_3]$	181	$[VOL_2]4H_2O$	181
$[CrL_3]$	181	$[UO_2L_2]H_2O$	181

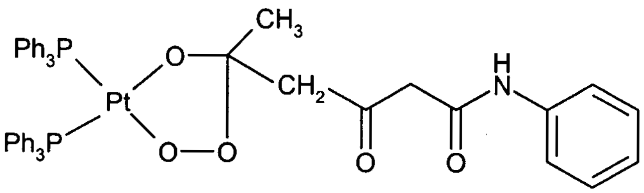
Other bonding modes of acetoacetanilides

Reaction of the platinum or palladium(II)chloride complexes of the type [MCl_2L_2], M = Pd, L_2 = 2,2′–bipyridyl; M = Pt, L = PPh_3 or L_2 = cycloocta–1,5–diene or [$Ph_2P(CH_2)_3PPh_2$] with acetoacetanilide mediated by Ag(1)oxide gave high yield of metallalactum complexes **21**[189].



21

The reaction of acetoacetanilide with the zerovalent platinum complex [Pt(*trans*Ph–CH=CH–Ph)($(PPh_3)_2$)] in air gives exclusively the peroxometallacyclic complex **22**[189].



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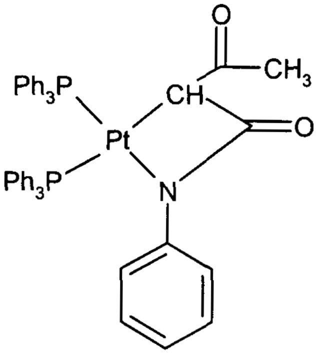
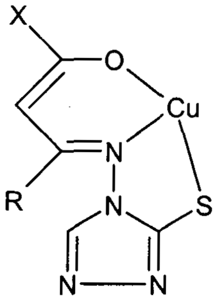
The reaction with [$Pt(PPh_3)_4$] gave a mixture of **22** and the platinalactum complex **23**[189].



23

Schiff's base complexes of acetoacetanilide

The schiff's base complexes of acetoacetanilide with various amines were reported[191-196]. The schiff's bases behave as tridentate dibasic ligands and form metal chelates with 1:1 metal–ligand stoichiometry of the type **24**[197].

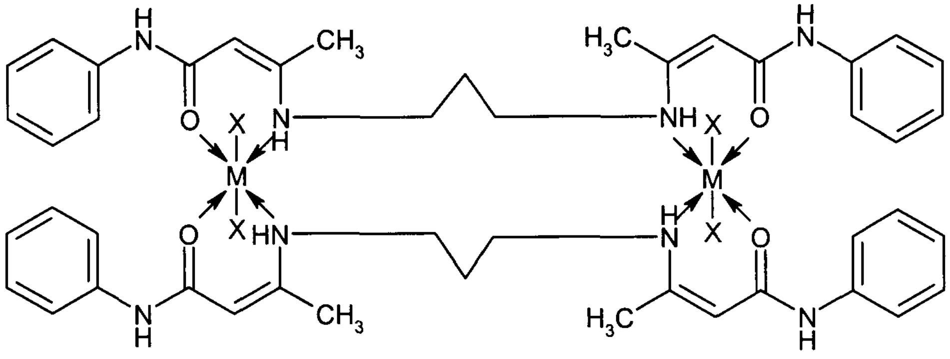


24

R = CH_3, X = NHC_6H_5, $NHC_6H_4CH_3$, $NHC_6H_4OCH_3$

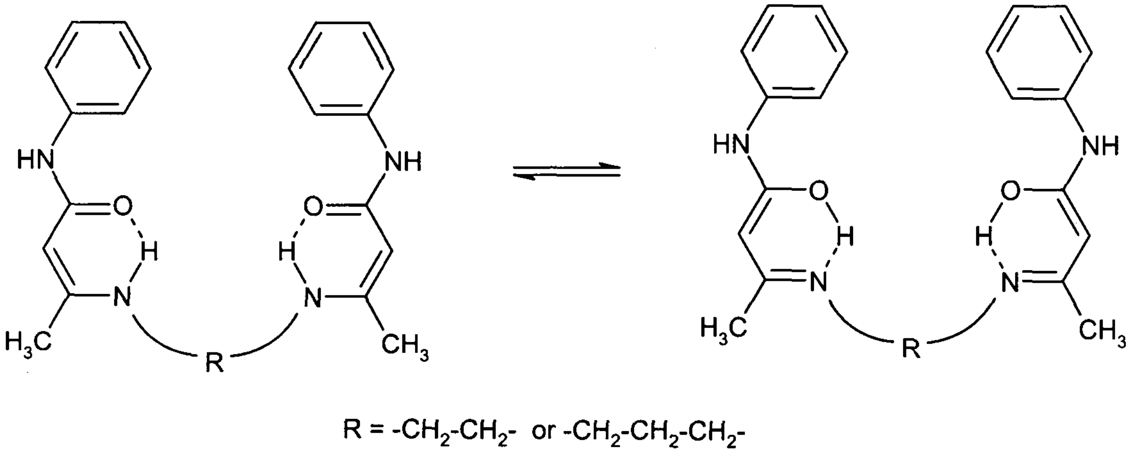
R = C_6H_5, X = NHC_6H_5

Schiff's base complexes of acetoacetanilide with 1,3-diaminopropane having the composition $[CoL_2X_4]$ where X = Cl, Br, NO_3 or ClO_4; $[Cu_2L_2(NO_3)_4]$, $[Zn_2L_2X_4]$ where X = Cl, SCN or ClO_4; $[CuCl_2L]$ and $[Zn_2Br_2L]$ have been synthesised[198], where L is the ONNO tetradentate ligand, N,N'-bis(acetoactanilide)-1,3-diaminopropane. The structure of type **25** have been suggested for the dimeric complex.



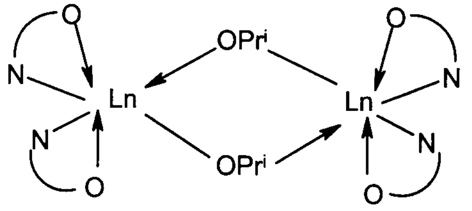
25

The reactions of β-amidoamines such as N,N′-ethylenebis(acetoacetanilideimine) and N,N′-propylenebis (acetoacetanilideimine)[199,200] in different stoichiometric ratios (1:1, 1:2 and 2:3) yielded different substituted products of the type [Ln(OPr^i)(aa)], [Ln(aa)(aaH)] and [$Ln_2(aa)_3$] where aa^{-2} is the anion of the corresponding bifunctional quadridentate β-amidoamine. The schiff's bases exist in tautomeric forms **26** and **27**.



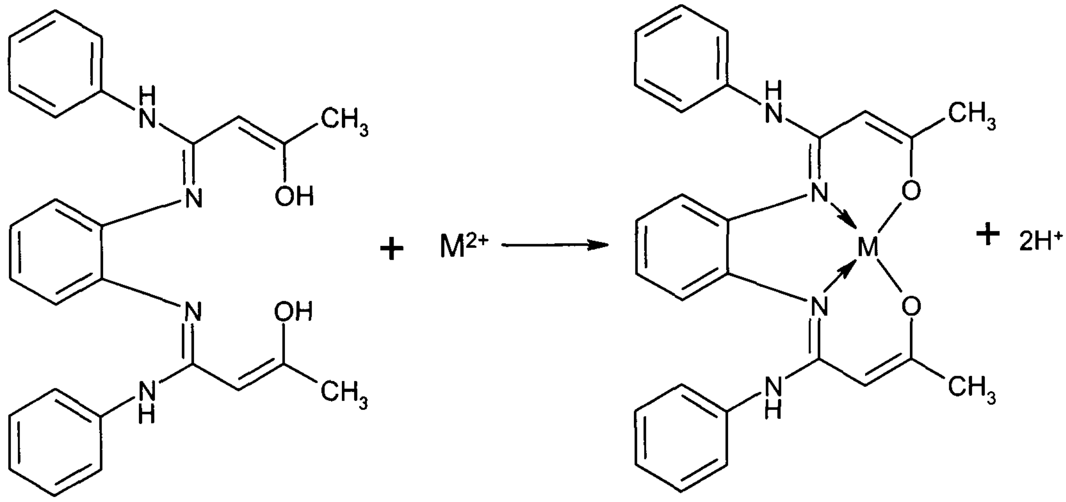
26 **27**

The reactions of β-amido amines with lanthanide isopropoxides in 1:1 molar ratio resulted in the synthesis of monoisopropoxylanthanide-N,N′-ethylenebis(acetoacetanilideimine) or N,N′-propylenebis (acetoacetanilideimine) derivative, **28**. However the reactions of lanthanide isopropoxides with β-amidoamines in the molar ratio 1:2 and 2:3 were found to be monomeric.



28

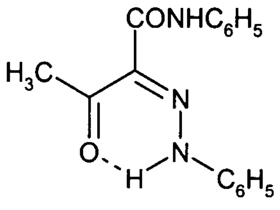
The schiff's base **29** formed by the condensation of o-phenylene diamine with acetoacetanilide form complexes of the type **30** with Cu(II), Ni(II), Mn(II), Zn(II) and VO(II)[201]. The ligand has both N and O donar sites. It coordinates with the metal ion in a tetradentate manner through the enolisable carbonyl group of the acetoacetanilide moiety and the azomethine nitrogen atom. Magnetic succeptibility values of the complexes at room temperature were consistent with square planar geometry around the central metal ion except for the Mn(II) and VO(II) complexes which show octahedral and square pyramidal geometry respectively[201].



29 **30**

Metal complexes of arylazoacetoacetanilide

Coupling of benzenediazonium salt with acetoacetanilide resulted phenylazoacetoacetanilide[202] which exist in the intra molecularly hydrogen bonded hydrazone form **31**. The compound form stable complexes with Cu(II), Ni(II), Co(II), Fe(II), Pd(II), UO_2(II)and VO(II)[203]. Analytical data correspond to 1:2 stoichiometry for the metal chelates. A 1:1 complex **32** with Cu(II)acetate was also characterised. The Ni(II), Fe(II) and Co(II) complexes **33** possess octahedral coordination[204,205] while Pd(II) formed a square planar complex **34**[206]. The UO_2(II) and VO(II) complexes **35** and **36** were pentagonal bipyramidal and square pyramidal respectively[207,208].



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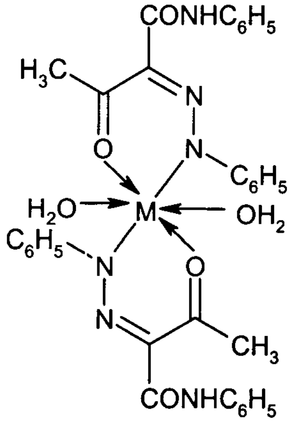

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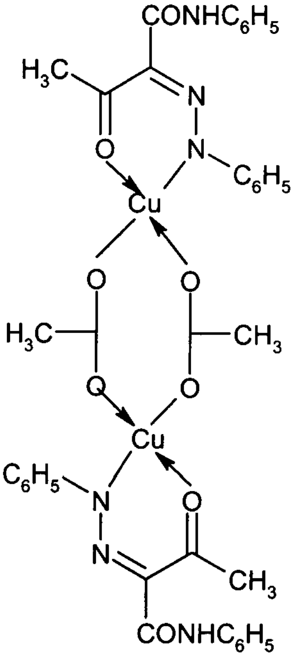

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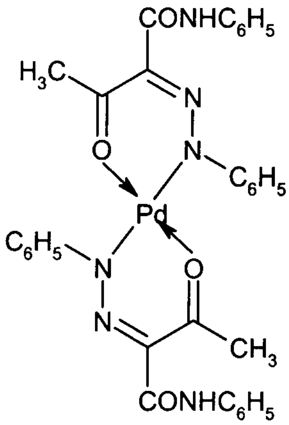

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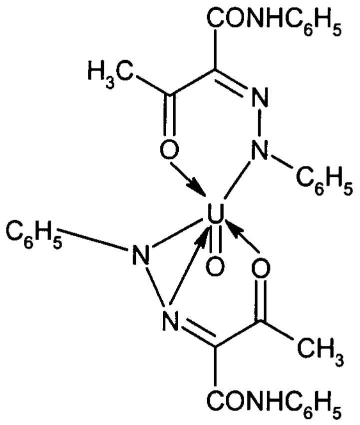

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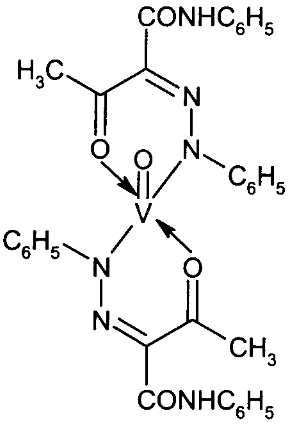
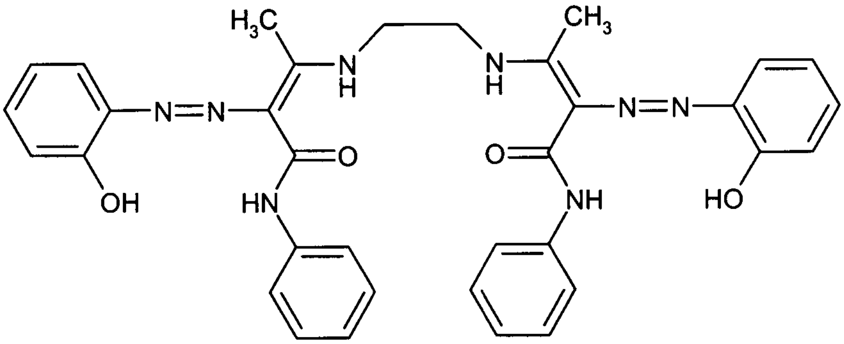
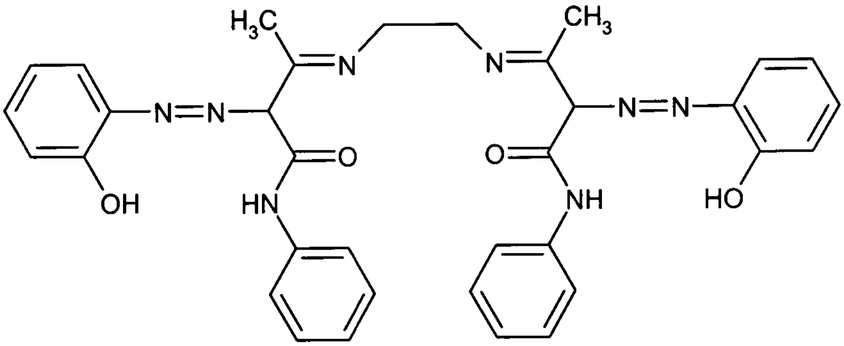


36

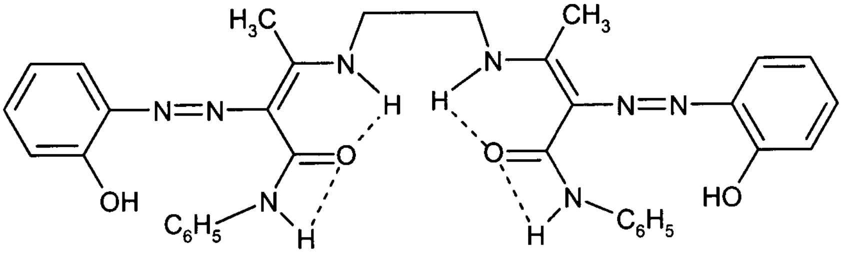
The schiff's base N,N′-bis(acetoacetanilide)ethylenediamine on coupling with the diazonium salt of o-aminophenol produced a macrocyclic ligand system[209] **37–39** which form polymetallic complexes **40–41** with Co(II), Ni(II), Cu(II), Zn(II), Hg(II) and Cd(II)[210].



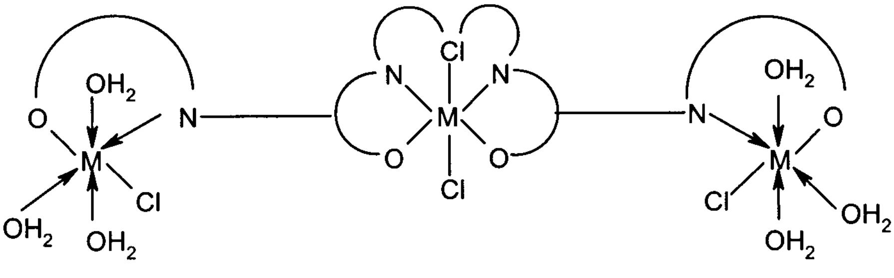
37 (ketoamine)



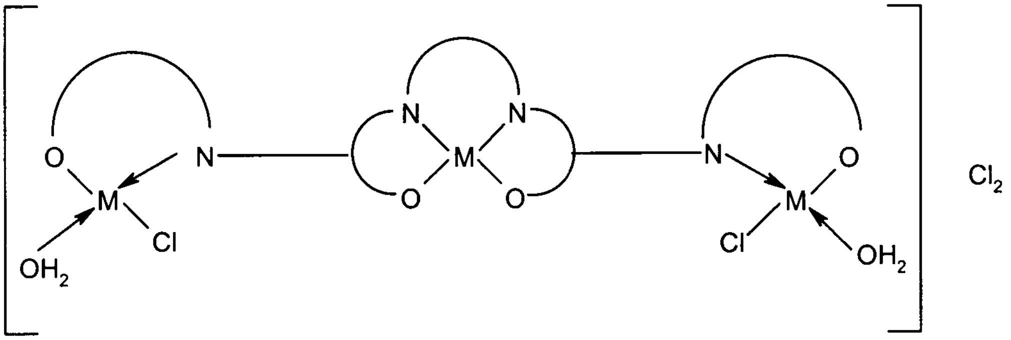
38 (ketoimine)



39 (Hydrogen bonded)



40 (M = Co(II), Ni(II), Cu(II))



41 (M = Zn(II), Cd(II), Hg(II))

Acetoacetanilide condense with hydroxylamine to form the oxime 3-hydroxyimino-1-N-phenylaminobutane-1-one[211]. Their Cr(III) and Fe(III) complexes with octahedral coordination of the type $[M(HL)_2X_2]X$ where X = Cl^-, Br^-, NO_3^-, NCS^- and ClO_4^- have been reported recently[212].

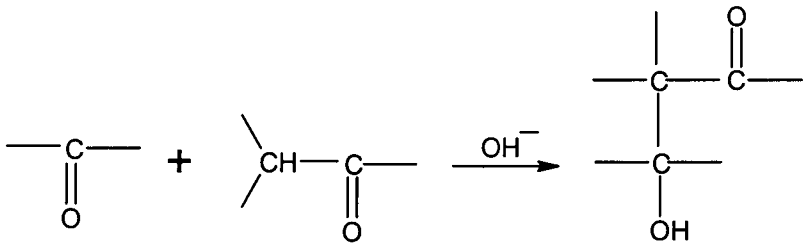
PART III

METAL COMPLEXES OF CONJUGATED β-KETOANILIDES

METAL COMPLEXES OF CONJUGATED β-KETOANILIDES

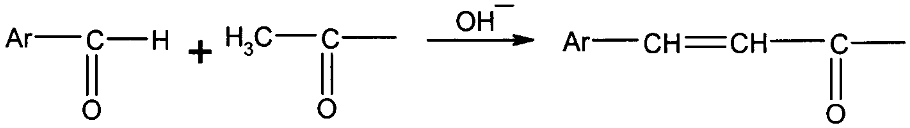
Introduction

Conjugated carbonyl compounds are usually prepared by the self condensation of aldehydes and ketones containing α-hydrogen with dil.alkali. This reaction, the so called aldol condensation, in most cases give rise to mixture of products, especially when the reaction is performed with two different carbonyl compounds both having α-hydrogen. However, if one of the carbonyl compounds lacks α-hydrogen, only one product can be isolated besides the self-condensation of the carbonyl compound containing α-hydrogen (scheme 3.1).



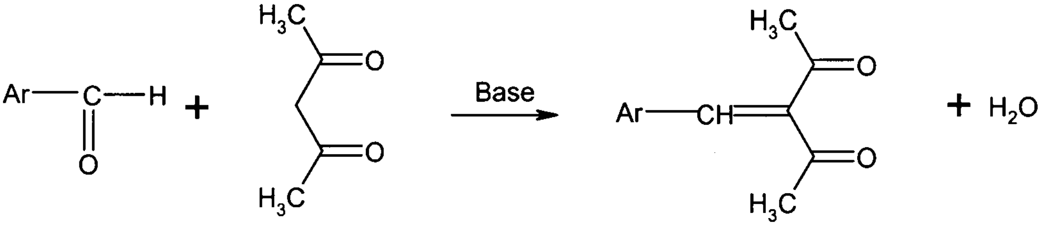
Scheme 3.1

Aromatic aldehydes condense with aliphatic aldehydes and ketones containing α-hydrogen to form α,β-unsaturated carbonyl compounds. This Claisen-Schmidt reaction (scheme 3.2), a modification of aldol condensation[215,216], is a highly useful method for the synthesis of numerous compounds having diverse uses[217-219].



Scheme 3.2

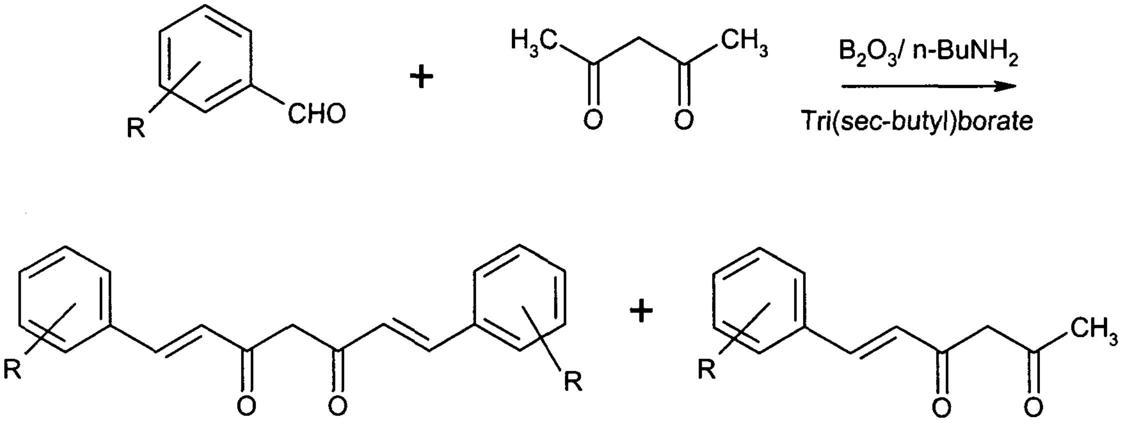
The β-dicarbonyl compounds in which a methylene group interposed between two electron withdrawing carbonyl groups usually undergo Knoevenagel condensation[219] with bases. In these case the more acidic methylene hydrogen is lost by the attack of the base to form a carbanion. This carbanion, like aldol and Claisen reaction, make a nucleophilic attack at the carbonyl carbon of aromatic aldehyde or ketone to form products of the type **1** given in scheme 3.3. This reaction has been utilised for the synthesis of numerous structurally and practically important compounds using different aromatic aldehydes and β-dicarbonyl compounds[220-225].



1

Scheme 3.3

Inorder to perform the Claisen-Schmidt reaction of these 1,3-dicarbonyl compounds, the active methylene group should be protected so that the condensation of aldehyde will occur at the terminal alkyl groups, if present. This type of methylene group protection and subsequent Claisen reaction was carried out in acetylacetone by Povoloni *et al*[226] and later modified by Pabon[227,228] for the synthesis of curcuminoids and other 1,7-diarylheptanoids **2** from vanillin and acetylacetone at room temperature in presence of B_2O_3 and trisec(butyl)borate using n-bulylamine as the condensing agents. The reaction also give some amount of the moncondensation product called 6-arylhexanoids **3** (scheme 3.4). The use of B_2O_3 and tri(sec-butyl)borate is to prevent the condensation of the aldehyde at the methylene carbon (Knoevenagel condensation) by the formation of an acetylacetone-boron complex. Thus the terminal methyl groups can undergo Claisen reaction with the aromatic aldehyde.

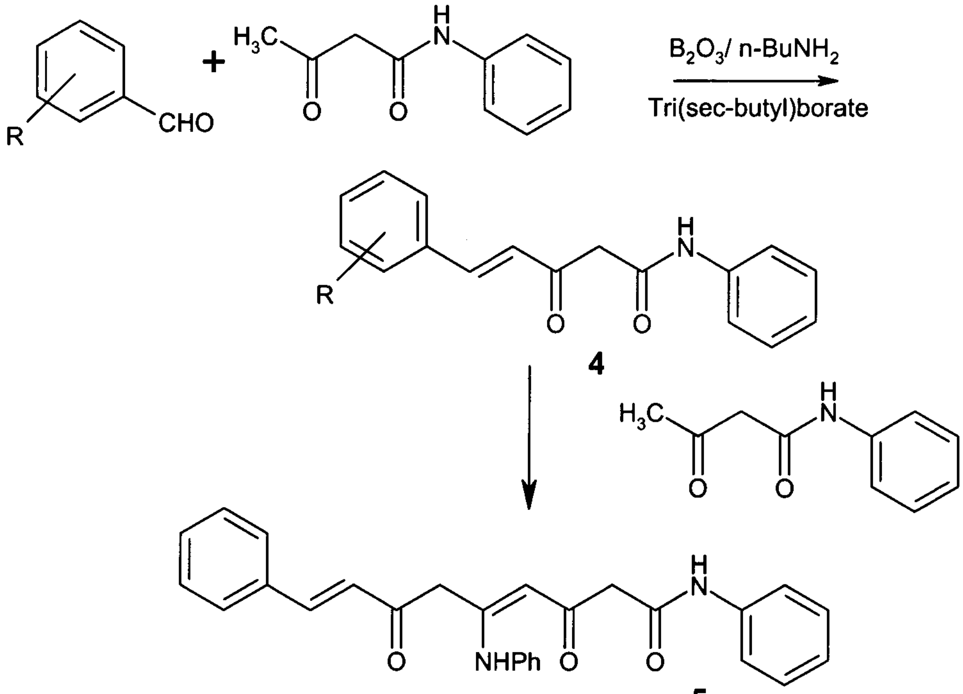


2 **3**

Scheme 3.4

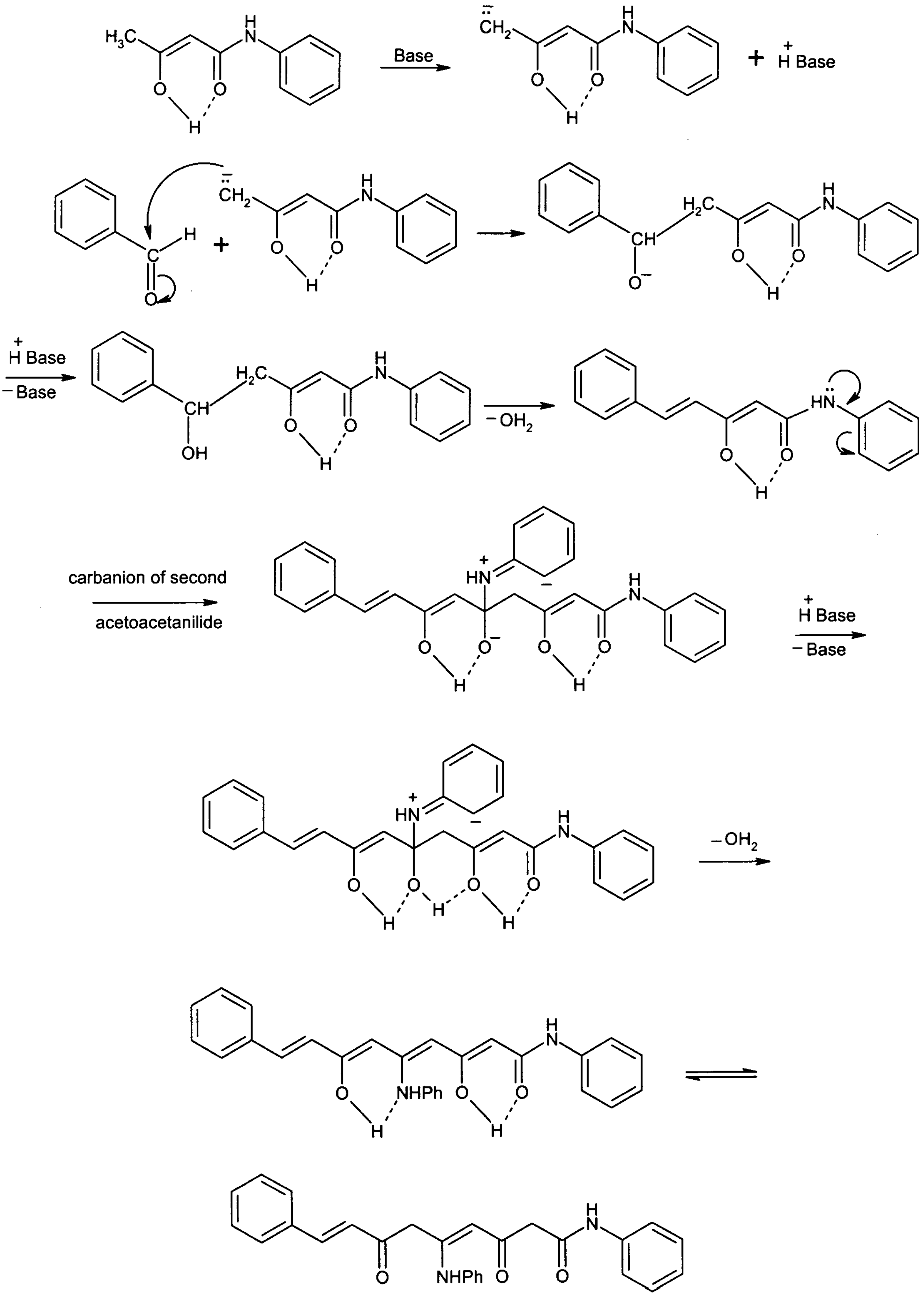
Since acetylacetone and benzoylacetone undergo Claisen reaction at the γ-methyl groups with various aromatic aldehydes, other β-dicarbonyl compounds like β-ketoamides and β-ketoesters with one γ-methyl group may also undergo the reaction that lead to the formation of α,β-unsaturated dicarbonyl compounds. However, unlike acetylacetone, benzoylacetone, etc. the carbonyl group of these 1,3-dicarbonyl compounds are linked to different heteroatoms such as

N,O etc. So some deviation from the normally expected pathway may take place by the interaction of amide nitrogen or ester oxygen with the carbonyl groups and result in the formation of unexpected products. This observation has been fully justified in the present investigation. Thus two types of unsaturated ketoanilides **4** (monocondensation product) and **5** (bis condensation product) have been isolated and characterised by the reaction between acetoacetanilide and various aromatic aldehydes. This reaction can be represented as in scheme 3.5.



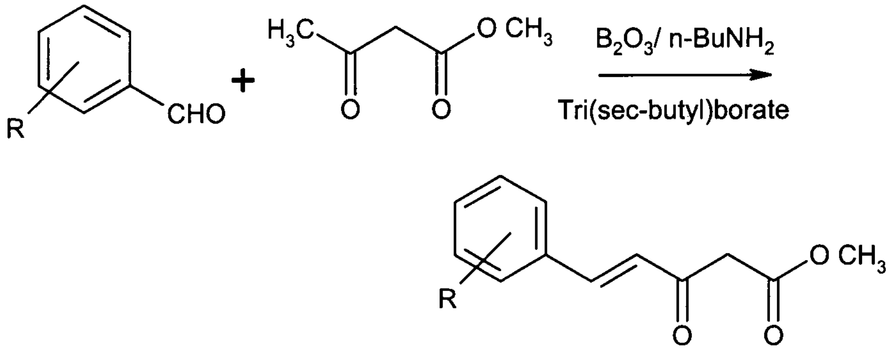
Scheme 3.5

The formation of various products can be fully justified by considering the reaction scheme 3.6. Thus the reaction of various aromatic aldehydes with acetoacetanilide resulted in the formation of not only the expected unsaturated β-ketoanilide **4**, but also an interesting class of tricarbonyl compounds **5**. Both these types of carbonyl compounds form well defined complexes with various metal ions.


Base
+ H Base
carbanion of second acetoacetanilide
H Base
− Base
− OH2
NHPh

Scheme 3.6

When the condensation reaction was carried out with methylacetoacetate using the same procedure for other 1,3-diketones, a monocondensation product was formed as in scheme 3.7. So, it can be inferred that the ester group do not interfere with the methylene protected Claisen-Schmidt reaction.



6

Scheme 3.7

For convenience this part is divided into five chapters based on the nature of the aryl groups of the aldehydes used for the synthesis of the conjugated ketoanilides. Thus in **chapter 1** synthesis and characterisation of mono and biscondensation products of benzaldehyde/ substituted benzaldehyde and their metal complexes are discussed. Synthesis and characterisation of the unsaturated anilides obtained from the condensation of naphthaldehyde/ 2-hydroxynaphthaldehyde and their metal complexes are considered in **chapter 2**. In **chapter 3** details on the compounds obtained from cinnamaldehyde are discussed. condensation products of acetoacetanilide with certain heteroaryl aldehydes are included in **chapter 4**. Results obtained from some of the biological studies carried with these compounds are also provided. Details on the synthesis and characterisation of certain β-ketoesters and Cu(II) complexes are discussed in **chapter 5.**

MATERIALS, INSTRUMENTS AND METHODS

Materials

Chemicals used for synthesis were of C.P. grade. For analytical purposes 'AnalaR' grade chemicals were employed. Commercial solvents were distilled and used for synthesis. Solvents purified by methods recommended by Weissberger[229] were employed for physical and physico-chemical measurements.

For the synthesis of complexes metal acetates were used except in the case of Fe(III) for which anhydrous $FeCl_3$ was used.

Only compounds isolated analytically pure are reported in this Thesis. The complexes reported here in are stable and have good keeping qualities. Compounds for recording spectra were recrystallised from proper solvents several times till chromatographically pure (tlc-silicagel).

Instruments

Instruments used in this investigation are

1. UV-1601 Schimadzu recording spectrophotometer.
2. 8101 Schimadzu-FTIR spectrometer.
3. Varian 300 NMR spectrometer.
4. Jeol 400 NMR spectrometer.
5. Jeol sx-102 (FAB) mass spectrometer.

6. Heraeus CHN-O-rapid analyser.
7. Perkin Elmer 2380-Atomic absorption spectrophotometer.
8. Varian E 112 ESR spectrometer.
9. Systronic pH meter.
10. Toshniwal conductivity bridge.
11. Gouy type magnetic balance.

Methods

Elemental analysis: Metal complexes were analysed by standard methods[230]. Metal percentages were recorded using atomic absorption spectrophotometer after decomposing them with concentrated sulfuric-nitric acid mixture. Carbon, hydrogen and nitrogen percentages reported are by microanalysis carried out at RSIC, CDRI, Lucknow.

UV-visible spectra were recorded from solution (10^{-3}M) of compounds in ethanol unless otherwise mentioned.

IR spectra of compound were recorded from discs with KBr. Bands were calibrated using the nearest polystyrene bands.

^{1}H NMR spectra were recorded using $CDCl_3$/dmso-d_6 as solvents and TMS as internal reference.

FAB mass spectra were recorded at room temperature using Argon (6KV, 10 mA) 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, 307. If metal ions such as Na^+ are present these peaks may be shifted accordingly.

Molar conductance of the complexes were determined in DMF at 28 ± 1^0C using solution of about 10^{-3} M concentration.

Magnetic susceptibility was determined at room temperature (28 ± 1^0C) using $Hg[Co(NCS)_4]$ as standard[263].

Molecular weight of compounds reported were determined by Rast's method[264] using naphthalene/ camphor as medium.

CHAPTER 1

METAL COMPLEXES OF CONJUGATED DIKETOANILIDES AND β-KETOANILIDES

Synthesis of the conjugated ketoanilides

The unsaturated β-ketoanilides were synthesised by the reaction between benzaldehyde and substituted benzaldehyde with acetoacetanilide in presence of boric oxide and tri(sec-butyl)borate using n-butylamine as the condensing agent. The reaction lead to the formation of two compounds and these were separated by column chromatography. A typical procedure for the synthesis is given below.

Acetoacetanilide (1.77 g, 0.01 mol) and boric oxide (0.35 g, 0.005 mol) were mixed and made into a paste with dry ethylacetate and stirred for about 1h at room temperature on a magnetic stirrer. To this a solution of aromatic aldehyde (0.01 mol) and tri(sec-butyl)borate (4.6 g, 0.02 mol) dissolved in dry ethylacetate was added and stirred for ~5h with the slow addition of n-butylamine (0.5 mL in 5 mL dry ethylacetate) in drops and the reaction mixture was kept overnight. Hot dil. HCl (0.4 M, 7.5 mL) was added and again stirred for lh. The mixture was extracted repeatedly with ethylacetate and the combined extracts were evaporated to dryness on a water bath to get a pasty mass.

To this 10 mL of 2 M HCl was added and kept for ~24h. The solution was stirred well and the precipitate formed was filtered.

From tlc it was revealed that only one product was formed with 4-hydroxybenzaldeyde, vanillin, 2-chlorobenzaldehyde and 4-chlorobenzaldehyde. However, the presence of two well defined spots in tlc revealed the presence of two compounds in the case of the products obtained from benzaldehyde, 4-methoxybenzaldehyde, 2-nitrobenzaldehyde, piperonal, veratraldehyde and 2,4-dimethoxybenzaldehyde. The mixture of compounds obtained were quantitatively separated by column chromatography as outlined below.

The crude product was dissolved in minimum quantity of dry ethylacetate and placed over a column (2x100 cm) densely packed with silicagel (mesh 60-120) and eluted with 3:5 v/v chloroform-acetone mixture at a uniform flow rate of 2 mL per min. As the elution proceeds, two bands were developed in the column, a pale yellow lower band and an orange red upper band. The lower region was collected as 10 mL aliquots in separate tubes and in each case the purity was established by tlc. The combined eluates on evoperation gave the pure unsaturated β-ketoanilide **4**.

The elution was then continued using 1:1 v/v mixture of chloroform and acetone to recover the orange red band retained in the upper portion of the column. The eluates were collected in aliquots of

10 mL in separate tubes, checked by tlc and the combined extracts on removing the solvent in vacuum yielded the unsaturated diketoanilides **5**. All the compounds isolated were recrystallised from hot chloroform to give spectroscopically pure material. The formation of the mono (**4**) and bis (**5**) condensation products can be fully justified by considering the electronic and steric effect of the phenyl substituents.

Thus it can be seen that, if the co-planarity of the monocondensation product is not lost by the substituents on the phenyl ring, the expected substituent effect is observed. But if the co-planarity is lost by bulky substituents on the phenyl ring, the electronic environment of the amide carbonyl is independent of the resonance effects of the substituents on the phenyl ring. But still inductive effects may alter slightly the reactivity of the amide carbonyl. In such cases the monoconodensation products may not undergo further condensation completely so that mixture of products are observed. In some cases, eventhough the resonance effects diminish the electron deficiency on the amide carbonyl, the mono condensation product is completely transformed in to the tricarbonyl compound. This may be due to the extended conjugation in the resulting product. Thus it is obvious that the electronic and steric environments of the phenyl substituents have marked effect on the second condensation and it is the $-NHC_6H_5$ group that promote the diketoanilide formation drastically. Benzaldehyde which do not carry any substituent give predominantly the triketone as the major product is indicative of the above facts. The variation in the proportion of both products can conveniently be explained by the competition between the electronic and steric effects of the substituents on the phenyl ring.

Inorder to have a meaningful discussion on the structural characteristics of these two types of conjugated β-ketoanilides, their analytical and spectral data are presented separately in two sections. **section 1** is on unsaturated diketoanilide and **section 2** on the unsaturated β-ketoanilide. Synthesis and characterisation of metal complexes of these two types of conjugated ketoanilides are included in each of these sections.

SECTION 1

METAL COMPLEXES OF UNSATURATED DIKETOANILIDES

Synthesis of metal complexes

The Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) complexes of the compounds were synthesised as follows.

To a refluxing solution of the compound in ethanol (0.001 mol, 20 mL) an aqueous solution of metal acetates (0.001 mol, 15 mL) was added drop by drop with stirring. The pH of the solution was adjusted around 6 using sodium acetate and refluxing was continued for ~4h. The solution was concentrated to half the volume and then cooled in ice. The precipitated complex was filtered, washed several times with water, then with ethanol, and recrystallised from hot methanol. The crystals were dried in vacuum.

Results and Discussion

Characterisation of the unsaturated diketoanilides

The aldehydes used for the synthesis of the conjugated β-ketoanilides in this investigation are brought in table 3.1. All the compounds are crystalline in nature with an orange red colour and are freely soluble in common organic solvents.

The results of elements analysis and molecular weight determination of the compounds given in table 3.2 suggest that two equivalents of acetoacetanilide has condensed with one equivalent of aromatic aldehyde in all cases. In the present study a detailed and systematic spectral investigation of the conjugated diketoanilides with a view to establish their structure and coordination behaviour were carried out on the basis of their UV, IR, ^{1}H NMR and mass spectral data.

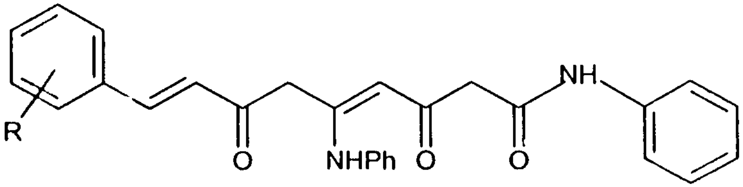
UV spectra

The UV absorption maxima of 1,3-dicarbonyl compounds are mainly due to the n→π* and π→π* transitions of the carbonyl and olefinic groups[42,104,231-233]. Depending on the degree of enolisation, the n→π* absorption of the carbonyl chromophore may vary. The extent of enolisation, degree of conjugation and the electronic effects of the groups attached to the dicarbonyl function have prominent influence on the position of the n→π* and π→π* absorption of β-dicarbonyl compounds.

The UV spectra of acetoacetanilide show a λ_{max} at ~246 nm in 95% ethanol (10^{-3} M) due to π→π* transition. The n→π* band occurs at longer λ value ~390 nm. In the unsaturated diketoanilide considered in this investigation the three carbonyl groups are in different electronic environment. Their extended conjugation and degree of enolisation influence the absorption maxima. The UV absorption maxima of the compounds included in table 3.2 clearly suggest that the position of the two prominent absorption maxima are strongly dependent on the extent of conjugation.

Table 3.1

Synthetic details of unsaturated diketoanilides



Compounds	Aldehyde used for synthesis	R	Systematic name	Yield (%)
1a	Benzaldehyde	H	1,5-Bis(N-phenylamino)-9-phenyl-4,8-nonadien-1,3,7-trione	50
2a	Salicylaldehyde	2-OH	1,5-Bis(N-phenylamino)-9-(2′-hydroxy)phenyl-4,8-nonadien-1,3,7-trione	30
3a	o-Chlorobenzaldehyde	2-Cl	1,5-Bis(N-phenylamino)-9-(2′-chloro)phenyl-4,8-nonadien-1,3,7-trione	70
4a	o-Nitrobenzaldehyde	2-NO_2	1,5-Bis(N-phenylamino)-9-(2′-nitro)phenyl-4,8-nonadien-1,3,7-trione	75
5a	p-Hydroxybenzaldehyde	4-OH	1,5-Bis(N-phenylamino)-9-(4′-hydroxy)phenyl-4,8-nonadien-1,3,7-trione	40
6a	p-Chlorobenzaldehyde	4-Cl	1,5-Bis(N-phenylamino)-9-(4′-chloro)phenyl-4,8-nonadien-1,3,7-trione	65

Contd ....

7a	p-Methoxybenzaldehyde	4-OCH_3	1,5-Bis(N-phenylamino)-9-(4′-methoxy)phenyl-4,8-nonadien-1,3,7-trione	35
8a	p-Ethoxybenzaldehyde	4-OC_2H_5	1,5-Bis(N-phenylamino)-9-(4′-ethoxy)phenyl-4,8-nonadien-1,3,7-trione	50
9a	p-N,N-Dimethylaminobenzaldehyde	4-$N(CH_3)_2$	1,5-Bis(N-phenylamino)-9-(4′-N,N-dimethylamino)phenyl-4,8-nonadien-1,3,7-trione	55
10a	Vanillin	3-OCH_3, 4-OH	1,5-Bis(N-phenylamino)-9-(3′-methoxy-4-hydroxy)phenyl-4,8-nonadien-1,3,7-trione	45
11a	Veratraldehyde	3-OCH_3, 4-OCH_3	1,5-Bis(N-phenylamino)-9-(3′,4′-dimethoxy)phenyl-4,8-nonadien-1,3,7-trione	45
12a	2,4-Dimethoxybenzaldehyde	2-OCH_3, 4-OCH_3	1,5-Bis(N-phenylamino)-9-(2′,4′-dimethoxy)phenyl-4,8-nonadien-1,3,7-trione	40
13a	Piperonal	3-OCH_2O-4	1,5-Bis(N-phenylamino)-9-(3′,4′-methylenedioxy)phenyl-4,8-nonadien-1,3,7-trione	40

Table 3.2

Physical, analytical and UV spectral data of the unsaturated diketoanilides

Compounds	MP (^{0}C)	Elemental analysis (%)			Mol. Weight	λ_{max} (nm)	log ∈
		C	H	N			
		Found/ (calcd)					
1a	110	76.34 (76.42)	5.62 (5.62)	6.71 (6.60)	424 (425)	255 355	4.01 4.64
2a	58	73.99 (74.52)	6.20 (6.21)	9.01 (8.99)	465 (468)	278 392	4.01 4.80
3a	90	70.59 (70.67)	5.04 (5.02)	6.13 (6.11)	458 (460)	246 343	4.04 4.32
4a	110	68.84 (69.08)	5.01 (4.90)	9.02 (8.96)	466 (469)	260 351	4.05 4.63
5a	105	73.54 (73.65)	5.42 (5.45)	6.34 (6.36)	440 (441)	265 372	4.07 4.77
6a	116	70.62 (70.67)	5.01 (5.02)	6.22 (6.11)	462 (460)	250 351	4.02 4.81
7a	88	73.56 (74.00)	5.63 (5.73)	6.04 (6.17)	451 (455)	266 384	4.07 4.82
8a	84	74.04 (74.36)	6.02 (5.98)	6.04 (5.98)	466 (469)	265 383	4.09 4.91
9a	54	73.99 (74.52)	6.20 (6.21)	9.01 (8.99)	465 (468)	270 392	4.01 4.80
10a	109	71.48 (71.49)	5.61 (5.53)	5.99 (5.96)	468 (471)	271 392	4.08 4.69
11a	112	72.10 (71.90)	5.99 (5.79)	5.89 (5.97)	483 (485)	270 394	4.08 4.68
12a	72	72.10 (71.90)	5.99 (5.79)	5.89 (5.97)	482 (485)	268 389	4.02 4.81
13a	84	71.03 (71.79)	5.10 (5.13)	6.01 (5.98)	468 (469)	267 391	4.06 4.70

IR spectra

IR spectra is a powerful tool in determining the structure of organic compounds especially compounds containing functional groups such as C=O, C=N, N–H, O–H, etc. Fortunately the compounds considered in this investigation contain many of these functional groups. In the vapour state and in non polar solvents 1,3-dicarbonyl compounds generally exist as the tautomeric mixture of diketo and enol forms[52,234-236]. Assignment of various bands in the enol tautomer is comparatively difficult. The enolic OH stretching absorption is usually seen as a broad band at 2700-3000 cm^{-1} due to strong intramolecular hydrogen bonding[237,238].

Primary and secondary amides have a tendency to form hydrogen bonded chain of the type $N–H\cdots O=C$. This results in the lowering of both N–H and C=O stretching frequencies. The conjugation of π electrons of the C=O bond and NH lone pair decreases the amide carbonyl stretching frequency. Open chain secondary amides in the solid state show the amide I band at 1680–1630 cm^{-1}. Conjugation and inductive effect of the N-substituent have marked effect on the amide I frequency. Amide II is a mixed vibration of N–H bending and C–N stretching and appears at 1570–1510 cm^{-1}. Amide III band due to mixed vibration involving C–N stretching and N–H bending is usually at

1310–1200 cm^{-1}. Amide IV band due to O=C–N bending is at 620 cm^{-1}. Amide V band due to N–H out of plane deformation is at 700 cm^{-1}. Amide VI band due to C=O out of plane bending is around 600 cm^{-1}.

Acetoactanilide shows two strong bands at 1727 and 1667 cm^{-1} assignable to acetyl carbonyl and amide carbonyl respectively[106,239]. Although acetoacetanilide has keto and enol tautomeric forms, no band has been assigned yet for the conjugated double bond system in its enol. In α-chloroacetoacetanilide, which is considered to have greater enol content, a band at 1600 cm^{-1} is relatively more intense and broad. Actually, among the four skeltol C–C vibrational bands of the phenyl ring at 1600–1450 cm^{-1}, the band due to the conjugated double bond of enol of β-ketoanilides get superimposed on the 1600 cm^{-1} band of the phenyl ring. In the spectra of N,N-diethylacetoacetanilide the amide carbonyl band is at 1640 cm^{-1} where as in acetoacetanilide, it is at 1667 cm^{-1}. This is due to the weak amide resonance which result in the withdrawal of election density on the nitrogen by the phenyl ring[235,240].

The N–H and O–H region of the spectrum of β-ketoanilides show considerably broad bands at 3400–3300 cm^{-1}. In acetoacetanilide it is at 3270 cm^{-1}. A weaker band may appear at about 3100 cm^{-1} in seconding amides. It is attributed to a fermi resonance overtone of the 1550 cm^{-1} band.

The observed IR spectra of the unsaturated diketoanilides considered can be conveniently explained on the basis of the structure **5** of the compounds. The spectra in the region 1600–1800 cm^{-1} show three intense absorptions at ~1720 cm^{-1}, ~1660 cm^{-1} and ~1600 cm^{-1}. The carbonyl stretching frequency of anilides are strongly dependent on the magnitude of the nitrogen lone pair density of the PhNHCO– group. Values as high as 1779 cm^{-1} has been reported for the amide carbonyl stretching in certain anilides[241]. Thus the band at ~1720 cm^{-1} can confidently be assigned to the stretching of the amide carbonyl of the structure **5**. Usually C=O stretching frequency of amide carbonyl of the structures of the type **5** can be expected at much lower value compared to acetoacetanilide. But the electron withdrawing effect of the groups attached to the carbonyl function together with possibility of non-linearity of the structure in view of the presence of bulky substituents, will strengthen the amide C=O force constant and there by its stretching. Therefore it is not unexpected of these type of structures to show amide carbonyl stretching at much higher value.

Similarly based on the spectral data of related compounds[234-236] the band at ~1600 cm^{-1} can safely be assigned to a conjugated and fully enolised carbonyl group. The cinnamoyl carbonyl group of structure **5** can very well enolise to form an intramolecularly hydrogen bonded structure. Therefore the band at ~1600 cm^{-1} is due to the cinnamoyl carbonyl of structure **5**. Spectra of typical compounds in the region 1400-1800 are reproduced in fig. **3.1-3.4**.

Spectra of the compounds in the region below 1600 cm^{-1} show several strong and medium intensity bands. These bands can be assigned to various C=C and C=N stretching vibrations and to N–H, N–C=O bending, N–H out of plane deformation and C=O out of plane bending, etc. The X–H stretching region of the spectra fully support the structure **5** proposed for the compounds. A comparatively broad band present in the region 2500–3500 cm^{-1} is expected of the intramolecularly hydrogen bonded structure.

IR spectra of all the compounds showed a prominent band at ~976 cm^{-1} typical of *trans* –CH=CH– absorption as the *cis*-ethylenic double bonds usually show weak intensity bands at a much lower region. Important bands that appeared in the spectra of the compounds are given in table 3.3.

Table 3.3

Characteristic IR data (cm^{-1}) of unsaturated diketoanilides

Compounds													Probable assignments
1a	**2a**	**3a**	**4a**	**5a**	**6a**	**7a**	**8a**	**9a**	**10a**	**11a**	**12a**	**13a**	
1721	1710	1710	1714	1715	1715	1712	1711	1716	1717	1705	1720	1718	ν (C=O) amide
1659	1658	1676	1678	1670	1660	1664	1662	1659	1655	1662	1666	1660	ν (C=O) α,β-unsaturated
1599	1620	1620	1634	1599	1612	1610	1618	1618	1599	1616	1610	1620	ν (C=O) chelated
1595	1599	1598	1597	1545	1598	1570	1599	1597	1580	1597	1600	1596	ν(C=C) phenyl/ ν(C=C) alkenyl/ ν amide II
1545	1541	1536	1540	1516	1539	1540	1538	1536	1541	1536	1543	1538	
1498	1494	1486	1504	1498	1516	1518	1502	1503	1498	1494	1501	1510	
1530	1532	1518	1512	1516	1520	1515	1516	1519	1518	1520	1512	1529	
1248	1238	1234	1242	1236	1240	1251	1248	1238	1252	1251	1263	1236	ν amide III
967	970	964	968	970	968	968	968	976	974	974	970	976	ν CH=CH trans
693	691	690	694	693	692	690	692	690	692	692	691	692	ν amide V
656	654	656	654	654	656	658	660	664	669	670	640	672	ν amide IV
617	604	618	618	617	614	610	608	606	604	610	573	608	ν amide VI

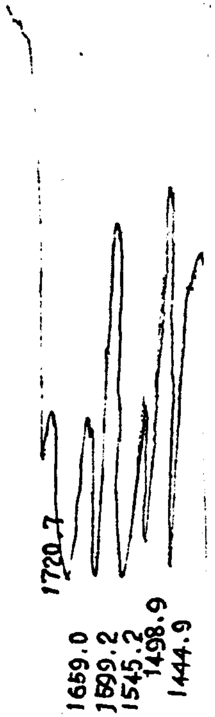


Fig 3·1
IR spectra of 1a

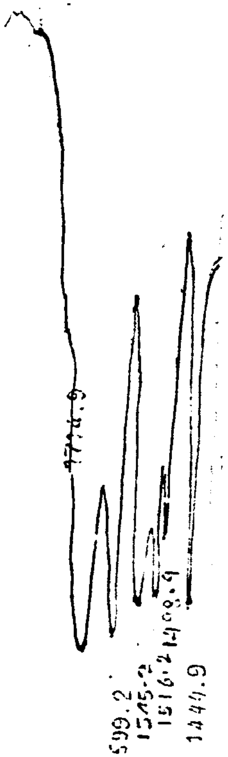


Fig 3·2
IR spectra of 5a

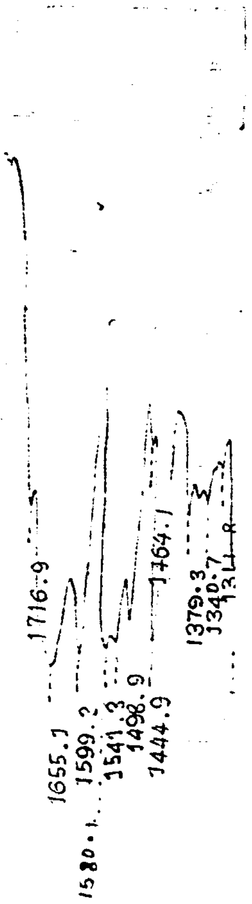


Fig 3·3
IR spectra of 10a

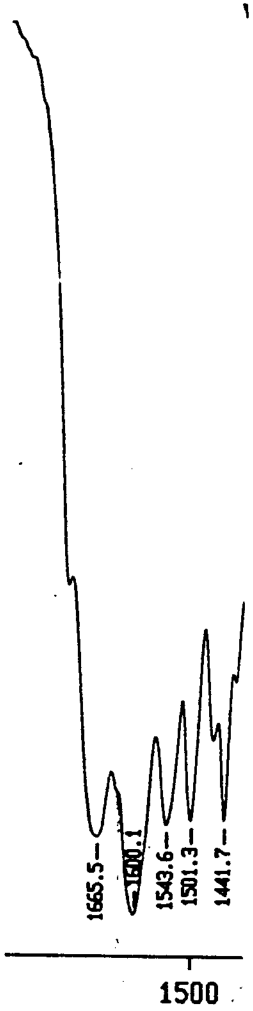


Fig 3·4
IR spectra of 12a

^{1}H NMR Spectra

The use of NMR spectroscopy in settling the structural problems of organic compounds especially 1,3-dicarbonyl compounds are well documented in the literature[52,242-244]. The keto–enol tautomerism of β-dicarbonyl compounds have been studied precisely by this spectral technique. The resonance signal of the proton involved in intramolecular hydrogen bonding generally appears in the low field region of the spectra. However such protons are prone to rapid exchange at room temperature. The enol proton signal of 1,3-dicarbonyl compounds such as 1,3-diketones (acetylacetone, benzoylacetone, etc.) appears at δ~16 ppm. The position of the methine signal, characteristic of the enol form, is also influenced by the electronic effects of the groups attached to the carbonyl function[243].

