LANTHANIDE COMPLEXES OF CURCUMINOIDS

THESIS SUBMITTED
TO THE UNIVERSITY OF CALICUT
IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN THE FACULTY OF SCIENCE

By

MALINI P.T.

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UNIVERSITY OF CALICUT
KERALA - 673 635
INDIA

JULY 2004

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DECLARATION

Certified that the thesis bound herewith is an authentic record of the research work on **LANTHANIDE COMPLEXES OF CURCUMINOIDS**, carried out by me under the supervision of Dr. K. Krishnankutty, Professor, Department of Chemistry, University of Calicut in partial fulfilment of the requirements for the award of the degree of the Doctor of Philosophy in Chemistry of the University of Calicut, and further that no part thereof has been presented before for any other degree.

Calicut University,
02.07.2004.

Malini P.T.

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CERTIFICATE

This is to certify that the thesis entitled **LANTHANIDE COMPLEXES OF CURCUMINOIDS** is an authentic record of the research work carried out by **Smt. Malini P.T.**, under my supervision in partial fulfilment of the requirements for the award of the degree of the Doctor of Philosophy in Chemistry of the University of Calicut. This work or part thereof has not been presented before for the award of any other degree.

Dr. K. Krishnankutty
(Supervising Teacher)
Professor
Department of Chemistry
University of Calicut.

Calicut University,
02.07.2004.

M

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I am also indebted to my parents and husband for their constant encouragement, love and moral boost which played a key role in the completion of this work nicely.

My sincere thanks to M/s Bina Photostat, Chenakkal, for their wonderful job in processing of the manuscript.

Malini P.T.

PREFACE

Active chemical constituents of a number of medicinal plants contain functional groups such as –OH, C=O, OCH_3, etc. that can form stable bonds with various metal ions. Many of the biological significance of these plant chemicals are associated with their ability to form complexes with various biologically important metal ions and other inorganic species. Therefore, studies on the coordination behaviour of synthetic analogues of active chemical components of medicinal plants have considerable importance. The present investigation is mainly on these aspects of certain synthetic analogous of natural curcuminoids. Curcuminoids are the active chemical constituents present in the traditional Indian medicinal plant turmeric (*Curcuma longa*). Synthesis and characterisation of lanthanide complexes of a series of curcuminoid analogues are considered in this study from a structural point of view. The antioxidant activity of these compounds are also included in this work.

The Thesis is divided into two parts.

Part I : General Introduction

Structurally, curcuminoids are a group of naturally occurring β-diketones in which the diketo function is directly attached to olefinic groups. Therefore, some of the salient features β-diketones and metal β-diketonates are briefly discussed in this part. Importance of coordinatin chemistry in biological processes has been highlighted. Reported studies on synthetic and structural aspects of curcuminoids and their metal complexes are briefly mentioned. Therefore no separate review is included. Various biochemical and medicinal applications of turmeric and curcuminoids have been cited. Need for further studies and importance of the present investigation have been interspearsed at appropriate places.

Results of the present investigations are presented in **Part II**. This part is divided into four chapters.

In **chapter 1**, details on the synthesis and characteristisation of lanthanide complexes of ten synthetic curcuminoids, (1,7-diarylheptanoids) are discussed. Infrared, ^1H nmr and mass spectral data have been successfully employed in establishing the structure and nature of bonding in these complexes. The spectral and analytical data clearly revealed the formation of three types of complexes, namely $[LnL_2(X)(H_2O)_2]$ where $X = Cl^-$, NO_3^-; $[LnL_2(NO_3)_2(H_2O)_2]$ and $[LnL_3(H_2O)_2]$, where L = the deprotonated ligand HL. The monobasic bidentate nature of the 1,7-diarylheptanoids in which the diketo oxygens are involved in bonding has been unequivocally established from the spectral data.

Electronic absorption and fluorescence emission spectral data of the 1,7-diarylheptanoids and their lanthanide complexes have also been discussed separately.

Thermogram of some of the complexes were studied and compared with the reported data on lanthanide β-diketonates.

In **chapter 2**, the synthesis and characterisation of dioxouranium(VI) complexes of some of the diarylheptanoids are considered. The $[UO_2L_2]$ stoichiometry and bidentate coordination of the ligands in these complexes have been established from spectral and analytical data.

Synthesis and characterisation of aluminium(III) complexes of the curcuminoids are presented in **chapter 3**. The use of ir, nmr and mass spectral data in elucidating the structure and nature of bonding in these type of complexes has been illuminated in this chapter.

Results of studies on antioxidant activity of the curcuminoids and their metal complexes are considered in **chapter 4**. Experimental aspects are given in detail and the data are presented graphically. All the curcuminoids exhibited antioxidant activity significantly. Structural influence and effect of complexation on the antioxidant activity has also been discussed.

References are given in the order cited.

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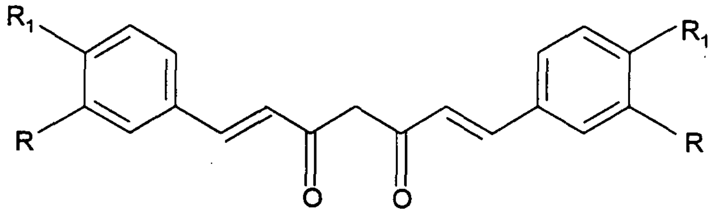
NOMENCLATURE AND ABBREVIATIONS

Names indicating the source of the compounds is a usual practice of naming the active chemical constituents isolated from natural products. Thus the name curcuminoids was given to a group of structurally related compounds present in the yellow pigment of the medicinal plant *Curcuma longa* Linn. (turmeric). Structurally they are 1,3-diketones of the type given below.



Synthetic analogues of these "unsaturated" β-diketones are also known by the term curcuminoids. Systematically these compounds are 1,7-diarylhepta-1,6-diene-3,5-diones and for brevity they are sometimes referred as 1,7-diarylheptanoids. Both these and the trivial name, curcuminoid are freely used in the present investigation.

Important abbreviations used in the thesis are:

Ar	aryl group
BM	Bohr Magneton
dmf	dimethylformamide

dmso	dimethylsulfoxide
FAB	Fast atom bombardment
Fig.	figure(s)
h	hour
Hz	Hertz
J	Coupling onstant
L	Deprotonated ligand
Ln	Lanthanide ion
M	Central metal ion in a metal complex
M.P.	Melting point
Ph	Phenyl group
ppb	Parts per billion
ppm	Parts per million
tlc	thin layer chromatography
μ_{eff}	Effective magnetic moment in Bohr magnetons
μL	microlitre (10^{-6} L)
X	Cl^-, NO_3^-, etc.

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 ^1H 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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PART I

GENERAL INTRODUCTION

GENERAL INTRODUCTION

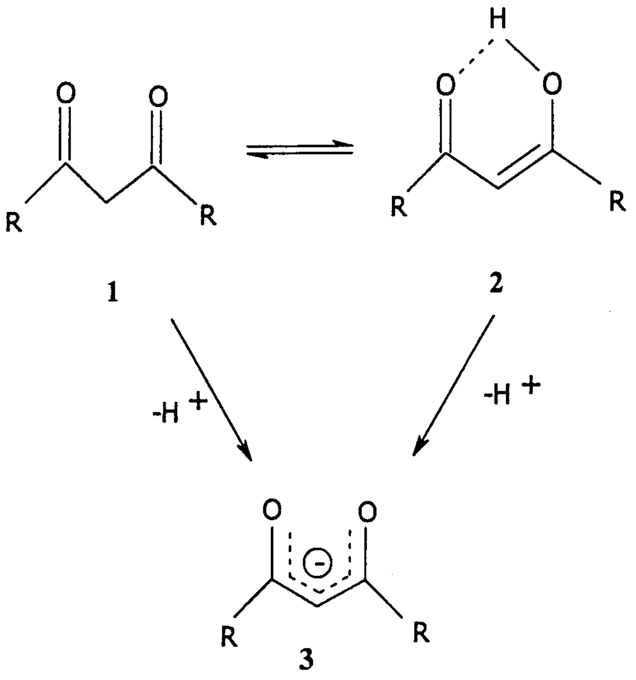
One of the fascinating features of modern coordination chemistry is the ever increasing academic, commercial and biochemical interest exhibited by metal complexes of organic molecules, both natural and synthetic.[1,2] This is mainly because of the ability of coordinated metal atom/ion to influence the reactivity of the organic compound. Thus, numerous highly efficient catalytic systems based on metal complexes are available. Similarly several synthetic metal complexes which mimic the behaviour of complex biomolecules are known and at present the study of such compounds are receiving much attention.[2-4] Although, the results obtained so far do not always parallel those in nature, a knowledge of the chemistry is being built up and the biochemical role of metal ions in natural ligand systems is beginning to be better understood.[5]

The structure, properties and uses of metal complexes are dependent both on the nature of the metal ion and the type of the ligand coordinated. The variation in metal ions is considerable, on the other hand, because of the developments in modern synthetic organic chemistry, variations in ligand systems is virtually limitless. Thus thousands of new ligand systems have been developed in recent years. This trend is evident from the reports on numerous compounds based on 1,3-diketones and related compounds.

The 1,3-diketones have several interesting structural features. They serve as the best example of keto-enol tautomerism and intramolecular hydrogen bonding. For a coordination chemist, perhaps, the most important aspect of β-diketones is their ability to form complexes with various metal ions. The 1,3-diketones still serves as the starting material for the design and synthesis of a large number of compounds having wide application in many fields. Therefore, investigations on metal complexes of different types of 1,3-diketones have considerable importance. The present investigation is mainly on certain structural and biochemical aspects of lanthanide complexes of a series of 'unsaturated' 1,3-diketones. Therefore, some of the salient features of 1,3-diketones and metal 1,3-diketonates which are quite pertinent to the present study are briefly discussed below.

Tautomerism of β-diketones

Since the preparation of acetylacetone and similar 1,3-dicarbonyl compounds in the later half of the 19th century, organic chemist has considerable interest in their properties, especially their ability to exhibit keto-enol tautomerism. The 1,3-diketones contain a methylene group or a substituted methylene group which is interposed between acyl or aroyl groups. Usually, 1,3-diketones exist as a mixture of keto **1** and enol **2** forms related by a 1,3-hydrogen shift.



Usually, the enolic form is favoured in nonpolar solvents and simultaneous conjugation and chelation through hydrogen bonding is responsible for the stability of the enol tautomers The proportion of the enol tautomers formed are influened by a number of factors like solvent, temperature and substituents. In general, the amount of enol form decreases when a bulky alkyl substituent is present at the α-position. This can be attributed to the steric hindrance offered by the bulky group together with inductive effects of the alkyl groups.[6-8] Presence of electron withdrawing groups such as Cl^-, Br^-, CN^- & CH_3COO^- at the α-position increases the proportion of the enol tautomers. The enolization also increases [9, 10] when the compounds are fluorinated or contain an aromatic ring.[32] The removal of hydrogens from the enol and keto forms generate the 1,3-diketonate anion **3**, which is main source of the coordination chemistry of 1,3-diketones.

Metal complexes of 1,3-diketones

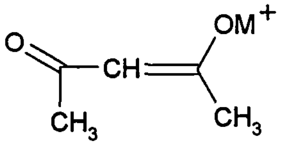
The coordinating abilities of 1,3-diketones were recognized as early as in 1887 when, Combes reported the synthesis of beryllium acetylacetonate.[11] This was followed by the pioneering work of Werner[12], Morgan[13,14] and Sidgwick[15] and confirmed the bidentate chelating character of these ligands. The diketonate anion, being a powerful chelating agent, form complexes with virtually almost all the metal and metalloid ions in the periodic table.

During 1896-1899 Urbain prepared hydrated tris(acetylacetonates) of lanthanum, yttrium and gadolinium[16-19]. In 1965, Mehrotra *et al.*[20] prepared pure tris(acetylacetonates) of praseodymium and neodymium, and the method was extended to the synthesis of pure tris-β-diketonates of other lanthanide elements.[21-28] Synthesis, purification, spectral characterization, stability and applications of lanthanide complexes of a number of β-diketones have also been reported.[205-208] Literature on 1,3-diketones and metal 1,3-diketonates are so voluminous that even an attempt to summarise is purposefully avoided. However, since β-diketones can be bonded to metal ions in a variety of ways[29-31], the different coordination modes reported are briefly mentioned below.[32-35]

Depending upon the bonding of metal atoms with the diketones, metal β-diketonates can be divided into four categories. (1) Oxygen bonded (2) Carbon bonded (3) Both carbon bonded and oxygen bonded and (4) Olefin bonded.

1) Oxygen bonded β-diketonate complexes

Several types of oxygen bonded β-diketonate complexes are known. It can function as a unidentate anion and form simple salts with electropositive metals,[34-36] which have typical salt like properties as in structure 4.



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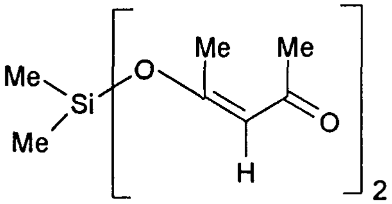
Another example for unidentate oxygen coordination is the tetrahedral silicon complex 5. The stability of this complex has been explained on the basis of participation of the d-orbitals of silicon in bonding.



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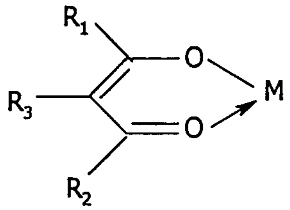
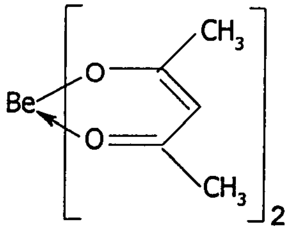
The usual mode of bonding of β-diketone is the formation of a six-membered C_3O_2M metal chelate ring in which it function as a monobasic bidentate ligand as in structure **6.** Delocalisation of the electron cloud of the chelate ring endow it with a certain amount of aromatic character as evident from the ability of such complex to undergo facile electrophilic substitution at the 2-carbon atom of the 1,3-diketone moiety.[37-40]



6

The enolate ion is mono basic, therefore, metal ion can react with one or more of the enolate ions to give either neutral or charged molecules depending on the coordination number (m) and valency (n) of the central metal atom. Thus three different types of complexes are possible.

i) When m = 2n, the metal β-diketonate so formed behaves as a neutral molecule. Some examples of this class of compounds[36,38-42] are given in structure as 7-9.



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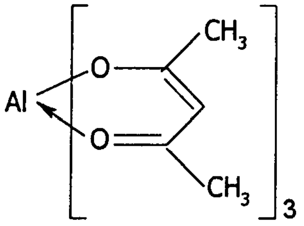

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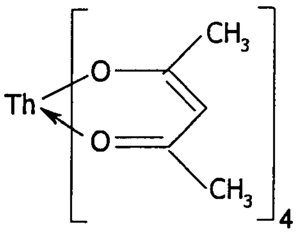


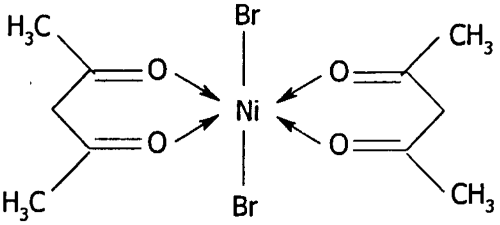
9

2) When m > 2n, the complexes behave as lewis acids and attain the desired coordination either by adduct formation or by polymerization. Examples of this type are given in structures **10-12**.

$[Ni(acac)_2\,bipy]$ $[Co\,(acac)_2]_4$ $[Zn(acac)_2\,(NH_3)_2]$

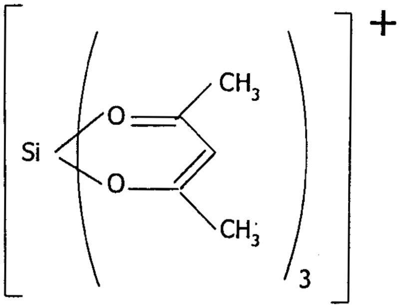
10 **11** **12**

When both carbonyl oxygens of the keto form of the ligand act as donor atoms,[43,44] β-diketones function as neutral ligand as in structure 13.



13

iii) When m < 2n, β-diketonates of the type **14-17** are well known in literature.



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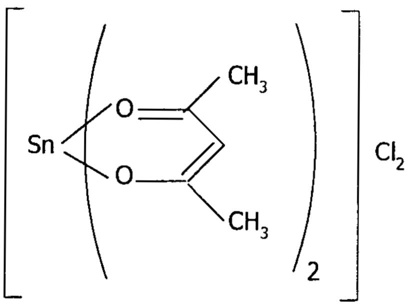

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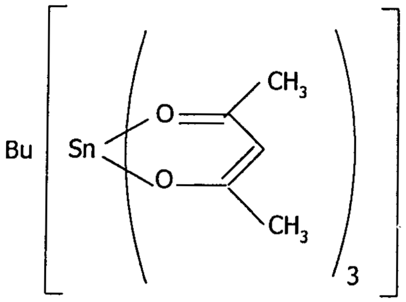

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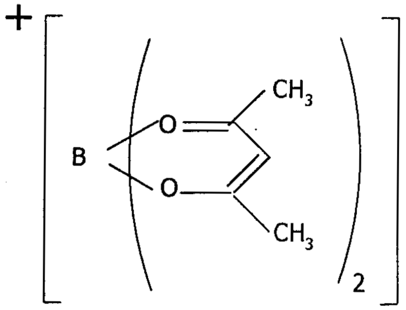
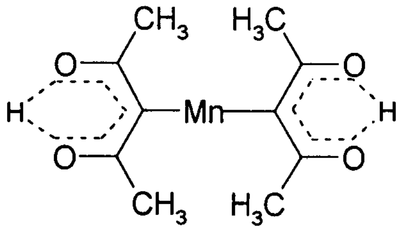


17

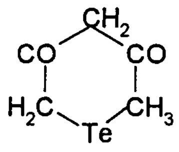
2) Carbon bonded complexes

In this category both terminal as well as the central carbon bonded β-diketone complexes are known. In β-diketonates of S, Se, Te, Au and Hg, the ligand moiety bonds through the carbon atom and the carbonyl oxygens do not participate in the bonding[45-57]. Typical examples are given in structures **18-22**.



18

(M = S; n = 1,2; M = Se, n = 2)



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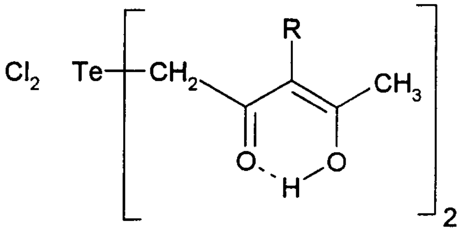

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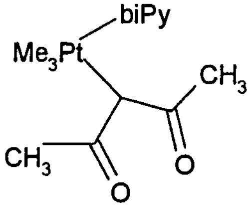


21

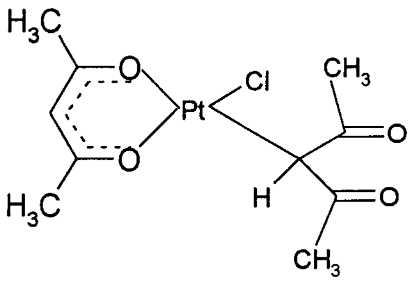
L_3 Au (A)

22

(A = acac, bzac
L = Ph_3P, Ph_2Et P, Et_3P)

3) Both carbon – bonded and oxygen-bonded complexes

Metal β-diketonates in which the metal atom is bonded to one ligand moiety through both the carbonyl oxygen, while the other through the 2-carbon atom are also quite common.[45,48] Examples of this class of compounds are shown in structures **23-25**.



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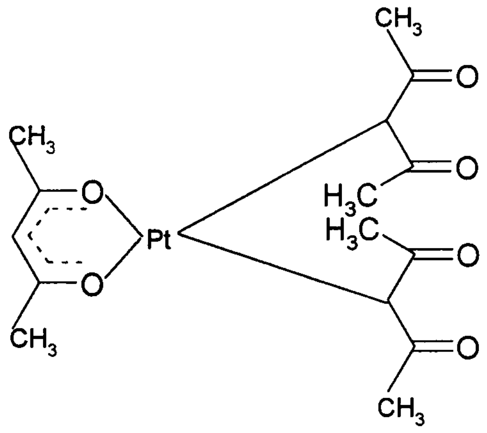

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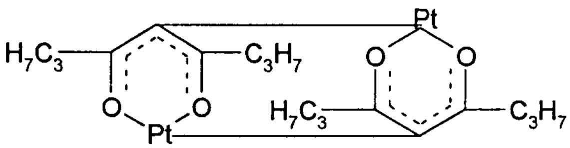
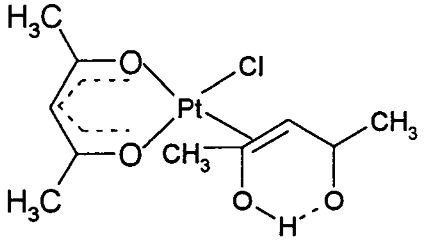


25

4) Olefin bonded complexes

β-Diketonates of certain metals are known in which the metal ion is directly attached to the olefinic, >C=C<, system.[33,49,50] Examples of complexes of this type are given in structures **26-28**.



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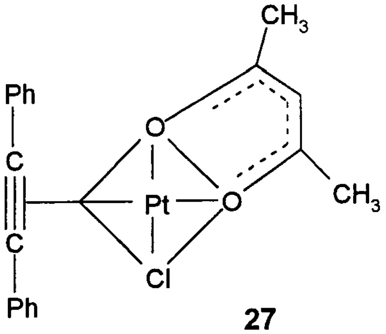

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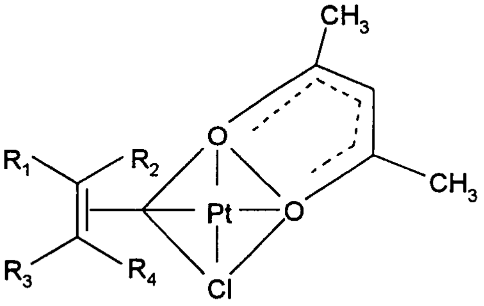

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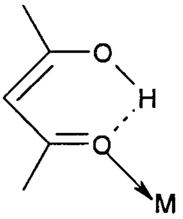
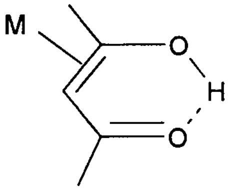
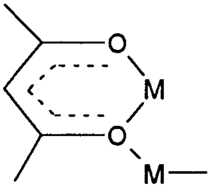
In addition to the above mentioned bonding modes, β-diketones are known to function as ligands in several other ways. Thus apart from the neutral and monoanionic nature of β-diketones in complexes, their ability to function as dianionic and even trianionic ligands are also well established.[37] Some of these unusual bonding modes exhibited by β-diketones are given below.

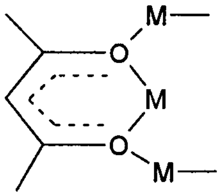
i) Neutral molecule

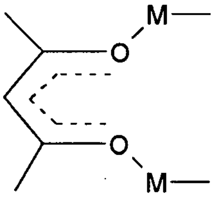


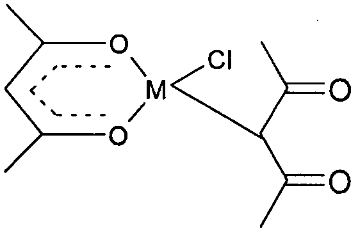


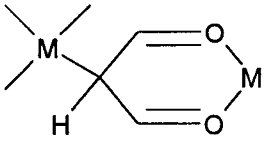
ii) Mono anions

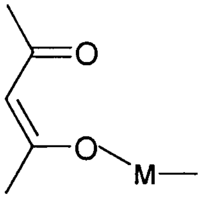


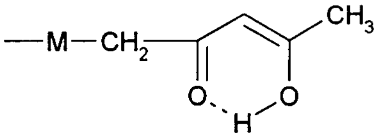




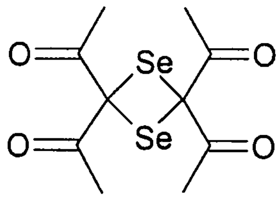


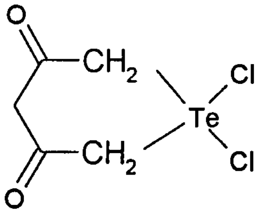


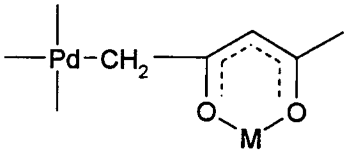




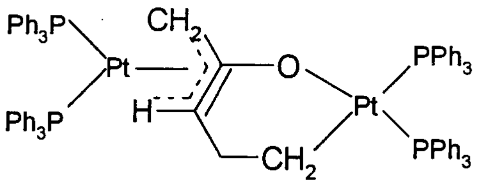
Dianions







Trianion



Structural characterization of metal complexes of 1,3-diketones

Almost all the available spectral techniques as well as diffraction data along with other physical and chemical methods have been extensively employed in studying the structure and nature of bonding in various metal 1,3-diketonates.[37] Thus, the uv-visible absorption spectral data together with magnetic moment values have been widely employed in establishing the structure and stereochemistry of the various metal diketonates. The importance of ir, nmr and esr spectral data in elucidating the structure and nature of bonding in coordination compounds were infact started with the application of these techniques in metal β-diketonates. Similarly the X-ray diffraction data provided the correct disposition of the ligands in metal complexes of β-diketones. The importance of these spectral studies are briefly outlined below.

Electronic Spectra

Interpretation of electronic absorption spectral data in establishing the structure and nature of bonding of metal β-diketonates has been a major research activity in coordination chemistry for a long time. Thus numerous reports exist on uv-visible spectral data of metal β-diketonates. Theoretical calculations based on SCF and LCAO-MO calculations of the various absorptions are also available particularly in the case of metal acetylacetonates. Thus, for instance, the strong broad absorption bands appearing at ~ 34700 cm^{-1} and 49500 cm^{-1} of metal acetylacetonates have been assigned to various π-π^* transitions. Similarly, almost all the observed electronic spectral bands have been justified on the basis of various MO calculations.[51-59]

The uv-visible absorption spectral data of several lanthanide β-diketonates were also employed not only in determining the structure and bonding but also in establishing the stoichiometry particularly the degree of hydration of the complexes.[60]

IR spectra

Vibrational spectroscopy is one of the most important available technique for establishing the structure and nature of bonding of coordination compounds particularly metal complexes of organic ligands. This aspect of ir spectra of the coordination compounds has been well illuminated from the reported ir studies on various metal β-diketonates.

Studies on the ir spectra of metal β-diketonates were initiated during the second half of the last century. Infrared spectra of metal β-diketonates provide valuable information regarding the nature of bonding of the diketo group attached to the metal. In addition, conclusive evidence for the quasi-aromatic behaviour of the six membered C_3O_2M chelate ring and various other structural features of metal β-diketonate has also been deduced from ir data. Importance of ir spectra in establishing the keto-enol tautomers of β-diketones has been well established.[61-62] For example characteristic carbonyl band of the enol form of acetylacetone appeared at 1613 cm^{-1} and that of diketo form at 1725 cm^{-1}. Presence of a broad band at 2700-3000 cm^{-1} is an indication of the intramolecularly hydrogen-bonded enol form of β-diketones.[63,64] Upon complexation, the carbonyl stretching frequency of

1,3-diketones shows a shift (10-50 cm^{-1}) to lower values and additional bands due to $\nu_{M\text{-}O}$ vibrations appear in the region 400-500 cm^{-1}.

Misumi and Iwasaki[65] reported the ir spectra of tris(acetylacetonates) of praseodymium, neodymium, europium, gadolinium and erbium. These complexes show the presence of pure M-O stretching bands on the region 420-432 and 304-322 cm^{-1}. In addition to these, the other metal-oxygen stretching and vibration modes coupled with ring deformation and $C\text{-}CH_3$ bending have been observed at about 550 and 623-611 cm^{-1} respectively. The observed shifts of M-O stretching bands to higher frequency from praseodymium to erbium are in good agreement with the lanthanide contraction phenomenon.

NMR Spectra

NMR spectral studies of metal β-diketonates appear to have been initiated in 1958 by Holm and Cotton[57] who assigned the positions of methyl and methine (=CH-) protons in neutral metal acetylacetonates. They observed that the chemical shifts were close to those observed for olefinic protons and were nearly independent of the size, charge and π bonding ability of the metal ion. The position and nature of splitting of the signals depends on the mode of the coordination, nature of the substituents and the extent of delocalization in the chelate ring.[66-72] The *cis* enol proton chemical shift, δ(OHO)/ppm, of β-diketone and β-ketoaldehyde of general formulae R'COCH (R") COR have been reported.[73] Nonhebel [74,75] showed that the bulky substituents on the α and β sites not only shifted δ(OHO) down field but produced a sharper line.

X-Ray Diffraction studies

The m-chloro and m-bromo derivatives of dibenzoyl methane were the first β-diketones to be investigated by X-ray methods.[61,62,76] The crystal and molecular structures of several metal β-diketonates have been determined by the 3-dimensional X-ray method.[37]

Mass spectra

Mass spectroscopy is an efficient tool in the structure elucidation of coordination compounds.[77-79] Macdonald and Shammon[80] studied mass spectra of a series of metal acetylacetonates. The most intense peaks in the spectra are usually derived from the monomeric forms of the complexes, but rarely peaks due to dimer or even trimer have also been observed. These studies confirm the influence of the odd or even electron character of an ion on its dissociation reactions (Mac Lafferty)[81] and provided additional evidence[77-79] that odd electron ions can be changed to even electron ions and vice versa, by change of valency of the metal atom in the ions.

Thermogravimetric studies

Thermal anlysis is a well established method for the characterization of inorganic complexes. Sievers and co-workers[82,83] have made a detailed comparative study of the thermal stability of derivatives of lanthanons with different β-diketones. These workers found that size and extent of fluorination of the ligand along with careful selection of substituents attached to the donors, enhances the volatility and stability of resulting complexes.[83]

Applications and use of metal complexes of β-diketones

The use of metal chelates of β-diketones depends on their chemical reactivity coupled with their volatility and thermal and solvolytic stability. These properties have been exploited in solvent extraction studies of various ions, and gas chromatographic separations of several metals.

The application of certain coordinately unsaturated lanthanide chelates, called 'shift reagents' for n.m.r spectral elucidation has become an extremely useful analytical technique.[84-87] Addition of β-diketonates like $Cr(acac)_3$, $Eu(dpm)_3$, $Eu(fod)_3$, $Pr(fod)_3$, etc. for measurements of carbon-13 n.m.r spectra is effective in reducing the normally long longitudinal relaxation times, thus minimizing saturation effects and allowing more rapid collection of data.[88-92]

The chemistry of lanthanide β-diketonates has assumed considerable importance because of their practical use as potential laser materials.[93-97] Since the development of gas chromatography as an efficient technique for separation and estimation of different species, volatile compounds of metals have assumed special significance. Amongst the numerous class of inorganic compounds, many β-diketone derivatives especially fluorinated β-diketone derivatives appear to be especially suitable.[98-102] Fluorinated β-diketones are highly useful in the solvent extraction of metals.[103-107] Metal complexes of β-diketones are used as fuel additives,[108] as supercritical fluids for waste clean up[109] in superconducting thin film manufacturing[110] and in production of homogeneous and heterogeneous catalysts.[111,112] Iron(II) and iron(III) chelates of β-diketone are used as catalysts for the removal of hydrogen sulphide from natural gas.[113]

Time resolved fluorescence spectra of europium chelates of β-diketones is one of the most rapidly growing areas of application of fluorescence spectroscopy. Highy sensitive time-resolved fluorometric determination of estrogens by HPLC using europium β-diketonate are reported.[200] Microsecond time-resolved fluorimetry (TRF) of europium chelates was introduced in the area of nucleic acid hybridization assays and immunoassays of proteins.[201-208]

Naturally occurring β-diketones

Majority of the reported studied on metal β-diketonates are based on synthetic β-diketones in which the diketo function is directly linked to alkyl/aryl groups. However active chemical components of several medicinal plants contain one or more carbonyl group as essential functional group. Many of the medicinal and other biological properties of these plants are due to the presence of these type of compounds.

Several plant species are known to exert wide range of beneficial physiological effects in addition to aroma and flavour. Even in the modern world, nature is still the greatest source of drugs and pharmaceuticals. The Indian subcontinent is endowed with rich and diverse local health traditions which is matched with an equally rich and diverse plant genetic resources.[114] The classical systems of medicine are also based on herbal medicine.

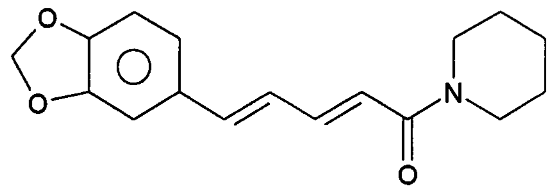
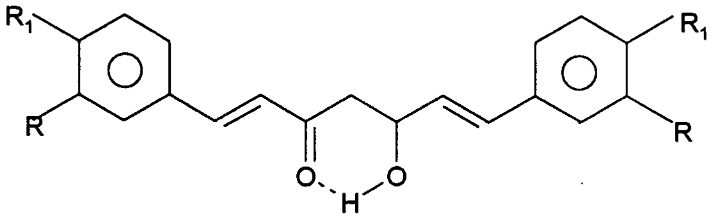
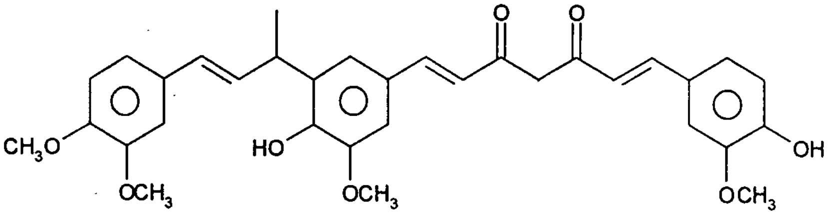
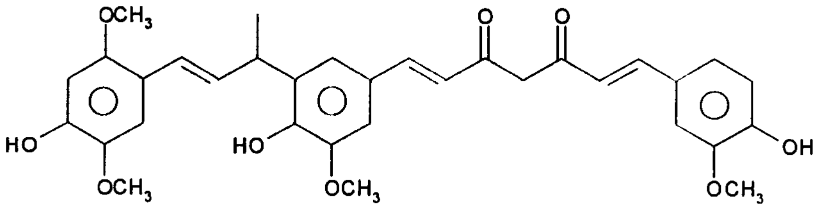
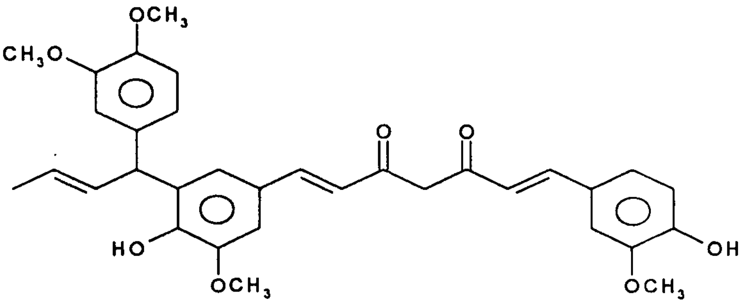
Herbs and herbal constituents are found to be safe and function as natural remedies to many tragic illness. Powerful antioxidants originating from edible and medicinal plants have been extensively investigated as important inhibitory materials for the prevention of oxidative deterioration of lipids. Recently it has been shown that peroxidation in living organism is closely related to the initiation of some human diseases, such as cancer, coronary heart disease and Alzheimer's disease. Ingestion of antioxidants may possibly prevent these diseases.[115,116]

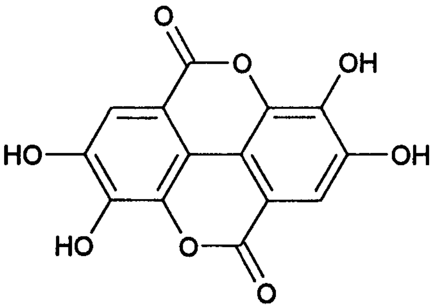
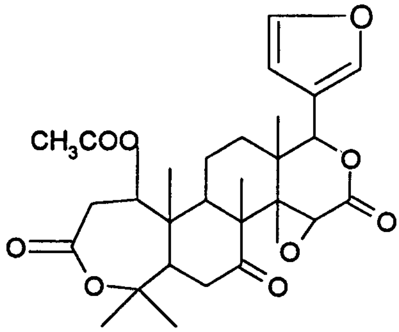
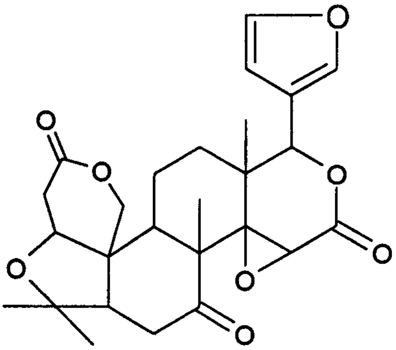
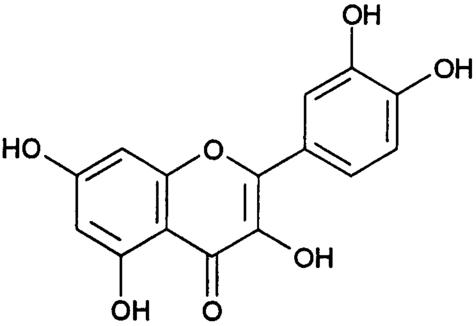
The state of health is a result of body's ability to recover from the continuous challenges posed by toxic substances entering through air, food and water. The most vivid example of this struggle, is our defence against chemicals that cause cancer. Most cancer causing compounds (carcinogens) undergo metabolic change in the body to 'activated' carcinogens. The 'activated' carcinogen binds to the cell DNA, and damages it forming the so called DNA adducts. Chemoprevention includes the use of pharmacologic or natural agents that inhibit the development of invasive cancer either by blocking the DNA damage that initiates carcinogenesis or by arresting or reversing the progression of premalignant cells in which such damage has already occurred.[117]

Foods of plant origin contain many bioactive compounds in addition to vitamins and minerals. These phytochemicals belongs to several classes of organic compounds such as sulphur containing compounds, terpenoids, flavanoids, polyphenols, carbonyl compounds, etc. Some of the naturally occurring carbonyl compounds and their main plant sources are given in Table 1. In addition to carbonyl group, several other functional groups are also present in these compounds.