The ^{1}H NMR spectra of the compounds **1a-3a** displayed a one proton singlet at ~13 ppm and another singlet at ~6 ppm assignable respectively to the strong intramolecularly hydrogen bonded enolic proton and to the methine hydrogen.

The CH_3 singlet of acetoacetailide is at δ2.17 ppm. But in the spectra of the ligands no signal is observed in this region supporting the involvement of γ-methyl groups in condensation. The CH_2 singlet of acetoactanilide at δ3.5 ppm has not changed appreciably in the spectra of the compounds which support the non-enolic nature of the active methylene group of the β-dicarbonyl function. The NH singlet of acetoacetanilide is observed at δ9.04 ppm which shift to downfield in the spectra of the compounds due to strong external conjugation. Further, two separate signals due to the NH protons are also appeared in the spectra indicating the presence of two NH groups. The region at ~δ7 ppm of the NMR spectra of all the compounds are highly complicated due to the absorption of various aromatic hydrogens lying in different environments. Some of the spectra are given in fig. **3.5-3.6**. The assignment of various proton signals observed in the ^{1}H NMR spectra of the ligands are assembled in table 3.4.

Table 3.4
Characteristic ^{1}H NMR spectral data of the unsaturated diketoanilides

Compounds	Chemical shift δppm					
	OH	NH	CH=CH	Methine	CH$_2$	Phenyl substituent
1a	13.178	10.103 9.876	8.201 8.001	6.898	3.585	-
2a	13.124	9.887 9.432	8.624 8.314	6.929	3.586	10.158
3a	12.346	9.801 10.004	8.698 8.512	6.975	3.662	-
4a	13.426	8.989 9.762	8.28 8.221	7.289	3.591	-
5a	13.042	9.219 9.843	8.891 7.671	6.719	3.582	10.042
6a	14.737	9.887 9.762	8.025 7.996	6.987	3.899	-
7a	12.042	10.104 9.844	8.189 8.027	6.942	3.800	3.894
8a	12.747	9.866 9.654	8.184 7.846	6.999	3.949	4.068
9a	12.344	9.739 9.456	8.604 8.608	6.724	3.566	2.932
10a	12.104	9.807 9.708	8.024 8.354	6.969	3.588	10.158 3.921
11a	13.042	10.092 9.842	7.659 7.639	6.858	3.794	3.860 3.830
12a	13.842	10.289 9.765	8.399 8.012	6.453	3.904	3.861 3.834
13a	12.945	9.814 9.844	8.142 7.679	6.796	3.705	6.001

Fig. 3.5 ^{1}H NMR spectrum of **2a**

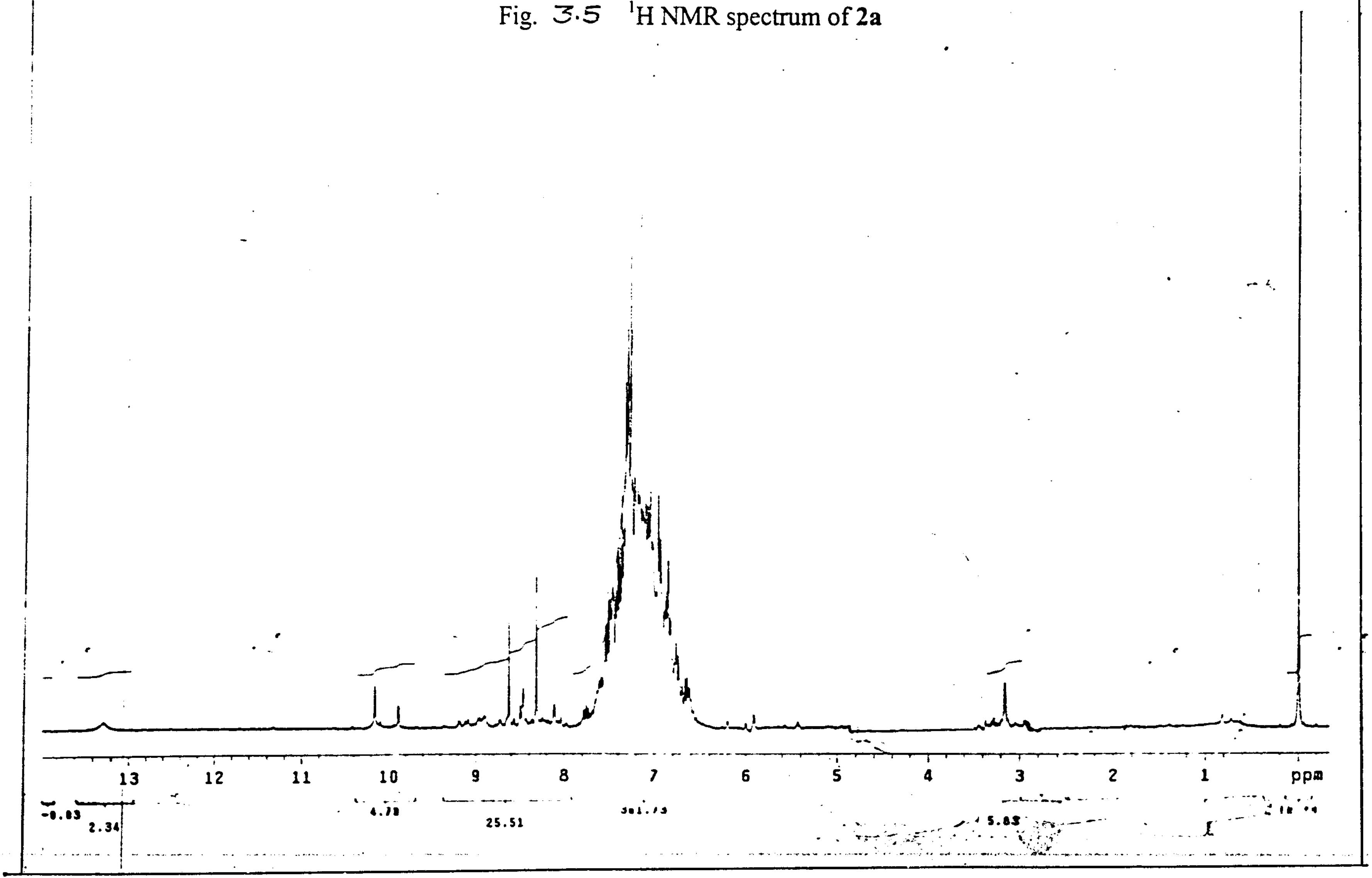
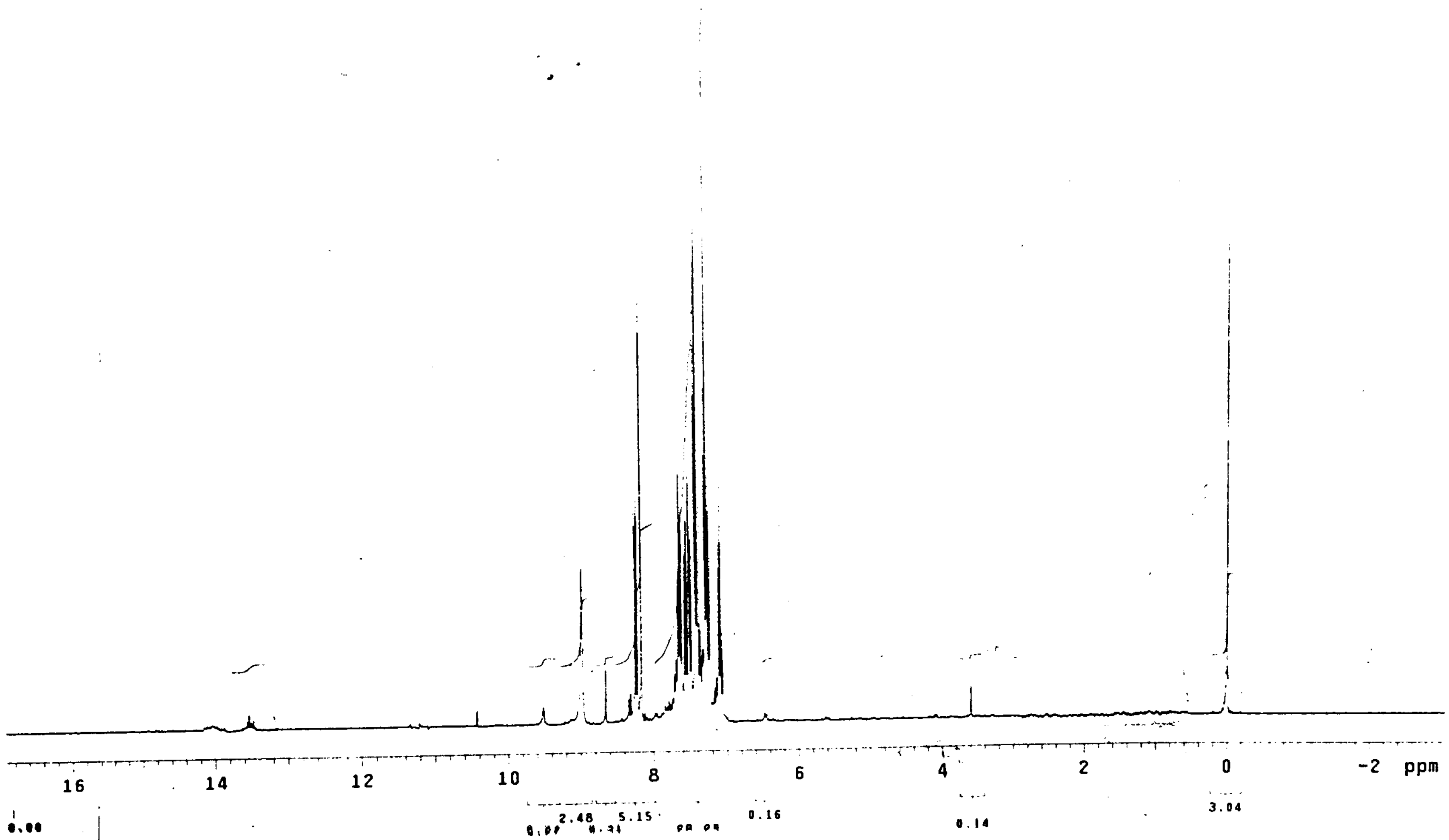


Fig. 3.6 ^{1}H NMR spectrum of **4a**



Mass spectra

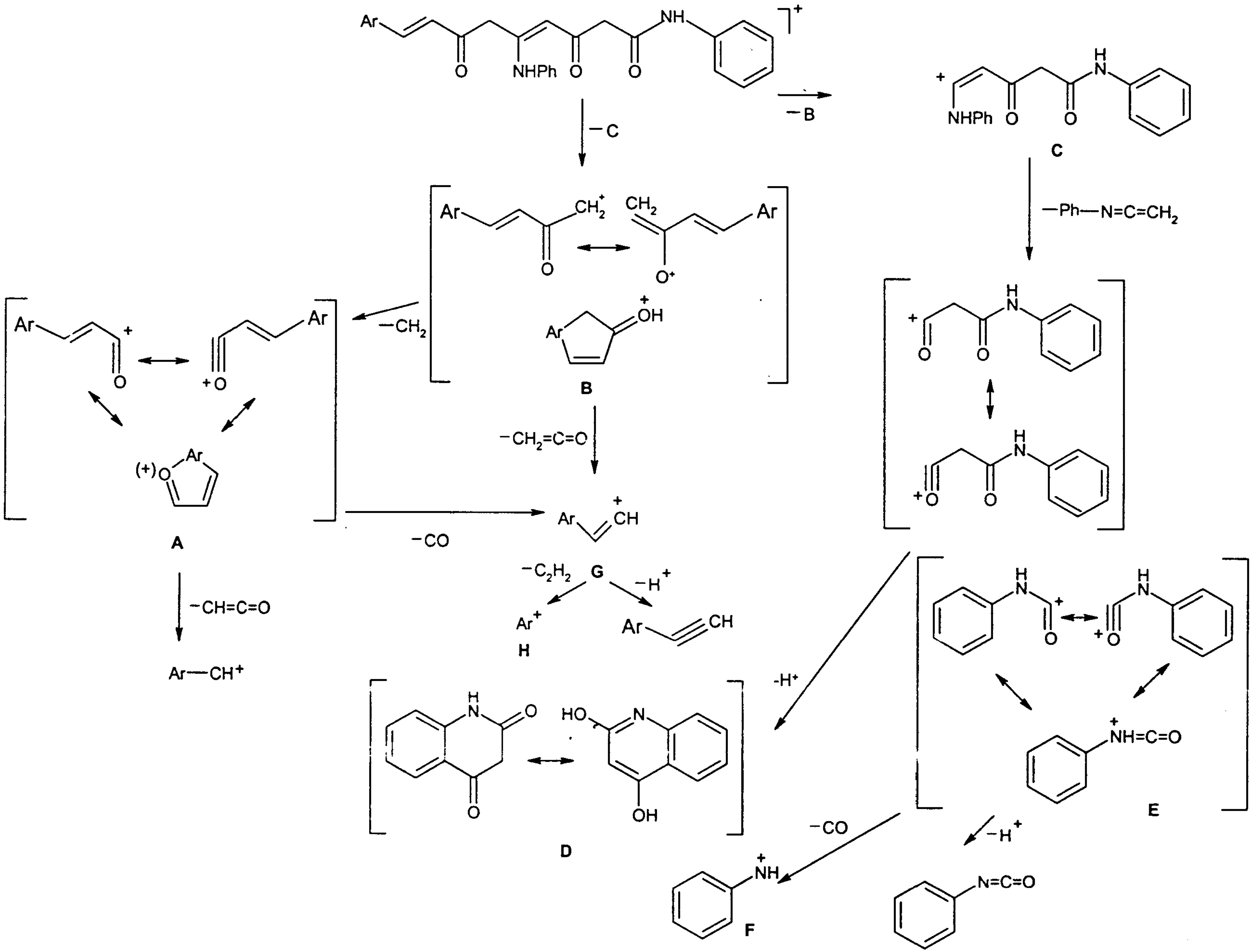
The potential of mass spectrometry in determining the structure of organic compounds including 1,3-dicarbonyl compounds are well demonstrated in the literature[245,246]. Detailed mass spectral analysis of different types of 1,3-dicarbonyl compounds are availableand were useful in determining their structure.

The fact that the condensation between acetoacetanilide and aromatic aldehyde takesplace in a 2:1 ratio is clearly evident from the molecular ion peak. The peaks **A** and **B** confirm the condensation of the γ-methyl group of acetoacetanilide with aromatic aldehyde. The peak $[C_6H_5NHCO]^+$ supports the presence of anilide group in the condensation product so that the group is not hydrolysed during the reaction condition. This is also confirmed by the $[P - C_6H_5NHCO]^+$ peak in the spectra. The absence of $[P - 2C_6H_5NHCO]^+$ peak indicates that only one amide carbonyl group is free in the product. The peak **B** clearly states that the active methylene group is protected through out the course of the reaction. Intense peaks due to the elimination of $[C_3HO_2]^+$ from the molecular ion is a most common feature of the mass spectra of 1,3-dicarbonyl compounds, having at least one aroyl group. The important peaks observed are shown in table 3.5 and typical spectra are reproduced in fig. **3.7-3.19**. Prominent peaks appeared in the spectra of all the diketoanilides can be conveniently accounted by the fragmentation pattern given in scheme 3.7.

Table 3.5

Important fragments observed in the FAB mass spectra of unsaturated diketoanilides

Compounds	P^+	A	B	C	D	E	G	H	P – D	P – E	P – F	P – E – F
1a	425	131	145	280	162	120	103	-	263	305	333	213
2a	441	147	161	280	162	120	119	-	279	221	249	229
3a	460	166	180	280	162	120	138	112	298	340	368	248
4a	470	176	190	280	162	120	148	122	308	350	378	258
5a	441	147	161	280	162	120	119	-	279	221	249	229
6a	460	166	180	280	162	120	138	112	298	340	368	248
7a	455	161	175	280	162	120	133	107	293	335	363	243
8a	469	175	189	280	162	120	145	119	307	349	117	257
9a	468	174	188	280	162	120	144	118	306	348	376	256
10a	471	177	191	280	162	120	149	123	309	351	379	259
11a	485	191	205	280	162	120	163	137	323	365	393	273
12a	485	191	205	230	162	120	163	137	323	365	393	273
13a	469	175	189	280	162	120	145	119	307	349	117	257