Table 1

Active constituents of some common spices and medicinal plants

Spice (Plant species)/ Active Principle	Structure
Black pepper (*Piper nigrum*) piperine	
Turmeric (*Curcuma longa*) Curcuminoids	
Indonesian medicinal ginger (*Zingiber cassumunar*) Cassumunin A	
Cassumunin B	
Cassumunin C	

Fruits and nuts (grapes, strawberries) Ellagic acid	
Terpenoids Citrus fruits Nomillin	
Limonin	
Flavanoids and flavanone Most vegetable fruits and cereal grains Quercetin	

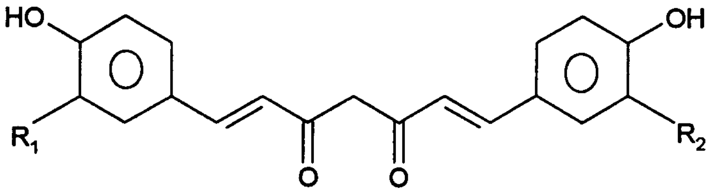
Among the various naturally occurring carbonyl compounds, curcuminoids possess several interesting structural features and numerous practical applications. Structurally they are typical 1,3-diketones in which diketo function is directly attached to olefinic groups. Recently metal complexes of curcuminoids and several structurally related compounds have been synthesized and characterized.[132-137] Since the present investigation is mainly on lanthanide complexes of curcuminoids, some of the chemical and biochemical aspects of curcuminoids are briefly mentioned below.

Curcuminoids

The main source of curcuminoids is the herbaceous Indian medicinal plant turmeric (*Curcuma longa* Linn.). Turmeric is used as a spice in Indian cooking and also as a house hold medicine. Its pharmacological properties are well documented in ancient Indian literature.[118,119] Turmeric is a common ingredient used on traditional cosmetics and in many traditional Indian ceremonies. Turmeric occupies an important position in the life of Indian people as a common remedy for many diseases. A paste of turmeric and slaked lime is an house hold remedy for grains, muscular pain and inflamed joints. Turmeric powder was used against biliary disorders, anorexia, coryza, cough, diabetic wounds, hepatitic disorders, rheumatism and sinusitis.[118-129]

Constitution of curcuminoids

Natural curcumin isolated from turmeric contains three well defined yellow compounds.[123] In 1953, Sreenivasan *et al* separated these three curcuminoids using column chromatography over silica gel.[124] Later these compounds were identified.[123-124] as curcumin I (diferuloyl methane) as the major component, curcumin II (feruloyl-p-hydroxy cinnmoylmethane) and curcumin III [bis-(*p*-hydroxycinnamoyl methane].



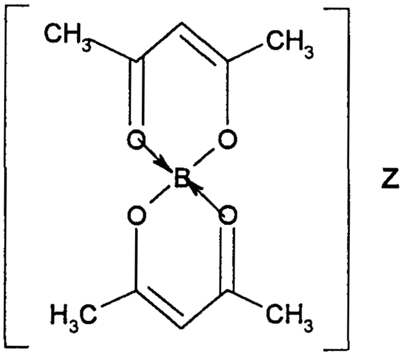
	R_1	R_2
Curcumin I	OCH_3	OCH_3
II	OCH_3	H
III	H	H

The structure of the compounds were later confirmed by chemical degradation studies.[128]

Synthesis of 1,7-diarylheptanoids

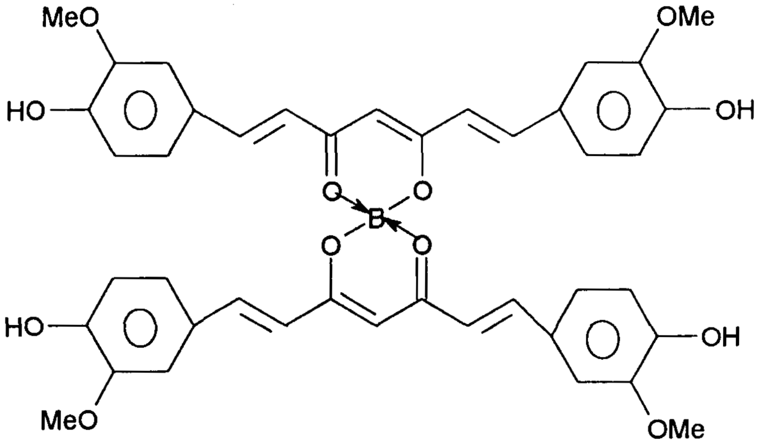
The synthesis of curcumin was first reported in 1913 by Lampe and Milobedzka.[125] This method was further improved by Povoloni.[126] H.J.J. Pabon developed a general method of synthesis for curcuminoids[127] and related 1,7-diarylheptanoids in good yield. This method involve the condensation of an aromatic aldehyde and acetylacetone in presence of B_2O_3, tri(sec butyl) borate and n-butylamine. The reaction was carried out in dry ethyl acetate in the temperature range 85-110°C.

According to Pabon, the acetylacetone-boric oxide complex, **29** is first formed. The methyl group of this complex then condenses with the aromatic aldehyde to form **30** which on acidification with con. HCl gives free curcumin.



$Z^- = OH^-$ or BO_2^-

29



30

Using this method, more than thirty curcuminoid analogues have been synthesized.

Structure of curcuminoids

Electronic, ir, nmr and mass spectral data of curcuminoids and a number of 1,7-diarylheptanoids have been reported.[118,128] Spectral analysis established that the curcuminoids exist predominantly in the intramolecularly hydrogen bonded enol form[130]. The crystal and molecular structure of curcumin 1 has been reported[121, 131] by X-ray crystallographic methods. These data will be quoted at appropriate places while discussing the results of the present investigation.

Metal complexes of curcuminoids

In a typical Hindu religions ceremony, turmeric is mixed with $Ca(OH)_2$ and rice. In this process the natural yellow colour of turmeric turns to a deep red colour. The colour change may be due to the interaction of curcuminoids with calcium ions. The Ca^{2+} ions may replace either enolic/phenolic proton, and changes the chromophoric group. A gold(I) complex of curcumin 1 was reported to possess antiarthritic activity.[129] Recently synthesis and characterization of stable Cu^{2+}, Ni^{2+}, Co^{2+}, Zn^{2+} and Pd^{2+} complexes of some synthetic curcuminoids were appeared in the literature.[132-134] Antitumour studies of metal chelates of these synthetic curcuminoids were also reported.[135-137]

Free radical scavenging and antioxidant efficiency of curcuminoids

Free radicals are produced in biological systems by the ionization of water by X-rays,[138] through metabolism, by triggered inflammatory phagocytes to reactive oxidants[139] and during oxidative phosphorylation.[140] These free radicals are highly reactive species, which react with biological compounds causing tissue damage. Antioxidants can counteract against this free radicals.

Curcuminoids are natural phenolic compounds, with potent anti-oxidant properties. Both turmeric and curcuminoids inhibited generation of potent free radicals like super oxide and hydroxyl radicals.[141] The antioxidant properties of curcumin in prevention of lipid peroxidation, another process that generates free radicals is well recognized.[142,143] The primary role of curcumin as a lipid soluble antioxidant is to intercept peroxyl free radicals formed during lipid peroxidation. This prevents free radical chain reactions which deteriorate the lipid membrane.[144]

Medicinal uses of turmeric and curcuminoids

Turmeric is a traditional house hold Indian medicine.[159] Certain studies revealed that the topical applications of curcuminoids in patients improve wound healing significantly and protect tissues from oxidative damage.[145] It is used as an anthelminti. Chemopreventive effect of turmeric against stomach and skin tumours have been studied.[160-162] Turmeric has antimutagenic,[163,164] property and prevents the DNA damage induced by smoke.[165,166] and lipid peroxidation and prevent BP-DNA adduct formation.[166] Studies have shown that many of the biological properties of turmeric are due to the presence of the curcuminoids. [131,175-178,142,167-174]

Pharmacological studies revealed that synthetic curcuminoids also have antimicrobial, anti inflammatory and anticarcinogenic activities.[152,168,169,179-196] Curcuminoids inhibits 4-nitroquinoline-1-oxide induced oral carcinogenesis[173], azoxymethane induced small and large intestinal carcinogenesis[174] and azoxy methane induced colon carcinogenesis.[197] Antimutagenic and anticarcinogenic activity of natural and several synthetic curcuminoids have been studied.[176] Antitumour and free radical scavenging activity of some synthetic curcuminoids were analysed and reported.[135-137,198]

In view of the recently discovered applications, the properties of natural and synthetic curcuminoids can best be summarized as protective properties. Turmeric and curcuminoids can exert protection either directly, by shielding the biomolecules, or indirectly by stimulating the natural detoxification and defence mechanisms of the body.[199] Curcuminoids also play a role in protecting some drugs from physico-chemical degradation. Addition of curcumin to the cardiovascular drug nifedipine, prevented degradation of nifedipine due to uv light.

One of the important protective mechanisms of turmeric extract and the curcuminoids is the protection against side effects produced by drug therapy. A potential preventive role of curcumin on DNA adduct formation with the carcinogen has been studied in vitro.[146] Additionally, *in vivo* studies on rats were also performed. As compared to the control animals, rats fed with curcumin showed decrease in levels of DNA adduct in the liver cells.[147] This decrease could be explained by the competitive binding of curcumin to the active site of benzopyrene, preventing cellular DNA adduct formation.

Because of the cytotoxic nature, anticancer drugs do not discriminate between cancer cells and normal cells, and could cause damage to non-cancerous tissue as well. Curcumin administered to mice along with anti-cancer drug, cyclophosphamide, increased the life span of animals and reduced bone marrow and liver toxicity of cyclophosphamide.[148] Curcuminoids, by virtue of their antioxidant activity, scavenge free radicals as well as prevent their formation, thereby eliminating the toxic effects of the drug.

The effect of combining curcumin with cisplatin was evaluated.[149] Clinical use of cisplatin is limited because of its severe toxicity leading to kidney failure. Studies showed that curcumin administered to mice along with the drug decreased the side effects of the drug therapy. Additionally kidney lipid peroxidation was reduced. Curcumin inhibited the H_2O_2 and nitrite induced lipid peroxidation and haemolysis of erythrocytes in vitro.[150,151]

The hepatoprotective action of an alcoholic extract of curcumin against CCl_4-induced liver injury *in vitro*[152] and *in vivo*[153] was tested. Curcumin significantly reduced the urinary excretion of tobacco mutagens, and also enhanced the activity of enzymes to detoxify cigarette smoke mutagens and carcinogens.[154,155] Curcumin also inhibits *in vitro* production of aflatoxins which causes injury to the liver.[156] Probably one of most discussed properties of curcuminoids is their anti-HIV effect demonstrated during *in vitro* and *in vivo* experiments, including a limited number of human studies.[157,158]

Importance of the present investigation

Coordination chemistry of biologically important plant products have gained considerable importance in recent years. This is evident from the numerous reports on medicinal and other aspects of curcuminoids and allied derivatives. However metal complexes of curcuminoids have not received as much attention as they deserve. **The present investigation is mainly on the synthesis and characterization of lanthanide complexes of a series of synthetic curcuminoid analogues. Also included the complexes of dioxouranium(VI) and aluminium(III). The antioxidant activity of these curcuminoids and their metal complexes are also studied in detail.**

LANTHANIDE COMPLEXES OF CURCUMINOIDS

THESIS SUBMITTED
TO THE UNIVERSITY OF CALICUT
IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN THE FACULTY OF SCIENCE

By

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Forwarded

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JULY 2004

PART II

SYNTHESIS, CHARACTERISATION AND ANTIOXIDANT ACTIVITY OF LANTHANIDE COMPLEXES OF 1,7-DIARYLHEPTANOIDS

Extensive literature is available on various aspects of lanthanide complexes of several β-diketones. These complexes include neutral, anionic and mixed ligand systems having different stoichiometry. The importance of metal complexes of naturally occurring β-diketones such as curcuminoids have been detailed in the introduction. In the present investigation lanthanide complexes of a series of synthetic curcuminoids (1,7-diarylheptanoids) have been studied from a structural context. The results are discussed in **chapter 1**. In the actinide series, dioxouranium(VI) formed well-defined complexes with these diarylheptanoids. Aluminium(III) also formed stable complexes with these β-diketones. These results are included separately (**chapter 2** and **3**). The antioxidant activity of the curcuminoids and their metal complexes are presented in **chapter 4**.

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[210] were employed for physical and physico-chemical measurements.

The following metal salts were used for the synthesis of metal complexes: Lanthanide(III) oxides, dioxouranium(VI) acetate and aluminium(III) nitrate.

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-silica gel).

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. 1001 spectronic, Bauch and Lomb spectrophotometer
9. Systronic pH meter
10. Toshniwal conductivity bridge
11. Mettler Toledo STARc thermal analysis system. Model: TGA/SDTA 851e.
12. Gouy type magnetic balance.

Methods

Elemental analysis: Metal complexes were analysed by standard methods.[211] Metal percentages were recorded using atomic absorption spectrophotometer after decomposing them with concentrated sulphuric-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.

Infrared spectra of compounds 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 mkatrix 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.

EI mass spectra were recorded by imparting vapourised sample molecules with a beam of electrons at 70 eV.

TG were recorded in N_2 atmosphere at a flow rate 80 ml/minute.

Emission spectra were measured in DMSO (1×10^{-6} moles/litre) in the range 450-700 nm.

Molar conductance[245] of the complexes were determined in dmf at $28 \pm 1°C$ using solution of about 1×10^{-3} M.

Magnetic susceptibility was determined at room temperature ($28 \pm 1°C$) using $Hg[Co(NCS)_4]$ as standard.[246]

LANTHANIDE COMPLEXES OF CURCUMINOIDS

THESIS SUBMITTED
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By

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CHAPTER I

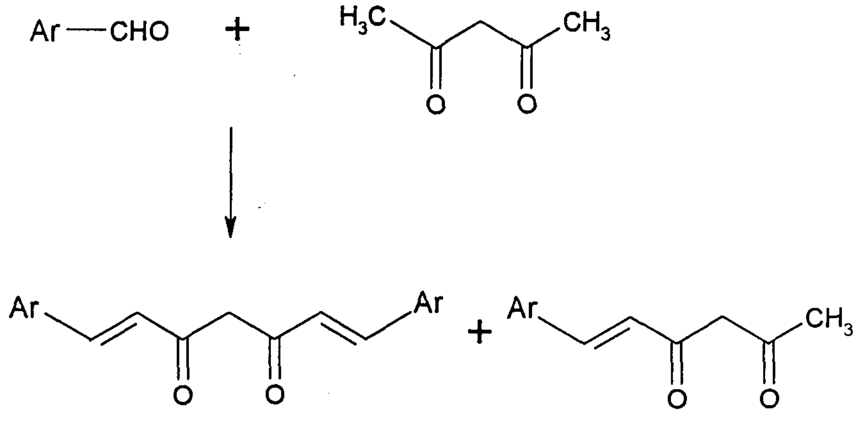
SYNTHESIS AND CHARACTERIZATION OF LANTHANIDE COMPLEXES OF 1,7-DIARYLHEPTANOIDS

SECTION 1

SYNTHESIS AND CHARACTERIZATION OF LANTHANIDE COMPLEXES OF 1,7-DIARYLHEPTANOIDS

Synthesis of 1,7-diarylheptanoids

The 1,7-diarylheptanoids were synthesized through the condensation of aromatic aldehydes with acetylacetone in presence of boric oxide and tri (sec-butyl) borate using n-butylamine as the condensing agent. The reaction leads to the formation of 1,7-diarylheptanoids as the major product along with small amounts of 6-arylhexanoids (Scheme 1.1). Pure 1,7-diarylheptanoids were separated by column chromatography. A typical procedure for the synthesis and purification of the 1,7-diarylheptanoids is outlined below.



Scheme 1.1

Acetylacetone (0.5g, 0.005 mol) and boric oxide (0.25 g, 0.0035 mol) were stirred for ~1h to yield acetyl acetone-boron complex. To this, a solution of aromatic aldehyde (0.01 mol) in dry ethyl acetate (7.5 mL) and tri (sec-butyl) borate (4.6 g, 0.02 mole) were added and stirred while maintaining temperature at about 80°C. n-Butylamine (0.1 mL) was added dropwise to the stirred solution during 40 min. Stirring was continued for ~ 4 h and the solution was set aside overnight. The mixture was again stirred for ~1h by adding hot (~60°C) hydrochloric acid (0.4M, 7.5 mL). The mixture was then extracted with ethyl acetate, the combined extracts were evaporated and the residual paste was stirred with HCl (50%, 10mL) for ~1h. The solid product separated was collected, washed with water and dried in vacuum. The quantitative separation of the 1,7-diarylheptanoid from 6-arylhexanoid were done by column chromatography using silica gel (mesh 60-120) as detailed below.

The solid product obtained was dissolved in minimum quantity of ethyl acetate and placed over a column (2 x 100 cm) densely packed with silica gel. The elution was done by1:5 v/v acetone-chloroform mixture. As the elution proceeds, two bands were developed in the column, a lower band of pale yellow and an upper band of yellow to orange red. The eluate from the lower band and the junction between the two bands were discarded.

The elution was then continued using a 2:1 v/v chloroform – acetone mixture to recover the upper orange-yellow band. The eluates were collected at regular interwals, checked by tlc, and the combined extracts on removing the solvent in vaccum yielded 1,7-diarylheptanoids. The compounds were further purified by recrystallisation from hot benzene.

Synthesis of lanthanide complexes of the 1,7-diarylheptanoids

The complexes of the various curcuminoid analogues with all the trivalent lanthanide series of metal ions except cerium, promethium, holmium and lutetium were prepared by the following general method. The lanthanide oxides (Ln_2O_3) were first dissolved in nitric acid. The solution was evaporated to a small volume, diluted with water and evaporated nearly to dryness to get the lanthanide nitrates. A methanolic solution (25 mL) of the metal nitrate (0.001 mol) was added slowly with stirring to a solution of the 1,7-diarylheptanoid (0.003 mol) in methanol (25 mL). The pH of the reaction mixture was carefully controlled in order to prevent the precipitation of the lanthanide hydroxide. In Table 1 the pH employed for the preparation of complexes along with the pH at which lanthanide hydroxide precipitation occur in aqueous and aq. methanol medium are given. The mixture was stirred for ~12h and concentrated to half the original volume. The precipitated complex on cooling to room temperature was filtered, washed with ethanol and recrystallised from hot methanol. Lanthanum and ytterbium complexes were prepared using their trichlorides.

Table 1

Precipitation pH of lanthanide complexes of curcuminoids

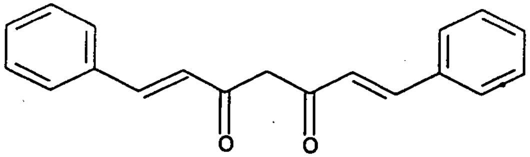
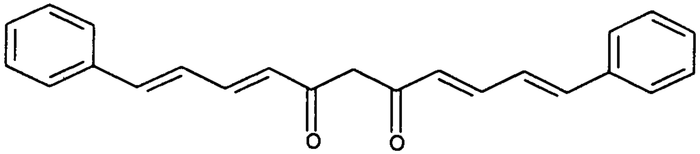
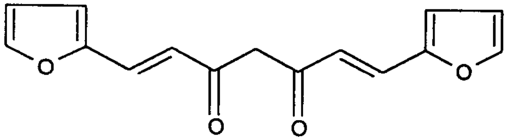
Metal (Ln^{3+}) ion	Precipitation pH of		
	Hydroxide from		Lanthanide complexes
	aqueous solution	1:3 v/v aqueous methanol	
La	7.64	7.56	6.7
Pr	7.52	7.5	6.6
Nd	7.48	7.41	6.6
Sm	6.82	6.78	6.5
Eu	7.40	7.24	6.6
Gd	6.35	6.30	6.5
Dy	7.06	7.08	6.4
Er	6.76	6.68	6.3
Yb	6.31	6.26	6.1
Tb	7.12	7.04	6.4

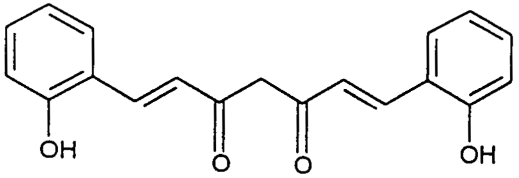
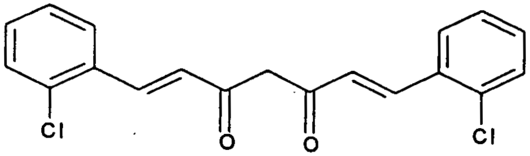
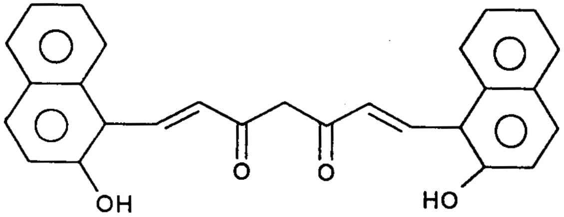
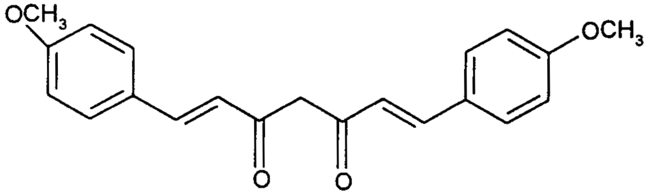
Results and Discussion

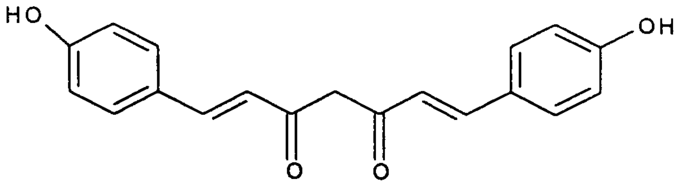
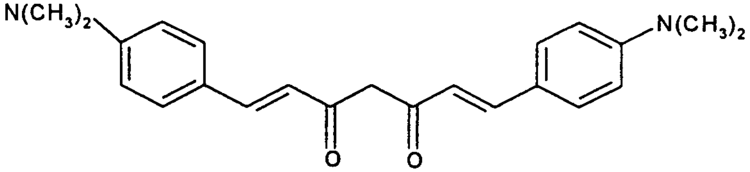
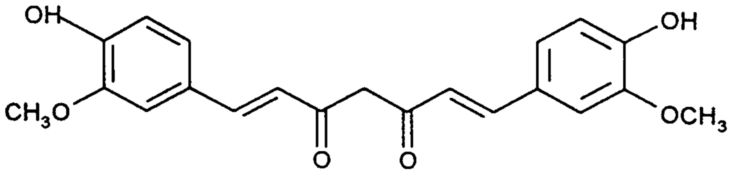
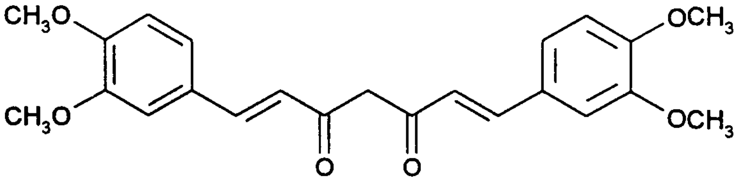
The 1,7-diarylheptanoids synthesized are given in Table 2 along with their systematic name and melting point found and reported. All the compounds are crystalline in nature, show sharp melting point that agree with reported values and further confirmed by mixed melting point determination. Infrared and nmr spectral data of the compounds are in total agreement with the reported values.

Table 2

Systematic name and structure of the 1,7-diarylheptanoids

Compounds	Aldehyde used for synthesis	Structure	Systematic name	M.P (°C) found	MP (°C) reported
1a	Benzaldehyde		1,7-diphenyl-1,6-heptadiene-3, 5 dione	159	160
1b	Cinnamaldehyde		1,1,1-diphenyl-1,3,8,10-undeccatetraene-5,7-dione	162	162
1c	Furfuraldehyde		1,7-difuryl-1,6-heptadiene-3,5-dione	144	145

1d	Salicylaldehyde		1,7-Bis (2-hydroxy phenyl) – 1,6-heptadiene-3,5-dione	120	120
1e	2-chlorobenzaldehyde		1,7-Bis (2-chlorophenyl)-1,6-heptadiene-3,5-dione	90	90
1f	2-hydroxy-naphthaldehyde		1,7-Bis (2-hydroxy napthyl) – 1,6-heptadiene-3, 5-dione	100	101
1g	4-methoxy Benzaldehyde		1,7-Bis (4-methoxyphenyl) – 1,6-heptadiene-3, 5-dione	108	08

1h	4-hydroxy benzal dehyde		1,7-Bis(4-hydroxy phenyl) – 1,6-heptadiene-3, 5-dione	133	132
1i	4-N,N-dimethyl aminobenzaldehyde		1,7-Bis(4-N, N-dimethyl amino phenyl) -1,6-heptadiene-3,5-dione	142	142
1j	4-hydroxy-3 methoxy benzaldehyde (Vanillin)		1,7-Bis(4-hydroxy-3-methoxy phenyl) ?	183	183
1k	3,4-dimethoxy benzaldehyde		1,7-Bis (3,4-dimethoxy phenyl) -1,6-heptadiene-3, 5-dione	216	218

Characterisation of lanthanide chelates of 1,7-diarylheptanoids

All the diarylheptanoids considered in this investigation formed stable crystalline and well defined complexes with the various lanthanide metal ions. They show sharp melting points and are soluble in common organic solvents like chloroform, benzene, dmf, dmso, etc.

The metal content of all the complexes were estimated after igniting to ~ 1000°C and weighed as Ln_2O_3. C, H and N percentages were determined by microanalytic technique. The observed elemental analytical data suggest that the complexes can be formulated into different types as given below.

	Types of complexes	Lanthanide	Ligands used (1a-1k)
1a.	$[LnL_2(Cl)(H_2O)_2]$	La	**1d - 1k**
b.	$[LnL_2(NO_3)(H_2O)_2]$	Pr, Nd, Sm, Gd, Dy, Er, Yb, and Eu	**1d - 1k**
2.	$[LnL_2(NO_3)_2(H_2O)_2]$	Tb	All
3.	$[LnL_3(H_2O)_2]$	La, Pr, Nd, Sm, Gd, Dy, Er, Yb, and Eu	**1a, 1b, 1c**

The C, H, N and metal percentages along with other physical data of $[LnL_2(X)(H_2O)_2]$ type and $[LnL_2(NO_3)_2(H_2O)_2]$ in tables 3-12 and that of $[LnL_3(H_2O)_2]$ in tables 13-19. Only analytically pure complexes are included in the table.

Table 3

Analytical and Characteristic ir spectral data of La(III) chelates of the 1,7-diaryl heptanoids, (HL)

La(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	La	Cl	Chelated ν_{CO}	HOH bending	$\nu_{La\text{-}O}$
1f	207	64.42 (63.26)	4.6 (4.1)	14.08 (13.56)	3.58 (3.46)	1582 (1637)	1628	410 418
Ig	216	58.05 (57.25)	4.99 (4.77)	15.92 (15.78)	4.2 (4.03)	1576 (1618)	1625	408 420
lh	203	56.01 (55.32)	4.36 (4.12)	16.69 (16.85)	4.14 (4.3)	1578 (1616)	1622	412 422
li	198	60.1 (59.2)	5.9 (5.79)	15.03 (14.9)	3.97 (3.8)	1585 (1631)	1629	405 416
lj	218	54.08 (53.37)	4.63 (4.45)	14.89 (14.71)	3.82 (3.75)	1580 (1619)	1628	410 421

*The calculated value corresponds to the $[LaL_2Cl(H_2O)_2]$composition where L stands for the deprotonated ligand HL.

Table 4

Analytical and Characteristic ir spectral data of Pr(III) chelates of the 1,7-diarylheptanoids, HL

Pr(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Pr	Chelated ν_{CO}	HOH bending	ν_{Pr-O}
1e	152	50.1 (49.3)	3.40 (3.24)	1.62 (1.51)	15.48 (15.23)	1581 (1638)	1629	411 420
1f	158	62.11 (61.54)	4.07 (3.99)	1.43 (1.32)	13.52 (13.38)	1587 (1637)	1624	419 457
1g	168	56.28 (55.45)	4.71 (4.62)	1.71 (1.54)	15.83 (15.5)	1583 (1618)	1627	409 417
1h	198	54.0 (53.46)	4.12 (3.99)	1.80 (1.64)	16.71 (16.52)	1586 (1616)	1621	410 418
1i	208	57.92 (57.45)	5.86 (5.62)	4.52 (4.37)	14.80 (14.66)	1582 (1631)	1628	408 417
1j	214	52.08 (51.8)	4.69 (4.32)	1.57 (1.44)	14.73 (14.48)	1576 (1619)	1623	409 419
1k	256	54.02 (53.64)	4.99 (4.86)	1.46 (1.36)	14.02 (13.69)	1581 (1622)	1621	408 420

*The calculated value corresponds to $[PrL_2(NO_3)(H_2O)_2]$ composition where L stands for the deprotonated ligand, HL.

Table 5

Analytical and Characteristic ir spectral data of Nd(III) chelates of the 1,7-diarylheptanoids, (HL)

Nd(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Nd	Chelated ν_{CO}	HOH bending	$\nu_{Nd\text{-}O}$
1e	168	50.0 (49.13)	3.40 (3.23)	1.58 (1.51)	16.08 (15.53)	1588 (1638)	1630	411 418
1f	153	61.52 (61.34)	4.04 (3.97)	1.49 (1.33)	14.06 (13.65)	1586 (1637)	1633	411 420
1g	204	55.68 (55.24)	4.71 (4.60)	1.62 (1.53)	16.08 (15.81)	1583 (1618)	1628	409 417
1h	196	53.92 (53.26)	4.02 (3.97)	1.71 (1.64)	17.05 (16.85)	1584 (1616)	1631	408 417
1i	207	57.68 (57.25)	5.82 (5.6)	4.42 (4.36)	15.06 (14.95)	1584 (1631)	1630	406 418
1j	200	52.34 (51.62)	4.54 (4.30)	1.51 (1.43)	14.99 (14.78)	1581 (1619)	1627	407 416
1k	248	53.96 (53.48)	5.12 (4.84)	1.48 (1.36)	14.12 (13.97)	1584 (1622)	1628	410 421

*The calculated value corresponds to $[NdL_2(NO_3)(H_2O)_2]$ composition where L stands for deprotonated ligand, HL.

Table 6

Analytical and characteristical ir spectra data of the Sm(III) chelates of the 1,7-diarylheptanoids (HL)

Sm(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Sm	Chelated ν_{CO}	HOH bending	ν_{Sm-O}
1f	172	61.42 (60.99)	4.12 (3.95)	1.48 (1.32)	14.62 (14.15)	1586 (1637)	1628	413 420
1g	184	55.14 (54.88)	4.83 (4.57)	1.71 (1.52)	16.74 (16.37)	1583 (1618)	1627	407 417
1h	197	53.12 (52.88)	4.18 (3.94)	1.79 (1.62)	17.85 (17.43)	1599 (1616)	1626	410 421
1i	224	51.72 (51.3)	4.59 (4.28)	1.58 (1.43)	15.74 (15.31)	1584 (1631)	1621	409 420

*The calculated value corresponds $[SmL_2(NO_3)(H_2O)_2]$ composition where L stands for deprotonated ligand.

Table 7

Analytical and Charactersitic ir spectral data of Gd(III) chelates of the 1,7-diarylheptanoids (HL)

Gd(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Sm	Chelated ν_{CO}	HOH bending	ν_{Gd-O}
1e	153	48.86 (48.44)	3.43 (3.19)	1.61 (1.49)	16.98 (16.71)	1583 (1638)	1627	409 419
1j	234	51.38 (50.95)	4.53 (4.25)	1.58 (1.42)	16.21 (15.89)	1589 (1619)	1630	407 418

*The calculated value corresponds to $[GdL_2(NO_3)(H_2O)_2]$ composition where L stands for deprotonated lignad.

Table 8
Analytical and Characteristic ir spectral data of Dy(III) chelates of the 1,7-diarylheptanoids (HL)

Dy(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Dy	Chelated ν_{CO}	HOH bending	$\nu_{Dy\text{-}O}$
1f	222	50.93 (50.68)	4.63 (4.22)	1.62 (1.41)	16.72 (16.34)	1587 (1637)	1627	403 417

*The calculated value corresponds to $(DyL_2(NO_3)(H_2O)_2]$ composition where L stands for deprotonated ligand.

Table 9
Analytical and Characteristic i.r. spectral data of Er(III) chelates of the 1,7-diarylheptanoids (HL)

Er(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Er	Chelated ν_{CO}	HOH bending	$\nu_{Er\text{-}O}$
1d	186	52.03 (51.86)	4.03 (3.87)	1.62 (1.59)	19.38 (9.02)	1588 (1623)	1630	404 416
1e	184	48.12 (47.94)	3.47 (3.15)	1.53 (1.47)	17.84 (17.58)	1581 (1638)	1628	408 417
1f	197	60.67 (60.04)	4.07 (3.89)	1.36 (1.30)	15.94 (15.50)	1586 (1637)	1627	410 419
1g	203	54.12 (53.88)	4.82 (4.49)	1.71 (1.50)	18.14 (17.88)	1576 (1618)	1623	405 415
1h	212	52.21 (51.86)	4.11 (3.87)	1.68 (1.59)	19.64 (19.02)	1586 (1616)	1626	407 418
1i	209	56.23 (55.91)	5.92 (5.47)	4.32 (4.25)	17.23 (16.94)	1583 (1631)	1625	407 420
1j	226	50.92 (50.44)	4.70 (4.2)	1.51 (1.4)	17.11 (16.74)	1589 (1619)	1624	410 418
1k	254	52.92 (52.31)	5.13 (4.74)	1.48 (1.33)	16.31 (15.85)	1581 (1622)	1626	408 419

*The calculated value corresponds to $[ErL_2(NO_3)(H_2O)_2]$ composition where L stands for the deprotonated ligand.

Table 10

Analytical and Characteristic i.r. spectral data of Tb(IV) chelates of the 1,7-diarylheptanoids, (HL)

Tb(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Tb	Chelated ν_{CO}	HOH bending	$\nu_{Tb\text{-}O}$
1a	214	52.96 (52.48)	4.18 (3.91)	3.46 (3.22)	18.73 (18.29)	1586 (1618)	1629	407 420
1f	171	57.69 (57.2)	4.08 (3.71)	20.63 (2.48)	14.71 (14.03)	1587 (1637)	1630	407 417
1j	234	48.17 (47.87)	4.32 (3.99)	2.81 (2.66)	15.73 (15.09)	1584 (1619)	1628	409 419

*The calculated value corresponds to $[TbL_2(NO_3)_2(H_2O)_2]$ composition where L stands for deprotonated ligand.

Table 11

Analytical and Characteristic i.r. spectral data of Eu(III) chelates of the 1,7-diarylheptanoids (HL)

Eu(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Eu	Chelated ν_{CO}	HOH bending	$\nu_{Eu\text{-}O}$
1d	186	52.92 (52.78)	4.14 (3.93)	1.73 (1.62)	17.79 (17.59)	1586 (1623)	1628	406 416
1f	194	61.13 (60.90)	4.12 (3.95)	1.52 (1.32)	14.53 (14.28)	1584 (1637)	1629	409 417
1g	183	54.99 (54.78)	4.79 (4.57)	1.71 (1.52)	16.83 (16.51)	1579 (1618)	1631	407 416
1h	198	52.96 (52.78)	4.12 (3.93)	1.83 (1.62)	17.62 (17.34)	1581 (1616)	1630	405 413
1j	214	51.53 (51.22)	4.62 (4.27)	1.61 (1.43)	15.71 (15.28)	1583 (1619)	1629	406 419

* The calculated value corresponds to $[EuL_2(NO_3)(H_2O)_2]$ composition where L stands for deprotonated ligand.

Table 12

Analytical and Characteristic i.r. spectral data of Yb(III) chelates of the 1,7-diarylheptanoids (HL)

Yb(III) Complexes of	MP (°C)	Elemental Analysis % (Found/ Calculated*)				Characteristic ir absorption bands (cm^{-1})		
		C	H	N	Yb	Chelated ν_{CO}	HOH bending	$\nu_{Yb\text{-}O}$
1f	182	59.99 (59.72)	3.98 (3.87)	1.52 (1.29)	16.13 (15.95)	1587 (1637)	1631	403 417
1g	174	53.92 (53.55)	4.63 (4.46)	1.62 (1.49)	18.52 (18.39)	1583 (1618)	1628	405 416
1h	201	51.79 (51.52)	3.99 (3.84)	1.79 (1.58)	19.83 (19.55)	1580 (1616)	126	407 419
1j	242	50.43 (50.15)	4.32 (4.18)	1.52 (1.39)	17.48 (17.22)	1583 (1619)	1629	406 417

* The calculated value corresponds to [$YbL_2(NO_3)$ $(H_2O)_2$] composition where L stands for deprotonated ligand.

Table 13

Analytical and Characteristic i.r. spectral data of La(III) chelates of 1,7-diarylheptanoids, (HL)

La(III) Complexes of	MP (°C)	Elemental analysis %, (Found/calculated*)			Characteristic ir absorption bands (cm^{-1})		
		C	H	La	Chelated ν_{CO}	HOH bending	$\nu_{La\text{-}O}$
1a	247	76.43 (76.01)	5.89 (5.44)	15.69 (15.44)	1579 (1618)	1629	407 418
1b	254	72.92 (72.26)	5.81 (5.32)	12.71 (12.12)	1591 (1621)	1632	408 417
1c	242	57.94 (57.45)	4.12 (3.74)	15.12 (14.78)	1592 (1624)	1627	406 418

*The calculated value corresponds to [$LaL_3(H_2O)_2$] composition where L stands for deprotonated ligand.

Table 14

Analytical and characteristic ir spectral data of Pr(III) chelates of the 1,7-diarylheptanoids (HL)

Pr(III) Complexes of	MP (°C)	Elemental analysis %, (Found/calculated*)			Characteristic ir absorption bands (cm^{-1})		
		C	H	Pr	Chelated ν_{CO}	HOH bending	ν_{Pr-O}
1a	248	8.59 (68.27)	5.03 (4.89)	14.72 (14.06)	1587 (1618)	1626	405 412
1b	254	(72.13)	(5.31)	(12.27)	1591 (1621)	1630	409 417
1c	238	57.74 (57.33)	5.74 (5.2)	15.28 (14.96)	1583 (1624)	1629	407 411

*The calculated value corresponds to $[PrL_3(H_2O)_2]$ composition where L stands for deprotonated ligand.

Table 15

Analytical and Characteristic i.r. spectral data of Nd(III) chelates of the 1,7-diaryl heptanoids (HL)

Nd(III) Complexes of	MP (°C)	Elemental analysis %, (Found/calculated*)			Characteristic ir absorption bands (cm^{-1})		
		C	H	Nd	Chelated ν_{CO}	HOH bending	ν_{Nd-O}
1a	262	68.82 (68.04)	5.14 (4.87)	14.92 (14.35)	1595 (1618)	1639	407 418
1b	256	72.42 (71.91)	5.83 (5.3)	12.92 (12.53)	1591 (1621)	1633	406 419
1c	243	57.88 (57.13)	5.89 (5.18)	15.92 (15.26)	1597 (1624)	1632	407 418

*The calculated value corresponds to $[NdL_3(H_2O)_2]$ composition where L stands for deprotonated ligand.

Table 16

Analytical data and Characteristic ir spectral data of Gd(III) chelates of the 1,7-diaryl heptanoids (HL)

Gd(III) Complexes of	MP (°C)	Elemental analysis %, (Found/calculated*)			Characteristic ir absorption bands (cm^{-1})		
		C	H	Gd	Chelated ν_{CO}	HOH bending	$\nu_{Gd\text{-}O}$
1a	274	67.92 (67.17)	5.24 (4.81)	15.94 (15.44)	1578 (1618)	1626	406 414
1c	268	56.93 (56.35)	4.18 (3.86)	16.97 (6.41)	1588 (1624)	1632	409 420

*The calculated value corresponds to [$GdL_3(H_2O)_2$] composition where L stands for deprotonated ligand.

Table 17

Analytical and Characteristic ir spectral data of Dy(III) chelates of 1,7-diaryl heptanoids (HL)

Dy(III) Complexes of	MP (°C)	Elemental analysis %, (Found/calculated*)			Characteristic ir absorption bands (cm^{-1})		
		C	H	Dy	Chelated ν_{CO}	HOH bending	$\nu_{Dy\text{-}O}$
1a	276	67.24 (66.83)	5.18 (4.79)	16.04 (15.88)	1590 (1618)	1639	411 417
1b	263	71.32 (70.8)	5.91 (5.22)	14.44 (13.89)	1584 (1621)	1630	407 419
1c	249	56.89 (56.05)	4.13 (3.84)	17.24 (16.87)	1591 (1624)	1629	405 417

*The calculated value corresponds to [$DyL_3(H_2O)_2$] composition where L stands for deprotonated ligand.

Table 18

Analytical and Characteristic ir spectral data of Er(III) chelates of 1,7-diaryl heptanoids (HL)

Er(III) Complexes of	MP (°C)	Elemental analysis %, (Found/calculated*)			Characteristic ir absorption bands (cm^{-1})		
		C	H	Er	Chelated ν_{CO}	HOH bending	ν_{Er-O}
1a	279	67.02 (66.52)	5.14 (4.77)	16.98 (16.27)	1584 (1618)	1639	409 417
1b	254	70.98 (70.51)	5.64 (5.19)	14.68 (14.24)	1582 (1621)	1629	411 422
1c	273	56.13 (55.77)	4.17 (3.82)	17.91 (17.27)	1588 (1624)	1632	412 420

* The calculated value corresponds to [$ErL_3(H_2O)_2$] composition where L stands for deprotonated ligand.

Table 19

Analytical and Characteristic ir spectral data of Yb(III) chelates of 1,7-diaryl heptanoids (HL)

Yb(III) Complexes of	MP (°C)	Elemental analysis %, (Found/calculated*)			Characteristic ir absorption bands (cm^{-1})		
		C	H	Yb	Chelated ν_{CO}	HOH bending	ν_{Yb-O}
1b	224	69.32 (69.11)	5.48 (5.26)	14.68 (14.44)	1581 (1618)	1630	407 419

*The calculated value corresponds to [$YbL_3(H_2O)_3$ composition, where L stands for deprotonated ligand.

All the complexes are non ionic in dmf. The lanthanum complexes are diamagnetic. The observed magnetic moment data of all other complexes agree with the tripositive oxidation state of the metal ion except for terbium. In the case of terbium, the metal ion appeared to be in Tb^{4+} oxidation state. This is expected in view of the stability of the f^7 electronic configuration of Tb^{4+}. The μ_{eff} values of the lanthanide complexes of all the diaryl heptanoids are well within the range expected. The observed data are in the range as given in Table 20.

Table 20

The observed magnetic moment values of the lanthanide complexes of the curcuminoids

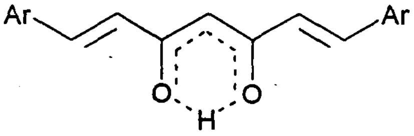
Lanthanide ion	Magnetic moment (μ_{eff}) in B.M.
La	diamagnetic
Pr	3.26 – 3.30
Nd	3.20 – 3.28
Sm	2.1 – 2.05
Eu	3.75 – 3.80
Gd	7.80 – 7.90
Dy	9.60 – 9.75
Er	9.18 – 9.24
Yb	4.18 – 4.25
Tb	7.80 – 7.90

The structure and nature of bonding of the complexes are discussed based on their ir, nmr and mass spectral data.

Infra red spectra

Infrared spectra is one of the most important tool available for establishing the structure and nature of bonding of metal complexes of organic molecules. This is particularly true in the case of metal complexes of β-diketones.[37-40,209] In β-diketones, the most important functional group available for characterization is the carbonyl groups. The carbonyl absorptions are sensitive to both chemical and physical effects, and due allowances must be made in assigning the likely position of ν_{CO} in a given structure. Many factors are involved in determining the precise frequency of a given carbonyl group. These include not only those such as inductive, resonance and field effects, which alter the force constant of the carbonyl bond but also physical features such as mass and angle effects, vibrational coupling and changes in the adjacent bonds. Phase changes, solvent effects, hydrogen bonding and extended conjugation also play significant role in determining the exact position and nature of the CO stretching band.

From ir spectral data, it has been well demonstrated[64] that the curcuminoids exist predominantly in the intramolecularly hydrogen bonded enol form 1. Thus the ir spectra of all the curcuminoids show an intense band at ~ 1620 cm^{-1}. This band has been assigned as due to the stretching of the strong intramolecularly hydrogen bonded diketo function of the structure **1**.



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Compared to other β-diketones such as acetylacetone, benzoylacetone, dibenzoylmethane, etc. the υ_{CO} of curcuminoids appear appreciably at very low frequency due to the extended conjugation, present in these type of compounds. That the compound exist in the intra molecularly hydrogen bonded structure **1** is also evident from the presence of a broad band in the region 2500 – 3500 cm^{-1} due to the O . . . H . . . O group of the enol form.

Infrared spectra of metal β-diketonates of the type $M(dik)_2$ and $M(dik)_3$ have been studied extensively.[247] Theoretical band assignments based on normal co-ordinate analysis of 1:1, 1:2 and 1:3 models of various acetyl acetonate complexes were also reported. In general, upon complexation the ν_{CO} frequency of the diketo group decrease appreciably to low values and additional bands due to $\upsilon_{M\text{-}O}$ appear in the low frequency region of the spectra of the complexes.

Although the complexes of curcuminoids obtained in the present study differ in their molecular formulae, all the complexes contain at least two ligand molecules. Therefore, the ir spectra of the complexes should exhibit certain similar features particularly in the double bond region. The recorded spectra of the complexes in the 1500-1800 cm^{-1} region display several common bands. The ν_{CO} band of the free ligand due to the intramolecularly hydrogen bonded diketo function disappeared in the spectra of all the complexes. Instead a new band appeared at ~ 1580 cm^{-1} assignable to metal bonded carbonyl group. This indicate the replacement of the chelated proton by metal ion. Spectra of the free ligands in the region 2500-4000 cm^{-1} is appreciably broadened due to the intra molecularly hydrogen bonded nature of the enolic form as in structure **1**. However well defined bands are present in the range 2900-3100 cm^{-1} assignable to various $\nu_{C\text{-}H}$ vibrations.

In the spectra of all the metal complexes, the intensity and breadth of the band in the 2500-3100 cm^{-1} region increased appreciably. This indicate the presence of different types of O-H vibrations in the molecule. Considering the fact that the enol proton is replaced by metal ion thereby eliminating the possibility of hydrogen bonding of the enol group, the observed nature of the broad band in the X-H region can only arise as due to the presence of H_2O molecules. Thus it can be presumed that the X-H region of the ir spectra strongly support the presence of H_2O molecules in the complexes thereby justifying their formulation.

A common characteristics of the spectra of all the complexes is the presence of two or more weak but prominent band in the range 1630-1660 cm^1. This region in the case of 1,3-dicarbonyl compounds and their metal complexes is usually associated with the stretching of free or metal bonded carbonyl function. But from the observed breadth and intensity, these band cannot be assigned to the carbonyl function of the compounds under investigation. Several studies on the ir spectra of lanthanide complexes of β-diketones revealed that complexes contain both co-ordinated and hydrated H_2O show characteristic absorption in the range 1630-1680 cm^{-1} due to H-OH bending. This observation has been well confirmed in the case of several hydrated lanthanide complexes of β-diketones.[64,247] Thus the observed bands in the region 1630 – 1660 cm^{-1} in the case of the complexes under study can safely be assigned to HOH bending of the water molecules present in the compounds. The observed broadness of the band in the region 2500 – 4000 cm^{-1} can also be accounted by the presence of both inter and intra molecular hydrogen bonding of different types although it is not possible to distinguish them.

Spectra of the compouns in the low frequency region show several new bands not found in the respective ligand spectra. These bands can be assigned to various υ_{M-O} vibrations. Characteristic ir spectral bands of the complexes are given in tables 3-19.

A comparison of the spectra of the three types of complexes in the different regions revealed conclusive evidences regarding their formulation. These aspects of the spectra of the complexes are discussed below separately.

Spectra of $[LnL_2X(H_2O)_2]$

Presence of coordinated water molecules in these types of complexes is clearly indicated from the appearance of bands assignable to H-OH bending ~ 1630 cm^{-1}. The origin of the broad band in the region 2500-3800 cm^{-1} in the spectrum of these complexes can be explained as due to the existence of both inter and intra molecular hydrogen bonding.

In the far ir region, spectra of complexes where $X = Cl^-$ (for eg. $[LaL_2Cl(H_2O)_2]$, displayed medium intensity band at 350 cm^{-1}. These bands are not present in the spectra of complexes where $X = NO_3^-$. Therefore these bands in the chloro complexes are undoubtedly due to υ_{M-Cl} vibrations.

The spectra of $[LnL_2(NO_3)\ (H_2O)_2]$ type of complexes have several characteristic features not observed in the spectra of other types of complexes. The presence of nitrate ion is clearly indicated in the ir spectra of these types of complexes. Nitrate ion can show a variety of bonding modes towards metal ions. It may be unidentate, symmetric or unsymmetric chelating bidentate or bridging bidentate. Though symmetry of the nitrate ion differs very little among these different structures, unidentate and bidentate bonding are easily distinguishable from ir spectra. Unidentate and bidentate chelating nitrates generally show three bands as follows.

	Unidentate (cm^{-1})	Bidentate Chelating (cm^{-1})
$\nu_a (NO_2)$	~ 1420	~1290
$\nu_s (NO_2)$	~ 1305	~1025
$\nu_{N=O}$	~ 1010	~1475

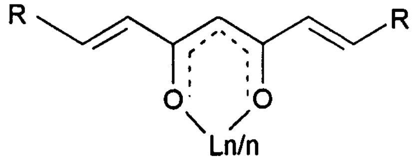
The separation of the two highest frequency bands is less for unidentate (~115 cm^{-1}) than for bidentate (~185 cm^{-1}).

The spectra of the lanthanide complexes of the type considered show two medium intensity bands at ~1300 cm^{-1} and ~1020 cm^{-1} assignable respectively to the asymmetric and symmetric stretching of NO_3 group. The separation between these two bands is found to be ~180 cm^{-1} indicating that the NO_3 group bonded as a chelating bidentate ligand. Further the bidentate chelation of NO_3^- is evident from the presence of a band at ~ 1470 cm^{-1} in the spectrum of all the complexes.

Spectra of [$LnL_3 (H_2O)_2$ complexes

The finger print region of the spectra of this type of complexes differ appreciably from the spectra of other types of complexes. All the spectra show prominent weak bands in the range 1630-1640 cm^{-1} assignable to the H-O-H bending mode of H_2O. The spectra in the X-H region also support the presence of H_2O in the complexes. The slightly broadened band in the region 2500-3800 cm^{-1} correspond to the stretching of O-H group of hydrogen bonded water molecules, probably intermolecular hydrogen bonding. The stretching of various C-H vibrations below the broad band are clearly indicated in the spectra. Absence of any band assignable to coordinated nitrate or chloro groups clearly support the 1:3 metal ligand stoichiometry of the complex.

Thus the formulaticn of different types of complex species of lanthanides with curcuminoids are easily distinguishable from ir spectra. Further the spectral data strongly support the monobasic bidentate coordination of the 1,7-diarylheptanoids as in structure 2.



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NMR spectra

The ^{1}H nmr spectra of only typical diamagnetic complexes were obtained. Representative spectra of all the four types of complexes appear to be very similar in the nature and position of various proton resonance signals. All the spectra clearly indicated the presence of H_2O in the complexes. A comparison of the spectra of the complexes with those of the ligands revealed several interesting information regarding the nature of bonding of the various ligand species in the complex. The low field signal due to the enolic proton of the free ligand at $\delta\sim16$ ppm disappeared in the spectra of all the complexes. This indicate the replacement of the enolic proton by metal ion as in structure 2. From comparison, the reported spectrum of **1f** and the spectrum of its lanthanum complex are given in figures 2 & 3. In the spectrum of complexes of the curcuminoids containing OH groups in the aryl ring, (Fig. 3) the phenolic proton signals remained almost unaffected indicating that only the enolic proton of the ligand is involved in complexation. This observation confirm to the monobasic bidentate coordination of the ligands in their metal complexes. The integrated intensities of the various protons especially the methylene and alkenyl protons agree well with the formula.

Mass spectra

The FAB mass spectra of representative complexes of all the three types have been obtained. These spectra unequivocally support the

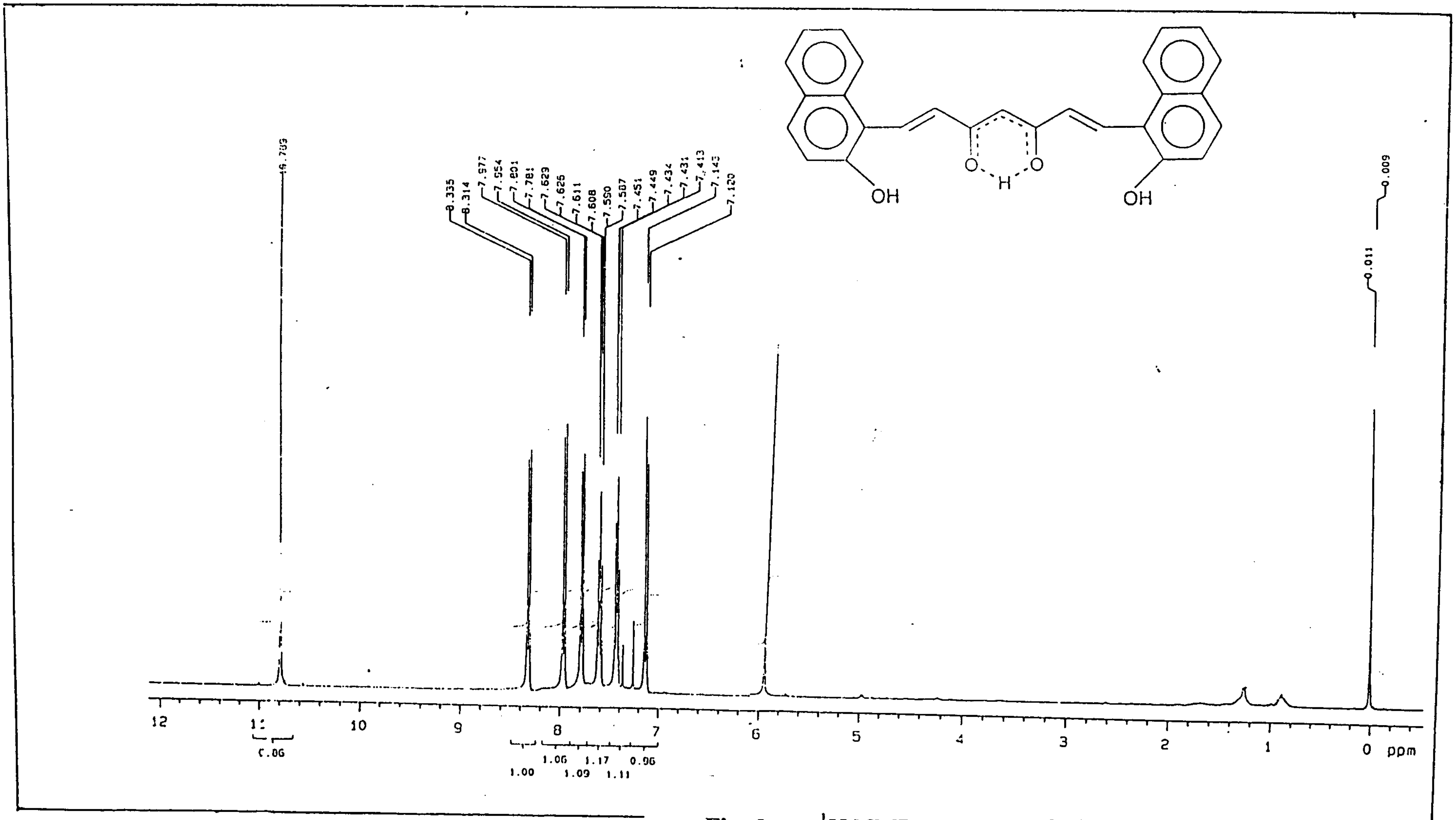

Fig. 2. ^{1}H NMR spectrum of **1f**

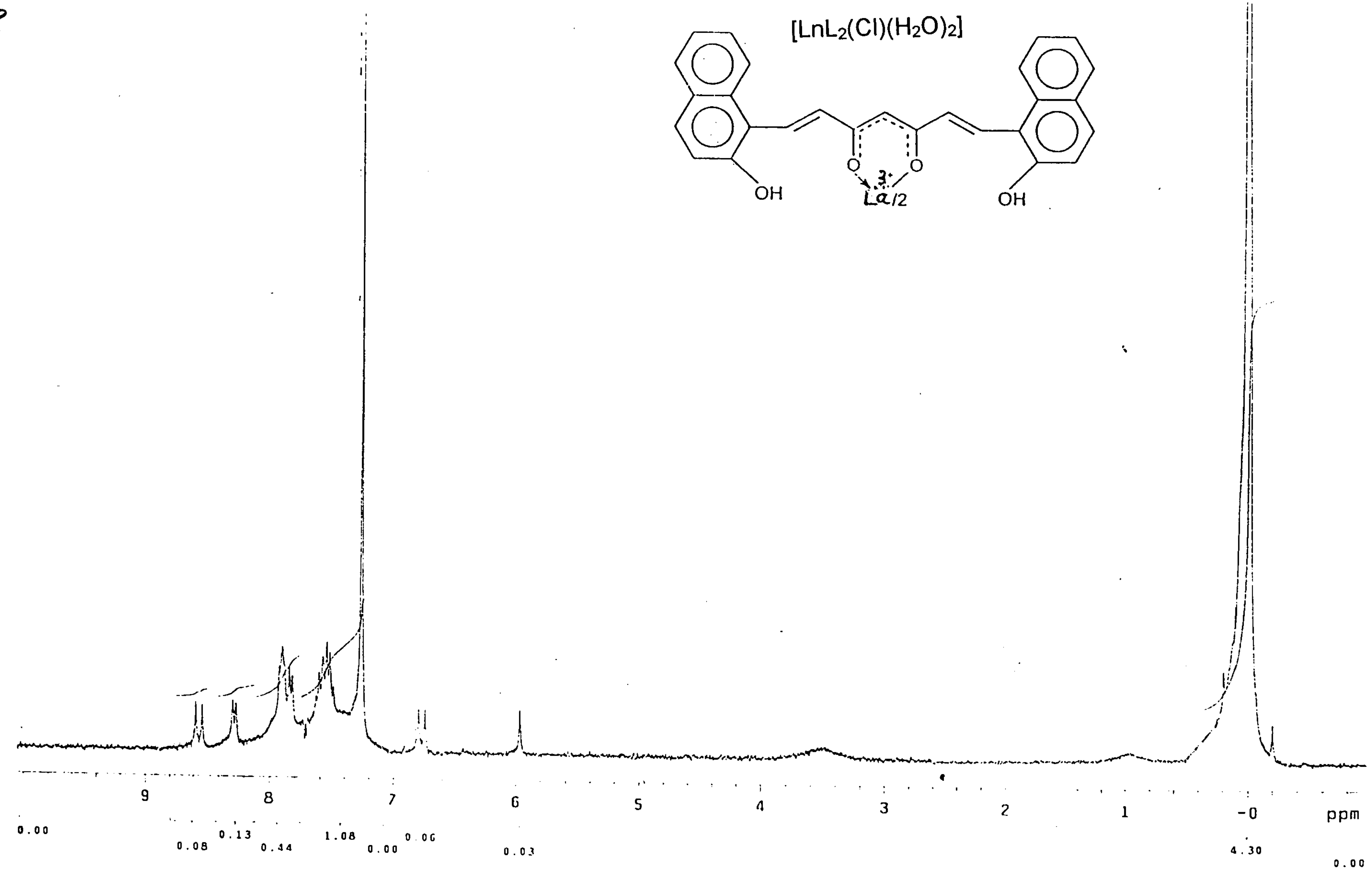

Fig. 3. ^{1}H NMR spectrum of Lanthanum(III) complex of **1f**

formulation of all the complexes of lanthanides with curcuminoids. Therefore the different types are discussed separately.

Mass spectra of $(LnL_2Cl\ (H_2O)_2$

The spectra of $[LaL_2Cl(H_2O_2]$ where L = **1j** and **1f** is represented in figures 4 & 5. The spectrum shows a prominent peak at m/z 873 which correspond to $(LnL_2]^+$, whereas the spectrum of $[LaL_2Cl(H_2O)_2]$ where L = **1f** shows two peaks at 988 and 990 with relative intensity of 2:1. The origin of these peaks can be traced as due to the $[LaL_2Cl]^+$ ion. The observed intensity of these peaks correspond to the isotopic abundance of ^{35}Cl and ^{37}Cl. Other prominent peaks in the spectrum are due to the ligand fragments.

Spectra of $[LnL2(NO_3)_2(H_2O)_2]$

The spectrum of $[TbL_2(NO_3)_2]$ where L = lj is given in figure 6. The spectrum shows a comparatively intense peak at m/z 1017. No other peak is present within ± 6 mass unit. This corresponds to the m/z of $[TbL_2(NO_3)_2]^+$ ion thereby confirming the formulation of the complexes since the natural abundance of ^{159}Tb is 100%. However an intense peak observed at m/z 905 corresponds to $[TbL_2]$. Other important peaks are due to the elimination of ligand substituents and fragments from the parent ion. Thus all spectral data support the Tb^{4+} oxidation state in its complexes.

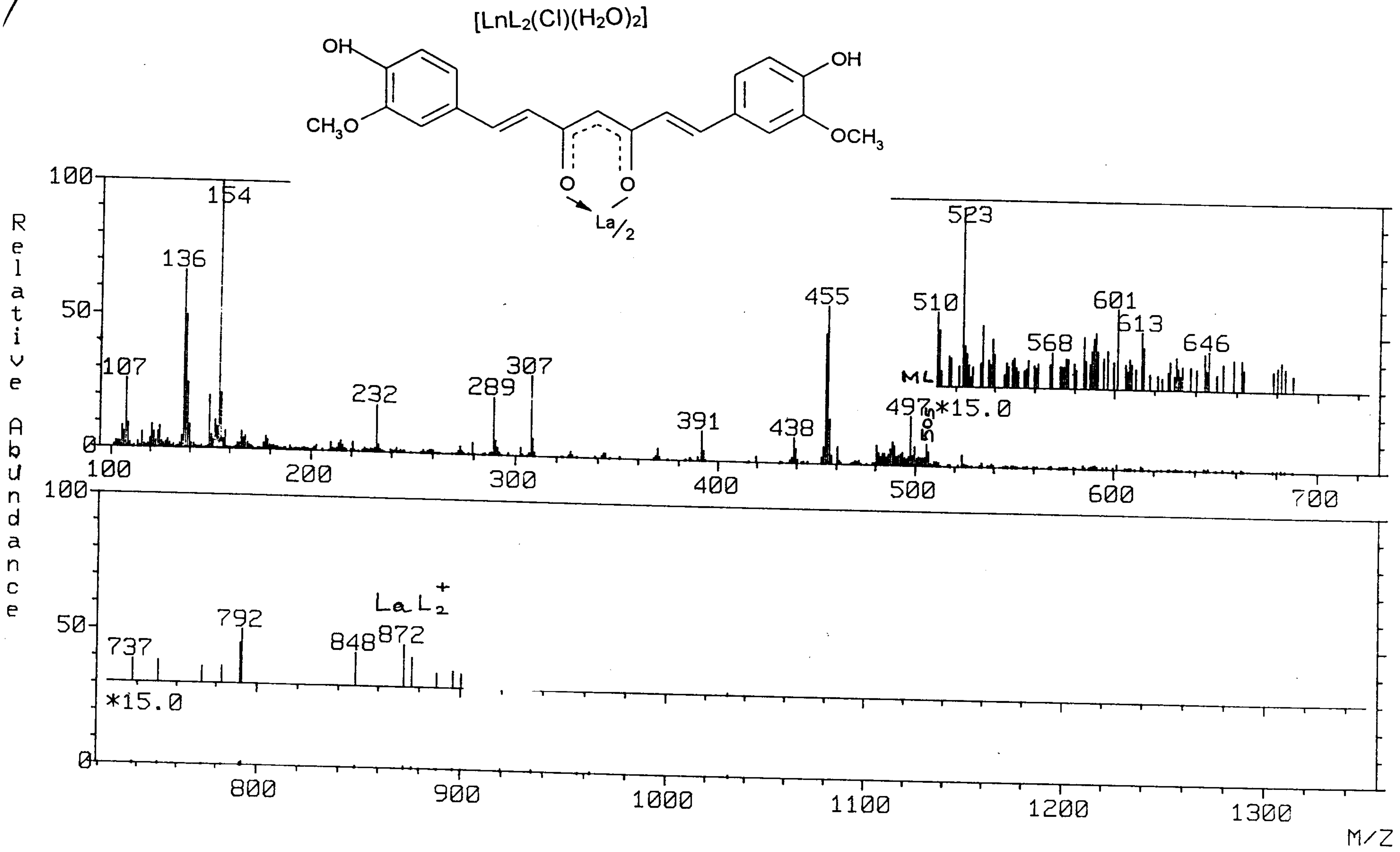

Fig. 4. Mass spectrum of Lanthanum(III) complex of **1j**

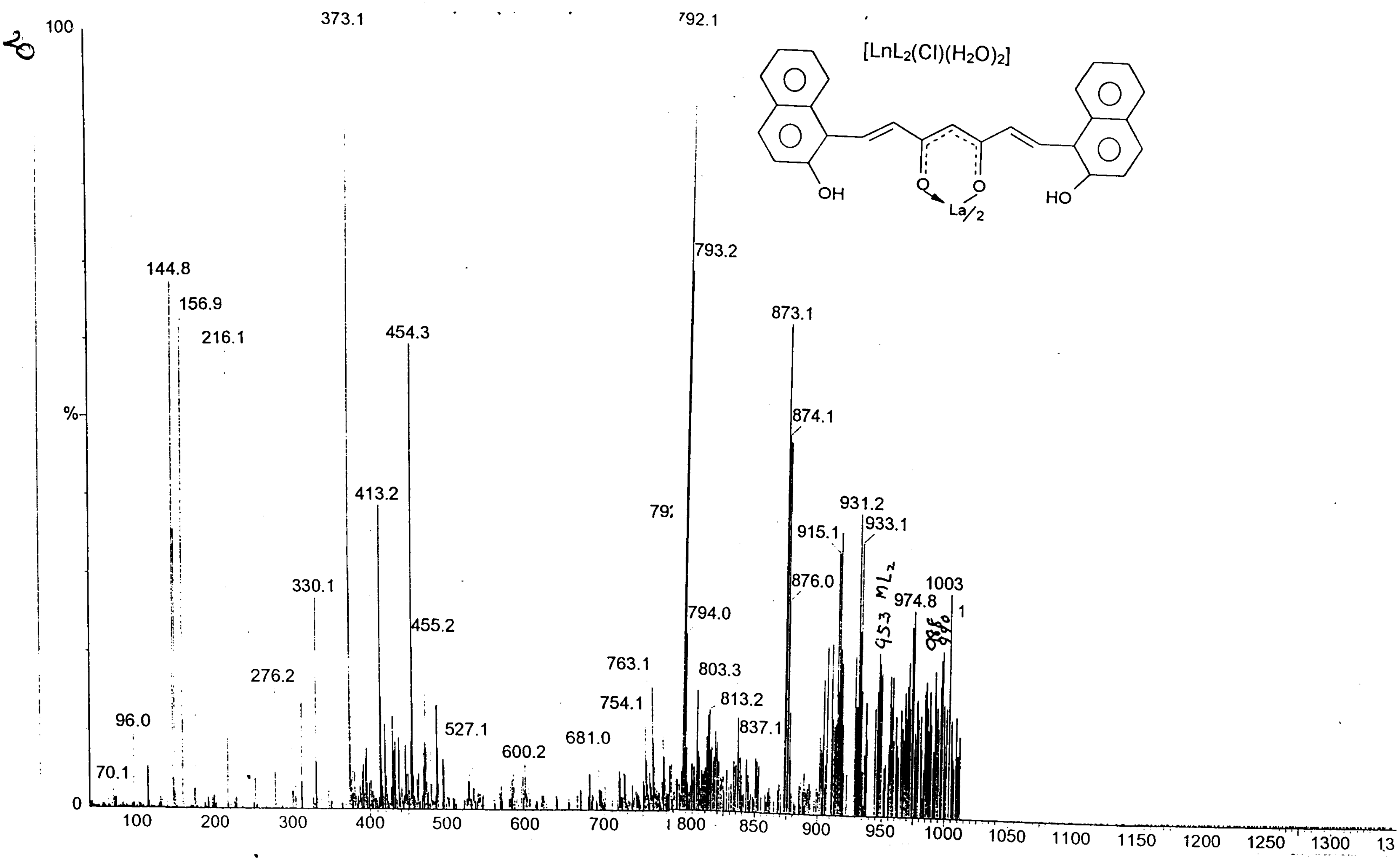

Fig. 5. Mass spectrum of Lanthanum(III) complex of **1f**

$[LnL_2(NO_3)_2(H_2O)_2]$

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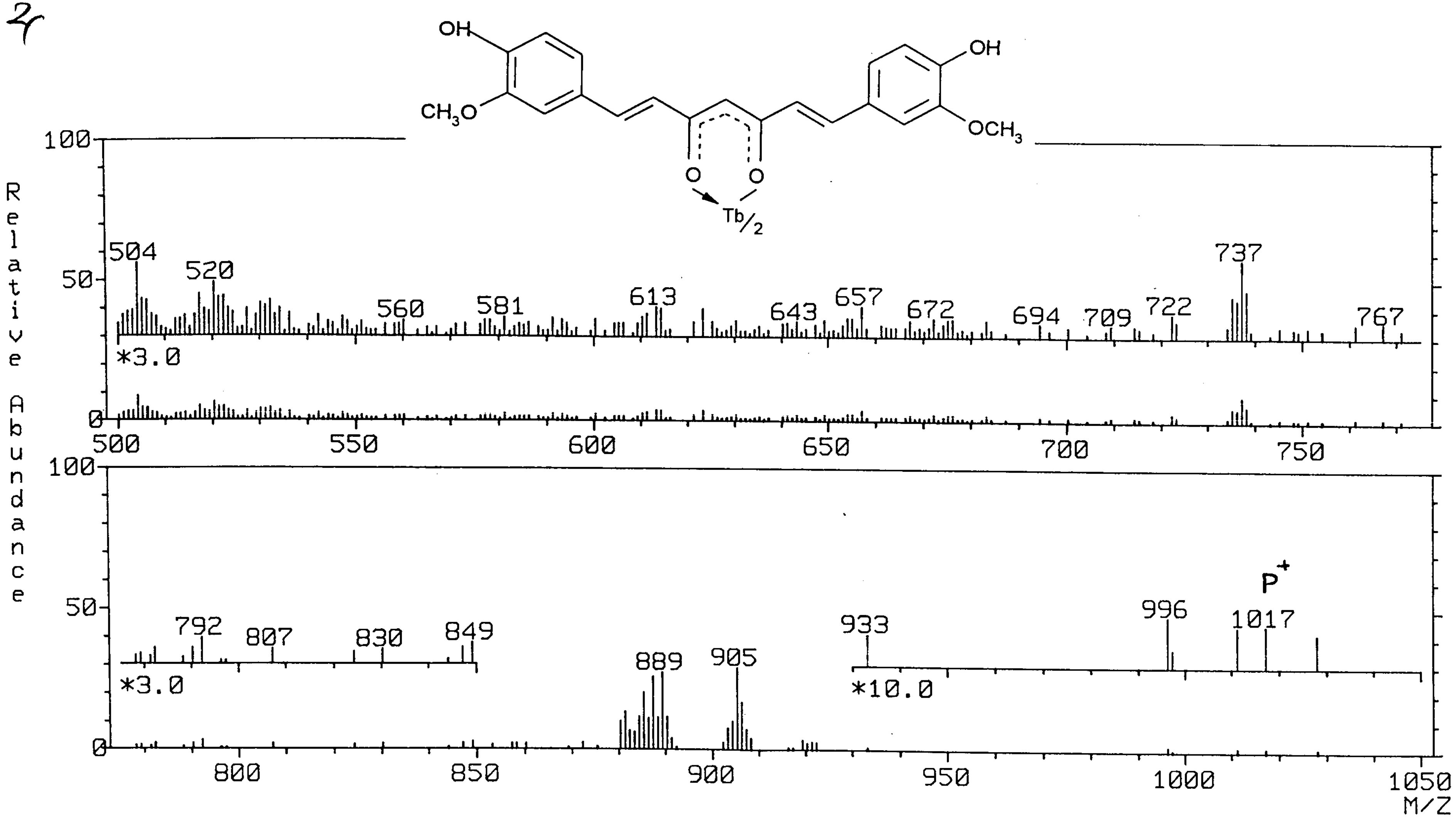

Fig. 6. Mass spectrum of Terbium(IV) complex of **1j**

Spectra of [$LnL_2(NO_3)(H_2O_2$]

Spectra of typical complexes of this group are given in figures 7-12. All the spectra show peaks corresponding to [$LnL_2(NO_3)]^+$and [$LnL_2]^+$ in the expected isotopic abundance of the metal. Other prominent peaks are due to ligand fragments.

Spectra of [$LnL_3(H_2O)_2$]

The analytical data of complexes of **1a**, **1b** and **1c** correspond to ML_3 stoichiometry. This was further confirmed from the mass spectrum of neodymium complex of **1b**. The spectrum revealed the presence of a peak due to LnL_3 stoichiometry at m/z 1122 (Figure 13). The spectrum also contains intense peaks due to ML_2^+, ML^+, etc. ions.