−C
−B
C
−Ph—N=C=CH₂
−CH₂
B
−CH₂=C=O
A
−CO
G
−C₂H₂
−H⁺
H
−CH=C=O
Ar—CH⁺
-H⁺
D
E
−CO
−H⁺
F
N=C=O
NH=C=O

Scheme 3.7

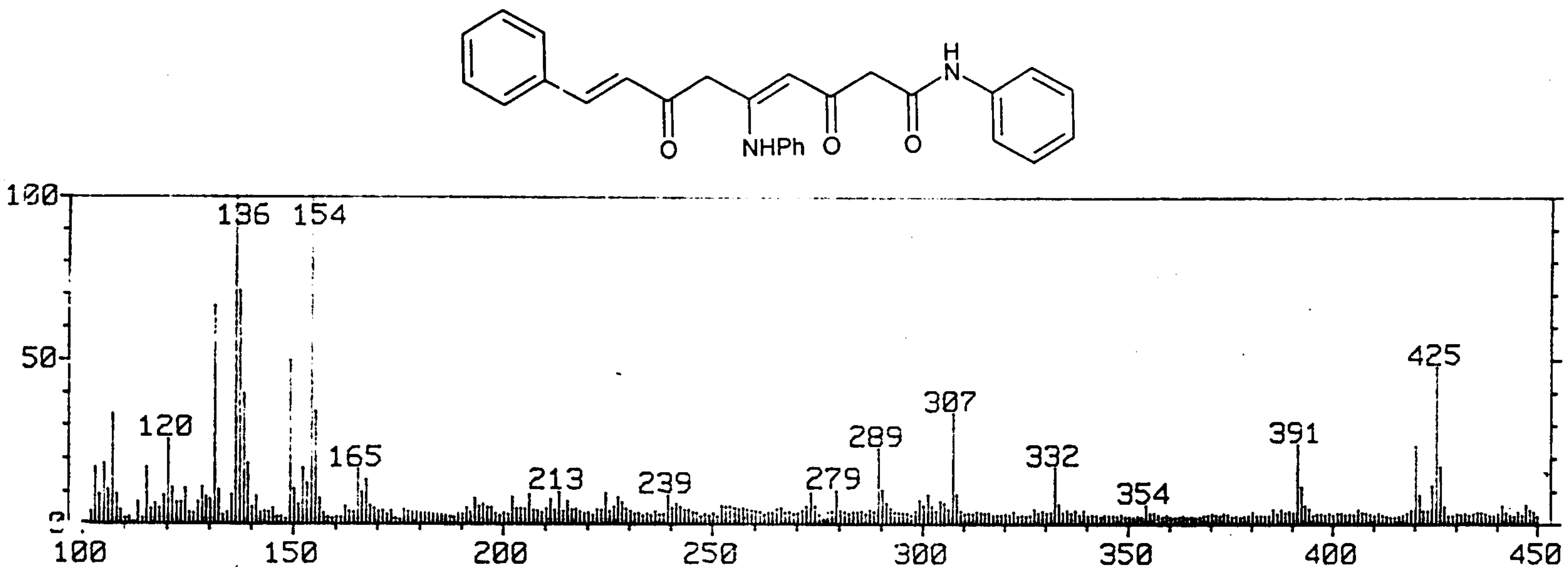


Fig.3.7. FAB Mass spectrum of **1a**

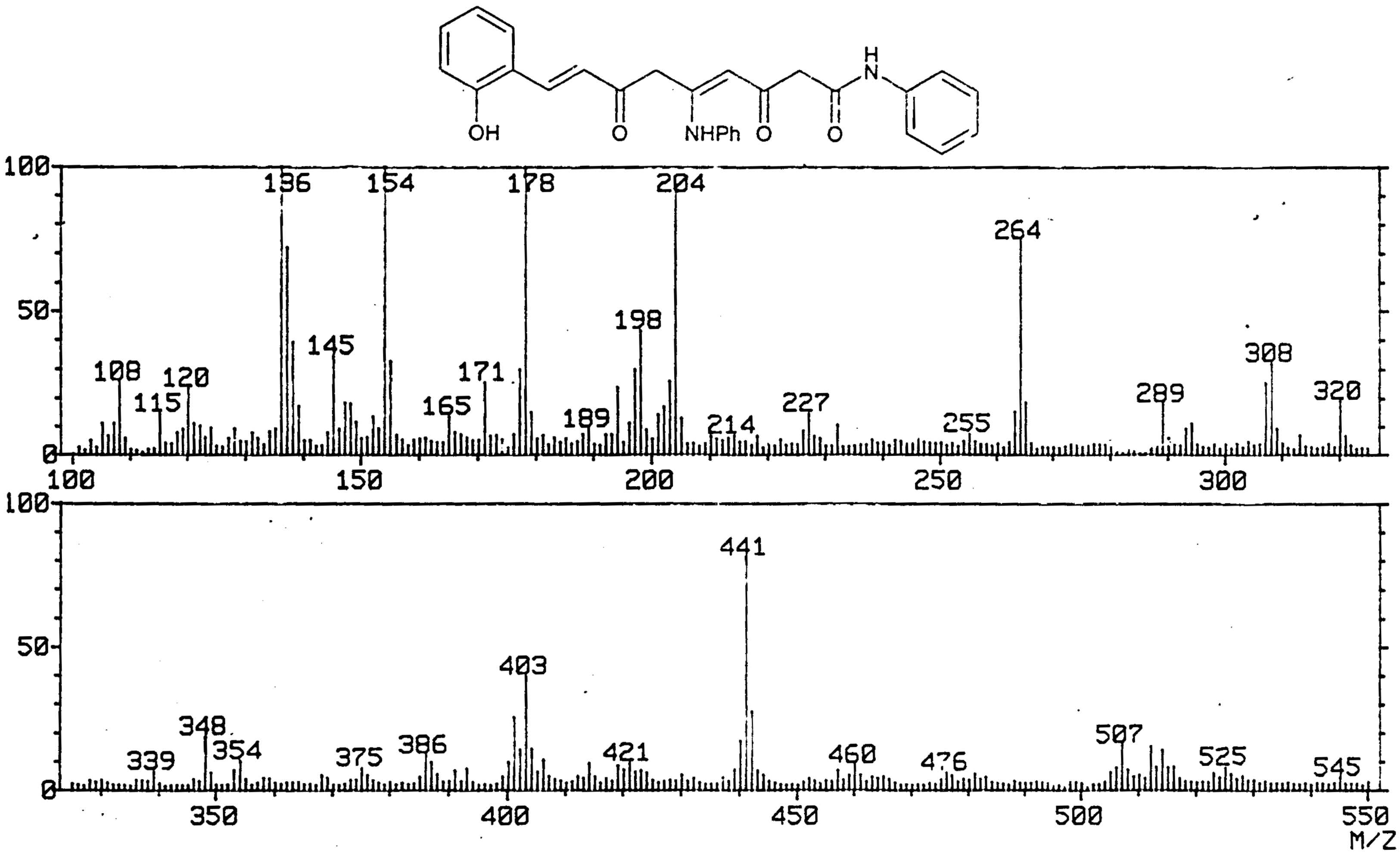


Fig. 3·8. FAB Mass spectrum of **2a**

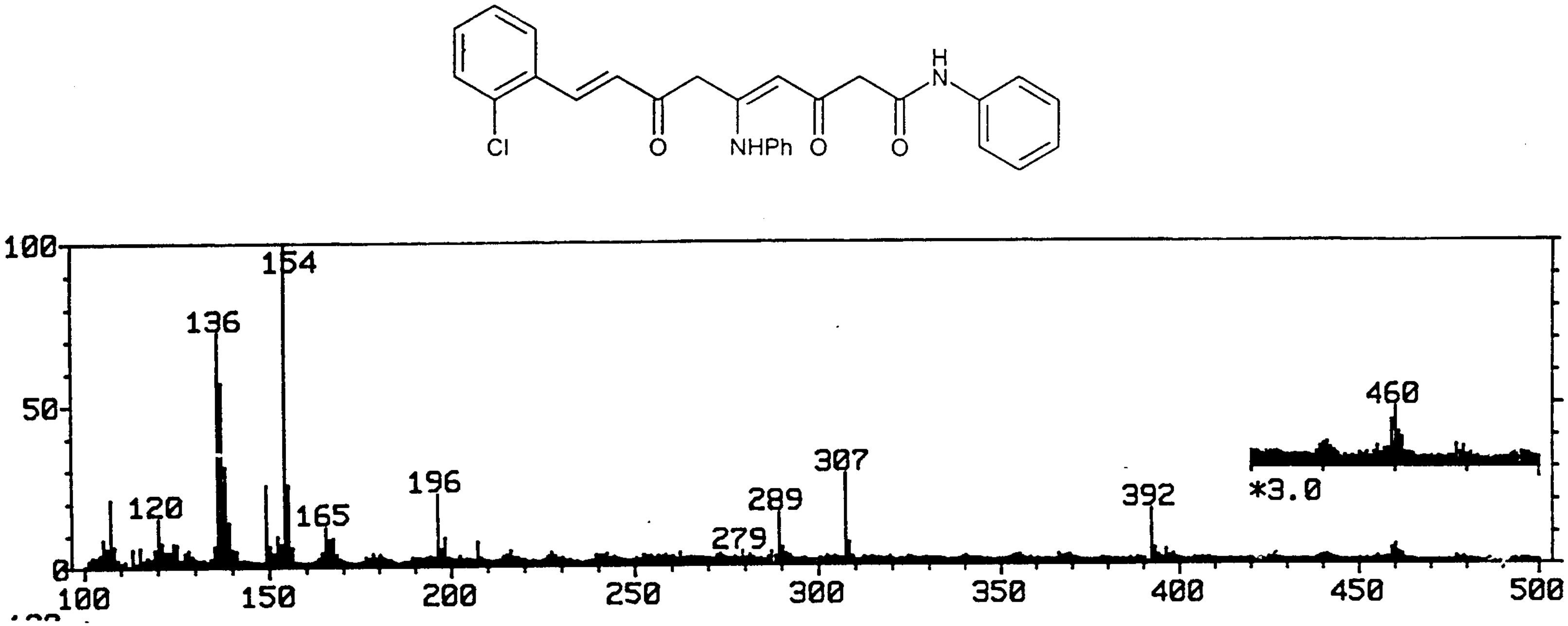


Fig. 3·9 FAB Mass spectrum of 3a

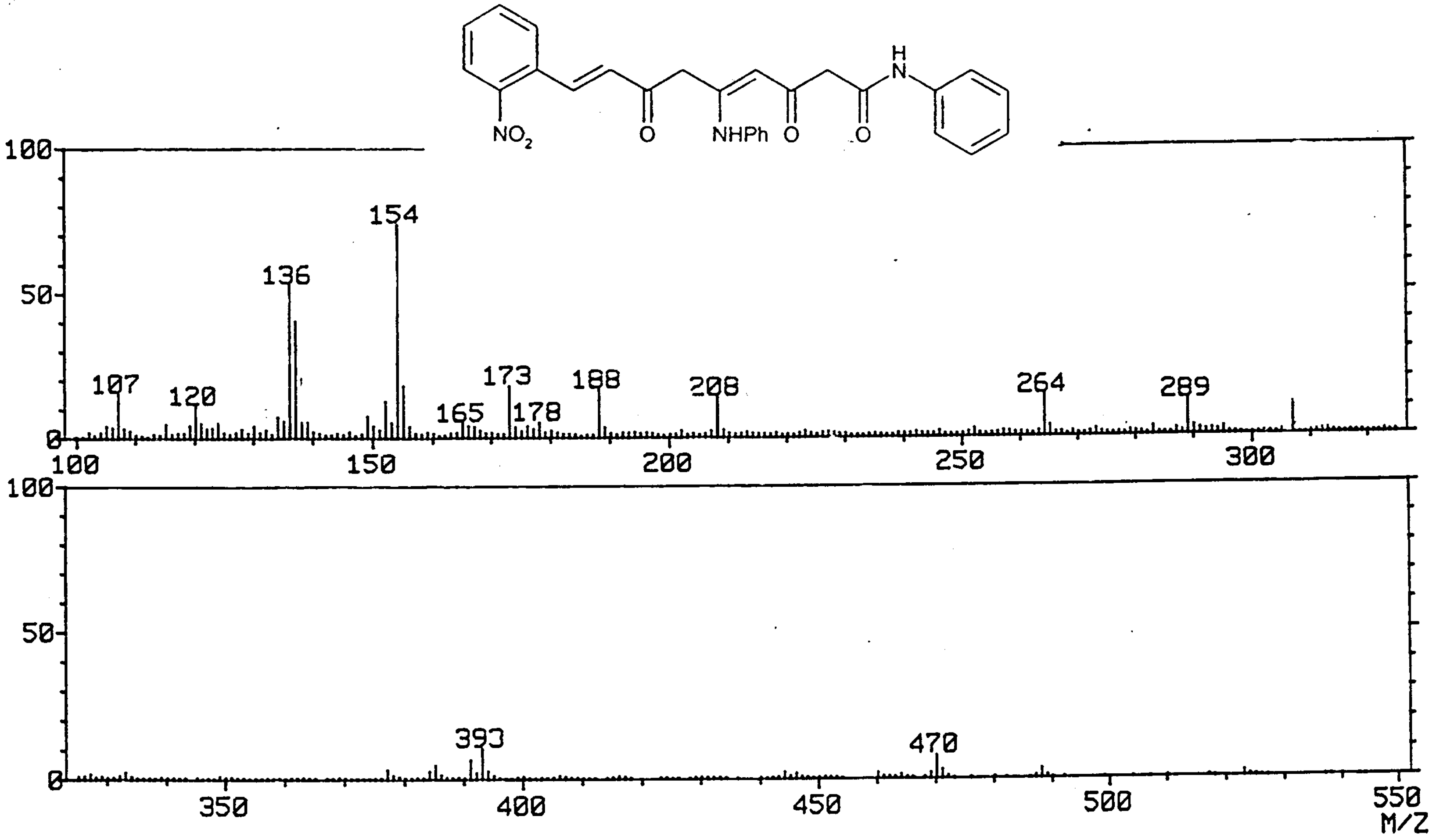


Fig. 3.10FAB Mass spectrum of **4a**

76 E

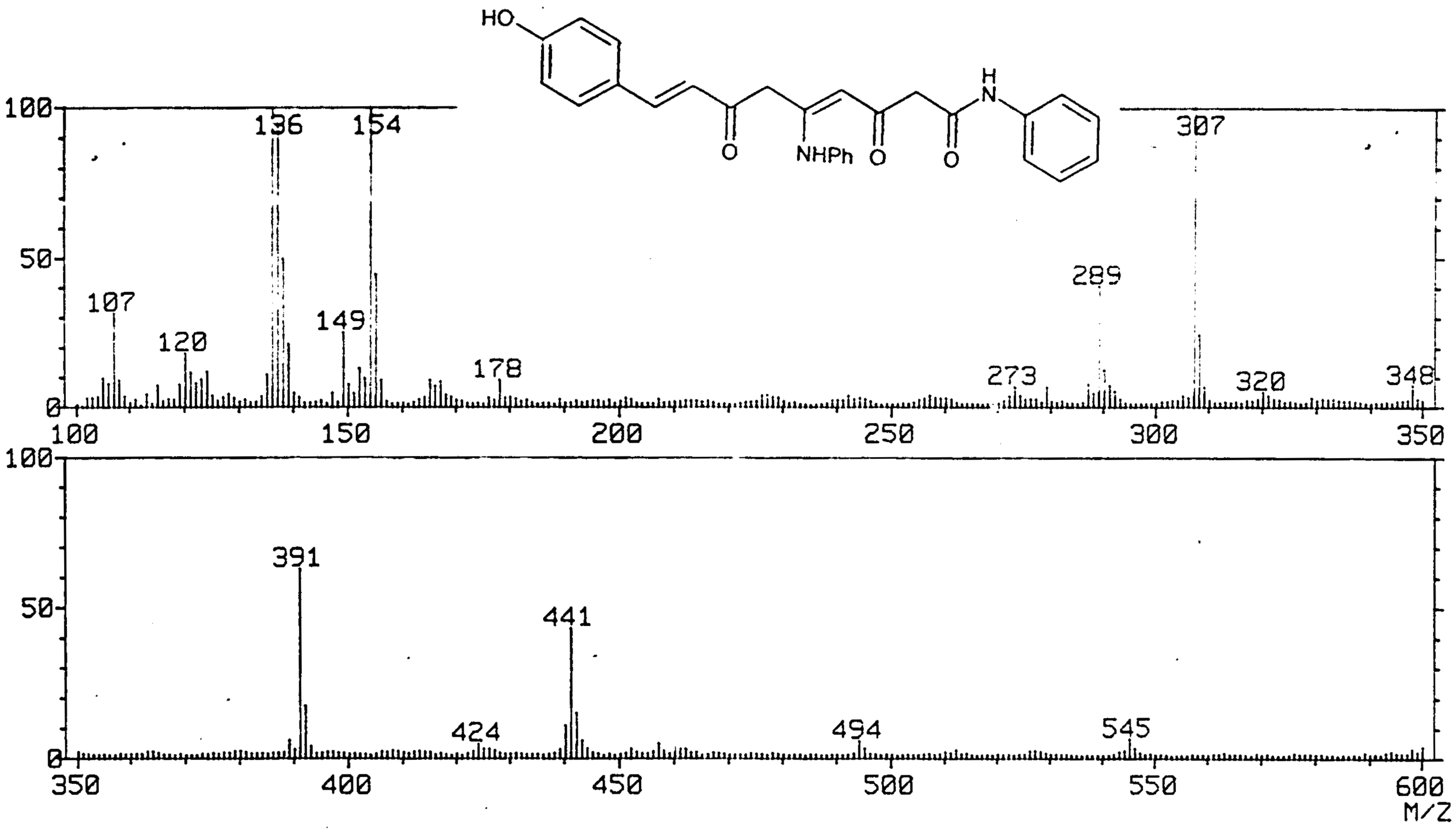


Fig.3.11 FAB Mass spectrum of **5a**

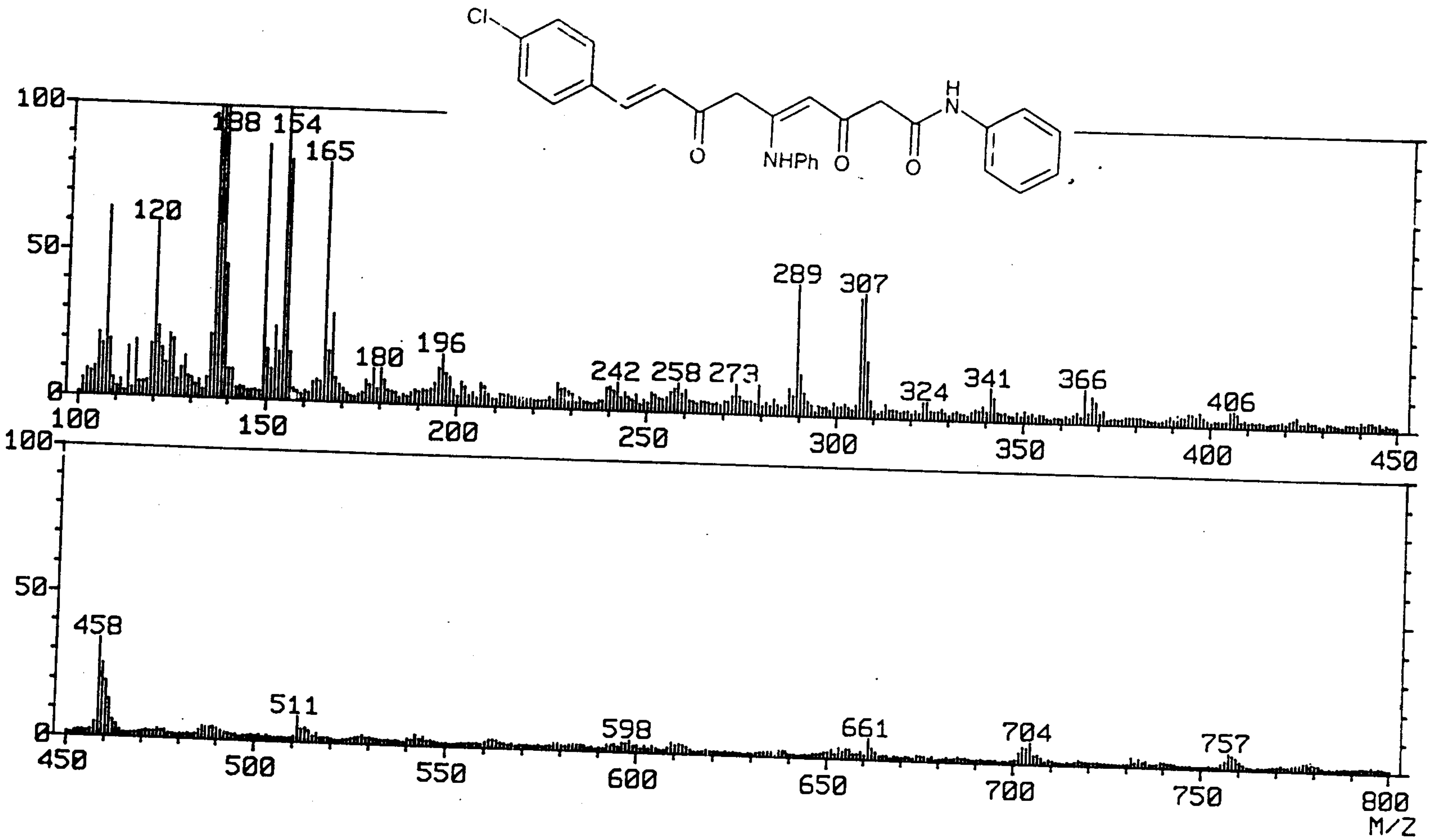


Fig. 3.12. FAB Mass spectrum of **6a**

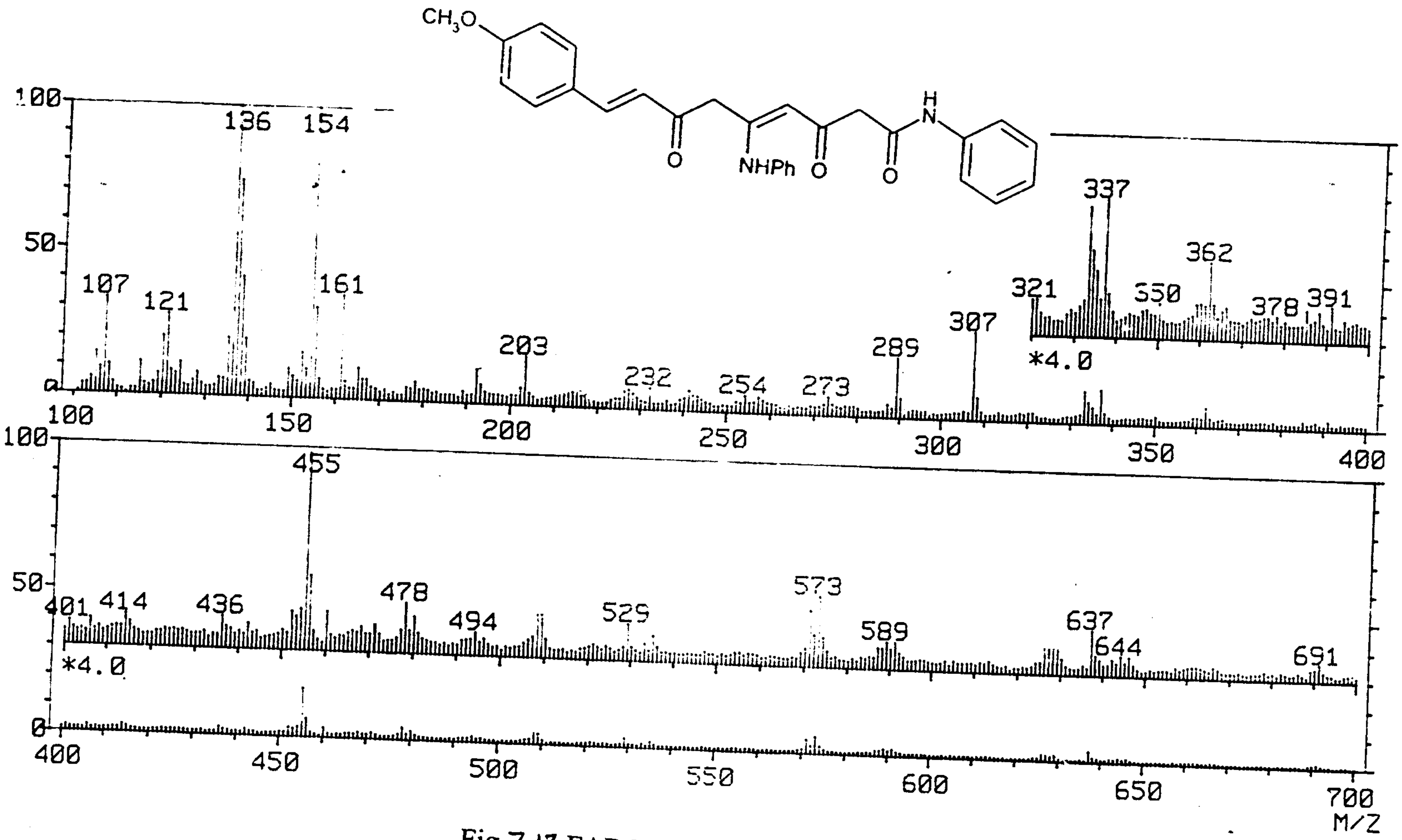


Fig. 3.13. FAB Mass spectrum of **7a**

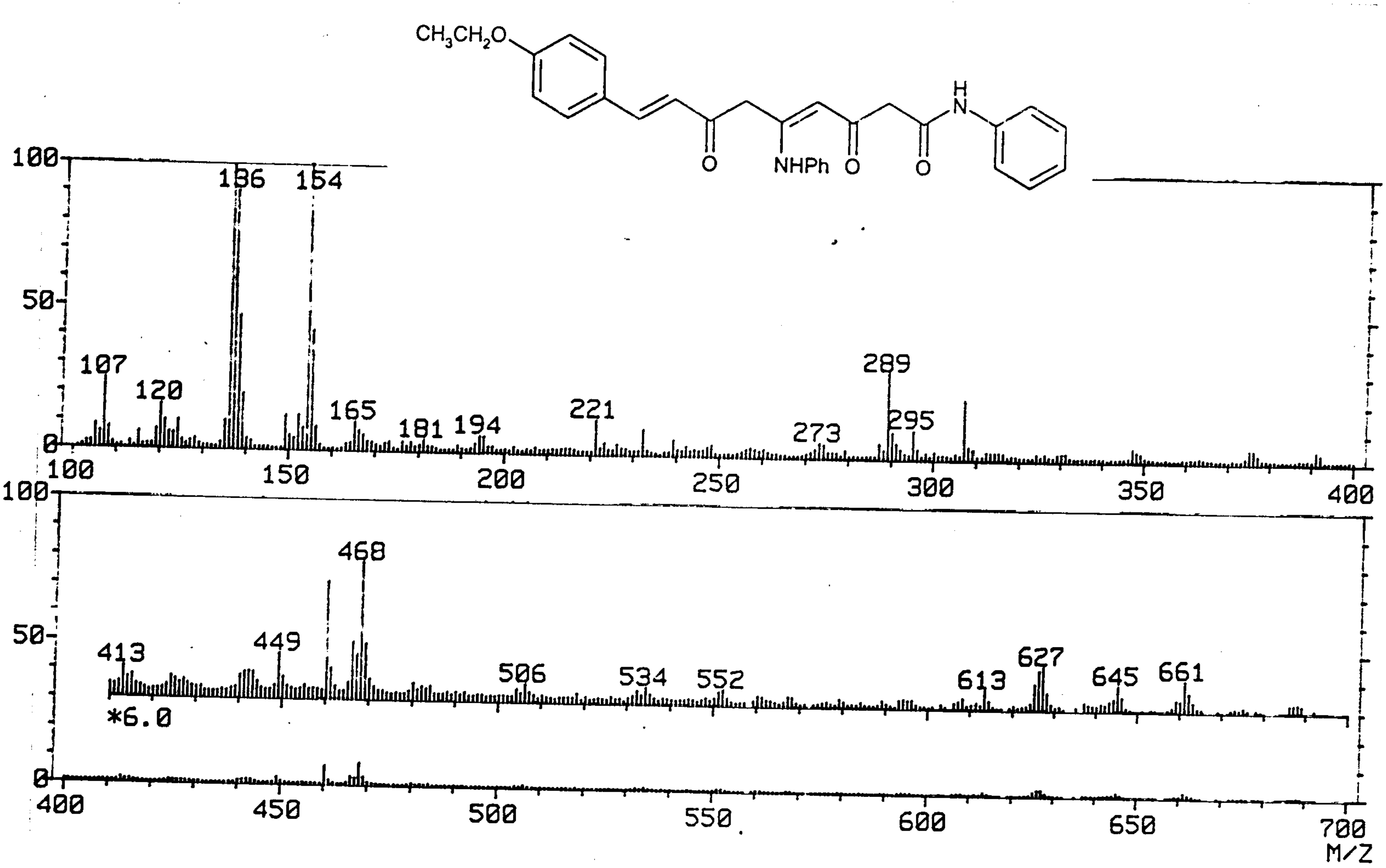


Fig. 3.14 FAB Mass spectrum of **8a**

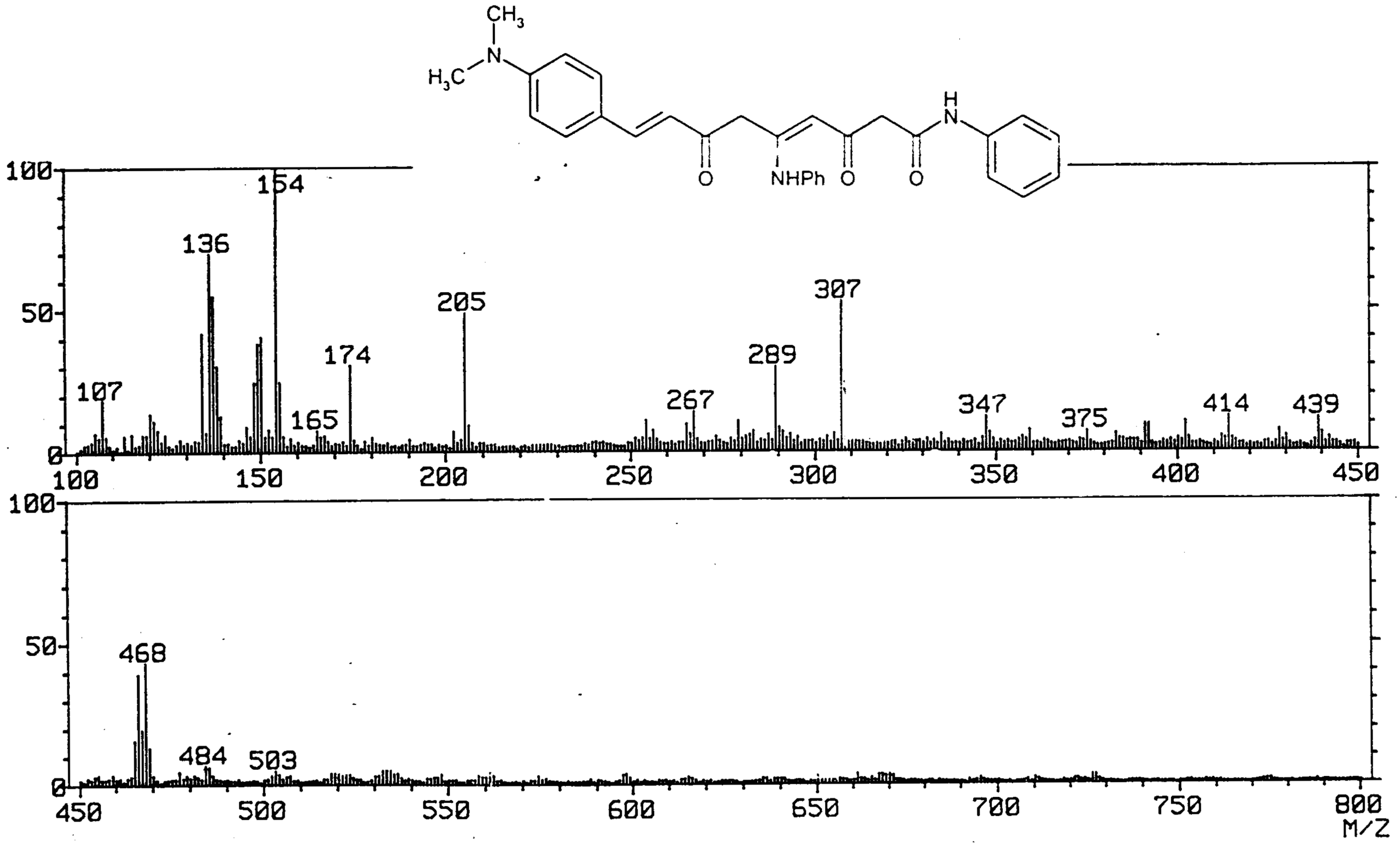


Fig.3.15 FAB Mass spectrum of **9a**

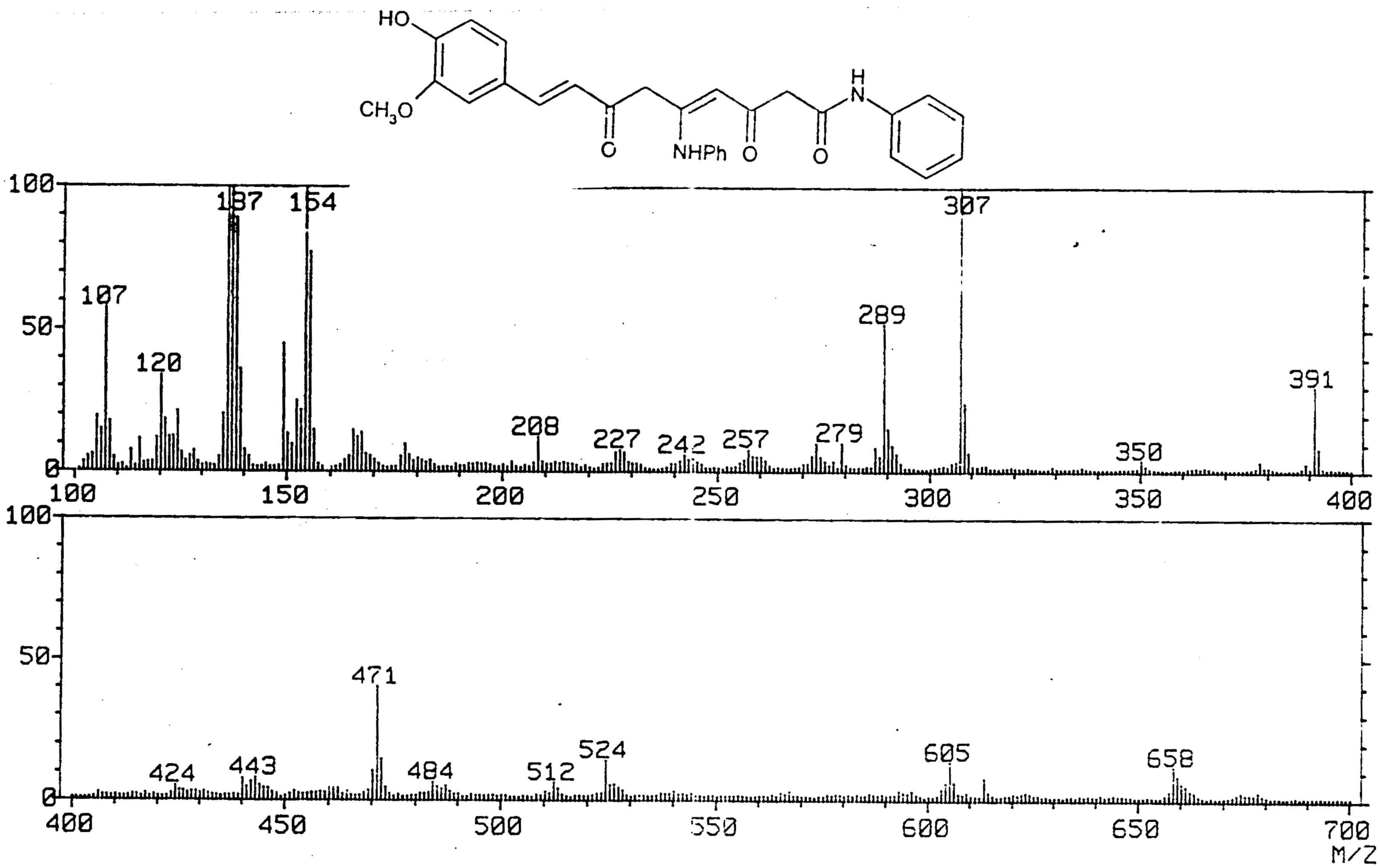


Fig.3.16.FAB Mass spectrum of **10a**

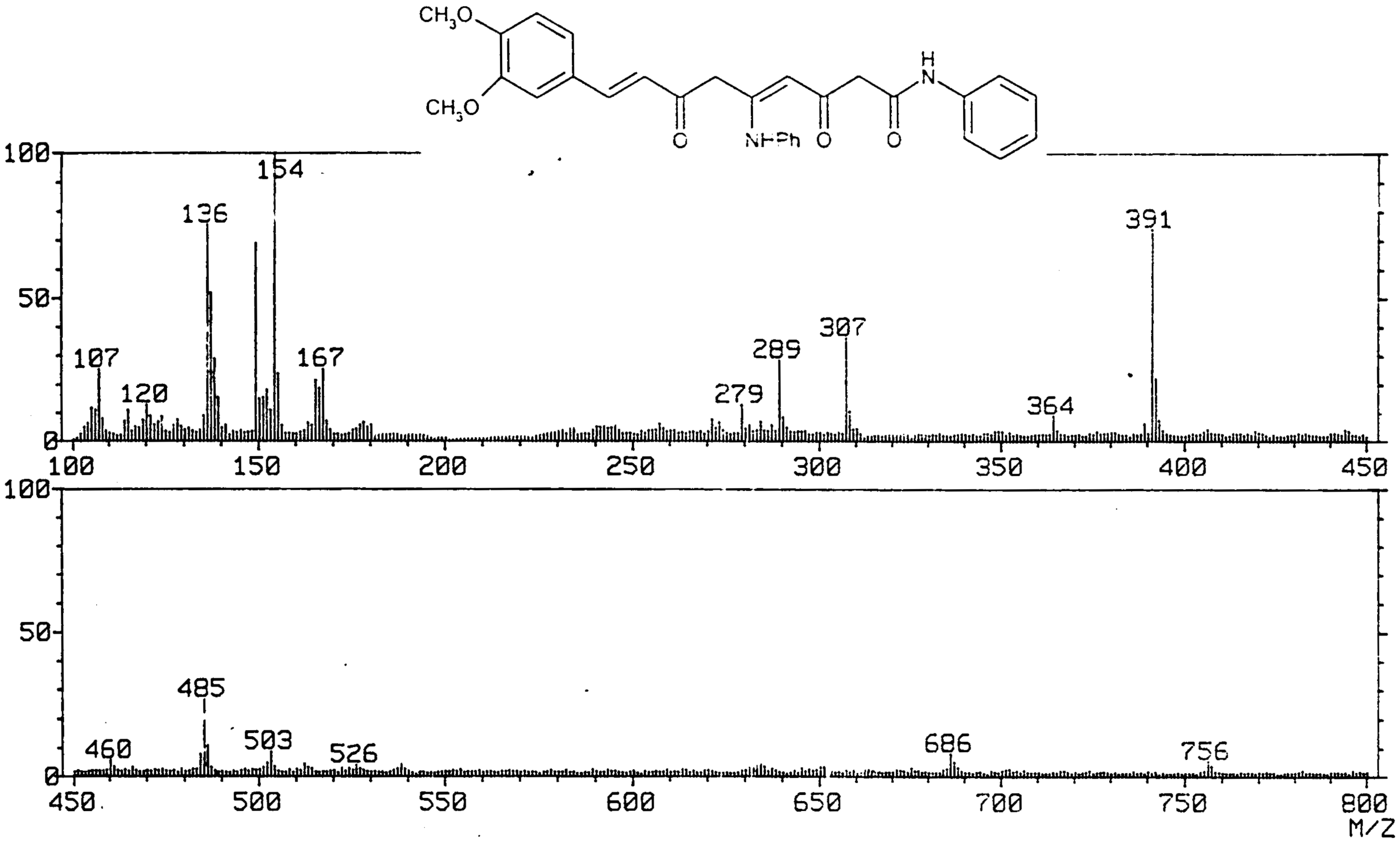


Fig. 3.17. FAB Mass spectrum of **11a**

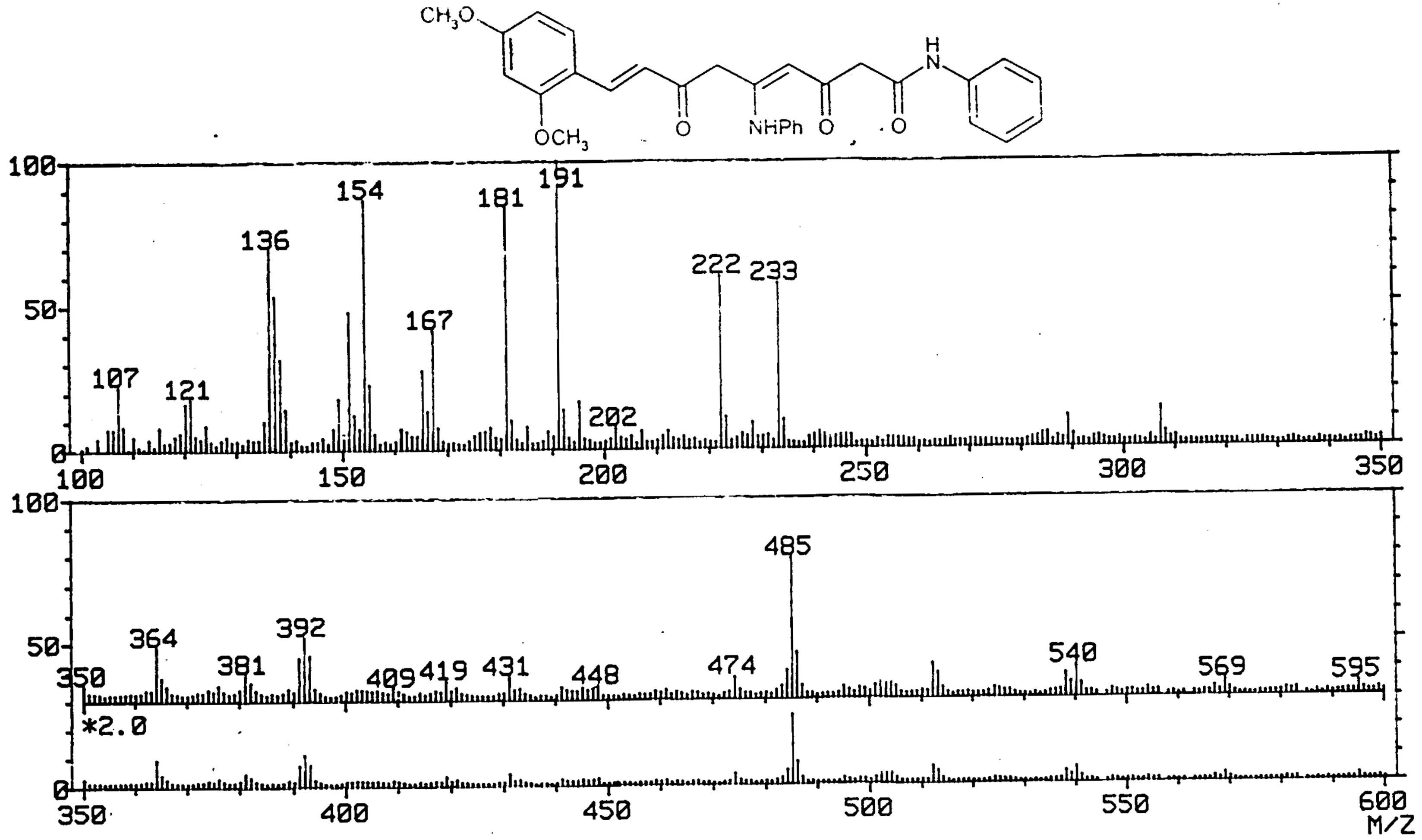


Fig. 3.18. FAB Mass spectrum of **12a**

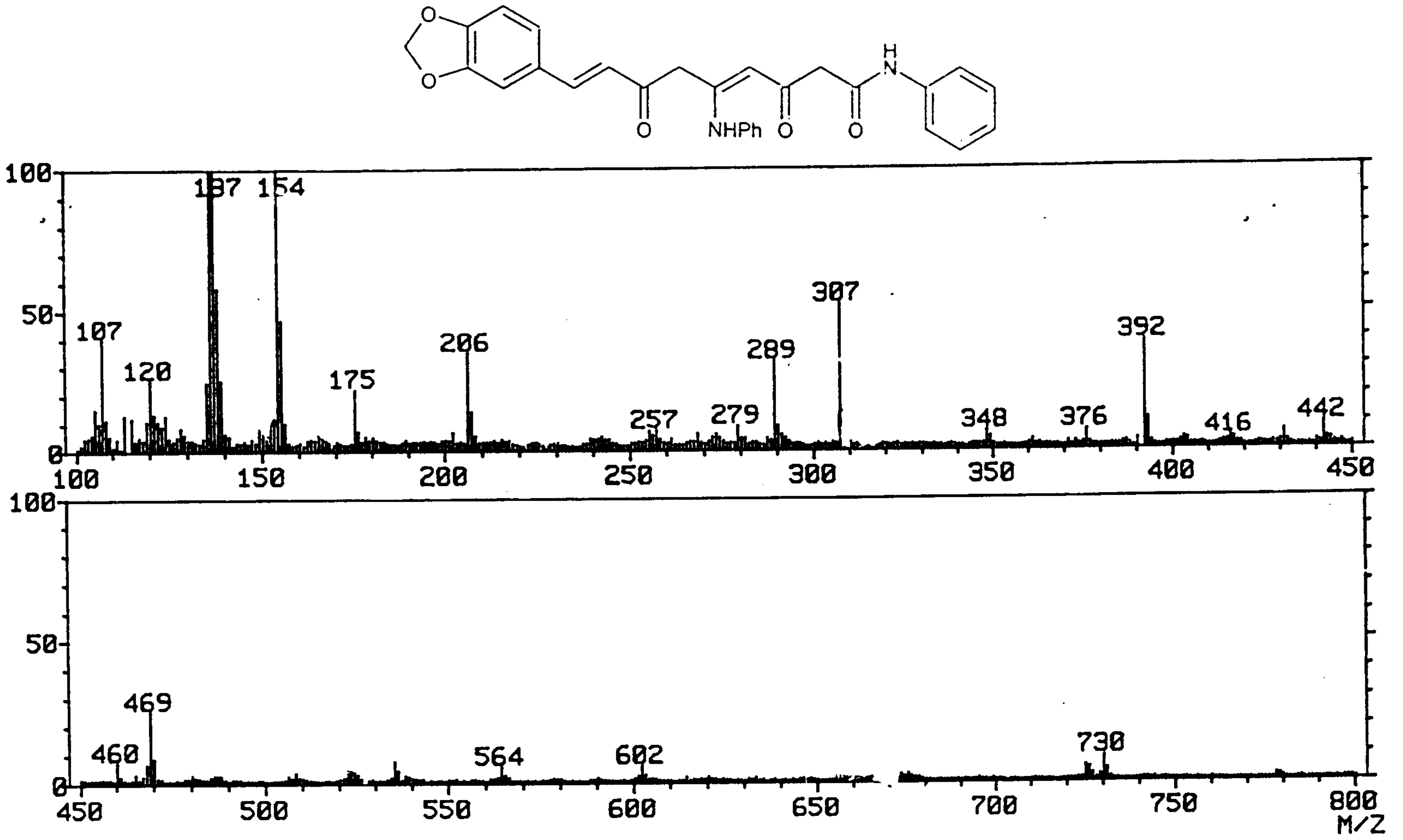
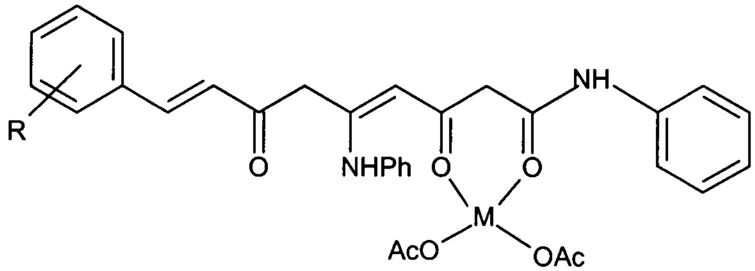


Fig. 3.19 FAB Mass spectrum of 13a

Characterisation of the metal chelates

Analytical and physical data of the metal chelates are given in table 3.6–3.10. The observed elemental analysis data of the chelates agreed well with their 1:1 metal-ligand stoichiometry. Complexes obtained in pure form are only reported. All metal complexes behaved as non-electrolytes in DMF (specific conductance <10 $\Omega^{-1}cm^{-1}$; 10^{-3} M solution). Cu(II) and Co(II) complexes showed normal magnetic moments while Ni(II), Zn(II) and Cd(II) chelates are diamagnetic.

The observed UV, IR, ^{1}HNMR and mass spectra of the complexes are in agreement with structure **6**.



6

UV spectra

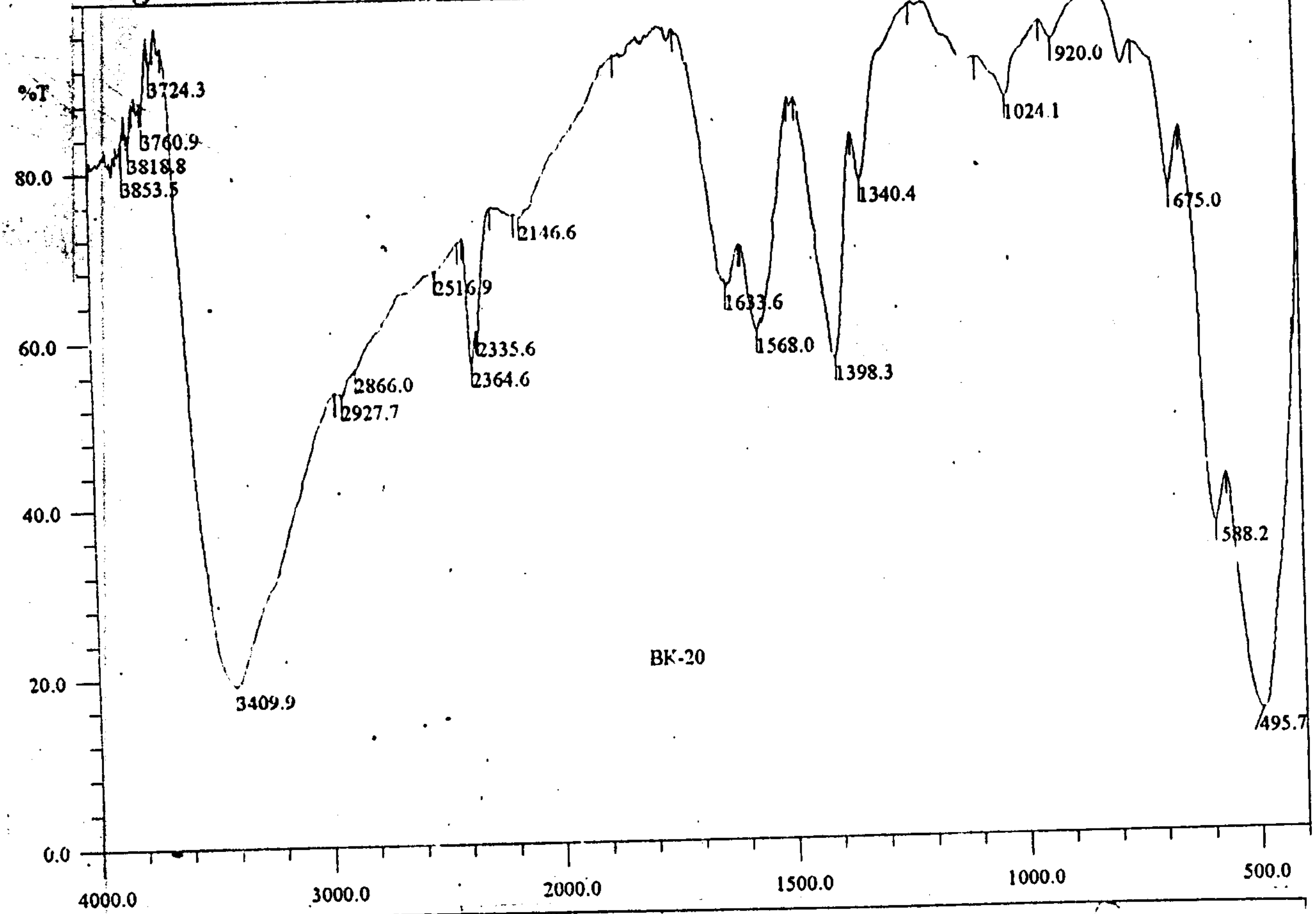
The UV absorption maxima of the metal chelates bear close resemblance with the free ligands. So it can be inferred that no structural alteration of the ligand has occurred during complexation. However the values shifted slightly to longer wave length in the spectra of the metal complexes indicating the involvement of the carbonyl oxygens in metal complexation[15,247,248].

IR spectra

The exact complexing site of a polydentate ligand such as those containing different carbonyl groups can be revealed from IR spectroscopy[15-18,19]. Acetoacetanilide shows three bands at 3420, 3295 and 3250 cm^{-1} which can be assigned to NH stretching vibrations of the anilide group. These bands appeared in the complexes as a strong and broad band and do not show any appreciable shift on complex formation and suggest the non coordination of NH group of anilide to the metal atom. The 3500–3000 cm^{-1} region of the IR spectra of the unsaturated diketoanilides and their complexes do not show any marked difference which indicate that the hydrogen bonded enolic OH is not replaced or involved in complex formation. The band at ~1720 cm^{-1} of the free ligand disappeared in the spectra of all the complexes and instead a comparatively broad and intense band appeared at ~1650 cm^{-1} and no other band is observed in the region 1600–1800 cm^{-1}. This indicate not only the amide carbonyl but also the alkenyl carbonyl is also affected appreciably as a result of metal coordination. The band at ~1650 cm^{-1} can arise only as due to metal bonded carbonyl function. The broad nature suggest that both the metal bonded carbonyl groups undergo stretching in this range. The amide II and III bands in ligands do not undergo any appreciable shifts and remain unaffected on complexation, while, the amide IV band at ~960 cm^{-1} shifted to higher frequency in the complexes. These observations suggest that bonding takes place through both the dicarbonyl oxygens atoms of the ligand and not through the nitrogen atom of the anilide moiety. Monodentate -OAc usually show two bands at ~1620 $cm^{-1}$and ~1310 cm^{-1} due to antisymmetric and symmetric stretching respectively[265]. Since carbonyl absorption of the compounds also appeared in this region the band at ~1620 cm^{-1} could not be located. However a medium intensity band observed at ~1320 cm^{-1} suggest the coordination of the acetate groups. The Co(II) complexes showed bands at ~3220 cm^{-1} indicating the presence of coordinated water molecules.

The important IR peaks of various complexes are listed in table 3.6–3.10. In conformity with the structure **6** spectra of the chelates showed additional bands at ~460 cm^{-1} and ~425 cm^{-1} assignable to $\nu_{M\text{-}O}$ vibrations. Thus IR spectra of the complexes support the neutral bidentate coordination of the unsaturated diketoanilides. Typical spectra are reproduced in fig. **3.20-3.23**.

Fig 3.20 IR spectrum of Cd(II) complex of 2a



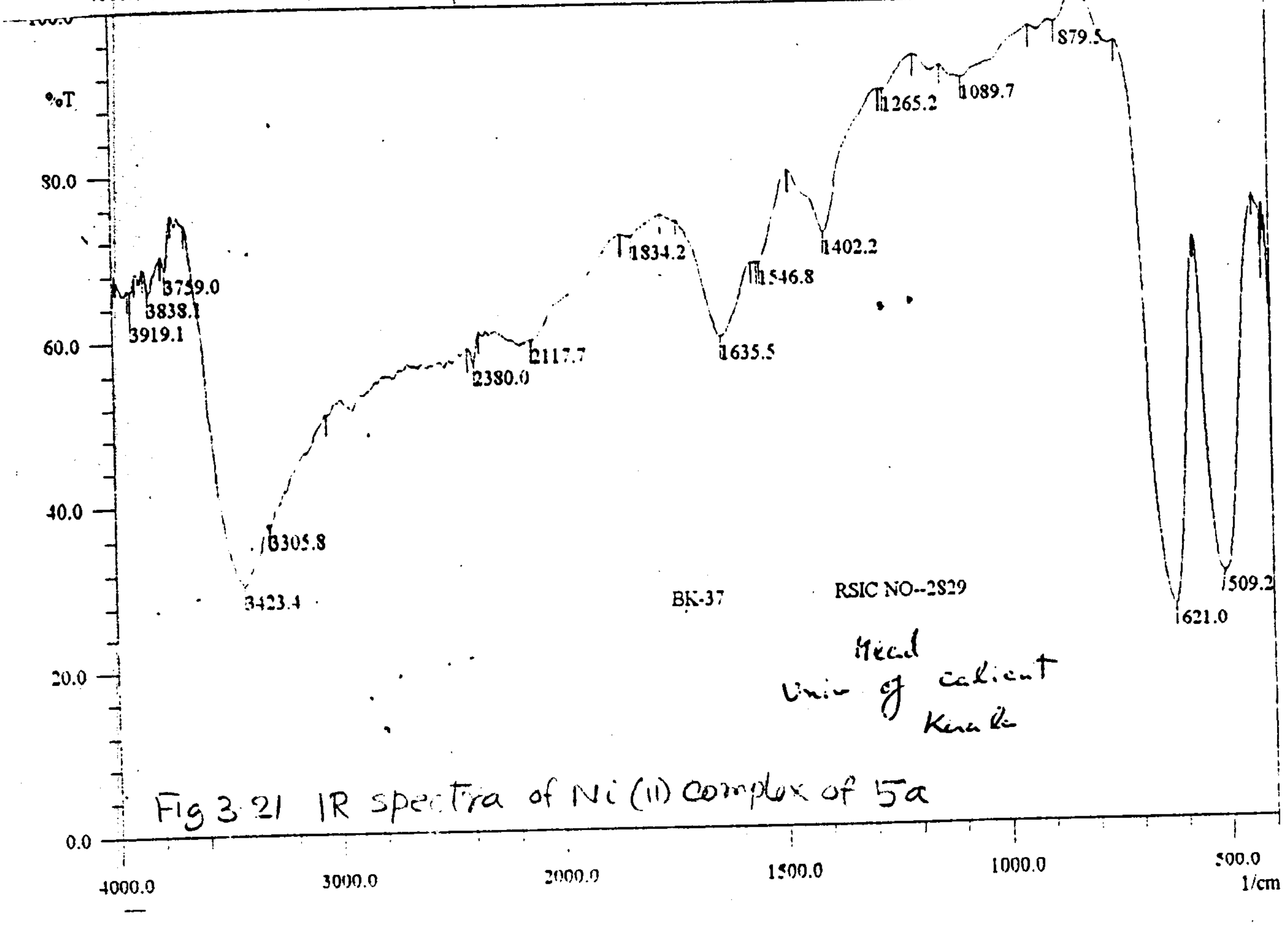


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Fig 3.21 IR spectra of Ni (II) complex of 5a

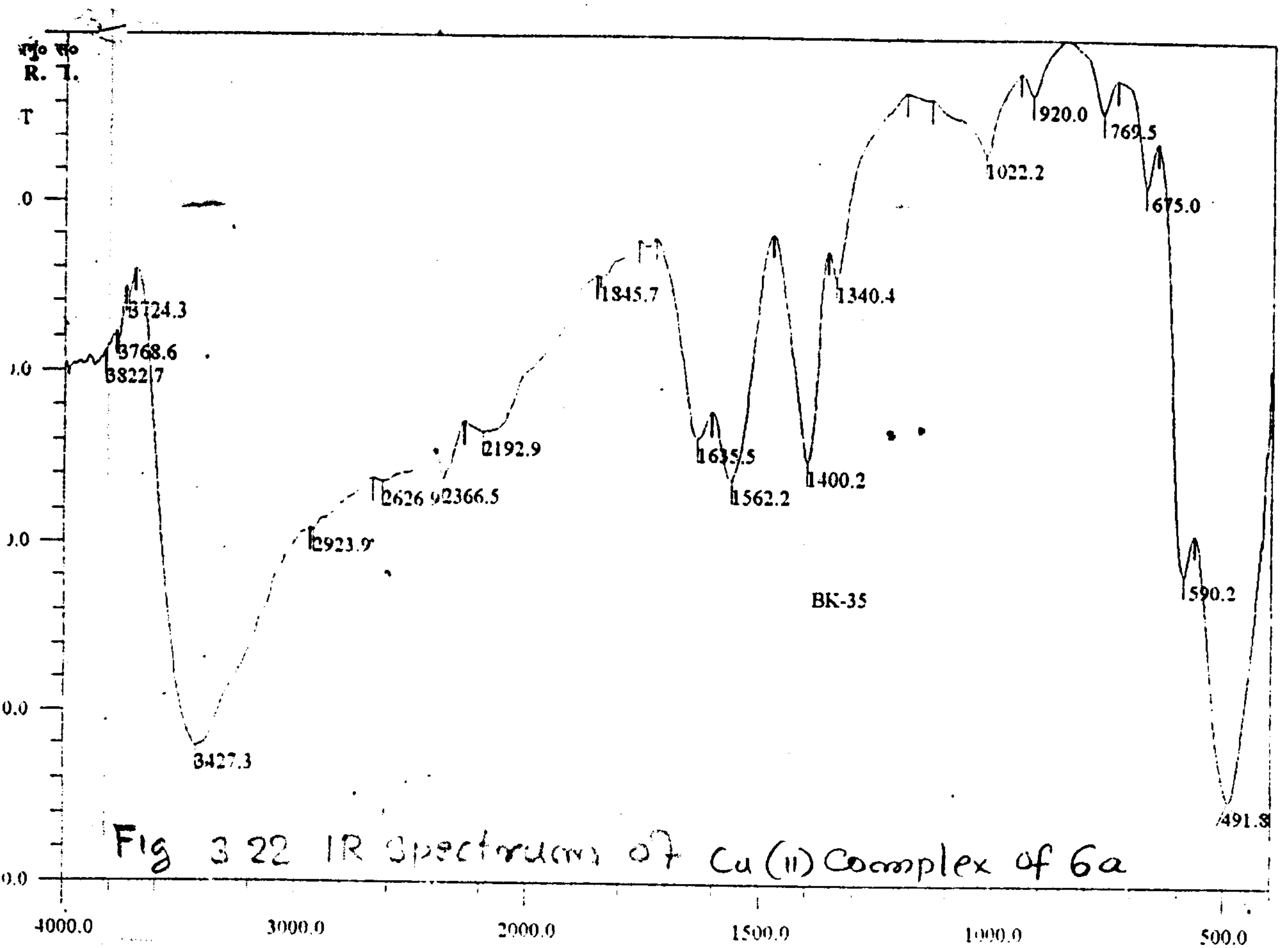


Fig 3.22 IR spectrum of Cu(II) complex of 6a

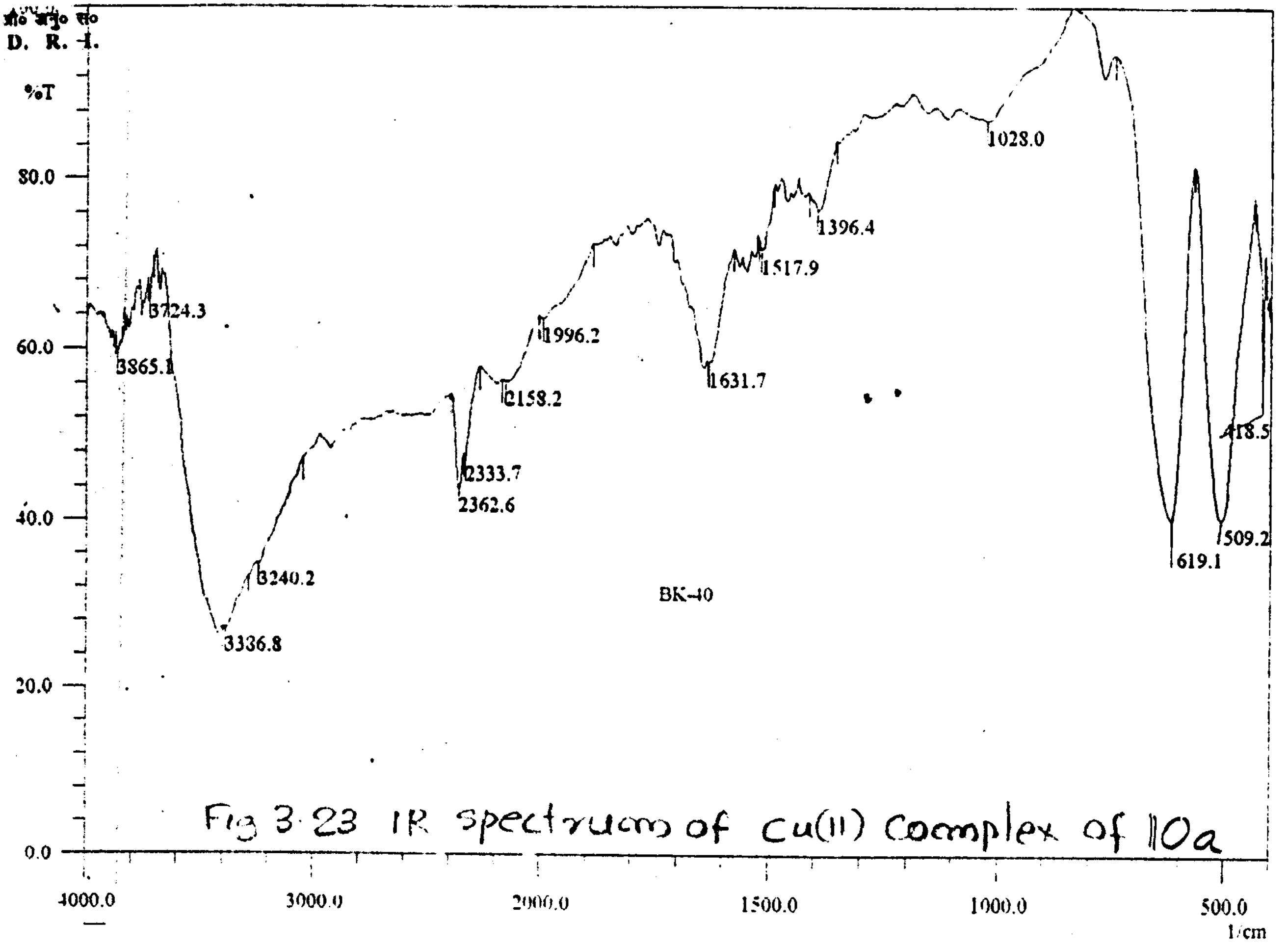


Fig 3.23 IR spectrum of Cu(II) complex of 10a

Table 3.6

Physical, analytical and IR data of the Co(II) chelates of the unsaturated diketoanilides, (HL)

Co(II) Chelate of	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)*				Characteristic IR absorption bands (cm^{-1})	
			C	H	N	Co	νC=O	νM-O
1a	176	4.61	61.76 (61.90)	5.04 (4.99)	4.61 (4.66)	9.85 (9.82)	1640	414 470
2a	184	4.89	60.94 (60.29)	4.80 (4.86)	4.52 (4.54)	9.04 (9.56)	1635	416 490
3a	196	4.62	58.12 (58.49)	4.52 (4.56)	4.38 (4.40)	9.04 (9.28)	1642	424 486
5a	208	4.78	60.14 (60.29)	4.74 (4.86)	4.50 (4.54)	9.42 (9.56)	1643	428 475
9a	214	4.63	60.11 (60.76)	5.06 (5.54)	6.92 (6.65)	8.94 (9.34)	1635	410 472
11a	188	4.87	59.84 (59.90)	5.12 (5.14)	4.21 (4.24)	9.01 (8.93)	1638	418 476
13a	192	4.54	61.01 (61.05)	4.71 (4.77)	4.36 (4.45)	9.24 (9.38)	1637	420 474

* *The calculated value corresponds to the* $[Co(HL)(OAc)_2(H_2O)_2]$ *composition*

Table 3.7

Physical, analytical and IR data of the Ni(II) chelates of the unsaturated diketoanilides, (HL)

Ni(II) Chelate of	MP °C	Elemental analysis (%) Found/(Calcd)*				Characteristic IR absorption bands (cm^{-1})	
		C	H	N	Ni	νC=O	νM-O
1a	204	60.92	5.20	4.68	9.81	1640	416
		(61.90)	(4.99)	(4.66)	(9.82)		474
5a	184	60.28	4.81	4.34	9.60	1635	415
		(60.29)	(4.86)	(4.54)	(9.56)		486
6a	178	58.04	4.54	4.30	9.14	1646	420
		(58.49)	(4.56)	(4.40)	(9.28)		484
7a	164	60.52	5.14	4.40	9.31	1645	418
		(60.86)	(5.07)	(4.43)	(9.35)		479
9a	176	60.74	5.48	6.60	9.32	1636	412
		(60.76)	(5.54)	(6.65)	(9.34)		470
10a	158	59.32	4.94	4.30	9.08	1630	416
		(59.35)	(4.95)	(4.33)	(9.11)		484
11a	156	59.84	5.16	4.26	8.74	1635	415
		(59.90)	(5.14)	(4.24)	(8.93)		490

* *The calculated value corresponds to the [Ni(HL)(OAc)$_2$] composition.*

Table 3.8

Physical, analytical and IR data of the Copper(II) chelates of the unsaturated diketoanilides, (HL)

Copper(II) Chelate of	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)*				Characteristic IR absorption bands (cm^{-1})	
			C	H	N	Cu	νC=O	νM-O
1a	174	1.76	63.12 (61.39)	5.04 (4.95)	5.12 (4.62)	9.86 (10.56)	1632	418 464
2a	176	1.74	58.94 (59.81)	4.80 (4.82)	4.54 (4.50)	10.24 (10.29)	1648	420 472
3a	188	1.75	57.42 (58.03)	4.47 (4.52)	4.28 (4.37)	9.06 (9.98)	1649	424 480
4a	166	1.74	57.04 (57.14)	4.04 (4.45)	6.44 (6.45)	9.94 (9.83)	1642	418 472
5a	190	1.77	59.70 (59.81)	4.64 (4.82)	4.40 (4.50)	9.98 (10.29)	1638	425 472
6a	172	1.76	58.12 (58.03)	4.40 (4.52)	4.31 (4.37)	9.46 (9.98)	1635	430 491
7a	158	1.78	59.44 (60.38)	5.01 (5.03)	4.20 (4.40)	9.91 (10.06)	1638	428 470
8a	164	1.73	60.14 (60.92)	5.04 (5.23)	4.29 (4.31)	9.76 (9.85)	1630	424 486
9a	192	1.74	59.42 (60.28)	5.34 (5.49)	6.54 (6.59)	10.11 (10.05)	1635	416 475
10a	198	1.75	57.40 (58.90)	4.61 (4.91)	4.28 (4.30)	9.54 (9.82)	1632	418 486
11a	210	1.76	59.01 (59.46)	5.07 (5.11)	4.18 (4.20)	9.48 (9.61)	1642	420 480
12a	156	1.77	58.48 (59.46)	5.07 (5.11)	4.04 (4.20)	9.54 (9.61)	1647	427 492
13a	172	1.74	60.18 (60.57)	4.70 (4.73)	4.50 (4.42)	9.92 (10.09)	1644	430 480

** The calculated value corresponds to the [Cu(HL)(OAc)$_2$] composition.*

Table 3.9

Physical, analytical and IR data of the Zn(II) chelates of the unsaturated diketoanilides, (HL)

Zn(II) Chelate of	MP °C	Elemental analysis (%) Found/(Calcd)*				Characteristic IR absorption bands (cm^{-1})	
		C	H	N	Zn	νC=O	νM-O
1a	144	60.74	4.84	4.59	10.64	1634	425
		(61.29)	(4.94)	(4.61)	(10.71)		490
2a	156	60.14	4.92	4.31	10.14	1640	418
		(59.71)	(4.81)	(4.41)	(10.43)		476
3a	174	58.14	4.54	4.24	10.22	1641	420
		(58.03)	(4.52)	(4.37)	(10.14)		486
8a	168	59.88	5.14	4.28	10.04	1640	412
		(60.82)	(5.22)	(4.30)	(9.98)		491
13a	182	60.14	4.68	4.40	10.12	1638	425
		(60.47)	(4.27)	(4.41)	(10.24)		484

* *The calculated value corresponds to the [Zn(HL)(OAc)$_2$] composition.*

Table 3.10

Physical, analytical and IR data of the Cd(II) chelates of the unsaturated diketoanilides, (HL)

Zn(II) Chelate of	MP °C	Elemental analysis (%) Found/(Calcd)*				Characteristic IR absorption bands (cm^{-1})	
		C	H	N	Zn	νC=O	νM-O
1a	136	57.04	4.46	4.14	16.72	1642	420
		(56.88)	(4.59)	(4.28)	(17.13)		470
2a	132	55.06	4.44	4.04	15.76	1634	418
		(55.52)	(4.48)	(4.18)	(16.70)		484
3a	126	53.06	4.14	4.05	16.21	1637	421
		(54.07)	(4.22)	(4.07)	(16.28)		492
5a	134	55.06	4.38	4.04	15.74	1638	419
		(55.52)	(4.48)	(4.18)	(16.70)		486
7a	128	55.74	4.61	3.88	16.34	1637	416
		(56.14)	(4.68)	(4.09)	(16.37)		492
8a	126	56.66	4.85	3.96	15.54	1635	417
		(56.73)	(4.87)	(4.01)	(16.05)		486
11a	132	54.96	4.72	4.01	14.98	1641	420
		(55.46)	(4.76)	(3.92)	(15.69)		491
13a	140	56.28	4.39	4.18	16.34	1640	412
		(56.30)	(4.40)	(4.11)	(16.42)		479

* *The calculated value corresponds to the [Cd(HL)(OAc)$_2$] composition.*

^{1}H NMR spectra

NMR spectroscopy is an important tool in assigning the actual coordination behaviour of 1,3-dicarbonyl compounds[242-244]. The usual complexing mode of 1,3-dicarbonyl compounds is the replacement of enolic proton by metal cation. This chelating mode can clearly be visualised by examining the downfield region of the spectra. The ^{1}H NMR spectra of the diamagnetic Ni(II) complexes showed the enolic OH proton signal of the ligand at ~13 ppm indicating the non-involvement of the enolic proton in complexation . However the methylene proton signal shifted appreciably to down field indicating the involvement of the β-dicarbonyl function in complexation as in structure **6**. Unlike in the spectra of the ligands, the complexes show a signal at ~δ2.5 ppm indicating acetate coordination and from the intensity, it can be inferred the presence of two acetate groups. The presence of proton signal at ~9.5 ppm in the spectra of complexes indicate that the NH groups are not involved in coordination.

Mass spectra

The potential of mass spectrometry in the structural elucidation of coordination compounds has been well illuminated in the case metal complexes of β-dicarbonyl compounds.[15,250-254]. In recent years, with the advent of highly efficient direct evaporation inlet systems, the problems with low volatility and thermal instability which are encountered frequently when dealing with metal complexes have to some extent been overcome. It has been shown from the mass spectral analysis of Cu(II)diketonates that stepwise removal of alkyl/aryl group(s) is a characteristic feature of all the complexes. Even though detailed mass spectral analysis of β-diketonate complexes with acetylacetone and related diketones are available, only meager attention was given to similar complexes of other 1,3-dicarbonyl compounds, especially β-ketoanilides.

The FAB mass spectra of all Cu(II) complexes show intense molecular on peaks. Peaks due to the removal of one or both acetate groups are characteristic of all the spectra. The fragments observed in the ligand spectra are also found in the spectra of the complexes which indicate that no structural alternation of the ligand has occurred during complexation. The peaks due to $[CuL]^+$ and L^+ are also observed in the spectra. The loss of $[C_6H_5NH]^+$ and $[C_6H_5NHCO]^+$ are found in the spectra of metal chelates like those of the ligands. The spectra of all the chelates contain a large number of fragments containing copper. These are easily identified because of 2:1 natural abundance of ^{63}Cu and ^{65}Cu isotopes. Typical spectra are reproduced in fig. **3.24-3.29**.

Geometrical structure of the complexes

In the copper(II) complexes the presence of a broad visible band at ~15,000 cm^{-1} and the measured μ_{eff} values (1.72-1.78B.M.) support the square-palanar structure. Square-planar copper(II) complexes undergo a change to octahedral symmetry in the presence of donor solvents. When the spectra of the chelates were measured in pyridine (10^{-3} M solution) a broad absorption band centred at ~11,250 cm^{-1} was observed which indicates the formation of pyridine adducts of the planar $[Cu(HL)(OAc)_2]$ complexes. The visible spectra of Co^{2+} complexes are showed a broad band with maxima at ~19,100 cm^{-1}. In some cases a shoulder appeared on this band at ~20,800 cm^{-1}. These values along with the observed magnetic moment in the range 4.70–4.9 B.M. suggest the octahedral geometry of the complexes. The observed diamagnetism and broad medium-intensity band at ~17,800 cm^{-1} in the visible spectra of the nickel(II) chelates undoubtedly suggest their square planar geometry. In conformity with this observation the visible spectra of the chelates in pyridine solution (10^{-3} M) showed three bands corresponding to configurational change from square planar to octahedral due to the association of pyridine. The three well-seperated absorption bands at λ_{max} ~8,234, ~13,556 and ~24,349 cm^{-1} correspond to the transitions $^3A_{2g} \rightarrow {}^3T_{2g}$; $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g} \rightarrow {}^3T_{1g}(P)$, respectively.

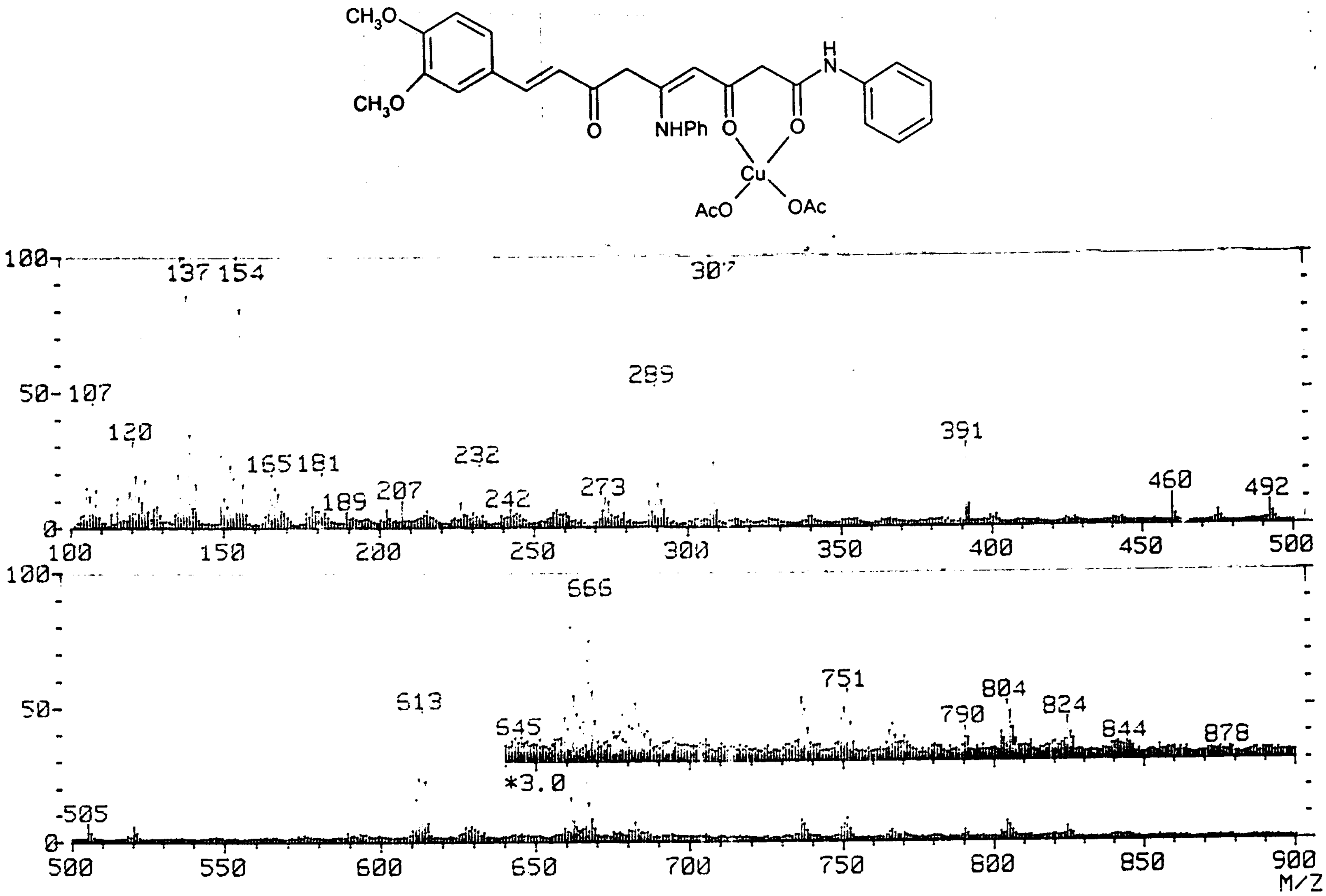


Fig.3.24FAB Mass spectrum of Cu(II) complex of **11a**

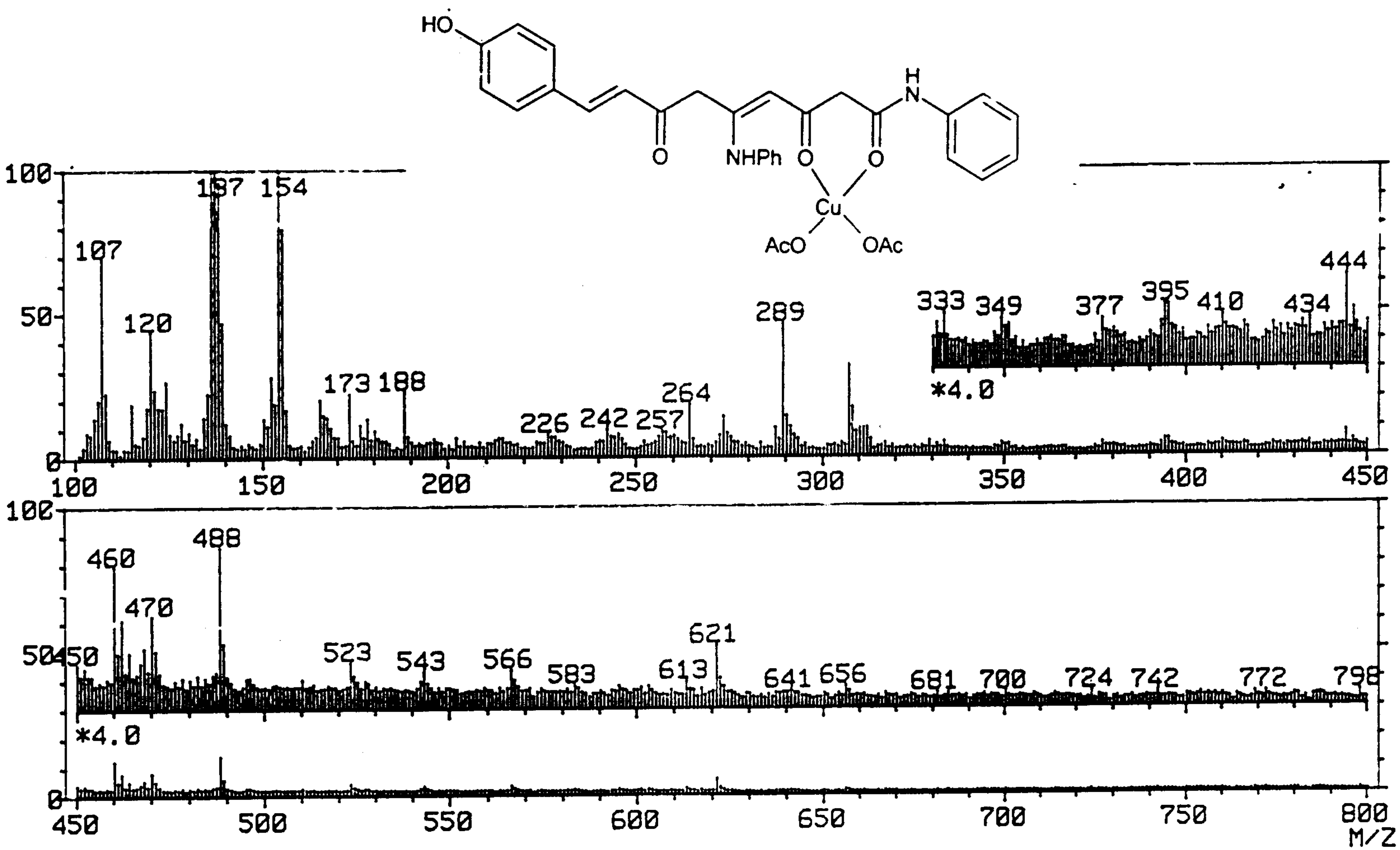


Fig.3.25 FAB Mass spectrum of Cu(II) complex of **5a**

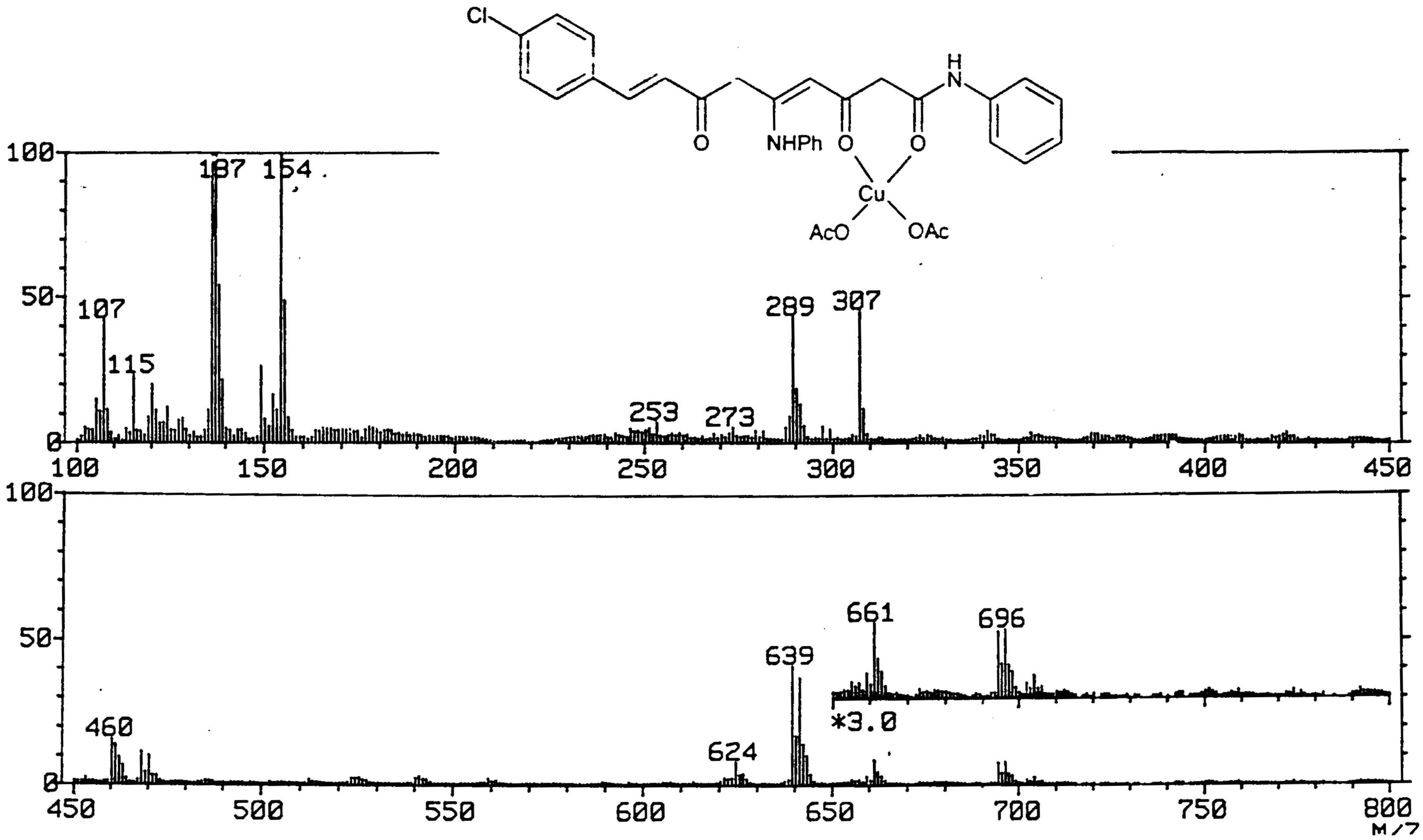


Fig.3.26 FAB Mass spectrum of Cu(II) complex of **6a**

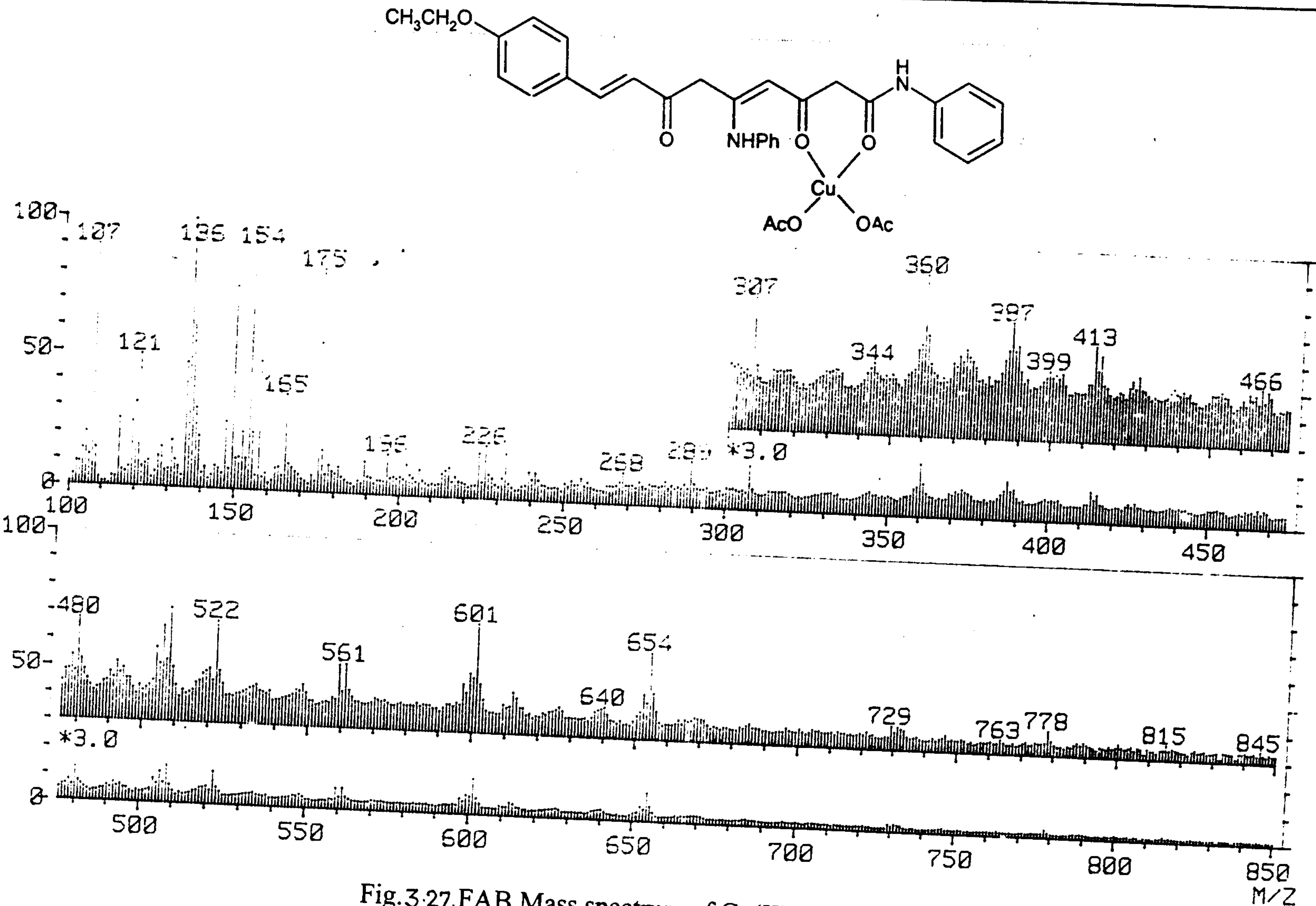


Fig.3.27 FAB Mass spectrum of Cu(II) complex of **8a**

86·E →

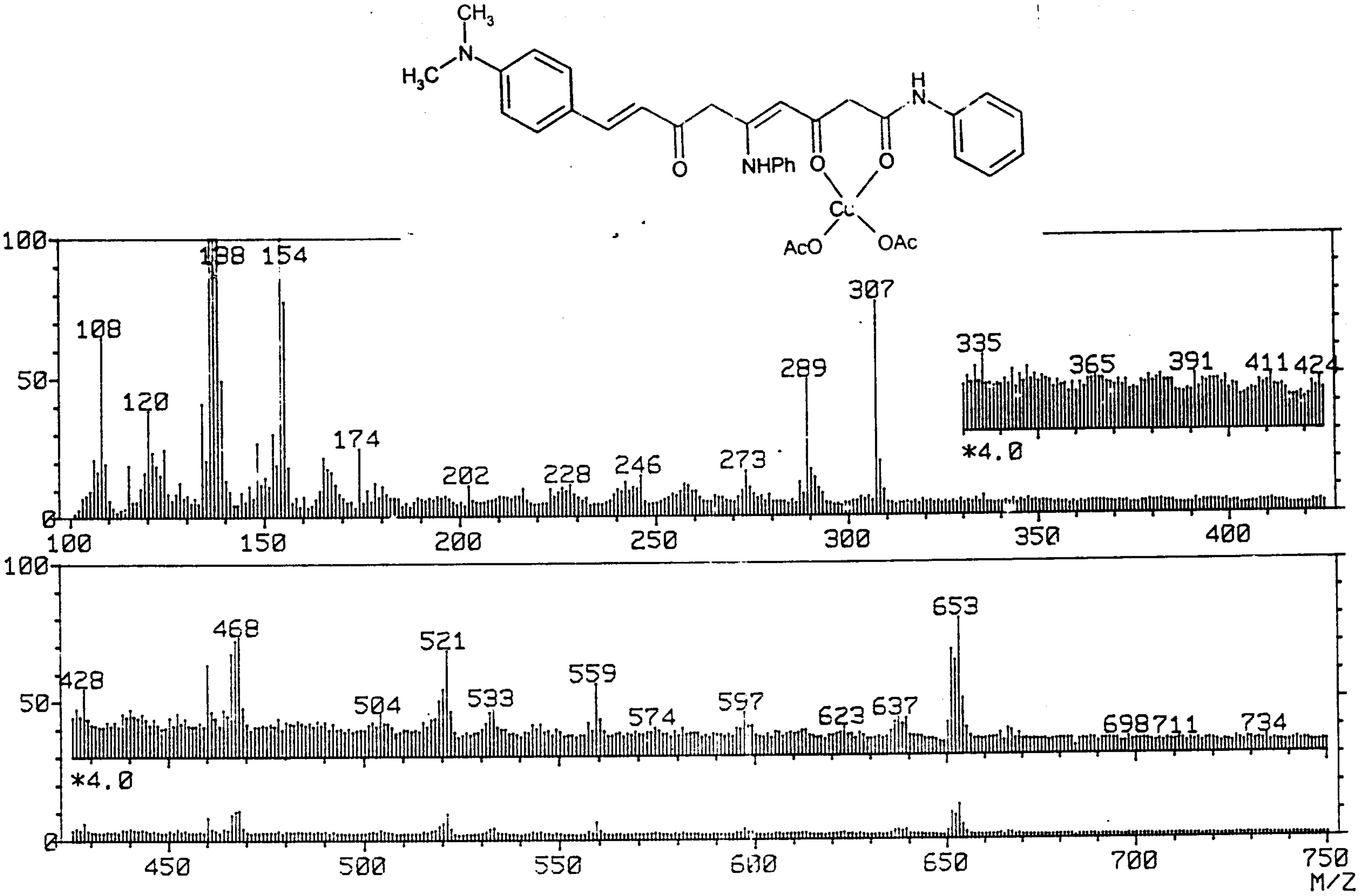


Fig. 3.28 FAB Mass spectrum of Cu(II) complex of **9a**

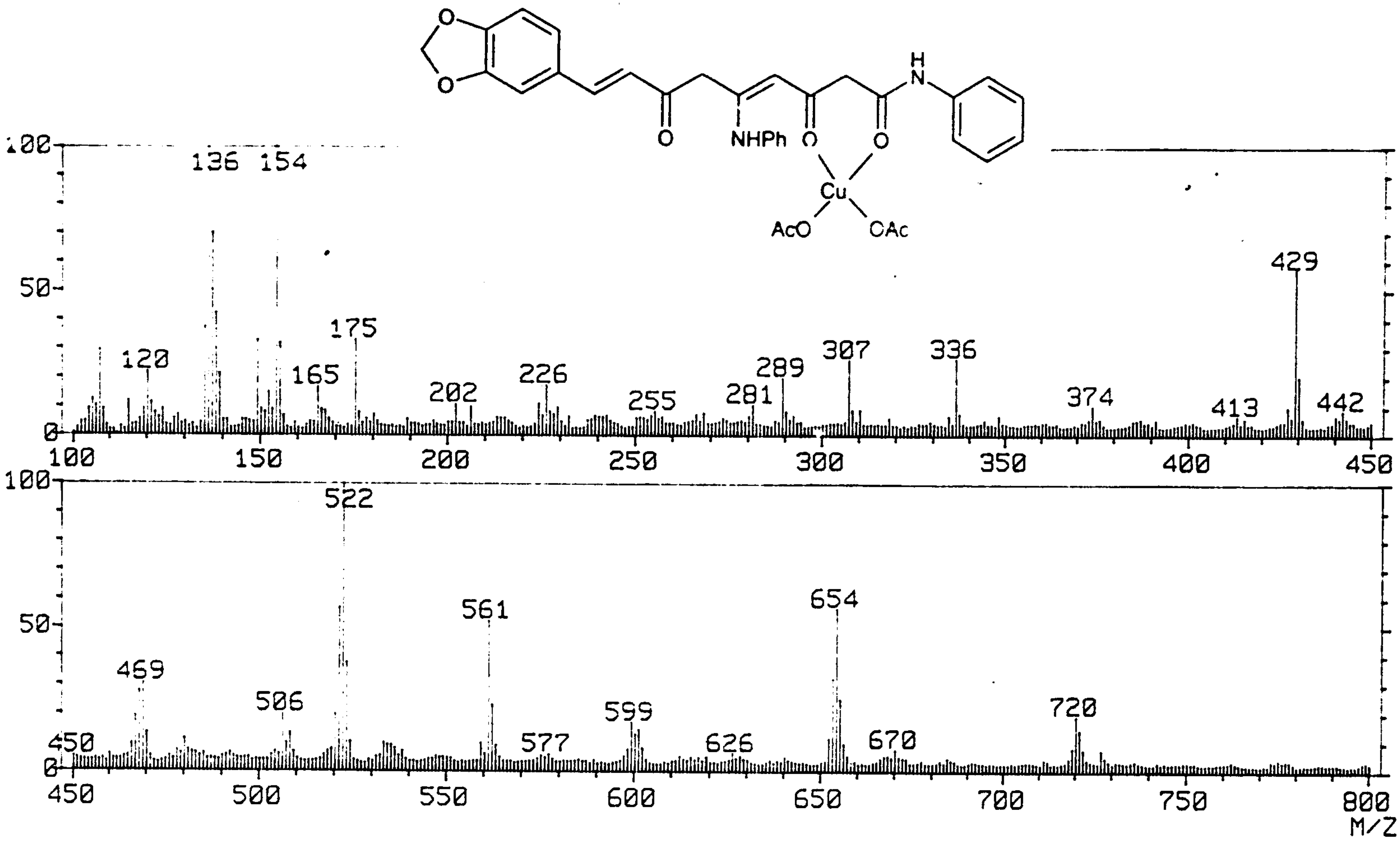


Fig.3.29 FAB Mass spectrum of Cu(II) complex of **13a**

SECTION 2

METAL COMPLEXES OF UNSATURATED β-KETOANILIDES

The unsaturated β-ketoanilides considered in this section are the monocondensation products formed as discussed in **section 1**.

The condensation of acetoacetanilide with benzaldehyde, p-methoxybenzaldehyde, p-ethoxybenzaldehyde, p-N,N-dimethylaminobenzaldehyde, salicylaldehyde, o-nitrobenzaldehyde, piperonal, vertraldehyde and 2,4-dimethoxybenzaldehyde yielded the unsaturated β-ketoanilide along with the diketoanilides (experimental details are given in **section 1**). These β-ketoanilides formed well defined complexes with Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Fe(III). The methods of synthesis of the complexes are given below.

To a refluxing solution of the compound in ethanol (0.002 mol, 20 mL) an aqueous solution of metal(II)acetates (0.001 mol, 15 mL) was added drop by drop with stirring. The pH of the solution was adjusted around 6 using sodium acetate and refluxing was continued for ~4h. The solution was concentrated to half the volume and then cooled in ice and the precipitated complex was filtered, washed several times with water, then with ethanol, and recrystallised from hot methanol. The crystals were dried in vacuum.

Fe(III) complexes were prepared as follows. To a refluxing solution of the compound in methanol (0.003 mol, 25 ml) slowly added a solution of anhydrous $FeCl_3$ in methanol (0.001 mol, 15 mL) with vigorous stirring. The mixture was then refluxed for ~2h, cooled to room temperature and the precipitated complex was filtered, washed with methanol and recrystallised from hot chloroform. The crystals were dried in vacuum.

Results and Discussion

The aldehydes used for the synthesis of the unsaturated acetoacetanilides in the investigation are brought in table 3.11 along with their systematic name and yield obtained. All the compounds are crystalline in nature with an yellow colour and are freely soluble in common organic solvents.

The results of elemental analysis and molecular weight determination of the compounds given in table 3.12 suggest that the condensation between aromatic aldehyde and acetoacetanilide takesplace in a 1:1 ratio (scheme 3.8). The UV, IR, ^1H NMR and mass spectral data of the compounds are in agreement with the structure **4**.

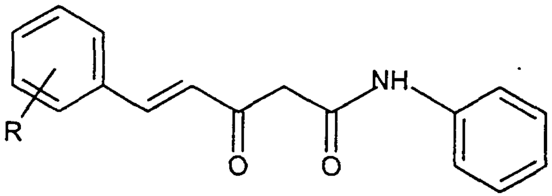
Characterisation of the unsaturated β-ketoanilides

UV spectra

The UV spectra of the compounds show two broad bands with maxima at ~380 nm and ~260 nm due to the various $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. The bands are considerably broader than the absorption of acetoacetanilide which suggests that more than one $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition exist in these compounds.

Table 3.14

Synthetic details of unsaturated β-ketoanilides



Compounds	Aldehyde used for synthesis	R	Systematic name	Yield (%)
1b	Benzaldehyde	H	1-(N-phenyl)amino-5-phenyl-4-penten-1,3-dione	60
2b	Salicylaldehyde	2-OH	1-(N-phenyl)amino-5-(2′-hydroxy)phenyl-4-penten-1,3-dione	62
3b	o-Nitrobenzaldehyde	$2\text{-}NO_2$	1-(N-phenyl)amino-5-(2′-nitro)phenyl-4-penten-1,3-dione	75
4b	p-Methoxybenzaldehyde	$4\text{-}OCH_3$	1-(N-phenyl)amino-5-(2′-methoxy)phenyl-4-penten-1,3-dione	54
5b	p-Ethoxybenzaldehyde	$4\text{-}OC_2H_5$	1-(N-phenyl)amino-5-(2′-ethoxy)phenyl-4-penten-1,3-dione	58
6b	p-N,N-Dimethylaminobenzaldehyde	$4\text{-}N(CH_3)_2$	1-(N-phenyl)amino-5-(2′-N,N-dimethylamino)phenyl-4-penten-1,3-dione	57
7b	Veratraldehyde	$3\text{-}OCH_3$, $4\text{-}OCH_3$	1-(N-phenyl)amino-5-(3′,4′-dimethoxy)phenyl-4-penten-1,3-dione	64
8b	2,4-Dimethoxybenzaldehyde	$2\text{-}OCH_3$, $4\text{-}OCH_3$	1-(N-phenyl)amino-5-(2′,4′-dimethoxy)phenyl-4-penten-1,3-dione	61
9b	Piperonal	$3\text{-}OCH_2O\text{-}4$	1-(N-phenyl)amino-5-(3′,4′-methylenedioxy)phenyl-4-penten-1,3-dione	48

Table 3.12

Physical, analytical and UV spectral data of the unsaturated β-ketoanilides

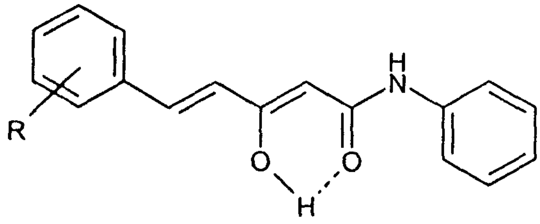
Compounds	MP (^{0}C)	Elemental analysis (%)			Mol. Weight	λ_{max} (nm)	log ϵ
		C	H	N			
		Found/ (calcd)					
1b	98	75.48	5.58	5.37	262	264	4.09
		(76.98)	(5.66)	(5.28)	(265)	374	4.84
2b	64	72.35	5.80	5.02	280	266	4.04
		(72.60)	(5.34)	(4.98)	(281)	375	4.92
3b	112	66.04	5.04	9.13	312	260	4.02
		(65.80)	(4.83)	(9.03)	(310)	370	4.54
4b	98	72.98	5.74	4.18	293	270	4.04
		(73.22)	(5.76)	(4.75)	(295)	392	4.68
5b	104	73.42	5.54	3.68	306	274	4.07
		(73.79)	(5.47)	(3.88)	(309)	396	4.97
6b	118	73.42	6.39	9.11	306	270	4.10
		(74.03)	(6.49)	(9.09)	(308)	394	4.84
7b	86	70.42	4.81	4.48	307	268	4.06
		(69.90)	(4.85)	(4.53)	(309)	379	4.91
8b	74	70.28	5.90	4.29	321	270	4.07
		(70.15)	(5.85)	(4.31)	(325)	376	4.95
9b	112	69.74	5.82	4.27	323	272	4.04
		(70.15)	(5.85)	(4.31)	(325)	390	4.75

IR spectra

The observed IR bands of the complex are easy to interpret compared to acetoacetanilide. Acetoacetanilide exist predominantly in the keto form with very small percentage of the enol content. Therefore the most characteristic bands in the IR spectrum of acetoacetanilide due to the amide carbonyl and acetyl carbonyl occur at ~1667 cm^{-1} and ~1720 cm^{-1} respectively. Thus the spectrum of acetoacetanilide is dominated by two intense and well defined absorption in the region 1650–1800 cm^{-1}. When acetyl group (CH_3CO) of acetoacetanilide is replaced by a cinnamoyl group (Ph-CH=CH-CO), drastic changes may occur in this region of the spectrum. This is fully justified from the recorded IR spectra of the compounds considered in this section.

Thus the spectra of all the compounds show only one intense absorption in the region 1650-1800 cm^{-1}. This band cannot be assigned to a cinnamoyl carbonyl stretching because such conjugated carbonyl groups usually absorb in the 1600–1650 cm^{-1} region. Therefor the band at ~1670 cm^{-1} of the compounds originate definitely due to the stretching of the amide carbonyl. Another prominent band appeared in the spectra of the compounds are at or near 1640 cm^{-1}. This band cannot be assigned to a cinnamoyl carbonyl. But this can be very well attributed to partially enolised cinnamoyl carbonyl function. Thus it can be clearly stated that the cinnamoyl carbonyl has enolised and hydrogen bonding may decrease the force constant of the carbonyl group and thereby shifted to low stretching frequencies.

From the IR spectra of the compounds in the region 1600–1800 cm^{-1} clearly demonstrate that the compounds are cinnamoyl acetanilides where the cinnamoyl carbonyl group has enolised and involved in intramolecular hydrogen bonding with the amide carbonyl as in structure 7.



7

The spectra of the compounds in the region 1500–1600 cm^{-1} showed several medium intensity bands assignable to various olefinic and aromatic C=C stretching. A prominent band observed at ~1525 cm^{-1} in the spectra is characteristic of the N–H deformation vibration. That the compounds exist in intramolecularly hydrogen bonded structure 7 is evident from the presence of a broad band due to the O–H·····N group in the region 3400 cm^{-1}. Weak and medium intensity bands assignable to the stretching of NH and various ν_{C-H} vibrations are also observed in the spectra.Some typical spectra are reprroduced in fig. **3.30-3.31** Important IR bands and their probable assignments are given in table 3.13.

Table 3.13

Characteristic IR data (cm^{-1}) of unsaturated β-ketoanilides

Compounds									Probable assignments
1b	**2b**	**3b**	**4b**	**5b**	**6b**	**7b**	**8b**	**9b**	
1670	1666	1678	1677	1672	1664	1667	1665	1662	ν (C=O) amide
1638	1640	1642	1632	1640	1638	1644	1645	1647	ν (C=O) chelated
1580	1590	1597	1596	1596	1590	1587	1585	1586	ν(C=C) phenyl/ ν(C=C) alkenyl / νamide II
1545	1542	1573	1564	1574	1573	1573	1569	1564	
1528	1536	1546	1536	1542	1536	1540	1537	1539	
1525	1518	1512	1513	1512	1515	1520	1516	1517	
1240	1232	1238	1214	1244	1236	1245	1252	1260	ν amide III
967	969	970	976	978	974	975	973	980	ν CH=CH trans
690	693	694	692	690	691	696	699	700	ν amide V
656	655	660	658	659	657	652	659	662	ν amide IV
610	608	617	610	618	614	609	604	600	ν amide VI

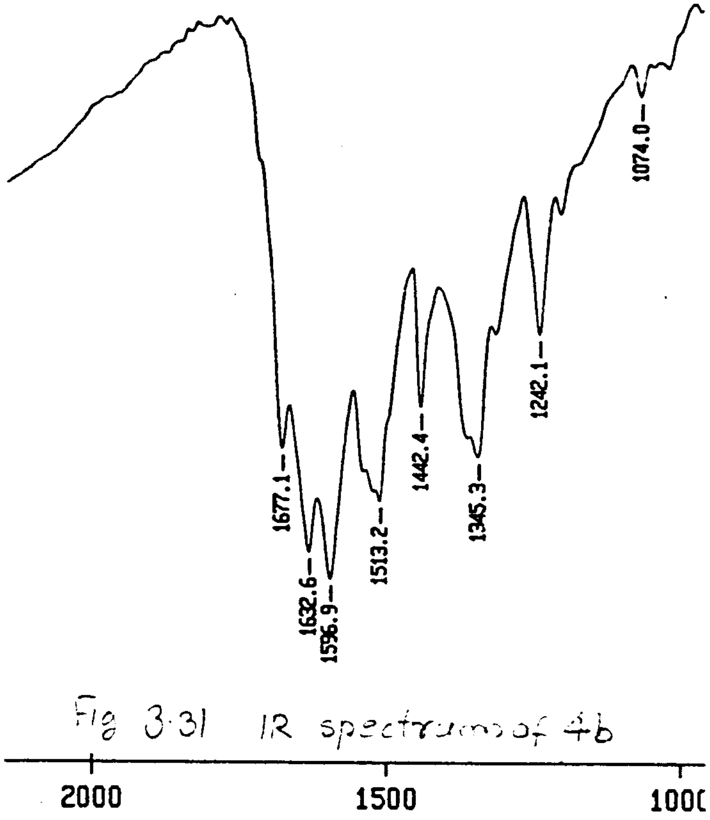


Fig 3·31 IR spectrum of 4b

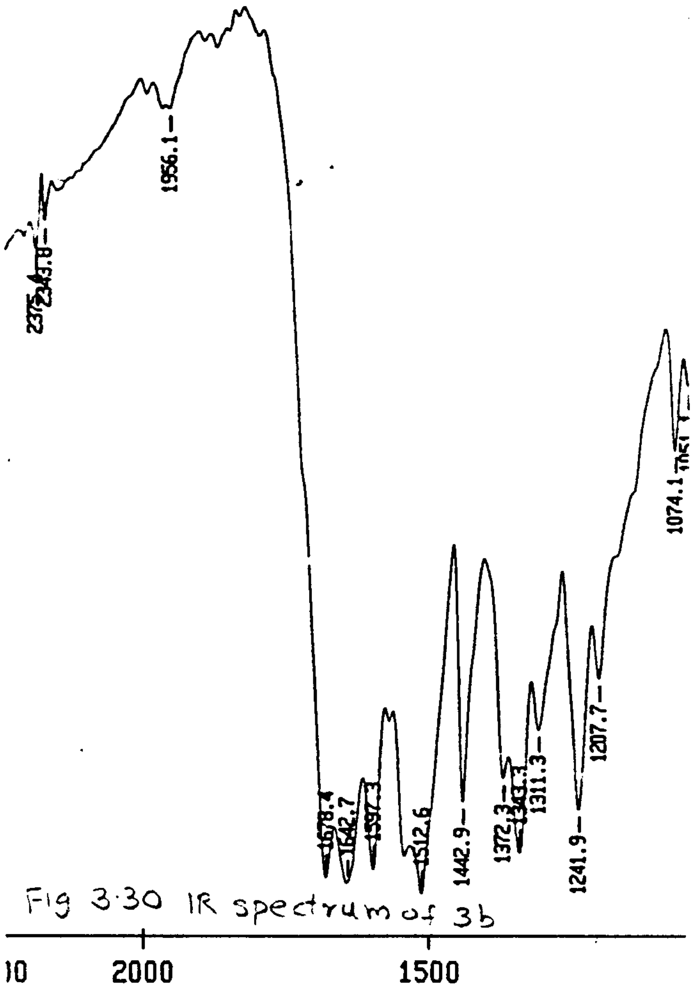


Fig 3·30 IR spectrum of 3b

^{1}H NMR spectra

That acetoacetanilide exist predominantly in the keto form has been clearly demonstrated from the ^{1}H NMR spectral studies[52,242-244]. Thus signals due to the enol proton was not observed in the reported spectrum of acetoacetanilide. The methylene protons showed resonance signals at ~3.5 ppm and the methyl protons at ~2.17 ppm. The most characteristic feature of the spectrum is a one proton signal at ~9 ppm due to the amide group.

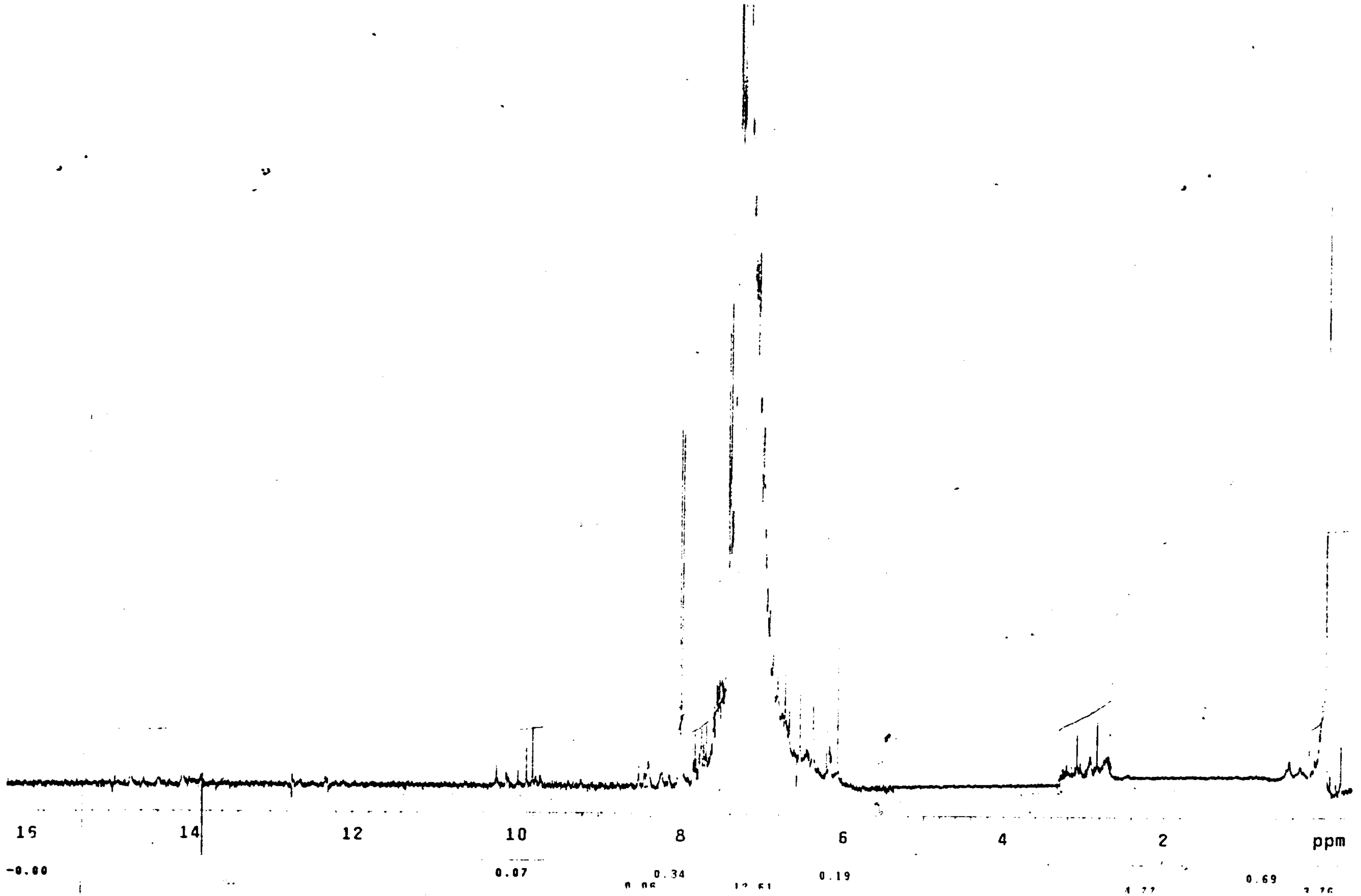
The ^{1}H NMR spectra of all the unsaturated β-ketoanilide show a one proton sliglity broadened signal in the range δ9–10 ppm and another one proton signal between δ12–13 ppm. The former signal is undoubtedly due to the NH proton. The existence of the later signal can only be accounted as arising from an enolisable carbonyl group. The spectra of the compounds do not contain any signal arising from the resonance of a methyl group. However the spectra displayed two one proton signals at ~8 ppm and a one proton signal at ~4 ppm. The former signals can conveniently be accounted as due to the olefinic protons and later to the methylene proton of the dicarbonyl function. The spectra also displayed a weak two proton signal of less intensity compared to the methylene proton at ~3.5 ppm similar to the OC-CH_2-CO protons of acetoacetanilide. Thus it can be stated that the enolisation is not complete and the compounds exist as a mixture of both the keto and enol forms. However, by considering the intensity of the O–C=CH–C=O and O=C–CH_2–C=O proton signals it can be inferred that the enol tautomer predominate. Integrated intensities of all the signals agree with the structure **7**. The spectral data are presented in table 3.14 and a typical spectrum is reproduced in fig. **3.32**.

Table 3.14

Characteristic ^1H NMR spectral data of the unsaturated β-ketoanilide

Compounds	Chemical shift δppm					
	OH	NH	CH=CH	Methine	CH_2	Phenyl Substituent
1b	12.168	9.103	8.204	6.997	3.684	-
2b	13.123	9.987	8.624	6.928	3.684	10.047
3b	12.745	8.884	8.247	7.384	3.592	-
4b	12.045	9.402	8.034	6.942	3.814	3.836
5b	12.456	9.882	8.967	6.976	3.948	4.068
6b	12.948	9.764	8.598	6.704	3.664	3.048
7b	12.444	10.006	7.648	6.884	3.796	3.784 3.946
8b	13.947	10.345	8.114	6.581	3.904	3.846 3.792
9b	12.947	9.804	7.678	6.748	3.705	6.024

Fig. 3.32 ^{1}H NMR spectrum of **2b**

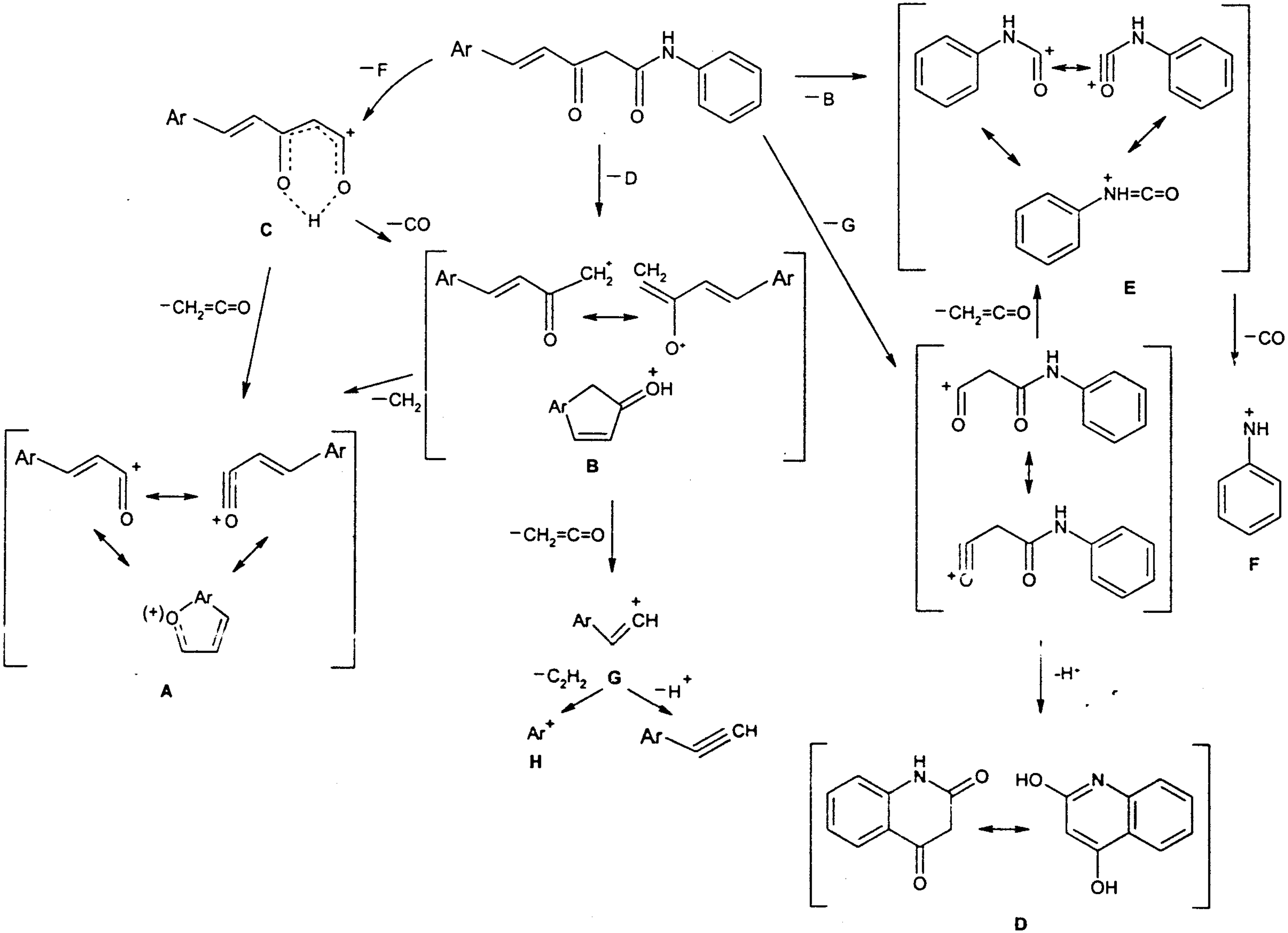


Mass Spectra

Mass spectra of all compounds showed intense molecular ion peak $P^+/(P + 1)^+$ thereby confirming the formation of the monocondensation product of the reaction between the various aldehydes and acetoacetanilide. $(P - C_6H_5)^+$, $(P - C_6H_5NH)^+$, $(P - C_6H_5NHCO)^+$, $(P - ArC_2H_2)^+$, etc. are characteristic of all the spectra. The important fragments appeared in the spectra can be explained by considering the fragmentation pattern given in Scheme 3.8. The m/z values of major peaks are tabulated in table 3.15. Some of the spectra are reproduced in fig. **3.33-3.41**.

Table 3.15
Important fragments observed in the FAB mass spectra of unsaturated β-ketoanilides

Compounds	P^+	A	B	C	D	E	G	H
1b	265	131	145	173	162	120	103	-
2b	281	147	161	189	162	120	119	-
3b	310	176	190	218	162	120	148	122
4b	295	161	175	203	162	120	133	107
5b	309	175	189	217	162	120	145	119
6b	308	174	188	216	162	120	144	118
7b	309	175	189	217	162	120	145	119
8b	325	191	205	233	162	120	163	137
9b	325	191	205	233	162	120	163	137


Ar
H
N
O
O
−F
−B
−D
−G
Ar
+
O
O
H
C
−CO
−CH₂=C=O
Ar
CH₂⁺
O
CH₂
Ar
O⁺
+
Ar
OH
B
−CH₂
Ar
+
O
Ar
+O
(+)O
Ar
A
−CH₂=C=O
Ar
+
CH
−C₂H₂
G
−H⁺
Ar⁺
H
Ar
CH
H
N
+
O
H
N
+O
+
NH=C=O
E
−CH₂=C=O
+
O
H
N
O
+O
H
N
O
−CO
+
NH
F
-H⁺
H
N
O
O
HO
N
OH
D

Scheme 3.8

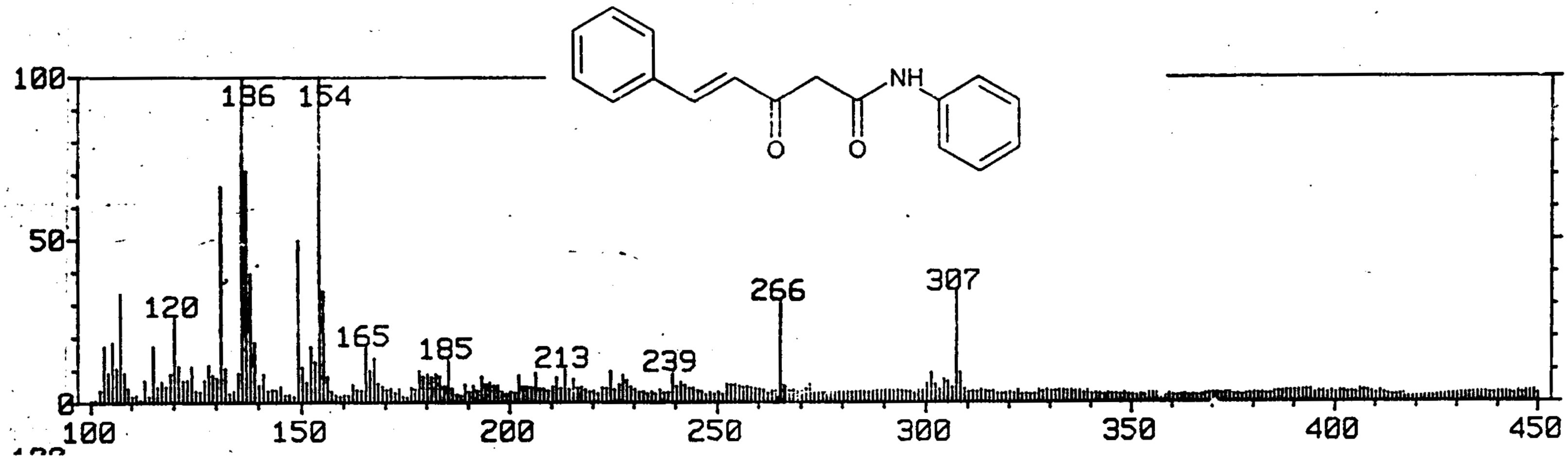


Fig. 3.33 FAB Mass spectrum of **1b**

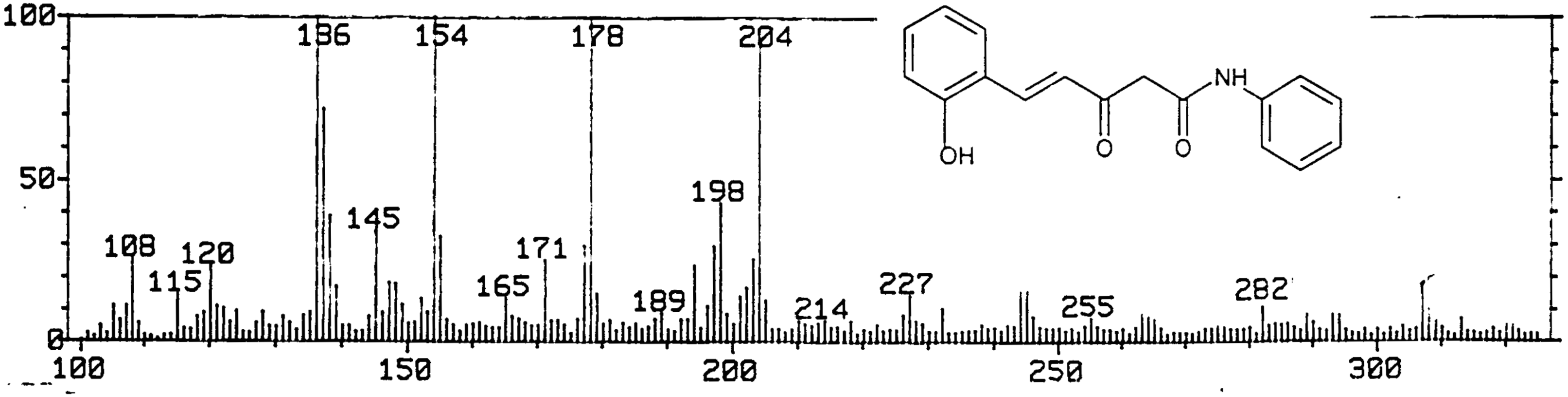


Fig. 3.34 FAB Mass spectrum of **2b**

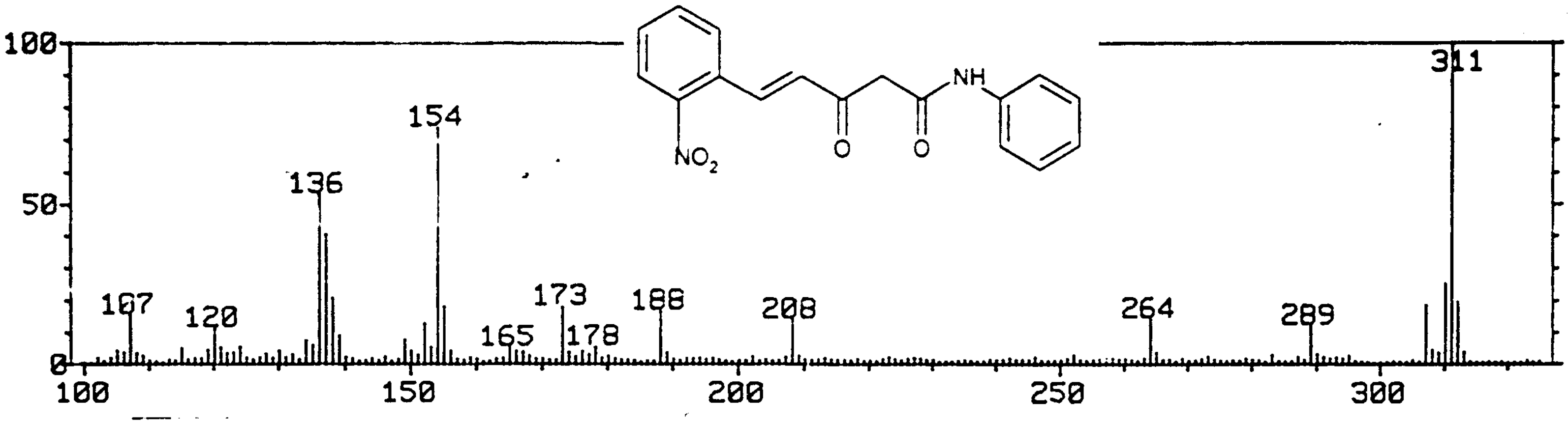


Fig.3.35 FAB Mass spectrum of **3b**

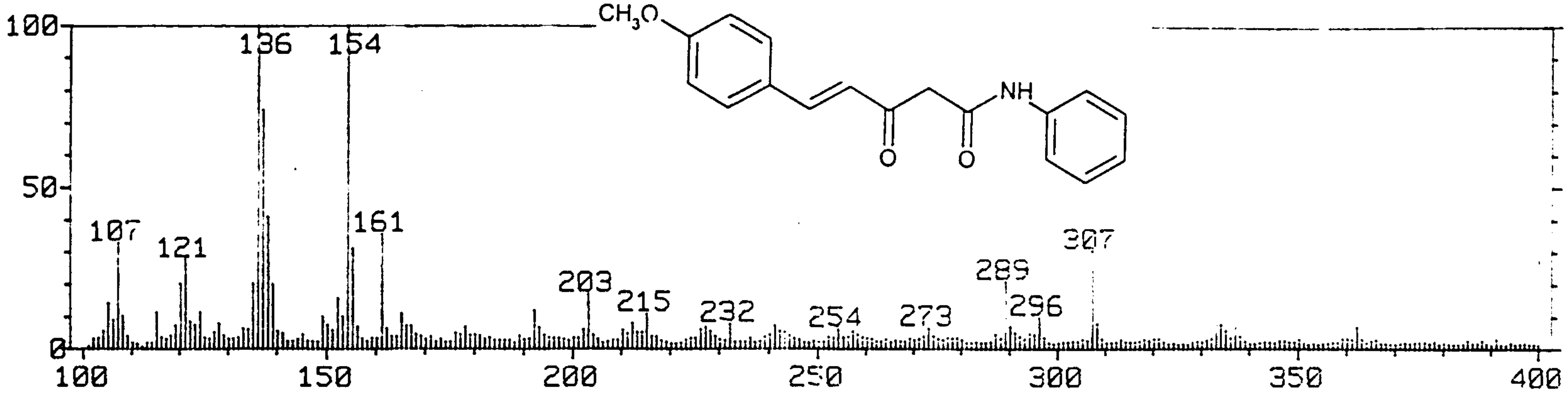


Fig.3.36 FAB Mass spectrum of **4b**

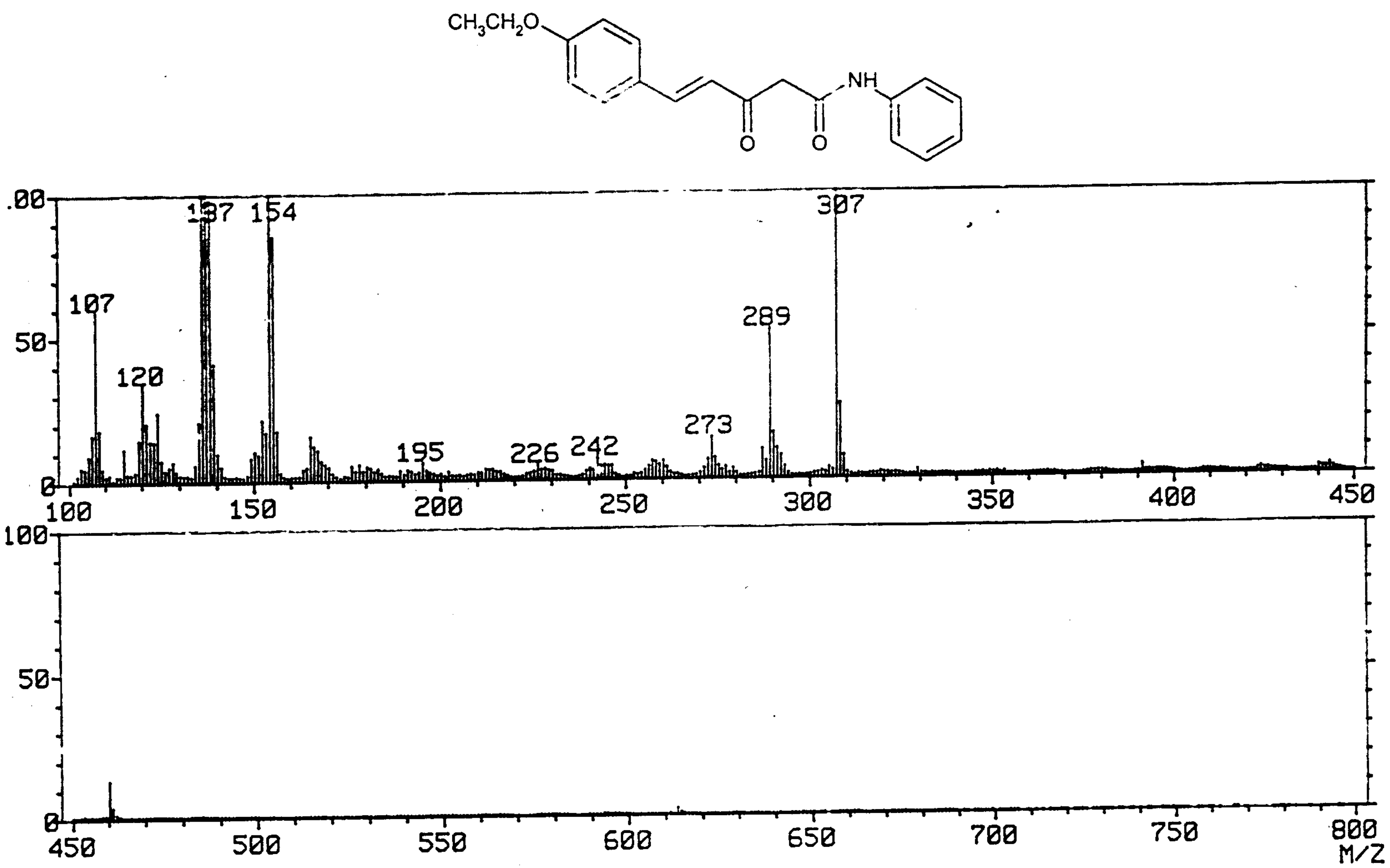


Fig.3.37.FAB Mass spectrum of **5b**

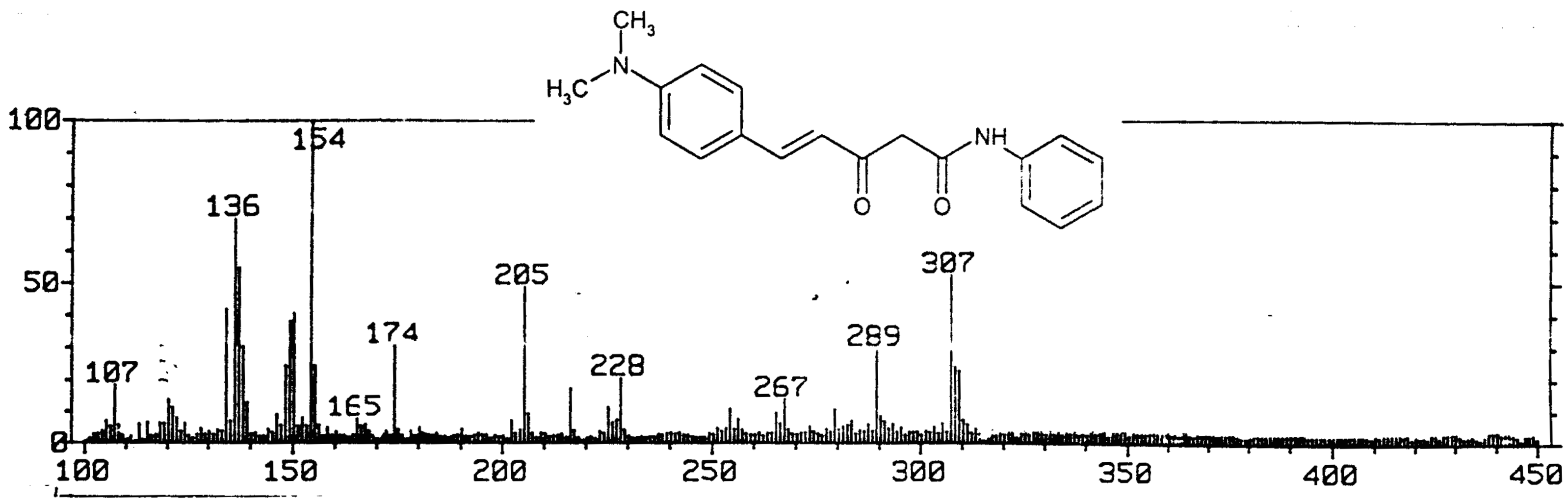


Fig.3.38 FAB Mass spectrum of **6b**

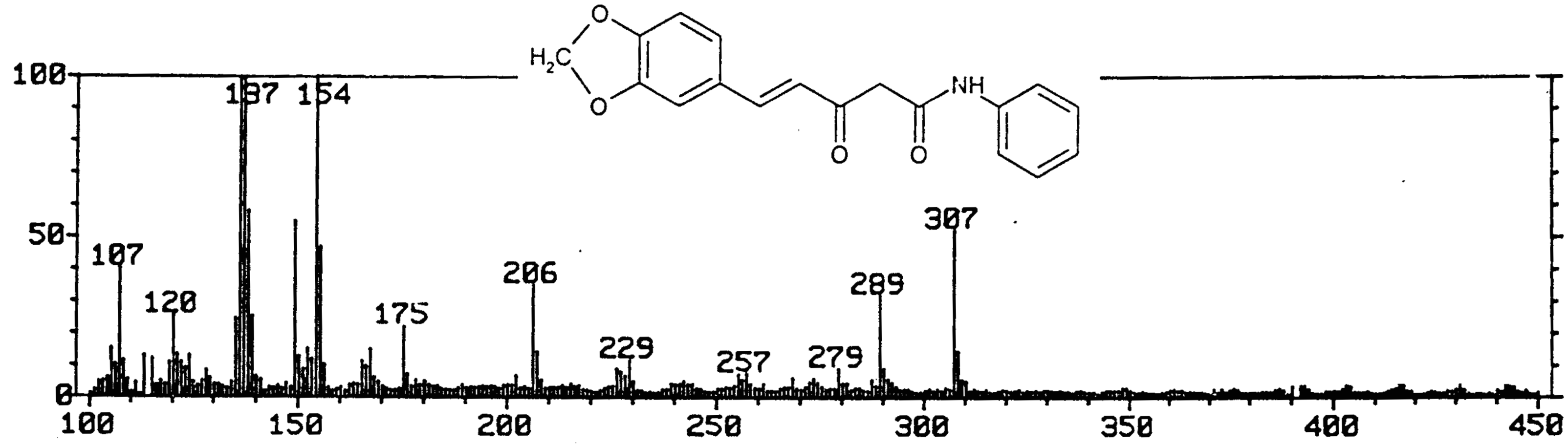


Fig.3.39 FAB Mass spectrum of **7b**

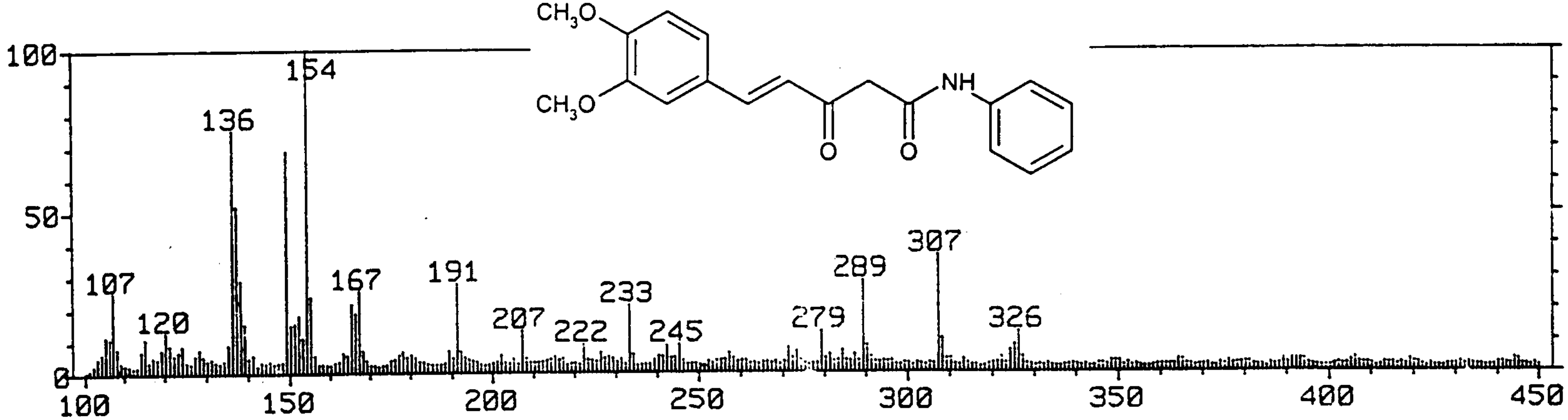


Fig.3.40 FAB Mass spectrum of **8b**

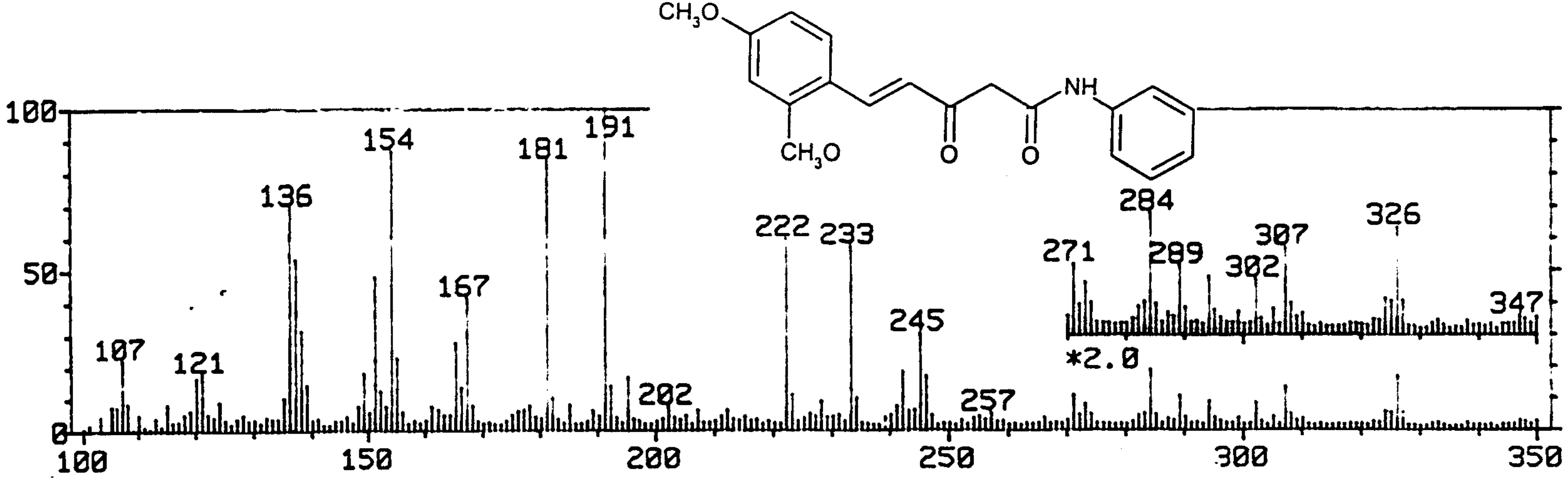
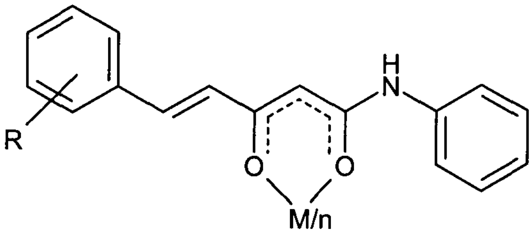


Fig.3.41 FAB Mass spectrum of **9b**

Characterisation of Metal Complexes

Analytical and physical data of the complexes are given in table 3.16–3.21. The observed elemental analysis data of the complexes agreed well with their 1:2 Metal–ligand stoichiometry except in the case of Fe(III) which are of [FeL_3] composition. All metal complexes behaved as non-electrolytes in DMF (specific conductance < $10\Omega^{-1}cm^{-1}$; 10^{-3} M solution). The Ni(II), Zn(II) and Cd(II) chelates are diamagnetic and all other complexes showed normal paramagnetic moment.

The observed UV, IR, NMR and mass spectra of the complexes are fully consistent with the structure **8** of the complexes.