$[LnL_2(NO_3)(H_2O)_2]$

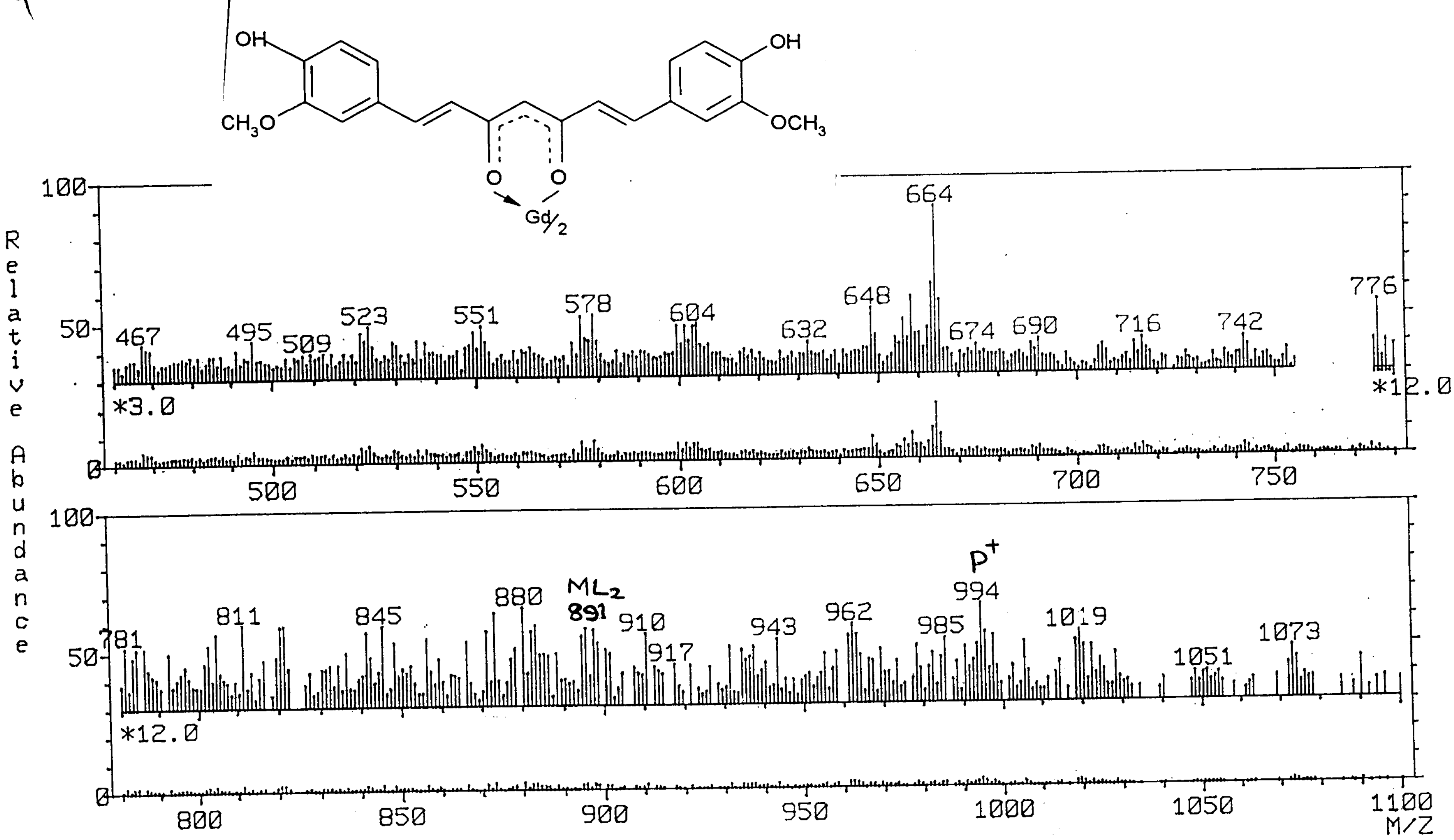

Fig. 7. Mass spectrum of Gadolinium(III) complex of **1j**

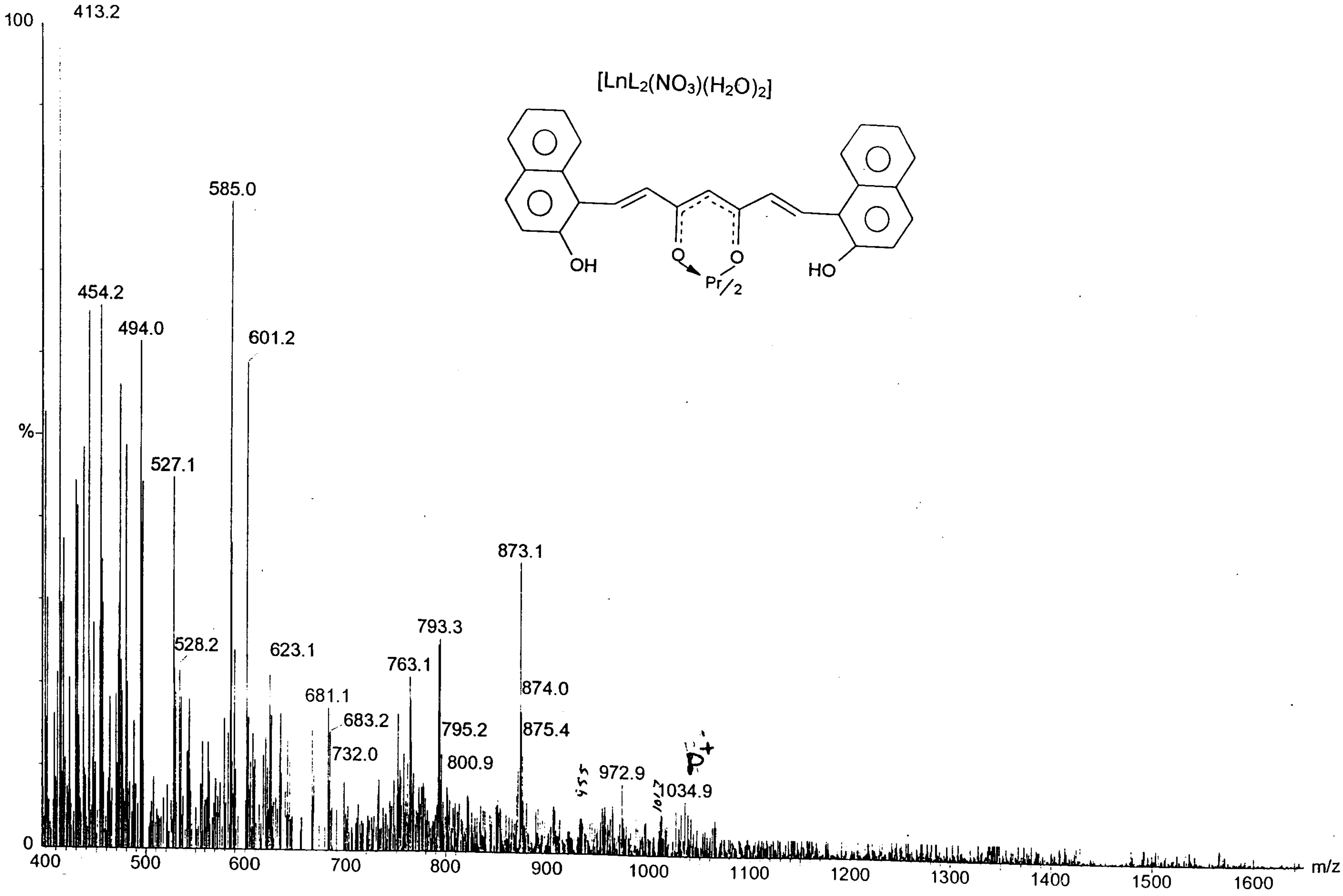

Fig. 8. Mass spectrum of Praseodymium(III) complex of **1f**

$[LnL_2(NO_3)(H_2O)_2]$

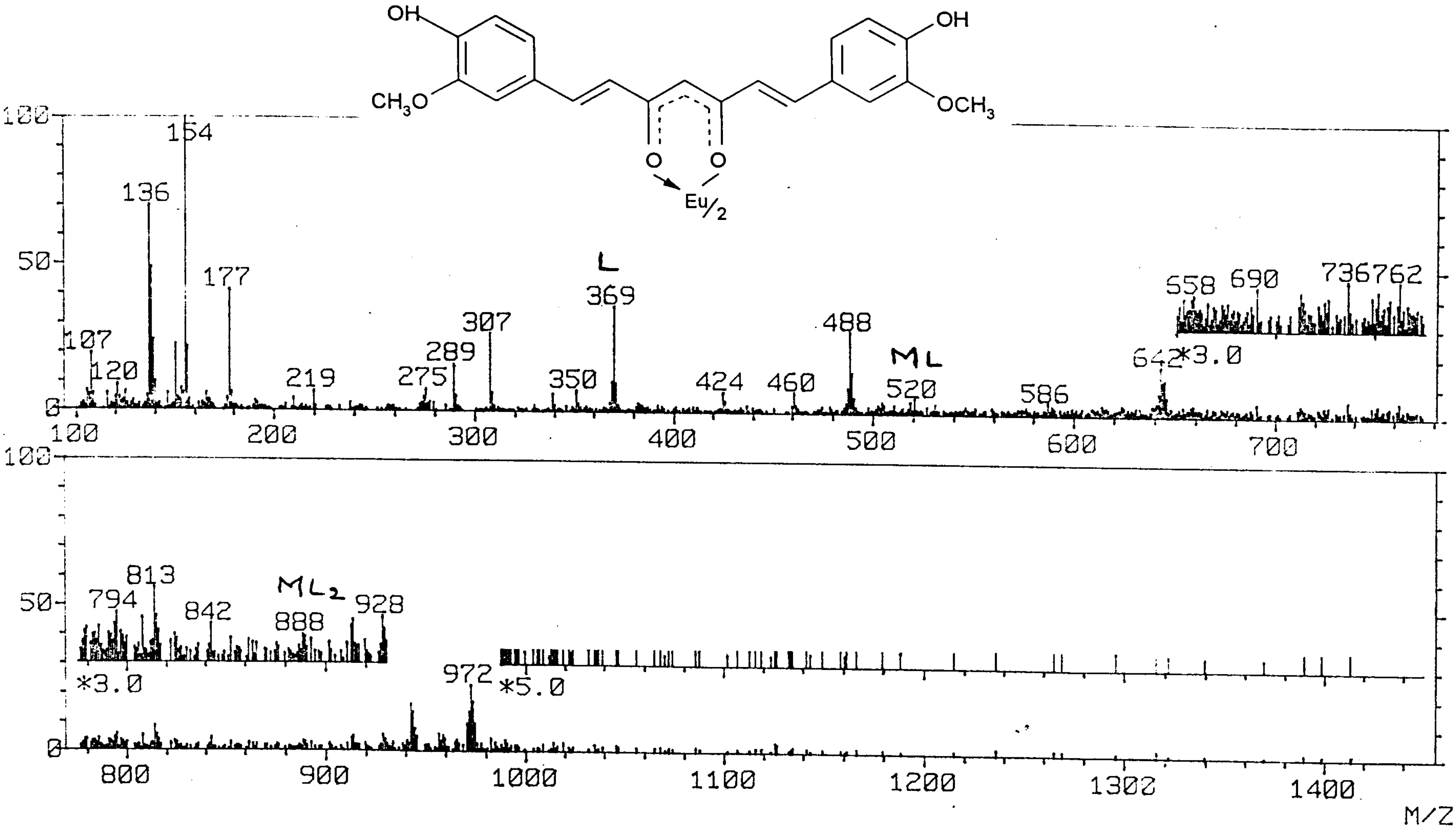

Fig. 9. Mass spectrum of Europium(III) complex of **1j**

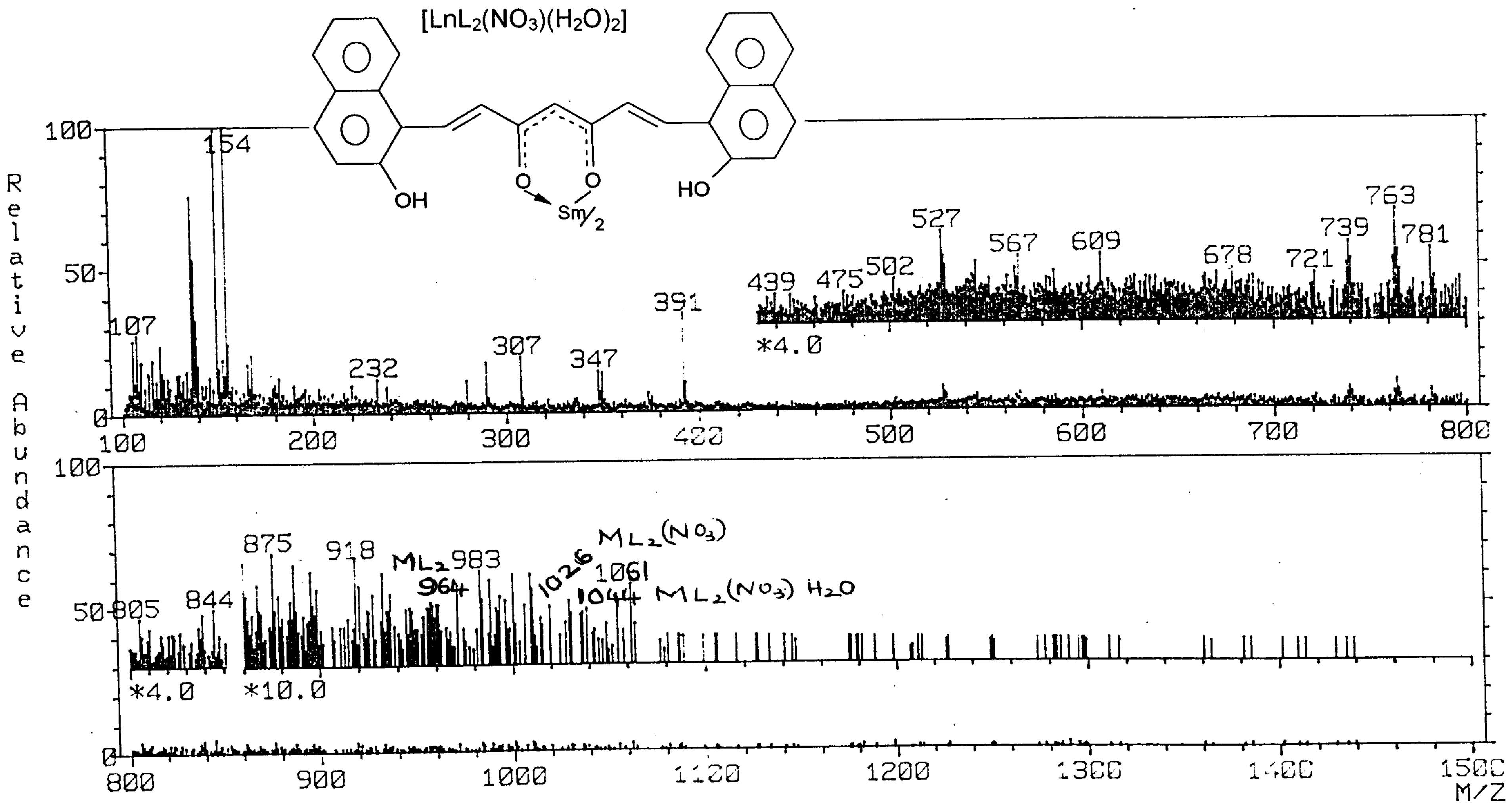

Fig. 10. Mass spectrum of Samarium(III) complex of **1f**

[$LnL_2(NO_3)(H_2O)_2$]

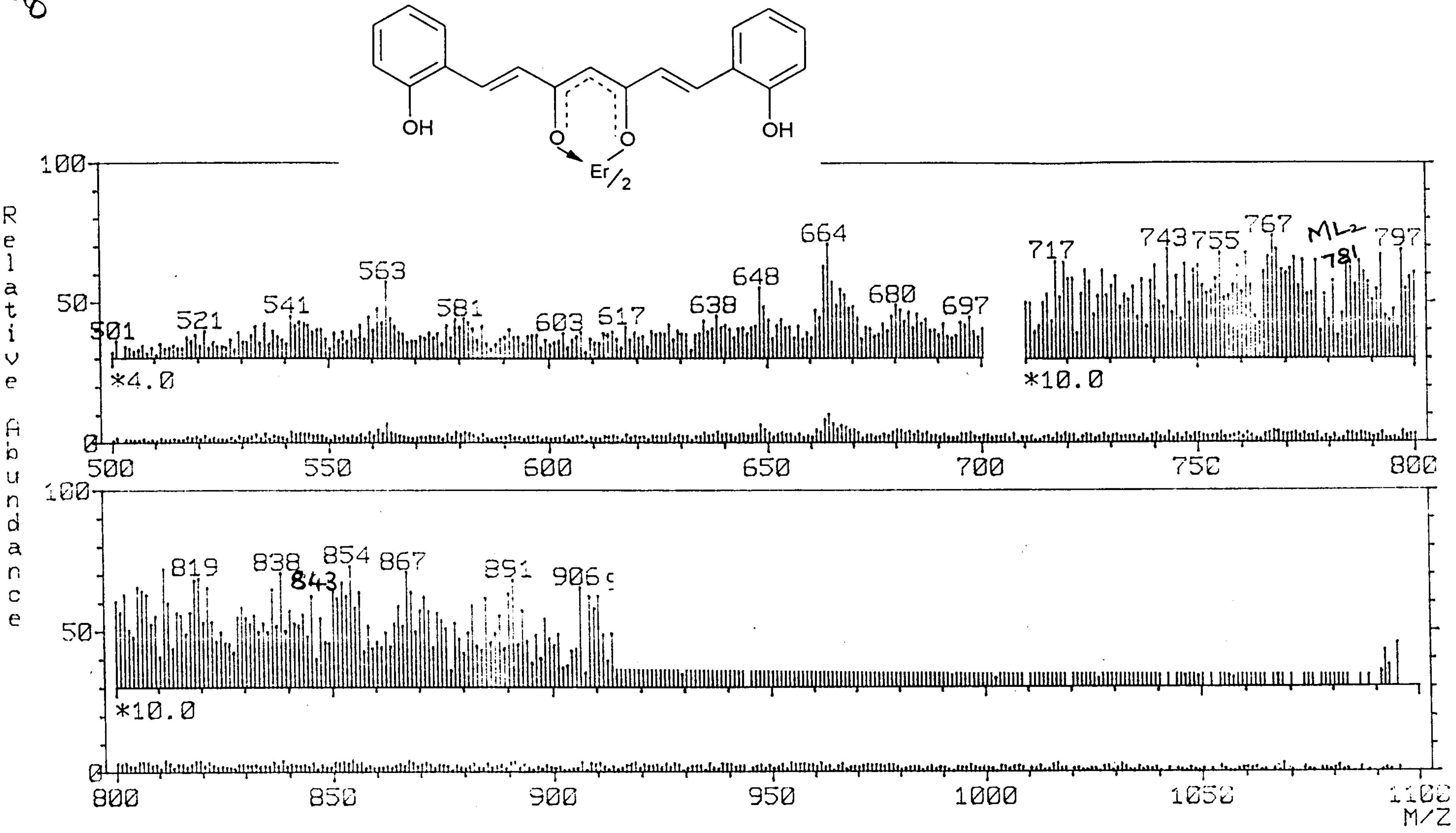

Fig. 11. Mass spectrum of Erbium(III) complex of **1d**

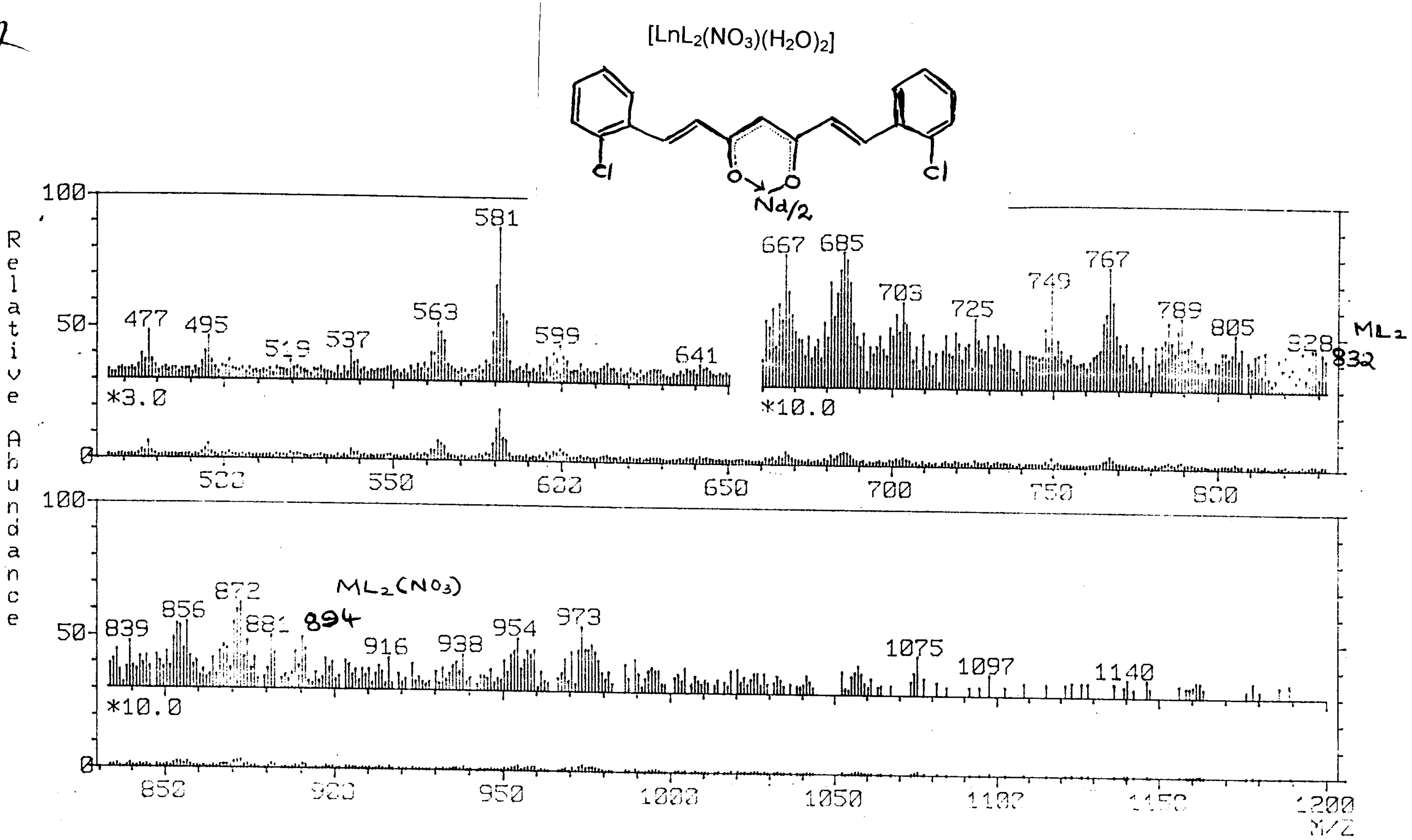

Fig. 12. Mass spectrum of Neodymium(III) complex of 1e

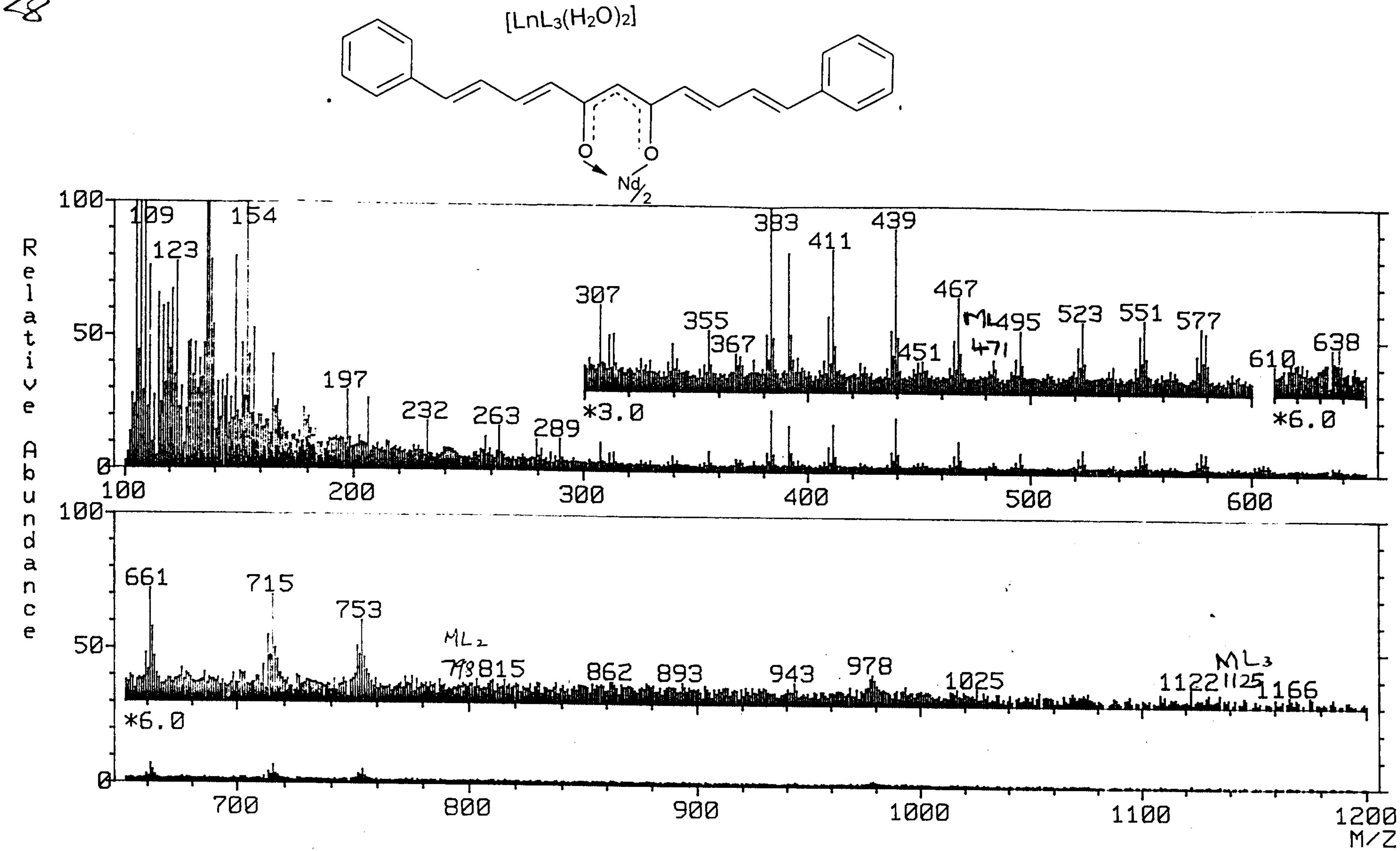

Fig. 13. Mass spectrum of Neodymium(III) complex of **1b**

Electronic Spectra

Electronic absorption spectra of several complexes of Ln^{3+} ion have been reported.[247] The absorptions are mainly due to f-f transitions. The intensity of the absorption bands has been studied both theoretically and experimentally. The theory has been reasonably successful in accounting for the intensity of most transitions on the basis of crystal field induced electric dipole transitions. The absorption bands that show abnormal variations in intensity and fine structure are termed as "hypersensitive". These variations are attributed to the action of a inhomogeneous field from the medium. These hypersensitive bands are strongly affected by changes in the symmetry of the field on the lanthanide ion.

β-Diketone complexes of lanthanides having coordination number six, seven or eight are well known. The absorption maxima, number of absorptions and their intensity are strongly dependent on the coordination environment. The electronic absorption spectral distribution of the typical Ln^{3+} complexes of the 1,7-diarylheptanoid, 1j are given in figure 14. The spectra of the free ligands exhibited two absorption maxima in the range 385-450 nm and at ~ 260 nm assignable respectively to the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions of the highly conjugated molecule. In the spectra of the complexes also these two bands are present with slight shift in position. Thus it can be

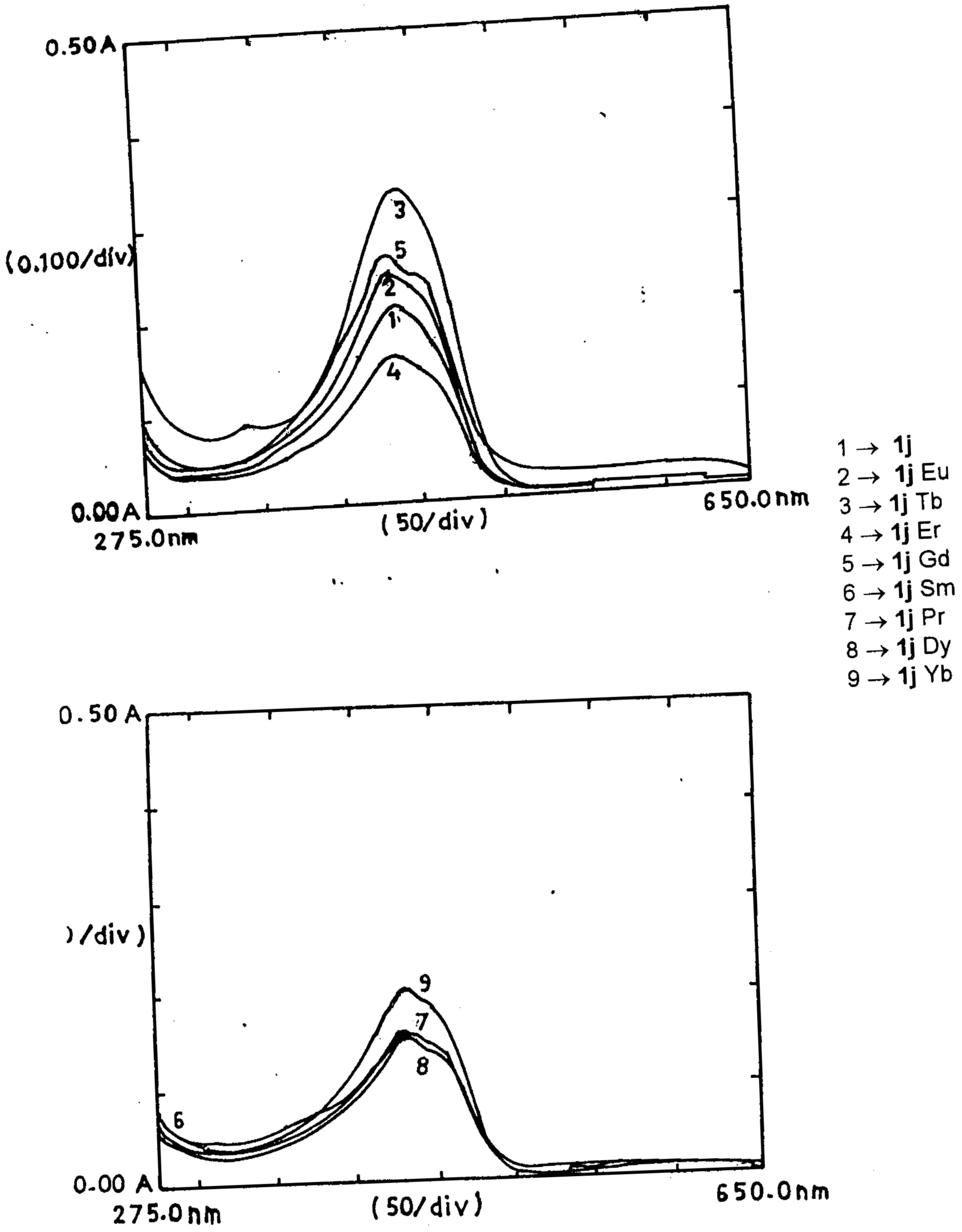

Fig. 14. Absorption spectra of **1j** and its complexes

presumed that no structural alterations of the ligands occurred during complexation.

The spectrum of all the complexes showed several weak absorption bonds in the low energy region. These bands are not so prominent in the spectra given in figure because of the very high intensity of various ligand transitions in the 350-450 nm region. Therefore, the observed λ_{max} of these bands of typical complexes are brought out in table 21.

The appearance of these longer wavelength bands clearly indicated complex formation and probable involvement of the f orbitals of the lanthanide ions. The origin of these weak transition can be associated with the various f-f transition possible in these complexes. Since the recorded spectra are not quantitative, specific assignment of the transitions are not possible and therefore no attempt is made in this regard. However the available data clearly justified complexation of the diarylheptanoids with the lanthanide ions.

Table 21

Electronic spectral data of lanthanide complexes of 1,7-diarylheptanoids

A. [$LnL_2X(H_2O)_2$] type complexes

Ln(III)	L	λ_{max}
La X = Cl^-	1f	602, 534, 506
	1g	534, 504, 484
	1h	506, 484
	1i	506, 456, 416
	1j	548, 532, 504
Pr X = NO_3^-	1e	508, 478, 436
	1f	786, 670, 646, 604
	1g	504, 486
	1h	550, 526, 506
	1i	506, 472, 448
	1j	580, 504, 432
	1k	538, 504
Nd X = NO_3^-	1e	506, 480
	1f	506, 440, 470
	1h	570, 550, 504
	1i	504, 460
	1j	740, 506, 422
	1k	582, 504
Sm X = NO_3^-	1f	506, 484, 444
	1j	668, 640, 614, 580, 431
Eu X = NO_3^-	1d	508, 466
	1f	506, 440
	1g	506, 484
	1h	506, 482
	1j	431
Gd	1j	585, 506, 432
Er	1d	504, 480
	1e	550, 528, 504
	1f	506, 430, 406
	1g	532, 502, 480
	1i	548, 504
	1j	587, 433, 506
Yb	1f	504, 438
	1j	432, 588, 608, 650, 682

B. $[TbL_2(NO_3)_2(H_2O)_2]$

Tb(III)	L	λ_{max}
La	1a	512, 478
	1c	512, 414
	1f	604, 504
	1j	581, 548, 538, 435

C. $[LnL_3(H_2O)_2]$ type complexes

LnII)	L	λ_{max}
La	1a	502, 424
	1c	502, 430
Pr	1a	618, 670, 564
	1b	632, 600, 534, 504
	1c	690, 618, 580
Nd	1a	508, 480
	1b	502, 482
Gd	1c	580, 510
Er	1a	506, 480
	1c	554, 528

SECTION 2

FLUORESCENCE SPECTRA OF CURCUMINOIDS AND THEIR LANTHANIDE COMPLEXES

Absorption of visible and/or uv radiation is a characteristic feature of transition metal complexes. However, very few complexes reemit even a small fraction of the absorbed radiation, because more efficient non radiative deexcitation pathways are available for these complexes. In the case of transition metal complexes, the d-electron excited states are strongly coupled to the environment through the ligand field which provides an efficient deexcitation mechanism that prevent luminescence.

The situation is entirely different in the case of lanthanide complexes. In these complexes, the lowest lying excited state is comprised of $4f^n$ configuration. The 4f orbitals of Ln(III) ions are largely shielded from the surrounding ligand field and their involvement in bonding with the ligands is minimum. Thus the ligand field splitting of 4f electrons in lanthanide complexes is only around 100 cm^{-1} compared to d-electrons involvement in transition metal complexes where the splitting is in the range 25000 cm^{-1}. As a result radiative deexcitation is frequent in lanthanide complexes. All of the Ln(III) ion are known to exhibit fluorescence, particularly in the solid state and anhydrous conditions. The fluorescence of Ln(III) complexes have been properly exploited in several areas of chemical sciences to give valuable information. Thus the application of Ln(III) complexes in photophysics, solid state studies, spectral investigations and even in solving several biochemical problems are well documented.[217,219]

Although the lanthanide elements are not known constituents of any naturally occurring biological systems, their importance in many biochemical investigations have been well established. This is mainly because of the several similarities between the coordination chemistry of Ln(III) ions and Ca(II) ions owing to their very similar ionic radii, preference to oxygen donor ligands, coordination number greater than 6, etc. This aspects of Ln(III), chemistry have been well studied.[217-221] In short, emission spectra of Ln(III) complexes can reveal a number of useful informations such as the nature of various electronic energy levels, influence of different ligands to the f electron, the nature of the coordinate bond, etc.

Most of the luminescence studies of Ln(III) ions and complexes are based on the five central ions namely Sm(III), Eu(III), Gd(III), Tb(III) and Dy(III). The luminescence of the remaining members are of little importance in coordination chemistry. This is mainly due to the comparatively low energy gap between various potential emissive levels. The energy levels of the five Ln(III) ions are given in figure 15.