8

n = 2 for Co(II), Ni(II), Cu(II), Zn(II) and Cd(II); n = 3 for Fe(III)

Table 3.16

Physical and analytical data of the Fe(III) chelates of the unsaturated β-ketoanilides

Fe(III) Chelate of	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)* C	H	N	Fe
1b	194	5.7	72.04 (72.26)	4.90 (4.96)	4.94 (4.96)	6.44 (6.50)
2b	186	5.8	68.34 (68.38)	4.69 (4.70)	4.65 (4.70)	5.98 (6.15)
3b	178	5.6	61.74 (62.13)	3.84 (3.96)	8.51 (8.53)	5.52 (5.59)
4b	214	5.8	68.18 (69.16)	5.04 (5.12)	4.47 (4.48)	5.58 (5.87)
5b	202	5.7	69.77 (69.87)	5.44 (5.52)	4.28 (4.29)	5.14 (5.62)
6b	196	5.7	69.48 (70.08)	5.80 (5.84)	8.62 (8.61)	5.60 (5.64)
7b	178	5.6	65.91 (66.40)	4.18 (4.30)	4.22 (4.30)	5.62 (5.64)
8b	184	5.7	65.84 (66.60)	5.24 (5.26)	3.98 (4.09)	5.31 (5.36)
9b	190	5.7	66.54 (66.60)	5.21 (5.26)	4.01 (4.09)	5.28 (5.36)

** The calculated value corresponds to the [FeL_3] composition where L stands for the deprotonated ligand.*

Table 3.17

Physical and analytical data of the Co(II) chelates of the unsaturated β-ketoanilides

Co(II) Chelate of	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)*			
			C	H	N	Co
1b	190	4.7	69.48 (69.51)	4.69 (4.77)	4.84 (4.77)	9.99 (10.05)
2b	192	4.8	65.11 (65.91)	4.48 (4.52)	4.51 (4.52)	9.43 (9.53)
6b	186	4.8	67.68 (67.76)	5.64 (5.65)	8.12 (8.32)	8.94 (8.77)
7b	208	4.7	63.11 (64.00)	4.13 (4.15)	4.10 (4.15)	8.71 (8.74)
8b	198	4.8	64.38 (64.49)	4.99 (5.09)	3.94 (3.96)	8.30 (8.34)

* *The calculated value corresponds to the* $[CoL_2(H_2O)_2]$ *composition where L stands for the deprotonated ligand.*

Table 3.18

Physical and analytical data of the Ni(II) chelates of the unsaturated β-ketoanilides

Ni(II) Chelate of	MP °C	Elemental analysis (%) Found/(Calcd)*			
		C	H	N	Ni
1b	160	69.33 (69.51)	4.62 (4.77)	4.74 (4.77)	9.94 (10.05)
4b	140	65.84 (66.77)	5.20 (5.25)	4.30 (4.32)	9.09 (9.12)
6b	138	67.18 (67.76)	5.63 (5.65)	8.31 (8.32)	8.74 (8.77)
8b	194	64.36 (64.49)	5.01 (5.09)	3.84 (3.96)	8.31 (8.34)

* *The calculated value corresponds to the* $[NiL_2]$ *composition where L stands for the deprotonated ligand.*

Table 3.19

Physical and analytical data of the Cu(II) chelates of the unsaturated β-ketoanilides

Copper(II) Chelate of	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)* C	H	N	Cu
1b	176	1.77	77.04 (77.27)	4.70 (4.74)	4.71 (4.74)	10.64 (10.66)
2b	198	1.80	65.38 (65.9)	4.46 (4.49)	4.44 (4.49)	10.08 (10.11)
3b	214	1.79	58.44 (59.91)	3.78 (3.82)	4.03 (4.11)	9.07 (9.25)
4b	186	1.78	65.44 (566.36)	4.88 (4.92)	4.18 (4.30)	9.46 (9.68)
5b	198	1.76	67.09 (67.16)	5.14 (5.30)	4.11 (4.12)	9.18 (9.28)
6b	178	1.80	66.84 (67.36)	5.42 (5.62)	8.04 (8.28)	9.24 (9.31)
7b	184	1.79	62.84 (63.62)	4.06 (4.12)	4.11 (4.12)	9.24 (9.28)
8b	168	1.74	63.98 (64.14)	5.06 (5.06)	3.93 (3.94)	8.88 (8.86)
9b	190	1.75	64.02 (64.14)	5.01 (5.06)	3.84 (3.94)	8.79 (8.86)

* *The calculated value corresponds to the [CuL_2] composition where L stands for the deprotonated ligand.*

Table 3.20

Physical and analytical data of the Zn(II) chelates of the unsaturated β-ketoanilides

Zn(II) Chelate of	MP °C	Elemental analysis (%) Found/(Calcd)*			
		C	H	N	Zn
1b	150	68.71 (68.80)	4.70 (4.72)	4.68 (4.72)	10.14 (10.96)
2b	162	64.34 (65.28)	4.46 (4.48)	4.44 (4.48)	9.98 (10.40)
3b	174	66.00 (66.16)	4.80 (4.90)	4.28 (4.29)	9.94 (9.95)
8b	148	63.54 (63.96)	5.04 (5.05)	3.92 (3.93)	8.88 (9.12)

* *The calculated value corresponds to the [ZnL$_2$] composition where L stands for the deprotonated ligand.*

Table 3.21

Physical and analytical data of the Cd(II) chelates of the unsaturated β-ketoanilides

Cd(II) Chelate of	MP °C	Elemental analysis (%) Found/(Calcd)*			
		C	H	N	Cd
1b	136	63.08 (63.75)	4.43 (4.38)	4.33 (4.38)	16.4 (17.5)
2b	148	59.94 (60.71)	4.16 (4.17)	4.14 (4.17)	16.54 (16.67)
4b	140	61.54 (61.71)	4.54 (4.57)	3.98 (4.00)	15.24 (16.00)
5b	154	61.94 (62.63)	5.19 (5.22)	3.81 (3.85)	14.98 (1538)
7b	146	59.31 (59.34)	3.76 (3.85)	3.81 (3.85)	15.34 (15.38)

* *The calculated value corresponds to the [CdL$_2$] composition where L stands for the deprotonated ligand.*

UV Spectra

In the UV region all the complexes exhibited two absorption maxima similar to the free ligands. However a slight shift to lower wave number compared to the ligand spectral maxima suggest that the carbonyl functions are bonded to the metal ions.

IR Spectra

The IR spectra of all the complexes in the 1600–1800 cm^{-1} region showed an intense and slightly broadened band in the range 1630 cm^{-1} irrespective of the nature of aryl groups and the metal ion. The observed broadening of the band suggest that, it is due to more than one carbonyl absorptions. Since bands due to the stretching of cinnamoyl and anilide carbonyls of the free ligands are absent in the spectra it can be presumed that the band appeared in the range 1630 cm^{-1} is due to metal bonded dicarbonyl functions. In acetoacetanilide complexes both the acetyl and amide carbonyls show appreciable decrease in frequencies up on complexation. Therefore by considering the position and slight broadening it can be presumed that the partially enolised cinnamoyl and amide carbonyl stretching frequencies of metal complex may absorb almost in identical values and may coalesce and appear as a broad band. Thus the band in the region 1630 cm^{-1} can safely be assigned to metal bonded dicarbonyl function.

That the carbonyl groups are involved in bonding with the metal as in structure 8 is further supported by the appearance of two medium intensity bands in the low frequency region at ~420 cm^{-1} and ~450 cm^{-1}

assignable to $\nu_{M\text{-}O}$ stretching of the complex. Important IR band and their probable assignments. are given in table 3.22–3.28 and typical spectra are reproduced in fig. **3.42-3.45**.

Table 3.22

Characteristic IR and UV spectral data of Fe(III) complexes

Fe(III) chelates of	Characteristic IR stretching bands (cm^{-1})			λ_{max}
	C=O	C=C (alkenyl/phenyl)	Fe-O	(nm)
1b	1627	1502,1518,1534	409 474	265 375
2b	1625	1488,1502,1526	420 485	267 378
3b	1630	1514,1516,1536	418 490	262 374
4b	1629	1524,1536,1539	416 474	272 394
5b	1625	1506,1525,1544	421 496	276 402
6b	1626	1514,1546,1566	422 494	274 400
7b	1630	1507,1519,1579	425 476	269 358
8b	1629	1523,1554,1576	426 474	272 380
9b	1628	1512,1561,1571	425 485	273 404

Table 3.23

Characteristic IR and UV spectral data of Co(II) complexes

Co(II) chelates of	Characteristic IR stretching bands (cm^{-1})			λ_{max}
	C=O	C=C (alkenyl/phenyl)	Co-O	(nm)
1b	1626	1554,1565,1578	416 474	265 376
2b	1628	1511,1519,1587	417 496	267 378
6b	1629	1514,1516,1536	420 494	271 396
7b	1625	1524,1556,1537	425 496	270 380
8b	1630	1518,1556,1576	418 476	272 380

Table 3.24

Characteristic IR and UV spectral data of Ni(II) complexes

Ni(II) chelates of	Characteristic IR stretching bands (cm^{-1})			λ_{max}
	C=O	C=C (alkenyl/phenyl)	Ni-O	(nm)
1b	1628	1518,1537,1549	417 490	265 375
4b	1630	1514,1526,1539	416 475	272 396
6b	1625	1525,1565,1573	424 496	271 397
8b	1629	1535,1544,1576	425 485	274 380

Fig 3.42

IR spectra of Ni (II) complex of 1b

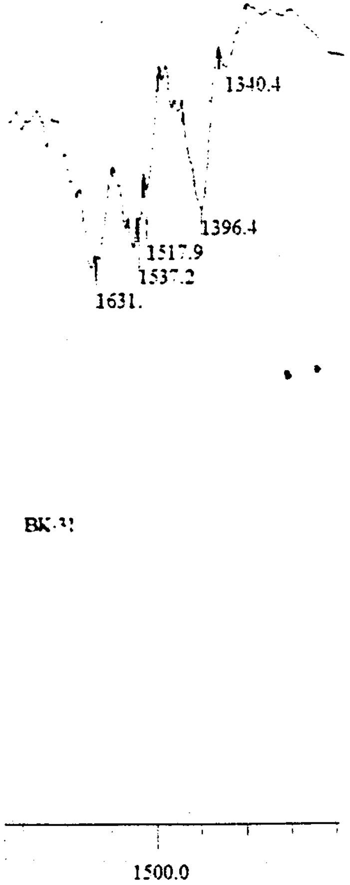


Fig 3.43

IR spectra of Cu(II) complex of 2b

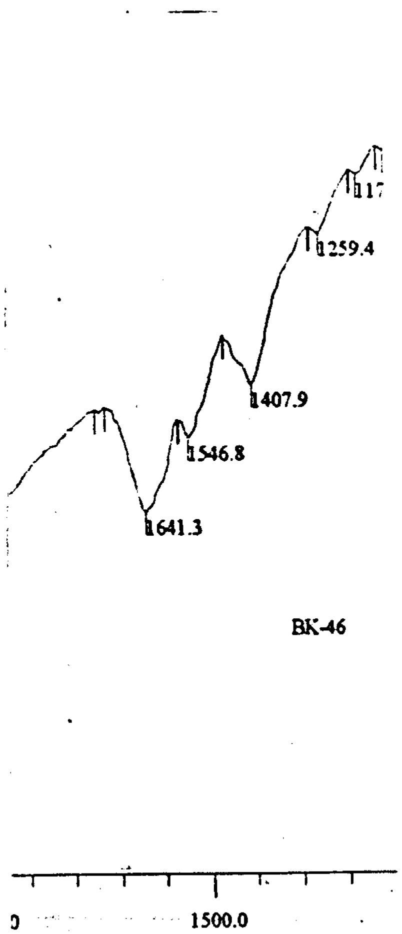


Fig 3.44

IR spectra of Cd (II) complex of 9b

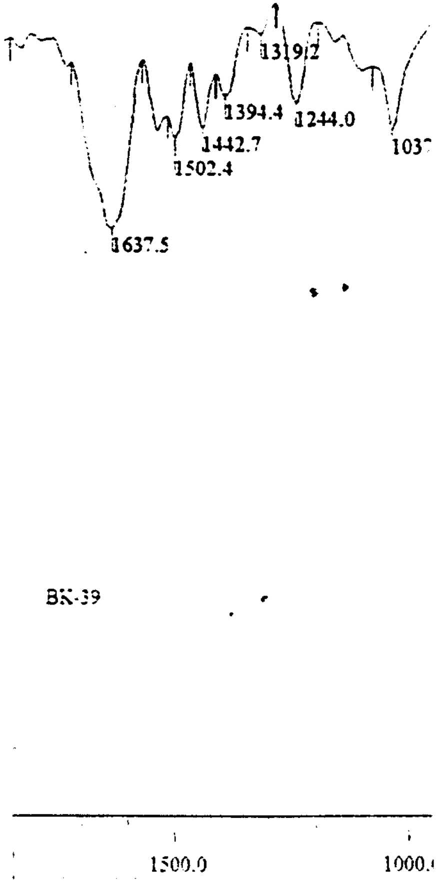


Fig 3.45

IR spectra of Fe(III) complex of 3(b)

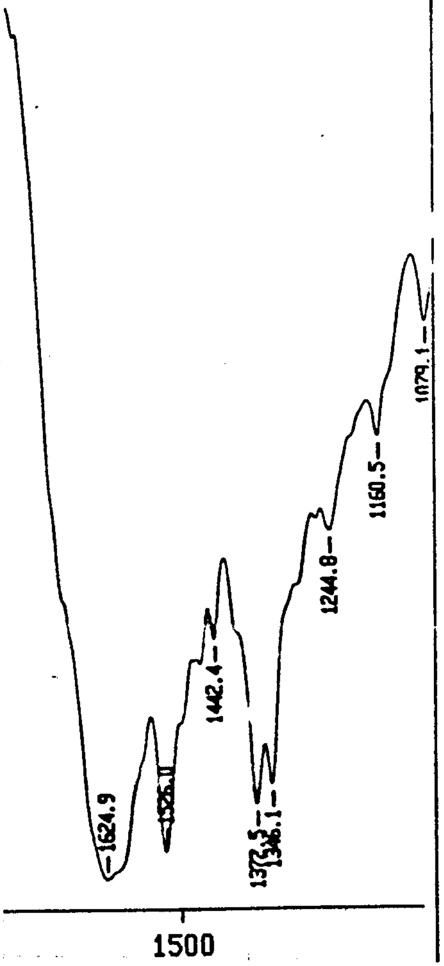


Table 3.25
Characteristic IR and UV spectral data of Cu(II) complexes

Cu (II) chelates of	Characteristic IR stretching bands (cm^{-1})			λ_{max}
	C=O	C=C (alkenyl/phenyl)	Cu-O	(nm)
1b	1630	1514,1516,1536	418 470	265 376
2b	1641	1516,1534,1546	416 485	266 376
3b	1627	1532,1545,1578	421 476	262 372
4b	1625	1532,1555,1586	422 474	274 396
5b	1626	1530,1544,1567	410 480	275 402
6b	1628	1545,1550,1577	412 474	272 398
7b	1630	1534,1546,1586	414 492	274 380
8b	1629	1514,1516,1536	421 498	271 377
9b	1627	1529,1539,1563	420 474	274 398

Table 3.26

Characteristic IR and UV spectral data of Zn(II) complexes

Zn(II) chelates of	Characteristic IR stretching bands (cm^{-1})			λ_{max}
	C=O	C=C (alkenyl/phenyl)	Zn-O	(nm)
1b	1628	1544,1556,1567	416 475	266 380
2b	1630	1564,1554,1578	420 477	270 676
3b	1624	1524,1564,1587	425 485	262 374
8b	1626	1523,1545,1535	426 490	272 377

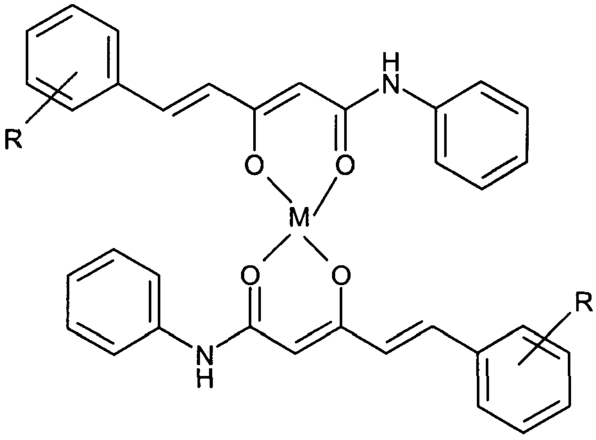
Table 3.27

Characteristic IR and UV spectral data of Cd(II) complexes

Cd(II) chelates of	Characteristic IR stretching bands (cm^{-1})			λ_{max}
	C=O	C=C (alkenyl/phenyl)	Cd-O	(nm)
1b	1630	1504,1519,1577	418 476	265 376
2b	1625	1515,1566,1565	425 470	267 376
4b	1627	1509,1554,1598	428 490	274 396
5b	1625	1512,1546,1587	434 476	270 395
7b	1630	1502,1518,1564	425 480	270 380
8b	1630	1518,1544,1587	416 494	272 390

^{1}H NMR Spectra

The most characteristic feature of ^{1}H NMR spectra of the diamagnetic complexes is the absence of the low field enol proton signal of the ligands. The NH proton signal remained almost unaffected. These strongly support that only the enol proton has been replaced by the metal ion and the amide nitrogen is excluded from coordination. The methylene proton signal shifted appreciably to low field compared to the shift in the olefinic protons. This may be due to the aromatic character that might have been imparted to the C_3O_2M ring system of the chelates by the highly conjugate groups attached to the dicarbonyl moiety. The integrated intensities of various aromatic and aliphatic protons agree well with the ML_2 stoichiometry of the complexes. Typical spectra are reproduced in figures. Since the olefinic protons of both of the two ligand molecules in the complexes give only one signal, it is quite evident that both the cinnamoyl group are in identical chemical environments. This is possible only with *trans* orientation as in structure **9**. Had the two cinnamoyl groups been in *cis* position strain releasing will definitely result in separate signals. That the phenolic OH group of **2b** is not involved in bonding with the metal ion is clearly indicated in the spectra of its Ni(II) complex.



9

Mass Spectra

The FAB mass spectra of the Cu(II) complexes are obtained and are assembled in figures. The spectra clearly show peaks corresponding to CuL_2 stoichiometry of the complexes. Stable peaks correspond to $[CuL]^+$, L^+, fragments of L^+ are also present in the spectra. The formation of major fragments can be accounted by considering the fragmentation pattern given in scheme 3.8. One of the typical spectra is reproduced in fig. **3.50**.

Geometrical structure of the complexes

Cu(II) complexes showed a broad visible band at ~15,000 cm^{-1} indicating the square-palanar structure. The complexes undergo a change to octahedral symmetry in the presence of donor solvents. When the spectra of the chelates were measured in pyridine (10^{-3} M solution) a broad absorption band centred at ~11,100 cm^{-1} was observed which indicates the formation of pyridine adducts of the planar [CuL_2] complexes. The visible spectra of Co^{2+} complexes are dominated by a broad band with maxima at ~19,200 cm^{-1}. In some cases a shoulder appeared on this band at ~20,700 cm^{-1}. These values together with the observed magnetic moment in the range 4.70–4.90 B.M. suggest the octahedral geometry of the complexes. The observed diamagnetism and broad medium-intensity band at ~17,600 cm^{-1} in the visible spectra of the Ni(II) chelates suggest their square-planar geometry. In conformity with this observation the visible spectra of the chelates in pyridine solution (10^{-3} M) showed three bands corresponding to configurational change from square-planar to octahedral due to the association of pyridine. The three well-seperated absorption bands at λ_{max} ~8,142, ~13,340 and ~24,456 cm^{-1} correspond to the transitions $^3A_{2g} \rightarrow {}^3T_{2g}$; $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g} \rightarrow {}^3T_{1g}(P)$, respectively.

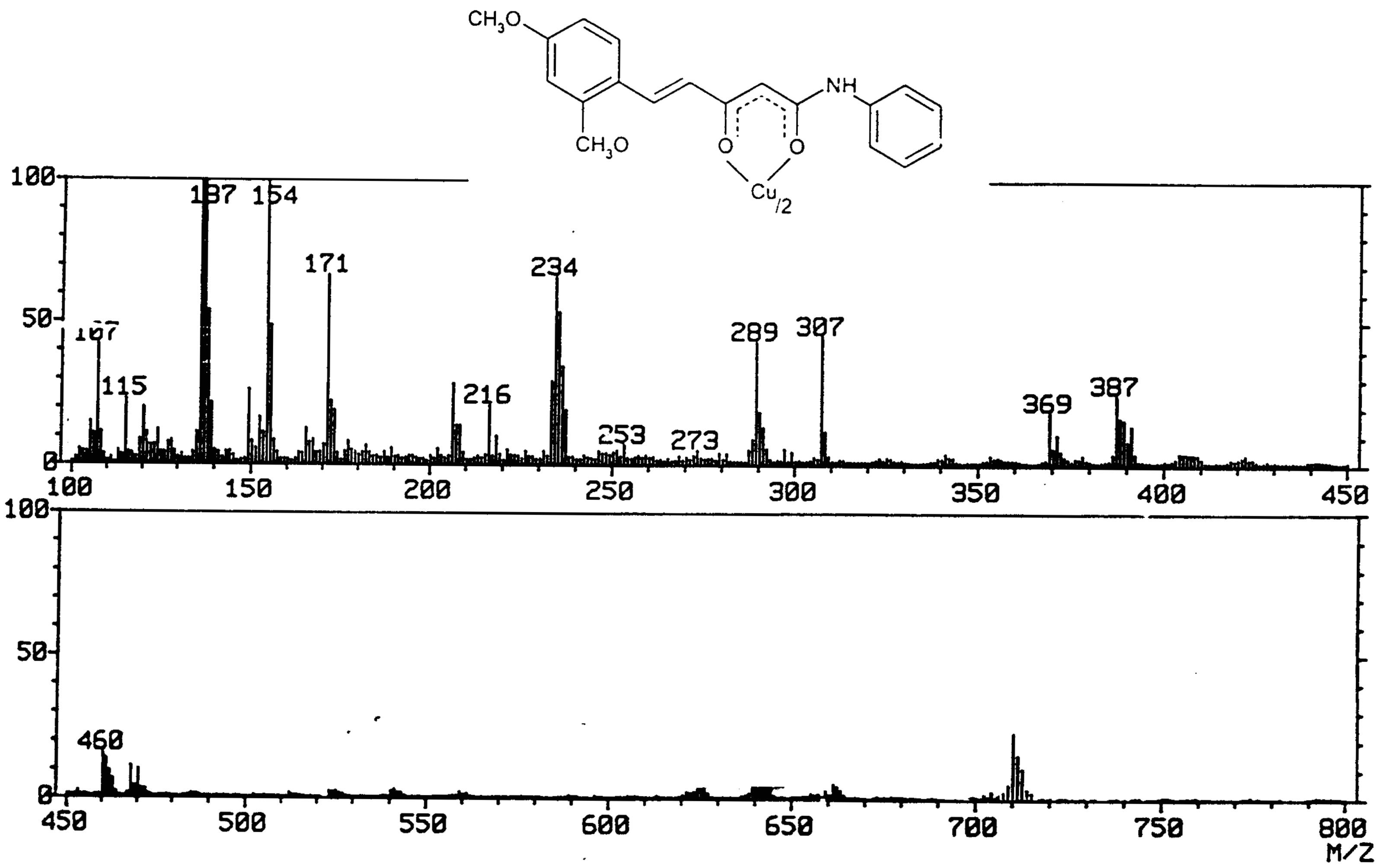


Fig.3.50 FAB Mass spectrum of Cu(II) complex of 9b

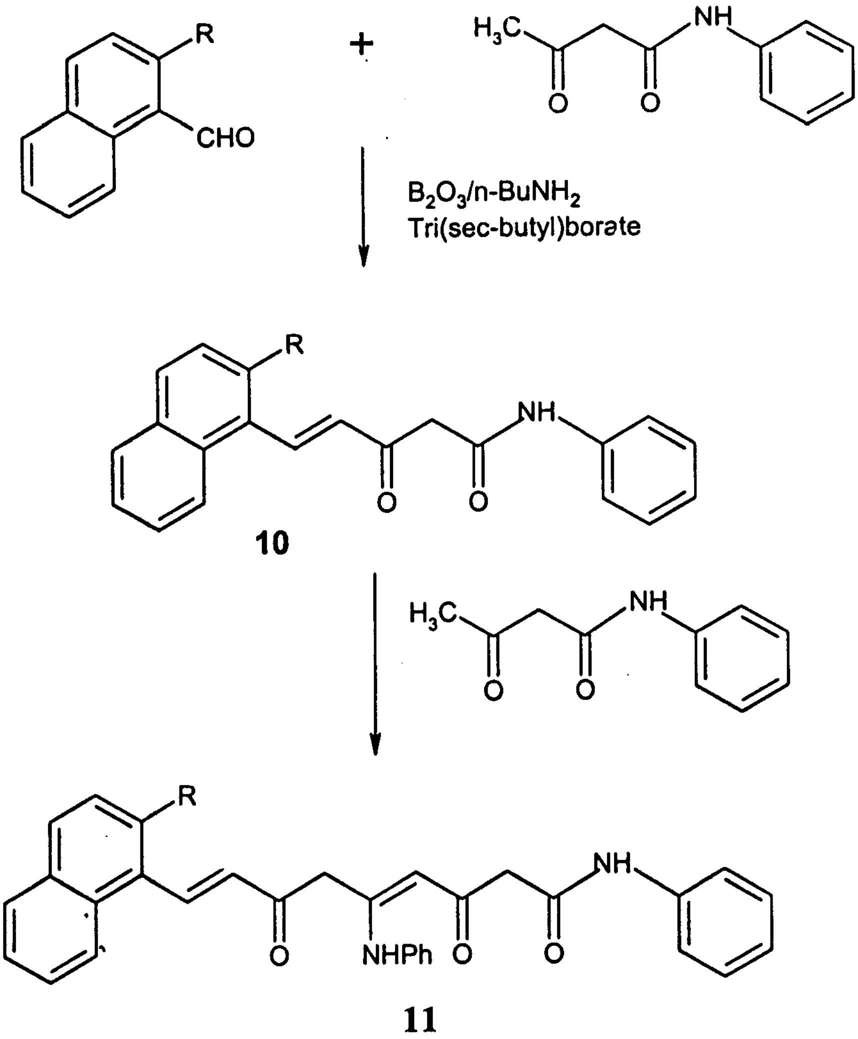
CHAPTER 2

CONJUGATED NAPHTHYL KETOANILIDES AND THEIR METAL COMPLEXES

Reaction of acetoacetanilide with benzaldehyde/substituted benzaldehyde in presence of B_2O_3, tri(sec-butyl)borate and n-butylamine yielded both the monocondensation product (unsaturated β-ketoanilide) and the biscondensation product (unsaturated diketoanilide) as discussed in **Chapter 1**. When the reaction was carried out using naphthalene-1-carbaldehyde and acetoacetanilide also resulted in the formation of two well defined compounds **10** and **11** and were separated in pure form by coloumn chromatography. Using analytical and various spectral data they were characterised as mono and biscondensation products, as in the reaction scheme 3.9. However, 2-hydroxynaphthalene-1-carbaldehyde formed only the monocondensation product **10**. This behaviour of 2-hydroxynaphthalene-1-carbaldeyde under the experimental conditions can be justified by considering the electronic effect of the 2-OH group in the naphthalene ring.

Both the mono and biscondensation products form well defined complexes with various transition and non-transition elements.

Analytical and spectral data of the compounds obtained from the first eluted product conform to structure **10** and second one to structure **11.** However tlc revealed only one product in the case of 2-hydroxynaphthalene-1-carbaldehyde.



Scheme 3.9

Structure **10** is an unsaturated β-ketoanilides having enolisable hydrogens. Structure **11** is evidently an unsaturated diketoanilide. For convenience this part is divided into two sections. Details on the characterisation and typical metal complexes of **10** are included in **section 1**. In **section 2** the characterisation of the unsaturated diketoanilide **11** and its typical metal chelates are included.

SECTION 1

Synthesis and characterisation of unsaturated β-ketoanilides and their metal complexes

The synthesis and chromatographic separation of the compounds are similar to that for the compounds considered in **Chapter 1**. The synthetic details of the compounds are given below.

Compounds	Aldehyde used for synthesis	R	Systematic name	Yield (%)
10b	Naphthalene-1-carbaldehyde	H	1-(N-phenyl)amino-5-naphthyl-4-penten-1,3-dione	50
11b	2-Hydroxynaphthalene-1-carbaldehyde	OH	1-(N-phenyl)amino-5-(2′-hydroxy)naphthyl-4-penten-1,3-dione	45

Synthesis of metal complexes

The general procedure adopted for the preparation of Co(II), Cu(II) and Zn(II) complexes are given below.

An ethanolic solution of the metal salt (0.001 mol, 20 mL) was added slowly with stirring to a solution of the compounds in methanol (0.002 mol,25 mL). The mixture was stirred well and sodium acetate was added to keep the pH around 6. The mixed solution was refluxed for ~ 2h and then the volume was reduced to half. On cooling to room temperature the complex gets precipitated. It was filtered, washed with

1:1 methanol-water mixture and dried. For purity, the compounds were recrystallised from hot chloroform.

Iron(III) complexes were prepared as follows. To a refluxing solution of the compounds in methanol (0.003 mol, 20 mL) slowly added a methanolic solution of anhydrous $FeCl_3$ (0.001 mol, 20 mL) with vigorous stirring. The mixture was then refluxed for ~2h and concentrated to half the original volume. It was then cooled in ice and the precipitated complex on cooling to ice cold temperature was filtered, washed with cold ethanol and recrystallised form hot chloroform. The complexes were dried in vacuum

Results and Discussion

Characterisation of the β-ketoanilides

The results of elemental analysis and molecular weight determination of the compounds are given in table 3.28. The compounds were characterised mainly on the basis of their UV, IR, NMR and mass spectral data and are discussed below.

UV Spectra

The UV spectra of the compounds are characterised by the presence of two absorption maxima (Table 3.28), the one at 370-400 nm corresponds to $n \rightarrow \pi^*$ transition and 260-270 nm to the $\pi \rightarrow \pi^*$ transition.

Table 3.28

Physical, analytical and UV spectral data of the unsaturated β-ketoanilides

Compounds	MP (^{0}C)	Elemental analysis (%) C	H	N	Mol. Weight	λ_{max} (nm)	log ϵ
		Found/ (calcd)					
10b	70	79.94 (80.00)	5.36 (5.40)	4.44 (4.44)	316 (315)	260 375	4.09 4.73
11b	72	77.48 (77.68)	5.64 (5.34)	4.92 (4.98)	329 (331)	265 394	4.07 4.64

IR Spectra

The IR spectra of the compounds in the 1600-1800 cm^{-1} are characterised by the presence of two strong bands at ~1670 cm^{-1} and at ~1630 cm^{-1} (Fig. **3.51** and **3.52**). The former band is undoubtedly due to the amide carbonyl. The band at ~1630 cm^{-1} can arise only due to the conjugated carbonyl group. The NH of amide and the intramolecular hydrogen bonded enolic group gives broad bands in the region 2600-3800 cm^{-1}. Characteristic absorption of amide group vibration like amide II,III,IV and V are also observed in this spectra. Important IR bands of the compounds are given in Table 3.29.

Fig 3.51 IR spectram of 10 b

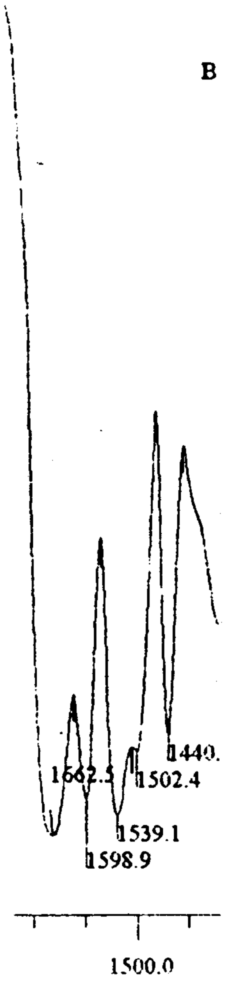


Fig. 3.52 IR spectram of 11b

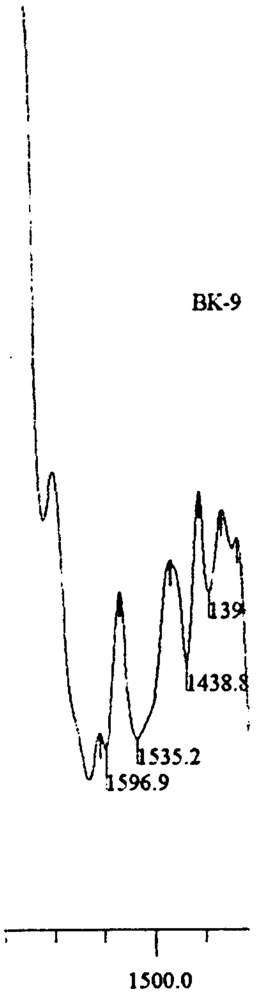


Table 3.29

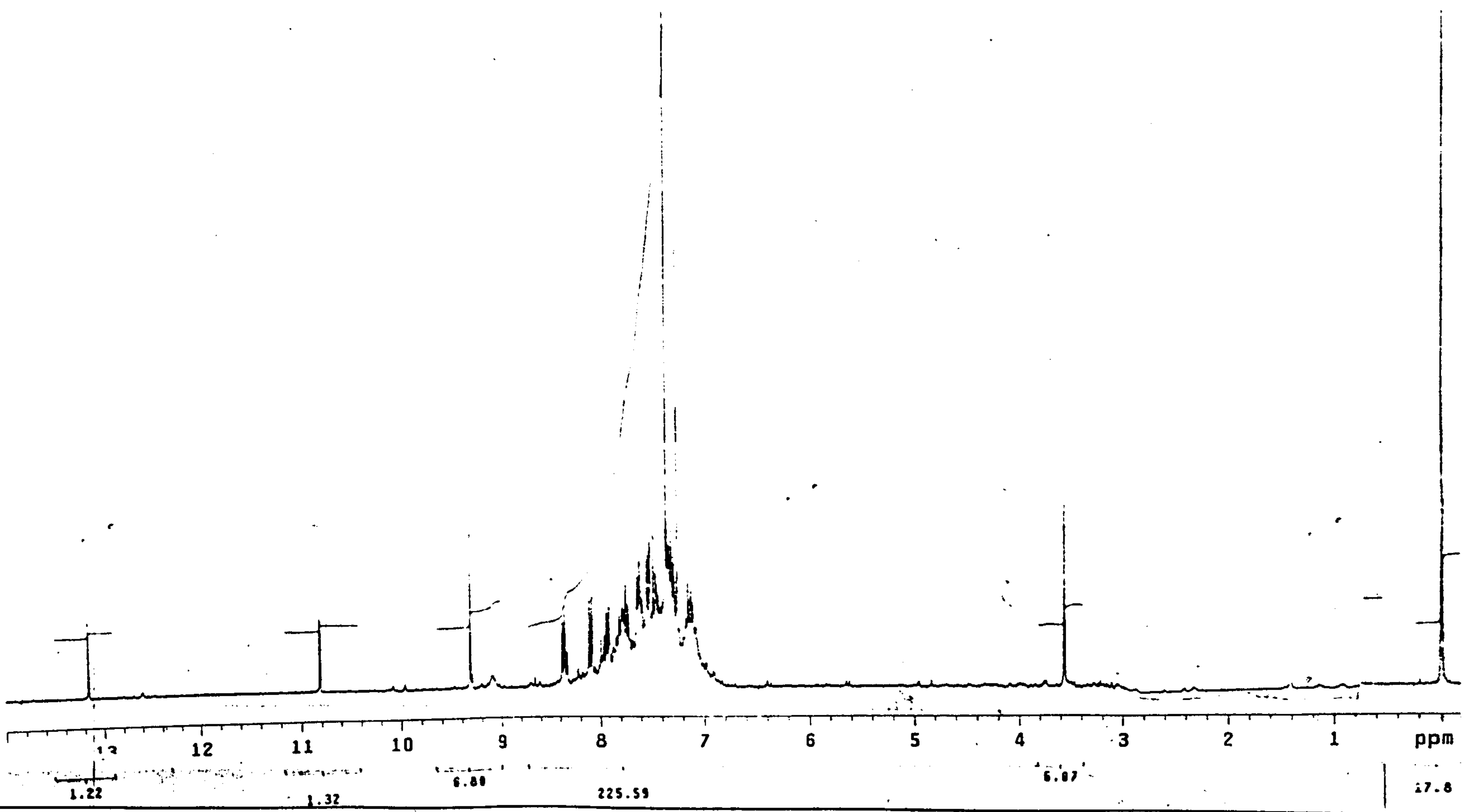
Characteristic IR data (cm^{-1}) of unsaturated β-ketoanilides

Compounds		Probable assignments
10b	11b	
1670	1665	ν (C=O) amide
1635	1636	ν (C=O) chelated
1598	1597	ν(C=C) phenyl
1539	1535	ν(C=C) alkenyl
1510	1515	ν amide II
1242	1238	ν amide III
976	974	ν CH=CH trans
686	688	ν amide V
650	652	ν amide IV
614	610	ν amide VI

^{1}H NMR Spectra

The ^{1}H NMR spectra of the compounds displayed a down field singlet at ~δ12 ppm and another singlet at ~δ 6 ppm assignable to the enol and methine protons respectively. The phenolic proton on the aryl ring of **11b** and the NH proton of anilide showed signals as expected. Aryl protons show signals in the range δ7-7.5 ppm. The assignment of

Fig. 3.53 ^{1}H NMR spectrum of **11b**



various proton signals observed in the ^{1}H NMR spectra of the compounds are assembled in table 3.30. The spectra of **11b** is given in Fig. **3.53**.

Table 3.30

Characteristic ^{1}H NMR spectral data of the unsaturated β-ketoanilides

Compounds	Chemical shift δppm					
	enolic OH	NH	CH=CH	Methine	CH_2	Phenyl substituent
10b	10.354	10.104	8.201 8.004	6.870	3.634	-
11b	13.258	9.318	8.386 8.353	6.928	3.568	10.814

Mass spectra

Mass spectra of the unsaturated β-ketoanilides show intense molecular ion peaks. Peaks corresponding to the $[P - C_6H_5NHCO]^+$ are characteristic of all the spectra. The possible fragmentation pattern of the compounds are consistent with scheme 3.8 of **Chapter 1** and the important peaks appeared in the spectra are tabulated in table 3.31. Spectra of the compounds are reproduced in fig 3.54-3.55.

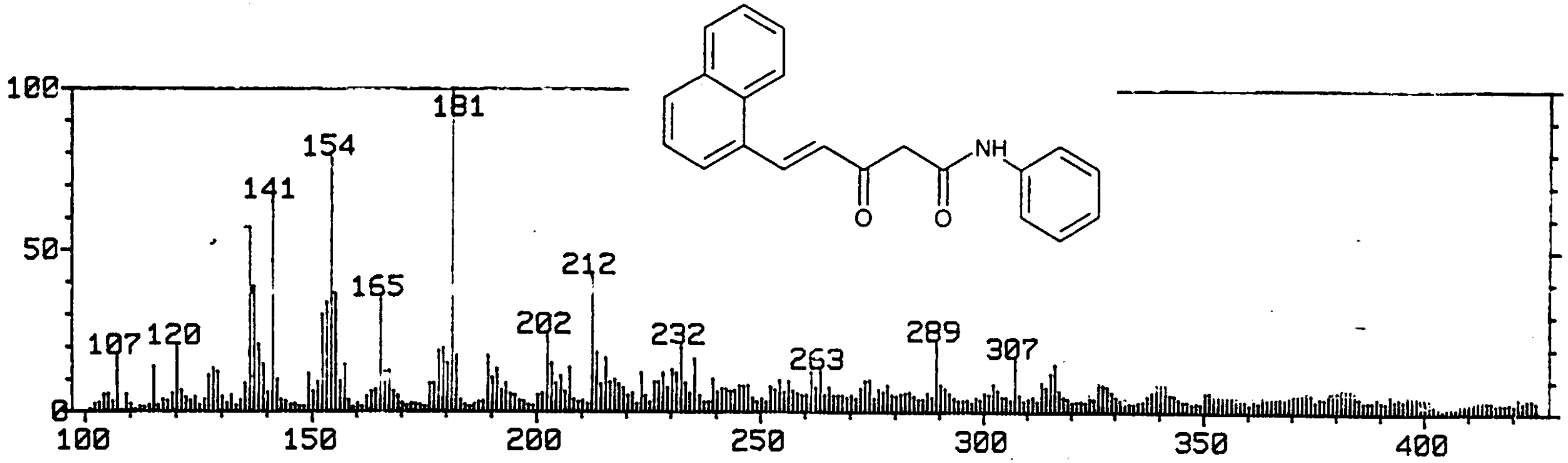


Fig.3.54 FAB Mass spectrum of **10b**

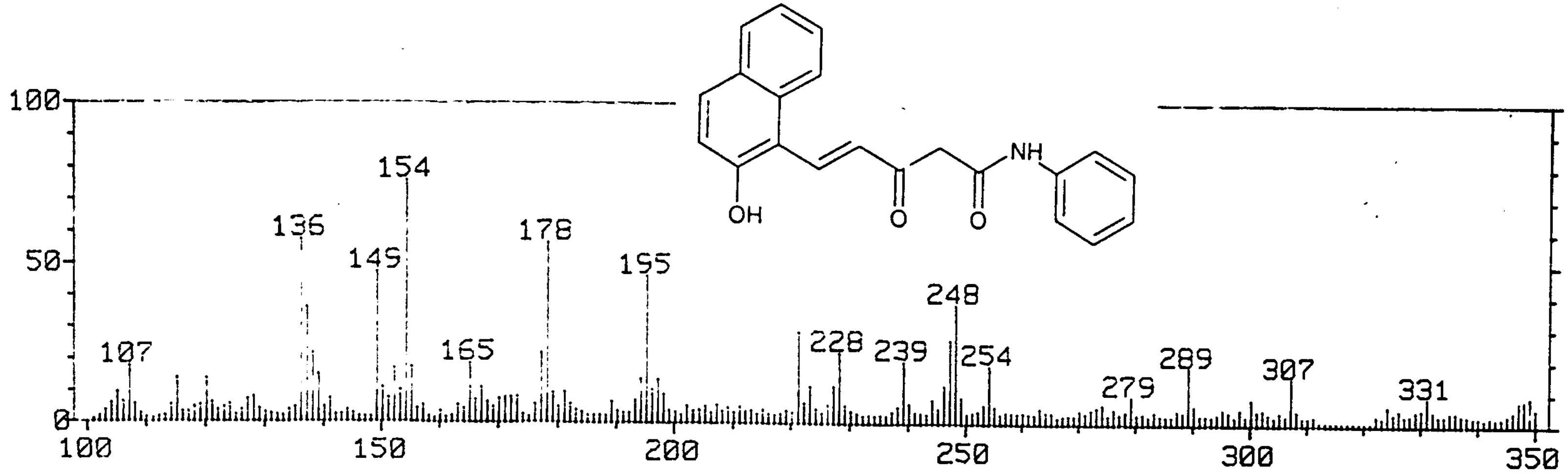


Fig.3.55FAB Mass spectrum of **11b**

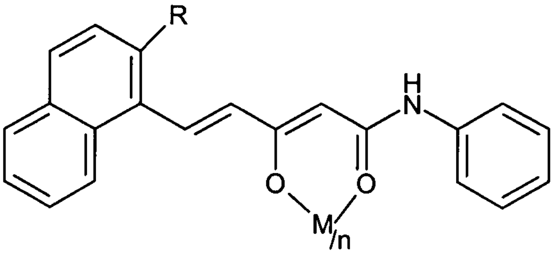
Table 3.31

Important fragments observed in the FAB mass spectra of unsaturated β-ketoanilides

Compounds	P^+	A	B	C	D	E	G	H
10b	315	181	195	223	162	120	153	127
11b	331	197	211	239	162	120	169	143

Characterisation of metal chelates

Elemental analytical data of the complexes of Co(II), Cu(II) and Zn(II) suggest their [ML_2] stoichiometry and [ML_3] for Fe(III) complexes. Analytical and physical data of the metal complexes are given in tables 3.32. Conductometric studies show that all the complexes behave as non electrolytes in dmf (specific conductance <10 $\Omega^{-1}cm^{-1}$ in 10^{-3} M solution) and do not contain the anion of the metal salt used for the preparation. Magnetic moment measurements show that Zn(II) complex is diamagnetic while Co(II), Cu(II) and Fe(III) complexes show normal magnetic moment. The UV, IR, NMR and mass spectral data suggest structure **12** of the complexes.



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n = 2 for Co(II), Cu(II) and Zn(II); n = 3 for Fe(III)

Table 3.32

Physical and analytical data of the metal chelates of the unsaturated β-ketoanilides

Metal ion	Ligand (HL)	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)*			
				C	H	N	Fe
Fe(III)	**10b**	176	5.76	75.44 (75.82)	4.79 (4.81)	4.19 (4.21)	5.48 (5.52)
	11b	148	5.78	72.34 (73.47)	4.60 (4.66)	4.06 (4.08)	5.30 (5.34)
Co(II)	**10b**	164	4.7	73.04 (73.06)	4.65 (4.66)	4.01 (4.08)	7.99 (8.59)
	11b	158	4.8	69.84 (70.10)	4.44 (4.45)	3.85 (3.89)	8.04 (8.21)
Cu(II)	**10b**	160	1.76	72.18 (72.94)	4.59 (4.63)	3.99 (4.05)	9.01 (9.12)
	11b	172	1.76	69.66 (69.71)	4.01 (4.43)	3.86 (3.87)	8.70 (8.71)
Zn(II)	**10b**	142	-	72.14 (72.73)	4.58 (4.62)	4.01 (4.04)	9.30 (9.38)
	11b	146	-	69.44 (69.52)	4.32 (4.41)	3.81 (3.86)	8.90 (8.97)

* *The calculated value corresponds to the* [ML_2] *composition for Cu(II) and Zn(II),* [$ML_2(H_2O)_2$] *for Co(II) and* [ML_3] *for Fe(III) where L stands for the deprotonated ligand.*

UV Spectra

The characteristic UV absorption maxima of the dicarbonyl compounds due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions show only slight bathochromic shifts in the spectra of the metal complexes. It is therefore, evident that no structural alteration has occurred to the ligand during complexation.

Infrared spectra

In the spectra of the metal complexes, the band due to hydrogen bonded dicarbonyl function of the ligands disappeared but instead a strong and slightly broadened band assignable to the stretching of the metal coordinated dicarbonyl group appeared at ~1620 cm^{-1} (Fig. **3.56-3.59**). The broad band in the region 3400-3800 cm^{-1} cleared up in the spectra of the complexes. However the spectra of the complexes of **11b** show a prominent band at ~3400 cm^{-1} due to the phenolic OH stretching. This indicated that the phenolic OH groups are not involved in complex formation. Spectra of the Co(II) complexes show characteristic bands at 3400 cm^{-1} and 3800 cm^{-1} due to coordinated water molecules. The various amide bands are only marginally altered in the spectra of the complexes. In agreement with this structure spectra of all complexes show bands at ~465 cm^{-1} and at ~420 cm^{-1} assignable to n(M-O) vibrations. Important ir bands of the complexes are included in table 3.33.

Fig 3.56
IR spectrum of Fe(III) complex of 11(b)

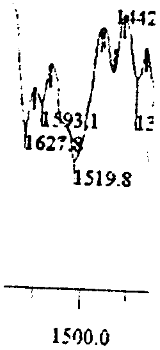


Fig 3.57
IR spectrum of Co(II) complex of 10(b)

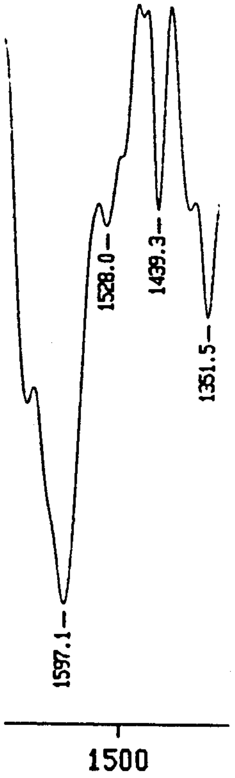


Fig 3.58
IR spectrum of Zn(II) complex of 11(b)

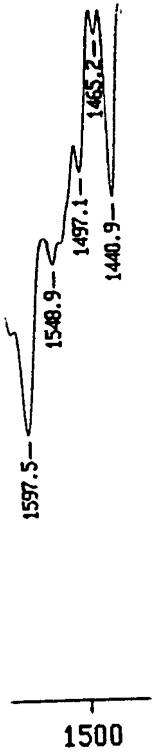


Fig 3.59
IR spectrum of Cu(II) complex of 11(b)

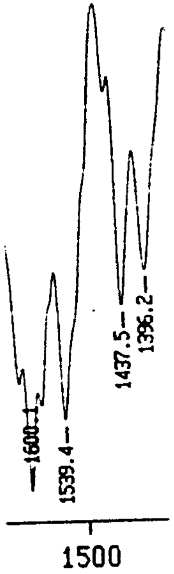


Table 3.33
Characteristic IR and UV spectral data of the metal complexes of unsaturated β-ketoanilides

Metal ion	Ligand	Characteristic ir stretching bands (cm^{-1})			λ_{max}
		C=O	C=C alkenyl/ phenyl	M-O	(nm)
Fe(III)	**10b**	1630	1586, 1546, 1518	424 496	275 391
	11b	1628	1593, 1536, 1520	417 475	270 406
Co(II)	**10b**	1630	1597, 1528, 1502	420 472	275 398
	11b	1625	1584, 1536, 1517	422 475	266 391
Cu(II)	**10b**	1626	1587, 1542, 1518	416 474	275 388
	11b	1622	1586, 1574, 1540	416 487	268 404
Zn(II)	**10b**	1630	1574, 1563, 1515	420 480	275 395
	11b	1629	1598, 1548, 1500	418 490	266 402

^{1}H NMR spectra

In the ^{1}H NMR spectra of the diamagnetic Zn(II) complexes the enolic proton singlet of the free ligand disappeared. However the phenolic OH signal of **1b** remain as such indicating its non involvement in coordination. The position of NH proton signal is only marginally altered in the complexes. Integrated intensities of the various proton signals agree well with the [ML_2] stoichiometry of the complexes.

Mass spectra

The FAB mass spectra of all the Cu(II) chelates show intense molecular ion peaks in conformity with their [CuL_2] stoichiometry. Peaks due to $[CuL]^+$ and fragments of L^+ are some times more intense. Peaks at m/z corresponding to $[P - nAr]^+$, $[P - nC_6NHCO]^+$ where n = 1 to 2 are present in the mass spectra of all the complexes. The spectra of the complexes are reproduced in fig. **3.60-3.61**.

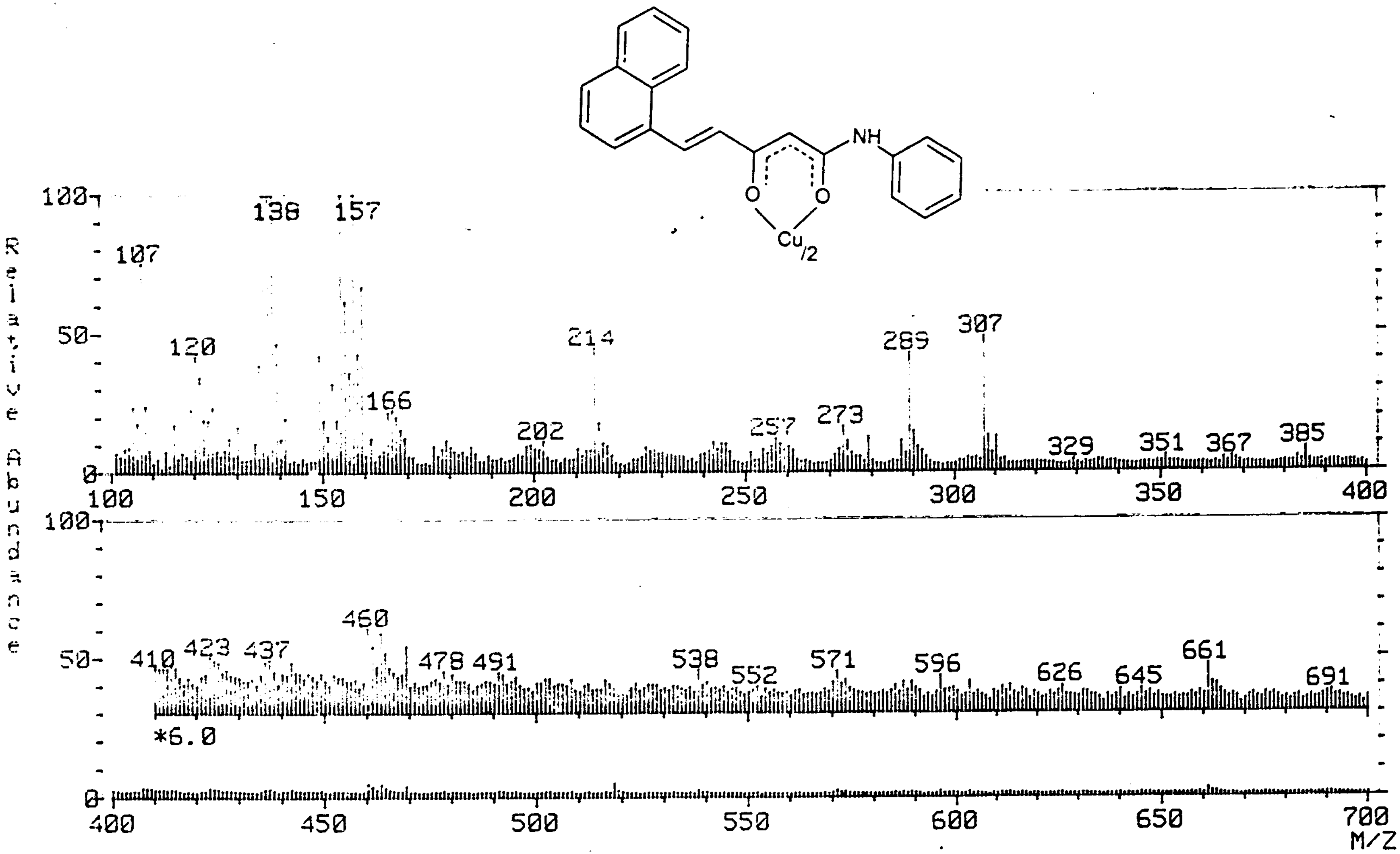


Fig. 3.60 FAB Mass spectrum of Cu(II) complex of **10b**

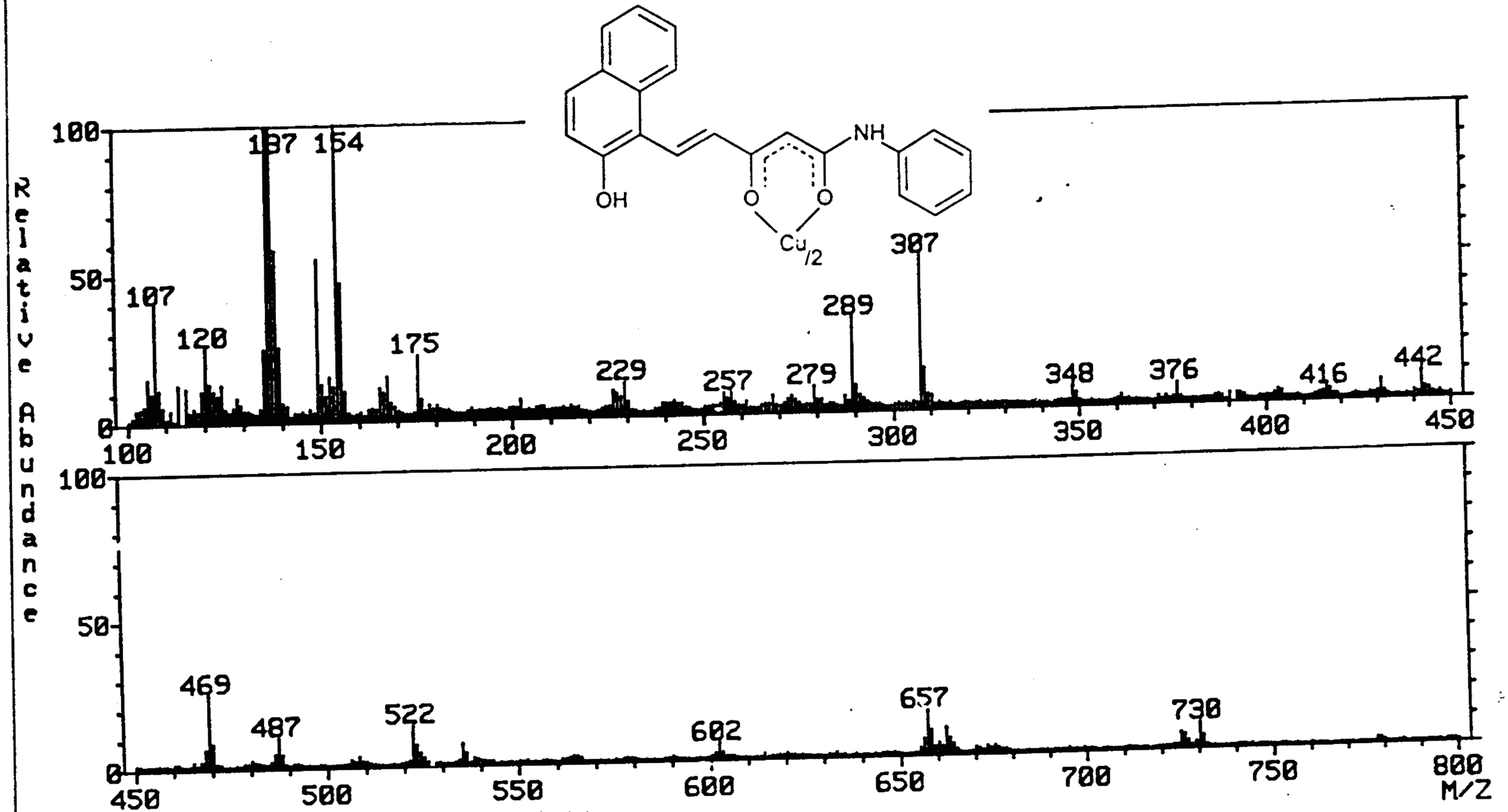


Fig.3·61 FAB Mass spectrum of Cu(II) complex of **11b**

SECTION 2

Synthesis and characterisation of unsaturated diketoanilide and its metal complexes

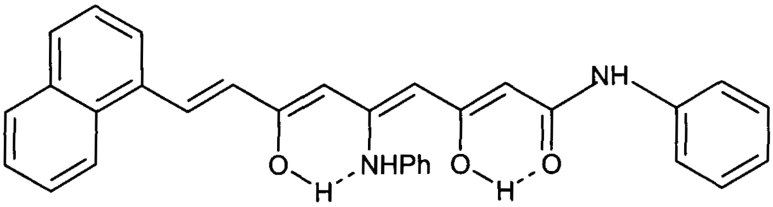
Synthesis of metal chelates

Co(II), Cu(II), and Zn(II) complexes of the compound was synthesised as follows.

To a refluxing solution of the compound in ethanol (0.001 mol, 20 mL), an aqueous solution of metal acetates (0.001 mol, 15 mL) was added drop by drop with stirring. The pH of the solution was adjusted around 6 using sodium acetate and refluxing was continued for ~4h. The solution was concentrated to half the volume. It was then cooled in ice and the precipitated complex was filtered, washed several times with water, then with ethanol and recrystallised from hot ethanol. The crystals were dried in vacuum.

Results and Discussion

The unsaturated diketoanilide and its complexes were characterised mainly on the basis of elemental analysis and IR, NMR and mass spectral data. Analytical and physical data of the compound and its metal complexes are given in table 3.34. The spectral data of the compound are in conformity with the intramolecularly hydrogen bonded enol form **13** and the analytical and spectral data of the complexes conform to structure **14**.



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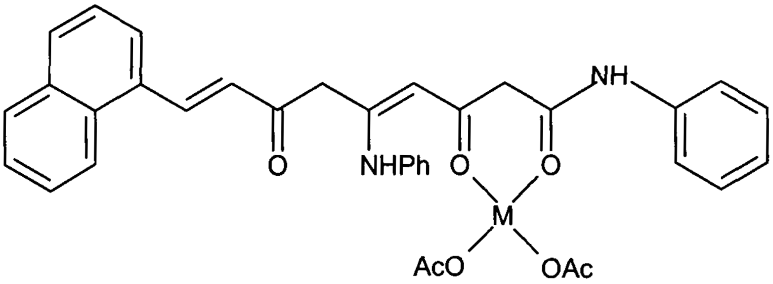

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Table3.34

Physical and analytical data of the unsaturated diketoanilide (HL) and its metal chelates

Compounds	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)			
			C	H	N	M
(HL)	88	-	79.10 (79.44)	5.49 (5.69)	5.78 (5.91)	-
[Co(HL)(OAc)$_2$ (H$_2$O)$_2$]	168	4.8	63.44 (64.52)	4.89 (4.92)	4.14 (4.30)	8.84 (9.06)
[Cu(HL)(OAc)$_2$]	178	1.76	64.01 (64.02)	4.74 (4.88)	4.22 (4.27)	8.77 (9.76)
[Zn(HL)(OAc)$_2$]	134	-	62.99 (63.93)	4.14 (4.87)	4.25 (426)	9.85 (9.89)

Infrared Spectra

Three distinct peaks are observed in the 1600–1800 cm^{-1} region of the spectrum of the compound. From a comparison of the spectral data of compounds these bands can be assigned as follows. The band at ~1600 cm^{-1} arises from the stretching of cinnamoyl carbonyl, the 1660 cm^{-1} peak due to α,β-unsaturated carbonyl group and the one at ~1700 cm^{-1} is due to the amide carbonyl. Broad bands are observed in the 3500–3000 cm^{-1} region due to the absorption by intramolecularly hydrogen bonded enolic OH and NH groups as in structure **13**. The bands observed in the region 1500-1600 cm^{-1} are due to various $\nu_{C=C}$ vibrations. The amide II, III & IV bands are observed at ~1530, ~1313 and ~666 cm^{-1} respectively.

In metal complexes the amide I band and the α,β-unsaturated carbonyl band of the compound are shifted markedly to higher wavelength indicating their involvement in complexation. The NH bands of anilide and OH band of enol in the range 3000-3500 cm^{-1} do not show any deviation from the ligand spectrum which undoubtedly explains the non involvement of nitrogen lone pair and enolic OH in chelation. The IR spectra of all the complexes showed a band at 1310 cm^{-1} indicating the presence of coordinated acetate group. The Co(II) complexes showed bands at ~3400 and ~3600cm^{-1} indicating the presence of coordinated water molecules. Spectra of the complexes show additional bands at ~460 cm^{-1} and ~425 cm^{-1} assignable to ν_{M-O} vibration. The important IR peaks are also listed in table 3.35.

Table 3.35

Characteristic IR and UV spectral data of complexes of unsaturated diketoanilide

Complex	Characteristic IR stretching bands (cm^{-1})			λ_{max}
	C=O enolic	C=O chelated	M-O	nm
Co(II)	1599	1634 1620	418 474	270 402
Cu(II)	1597	1637 1619	425 470	272 404
Zn(II)	1598	1635 1624	420 470	268 399

^{1}H NMR Spectra

The ^{1}H NMR spectra of the compound displayed a one proton singlet at δ 6.6 ppm and at δ11.5 ppm assignable to methine hydrogen and the intramolecularly hydrogen bonded enolic hydrogen respectively. The CH_3 singlet of acetoacetanilide at δ2.17 ppm is disappeared indicating their involvement in condensation with the aldehyde. The CH_2 singlet of acetoacetanilide at δ3.5 ppm is not changed appreciably in the spectra of the ligand. The NH singlet of anilide group at δ9.04 ppm is shifted to downfield due to strong external conjugation. Two signals appeared in this region indicating the presence of to NH groups. The region δ7-7.5 ppm contain a number of signals due to aromatic protons. The *trans* orientation of the alkenyl groups is indicated by the position of their signals and from the observed J values.

The non-involvement of enolic proton attached to the Ar-CH=CH- group in complexation is indicated by retaining of its signal in the ^1H NMR spectra of the diamagnetic Zn(II) at complex at δ11.5 ppm. That complexation has occurred by the replacement of enolic hydrogen of β-dicarbonyl moiety is indicated by disappearance of the OH signal in the spectra of the complex the resonance signal would have been disappeared. The methylene proton signal is shifted slightly to downfield indicating neutral coordination of the dicarbonyl moiety. Acetate coordination to maintain electrical neutrality is indicated by the signal at δ ppm. From the intensity, it can be inferred that there are two acetate groups per/metal atom. The position and intensity of the NH signals remain unaltered in the complexes indicating its non involvement in coordination.

Mass Spectra

The compound showed intense molecular ion peak characteristic of the condensation of acetoacetanilide and aromatic aldehyde in the 2:1 ratio. The peaks **A** and **B** confirm the condensation of γ-methyl group of acetoacetanilide with aromatic aldehyde. The retainment of anilide in the condensation product is confirmed by the $[C_6H_5\text{-NHCO}]^+$ peak in the spectrum of the ligands. The fragments produced may undergo rearrangement to produce stable cyclic species. The absence of

[P - 2C_6H_5NHCO]$^+$ group indicates that only one amide carbonyl group is free in the ligands. The protection of active methylene group throughout the course of the reaction is confirmed by the fragment **A**. The peaks ArCH=CH$^+$, Ar-C≡CH and Ar$^+$ etc. are also observed in the spectra. The formation of the important peaks can be conveniently explained by the fragmentation pattern given in scheme 3.7 of **Chapter 1**.

The FAB mass spectrum of the Cu(II) chelate show intense molecular ion peak. The peaks due to the successive removal of one or both acetate groups and the fragment of L$^+$ are observed in the spectra. The spectra of the diketoanilide and its Cu(II) complex are reproduced in fig. **3.62-3.63**.

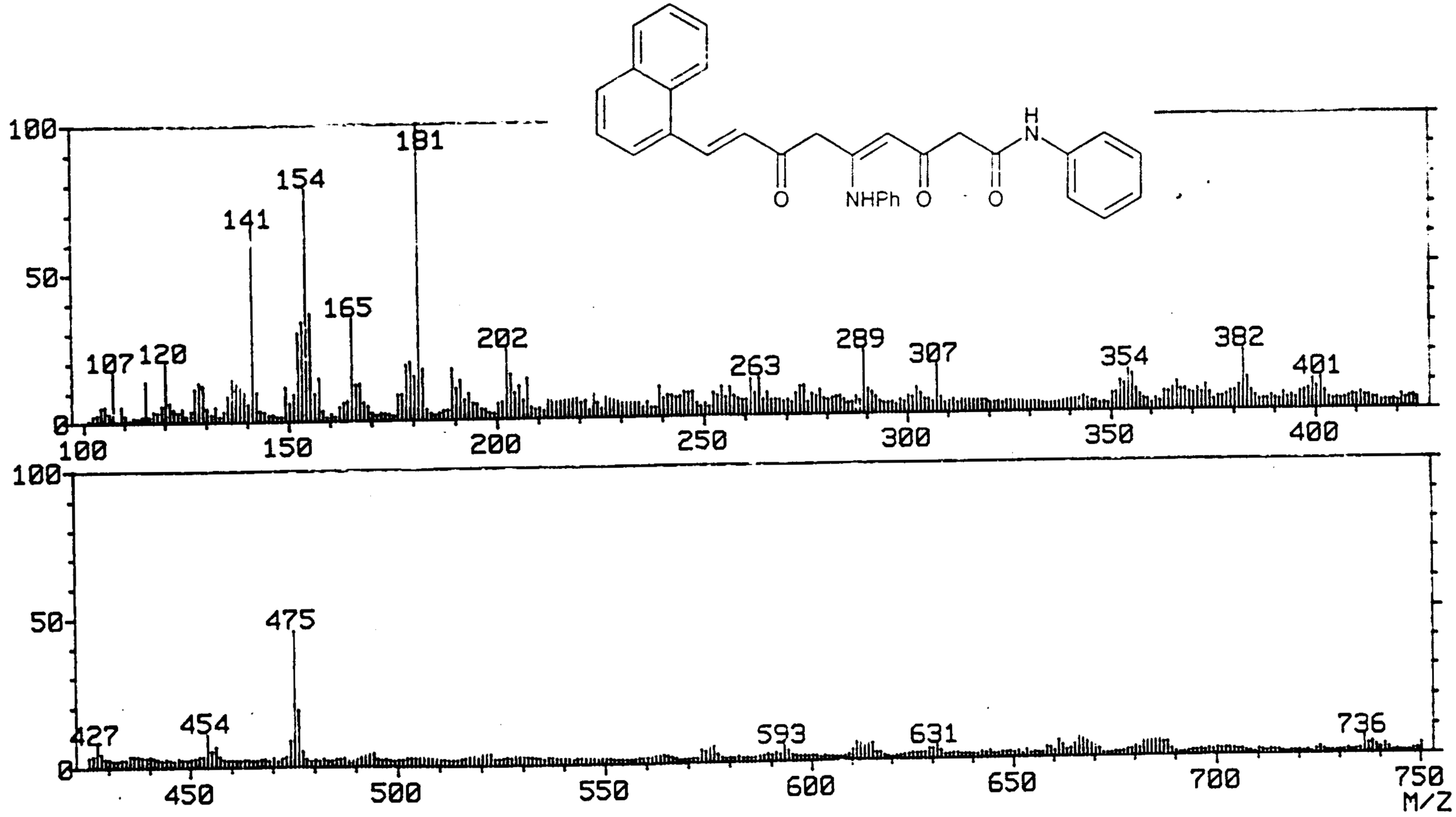


Fig.3.62 FAB Mass spectrum of **14a**

129.B

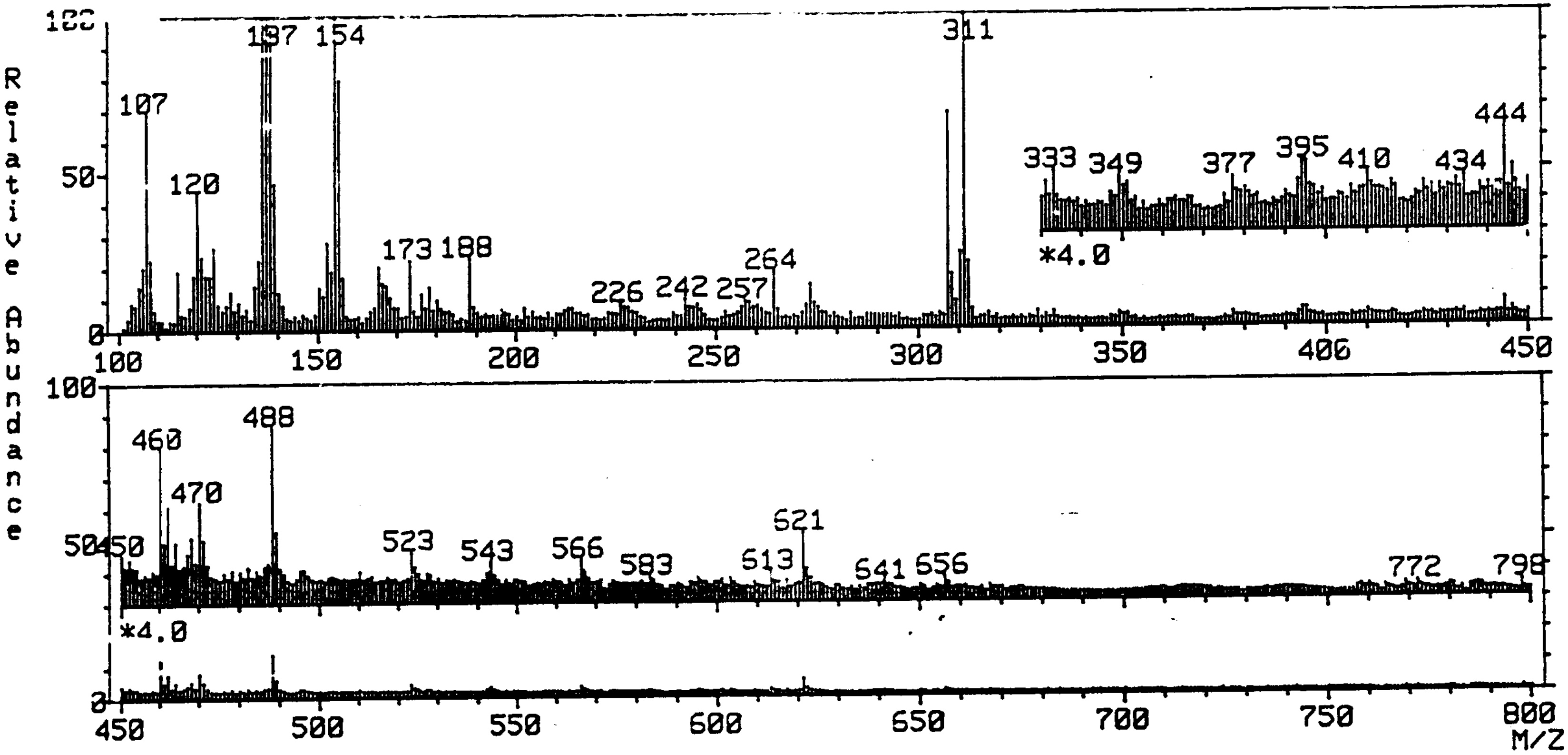


Fig.363 FAB Mass spectrum of Cu(II) complex of **13**

CHAPTER 3

SYNTHESIS AND CHARACTERISATION OF 1-PHENYLAMINO-7-PHENYL-4,6-HEPTADIEN-1,3-DIONE AND ITS METAL COMPLEXES

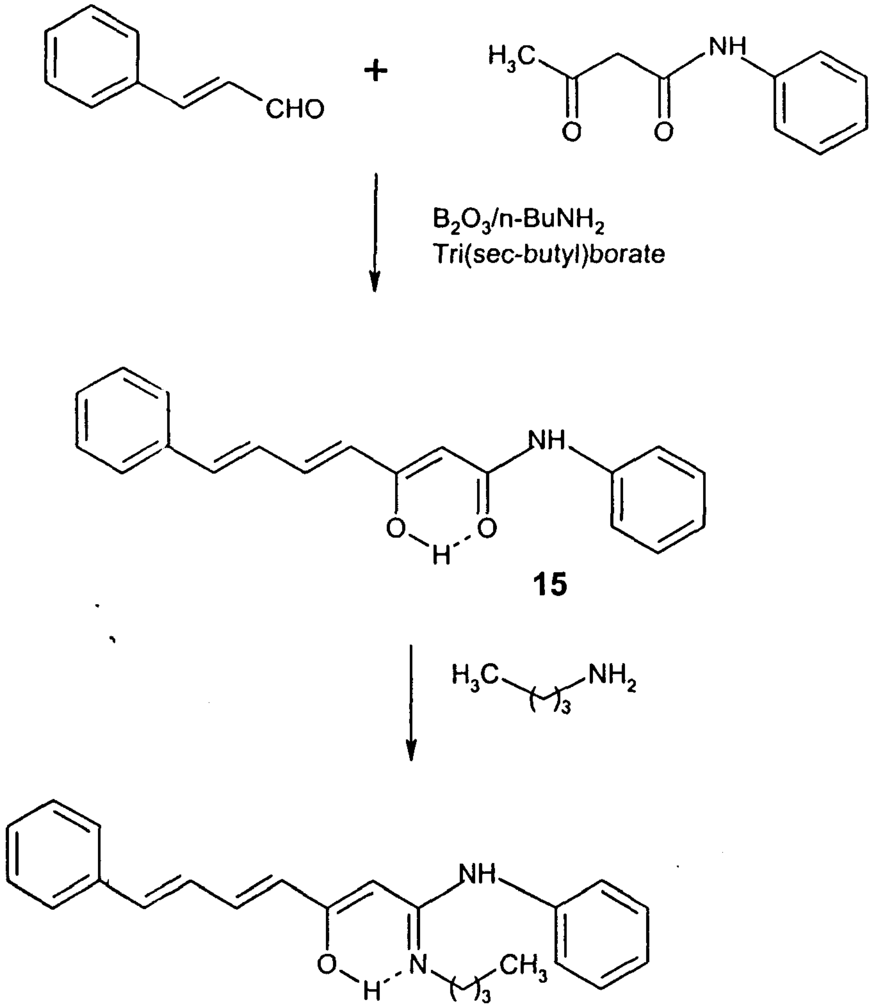
The reaction between cinnamaldehyde and acetoacetanilide in presence of boric oxide and tri(sec-butyl) borate with n-butylamine as the condensing agent resulted in the formation of more than one products. Chromatographic separation of the mixtures yielded two well defined compounds. Details on the synthesis, separation and purification of these two types of compounds and their typical metal chelates are presented in this part. Experimental details employed for the synthesis and separation of the two compounds are given below.

Acetoacetanilide (0.01 mol, 1.77 g) was stirred for ~1h with boricoxide (0.0035 mol, 0.25 g) to obtain acetoacetanilide-boron complex. To this reaction mixture cinnamaldehyde (0.01 mol, 1.37 g), dissolved in dry ethylacetate (5 mL) containing tri(sec-butyl)borate (0.002 mol, 4.6 g) were added. The reaction mixture was stirred on a magnetic stirrer and while stirring n-butylamine (0.5 mL dissolved in 5 mL dry ethylacetate) was added during 30 min. Stirring was continued for an additional period of ~5h and the solution were kept aside overnight. Hot (~60^{0}C) hydrochloric acid (0.1 M, 10 mL) was added and the mixture again stirred for ~1h. The organic layer separated was extracted with ethylacetate. The combined extract were evaporated to dryness and the residual paste was stirred with HCl (0.1 N, 25 mL) for ~1h. It was then kept aside overnight. The solid product separated was collected, washed with water and dried in vacuum. When the product obtained was subjected to tlc, two distinct spots were obtained. They were separated quantitatively by column chromatography using silicagel (60-120 mesh) as detailed below.

The product was dissolved in minimum amount of ethylacetate and placed over the column (2x200 cm) densely packed with silicagel. The eluting solvent used was 1:7 acetone-chloroform mixture. As the elution proceeds two bands were developed in the column, a bright yellow lower band and an orange red upper band. The lower region was collected as 10 mL aliquots in separate tubes and in each case, the homogeneity was established by tlc.

The elution was then continued using 1:3 mixture of chloroform and acetone to recover the orange red upper band. The two compounds isolated were recrystallised from hot benzene to give spectroscopically pure material.

Analytical and spectral data of the compounds eluted first from chomatographic column conform to structure **15**, the usual monocondensation product. But the second product on analysis is found to be an entirely different compound. A thorough investigation of the compound using different spectral techniques revealed that the compound is a Schiff's base **16** formed by the condensation between the amide carbonyl of the monocondensation product and the amino group of the butylamine. The formation of the two compounds can be explained by the reaction scheme 3.10.



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Scheme 3.10

Both these compounds formed stable metal complexes with various transition and non-transition elements. Analytical and spectral data useu for the characterisation of the two compounds and their metal complexes are discussed below.

Synthesis of metal complexes

Complexes of Ni(II), Cu(II), Zn(II) and Cd(II) with the unsaturated β-ketoanilide were prepared by the following general procedure.

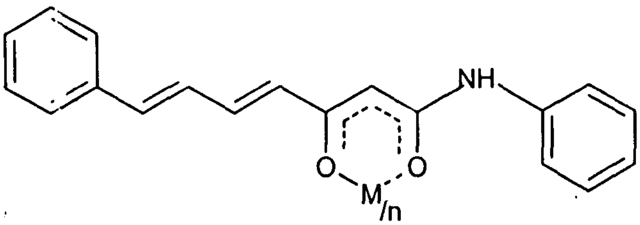
An ethanolic solution of the metal salt (0.001 mol, 20 mL) was added slowly with stirring to a solution of the compound in methanol (0.002 mol, 25 mL). The mixture was stirred well and sodium acetate was added to keep the pH around 6. It was then refluxed gently for ~3h and concentrated to half the original volume. On cooling to room temperature the complex gets precipitated. The precipitated product was filtered, washed with 1:1 methanol-water mixture and dried. For purity, the complexes were recrystallised from hot chloroform.

Fe(III) complex was prepared as follows. To a refluxing solution of the compound in methanol (0.003 mol, 15 mL) slowly added a solution of anhydrous $FeCl_3$ in methanol (0.001 mol, 20 mL) with vigorous stirring. The mixture was then refluxed for ~2h and the volume were reduced to half. It was then cooled in ice and the precipitated complex was filtered, washed with cold ethanol and recrystallised from hot chloroform. The crystels were dried in vacuum.

Results and Discussion

Electronic, IR, NMR and mass spectral data were examined thoroughly inorder to characterise the unsaturated β-ketoanilide and their metal complexes apart from elemental analysis, molecular weight determination, conductance and magnetic moment measurments.

Elemental analysis (C, H, N and metal percentages) and physical data of the complexes given in table 3.36 conform to the molecular formula of structure **17** of the compound. Conductometric studies show that all the complexes behave as non-electrolytes in dmf (specific conductance <10 $\Omega^{-1}cm^{-1}$ in 10^{-3} M solution) and do not contain the anion of the metal salt used for the preparation. Magnetic moment measurements show that Ni(II), Zn(II) and Cd(II) complexes are diamagnetic and all other complexes are paramagnetic.



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The spectral data of the compounds are discussed below.

UV Spectra

The UV spectra of the compounds in methanol show two absorption maxima. Based on earlier reports the band at 385 nm correspond to n→π* transition and the one at 286 nm is due to π→π* transition of the carbonyl chromophore. The slight shift of absorption maxima to longer wavelength in complexes indicate the involvement of the carbonyl oxygen in metal complexation.

Table 3.36

Physical and analytical data of the unsaturated β-ketoanilide (HL) and its metal chelates

Compounds	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)*			
			C	H	N	M
HL	85	-	78.24 (78.35)	5.80 (5.84)	4.76 (4.81)	-
[FeL$_3$]	172	5.8	73.81 (73.87)	5.12 (5.18)	4.60 (4.50)	5.29 (5.94)
[NiL$_2$]	154	-	71.10 (71.36)	5.10 (5.01)	4.28 (4.38)	9.12 (9.23)
[CuL$_2$]	198	1.77	70.61 (70.81)	4.92 (4.97)	4.32 (4.35)	9.87 (9.94)
[ZnL$_2$]	136	-	70.52 (70.70)	4.91 (4.96)	4.24 (4.34)	10.14 (10.08)
[CdL$_2$]	128	-	65.82 (65.90)	4.58 (4.62)	4.08 (4.05)	15.58 (16.18)

IR spectra

The IR spectrum of the unsaturated β-ketoanilide is characterised by the presence of two strong bands at 1615 cm^{-1} due to the highly conjugated carbonyl and at 1678 cm^{-1} due to the amide carbonyl. The broad band observed in the range 3000-3500 cm^{-1} is due to intramolecularly hydrogen bonded structure. The amide II to VI bands show absorptions as expected of the compound. The band at 969 cm^{-1} can be confidently assigned as due the *trans* CH=CH absorption.

The IR spectra of all the complexes are in full agreement with the structure **15**. In the spectra of metal complexes both the carbonyl stretching frequencies are shifted appreciably to lower values. Thus the amide carbonyl is shifted to ~1650 cm^{-1} and the other to ~1590 cm^{-1}. This strongly support the mode of coordination of the metal as in structure **15**. Alkenyl and aromatic stretching frequency appears between 1530-1585 cm^{-1}. The broad absorption of the ligand in the region 3000-3500 cm^{-1} cleared up in the spectra of metal complexes. Weak bands due to NH and various C–H stretches appeared in this range. Metal-oxygen stretching frequencies appeared at ~415 cm^{-1} and ~480 cm^{-1}. The important IR bands are listed in table 3.37.

Table 3.37

Characteristic IR and UV spectral data of the unsaturated β-ketoanilide and its metal complexes

Complex of	Characteristic IR stretching bands (cm^{-1})			
	C=O amide chelated	C=O enolic chelated	C=C alkenyl/ phenyl	M-O
Fe(III)	1650	1592	1520, 1535, 1576	424 476
Ni(II)	1640	1589	1518, 1544,1579	419 492
Cu(II)	1642	1594	1518, 1548, 1591	425 465
Zn(II)	1648	1595	1515, 1544, 1593	426 470
Cd(II)	1640	1593	1519, 1538, 1578	414 492

^{1}H NMR spectra

The ^{1}H NMR spectra of the compound displayed a one proton singlet at 14.1 ppm assignable to the strong intramolecularly hydrogen bonded enolic proton. The olefinic, aromatic protons and NH protons showed signals as expected. In the ^{1}H NMR spectra of the diamagnetic Ni(II) complex, the low field enolic proton singlet of the free ligand is absent. Methine proton singlet and aromatic proton signals shifted slightly to downfield. The resonance signals of alkenyl proton and NH singlet of anilide showed only marginal shifts. The integrated intensities of all the protons agree with the formulation of the complexes.

Mass Spectra

Mass spectrum of the compound shows the molecular ion peak at m/z 291in accordance with the formulation. Elimination of O, OH, CO, CH_2O, $C_3HO_2^+$ and $C_6H_5NHCO^+$ from the molecular ion characteristic of β-dicarbonyl compounds is clearly evident from the observed spectrum. Important peaks appeared in the spectrum of the compound can be conveniently accounted by the fragmentation pattern given in scheme 3.8 of **Chapter 1**.

The FAB mass spectra of the Cu(II) chelate showed relatively intense $(P + 1)^+$ peak corresponding to $[CuL_2]$ stoichiometry. The stepwise removal of aryl groups from the molecular ion is characteristic of the spectrum. Peaks due to the ML^+, L^+ and fragments of L^+ are also detected in the spectrum. The spectra of the diketoanilide and its Cu(II) complex are reproduced in fig **3.64-3.65**.

Characterisation of the Schiff's base and its Metal Complexes

Synthesis of metal complexes

Ni(II), Cu(II), Zn(II) and Cd(II) complexes of the schiff's base were synthesised as follows.

To a refluxing solution of the compound in ethanol (0.002 mol, 20 mL) an aqueous solution of metal acetate (0.001 mol, 15 mL) was added drop by drop with stirring. The pH of the solution was adjusted around 6 using sodium acetate and refluxing was continued for ~2h. The

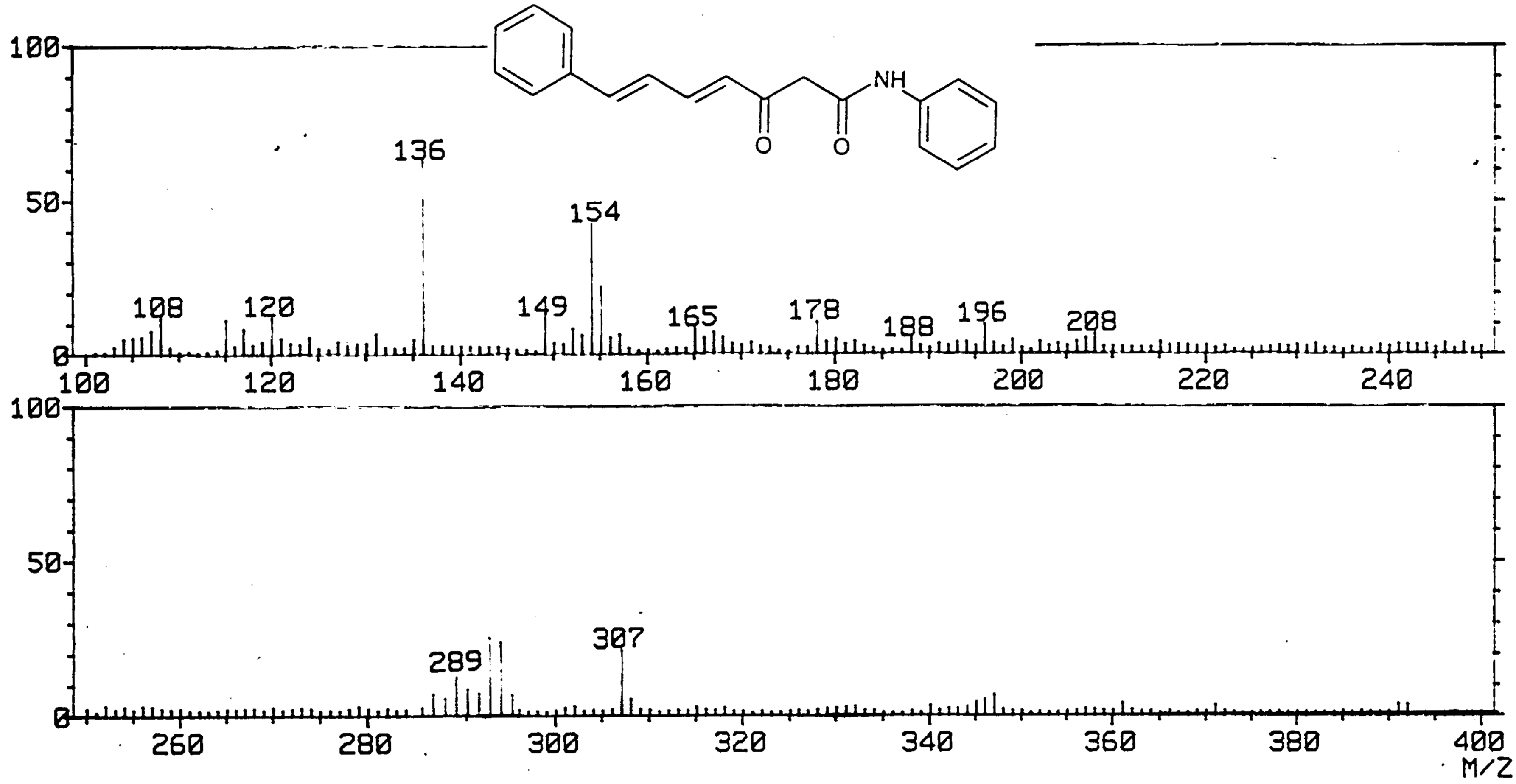


Fig. 3 ~~6~~4 FAB Mass spectrum of 15

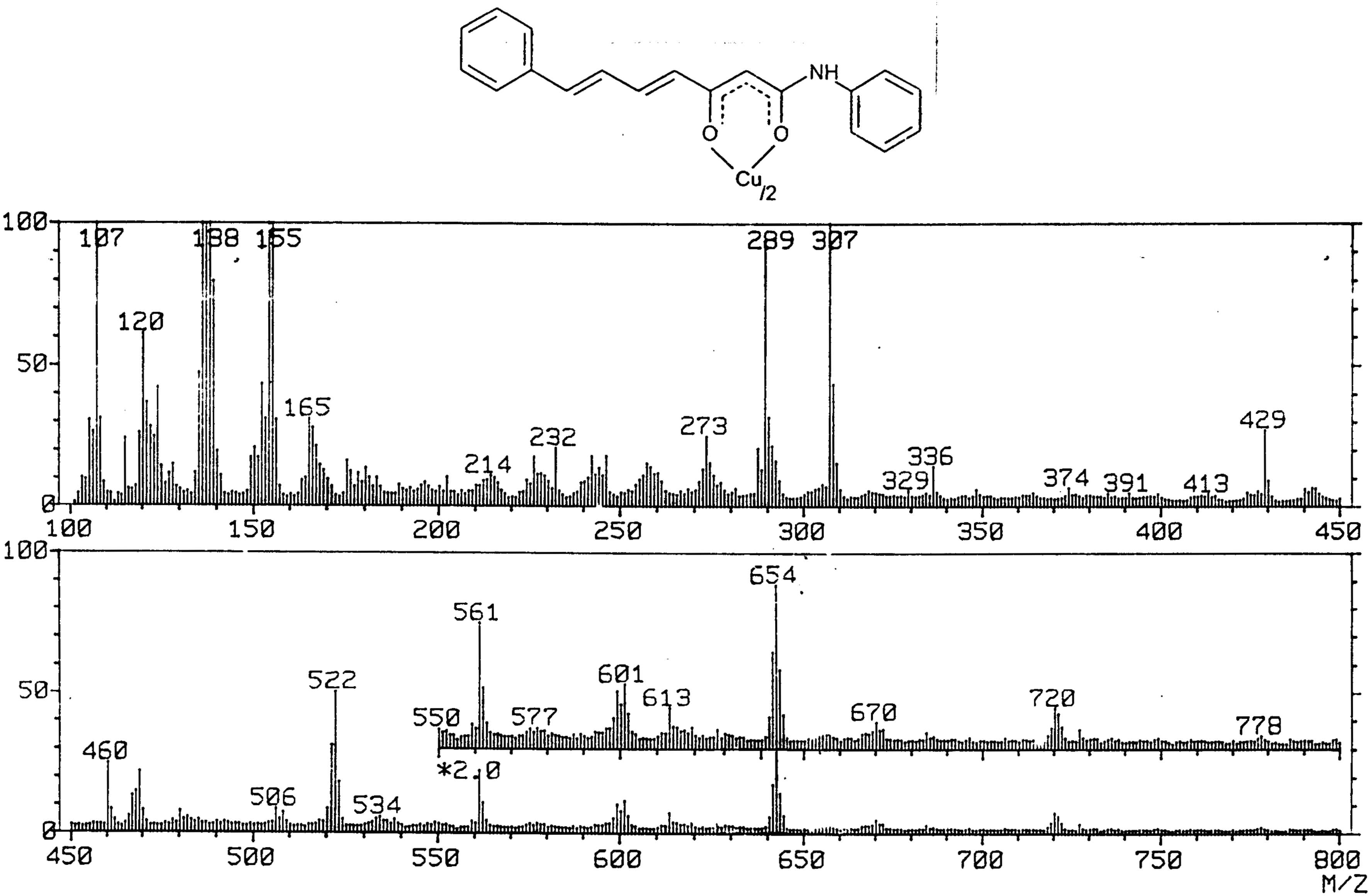


Fig.3.65.FAB Mass spectrum of Cu(II) complex of 15

solution was concentrated to half the volume. It was then cooled in ice and the precipitated complex was filtered, washed several times with water, then with ethanol and recrystallised from hot benzene. The crystels were dried in vacuum.

Fe(III) complex was prepared as follows. To a refluxing solution of the compound in methanol (0.003 mol, 20 mL) slowly added a solution of anhydrous $FeCl_3$ (0.001mol, 15mL) with vigorous stirring. The mixture was then refluxed for ~2h, cooled to room temperature and the precipitated complex was filtered, washed with methanol and then recrystallised from hot chloroform. The crystels were dried in vacuum.

Results and Discussion

Characterisation of the Schiff's base

The results of elemental analysis and molecular weight determination of the compound given in table 3.38 suggest that one equivalent of the unsaturated β-ketoanilide has condensed with n-butylamine to form the Schiff's base. The proposed structure **16** of the compound has been established from the UV, IR, NMR and mass spectral data. These data are briefly discussed below.

UV Spectra The UV spectra of the compound showed two broad absorption bands with λmax at 275 nm and 370 nm assignable to the $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ transition of the compound.

Table 3.38

Physical and analytical data of the Schiff's base (HL) and its metal chelates

Compounds	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)			
			C	H	N	M
HL	92	-	79.72 (79.77)	7.44 (7.51)	7.94 (8.09)	-
[FeL$_3$]	202	5.76	74.92 (75.96)	6.78 (6.88)	7.53 (7.71)	5.16 (5.05)
NiL$_2$]	196	-	72.72 (73.70)	6.54 (6.68)	7.42 (7.48)	7.68 (70.88)
[CuL$_2$]	154	1.77	72.39 (73.31)	6.54 (6.64)	7.48 (7.44)	8.33 (8.37)
[ZnL$_2$]	138	-	72.74 (73.11)	6.52 (6.62)	7.38 (7.42)	8.59 (8.61)
[CdL$_2$]	126	-	67.92 (68.83)	6.14 (6.23)	6.79 (6.98)	12.98 (13.97)

IR Spectra That the amide carbonyl has involved in the schiff's base formation is clearly indicated in the IR spectrum. Thus the band at ~1660 cm^{-1} due to amide carbonyl is absent in the spectrum and further no absorption band exist in the 1650-1800 cm^{-1} region. This clearly indicate that the compound does not contain not only amide carbonyl but also a free Ar-(CH=CH)$_2$-C=O function. However the spectrum of the compound in the region 1600-1650 cm^{-1} show two prominent bands. The C=N stretching of Schiff's base usually appear in the region 1640 cm^{-1}. Conjugation and hydrogen bonding have appreciable influence on the precise frequency of the band. Similarly enolisation of a highly conjugated carbonyl group and its engagement in hydrogen bonding show very low value for its stretching frequency. Considering all these factors together with the various probabilities of the condensation that can take place under the experimental condition employed, the two band observed at ~1620 $cm^{-1}$and 1640cm^{-1} can only be arised from the stretching of an enolised conjugated carbonyl that can engage in hydrogen bonding with an azomethine (C=N) group as in structure **16**. That strong intramolecular hydrogen bond as in structure **16** exist in the compound is clearly indicated from the presence of the broad band in the region 2800-3500 cm^{-1}. Thus the observed IR spectra of the compound unambiguously support the structure **16**. Further evidence for the proposed structure of the compound has obtained from the ^1H NMR spectra.

^{1}H NMR Spectra The ^1H NMR spectra of the ligand displayed two signals in the low field at 11.43 ppm and 9.5 ppm. These signals are easily assignable to intramolecularly hydrogen bonded enolic hydrogen and the anilide NH proton of structure **16**. Other signals observed in the spectra (Fig.) fully agree with the structure **16** of the schiff's base.

Mass Spectra The compound showed intense molecular ion peak at m/z 345 correspond to the molecular formula of the compound. That the compound is a schiff's base is clearly indicated from the prominent peaks appeared in the spectrum given in fig **3.66**.

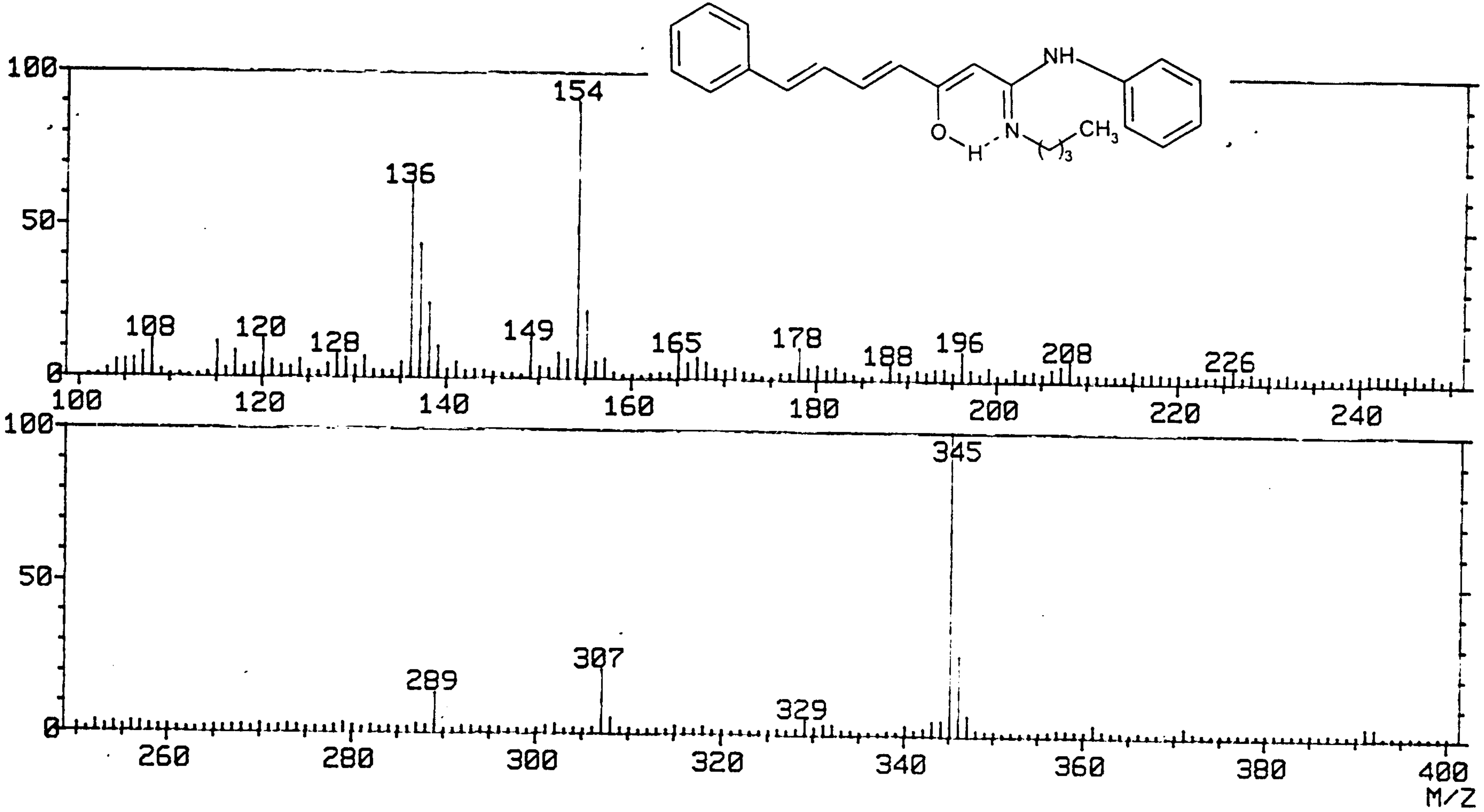
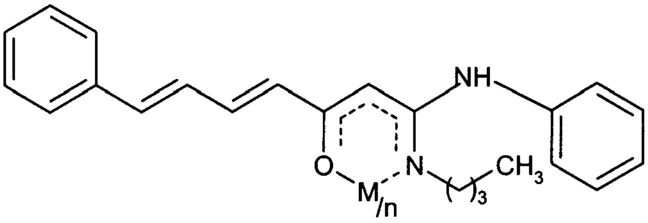


Fig. 3.66.FAB Mass spectrum of 16

Characterisation of the metal chelates

Analytical and physical data of the metal complexes are given in table 5.4. The observed elemental analysis data agreed well with their 1:2 metal-ligand stoichiometry for Ni(II), Cu(II), Zn(II) and Cd(II) and 1:3 for Fe(III) complex. Conductometric studies show that all the complexes behave as non-electrolytes in dmf (specific conductance <10 $\Omega^{-1}cm^{-1}$ in 10^{-3} M solution) and do not contain the anion of the metal salt used for the preparation. Magnetic moment measurements show that Ni(II), Zn(II) and Cd(II) complexes are diamagnetic while others show normal paramagnetic moment. The observed UV, IR, NMR and mass spectral data are in agreement with the structure **18** of the complexes.



18

UV Spectra The UV spectra of the complexes show close similarly with the ligands which indicate that no structural alteration of the ligand has occurred during complexation.

IR Spectra In the spectra of metal complexes both the bands in the region 1600-1650 cm^{-1} disappeared and no other band is observed in the region 1600-1800 cm^{-1}. Instead two prominent bands appeared at ~1595 cm^{-1} and ~1580 cm^{-1} due to metal-bonded C=O and C=N groups in addition to various alkenyl and aromatic C=C stretching frequencies that appeared in the range 1530-1585 cm^{-1} of the free ligand. The broad absorption of the ligand in the region 2700-3500 cm^{-1} cleared up in the spectra of metal complexes. However a medium intensity band at ~2900 cm^{-1} appeared due to NH stretching vibration. In accordance with this observation the new bands appeared at ~450 and ~530 cm^{-1} are due to M–O and M–N stretching frequencies. The characteristic IR bands and their probable assignments are given in table 3.39.

Table 3.39

Characteristic IR data (cm^{-1}) of the complexes of Schiff's base

Complexes					Probable assignments
Fe(III)	**Ni(II)**	**Cu(II)**	**Zn(II)**	**Cd(II)**	
1588	1591	1592	1591	1589	ν (C=N) chelated
1576	1582	1580	1576	1577	ν (C=O) chelated
1564	1564	1560	1558	1574	ν C=C alkenyl/ phenyl
1546	1548	1554	1546	1538	
1526	1528	1524	1525	1526	
2930	2970	3010	2846	2854	νN-H
446	450	436	427	430	ν M-O
530	528	532	531	527	ν M-N
970	972	971	970	972	ν CH=CH trans

^{1}H NMR Spectra In the ^{1}H NMR spectrum of the diamagnetic Ni(II) complex the low field enolic proton singlet of the free ligand disappeared and the NH proton signal slightly shifted to low field. The spectrum is reproduced in fig. The assignment of various signals given fully support the mode of coordination and the formulation of the complex.

Mass Spectra The FAB mass spectrum of the Cu(II) chelate of the compound shows the stepwise removal of the aryl and alkenyl groups. Molecular ion peak, fragments due to ML^+, L^+ and that of L^+ are also detected in the spectrum. A number of fragments containing copper are in agreement with the natural abundance of ^{63}Cu and ^{65}Cu isotopes are also present in the spectrum (fig.**3.67**).

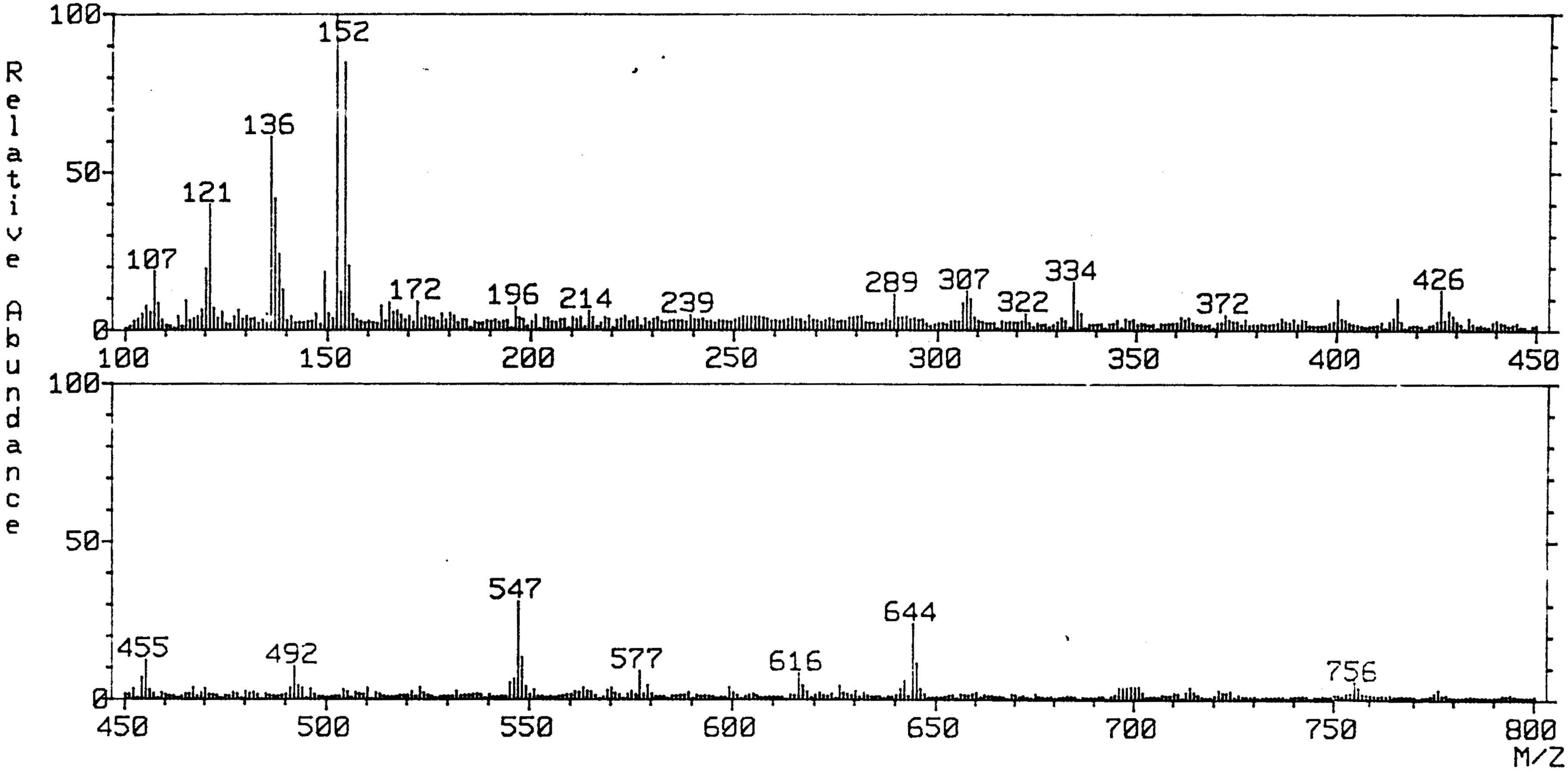


Fig.3.67 FAB Mass spectrum of Cu(II) complex of 16

CHAPTER 4

SYNTHESIS AND CHARACTERISATION OF HETEROARYL KETOANILIDES AND THEIR METAL COMPLEXES

Reaction of acetacetanilide with heteroaryl aldehydes in presence of boric oxide, tri(sec-butyl)borate and n-butylamine resulted in the formation of a new type of unsaturated β-ketoanilide. The heteroaryl aldehydes used were furan-2-carbaldehyde (furfural) and pyridine-2-carbaldehyde. Furfural yielded both the dicarbonyl and tricarbonyl compounds while pyridine-2-carbaldehyde formed only the tricarbonyl compound. The difference in the behaviour of the two aldehyde during the reaction can easily be explained. Since five membered rings are more strained than six membered rings the monocondensation product of furfural is unlikely to transform into the tricarbonyl compound. But in pyridine-2-carbaldehyde strong electron withdrawal of the nitrogen of the pyridine ring increase the nucleophilicity of amide carbonyl which can welcome easily another molecule of acetoacetanilide to form the tricarbonyl compound. Details on the synthesis, separation and purification of these unsaturated heteroaryl β-ketoanilides and their tricarbonyl compounds along with there typical metal complexes are presented in this part.

Experimental

Acetoacetanilide (1.77 g, 0.01 mol) and boric oxide (0.35 g, 0.005 mol) were mixed and made in to a paste with dry ethylacetate and stirred for ~1h at room temperature on a magnetic stirrer. To this a solution of heteroaryl aldehyde (0.01 mol) and tri(sec-butyl)borate (4.6 g, 0.02 mol) dissolved in dry ethylacetate was added and stirred for ~5h with the slow addition of n-butyl amine (0.5ml in 5ml dry ethylacetate) in drops and the reaction mixture was kept overnight. Hot dil. HCl (0.4M, 7.5 ml) was added and again stirred for lh. The mixture was extracted repeatedly with ethylacetate and the combined extracts were croperated to dryness on a water bath to get a pasty mass. To this 10 ml of 2M HCl was added and kept for ~24h. The solution was stirred well and the precipitate formed was filtered.

The presence of two well defined spots in tlc revealed the presence of two compounds in the case of the products obtained from furfural. But only one product was obtained with pyridine-2-carbaldehyde as revealed by tlc. The product were recrystallized from hot chloroform.

The mixture of compounds obtained from furfural were quantitatively separated by column chromatography as outlined below.

The crude product was dissolved in minimum quantity of dry ethylacetate and placed over a column (2x100 cm) densely packed with silicagel (mesh 60-120) and eluted with 3:2 v/v chloroform-acetone mixture at a uniform flow rate of 2 ml per min. As the elution proceeds, two bands were developed in the column, a pale yellow lower band and an orange red upper band. The lower region was collected as 10 mL aliquots in separate tubes and in each case the purtiy was established by tlc. The combined eluates on evoperation gave **19**, the pure unsaturated β-ketoanilide.

The elution was then continued using 1:1 v/v mixture of chloroform and acetone to recover the brick red band retained in the upper portion of the column. The eluates were collected in aliquots of 10 mL in separate tubes, checked by tlc and the combined extracts on removing the solvent in vaccum yielded the unsaturated diketoanilide **20**. All the compounds isolated were recrystallised from hot methanol to give spectroscopically pure material.

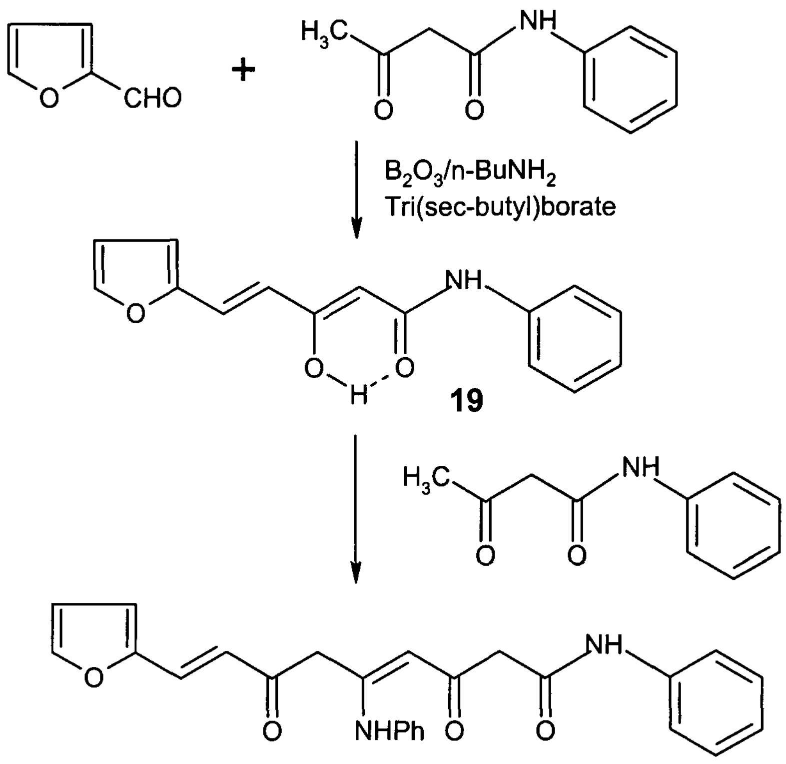
Both the mono and bis condensation products yielded complexes with various metal ions. This complexes were synthesised as detailed below.