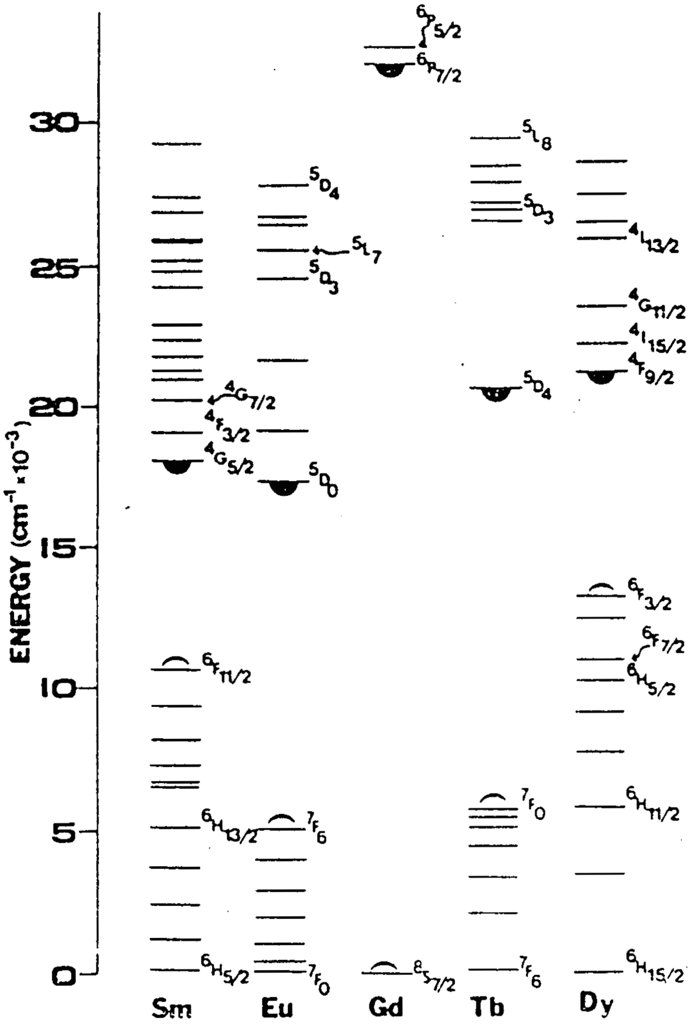

Figure 15 · Energy level diagrams for the central members of the Ln(III) ion series —●—, lowest luminescent level; —◠— highest level of the ground-state manifold.

The energy gap between the lowest lying emissive level and the highest level of the ground manifold of the five Ln(III) ions are 7400, 12150, 32000, 10800 and 7850 cm^{-1} respectively. A reasonably large energy gap is observed in the case of Eu(III) and Tb(III) and as a result these ions show strong fluorescence in the visible region.

Emission spectral studies on lanthanide chelates of organic ligands like salicylaldehyde, β-diketones, etc. were first reported by Weissmann in 1942.[222] The study showed the line like emissions characteristic of the f-f-transitions of Eu(III) chelates. With the advent of laser technology in the 1960's, numerous studies appeared regarding the luminescent behaviour of Ln(III) laser chelates.[218] These qualitative studies revealed several interesting aspects on lanthanide luminiscence. Some of the major conclusions are cited below.

Sensitisized emission from Ln(III) ion levels in chelates arises from intramolecular transfer from higher energy triplet state of the ligand following intersystem crossing from the ligand singlet state. The emission character are strongly dependent on the number and types of ligands coordinated to the Ln(III) ion. The nature of $^5D_0 \rightarrow {}^7F_0$ transitions in Eu(III) corresponds to the number of different complex species present. In the case of certain Eu(III) β-diketonate complexes, laser action was demonstrated for the $^5D_0 \rightarrow {}^7F_0$ transition. It is to be pointed out that with a few exceptions, most of the above early qualitative conclusions have been confirmed by more recent sophisticated studies.

The fluorescence and other photochemical properties of the major constituent of the natural curcuminoids, or curcumin I [bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene 3,5-dione), that is 1j of the present study, have been investigated by various group of workers.[223-225] The fluorescence intensity and the position of the most intense band of the compound were very sensitive to the nature of the solvent. A large red shift in fluorescence maximum was observed on going from toluene to alcohol ($\Delta\lambda$ 61 nm) and SDS micells ($\Delta\lambda$ 69 nm). The fluorescence quantum yield was highest in acetonitrile (0.104) compared to toluene (0.067), ethanol (.063) and dmf (0.027).

Eventhough 1j in its enol configuration may exist in several cis-trans isomeric forms, no wavelength dependence was reported on its fluorescence excitation spectrum. For instance in toluene, the excitation spectra recorded at five different wavelength were identical and overlapped well with the absorption spectrum. In the enol form of the compound, intramolecular conjugation of the π electrons may couple with the two feruloyl chromophore into one extended π electron system. The various photophysical properties of curcumin can be attributed to the extended conjugation of the molecule.[29,226]

Usually intramolecular hydrogen bonding provides a channel for fast radiationless deactivation of excited state *via* excited state H-atom transfer.[227] However, in aprotic media curcumin I fluoresce strongly and generates $^1O_2$, implying low non radiative singlet deactivation to the ground state and the formation of relatively long lived triplet state in solution.[228] It then follows that intramolecular hydrogen bonding must disappear when the compound is excited and the molecule undergoes ketonization. The large red shift observed fluorescence on going from non polar to polar solvents also indicate that singlet state must be very polar. Extended conjugation present in the molecule and the presence of electron donating substituents are all responsible for the higher fluorescence intensity of curcuminoids. Thus in short, the photochemical properties of curcuminoids are strongly dependent on their environment. It has been shows that not only the observed photochemical properties, but also the various biological activities are closely associated with the electronic and structural environment of the compounds.[229]

The fluorescence spectra of all the curcuminoids considered in this study and some of their lanthanide complexes were recorded in order to determine their fluorescence emission maxima and its dependence on aryl substituents. Emission spectra of the compounds were measured in dmso solution ($1x10^{-6}$M). Absorption spectra of all the compounds in the 275-650nm region showed two strong bands at ~580 and ~430nm. Therefore, the excitation wavelength employed for fluorescence measurements was at

~430nm. All the emission spectra reported here are uncorrected and no attempt was made to calculate the quantum yield of emission. The emission spectra are given in figures 16-18.

Several interesting conclusion can be derived from the observed fluorescence spectra of curcuminoids (a) Among the unsubstituted curcuminoids (1a–1c), fluorescence λ_{max} increased as the degree of conjugation increases. Thus for the 1,7-dinaphthyl derivative 1f, the λ^*_F is at 517 nm where as for 1,7-diphenyl analogues the λ^*_F is at 459 nm. This is expected in view of the fact that with increase in conjugation, the energy gap between the emission levels are decreased. (b) Phenyl substituents, in general increases the fluorescence wavelength maxima. Electron donating substituents in the *para* position of the phenyl rings showed longest λ_{max} of fluorescence. Thus the strong electron donating N,N-dimethyl group exhibited fluorescence at λmax 542 compared to 459 of the unsubstituted analogue. The λ_{max} decreases with decrease in electron donating ability of the substituents. The order observed is: p-$N(CH_3)_2$>p-OH>p-OC_2H_5>o-OH $\simeq$o-CH_3. When both –OH and –OCH_3 groups are present on the phenyl ring also showed an increase in λ_{max} of fluorescence. Electron donating substituents are expected to increase the electron density of the enol form which is responsible for the fluorescence of the curcumnoids. It has been reported that during excitation, ketonization will takes place and emission profile varies in the

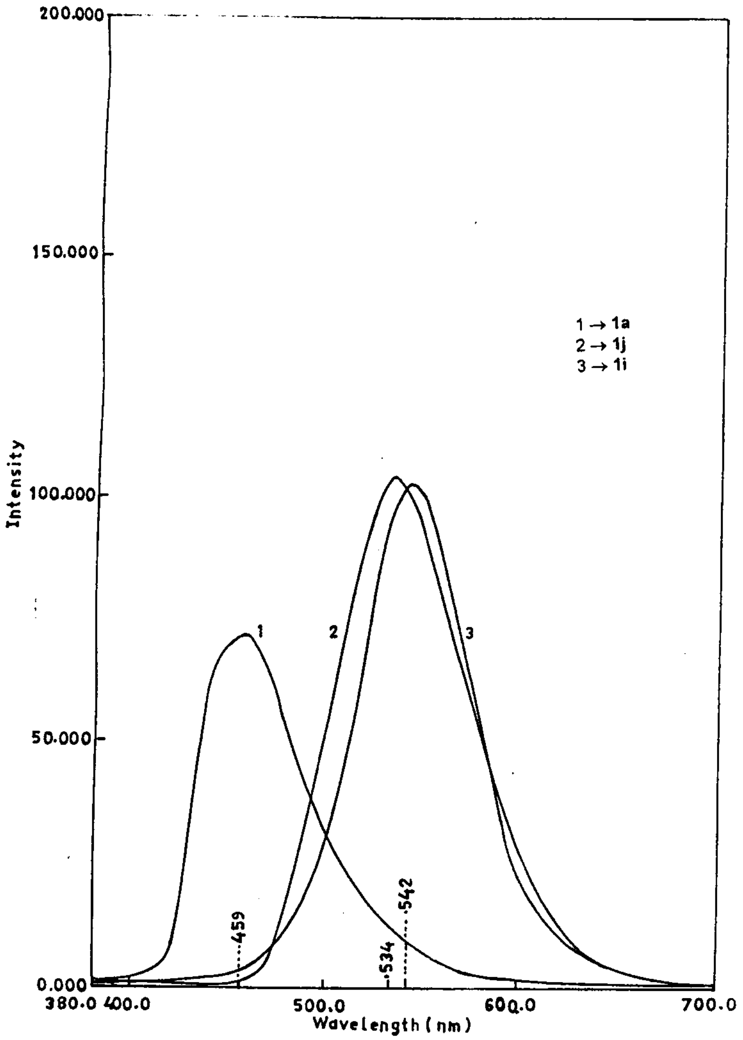

Fig. 16. Fluorescence spectra of 1,7-diarylheptanoids

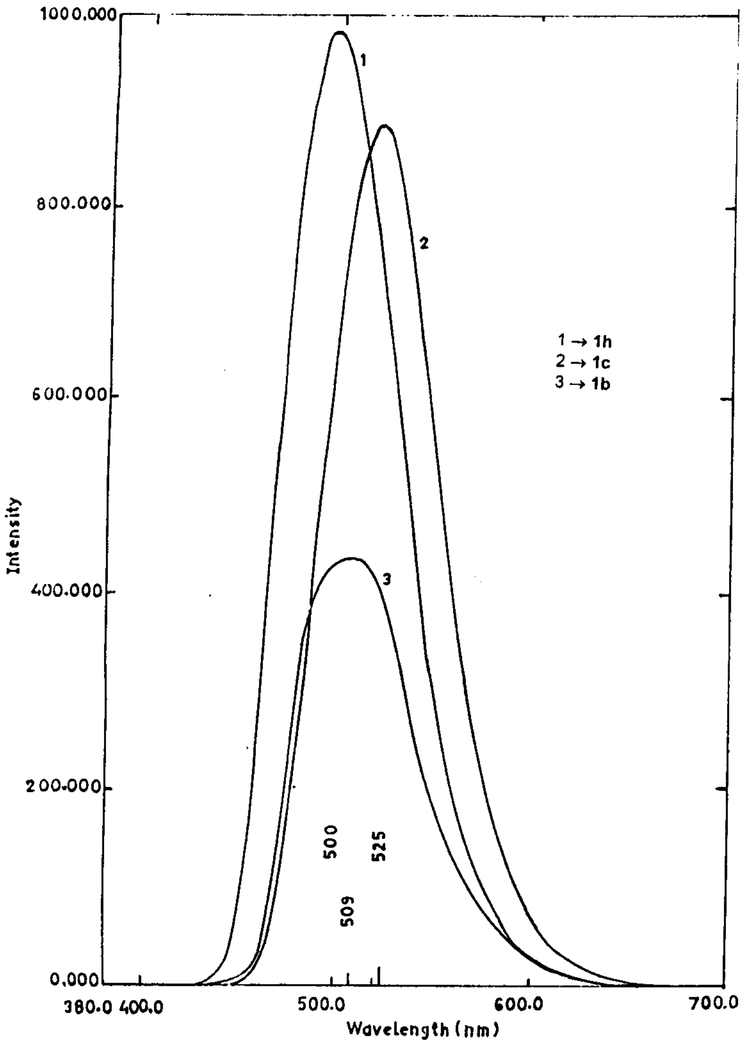

Fig. 17. Fluorescence spectra of 1,7-diarylheptanoids

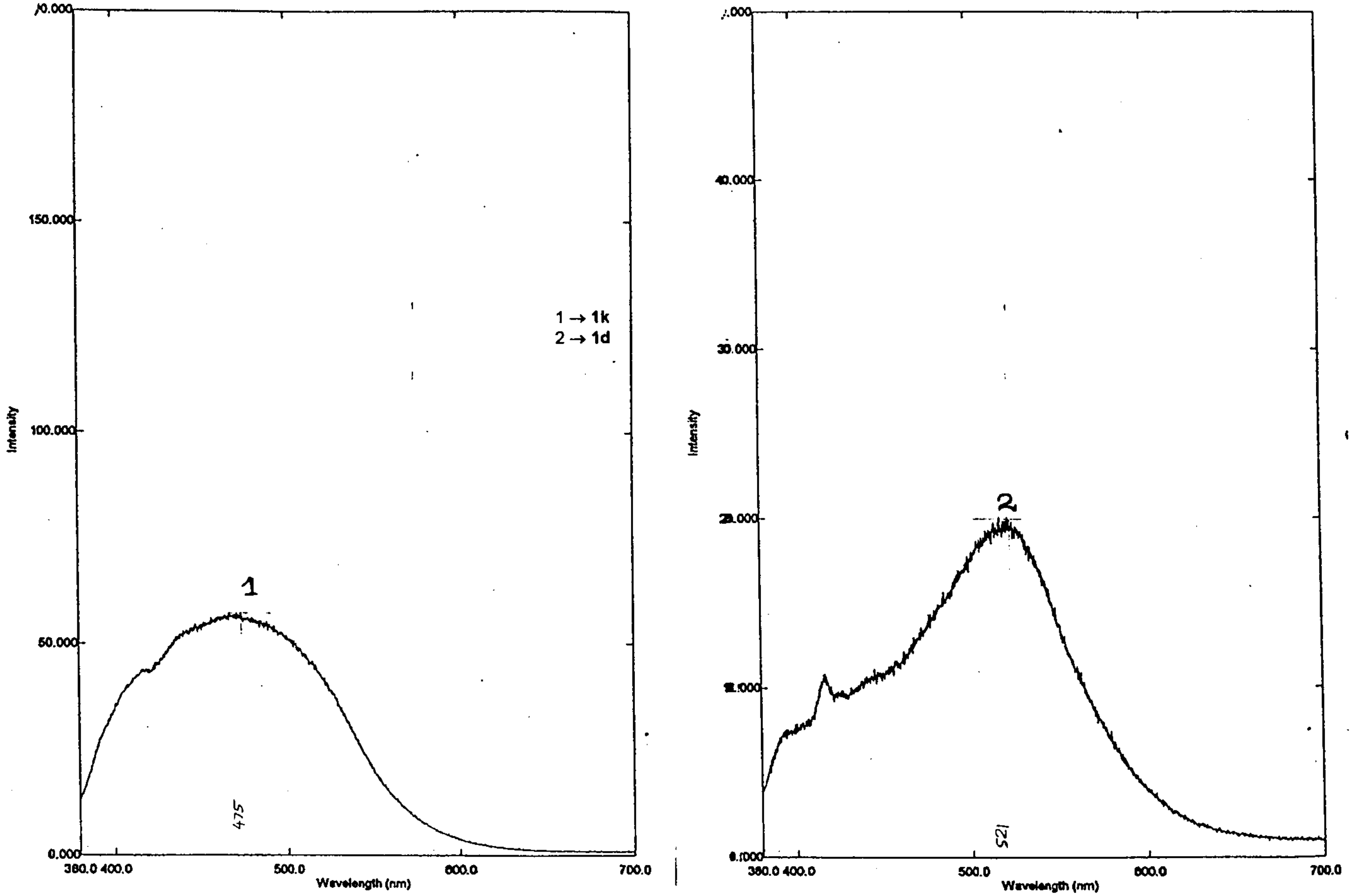

Fig. 18. Fluorescence spectra of 1,7-diarylheptanoids

solvent and substituents. Increase in electron density at the keto function may reduce the energy gap between the states involved in the emission processes. This may be the reason why electron donating substituents decreases the fluorescent energy. Thus it can be stated that not only the diketo functions is involved in the emission process but also the molecule as a whole is responsible. (c) The relative intensity of the λ^*_F do not permit any simple correlation with the structure or substituents on the aryl rings of the compounds. However, fluorescence intensity increases with increase in conjugation. The heteroaryl curcuminoid, 1c, showed the highest intensity. Similarly, electron donating substituents, such as and OH, OC_2H_5 at the *para* position of the phenyl rings also showed very high intensity of fluorescence. But the bulky p-$N(CH_3)_2$ and disubstituted derivatives showed relatively weak fluorescence. This may be attributed to the steric hindrance of the bulky and disubstituted derivatives that may facilitate radiationless decay of the excited state. More elaborate and detailed quantitative investigation is required to find out the actual cause of these observations.

TABLE 22

Fluorescence maxima and relative intensity of 1,7-diarylheptanoids*

Compound	Fluorescence λ_{max}	Relative Intensity
1a	459	75
1b	509	450
1c	500	990
1d	475	60
1h	525	900
1i	542	110
1j	534	115
1k	521	22.5

*Concentration 1 x 10^{-6} mol/l, Excitation wavelength 370 nm

The fluorescence spectra of the Ln(III) complex of the ligand 1j were recorded in order to study of effect of complexation on the fluorescent behaviour of the compound. The observed spectra are broad and the λmax of the fluorescence is very close to that of the ligand except that of the Eu(III) complex. The spectra of the complexes are given in figures 19, 20. From a comparison of the spectra of the complexes with that of ligand spectrum it can be stated that no appreciable change in the energy levels of the ligand occurred during complexation.

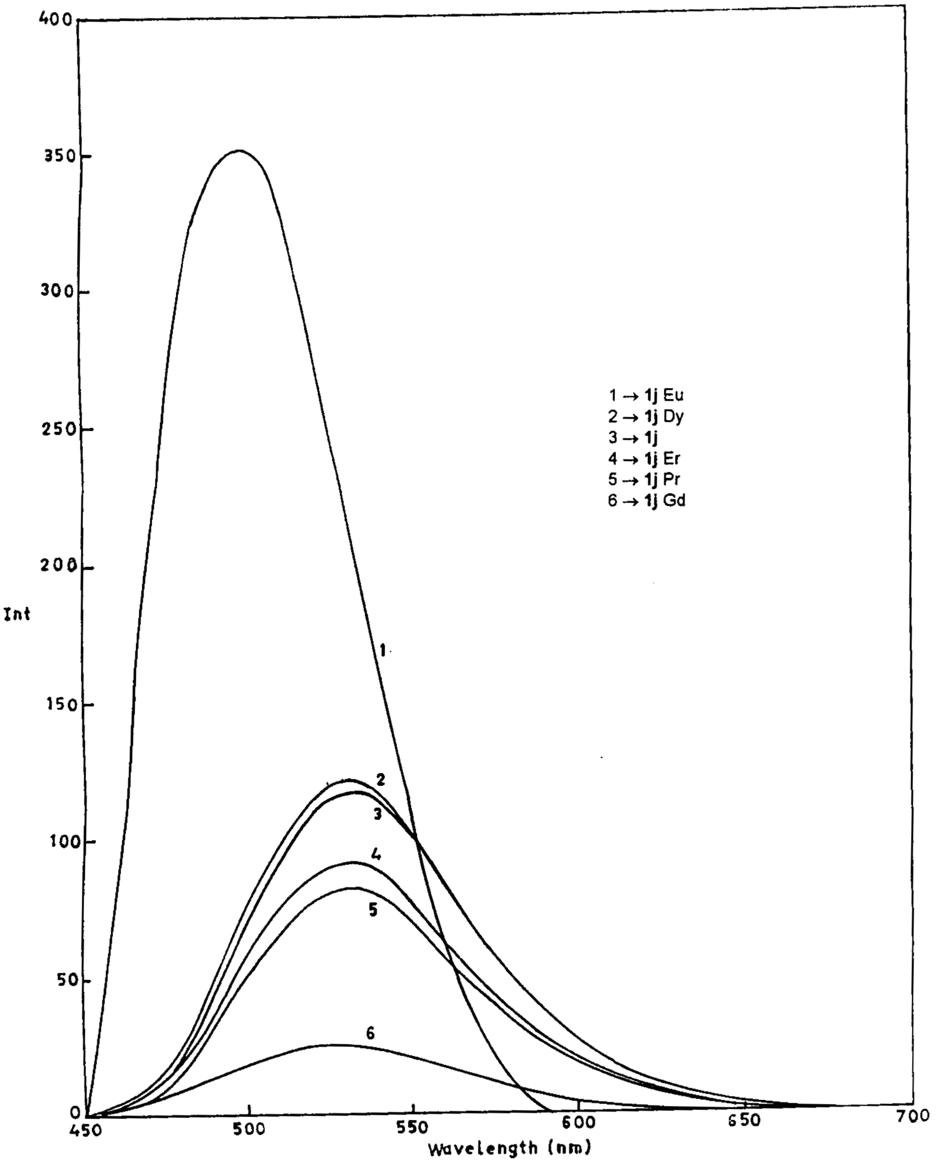

Fig. 19. Fluorescence spectra of **1j** and its complexes

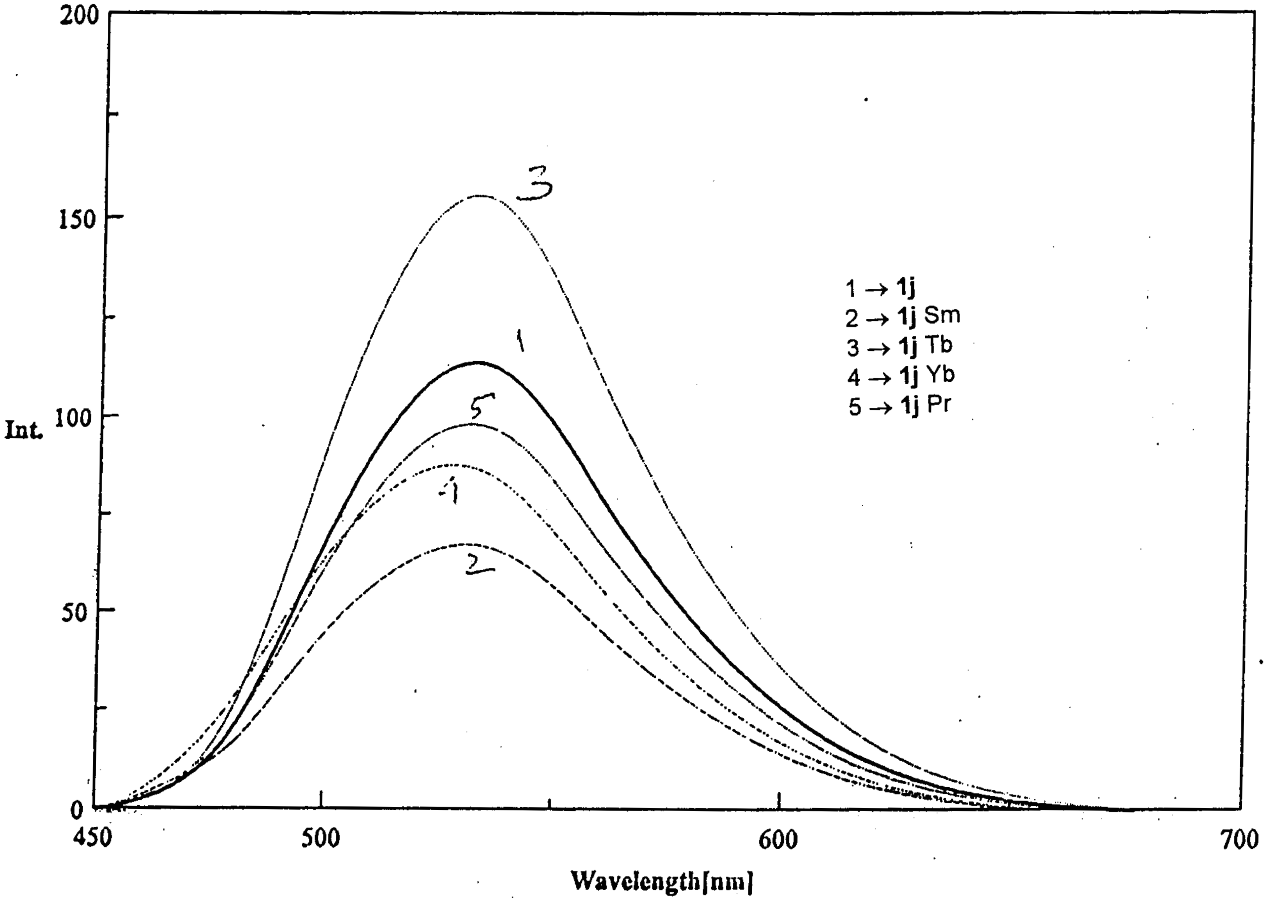

Fig. 20. Fluorescence spectra of **1j** and its complexes

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SECTION 3

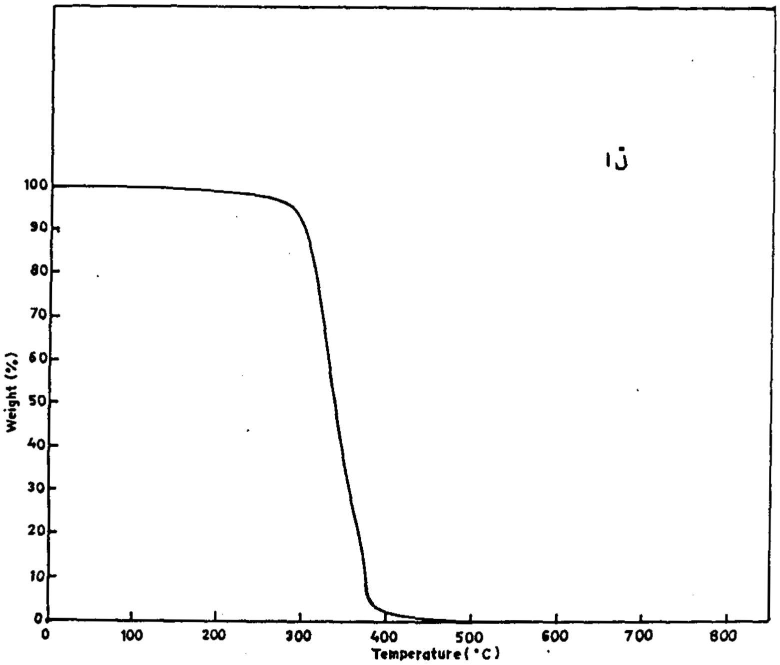
THERMOGRAVIEMTRIC STUDIES OF LANTHANIDE COMPLEXES OF 1,7-DIARYLHEPTANOIDS

Thermogravimetry is a powerful tool in coordination chemistry in several respects. For instance TG of a metal complexes can provide valuable informations regarding the thermal stability, volatility, the number and type of coordinated ligands and their mode of bonding, the nature of bonding of the different ligand in a mixed ligand complex, etc.[212-214] Several thermogravimetric investigations on metal complexes of β-diketones have been reported in view of their importance as volatile complexes in gas chromatographic studies.[215,216] The influence of substituents on β-diketones, the nature of the metal ion, the composition of the complex on the thermogram have been well explored by various investigators and yielded several interesting results.[215]

Many anhydrous lanthanide chelates of β-diketones are volatile at moderate temperatures (100-200°C). Thermograms of such chelate show smooth curve that approach 100% weight loss. It has been observed that as the radius of the Ln^{3+} ion decreases, the volatility of the chelates increases. Hydrated lanthanide β-diketones generally decrease the volatility and thermal stability, and decomposition of the chelates occur after loosing the water molecules.[213]

Inorder to get some idea regarding the volatility and thermal stability of the lanthanide chelates of the 1,7-diarylheptanoids, thermogram of some lanthanide chelates of **1j** was studied. The TG curves are redrawn in figures 21-24.

The first stage in all the thermograms correspond to the loss of water molecules below 150°C. The observed weight-loss at this stage agree with the formulation of the complex. The weight loss and second and third stage correspond to the loss of NO_2 from the complex. This was followed by the decomposition of the ligand moiety and formation of Ln_2O_3 takes place. In the thermogram of the terbium complex, there are four well defined stages. From the observed weight loss of each stage, it can be seen that the complex contain two ligand moiety and two nitrate groups.



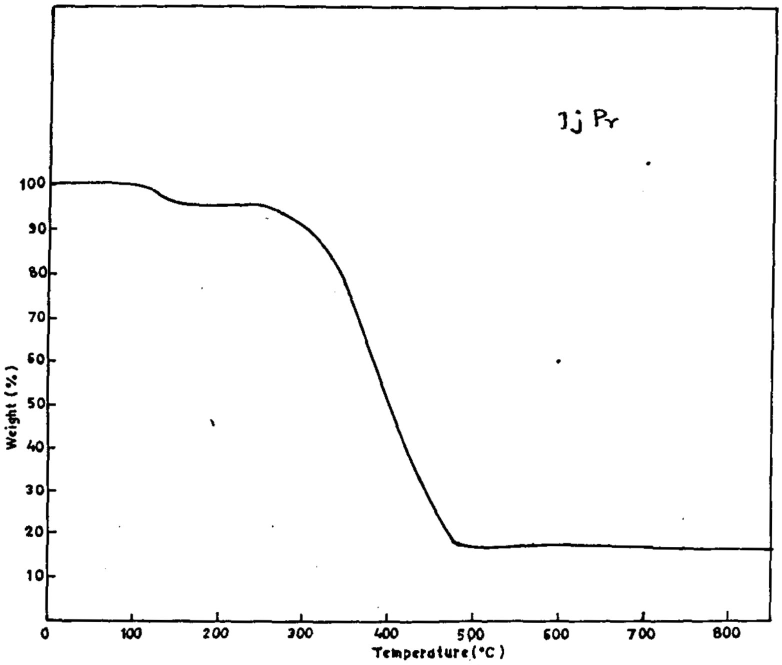


Fig. 21. Thermogram of 1j and its Praseodymium(III) complex

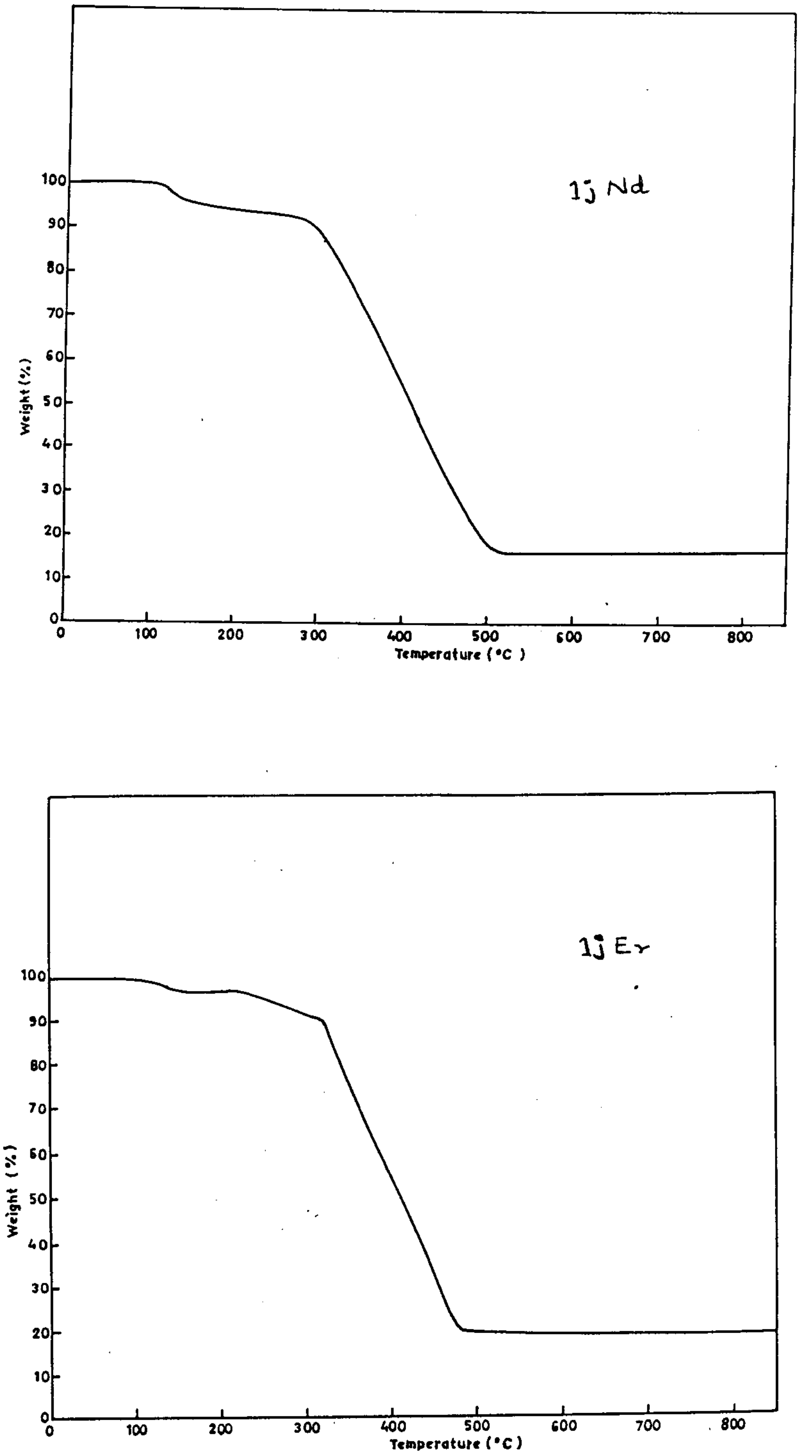
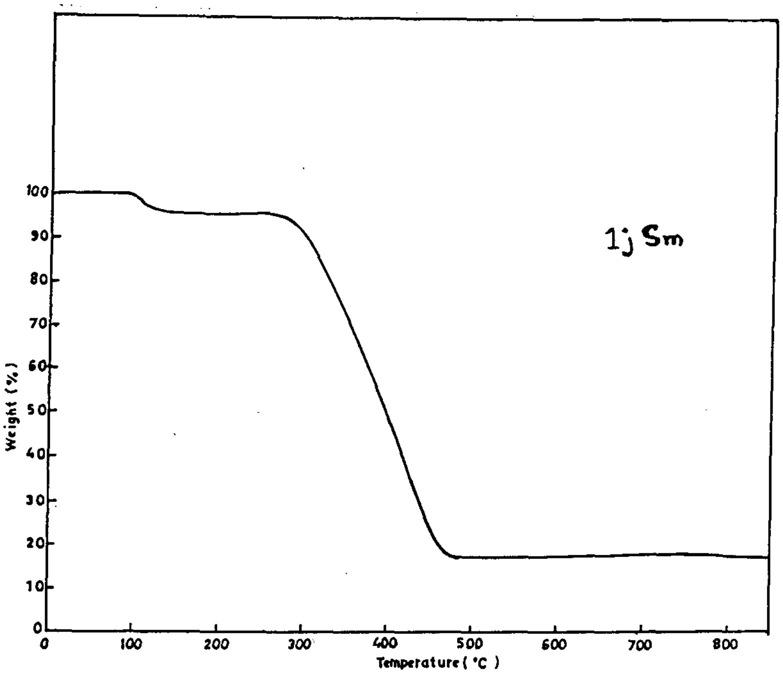


Fig. 22. Thermogram of Neodymium(III) and Erbium(III) complexes of 1j



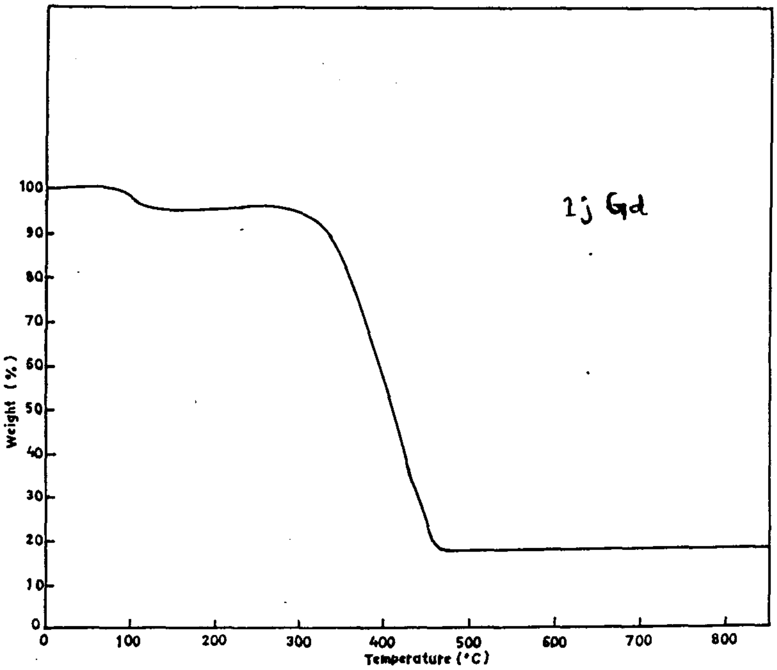


Fig. 23. Thermogram of Samarium(III) and Gadolinium(III) complexes of 1j.