Synthesis of metal chelates

Cu(II), Co(II), Ni(II), Zn(II) and Cd(II) chelates were synthesised from their metal acetates (0.001 mol in 25 mL 1:1v/v acetone-ethanol mixture by the addition of an ethanolic solution of the ligand (0.002 mol, 20 mL) followed by sodium acetate to maintain the pH around 6. The reaction mixture was refluxed for ~3h on a boiling water bath and then cooled to ~10^{0}C using an ice bath. The precipated product was separated, washed with methanol, dried in vacuum and recrytallised from hot benzene.

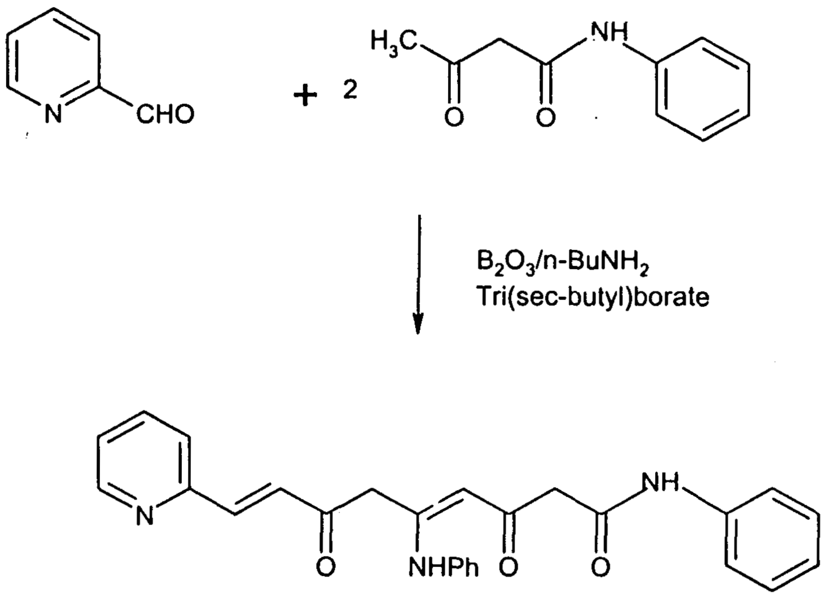
Results and Discussion

The observed C, H and N percentages together with mass spectra of the two condensation products clearly domenstrate that the compounds are of the type **19** and **20** and their formation can very well be recorded as in the reaction schemes 3.11-3.12. Further the UV, IR and NMR spectra of the two compounds fully support the structure. These analytical and spectral data of the two compounds are discussed below separately. Details on the characterisation of the metal complexes of the compounds are also discussed along with.



20 A

Scheme 3.11

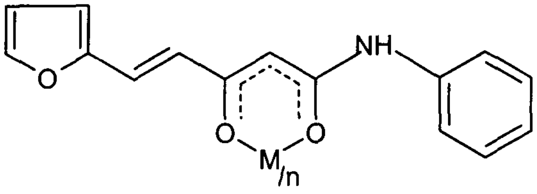


20 B

Scheme 3.12

Characterisation of the heteroaryl β-ketoanilides and its metal complexes

The elemental, analytical and other physical data of the compound and its stable complexes **21** are given in table 3.40. The data of the complex correspond to $[ML_2]$ stoichiometry expect for iron(III) which is $[ML_3]$. The detailed analysis of the various spectral data of the compound was carried out inorder to establish its tautomeric forms. The spectral data of the complexes were also considered with a view to establish the structure and nature of bonding.



21

n = 2;Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) n = 3; Fe(III)

UV Spectra The observed UV absorption maxima of the compound at 370 nm and 262 nm are assignable to various n→π* and π→π* transitions of the compound. These maxima showed slight bathochromic shifts in the spectra of the metal complexes indicating the involvement of the carbonyl groups in coordination.

Table 3.40

Physical and analytical data of the unsaturated β-ketoanilide (HL) and its metal chelates

Compounds	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)*			
			C	H	N	M
HL	88	-	69.76 (70.59)	5.04 (5.10)	5.36 (5.49)	-
[FeL$_3$]	176	5.77	65.84 (66.09)	4.36 (4.41)	5.01 (5.14)	6.66 (6.73)
[CoL$_2$]	148	4.7	62.50 (63.49)	4.13 (4.23)	4.91 (4.94)	10.14 (10.41)
[NiL$_2$]	138	-	63.04 (63.49)	4.12 (4.23)	4.64 (4.94)	10.08 (10.41)
[CuL$_2$]	194	1.76	62.88 (63.04)	4.10 (4.20)	4.88 (4.90)	10.94 (11.03)
[ZnL$_2$]	154	-	62.53 (62.83)	4.17 (4.19)	4.86 (4.89)	11.02 (11.34)
[CdL$_2$]	130	-	57.14 (58.06)	3.81 (3.87)	4.51 (4.52)	17.04 (18.06)

IR Spectra As expected of structure **19** the IR spectrum of the compound showed two intense bands in the region 1600-1800 cm^{-1} assignable to the amide and the conjugated carbonyl stretching. The NH of amide and the intramolecular hydrogen bonded enolic groups give broad bands in the region 2600-3800 cm^{-1}. Characteristic absorption of the anilide group are not altered.

In the spectra of the metal complexes the band due to hydrogen bonded dicarbonyl function of the ligand disappeared, but instead, a strong band assignable to the stretching of the metal coordinated dicarbonyl group appeared at ~1595 cm^{-1}. The broad band in the region 3400-3800 cm^{-1} cleared up in spectra of the complexes. The Co(II) complex showed band in this region indicating coordinated water molecules. The amide II→VI bands remain almost unaffected in spectra of the complexes. In agreement with the structure spectra of all compelxes show additional bands at ~425 cm^{-1} and at ~475 cm^{-1} assignable to $\nu_{M\text{-}O}$ vibrations. The important IR bands and their probable assignments are given in table 3.41.

Table 3.41

Characteristic ir data (cm^{-1}) of the complexes of unsaturated β-ketoanilide (HL)

Complexes						Probable assignments
[FeL$_3$]	**[CoL$_2$]**	**[NiL$_2$]**	**[CuL$_2$]**	**[ZnL$_2$]**	**[CdL$_2$]**	
1595	1596	1594	1593	1595	1594	ν (C=O) chelated
1515	1517	1518	1520	1519	1520	ν_{as}C-C –C
425 472	418 480	424 464	418 470	420 472	418 469	νM-O

^{1}H NMR Spectra The ^{1}H NMR spectra of the compound is characterised by a down field singlet at δ12.34 ppm and another singlet at δ6.04 ppm assignable to enol and methine protons of structure **19** respectively. In the ^{1}H NMR spectra of diamagnetic Ni(II) complex enolic proton singlet at δ12.34 ppm of the free ligand is disappeared supporting the replacement of enolic hydrogen during metal complexation. The position of the NH proton signal, alkenyl and aryl signals are only slightly affected.

Mass Spectra Mass spectrum of the compound showed intense molecular ion peak (Fig.**3.68**). Peaks corresponding to [C_6H_5NHCO]$^+$ and [P- C_6H_5NHCO]$^+$ are characteristic of the spectrum. The mass spectrum of Cu(II) chelate showed intense molecular ion peak in conformity with its [CuL$_2$] stoichiometry. Peaks due to [CuL]$^+$ and fragments of L$^+$ are also found in the spectra. Peaks at m/z corresponding to $[P - nAr]^+$ and $[P - n\ C_6H_5NHCO]^+$ where n = 1and 2 are also quite common. This spectrum is reproduced in fig. **3.69**. Thus all the analytical data fully support the structure **19** of the compound.

Characterisation of the heteroaryl diketoanilides and their metal complexes

Systematic names of the diketoanilides are given below.

Compounds	Aldehyde used for synthesis	Ar	Systematic name	Yield (%)
15a	Furfural	2-Furyl	1,5-Bis(N-phenylamino)-9-(2′-furyl) - 4,8-nonadien-1,3,7-trione	50
16a	Pyridine-2-carbaldehyde	2-Pyridyl	1,5-Bis(N-phenylamino)-9-(2′-pyridyl)-4,8-nonadien-1,3,7-trione	30

Analytical and physical data of the compounds and their metal complexes are given in table 3.42-3.43. The observed elemental analysis data of the complexes agreed well with their 1:1 metal ligand stoichiometry along with the anion of metal salt used for their preparation. However in the case of copper complexes of **16a**, the C, H, N and Cu percentages suggest the composition $[Cu_2L(OAc)_3]$. All metal complexes behaved as nonelectrolytes in dmf (specific conductance $<10\Omega^{-1}cm^{-1}$: 10^{-3} M solution). Cu(II) and Co(II) complexes showed normal magnetic moments while Ni(II), Zn(II) and Cd(II) complexes are diamagnetic. The observed UV, IR, NMR and mass spectral data of the Co(II), Ni(II), Zn(II) and Cd(II) complexes are in agreement with the structure **22** while the spectral data of the Cu(II) can be conveniently explained on the basis of structure **23**.

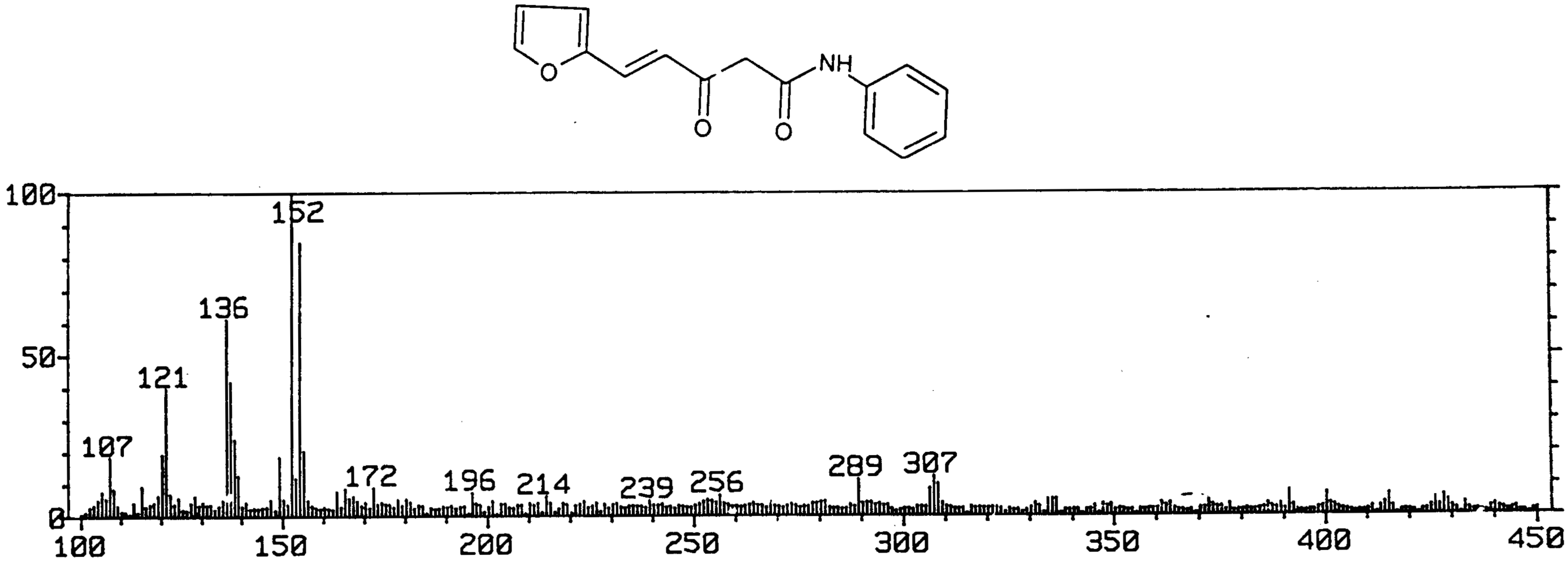


Fig. 3.68 FAB Mass spectrum of 19

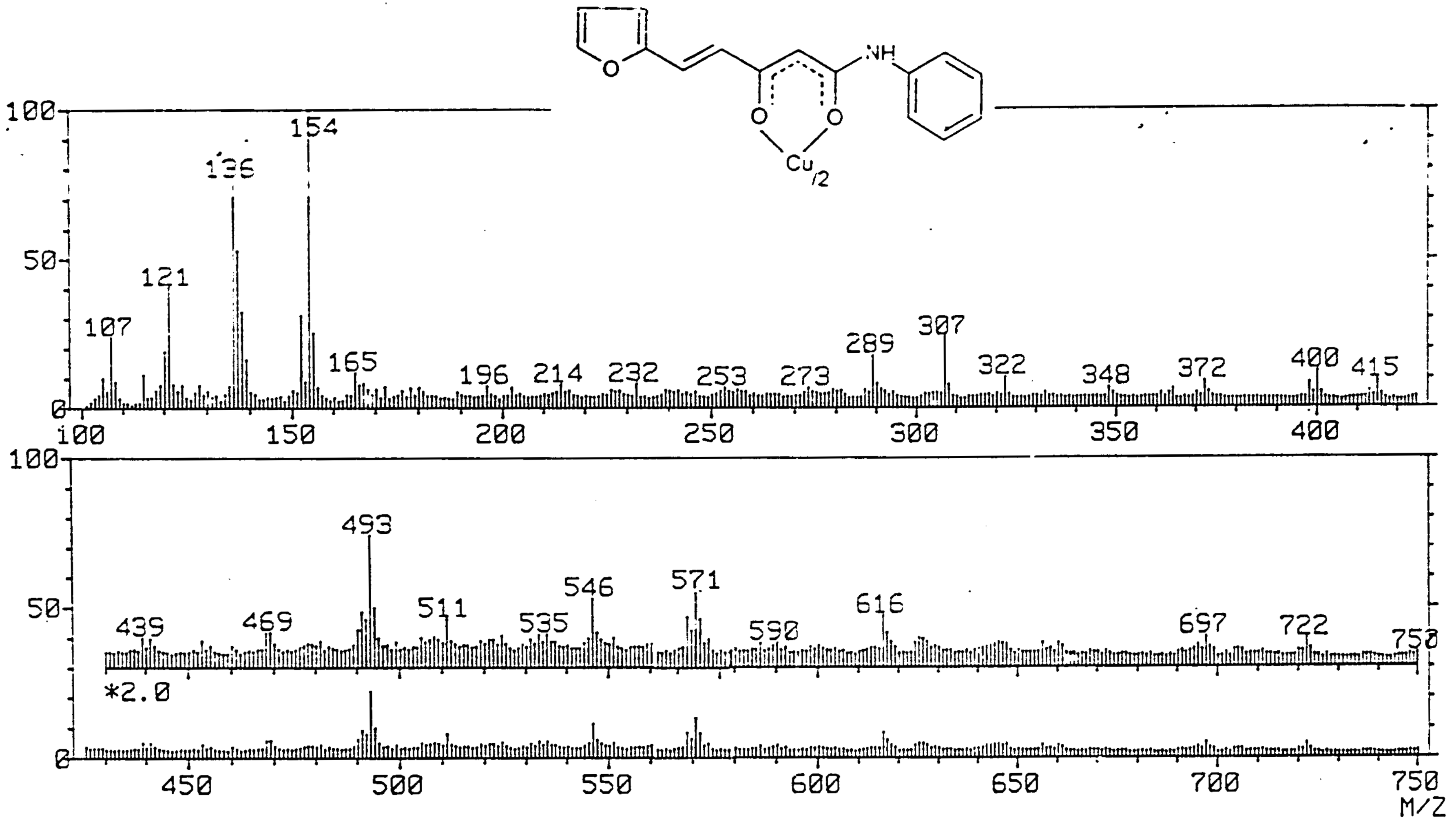
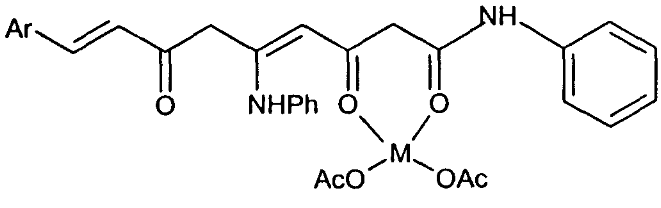
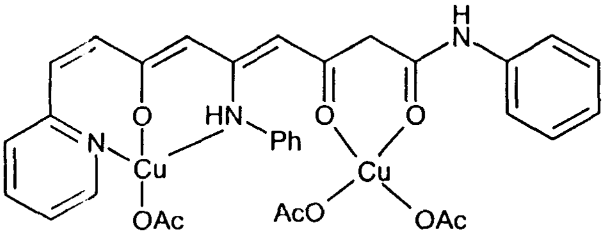


Fig. 3.69. FAB Mass spectrum of Cu(II) complex of **13b**



22



23

Table 3.42

Physical and analytical data of **15a** (HL) and its metal chelates

Compounds	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)* C	H	N	M
HL	56	-	71.34 (72.29)	5.14 (5.31)	6.74 (6.76)	59.01 (59.28)
$[Co(HL)(OAc)_2(H_2O)_2]$	174	4.77	58.11 (58.88)	4.73 (4.74)	4.72 (4.74)	8.99 (9.64)
$[Ni(HL)(OAc)_2]$	186	-	57.94 (58.88)	4.76 (4.74)	4.75 (4.74)	9.60 (9.64)
$[Cu(HL)(OAc)_2]$	194	1.76	58.14 (58.39)	4.65 (4.70)	4.69 (4.70)	9.84 (10.73)
$[Zn(HL)(OAc)_2]$	150	-	57.84 (58.89)	4.64 (4.69)	4.67 (4.69)	10.10 (10.89)
$[Cd(HL)(OAc)_2]$	134	-	53.34 (54.03)	4.28 (4.35)	4.30 (4.35)	16.74 (17.40)

Table 3.43

Physical and analytical data of the **16a** (HL) and its copper chelate

Compounds	MP °C	μ_{eff} BM	Elemental analysis (%) Found/(Calcd)*			
			C	H	N	Cu
HL	52	-	72.28 (73.41)	5.40 (5.41)	9.76 (9.88)	-
$[Cu_2L(OAc)_3]$	136	1.76	52.74 (52.82)	4.10 (4.13)	5.72 (5.78)	16.94 (17.50)

UV spectra The UV spectra of the compounds in 95% ethanol (10^{-3} M) show two bands at λ_{max} ~350 nm and ~250 nm assignable to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transition of the carbonyl group.The UV absorption bands of the complexes bear close resemblance with those of the ligands which indicate that no structural alteration of the ligand has occurred during complexation.

IR spectra Important IR bands and probable assignments given in table 3.44 support the structure **20 A** and **20 B** of the compounds. The amide I band the observed at 1661cm^{-1}. The broad bands observed at 3200-3500 cm^{-1} suggested the existence of the compounds in the intramolecularly hydrogen bonded form.

The amide I band and the α,β-unstaruated carbonyl band of the ligands are shifted to lower frequencies suggesting their involvement in complexation. The broad band observed in the range 3000-3500 cm^{-1} do not show any deviation from the ligand. The amide II and III bands in the ligands do not undergo any appreciable shifts and remain unaffected on complexation while the amide IV band at ~960 cm^{-1} is shifted to higher frequency in the complexes. These observation undoubtedly suggest that the complexation had taken place through both the carbonyl groups and not through the anilide nitrogens. The band at 1410 cm^{-1} in all the spectra indicate the coordination through acetate groups. The Co(II) complexes showed bands at ~3220 cm^{-1} indicating the presence of coordinated water molecules. The bands at ~460 cm^{-1} and ~425 cm^{-1} are due to ν_{M-O} vibrations. The important IR peaks of various complexes are listed in table 3.44.

The IR spectrum of the Cu(II) complex of **16a** showed significant difference from the spectra of other complexes. Thus the broad band observed of the ligand in the region 2800-3500 cm^{-1} due to the O-H...N hydrogen bonding almost disappeared and several band due to NH, CH, etc. vibrations appeared. This indicate that the enol proton has been replaced by the metal ion. Further the region 1600-1400 cm^{-1} of the complex also showed appreciable deviation from the ligand spectrum. Thus band due to the various C=C, C=N, etc. shifted to lower frequency presumably due to the coordination as in structure **23**.

Table 3.44

Characteristic IR data (cm^{-1}) of the unsaturated diketoanilides

Compounds		Probable assignments
15a	**16a**	
1718	1718	ν (C=O) amide
1660	1663	ν (C=O) α,β-unsaturated
1620	1620	ν (C=O) chelated
1600	1599	νC-C phenyl
1542	1545	νC-C alkenyl
1510	1510	ν amide II
1248	1239	ν amide III
978	977	ν CH=CH trans
692	691	ν amide V
645	644	ν amide IV
614	612	ν amide VI

^{1}H NMR spectra The ^{1}H NMR spectra of the ligands displayed a one proton singlet at ~δ6 ppm and another at ~δ12 ppm assignable to methine hydrogen and the intramolecularly hydrogen bonded enolic hydrogen respectively. The CH_2 singlet appeared at ~δ3.5 ppm. The NH singlet of anilide group at ~δ9 ppm is shifted considerably to down field due to strong external conjugation. Two NH singlet signals indicate the presence of two NH groups in different environments. The aromatic hydrogen lying in different environments make the δ7-8 ppm region of the spectrum highly complicated. The various proton signals are assembled in table 3.45.

That the enolic OH signal of the ligand at ~δ12 ppm is also present in the spectrum of diamagnetic Ni(II) complex indicate that the enol OH is not involved in complexation. The methylene proton signal is shifted slightly to down field indicating the coordination through the diacarbonyl groups. The noninvolvement of enolic OH and anilide NH in coordination is indicated by the position of their signals which remain unchanged in both ligand and the complexes. Acetate coordination is indicated by the position of their signals at ~δ2.5 ppm.

Table 3.45

Characteristic ^1H NMR Spectral data of the unsaturated diketoanilides

Compounds	Chemical shift δ ppm				
	OH	NH	CH=CH	Methine	CH_2
15a	12.140	8.202 8.341	8.098 7.631	6.857	3.587
16a	11.762	9.172 9.761	8.567 8.543	6.997	3.575

Mass Spectra Intense molecular ion peaks are observed in the mass spectra of the compounds. The fragments **A** and **B** undoubtedly explain the involvement of γ-methyl group of acetoacetanilide in the condensation with aromatic aldehyde. The peaks due to $[C_6H_5NHCO]^+$ and $[P - C_6H_5NHCO]^+$ are observed in the spectra of the compounds. The absence of $[P - 2C_6H_5NHCO]^+$ peak indicate that the two aminophenyl groups are lying in different environments. The fragment

A safely exclude the possibility of active methylene group in condensation. The formation of important peaks can be explained by fragmentation pattern given in scheme 3.7 of **Chaper 1** and the important peaks observed are shown in table 3.46. Spectra of the compounds are given in fig. **3.70-3.72**.

The FAB mass spectrum of the Cu(II) chelate is in total agreement with formulation of the complex. Thus molecular ion peak correspond to the stoichiometry appeared at m/z 727. The peaks due to the successive removal of acetate groups, CuL^+, L^+ and fragments of L^+ are characteristic feature of all the spectrum. The spectrum is reproduced in fig **3.73**. The spectra all the chelates contain large a number of fragments containing Cu.

Table 3.46

Important fragments observed in the FAB mass spectra

Compounds	P^+	A	B	C	D	E	G	H	P - D	P - E	P - F	P - E - F
15a	415	121	135	280	162	120	-	-	253	295	323	203
16a	425	131	145	280	162	120	103	-	263	305	333	213

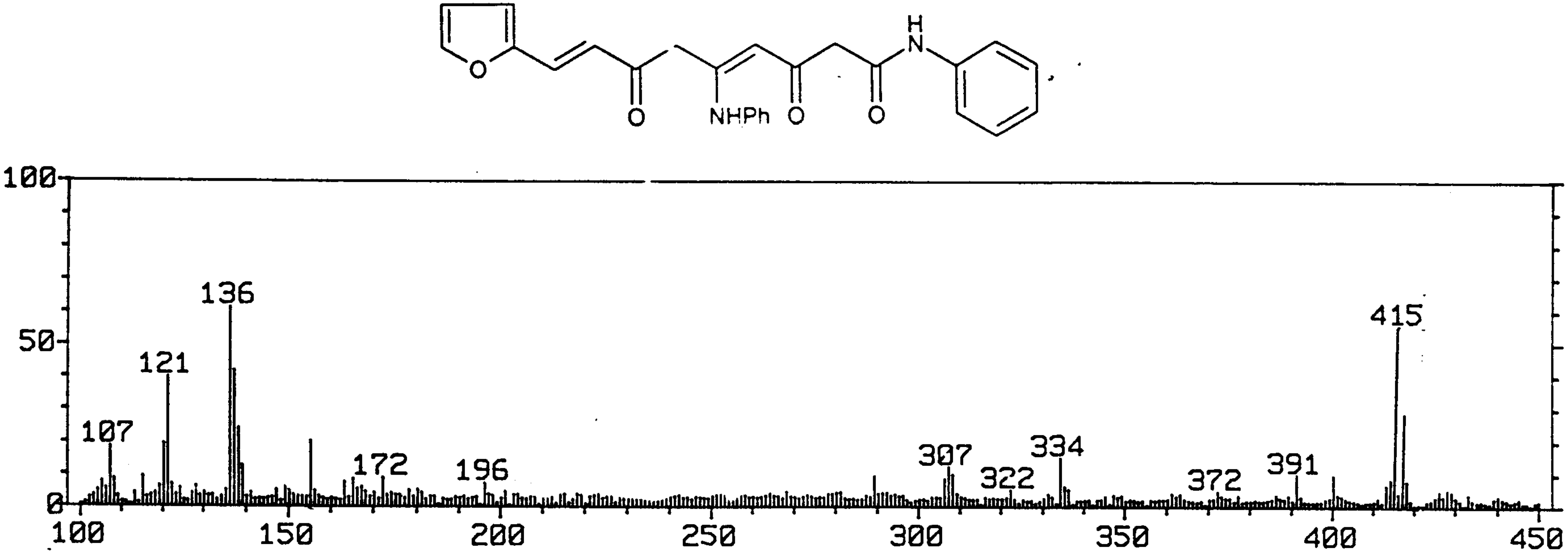


Fig. 3.70 FAB Mass spectrum of **15a**

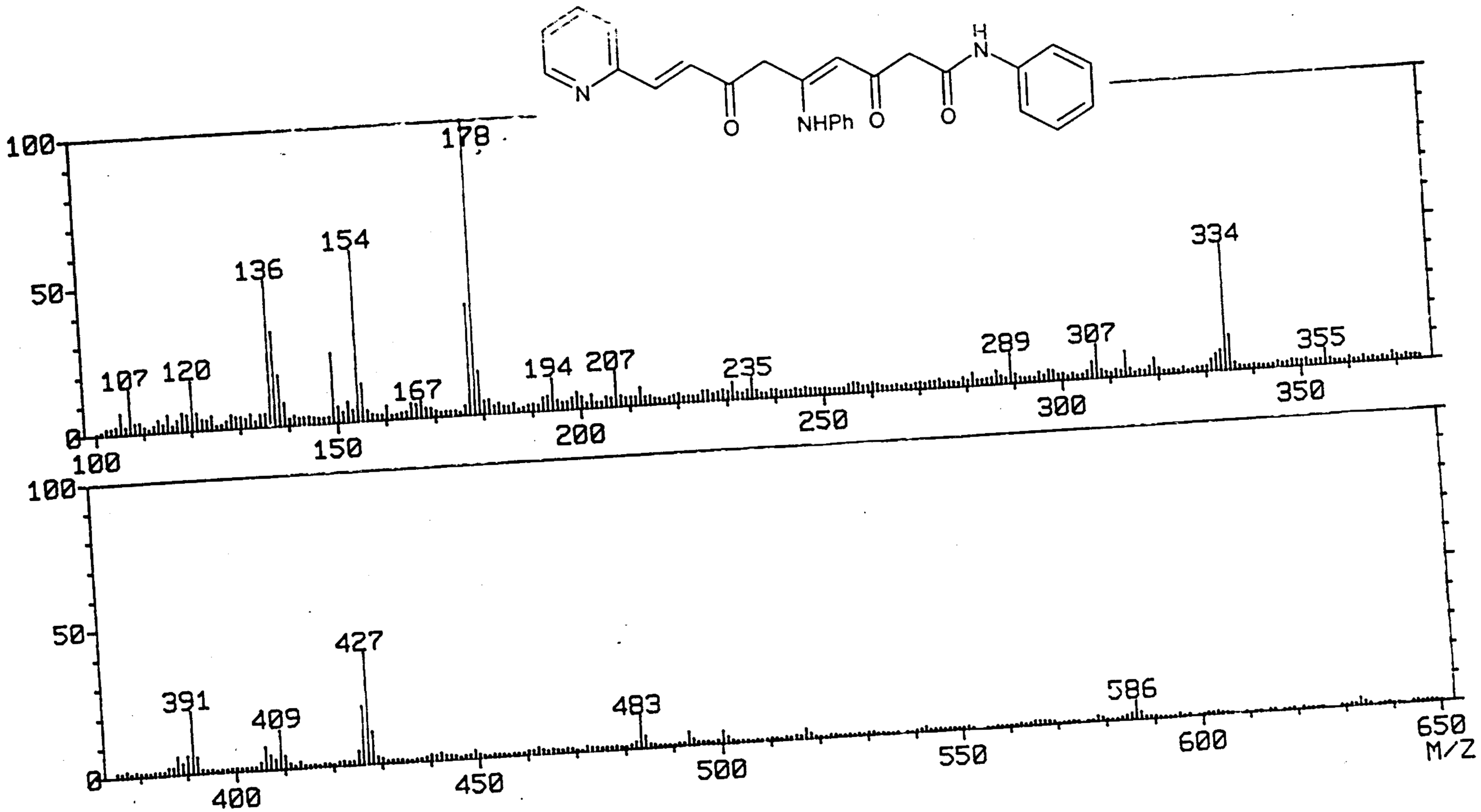


Fig. 3·71. FAB Mass spectrum of **16a**

159 C

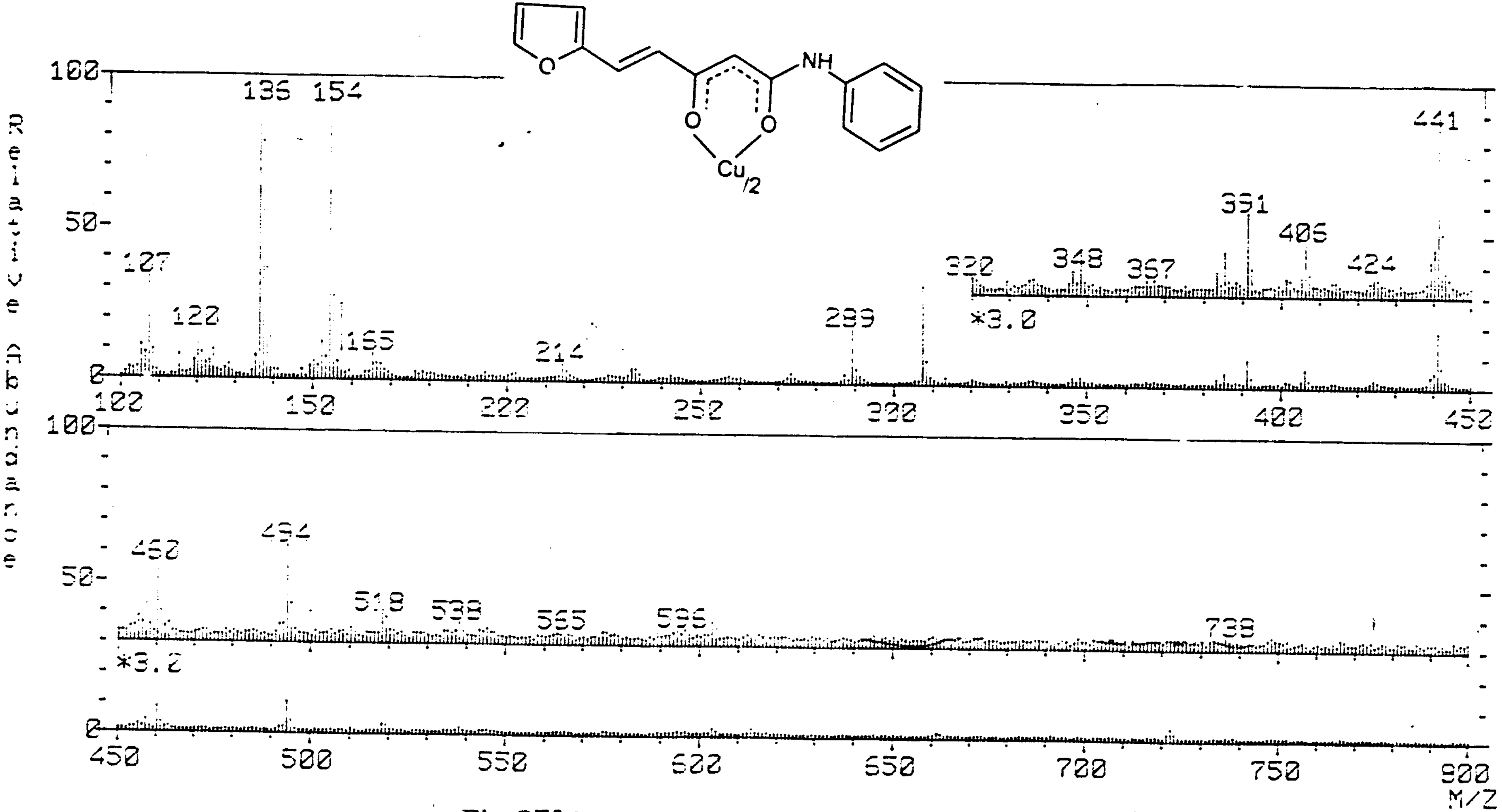


Fig. 3.72 FAB Mass spectrum of Cu(II) complex of 15a

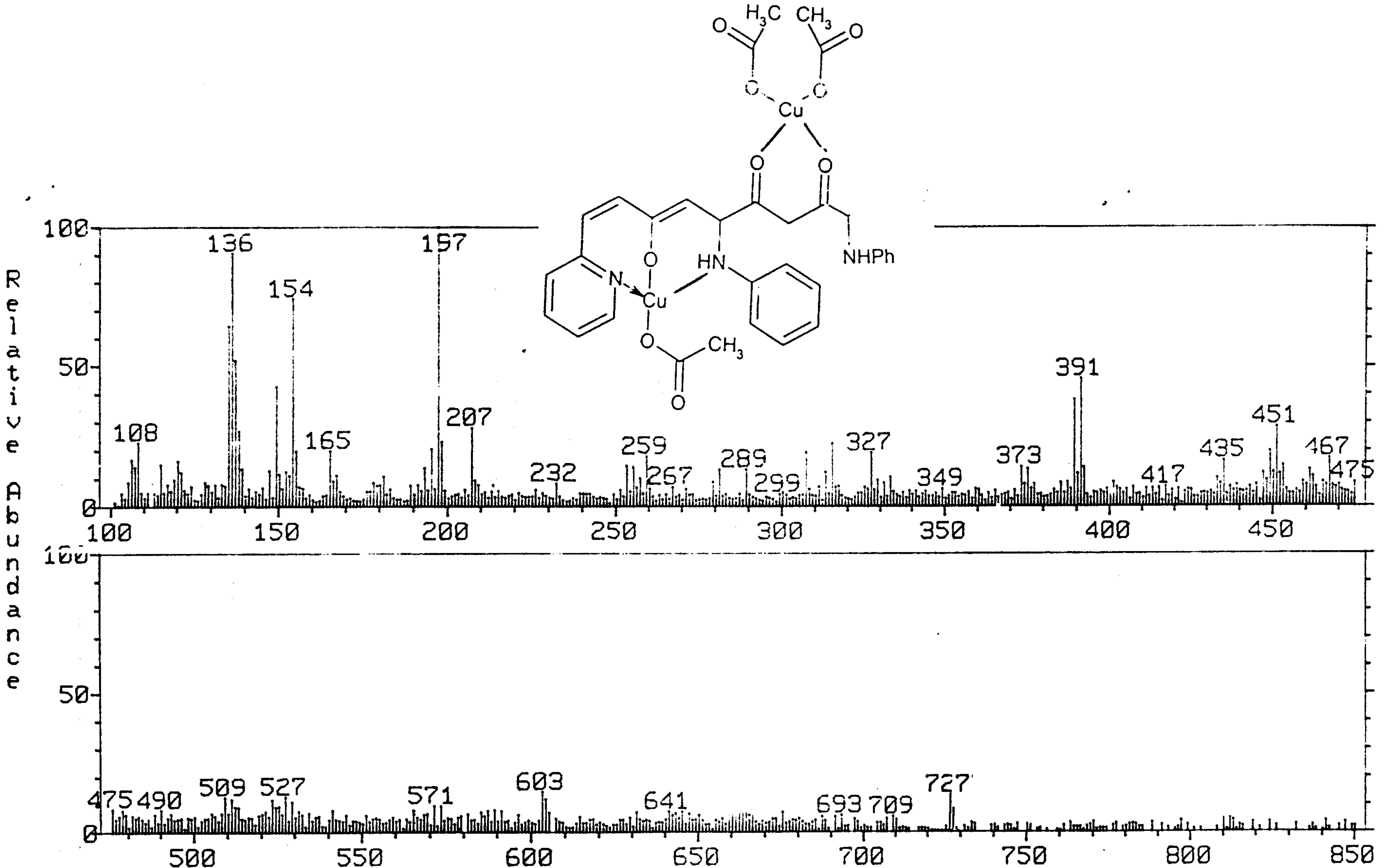


Fig. 3.73 FAB Mass spectrum of Cu(II) complex of **16a**

BIOLOGICAL STUDIES

Unsaturated β-dicarbonyl compounds such as curcuminoids are known to possess antifungal and antimicrobeal activities in addition to their numerous biological significance [245,259-261]. Since the unsaturated β-ketoanilides and diketoanilides considered in this investigation are structurally related to curcuminoids and also contain the heteroatom nitrogen, they can also exhibit antifungal and similar activities. Therefore, the antifungal activity of these unsaturated anilides with their typical metal complexes were also studied.

Three different fungal strains used[262] are given in table 3.47.

Table 3.47

Fungal strains used

Sl. No.	Fungal strain	Characteristics	Disease caused
1.	*Aspergillus niger*	Rapidly growing, white and filamentous, turning black	It causes infection of external ear
2.	*Aspergillus parasiticus*	Rapidly growing	It causes aspergillosis, which involve allergic manifestations, superficial infections etc.
3.	*Rhizopus oryzae*	Fast growing white cottony colony at 28°C	It is the most prevalent agent of mucormycosis.

Experimental

The tendency of a compound to block the microbial growth is one of the most important in clinical therapy and recently numerous automated systems are available for the determination of antimicrobial effectiveness. The disk diffusion technique is followed in the present investigation. The principle behind the assay technique is that when an antibiotic impregnated disk is placed on agar previously inoculated with the test organism the antibiotic diffuses rapidly outwards through the agar producing an antibiotic concentration gradient. A well-defined 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.

Nystatin was used as the standard for antifungal tests. Its aqueous suspension is stable for 10 min on heating to 100^0C and at pH 7. For the present investigation, a 1000 ppm solution in DMSO was used as the standard. Solutions of test compounds were prepared in DMSO and for sterilising all the media used were autoclaved at 121^0C for 20 minutes.

The medium for demonstration of antifungal tests were prepared by the following method. 20 g potato was cut in to small pieces and boiled with 100 ml distilled water. It is filtered through cotton and to the extract added 2 g glucose and 1.5 g agar and boiled. Its pH was adjusted to 5.7 using 10% HCl.

The medium was autoclaved for 20 min and when the temperature became 35-40^{0}C, the fungal spores were scrapped and added to the medium. Mixed well and carefully poured into clean autoclaved petridishes of 9 cm diameter and allowed to cool. Using an agar punch, wells (10 mm) were cut on these plates. In each well two drops of 1000 ppm solution of the compound were added. In each petriplate one well was used for DMSO and another one for the standard Nystatin. The wells were labelled properly and incubated at room temperature over night. The plates were prepared in duplicate. The antifungal activity was measured by noting the diameter of the inhibition zone around each well (mm).

Results and Discussion

Average diameter of the zone of inhibition observed for the compounds are given in table 3.48. These qualitative results reveal that both unsaturated ketoanilides show maximum activity against all tested organism than their metal complexes. The Cu(II) complexes are more active than others. Among the compounds those possessing –OH, -OR and Cl groups in the aromatic ring show maximum activity than the rest. Compounds possessing heterocyclic ring systems like furfural and pyridine-2-carbaldehyde are also found active. The activity of metal complexes are very low compared to ligands. Maximum activity is shown with *A. niger*, while practically, no activity is observed with *R. oryazea*.

Table 3.48

Results of studies on antimicrobial activity of unsaturated ketoanilides and their metal complexes

Unsaturated ketoanilides				Cu(II) complexes			Ni(II) complexes			Co(II) complexes		
Fungal strains				*Fungal strains*			*Fungal strains*			*Fungal strains*		
	1	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**
DMSO	8	8	8	8	8	8	8	8	8	8	8	8
Nystatin	10	10	10	10	10	10	10	10	10	10	10	10
2a	22	18	11	20	16	10	18	14	10	11	13	10
3a	23	16	14	21	15	10	20	15	10	12	13	11
4a	21	18	10	22	13	10	18	12	10	12	11	10
5a	25	15	10	21	14	11	20	14	11	11	11	11
6a	23	16	11	21	12	10	19	10	10	10	12	10
7a	24	18	12	18	17	11	14	17	11	12	13	10
8a	22	17	13	17	16	10	12	12	10	11	12	10
10a	22	17	13	18	12	10	11	10	10	13	10	11
11a	25	19	14	16	14	10	10	11	10	13	11	11
12a	23	15	10	17	12	11	14	10	11	12	12	10
15a	23	15	12	18	14	10	16	12	10	11	13	10
16a	18	18	13	16	13	12	10	13	12	12	12	11
2b	19	18	10	13	10	10	10	13	10	11	11	10
3b	18	18	11	14	12	10	10	12	10	12	10	10
4b	18	17	12	12	11	11	11	14	11	13	10	11
5b	19	19	11	12	10	10	12	10	10	10	12	10
7b	21	20	14	13	11	12	13	11	12	11	12	11
8b	20	16	13	10	10	11	10	11	11	12	10	11
9b	19	19	15	12	13	10	12	11	10	13	11	10

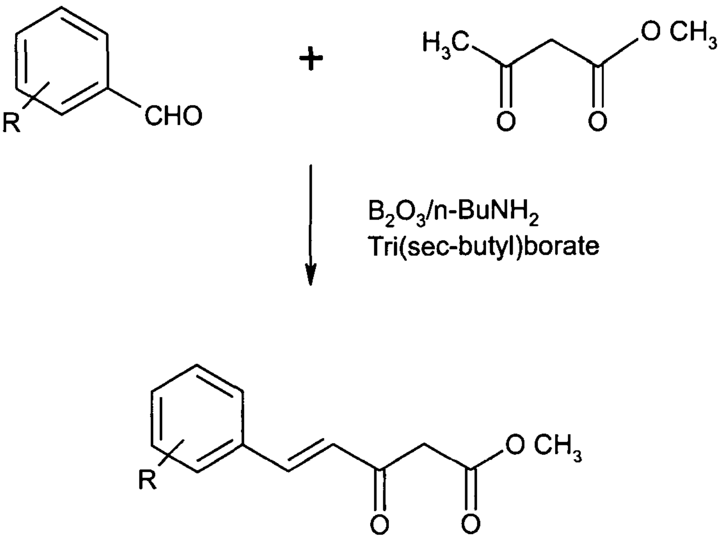
CHAPTER 5

SYNTHESIS AND CHARACTERISATION OF UNSATURATED β-KETOESTERS AND THEIR COPPER(II) COMPLEXES

Similar to β-ketoanilides, β-ketoesters having at least one acetyl group can undergo claisen condensation at the methyl group with aromatic aldehydes. The product will be a β-ketoester in which an olefinic group is directly attached to the dicarbonyl group. Such unsaturated β-ketoesters may also form stable metal complexes similar to β-ketoesters. This observation have been fully justified in the reaction between various aromatic aldehydes with methyl acetoacetate. Details on the synthesis and characterisation of these unsaturated β-ketoesters and their Cu(II) complexes are presented in this chapter.

Synthesis of the unsaturated β-ketoesters

The basic reaction is similar to that employed for the synthesis of unsaturated β-ketoanilides considered in the previous chapters. That is the dicarbonyl function (CO-CH_2–CO) is protected in the form of the boron complex in order to prevent the knoevenagel condensation so that only claisen condensation will take place at the CH_3 group of methyl acetoacetate to form structure **24** as in the reaction scheme 3.13. Unlike the β -ketoesters the reaction yielded only one product. The formation of tricarbonyl compounds discussed in the previous chapter were not found probably due to the decrease in electron density on the ester carbonyl (ester resonance). A typical procedure for the synthesis of the compounds are given below.



24
Scheme 3.13

Methyl acetoacetate (0.005 mol) and boric oxide (0.005 mol) were mixed thoroughly to get a pasty mass. The mixture was stirred for ~ 1 h at room temperature on a magnetic stirrer. To this mixture a solution of aromatic aldehyde (0.005 mol) and tri(sec–butyl)borate (0.02 mol) dissolved in dry ethyl acetate were added and the stirring was continued for ~6h with the slow addition of n-butylamine (0.5 mL in 5 mL dry ethyl acetate). The mixture is then kept aside overnight. HCl (0.01 M, 10 mL) was added and again stirred for ~1h, extracted repeatedly with ethyl acetate. The combined extracts were evaporated to dryness on a water bath. The pasty mass obtained was stirred with methanol (15 mL) for ~2h and was then kept in an ice bath with constant stirring for ~3h. The precipitated compound was filtered out 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.

Synthesis of Cu(II) complexes

To a refluxing solution of the compound (0.002 mol) in ethanol (20 mL), an ethanolic solution of Cu(II)acetate(0.001 mol, 15 mL) was added drop by drop with stirring. The pH of the solution was adjusted around 6 using sodium acetate and refluxing was continued for ~3h. The solution was concentrated to half the volume. The precipitated complex was separated by filteration, washed with water, then with methanol and recrystallised from hot ethanol.

Results and Discussion

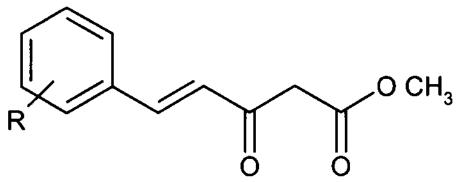
Characterisation of the unsaturated β-ketoesters

The compound obtained are yellow crystalline solids and are highly soluble in common organic solvents. The synthetic details of the compounds are given in table 3.49. The physical and analytical data of the compounds are given in table 3.50. 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.

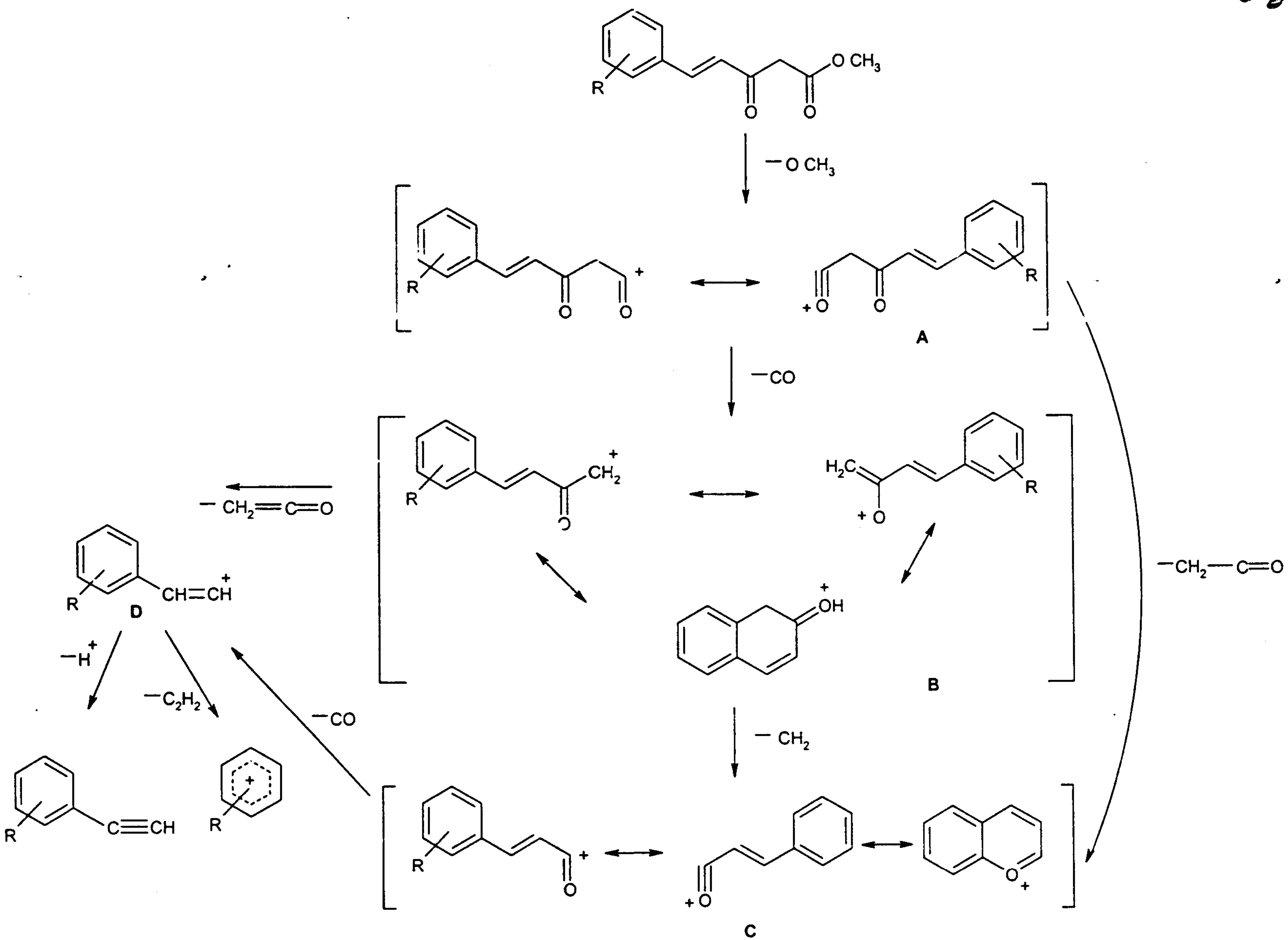
The mass spectra of the compounds **1d-3d** are in full agreement with the above observation. The spectra are reproduced in figures **3.74-3.76**. Prominent peak due to the molecular ion that correspond to the Claisen condensation product of structure **25** are present in all the spectra. The important peaks observed in the spectra of the compounds can also the explained by considering this structure. The probable fragmentation pattern of the compounds based on the various mass spectral peaks (table 3.51) are given in scheme 3.14.