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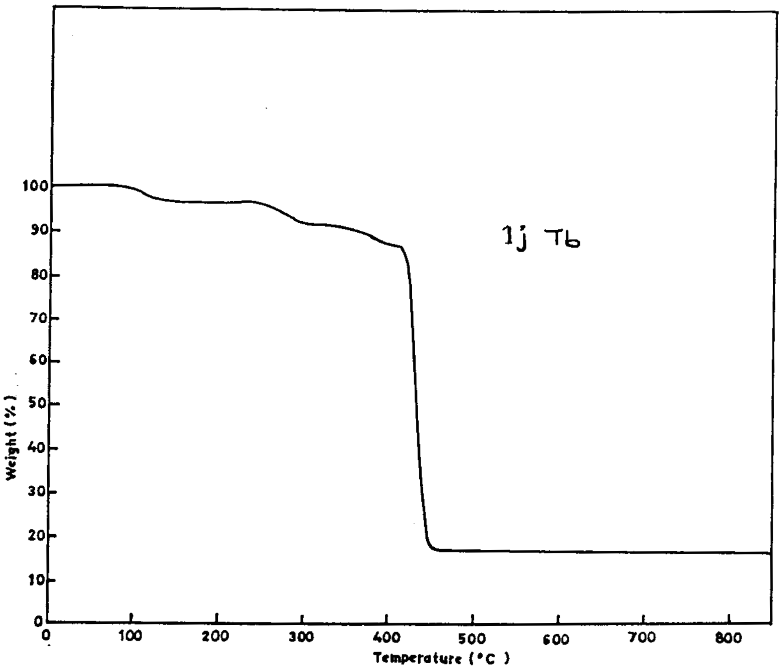

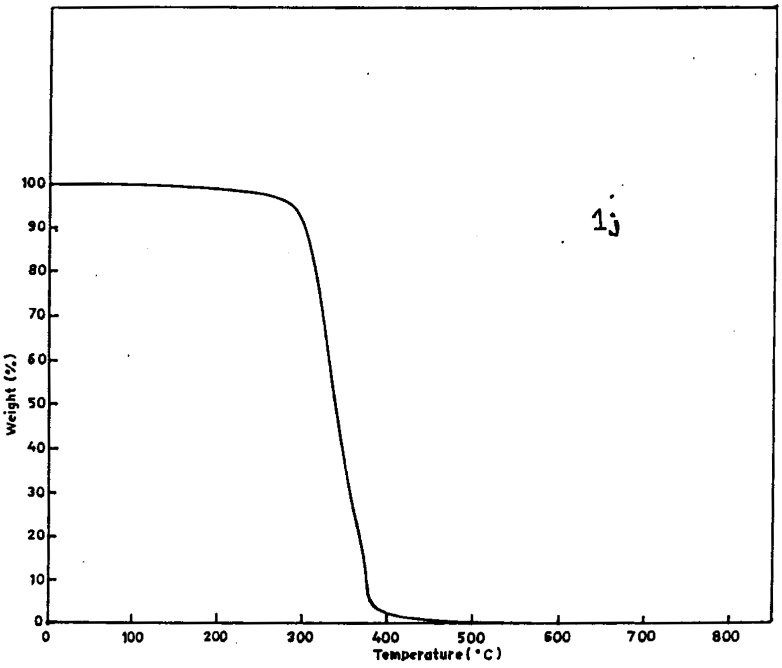

Fig. 24. Thermogram of **1j** and its Terbium(IV) complex

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TABLE 23

Thermal Decomposition of the 1j (HL) and its Pr(III), Nd(III), Er(III), Sm(III), Gd(III) and Tb(IV) Chelates

Compound/ complexes (molecular mass)	Temp. ranges in TG (°C)	Mass loss %		Pyrolysis %	Final product
		TG	Theoretical		
1j = HL $C_{21}H_{20}O_6$ (368)	280 - 390	100	100	100	-
$PrL_2(NO_3)(H_2O)_2$ (972.907)	100 - 150 240 - 390 300 - 480	3.4 4.9 75	3.60 4.89 75.44	83.33	Pr_2O_3
$NdL_2(NO_3)(H_2O)_2$ (976.24)	100 - 150 240 - 280 290 - 500	3.6 4.89 75	3.6 4.9 73.45	81.85	Nd_2O_3
$ErL_2(NO_3)(CH_2O)_2$ (999.26)	100 - 140 220 - 300 320 - 480	3.6 4.7 72	3.6 4.8 73.45	81.85	Er_2O_3
$SmL_2(NO_3)(H_2O)_2$ (982.35)	100 - 130 220 - 280 290 - 460	3.8 4.8 74	3.66 4.9 74.72	83.28	Sm_2O_3
$GdL_2(NO_3)(H_2O)_2$ (989.25)	80 - 120 260 - 320 320 - 480	3.7 5 73	3.64 4.9 74.2	82.74	Gd_2O_3
$TbL_2(NO_3)_2(H_2O)_2$ (1052.924)	80 - 120 240 - 300 325 - 410 420 - 500	3.4 4.5 4.7 70	3.5 4.6 4.9 69.71	82.71	Tb_2O_3

Although lanthanide chelates of β-diketones are volatile at moderate temperatures, no such behaviour is observed in the case of lanthanide chelates of the curcuminoids, probably due to the bulkiness of the ligands and mixed ligand nature of the complex. The most important conclusion that can be derived from the thermograms of the complexes is their stoichiometry and thereby the formulations as discussed.

LANTHANIDE COMPLEXES OF CURCUMINOIDS

THESIS SUBMITTED
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IN PARTIAL FULFILMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
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IN THE FACULTY OF SCIENCE

By

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JULY 2004

CHAPTER II

DIOXOURANIUM(VI) COMPLEXES OF THE 1,7-DIARYLHEPTANOIDS

DIOXOURANIUM(VI) COMPLEXES OF THE 1,7-DIARYLHEPTANOIDS

Synthesis

The general procedure adopted for the preparation of dioxouranium complexes is given below.

A methanolic solution (25 mL) of the metal salt (0.001 mol) was added slowly with stirring to a solution of the 1,7-diarylheptanoid (0.002 mol) in methanol (25 mL). The mixture was stirred well and refluxed gently for ~ 1 h and the volume was reduced to half. On cooling to room temperature the complex get precipitated, washed with 1:1 methanol-water mixture and dried in a vacuum desiccator. For purity, the compound was recrystallised from hot methanol.

Results and Discussion

The analytical and physical data of the complex are given in Table 24. The elemental analytical data of the complexes correspond to the $[UO_2L_2]$ stoichiometry. All the complexes are non-conducting in dmf (specific conductance $< 10\ \Omega^{-1}cm^{-1}$ in 10^{-3} M solution) and do not contain acetate anion of uranyl acetate used for the preparation.

Table 24

Physical and analytical data of the dioxouranium(VI) chelates of 1,7-diarylheptanoids, (HL)

Dioxouranium(VI) chelates	M.P. °C	Elemental analysis %, Found/Calculated*			
		C	H	N	U
1a	238	55.86 (55.61)	1.96 (1.83)	--	29.48 (29.02)
1b	252	59.98 (59.74)	2.42 (2.06)	--	26.08 (25.76)
1c	242	46.38 (46.15)	1.72 (1.41)	--	30.76 (30.51)
1f	262	60.06 (59.78)	1.98 (1.75)	--	22.18 (21.96)
1g	268	53.93 (53.62)	2.46 (2.02)	--	25.73 (25.32)
1h	265	51.83 (51.58)	1.89 (1.70)	--	27.18 (26.93)
1i	240	55.93 (55.64)	2.92 (2.52)	2.96 (2.82)	24.23 (23.99)
1j	293	50.53 (50.20)	2.02 (1.89)	--	23.94 (23.7)
1k	272	52.38 (52.07)	2.48 (2.17)	--	22.72 (22.46)

* The calculated value corresponds to the [UO_2L_2] composition where L stands for the deprotonated ligand.

Infrared spectra

The free ligand band at ~ 1620 cm^{-1} due to the intramolecularly hydrogen bonded diketo-function disappeared in the spectra of all the complexes. This indicate the involvement of the diketo function in bonding with the metal ion. Further, in the spectra of all the complexes, a new medium intensity band appeared at ~ 470 cm^{-1} and 418 cm^{-1} which are not observed in the spectra of the ligands. These bands are undoubtedly due to ν(M–O) vibrations. A comparatively intense band at ~ 920 cm^{-1} is due to UO_2 stretching.

The broad free ligand band in the region 2500-3500 cm^{-1} cleared up in the spectra of all the complexes and instead weak bands in the region 2000-2800 cm^{-1} appeared presumably due to various C–H stretching vibrations. However in the spectra of complexes of **1d, 1f, 1h** and **1j** which contain OH groups in the phenyl rings exhibited bands in the region 3600-3200 cm^{-1} due to ν_{OH}. This suggest that only the enolic proton of the diketo group is engaged in complexation and the –OH groups on the phenyl rings are unaffected. Thus the observed ir spectra strongly support structure **3** of the uranyl complexes. Characteristic ir bands of the complexes are given in table 25.

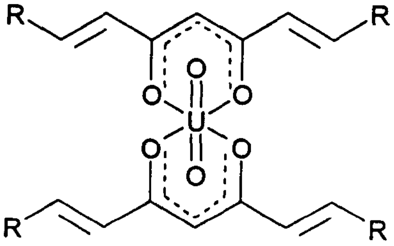

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Table 25

Characteristic ir spectral data of dioxouranium(VI) chelates of 1,7-diarylheptanoids (HL)

Dioxouranium(VI) chelates of	ν(C=O) chelated	ν(C–C–C)	ν(UO_2)	ν(U–O)
1a	1576	1509	916	473 419
1b	1580	1509	926	468 419
1c	1599	1503	923	472 418
1f	1595	1510	920	467 418
1g	1586	1512	918	469 420
1h	1572	1513	922	470 419
1i	1574	1516	923	471 417
1j	1597	1517	922	467 419
1k	1592	1509	920	473 416

NMR Spectra

The ^1H nmr spectra of the uranyl complexes of **1b** and **1f** clearly indicated the replacement of the enolic proton by the metal ion. Thus the low field signal at $\delta \sim 16$ ppm due to the intramolecularly hydrogen bonded enol

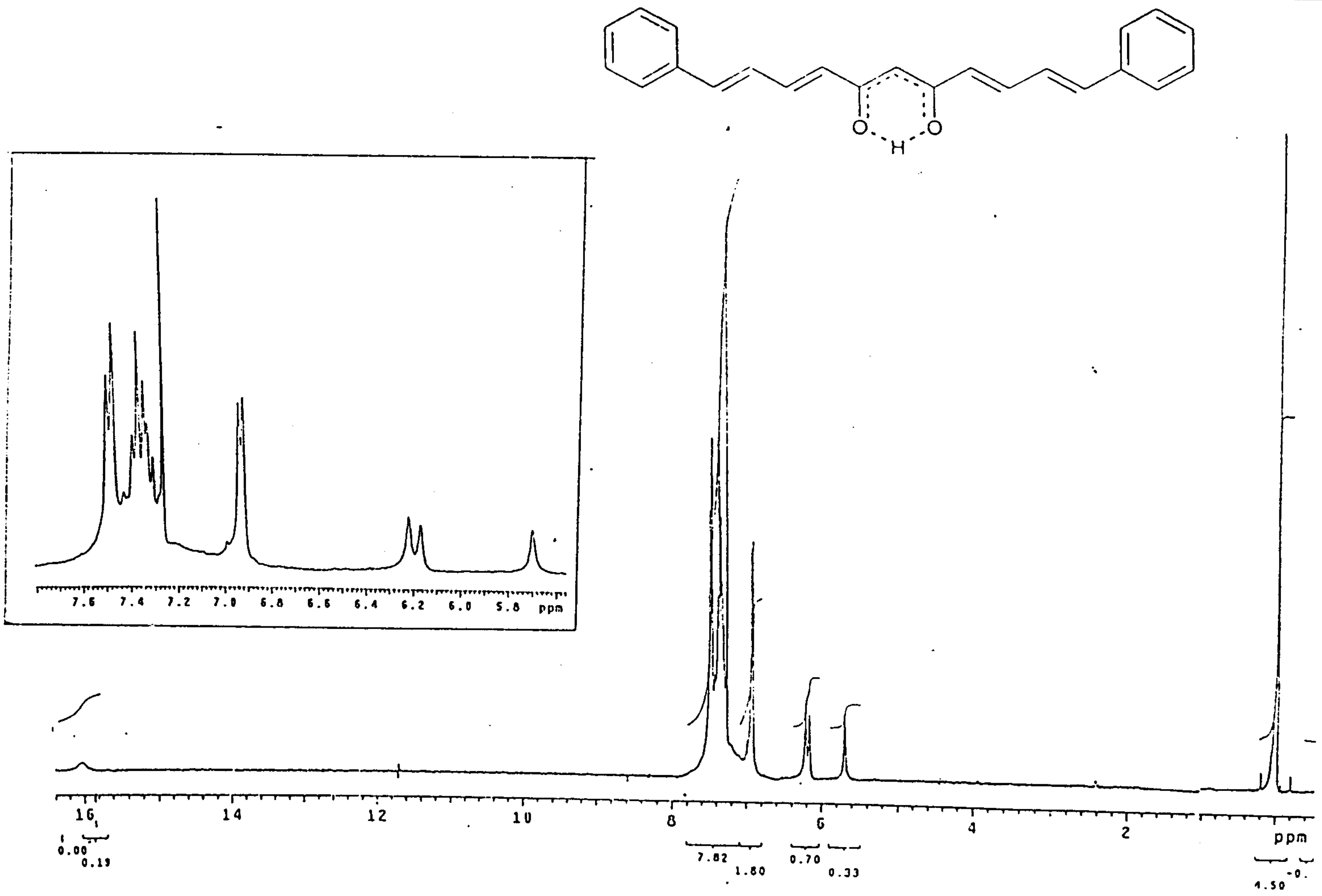


Fig. 25. ¹H NMR spectrum of 1b

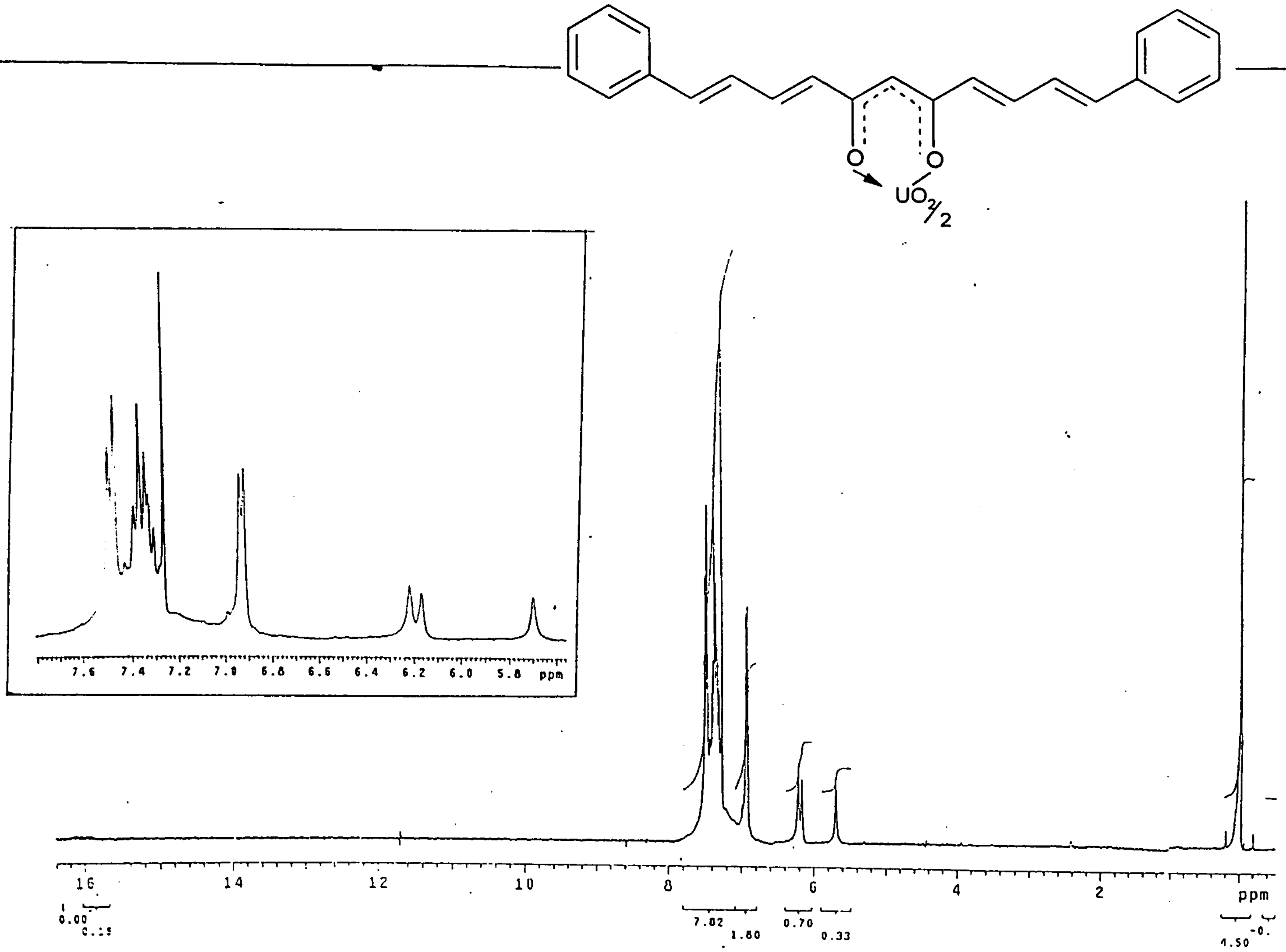


Fig. 26. ^{1}H NMR spectrum of Uranyl(VI) complex of **1b**

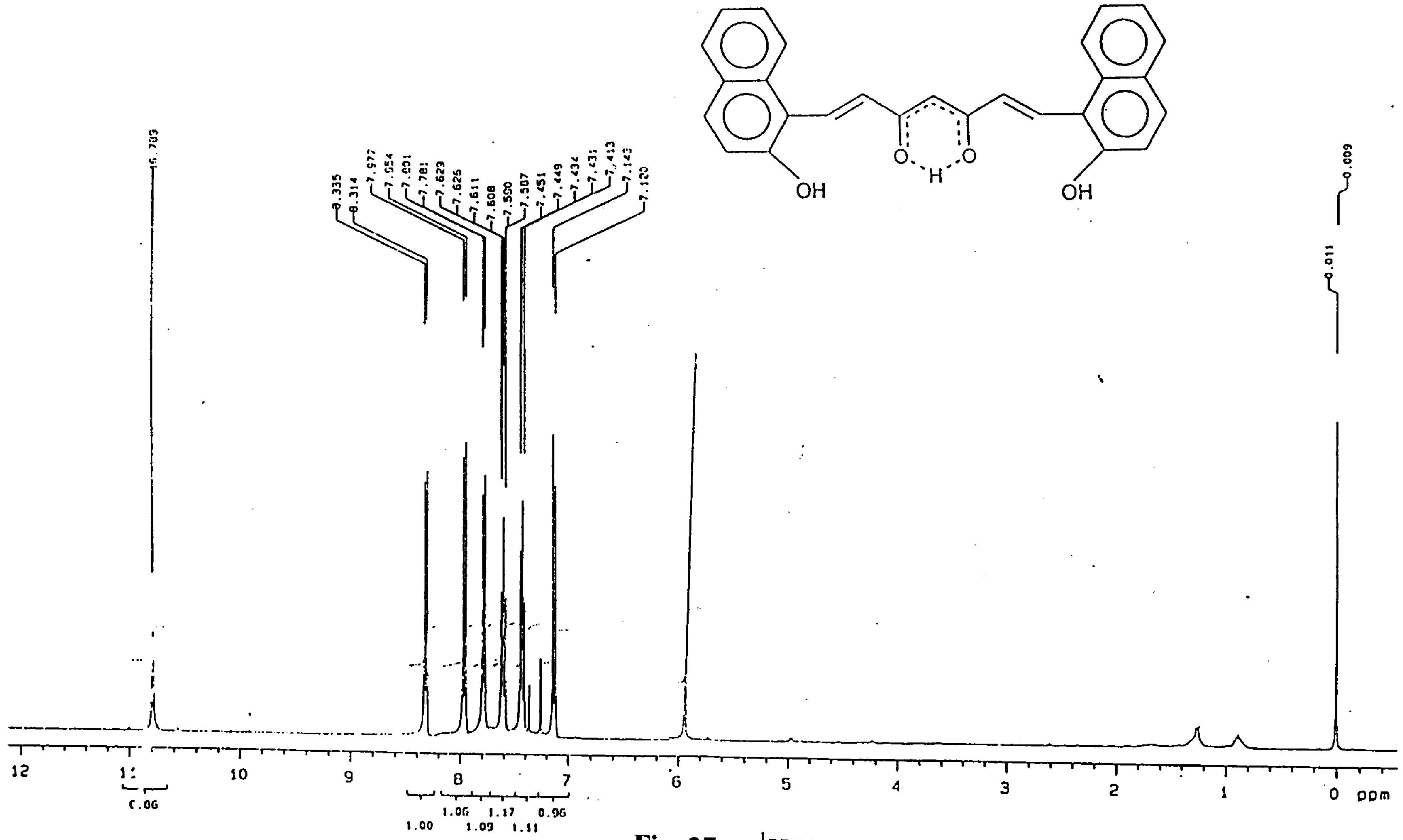


Fig. 27. ¹H NMR spectrum of **1f**

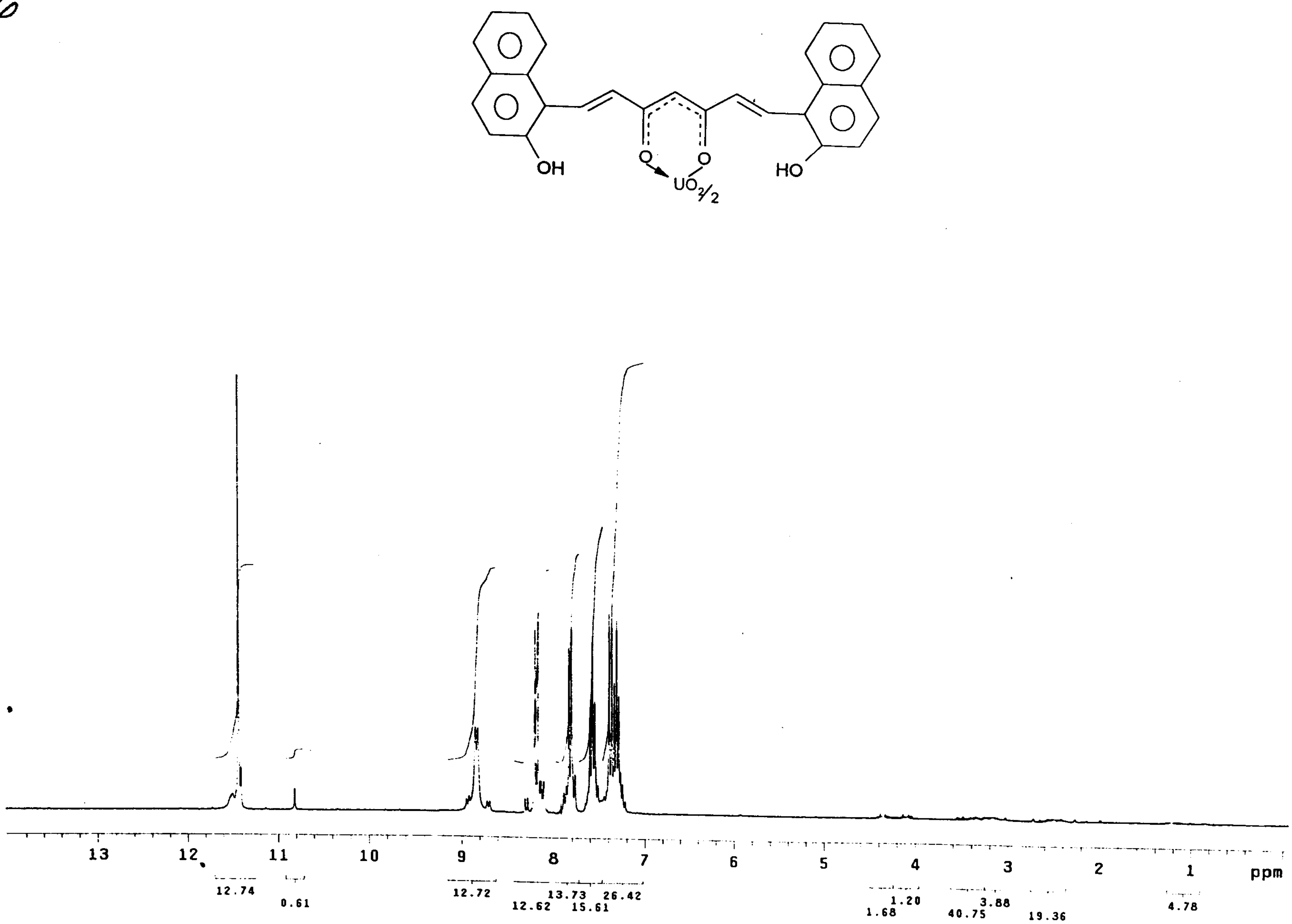
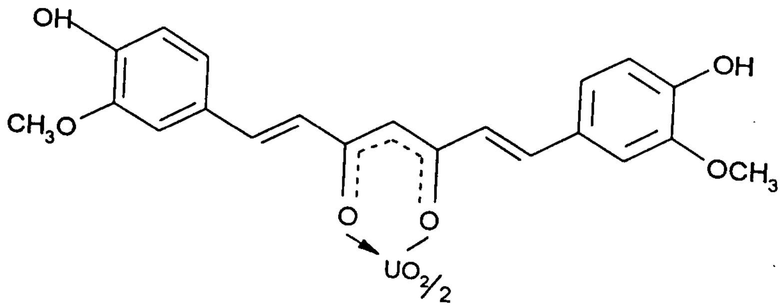


Fig. 28. ^{1}H NMR spectrum of Uranyl(VI) complex of **1f**

proton of the free ligand is absent in the spectra of the complexes. That the phenolic –OH group of **1f** is not involved in complex formation is well demonstrated in the spectrum from the presence of a signal at δ~ 11.5 ppm. The integrated intensity of the signal correspond to four protons thereby confirming the presence of two ligands in the complex. The measured frequency of this signal reveals that it is a combination of at least three resonance signals at δ 11.504,11.434 and 11.409 ppm. This point to the fact that the four –OH groups of the complex are not in identical environment. This can be attributed to steric factors. The integrated intensities of all the signals agree with the formulation of this complex. Spectra of **1b** and **1f** and their uranyl complexes are reproduced in figures 25-28.

Mass spectra

The FAB mass spectrum of the dioxouranium complex of 1j is given in figure 29. The spectrum displays a relatively intense (P+1) peak correspond to the stoichiometry $[UO_2L_2]$. The relative intensities of the peaks in the range 1003-1007 is in agreement with the natural abundance of various isotopes of uranium. Other prominent peaks are due to the elimination of OCH_3, H_2O, phenyl groups, C_2H_2, etc. from the molecular ion. Similarly an intense peak at m/z 637 is due to $[UO_2L]^+$ fragment. Thus the available spectral data agree with the structure **3** of the complexes.



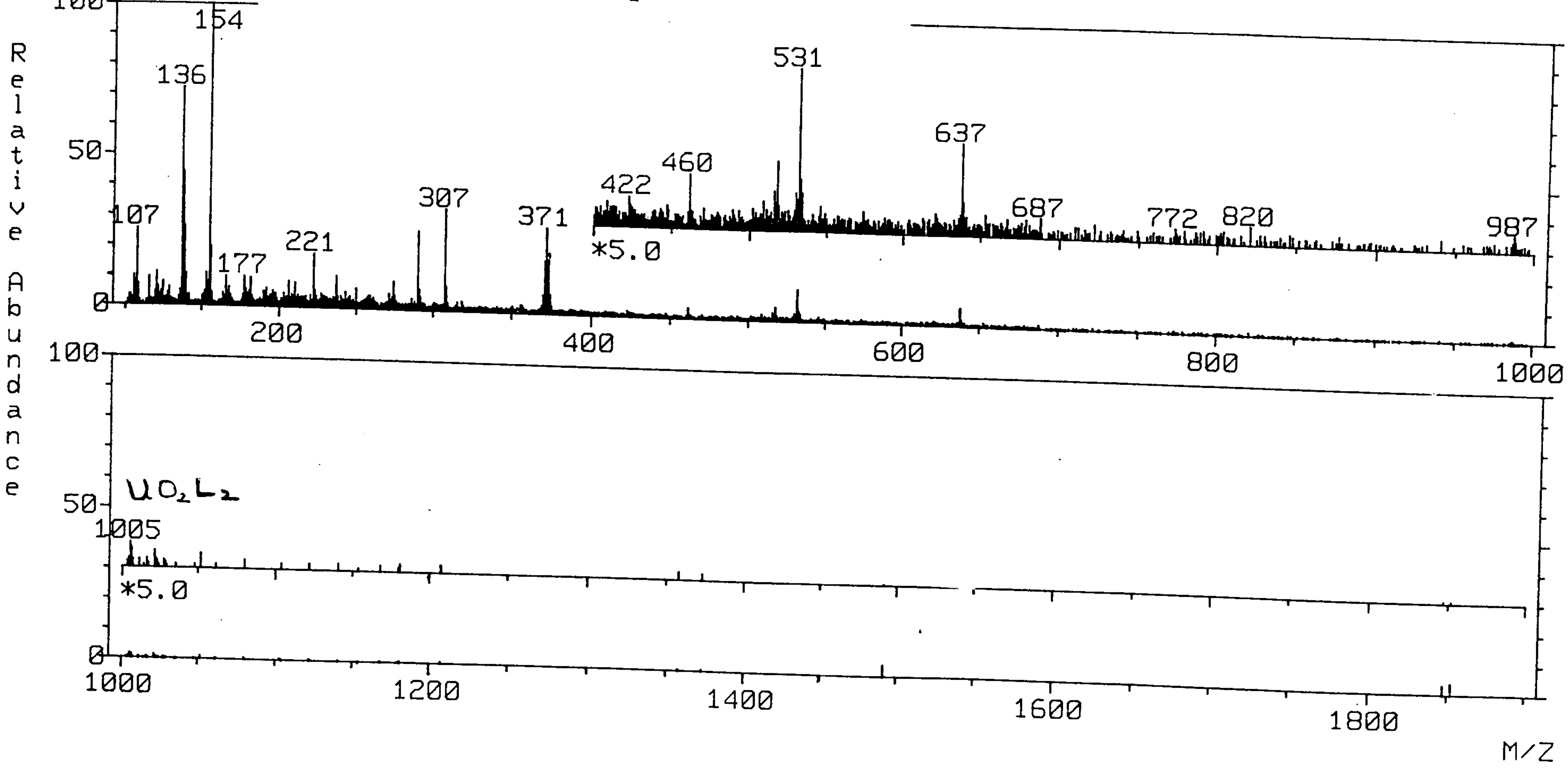


Fig. 29. Mass spectrum of Uranyl(VI) complex of **1j**

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JULY 2004

CHAPTER III

ALUMINIUM(III) COMPLEXES OF 1,7-DIARYLHEPTANOIDS

ALUMINIUM(III) COMPLEXES OF 1,7-DIARYLHEPTANOIDS

The 1,7-diarylheptanoids yielded well-defined complexes with aluminium(III). The synthesis and characterisation of these complexes are discussed below.

Synthesis of the complexes

The general procedure adopted for the preparation of Al(III) complexes is given below.

A methanolic solution (25 mL) of the aluminium nitrate, $Al(NO_3)_3.9H_2O$, (0.001 mol) was added slowly with stirring to a solution of the 1,7-diarylheptanoid (0.003 mol) in methanol (25 mL). The mixture was stirred well and refluxed gently for ~ 1 h and the volume was reduced to half. On cooling to room temperature the complex gets precipitated. It is then filtered, washed with 1:1 methanol-water mixture and dried in a vacuum desiccator. For purity, the compound was recrystallised from hot methanol.

Results and Discussion

The analytical and physical data of the complexes are given in table 26. The elemental analytical data of the complexes correspond to the $[AlL_3]$ stoichiometry. The complexes are non-conducting in dmf and do not contain the nitrate ion of the aluminium nitrate used for the preparation.

TABLE 26

Physical and Analytical data of the Aluminium(III) chelates of 1,7-diarylheptanoids (HL)

Aluminium(III) chelates	M.P. (°C)	Elemental analysis %, found/calculated*		
		C	H	Al
1a	190	80.63 (80.28)	5.61 (5.28)	3.24 (3.17)
1b	> 340	82.43 (82.14)	5.92 (5.65)	2.82 (2.68)
1d	> 320	72.47 (72.15)	4.93 (4.75)	2.98 (2.85)
1f	> 340	78.01 (77.88)	4.83 (4.56)	2.43 (2.16)
1j	> 300	67.52 (67.02)	5.28 (5.05)	2.63 (2.39)
1l	160	74.54 (74.19)	6.43 (6.18)	2.72 (2.42)

*The calculated value corresponds to the [AlL_3] composition where L stands for the deprotonated ligand HL.

Infrared spectra

The ir spectra of the complexes revealed that the enolic proton of the ligand has been replaced by the metal ion. Thus the broad band in the region 2500-3500 cm^{-1} of the ligand cleared up in the spectra of complexes and instead several weak bands in the region 2500-3200 cm^{-1}, due to various ν_{C-H} vibrations. The intramolecularly H-bonded carbonyl band of the ligand at ~1624 cm^{-1} shifted to ~ 1590 cm^{-1} in the spectra of complexes due to the metal coordination to the diketo function. The typical spectra of the free ligands and their complexes are reproduced in figures 30, 31.

NMR spectra

The ^{1}H nmr spectra of the complex clearly demonstrated the replacement of the enolic proton by Al(III) ion. The low field band at $\delta \sim 16$ ppm of the ligand disappeared in the spectra of the complexes. The spectra are reproduced in figures 32-35. The methylene and olefinic proton signals are slightly shifted to low field compared to the free ligand resonance which indicate more efficient delcoalization of the π-electron in the complexes.

Mass spectra

The most importance evidence regarding the formation of the trischelates were obtained from their mass spectra. The spectra clearly show relatively intense peak due to the molecular ion and a more intense peak due to $[AlL_2]^+$ ion. The spectra are reproduced in figures 36, 37. Several metal containing fragments are appeared in the low mass region of the spectrum.

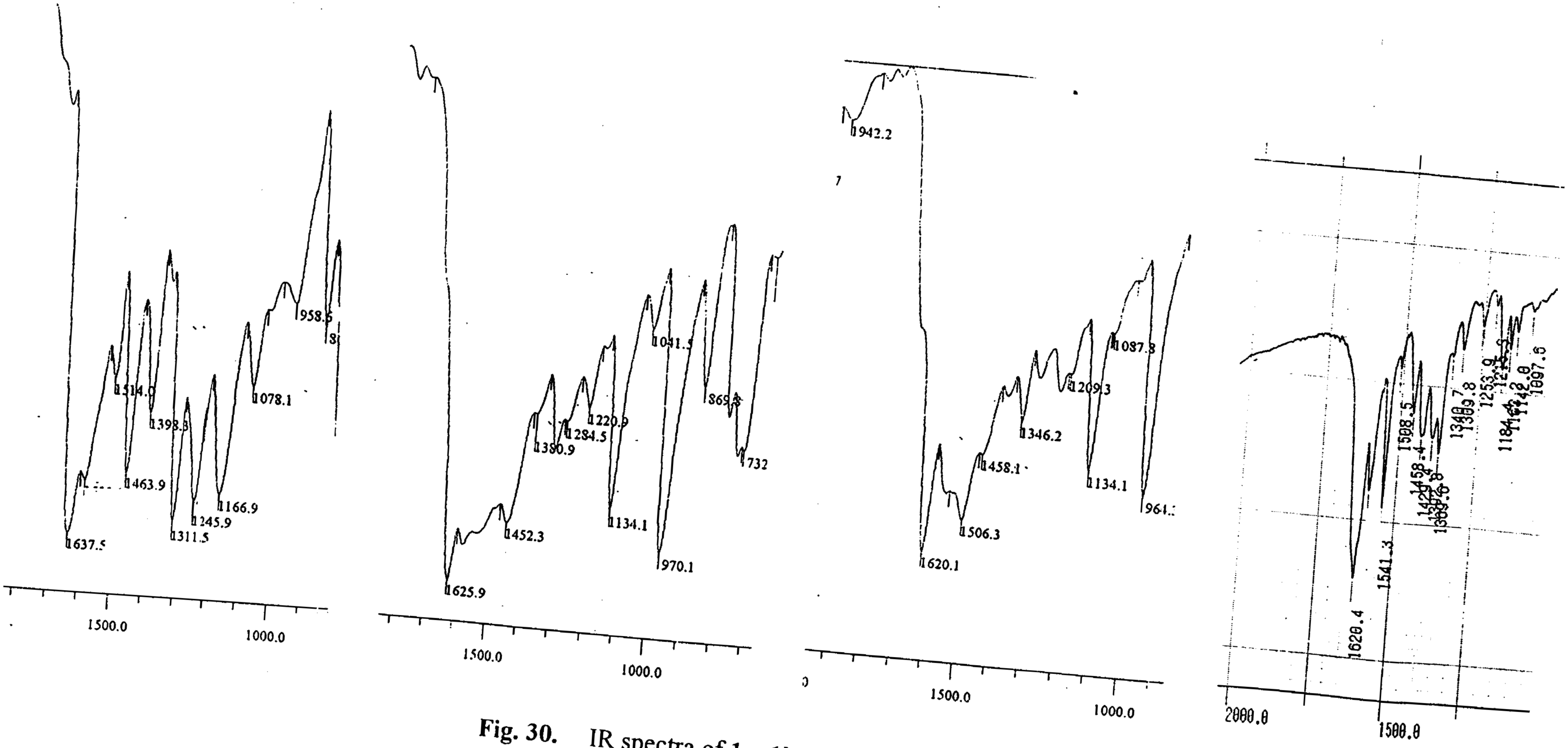


Fig. 30. IR spectra of **1a**, **1b**, **1j** and **1l**

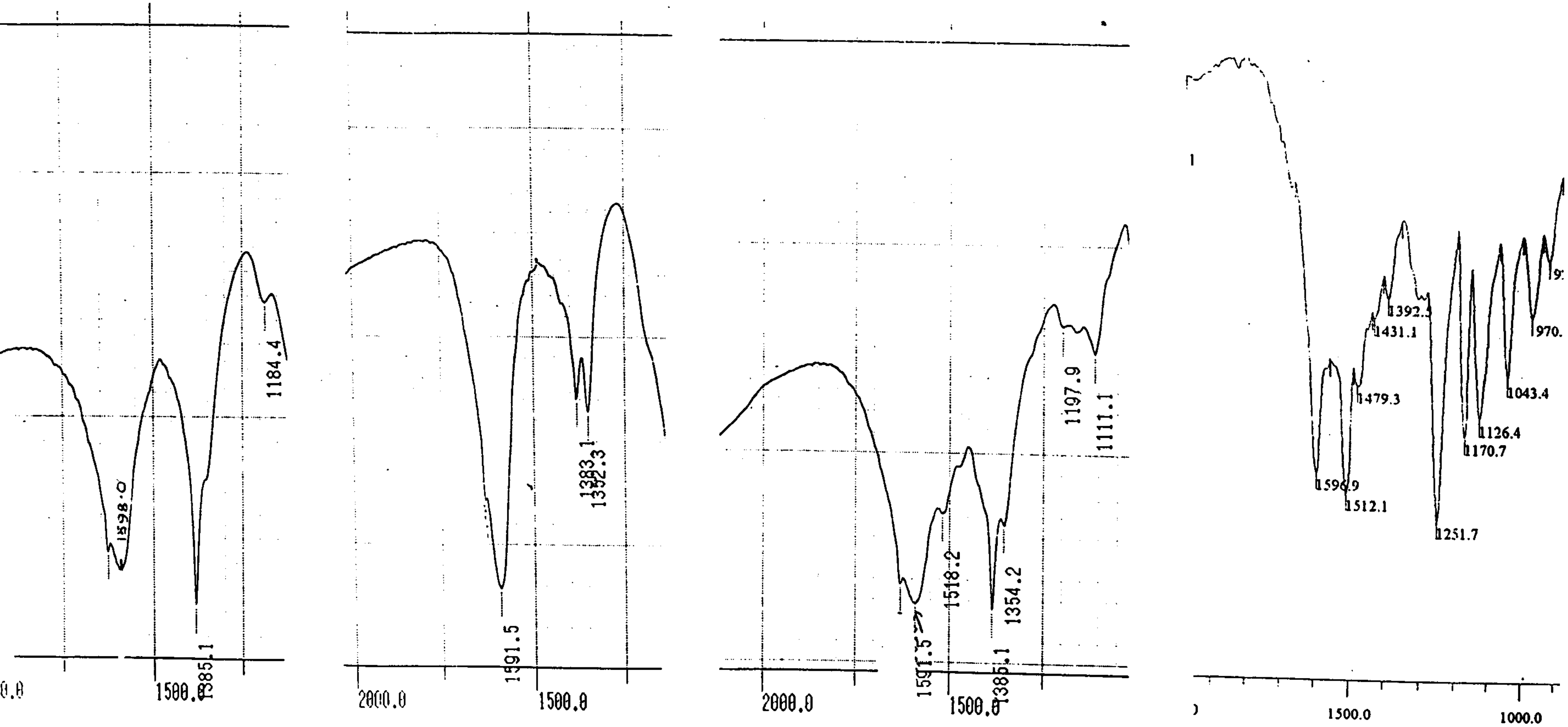


Fig. 31. IR spectra of Aluminium(III) complexes of **1a, 1b, 1j** and **1l**

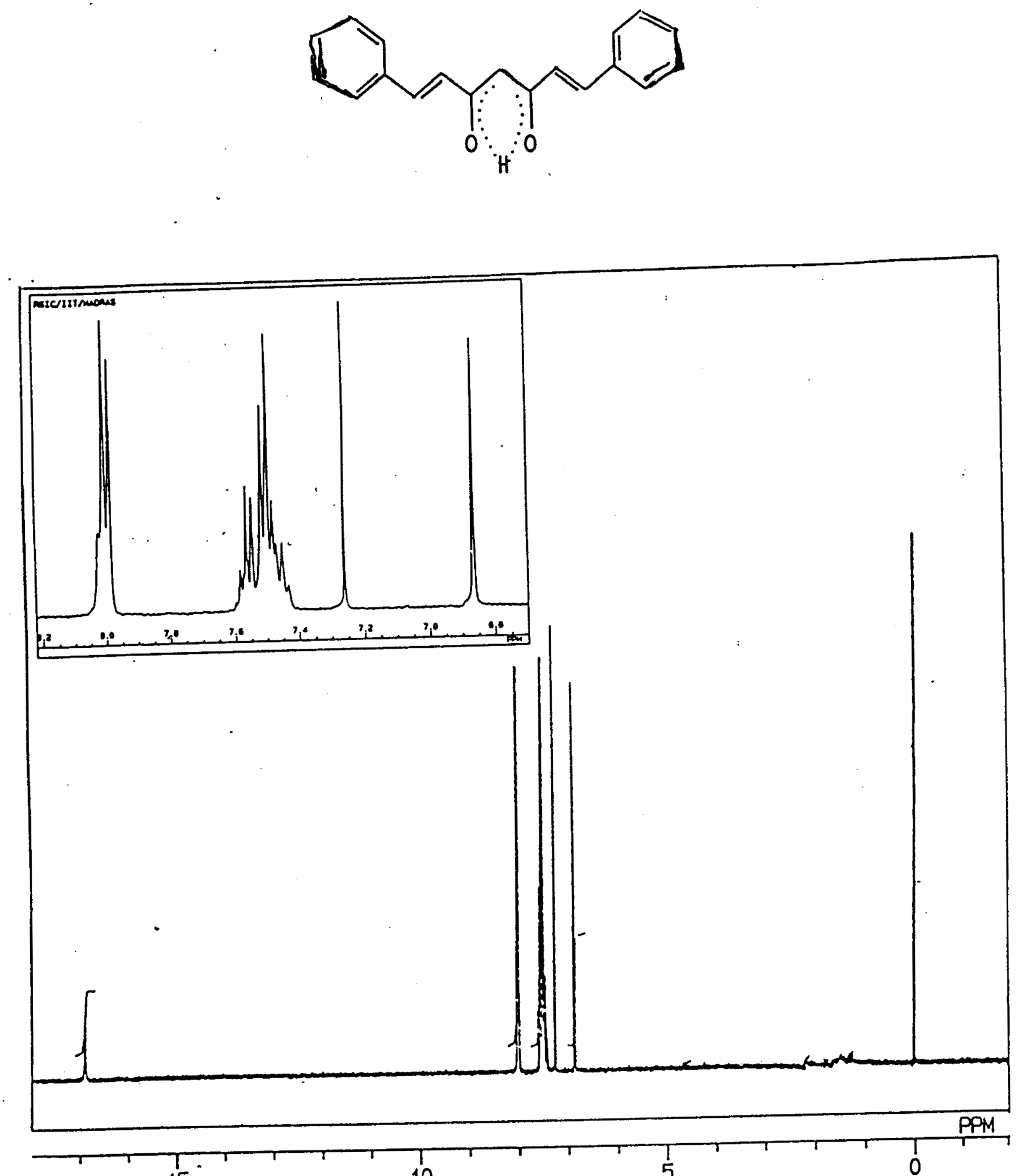
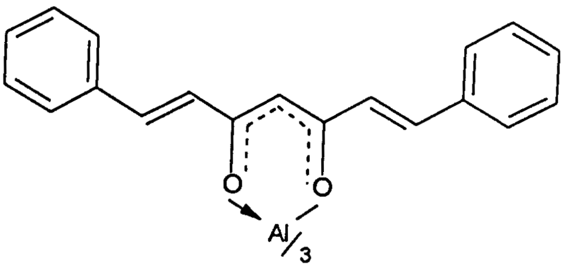


Fig. 32. ^{1}H NMR spectrum of **1a**



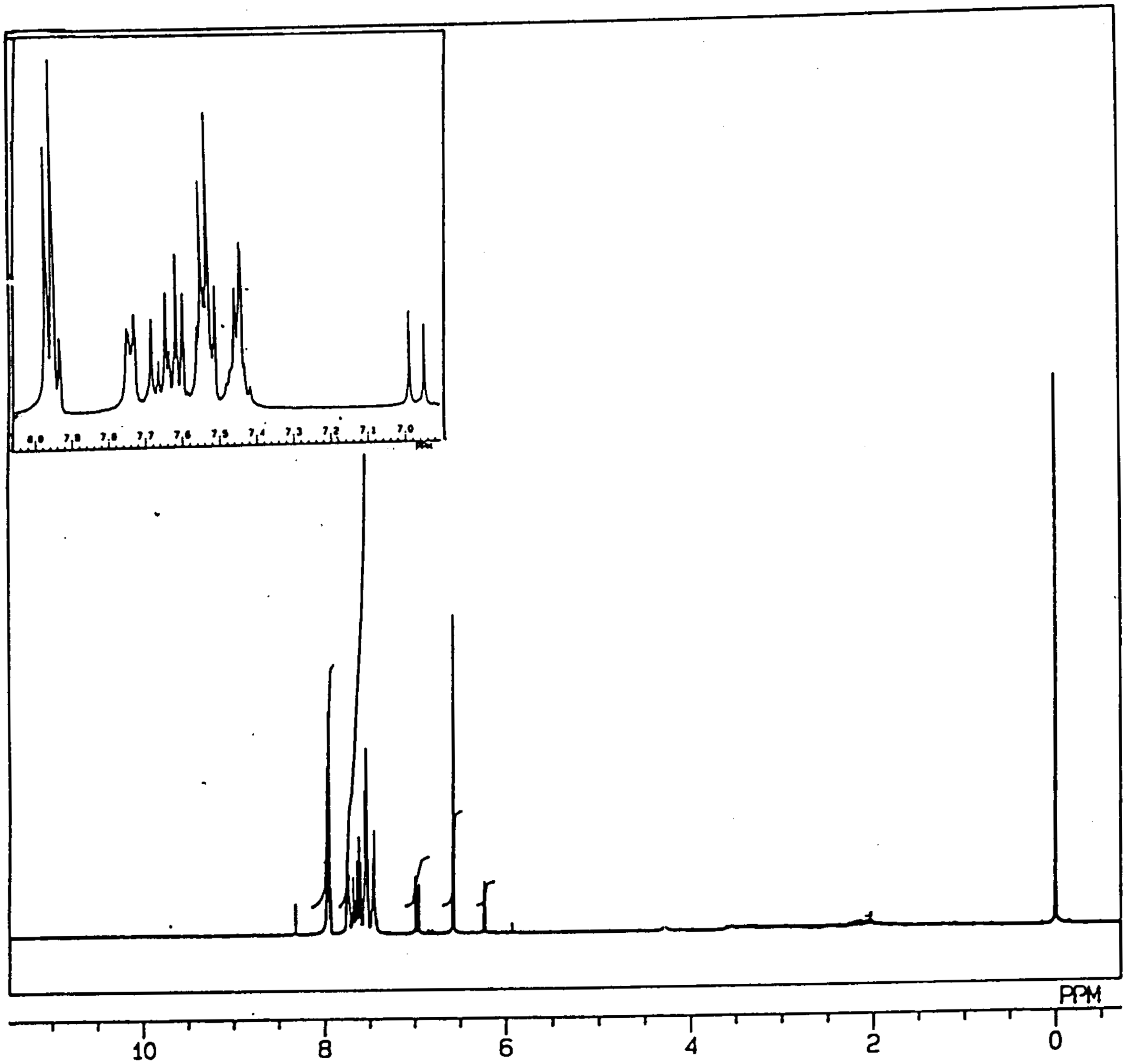


Fig. 33. ^{1}H NMR spectrum of Aluminium(III) complex of **1a**

51

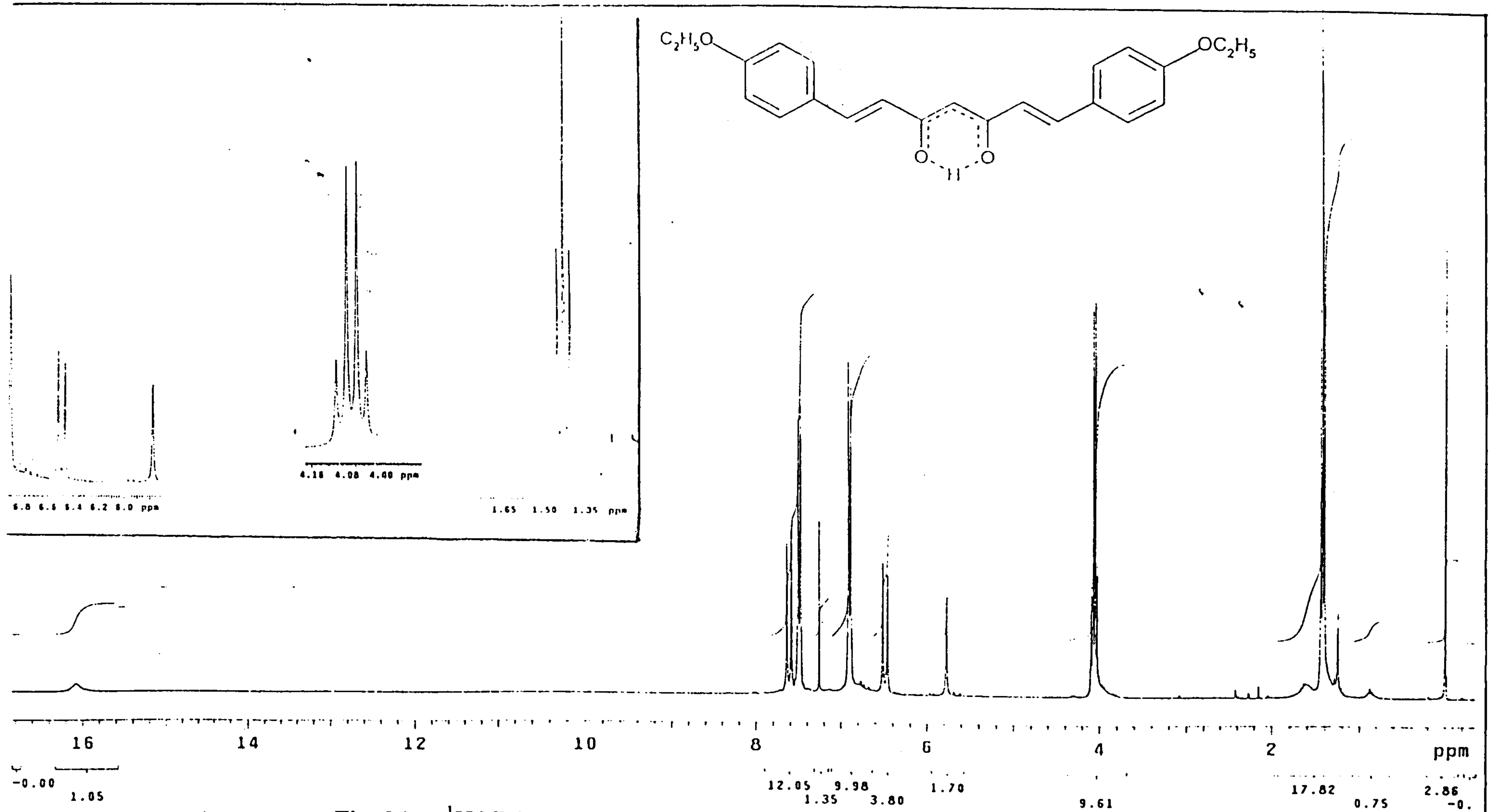


Fig. 34. ^{1}H NMR spectrum of 1l

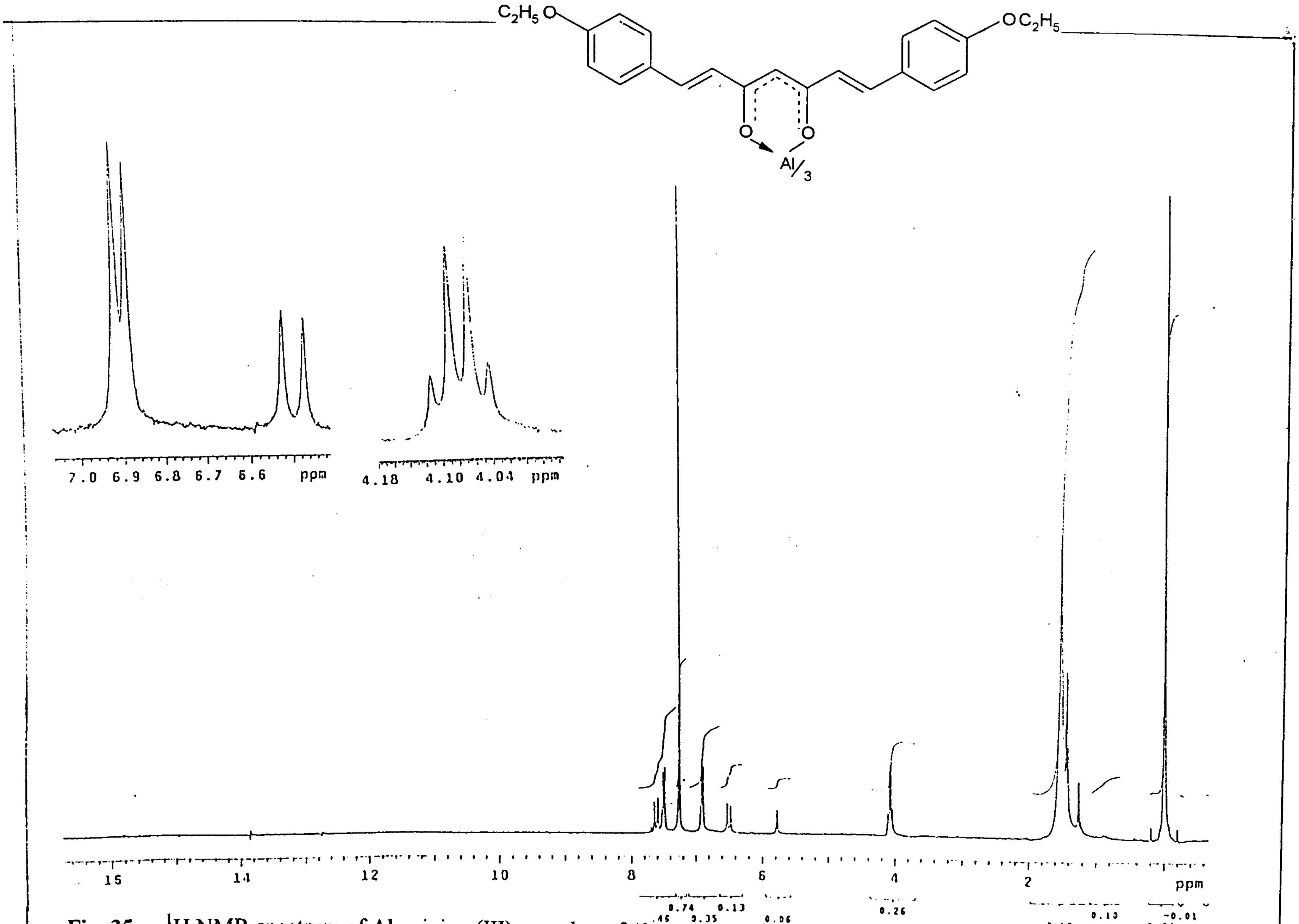


Fig. 35. ^{1}H NMR spectrum of Aluminium(III) complex of 1l

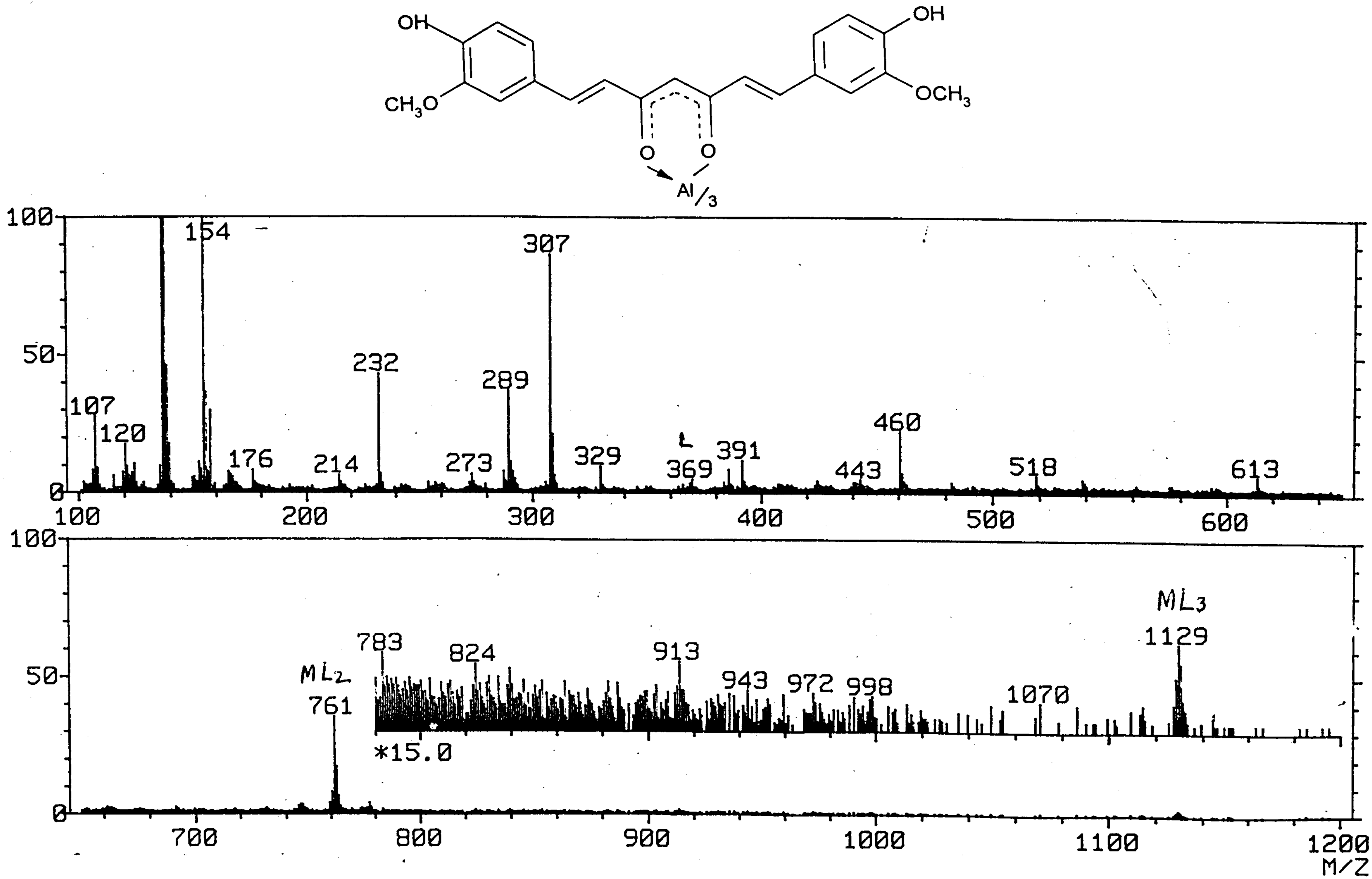


Fig. 36. Mass spectrum of Aluminium(III) complex of **1j**

50

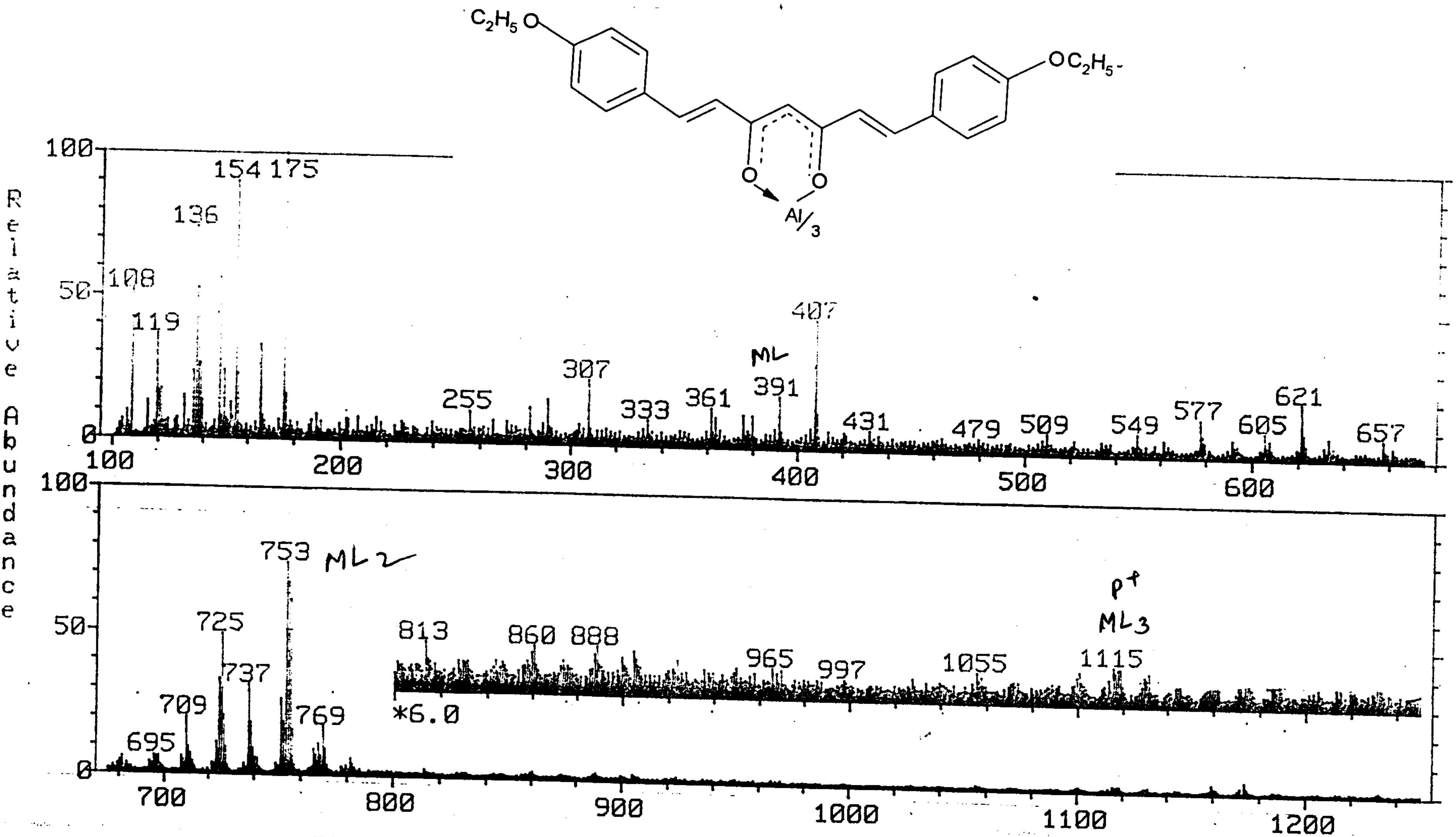


Fig. 37. Mass spectrum of Aluminium(III) complex of 1l

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CHAPTER IV

ANTIOXIDANT ACTIVITY OF THE 1,7-DIARYLHEPTANOIDS AND THEIR METAL COMPLEXES

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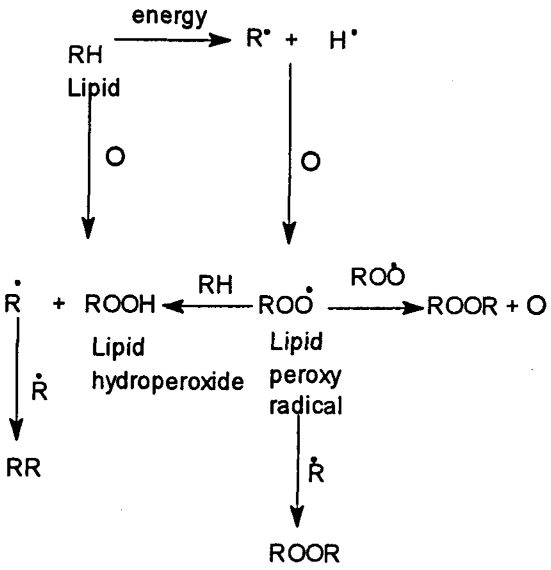
ANTIOXIDANT ACTIVITY OF THE 1,7-DIARYLHEPTANOIDS AND THEIR METAL COMPLEXES

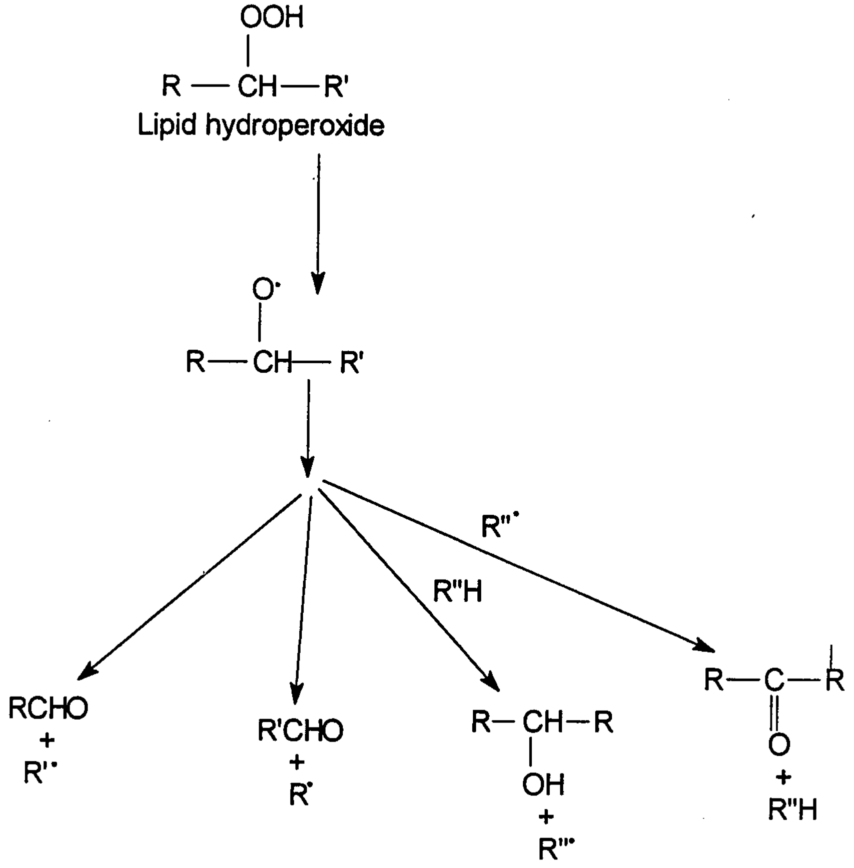
Copy ?

During the physiological process of respiration, inhaled and tissue incorporated oxygen oxidises cellular components and biomolecules. This process when tilted towards excessive activity, results in generation of oxidative products known as free radicals. A direct consequence of this is found in the rancidification of certain lipids.[230] The autoxidation of unsaturated fatty acid components of lipids is known to proceed by a free radical mechanism as shown in scheme 1.1.



Scheme 1.1

The hydroperoxides formed as the primary products are quite unstable and can produce more free radicals by degenrate branching and numerous unwanted secondary degradation products (scheme 1.2) of which the volatile aldehydes play significant role in imparting off-flavours to food stuffs even at ppb levels.[231]



Scheme 1.2

Free radicals such as ROO•, RO•, OH•, etc. can react at random by hydrogen abstraction and a variety of addition reactions to damage proteins, other lipids and vitamins (particularly vitamin A). The human body has built-in mechanisms to counteract free radicals. These mechanisms are collectively known as the body's antioxidant defence.

Synthetic organic chemists have developed many effective antioxidants for rubber, hydrocarbon fuels, plastics and food stuffs.[232] Propyl gallate, BHA (butylated hydroxyanisole) and BHT (butylated hydroxytoluene) are antioxidants used as food additives. Some vitamins (Vitamin E & C), minerals and natural compounds like phenols, flavonoids and carrotenoids have the ability to counteract free radicals by scavenging or neutralising the free radicals.

Curcuminoids are natural phenolic compounds, with potent antioxidant properties. Several research groups have recently provided convincing evidence for the antioxidant properties of curcuminoids and turmeric extracts.[142,233-238] Both turmeric and curcuminoids inhibited generation of potent free radicals like superoxide and hydroxyl radicals.[141] The antioxidant properties of curcumin in prevention of lipid peroxide, another process that generates free radicals, is well recognised.[143,233]

Curcuminoids, have been found both safe and effective antioxidants, and scavenge free radicals at the cost of becoming weak free radicals themselves. These "second hand" free radcials are unreactive products, and do not pose a health hazard. Also the curcuminoid free radicals, unlike those of synthetic phenolics like BHT or BHA are short lived, a feature that further adds to their safety.

In this investigation, the antioxidant activity of the 1,7-diarylheptanoids and their typical metal complexes were studied. The experimental details and results obtained are discussed below.

Experimental

The antioxidant assay is usually carried out on model systems such as methyl linoleate or linoleic acid and there are several methods to study the extent of activity.[239-243] In the 'thiocyanate method', the ability of lipid hydroperoxide (formed during the autoxidation of lipids such as linoleic acid) to oxidise $Fe^{2+} \rightarrow Fe^{3+}$ is exploited. In this method, the sample and linoleic acid in a water-ethanol medium is incubated at 40°C in the dark and the autoxidation is followed at intervals by measuring the absorbance (at 500 nm) of the red colour developed after the addition of ferrous salt and NH_4SCN. As the concentration of Fe^{3+} and hence absorbance depends on the extent of lipid autoxidation, the antioxidant activity of the sample can be judged qualitatively from a comparison of the absorbance of a control maintained under identical conditions. The antioxidant assay procedure employed is given below.

A solution (2.53%) of linoleic acid in 99.5% ethanol and 0.05 M phosphate buffer of pH 7 were prepared. Solution (4 mL) of the test compound (2 mg in 99.5% ethanol) was added to a solution mixture containing linoleic acid (4.1 mL), phosphate buffer (8 mL) and distilled water

(3.9 mL) taken in stoppered Erlenmaeyr flasks, and incubated at 40°C in the dark for 7-8 days. At periodic intervals during the incubation, 100 mL of the mixture was used for antioxidant assay by the thiocyanate method as described below.

The incubated solution (100 mL) was added to 75% ethanol (9.7 mL) and 30% ammonium thiocyanate (0.1 mL). Ferrous salt solution (0.1 mL, 2×10^{-2}M) in 3.5% HCl was then added and precisely after 3 min the absorbance of the red colour developed was measured at 500 nm. The antioxidant activity was judged from the decrease in the absorbance compared to the absorbance of a control maintained under identical condition.

Results and Discussion

The results of antioxidant activity of the eight synthetic curcuminoids obtained are presented graphically (absorbance at 500 nm vs number of days) in figure 38. The control is included in the figure to clarify the extent of activity. Antioxidant activity of the curcuminoid analogues correlates with their ability to scavenge reactive oxygen species.[244] The presence of a double bond in conjugation with each of the phenyl rings is responsible for this activity.

Among the compounds, highest antioxidant property is shown by **1f** and the lowest activity by **1g**. The observed order of the activity is

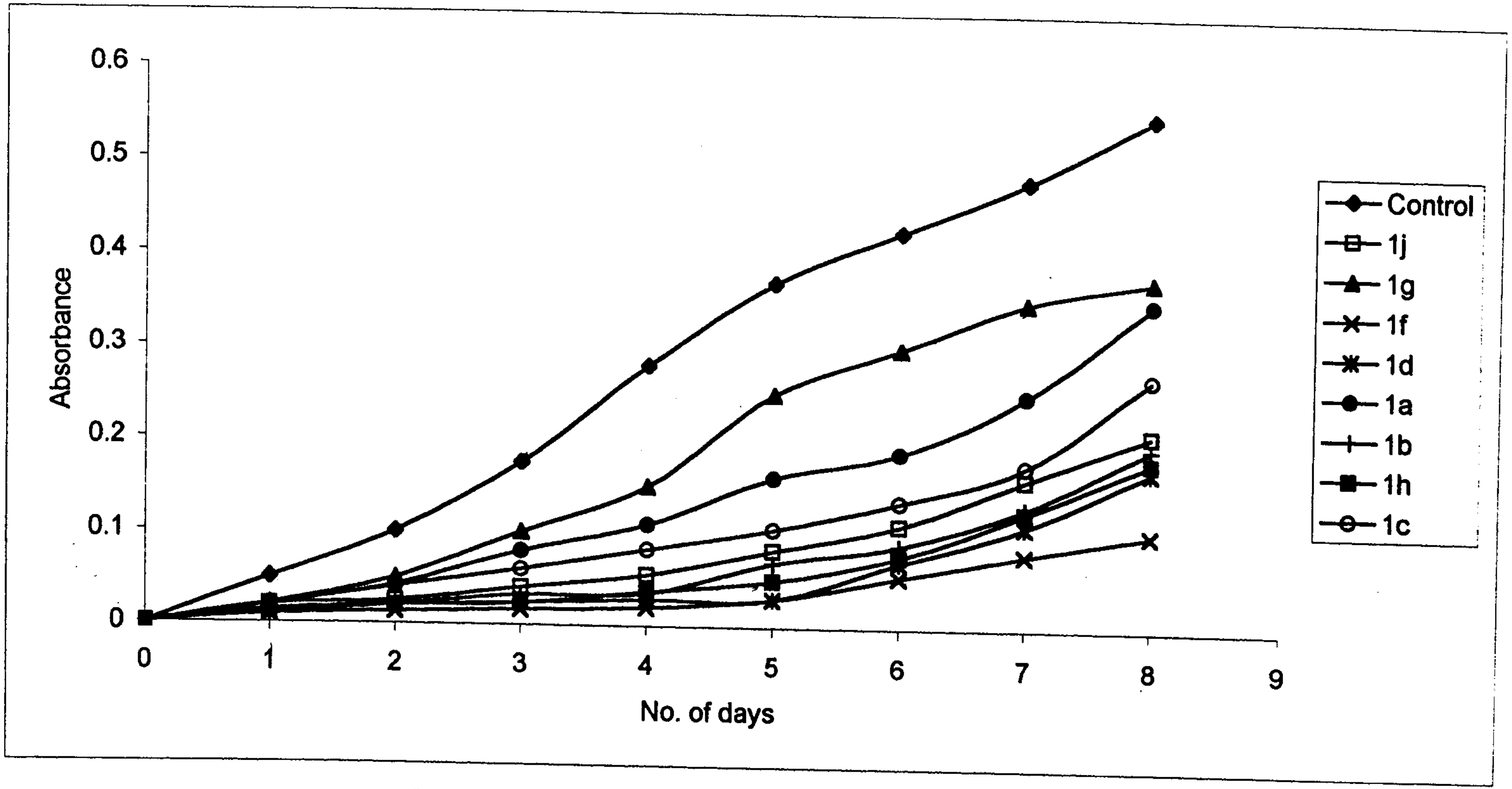


Fig. 38 Antioxidant assay of 1,7-diarylheptanoids

1f > **1d** > **1h** > **1b** ~ **1j** > **1c** > **1a** > **1g**. Since the structural unit in all the curcuminoids is the diketo function (predominantly enolised), the variation in activity of the compounds can arise only as due to the aryl substituents. Some of the major conclusions that can be derived from the results (figure 38) of antioxidant study of the compounds are

(a) Extended conjugation increases the activity, thus **1f** and **1b** show more activity than **1a**.