Table 3.49

Synthetic details of unsaturated β-ketoesters



Compounds	Aldehyde used for synthesis	R	Systematic name	Yield (%)
1d	p-Hydroxybenzaldehyde	4-OH	Methyl-[5-(4′-hydroxy) phenyl]-3-oxo-4-pentenoate	50
2d	p-N,N-dimethyaminobenzaldehyde	4-N$(CH_3)_2$	Methyl-[5-(4′-N,N-dimethylamino)phenyl]-3-oxo-4-pentenoate	30
3d	Vanillin	3-OCH_3 4-OH	Methyl-[5-(3′-methoxy-4’-hydroxy)phenyl]-3-oxo-4-pentenoate	70


O CH3
R
O
−O CH3
+
A
−CO
CH2
H2C
+ O
OH
B
−CH2=C=O
−CH2—C=O
CH=CH+
D
−H+
−C2H2
−CO
C≡CH
− CH2
+ O
C
O+

Scheme 3.14

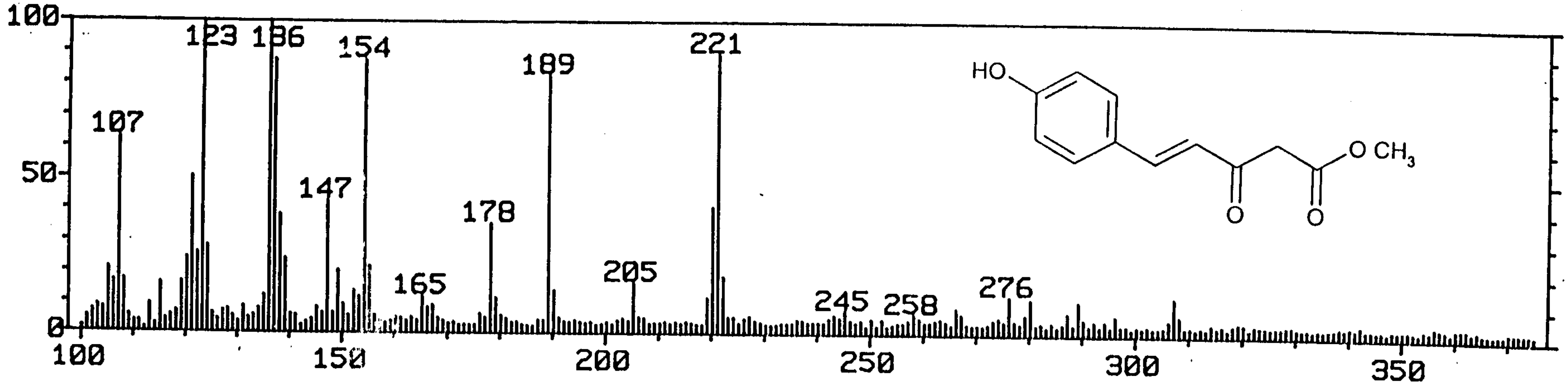


Fig 3-74 FAB Mass spectrum of **1d**

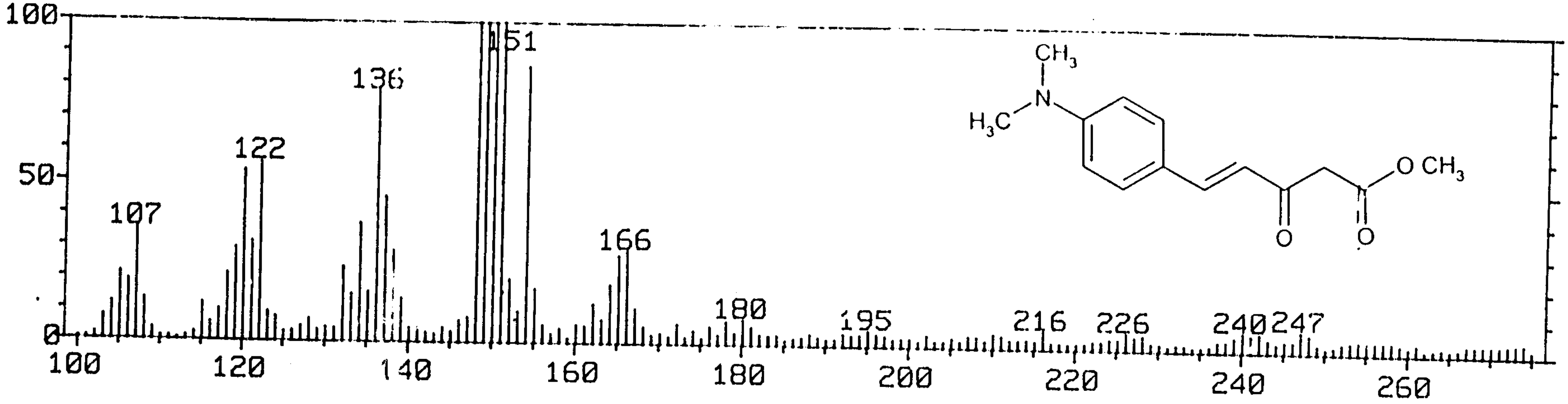


Fig 3.75.FAB Mass spectrum of **2d**

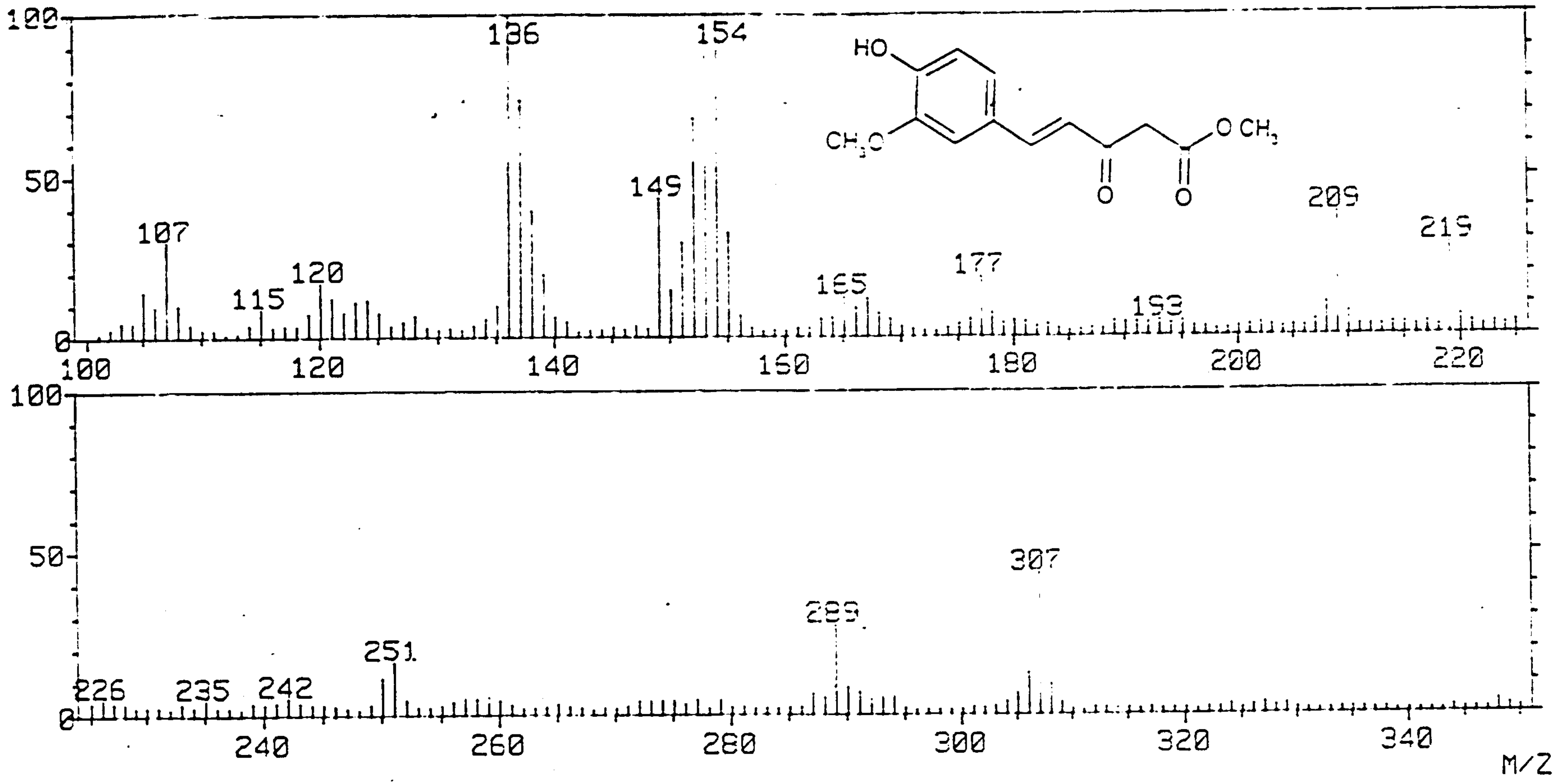


Fig. 3.76 FAB Mass spectrum of **3d**

Further evidence for the suggested structure of the compounds were obtained from their IR spectra. The spectra of compounds **1d-3d** in the region 1600-1800 cm^{-1} exhibit five strong bands assignable to specific functional groups. The spectra in the region are reproduced in fig. **3.77-3.79**.

The ester carbonyl of methylacetoacetate shows the carbonyl stretching band at ~1750 cm^{-1} and the acetyl carbonyl at ~1720 cm^{-1} as well as a band attributed to the β-hydroxy-α,β-unsaturated ester carbonyl of the enol form at ~1650 cm^{-1}. Thus the bands observed at ~ 1740 cm^{-1}, ~ 1670 cm^{-1} and ~1600 cm^{-1} are respectively due to 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 vibrations.

The broad peak in the region 2500-3500 cm^{-1} is due to the strong intramolecularly hydrogen bonded enol form of the compound.

Table 3.5C

Physical, analytical and UV spectral data of the unsaturated β-ketoesters

Compounds	MP (^{0}C)	Elemental analysis (%) C	H	Mol. Weight	λ_{max} (nm)	Log ε
		Found/ (calcd)				
1d	86	66.04 (65.45)	5.72 (5.45)	218 (220)	288 397	4.04 4.84
2d	57	68.45 (68.02)	6.72 (6.88)	246 (247)	260 386	4.07 4.89
3d	64	65.04 (65.40)	5.78 (5.60)	252 (250)	258 358	4.08 4.87

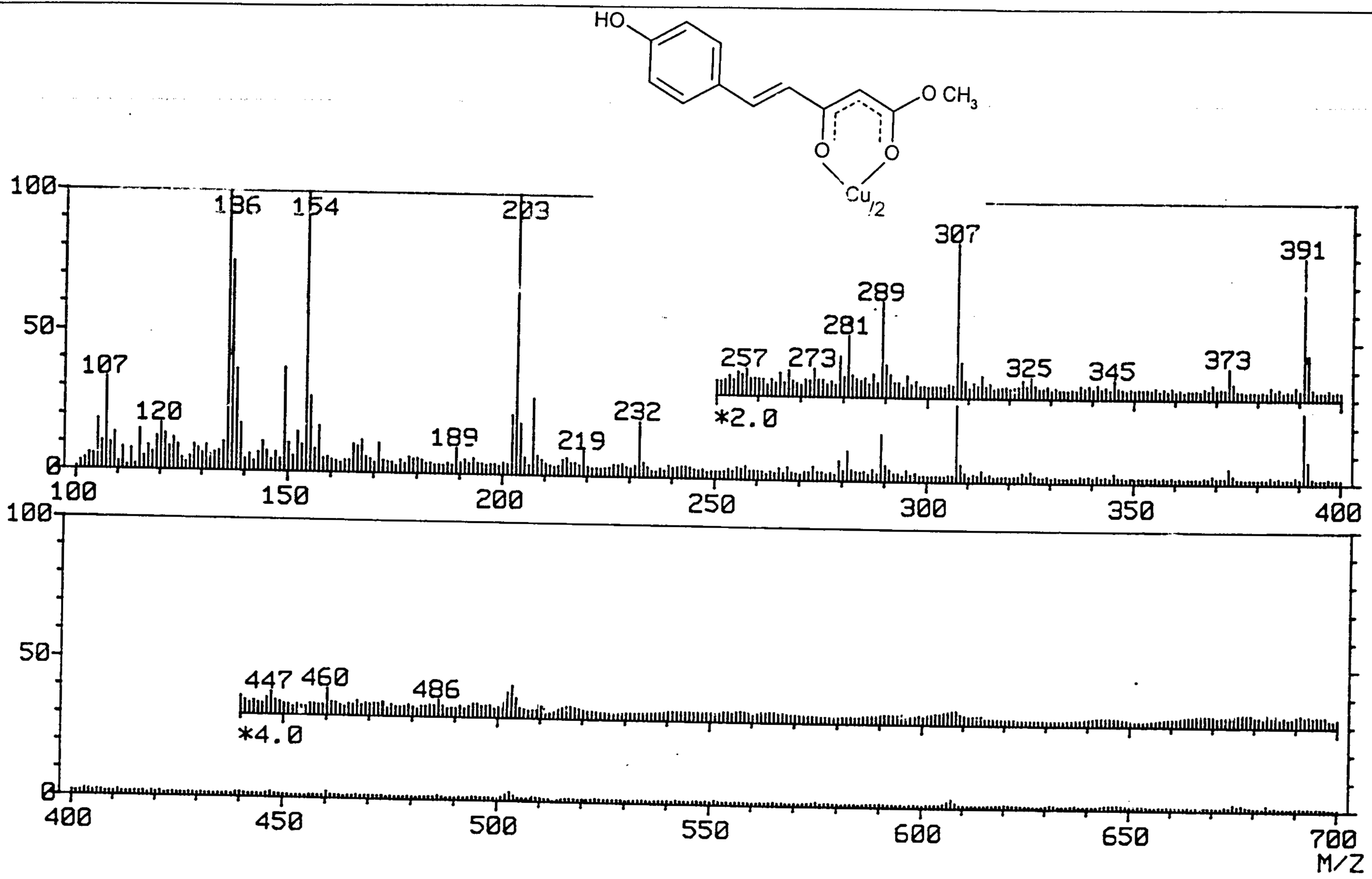


Fig. 3.80 FAB Mass spectrum of Cu(II) complex of **1d**

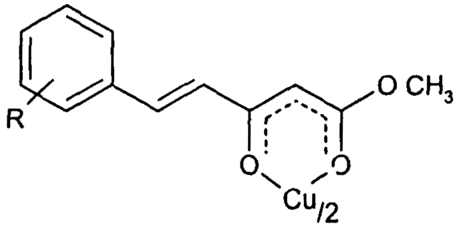
Table 3.51

Important fragments observed in the FAB mass spectra

Compounds	P^+	A	B	C	D
1d	220	189	161	147	119
2d	247	216	188	174	146
3d	250	219	191	177	149

Characterisation of Cu(II) chelates

Elemental analytical data of the Cu(II) complexes suggest [ML_2] stoichiometry. The IR and mass spectral data of the compounds suggest the structure **25** for the complexes.



25

The FAB mass spectra of the complexes reproduced in fig. 3.80-3.82 show intense molecular ion peaks. The peaks due to the successive elimination of anyl groups, -OCH_3 etc. are characteristic of the spectra.

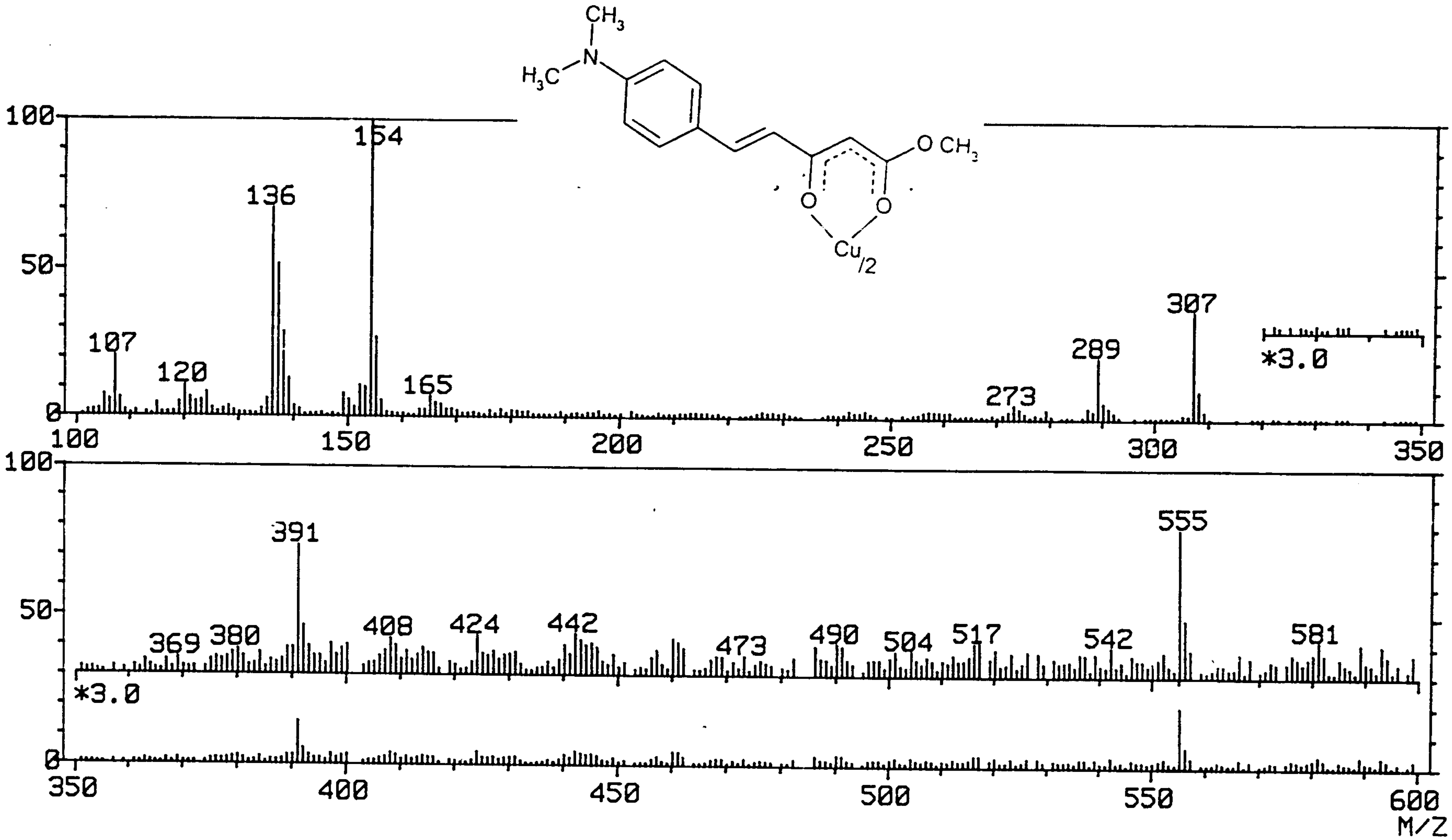


Fig.3.81 FAB Mass spectrum of Cu(II) complex of **2d**

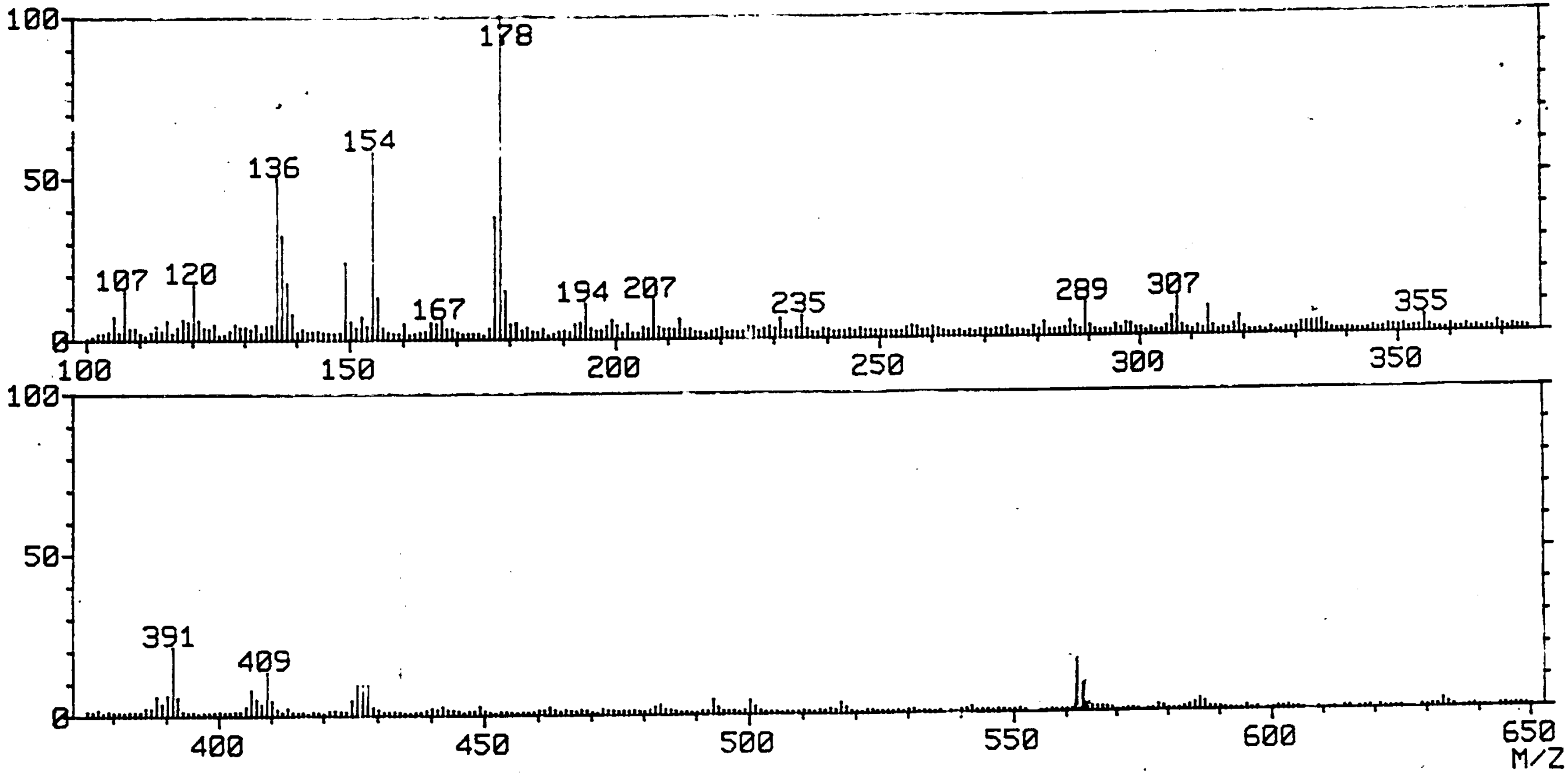


Fig. 3.82 FAB Mass spectrum of Cu(II) complex of 3d

In the IR spectra of the complexes of **1d–3d**, a new band appears at 1680 cm^{-1} assignable to the metal co-ordinated ester carbonyl. The band due to hydrogen bonded dicarbonyi function of the free lignands disappeared, but instead a strong band assignable to the stretching of the metal coordinated cimnamoyl carbonyl appeared at ~1595 cm^{-1} (fig **3.77-3.79**). Similarly the broad band due to the OH stretching of the free lignands in the region 3000-3800 cm^{-1} also cleared up in the spectra of all the complexes. However the spectra of the complexes **1d** show prominent band at 3400 cm^{-1} attributable to the stretching of the phenolic OH groups. In agreement with this structure spectra of all the complexes show additional bands at ~425 cm^{-1} and ~460 cm^{-1} assignable to $\nu_{M\text{-}0}$ vibration.

The measured magnetic moments of the complexes are in the range 1.70–1.80. This together with the observed visible absorption bands at ~15,000 cm^{-1}suggest square planar co-ordination around the Cu^{2+} ion.

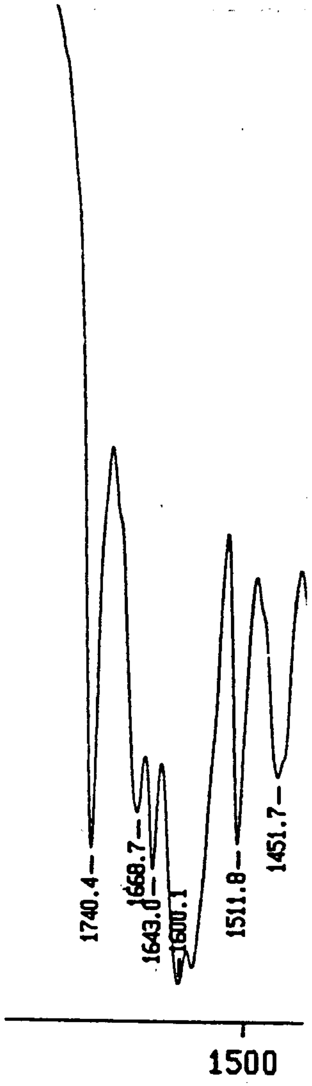


Fig 3·77.
IR spectra of 1d

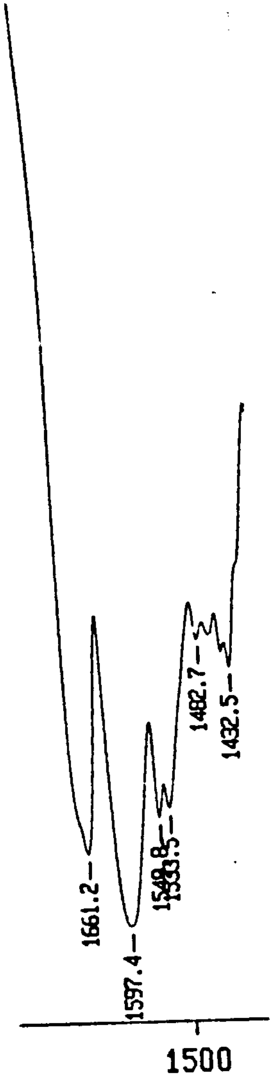


Fig 3·78
IR spectra of 2d

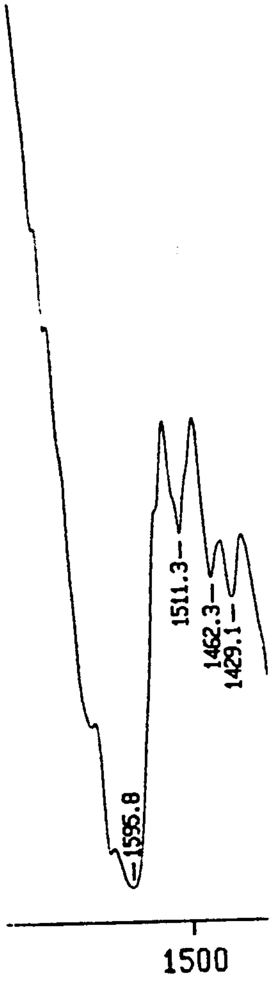


Fig 3·79
IR spectra of 3d

PART IV

REFERENCES

REFERENCES

1. C.F. Bell 'Principles and Applications of Metal Chelation'. Oxford University, London, (1978).
2. Gary Wulfsberg 'Inorganic Chemistry'. University Science Books, California, (2000).
3. J. C. Bailar. Jr.(ed). 'The Chemistry of the Co-ordination Compounds'. Reinhold, New York, (1956).
4. G. Wilkinson (ed. in Chief) 'Comprehensive Co-ordination Chemistry', 1st edn., Vol. **6**, Pergamon, New York, (1987).
5. R. G. Pearson, J. Am. Chem. Soc., **85**, 3553, (1963); J. Chem. Ed., **45**, 581, 643. (1968).
6. A. E. Martell and M. Calvin, 'Chemistry of Metal Chelate compounds', Prentice Hall, New York, (1952).
7. A. E. Martell (ed). 'Co-ordination Chemistry', ACS Monograph, 168, Van Norstrand – Reinhold, New York, (1971).
8. K. M. Smith (ed.), 'Porphyrins and Metalloporphyrins', Elsevier, Amsterdam, (1975).
9. G. A. Melson (ed.) 'Co-ordination Chemistry of Macrocyclic Compounds', Plenum, New York, (1979).
10. H. Irving and R. J. P. Williams, Nature, **162**, 746, (1948)
11. S. Ahrland, J. Chatt and N. R. Davis., Quart. Rev., **12**, 265.(1958)
12. J. P. Fackler Jr., Progr. Inorg. Chem., **7**, 361, (1966)

13. R. E. Sievers and J. J. Fortman., Co-ord. Chem. Rev., **6**, 331, (1971)

14. B. Bock, K. Flatau, H. Junge, M. Khur and H. Musso., Angew. Chem., Int. Edn. Engl., **10**, 225, (1971)

15. R. C. Mehrotra, R. Bohra and D. P. Gaud, 'Metal β-diketonates and Allied Derivatives', Academic, New York, (1978).

16. D. W. Thompson, 'Structure and Bonding', **9**, 27, (1970)

17. K. C. Joshi and V. N. Pathak, Co-ord. Chem. Rev., **22**, 37, (1977)

18. D. St., C. Black 'Comprehensive Co-ordination Chemistry', G. Wilkinson (ed. in Chief) Vol. **2**, Pergamon, New York, (1987).

19. S. Kawaguchi 'Variety in co-ordination modes of Ligands in Metal Complexes', Springer-Verlag, New York, (1988).

20. W. W. Mainke and R. E. Anderson, Anal. Chem., **24**, 708, (1952).

21. G.H. Morisson and H. Freiser 'Solvent Extraction in Analytical Chemistry'. John Wiley and Sons, New York, (1957).

22. E. H. Hufmann, G. N. Iddings, R. M. Osborane and G. V. Shalimoff, J. Am. Chem. Soc. **77**, 881, (1955).

23. Olof Samuelson 'Ion Exchange Separation in Analytical Chemistry'., John Wiley Son's, New York, (1963).

24. Friedrich Helfferich 'Ion exchange'., McGraw Hill Book Company, New York, (1963).

25. J. f. Steinbach and H. Frieser, Anal. Chem., **26**, 375, (1954).; A. Krishen and H. Frieser, Anal. Chem. **31**, 923, (1959).

26. C. Testa. Anal. Chim. Acta., **25**, 525, (1961).

27. R. A. Schneider, Anal. Chem., **34**, 522, (1962).

28. H. Onishi and C. V. Banks, Anal. Chem., **35**, 1887, (1963).

29. J. C. Brown, Adv. Chem. Ser., **93**. 162 (1977).

30. S.M. Khopkar and A.K. Day, Z. Anal. Chem., **171**, 241, (1959).

31. P. M. May, P. W. Linder, and D. R. Williams, J. Chem. Soc., Dalton Trans, 588, (1977).

32. M. N. Highes, 'Co-ordination Compounds in Biology' in Comprehensive Co-ordination Chemistry, Vol. **6**, G. Wilkinson (ed. in Chief). Pergman, New York (1987); H. F. Bienfact and F. Vander Mark in 'Metals and Micronutrients: Uptake and Utilisation by Plants', D. A. Robb and W. S. Pier point (eds.). Academic, London, (1983).; B. Lonnerdal, A. G. Stanislowski and L. S. Hurley, J. Inorg. Biochem., **12**, 71, (1980).

33. R. W. Hay and D. R. Williams, 'Specialist Periodical Reports: Amino acids, Peptides and Proteins'. The Chemical Society, London, (1982).

34. S. J. Angyal, Chem. Soc. Rev., **9**, 415. (1980).

35. E. L. Giroux and R. I. Henkin., Biochim., Biophys. Acta., **273**, 64, (1972).

36. M. W. Dennis, S. Stojan and B. Sarkar. Co-ord. Chem. Rev., **122**, 171, (1993).

37. S. K. Dhar (ed,) 'Metal Ions in Biological Systems'., Plenum, New York, (1973).

38. P. M. Harrison and R. J. Hoare., 'Metals in Biochemistry'., Chapman and hall, New York, (1980).

39. D. A. Phipps. 'Metals and Metabolism'., Oxford University, Oxford, (1976).

40. E. J. Underwood. 'Trace Elements in Human and Animal Nutrition', Academic, New York, (1971).

41. A. S. Brill, 'Transititon Metals in Biochemistry', Springer–Verlag, Berlin, (1977).

42. J. Emsely, 'Structure and Bonding', **57**, 147, (1984)

43. J. D. Park, H. A. Brown and J. R. Lachen. J. Am. Chem. Soc., **75**, 4573, (1953).

44. J. L. Burdett and M. T. Rogers., J. Am. Chem. Soc., **86**, 2105, (1964).

45. H. Koshimura, J. Saito and T. Okubo., Bull. Chem. Soc. Japan., **46**, 632, (1923).

46. E. Uhlemann and W. W. Suchan., Z. Anorg. Allg. Chem., **41**, 342, (1966).

47. G. Klose, P. H. Thomas, E. Uhlemann and J. Marki., Tetrahedron, **22**, 2695, (1966).

48. Z. Zuttante., J. Chem. Edn. **22**, 230, (1945).

49. A. E. Martell and M. Calvin "Chemistry of Metal Chelate Compounds', Prentice Hall Inc., Englewood Cliffs, New Jersey, **76**, 237, (1962).

50. L. Zahover and K. W. F. Kohlrausch, Ber., **738**, 1304 (1940); C. A., **35**, 2860, (1941).

51. G. W. Everett. Jr. and R. H. Holm, J. Am. Chem. Soc., **87**, 2117, (1965).

52. R. P. Barnes and A. K. Braden., J. Am. Chem. Soc., **65**, 1070 (1945).

53. P. Venugopalan, Ph. D. Thesis, Department of Chemistry, Calicut University, (1997).

54. A. Kettrup and M. Crote, Z. Anal. Chem. **269**, 118, (1974).

55. A. Kettrup and M. Crote., Monatsch. Chem., **104**, 1333, (1973).

56. R. C. Mehrotra., J. Indian Chem. Soc., **55**, 1, (1978).

57. D. Gardenic and B. Korpar-Colig., Proc. Chem. Soc., (London) 308, (1963).

58. P. W. N. M. Van Leewen., Recl. Trav. Chem., Pays Bas, **87**, 396, (1968).

59. Y. Nakamura and S. Kawaguchi., Chem. Commu., 716 (1968).

60. S. Koda, S. Oei, H. Kuroya, K. Isobe, Y, Nakamura and S. Kawaguchi, Chem. Commun. 1321, (1971).

61. A. Werner, Ber., **34**, 2584, (1901).

62. G. T. Morgan and H. W. Moss., Proc. Chem. Soc., **29**, 471, (1914).

63. G. T. Morgan and H. W. Moss., J. Chem. Soc., **105**, 189, (1914).

64. N.V. Sidgwick and F. M. Brewer., J. Chem. Soc., **127**, 237, (1925).

65. N. Thankarajan and D. N. Sen., Indian J. Chem., **6**, 278, (1968).

66. G. T. Behnke and K. Nakamoto., Inorg. Chem., **6**, 440, (1967)

67. Y. Nakamura and K. Nakamoto., Inorg. Chem., **14**, 63, (1975)

68. G. T.Morgan, H. D. K. Drew., J. Chem. Soc., **117**, 1456, (1920).

69. N.Yanase, Y. Nakamura, S.Kawaguchi., Inorg. Chem., **17**, 2874, (1978).; Z. Kanda, Y.Nakamura, S. Kawaguschi., Inorg. Chem., **17**, 910, (1978).; J. Lewis and C. Oldham. J. Chem. Soc. (**A**), 1456, (1966).

70. N. Yanase, Y. Nakamura and S. Kawaguchi., Inorg. Chem., **19**, 1575, (1980); S. Okeya, Y. Nakamura, T. Hinomoto and S. Kawaguchi., Bull. Chem. Soc. Japan, , **55**, 477, (1982).

71. A. Allen, J.Lewis, R. F.Long, C.Oldham, Nature (London) **202**, 589, (1964).

72. D. Gibson, J. Lewis, C. Oldham., J. Chem. Soc. (A), 1456 (1966).

73. N. Yanase, Y. Nakamura and S. Kawaguchi., Inorg. Chem., **19**, 1575, (1980)

74. A. Allen, J. Lewis, R. F.Long, C. Oldham, Nature (London), **202**, 589, (1964).; D. Gibson, J. Lewis, C. Oldham., J. Chem. Soc. (A) 72, (1967).

75. F. J. Welcher., "Organic Analytical Reagents", Vol. **I**, D. Van. Nostrand Company Inc., New York, 391, (1948)

76. A. T. Filipenko and L. J. Sarranskil, Russ. J. Inorg. Chem., **10**, 235 (1965).

77. F. A. Cotton and R. C. Elder., Inorg. Chem., **4**, 1145, (1965).; J. N. Collie and A. A. B. Reilley, J. Chem. Soc. **121**, 1984, (1922).

78. F. Sagara. H. Kobayashi and K. Ueno, Chem. Soc. Japan, **45**, 900, (1972)..

79. M. L. Miles, T. M. Harris and C. R. Hauser. J. Am. Chem. Soc. **85**, 3884, (1963).; F. Sagra, H. Kobayashi, K. Ueno., Bull. Chem. Soc. Japan., **45**, 794, (1972).

80. C. W. Dudley., T. N. Huckerby, C. oldham., J. Chem. Soc. **A**. 2605, (1970).

81. M. D. Glick., Inorg. Chem., **12**,1297,(1973); R. L. Lindvedt, L.L. Borer, D. P. Murtha, J. M. Kusaj, M. D. Glick., Inorg. Chem., **13**,18, (1974).

82. L. L Borer, W. Vanderbout., Inorg. Chem., **18**, 526, (1979).

83. M. D. Glick, R. L. Lintvedt., Prog. In. Chem., **21**, 223, (1976).; U. Casellato, P. A. Vigato., Co-ord. Chem. Rev., **23**, 31, (1977).

84. Ardrelczyk, R. L. Lintvedt., J. Am. Chem. Soc. **94**, 8633, (1972).

85. D. E. Fenton, C. M. Regan., U. Castellato, P. A. Vigato, M. Vidali., Inorg. Chim. Acta., **83**, 23, (1984).; D. E. Fenton, J. R. Tate, U. Castellato, S. Tambrini, P. A. Vigato, M. Vidali., **83**, 23, (1984).

86. T. Yano, T. Ushiyima, M. Sasaki, H. Kobayashi and K. Ueno., Bull. Chem. Soc., Japan., **45**, 2452, (1972).

87. C.C. Hinckley, J. Am. Chem. Soc,. **91**, 5160, (1969)

88. J.K.M. Sanders and D.H. Williams, Chem. Commun., 422, (1970)

89. D.S. Dyer, J.A. Cunningham, J.J. Brooks, R.E. Sievers and R.E. Rondean 'Nuclear Magnetic Resonance Shift Reagents' Academic Press, New York (1973).

90. B.C. Mayo, Chem. Soc. Rev. **2**, 49, (1973).

91. R. F. Sievers *et al* 'Co-ord. Chem. Rev. **128**, 285, (1963).

92. O.A. Gansow, A.R. Bruke and G.N. LaMar J. Chem. Soc. Chem. Commun., 456, (1972).

93. K. Tori, T. Tsushima, Y. Tamura, H. Shigemoto, T. Tsuji, H. Ishitobi and H. Tanida, Tetrahedron Lett., 3307, (1975)

94. F.A. Cotton, L.J. Kruczynski, B.L. Shapiro and L.F. Johnson J.Am. Chem. Soc., **94**, 6191, (1972).

95. S.J. Weissman. J. Chem. Phys. **10**, 214, (1942).

96. G.A. Crosby, R.E. Whan and R.M. Alire J. Chem. Phys., **34**, 743, (1961).

97. M. Lederer, Nature, **176**, 462, (1955).; R.W. Moshier and R.E. Sievers, 'Gas Chromatography of Metal Chelates', Pergamon Press, Oxford, (1965).

98. T. Shigematsu, M. Matsui and K. Utsunomiy Bull. Chem. Soc. Japan. **41**, 763, (1968).; C.A. Burgett and J.S. Fritz, Anal. Chem. **44**, 972, (1738).

99. H. Morisson and H. Freiser 'Solvent Extraction in Analytical Chemistry'. John Wiley and Sons, New York, (1957).; T. Shigematsu, M. Tabushi and M. Matsui, Bull. Chem. Soc. Japan, **37**, 1333, (1964).

100. J. Stary 'The Solvent Extraction in Metal Chelates' Pergamon Press, New York, (1964).; T.R. Sweet and H.W. Parlett Anal. Chem. **40**, 1885, (1968).

101. T. Masuda, H. Matsumura, Y. Oyama, Y. Takeda, A. Jitoe, K. Kida and K. Hidaka J. Nat. Prod , **61**, 609, (1998); T. Masuda and A. Jitoe J. Agric. Food Chem., **42**, 1850, (1994).

102.T. Osawa and M. Namiki J. Agric. Food Chem. **33(5)**, 777, (1985).

103.C.T. Ho, T.Osawa, M.T. Haung and Robert T. Rosen 'Food Phyto chemicals for cancer prevention II' ACS Symposium series 547, Washington DC, (1994).; M.T. Huang, T. Lysz, T. Ferraro, T.F.Abid, J.D. Laskin and A.H. Conney, Cancer Res., **51**, 813, (1991).

104.P. Venugopalan and K. Krishnankutty, J. Indian Chem. Soc., **75**, 98, (1998).

105 (a) L. Knorr, Liebigs Ann., **76**, 236, (1886); (b). H. O. Chaplin and L. Hunter, J. Chem. Soc. 484, (1939).

106. P. Umapathy and D. N. Sen. Indian. J. Chem., **6**, 516, (1968).

107. R. L. Dutta and A. Syamal. J. Indian. Chem. Soc. **44**, 381, (1967).

108. A. Syamal and A. Sarkar, Z. Anorg. Allg. Chem., **373**, 204, (1970).

109. A. D. Taneja, K. P. Srivastava and N. K. Agarwal. J. Inorg. Nucl. Chem., **34**, 3573, (1972).

110. P. Umapathy and D. N. Sen, Indian, J. Chem. **4**, 455, (1966).

111. M. N. Patel, C. B. Patel, and R. P. Patel, J. Indian Chem. Soc., **51**, 512, (1974).

112. A. Badilescue, Rev. Roun. Chim., **14**, 395, (1969).

113. L. Wolf and K. Wetsel, Chem. Ber., **90**, 1007, (1957).

114. A. Syamal, J. Indian Chem. Sco., **45**, 755, (1968).

115. A. P. Budhkar, P. Umapathy and D. N. Sen. Indian J. Chem. **9**, 376, (1973).

116. A. D. Taneja, K. P. Srivastava and N. K. Agrawal, J. Inorg. Nucl. Chem., **34**, 2980, (1972).

117. A. Syamal, J. Indian Chem. Soc., **45**, 904, (1968).

118. A. Syamal and R. L. Dutta, Indian J. Chem., **6**, 520, (1968).

119. A. Syamal and R. L. Dutta, J. Indian Chem. Soc., **45**, 1, (1968).

120. A. Syamal, J. Indian Chem. Soc., **45**, 374, (1968).

121. K. Gopalakrishnan, U. Chundesama and P. K. Bhattacharya, J. Indian Chem. Soc., **56**, 445, (1979).

122. N. K. Dutt and R. De., Indian J. Chem., **14 A**, 498, (1976).

123. J. N. Patil and D. N. Sen. Indian J. Chem., **11**, 782, (1973).

124. A Syamal, J. Indian Chem. Soc., **45**, 347, (1968).

125. S. K. Bhasin, P. Umapathy and D. N. Sen, J. Indian Chem. Soc., **49**, 1113, (1972).

126. U. Janardana Rao and A. P. B. Sinha., Indian J. Chem., **6**, 178, (1968).

127. J. N. Patil., D. N. Sen., Indian J. Chem., **12**, 189 ,(1974).

128. A. D. Taneja and K. P. Srivastava, J. Inorg. Nucl. Chem., **35**, 1397, (1973).

129. Z. P. Dudek and M. Barber, Inorg. Chem. **5**, 372, (1966).

130. A. Kettrup, P. Ackermann and W. Reipe, Z. Naturforsch D, **33**, 183, (1978).

131. K. Day, J. K. Bhar, K. C. Ray and S. K. Sen, J. Indian Chem. Soc., **52**, 999, (1975).

132. P. R. Johnson and D. A. Thernton, J. Inorg. Nucl. Chem., **37**, 461, (1975).

133. J. R. Horder and M. F. Lapport, J. Chem. Sec. A, 173, (1969).

134. R. L. Dutta and A. Syamal, 'Elements of Magnetochemicstry', East West Press, (1993).

135. R. C. Fay and T. S. Piper, J. Am. Chem. Soc. **84,** 2303, (1962).

136. D. N. Sen and P. Umapathy, Indian J. Chem. **4,** 454, (1966).

137. D. N. Sen and P. Umapathy, J. Indian Chem. Soc., **45,** 810, (1968).

138. C. Gopinathan and J. Gupta, Indian J. Chem., **12,** 103, (1974).

139. H. A. Patwardhan, S. S. Gopinathan and C. Gopinathan, Indian. J. Chem. **16A**, 224, (1978).

140. S. C. Chaudhary and J. Gupta., Indian J. Chem. **24A,** 150, (1985).

141. R. C. Paul, P. K. Gupta, M. Gulati and S. L. Chadha, Inorg. Nucl. Chem. Lett., **13,** 665, (1977).

142. R. C. Paul, P. K. Gupta, M. Gulati and S. L. Chadha, Inorg. Cjim. Acta, **20,** 7, (1976).

143. S. C. Chaudhany and J. Gupta., Indian J. Chem. **27A,** 914, (1988).

144. S. N. Poddar and D. K. Biswas. J. Inorg. Nucl. Chem. **31,** 565, (1969).

145. R. J. Cozens and K. S. Murray. Aust. J. Chem. **25,** 911, (1972).

146. K. Ueno and A. E. Martell, J. Phys. Chem.Ithaca **60,** 1270, (1956).

147. A. Syamal and V. D. Ghanekar, Indian J. Chem. **13,** 602, (1975).

148. M. E. Celap, M. J. Malinar and P. N. Radivojsa, Inorg. Chem., **14**, 2965, (1975).

149. Y. Shimura, J. Am. Chem. Soc., **73**, 5079, (1951).

150. N. Metsuoka, J. Hidaka and Y. Shimura, Bull. Chem. Soc. Jap., **39**, 1257, (1966).

151. A. Syamal and P. K. Mandal, synth. React. Inorg. Met – Org. Chem., **10** (4), 349, (1980).

152. A Syamal and P. K. Mandal, Transition Met. Chem., **3**, 292, (1978).

153. A. Syamal and P. K. Mandal, Transition Met. Chem, **4**, 348, (1979).

154. Bipin B. Mahaptra and D. Panda J. Indian Chem. Soc., **61**, 568, (1984).

155. Bipin B. Mahapatra and Basant. K. Patel, Indian J. Chem., **26A**, 623, (1987).

156. N. K. Dutt and R. De, J. Indian Chem. Soc., **48**, 981, (1971).

157. S. S. Gopinathan, C. Gopinathan and J. Gupta, Indian J. Chem., 12, 626, (1974).

158. C. Gopinathan, B. K. Pandit, S. S. Gopinathan, A. U. Sonsale and P. A. Awasker, Indian J. Chem., **13**, 516, (1975).

159. S. S. Gopinathan and C. Gopinathan, Indian J. Chem., **15A**, 660, (1977).

160. Bipin. B. Mahapatra and Dilip. K. Das, Indian J. Chem., **26A**, 173, (1987).

161. A. Syamal, D. H. Fricke, D. C. Pantalco. P. G. King, Johnson and R. Carl, J. Less Common Metals, **19**, 141, (1969).

162. A. Syamal, J. Indian Chem. Sci., **44**, 656, (1967).

163. A. D. Taneja, J. Inorg. Nucl. Chem., **35**, 3617, (1973).

164. A. Syamal, J. Inorg. Nucl. Chem., Lett. **4**, 543, (1968).

165. A. Syamal, Canadian J. Chem., **47**, 1693, (1969).

166. A. Syamal, J. Inorg. Nucl. Chem., **31**, 1869, (1969).

167. A. Symal, Z. Natur forsch. B, **25**, 567, (1972).

168. Bipin. B. Mahapatra and D. Panda. J. Inst. Chemists (India), **56**, 119, (1984).

169. F. Dias, C. Airoldi, C. Portela and G. F. de. Sa., J. Chem. Research(s) **15**, (1981).

170. W. Dietrich, H. K. Eisigen and H. P. Latscha, Z. Natur forsch., **35b**, 17, (1980).

171. S. N. Misra, T. N. Misra and R. C. Mehrotra, Aust. J. Chem, **21**, 797, (1968).

172. D. C. Bardley, F. M. Abad–El–Halim and W. Wardlaw, J. Chem. Soc., 3450, (1950).

173. D. C. Bardley, M. A. Saad and W. Wardlaw, J. Chem., 1091, 3488, (1954).

174. B. S. Sankhla, S. Mathur and M. Singh, Synth. Rect. Inorg. Met-org. Chem., **15**(5), 627, (1985).

175. Thankarajan and P. Sreeman, Ind. J. Chem., **20A**, 372, (1982)

176. A. Kettrup and W. Riepe, Z.Anal.chem., **252**, 1 (1970).

177. P. Sreeman. Ph.D. Thesis, Calicut University, (1980).

178. N. Thankarajan and P. Sreeman 'Indian J. of Chem.' **16A**, 611, (1978).

179. N. Thankarajan and P. Sreeman., Curr. Sci., **44**, 420, (1975).

180. N. Thankarajan and P. Sreeman., J. Indian Chem. Soc., **58**, 411, (1981).

181. N. Thankarajan and P. Sreeman., J. Indian Chem. Soc., **55**, 325, (1978).

182. J. M. Trivedi and C. M. Mehta, J. Indian Chem. Soc., 50, 133 (1973).

183. A. Kettrup and J. Abahagen, Z. Natur forsch B, **25**, 1382, (1970),

184. A. kettrup and J. Abahagen, Monatsch. Chem., **106**, 55, (1975),

185. R. J. Chudgar and K. N. Trivedi, J. Indian Chem. Soc., **46**, 537, (1969).

186. M. I. Ali, M. A. Abustate, N. M. Hass 'J. Chem. Eng. Data, **17**, 106, (1972).

187. K. Suruk and K. Yamassaki., J. Inorg. Nucl. Chem., **24**, 1093, (1986).

188. B. N. Barsoum, M. Essowy and M.A. F. Sharaf. Egypt. J. Chem., **31**, 6, 691 (1988).

189. William Henerson, John Fawcett, Raymond D. W. Kemmit, Clive Proctor, J. Chem. Soc., Dalton Trans., 3085, (1994).

190. R. C. Maurya, D. D. Mishra, D. K. Srivastava, P. K. Trivedi and I.B. Khan. Nat.Acad. Sci. Letters, **14**, 379, (1991).

191. S. K. Agrawal and J. P. Tandon., J. Inorg. Nucl. Chem., **37**, 949, (1975).

192. S. H. H. Chaston, S. E. Livingstone, T. N. Lockyer and J. S. Shannon, Aust. J. Chem., **18**, 1539, (1965).

193. R. K. Y. Ho and S. E. Livingstone, Aust. J. Chem. **18**, 659, (1965).

194. A. E. Landers and D. J. Phillips. Inorg.Chim Acta., **32**, 53, (1979).

195. A. K. Arivastva, V. B. Rana, M. Mohan, M. P. Swami and P. C. Jain, J. Inorg. Nucl. Chem., **37**, 723, (1975).

196. K. S. Shaka, J. Mohan, V. K. Chandha and H. K. Pujari, Indian J. Chem. **12**, 287, (1974).

197. A. Syamal and M. A. Bari Niazi, Synth. React. Inorg. Met-org. Chem., **15**(6), 805, (1985).

198. Bipin . B. Mahapatra, and Debendra Pandc., Transition Met-Chem., **9**, 117, (1984).

199. K. K. Deshmukh, A. M. Hundekar, S. D. Patil, C. I. Jose and D. N. Sen., J. Ind. Chem. Sci., **56**, 785, (1979).

200. B. S. Sankhla, S. Mathur and M. Singh, React. Inorg. Met-Org. Chem., **15**(8), 1121, (1985).

201. N. Raman, Y. Pitchaikani raja and A. Kulandaisamy, Proc. Indian Acd. Sci. (Chem. Sci). **113**, No.3, 183, (2001).

202. G. Rosini, J. Org. Chem., **39**, 3504, (1974).

203. A. Y. Desai and A. D. Sawant., Oriental J. Chem. **9**, No.4, 300, (1993).

204. Cotton F. A. and Wilkinson., G. Advanced Inorg. Chem. Int. Sci., 870 NY, (1967).

205. S. Khatavkar, and A. Deshmukh, J. Ind. Chem. Soc. **65**, 528, (1988).

206. C. J. Ballhausen, Introduction to Lignad Field Theory 251, McGrawHill series New York (1962); Agarwal, RC and Agarwal, G. K., J. Ind. Chem. Soc., **55**, 681, (1978).

207. U. Casellato, *et al.*, Co-ord. Chem. Rev., **26**, 85, (1978).

208. A. Deshmukh, Ph.D. thesis, Bombay University, (1989).

209. B. B. Mahapatra and S. K. Pujari, Transition Met. Chem., **8**, 202, (1983).

210. Bipin. B. Mahapatra and Dillip. K. Das., Synth. React. Inorg. Met-Org, Chem., **18** (10), 965, (1988).

211. Sharma. S. N., Orient. J. Chem., **15**(1), 165, (1999).

212. S. N. Sharma and P. K. Ambastha, Orient. J. Chem., **16**(1), 125, (2000).

213. Bipin. B. Mahapatra and D. Panda. J. Inst. Chemists (India), **56**, 119, (1984).

214. R. C. Maurya, D. D. Mishra, P. K. Trivedi, S. Mukherjee and D. K. Shrivastava., Synth. React. Inorg. Met-Org. Chem., **22**(4), 403, (1992).

215. A. Wurtz, Bull 'Soc. Chim. France (2), **17**, 436, (1872).

216. Schmidt 'J. Chem.Soc.(A) **40**, 247,889, (1881).; L. Claisen, J. Chem.Soc (A), **40**, 422, (1881); **46**, 1166, (1884).

217. C. R. Conrad and M.A. Dolliver, Org. Synth. Coll., **2**, 71, (1932).

218. E. P. Kohler and H. M. Chadwell, Org.Synth. Coll, **1**, 71, (1932).; W. Davey and I. R. Guilt. ,J. Chem. Soc., 1008, (1957).

219. E.Knoevenagel., J. Chem. Soc.(A). **66**,(1), 570, (1894).; E. Knoevenagel .,J. Chem. Soc.(A). **70** (1), 232, (1896).

220. B. D. Wilson, J. Org.Chem, **28**, 314, (1963).

221. M.E. McEntee and A. R. Pinter., J. Chem. Soc. 4419, (1957).

222. P. Delsest and R. Pallaud 'Compt. Rend., **246**, 1703, (1958); H Midorikawa, Bull. Chem.Soc. Japan, **27**, 149, (1954); H Midorikawa, Bull. Chem. Soc. Japan, **27**, 213, (1954).

223. E.Knoevenagel and W. Faber., Ber., **31**, 2773, (1898).

224. Galat, 'J.Am. Chem. Soc.', **70**, 2596, (1948).

225. Pandya and Pandya., Proc.Indian.Acad.Sci., **17A**, 3, (1943).

226. J. Povoloni, F. Gambarin and A.M. Grinzato, Ann. Chim. (Rome), **40**, 280, (1950).

227. H.J.J. Pabon, Rec., Trav. Chim., **83**, 379, (1964).

228. K.R. Srinivasan, J. Pharm. Parmacol, **5**, 448, (1953).

229. A. Weissberger, P.S. Proskauer, J.A. Hiddick and B.E. Troops and 'Organic solvents' **3**, Interscience, New York, (1956).

230. J. Baset, R.C. Denney, G.H Jeffery and J. Mandham (eds) 'Vogel's Text Book of Quantitative inorganic analysis' 4th Edn., ELBS and Longman, London, (1978).

231. J.G. Grasselli, 'CRC Atlas of spectral Data and Physical Constants of Organic compounds', CRC Press, Ohio, (1973).

232. G. Allen and R. A. Dwek., J. Chem. Soc., B. 161, (1966).

233. V. Gutman, Angew., Chem. Int. Edn. Engl., **9**, 843.L.J., (1970).

234. Bellamy, G.S. Spicer and J.D.H. Strickland, J. Chem. Soc., 4653, (1952).

235. L. J. Bellamy, 'The Infrared spectra of Complex Molecules' Vol.**2**. Chapman and Hall, London, (1980).

236 C. N. R. Rao, 'Chemical Applications of Infrared spectroscopy' Academic, London, (1973).

237 V.S. Govindarajan 'CRC Critical Reviews in Food Science and Nutrition', **12**, 199, (1980).

238 P.J. Roughley and D.A. Whiting, J. Chem. Soc. Perkin Trans,**1**, 2379, (1973).

239 R.L. Belford, A.R. Martell and M. Kalvin, J. Inorg Nucl. Chem. **2**, 11, (1956).

240 J. H. Robson and J. Reimhart, J. Am. Chem. Soc. **77**, 498, (1955).

241. Horak, Moravec and Pliva., Spetrochim. Acta, **21**,919, (1965).

242. D. C. Nonhebel, Tetrahedron., **24**, 1869, (1968).

243. R. L. Lintvedt and H. F. Holtzdaw., Jr., J. Am. Chem. Soc, **88**, 2713, (1966).

244. R. H. Holm and F. A. Cotton, J. Am. Chem. Soc., **67**, 2003, (1945).

245. J. H. Bowie, D. H. Williams, S. D. lawesson and G. Schroll, J. Org. Chem., **31**, 1384, (1966).

246.C. G. Macdonald and J. S. Shanon, Aus, J. Chem, **19**, 1545, (1966)

247.H. Irving and R.J.P. Williams, J. Chem. Soc., 3192, (1953).

248.J. P. Fackler, Jr. F. A. Cotton and D. W. Barnum, Inorg. Chem., **2**, 97, (1963).

249. J. M. Clark, Jr. and R. L. Switzer, 'Experimental Biochemistry' 2nd edn., W. H. Freeman and Company, SanFrancisco, (1977).

250. P.J. Roughley and D.A. Whiting, J. Chem. Soc. Perkin Trans.,**1**, 2379, (1973).

251. Z. Rapport, 'The chemistry of Enols'Wiley and Sons, Chichester, 1990.

252. H.H., Tonnesen, Ph.D. Thesis, Institute of Pharmacy, University of Oslo, Oslo, Norway, (1986).

253. Emily P. Pudele, and Michel Barber Inorg. Chem. **5**, No.3, 375 (1966).

254. S. K. Bhasin, P. Umapathy and D. N. Sen. J. Ind. Chem. Soc., **49**, 1113 (1972).

255. R. J. Anto, J. George, K.V. D. Babu, K. N. Rajasekharan and R. Kuttan, . Mutat. Res., **370 (2)**, 127, (1996).

256. M. T. Haung, Z. Y. Wang, C. A. Geogiadis, J. D. Lasken and A. H. Conney., Carcinogenesis, **13**, 2183, (1992).

257. M. T. Haung, R. C. Smart, C. Q. Wong and A. H. Conney, Cancer Res. **48**, 5941,(1988).

258. Y. Shing, H. Shung, T. Shizuko and Kazuo, Yakugaku Zasshi, **12**(4), 269, (1995).

259. A. Banerjee and S. S. Nigam, Indian J. Med. Res., **68**, 195. (1978).

260. S. Venkitaraman, Indian J. Physiol, Pharmacol, **22**, 237, (1978).

261. C. H. Collins and P. M. Lyne., Microbilogical methods., Butterworth., London, 414, (1970).

262. R. Ananthanarayanan and C.L.J. Paniker, "Textbook of Microbiology", Orient Longman (1984).

263. B.N. Figgis and R.S. Nyhlom, J. Chem. Soc., 4190, (1958).

264. F.G. Mann and B. C. Saunders, 'Practical Organic Chemistry', ELBS and Longman, London, (1975).

265. N. Nakamoto, 'Infrared Spectra and Raman Spectra of Inorganic and Coordination Compounds', John Wiley & Sons: New York, (1997).