(b) Presence of –OH group on the aryl ring markedly increased the activity.

(c) Since **1g** showed least activity, methoxy group is not the major contributor to the antioxidant activity.

(d) An –OH group ortho to the olefinic linkage is more favourable for antioxidant behaviour than an –OH group in the para position. This is evident from the data that **1h** shows less activity than **1d**.

Recent studies revealed that these synthetic curcuminoids possesses antitumour activity.[176] It has been shown that antitumour activity of compounds are closely related to the antioxidant activity also. A comparison of the reported antitumour activity of the curcuminoids considered in the present study with their antioxidant activity revealed that those curcuminoids having highest antitumour activity also exhibit maximum antioxidant activity.[36,37] The reported antitumour activity (reduction in tumour volume in mice) of the curcuminoids are given in the figure 39 and the observed antioxidant activity in figure 40.

Thus **1f** and **1d** which contain –OH group at the *ortho* position of the aryl ring exhibited maximum antioxidant and antitumour activity.

The antioxidant activity of typical lanthanide complexes of curcuminoids were also studied. The results showed that almost all the complexes have significant antioxidant activity. However, their activity is less than the corresponding free curcuminoids (Figures 41-48).

Complexes of those curcuminoids which contain free –OH groups also showed lower activity. Thus –OH group alone is not sufficient to promote antioxidant activity. This indicate the importance of free and enolised dicarbonyl moiety in antioxidant property of curcuminoids. During complexation, the enolic proton is removed with the formation of a six membered pseudo-aromatic C_3O_2M chelate ring with the metal ion thereby loosing the enolic nature of the curcuminoids. Earlier reports of certain transition metal complexes of some of the curcuminoids also showed less activity for complexes.[132] It has been reported that the antitumour activity of curcuminoids increases on complexation with metal ions such as copper(II). But, in general the antioxidant activity of metal complexes of curcuminoids decreases.

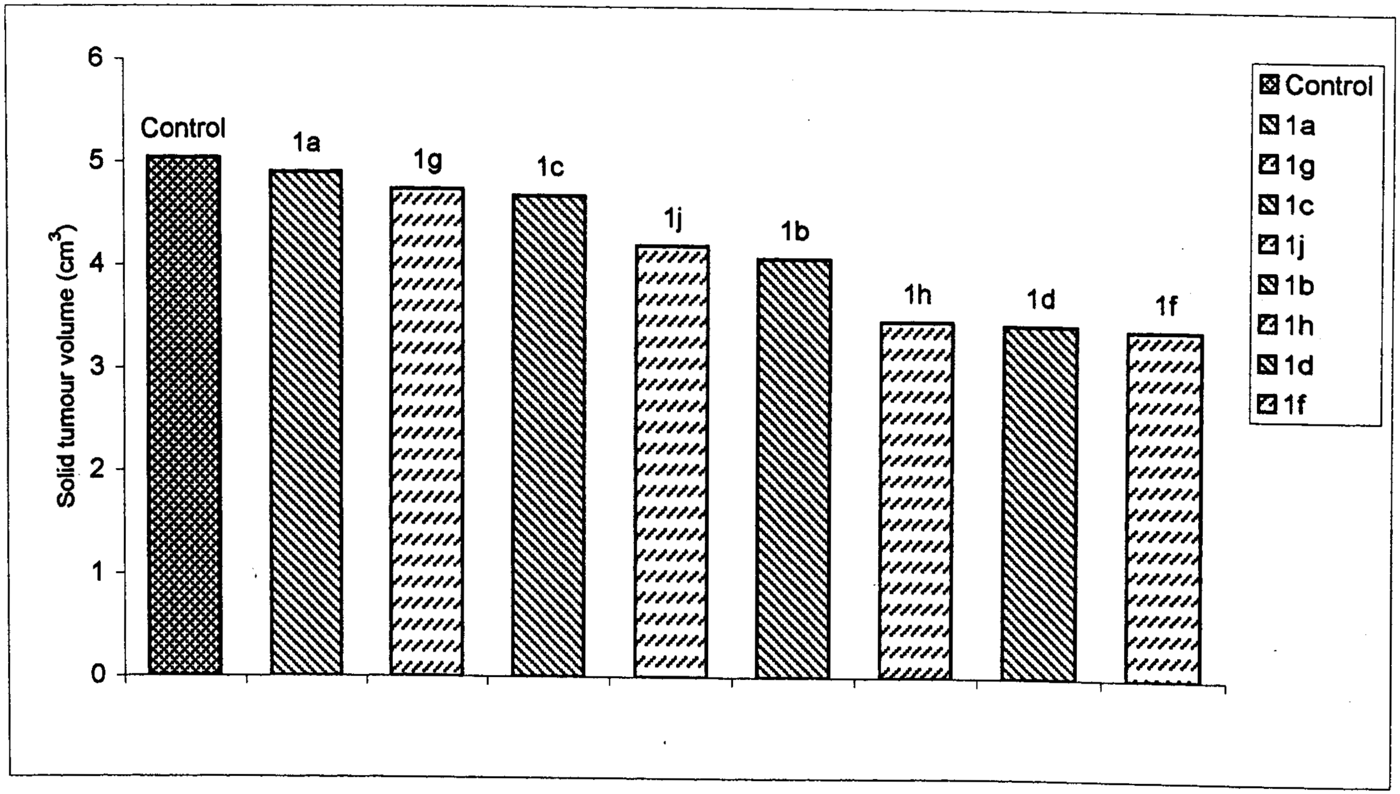


Fig. 39 Solid tumour volume on day - 31 with respect to control

58

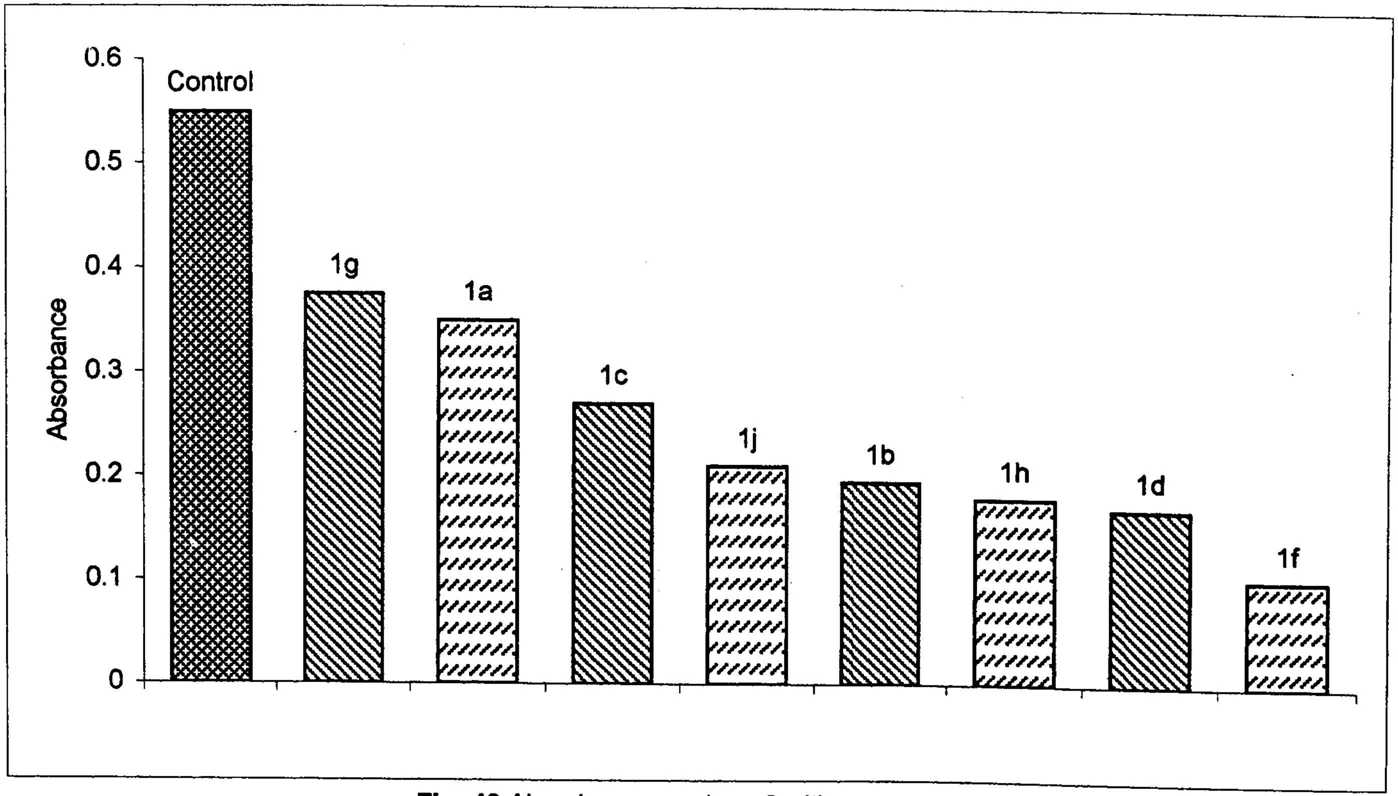


Fig. 40 Absorbance on day - 8 with respect to control

59

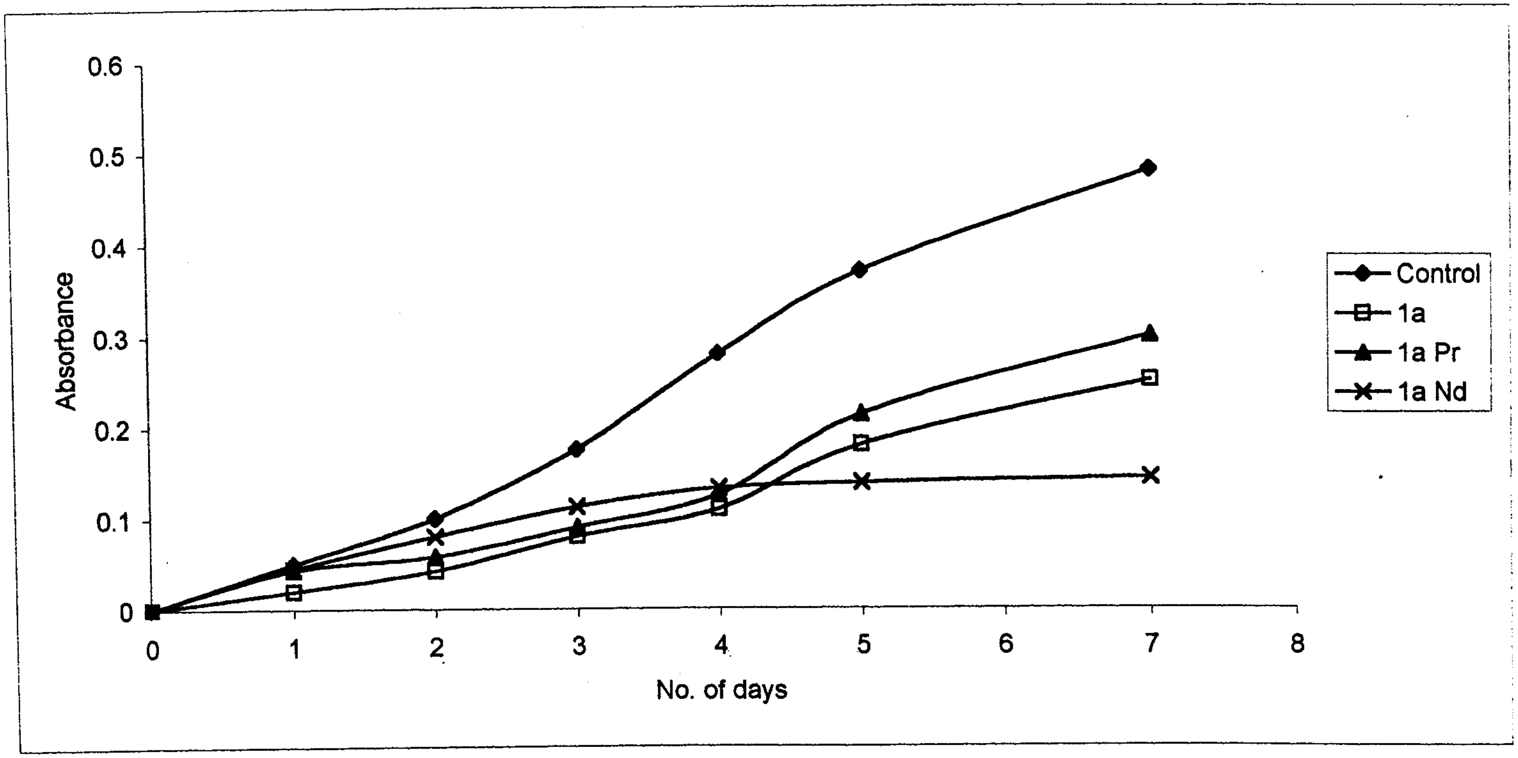


Fig. 41 Antioxidant assay of **1a** and its complexes

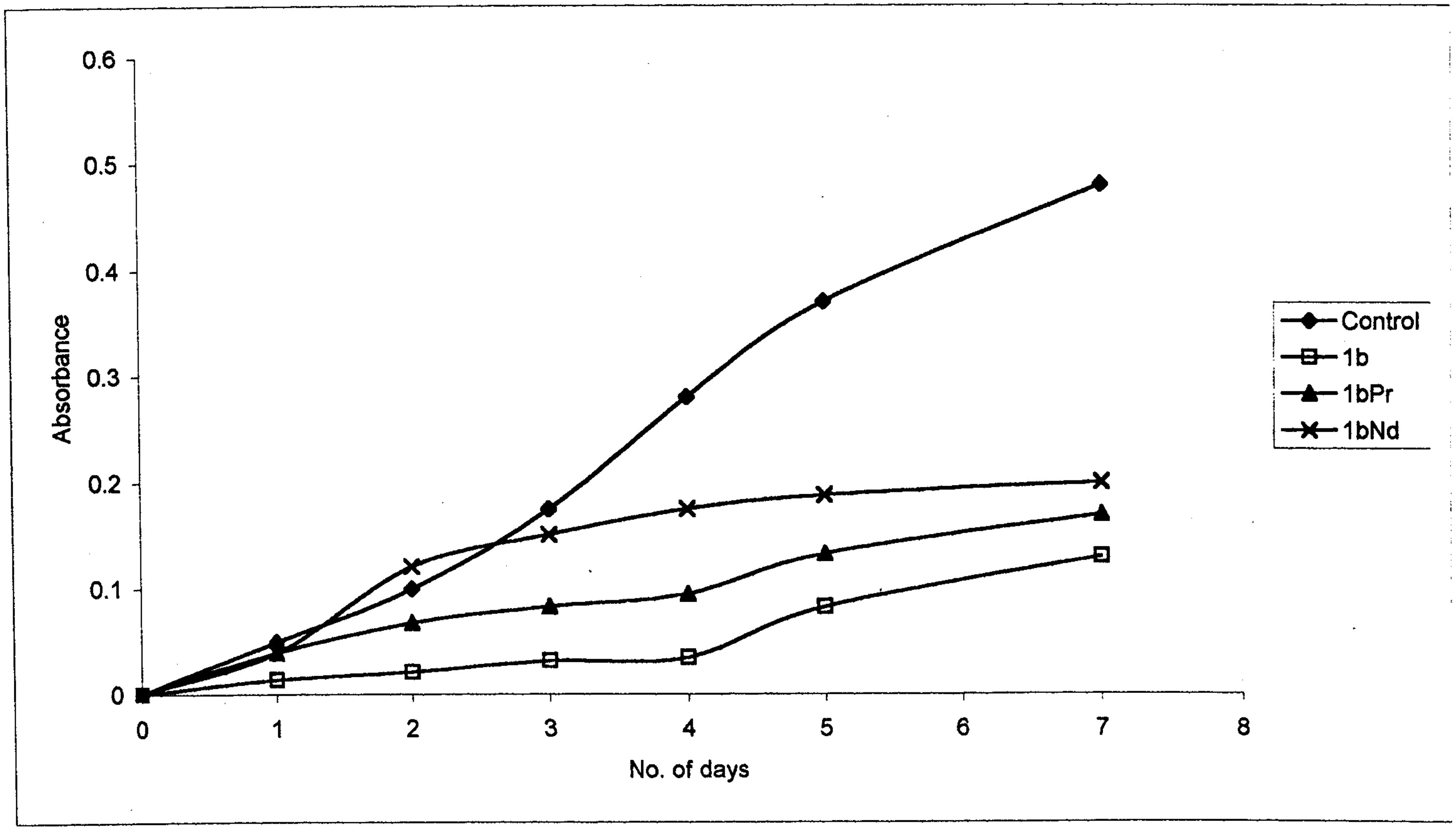


Fig. 42 Antioxidant assay of **1b** and its complexes

61

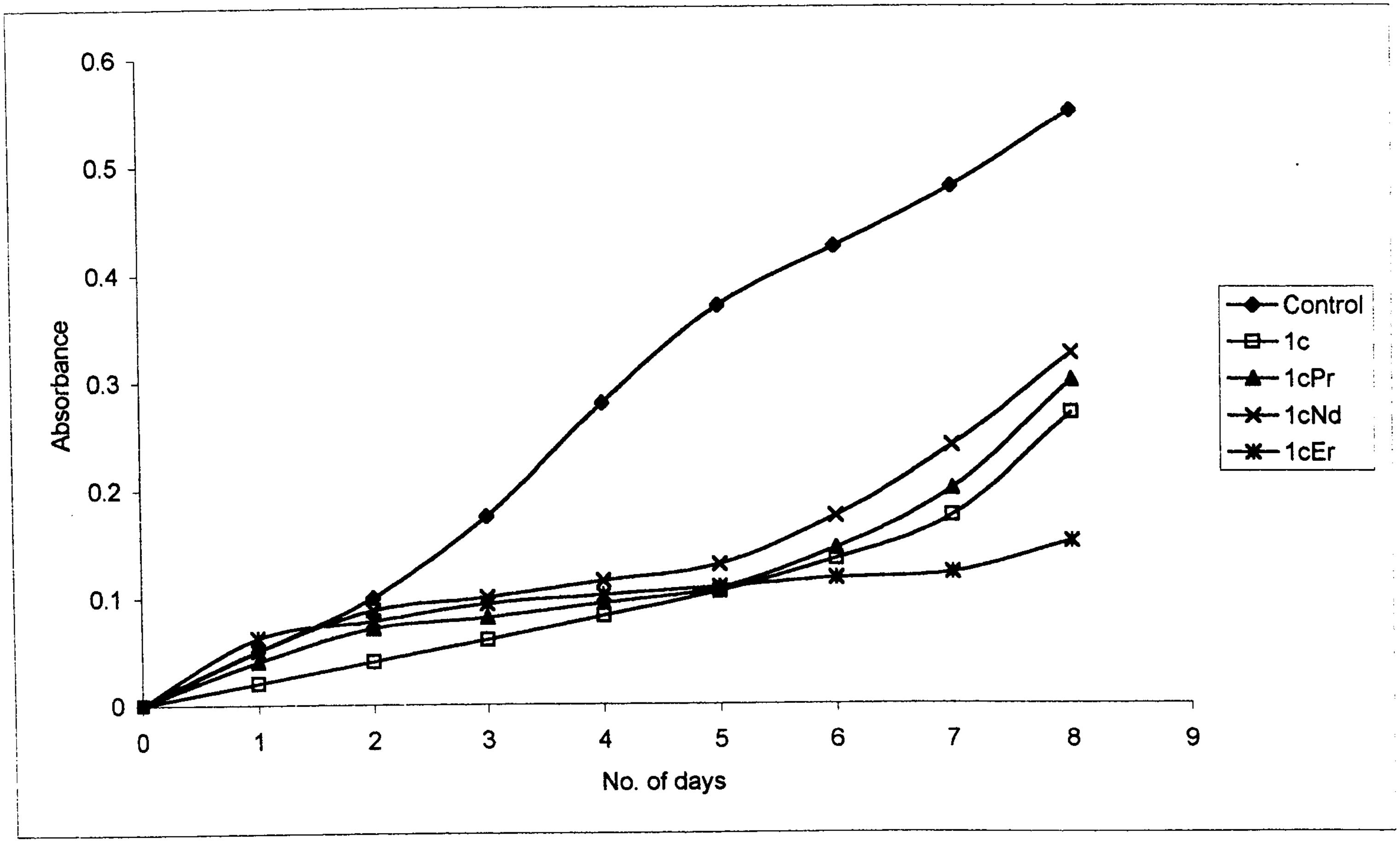


Fig. 43 Antioxidant assay of **1c** and its complexes

62

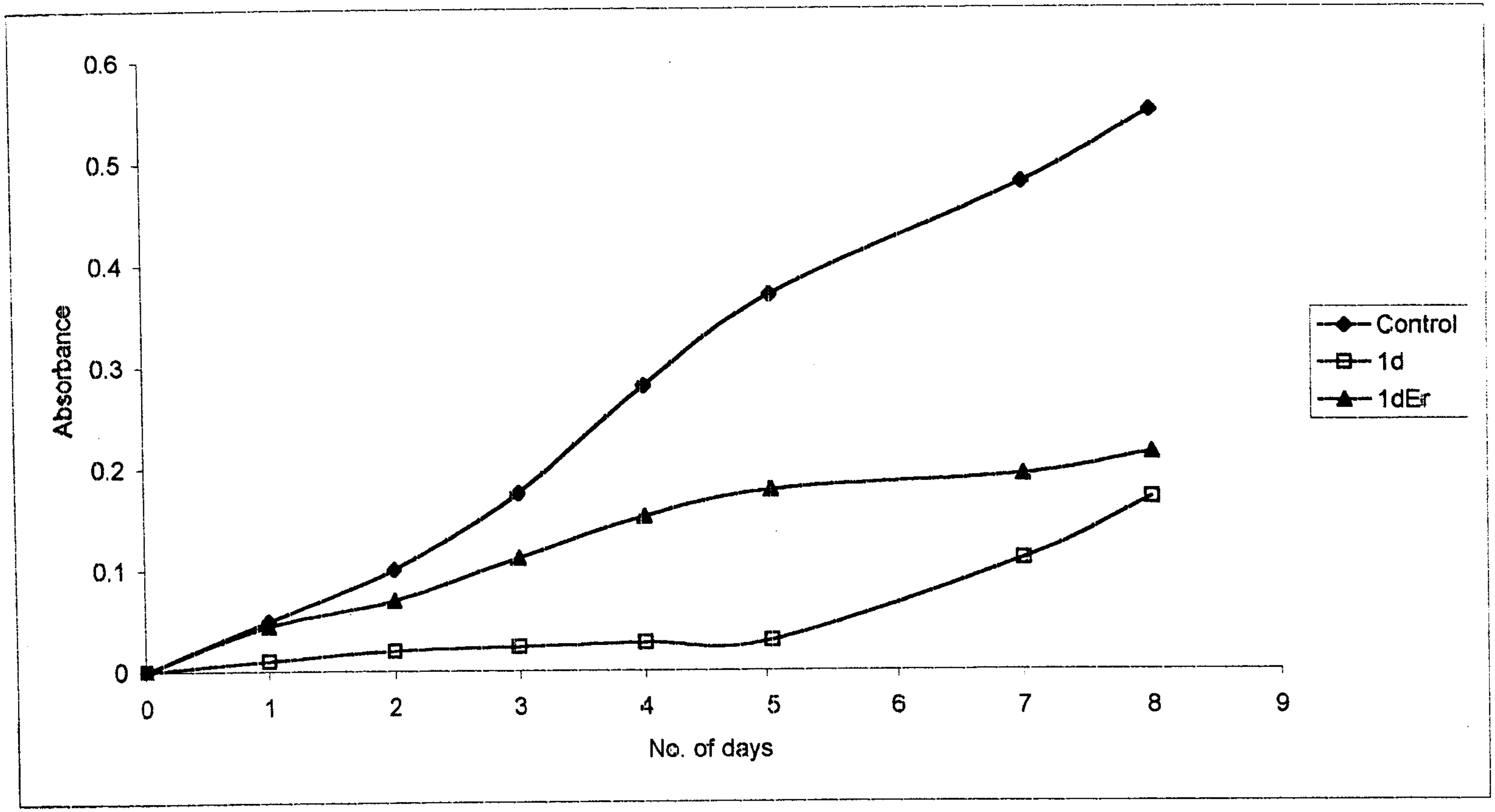


Fig. 44 Antioxidant assay of **1d** and its complexes

63

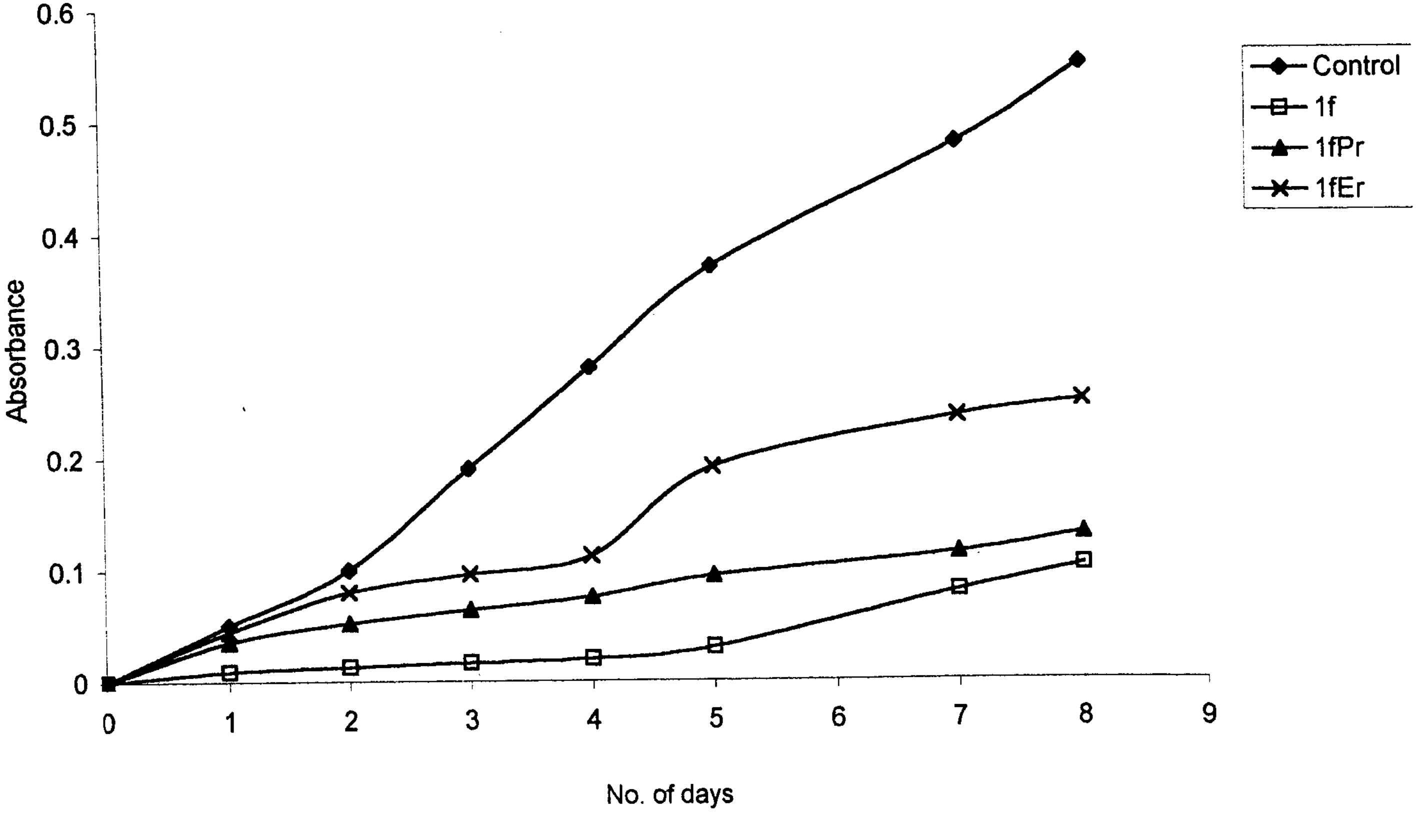


Fig. 45 Antioxidant assay of **1f** and its complexes

64

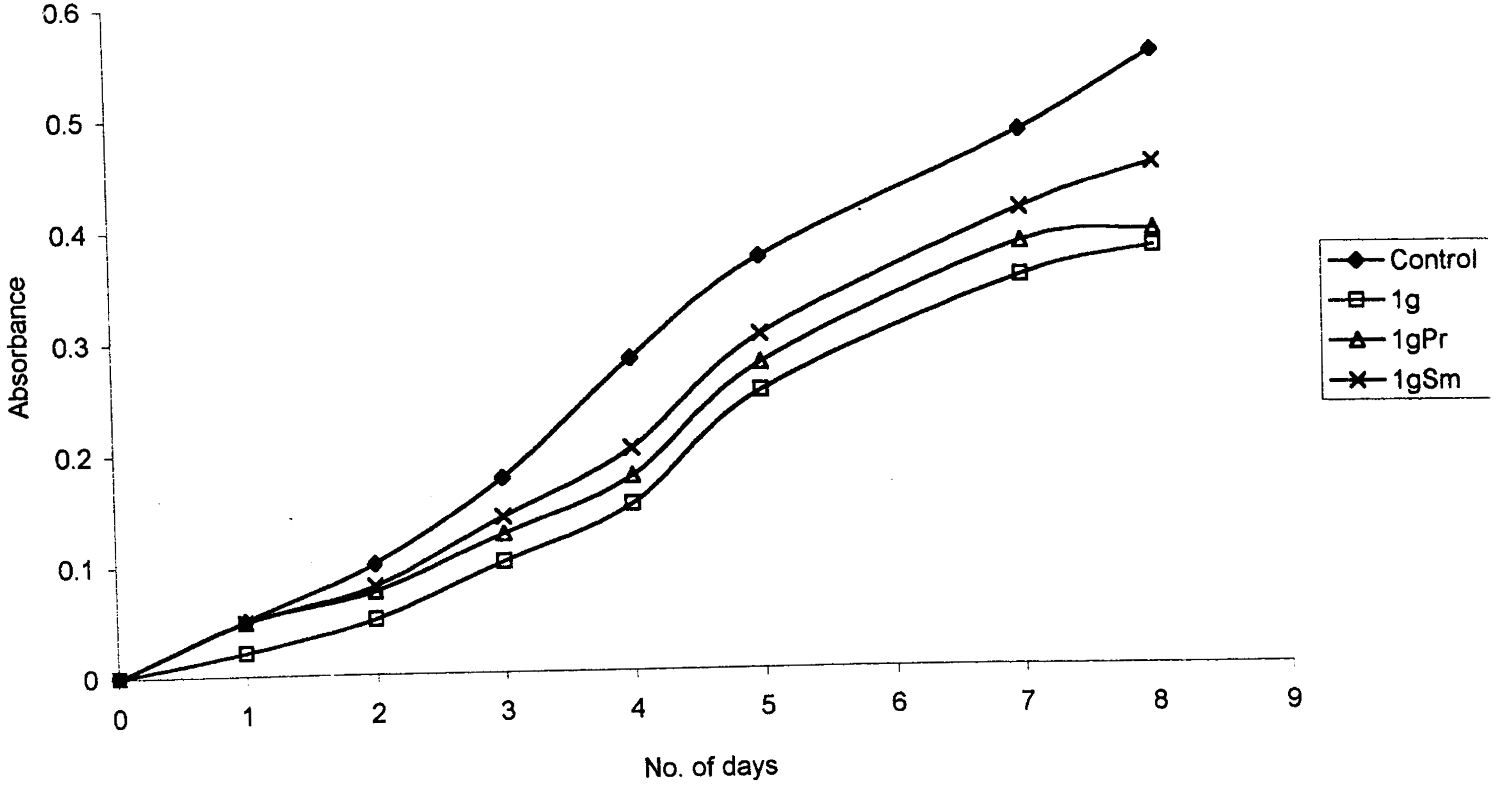


Fig. 46 Antioxidant assay of **1g** and its complexes

65

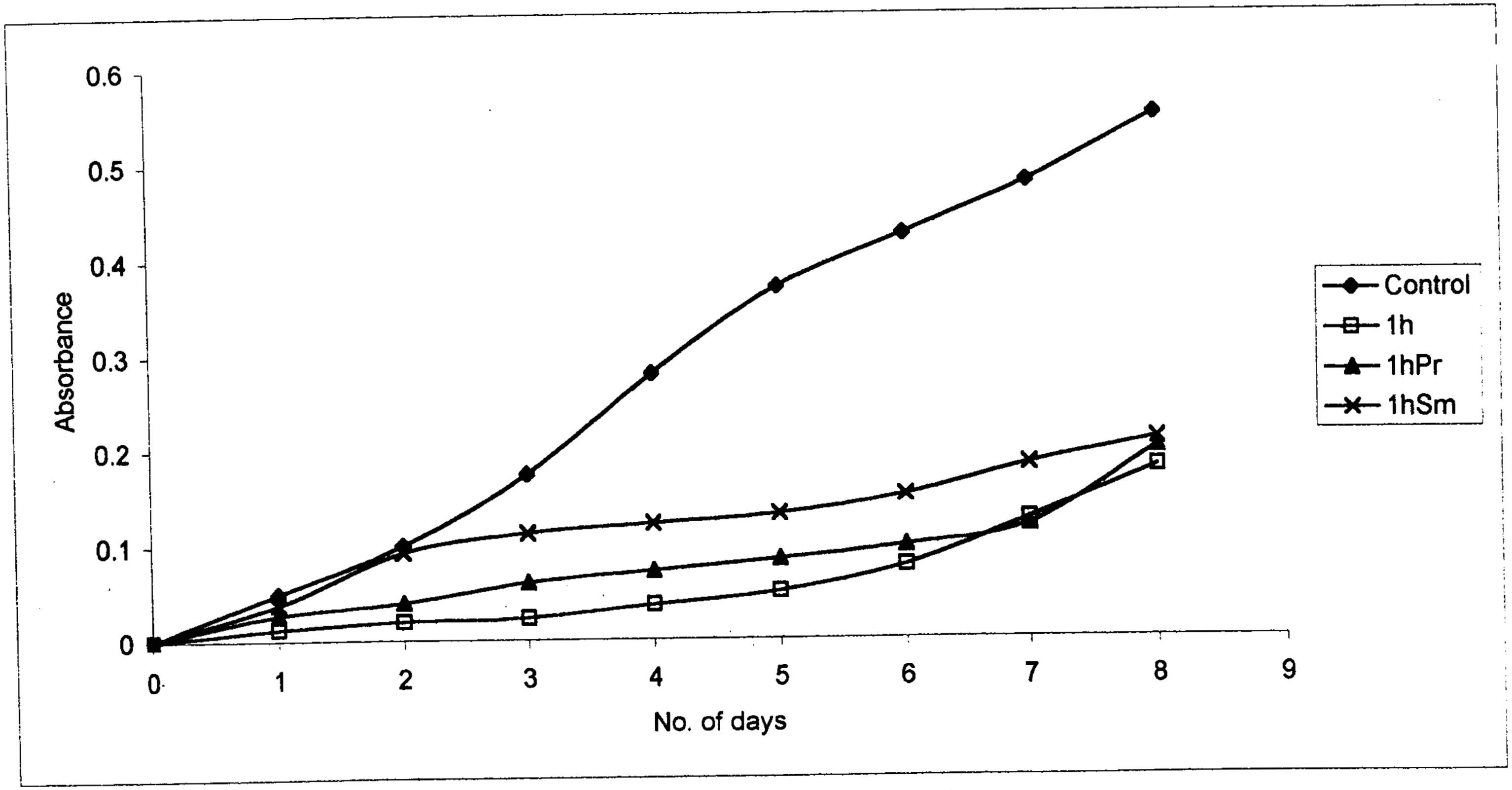


Fig. 47 Antioxidant assay of **1h** and its complexes

66

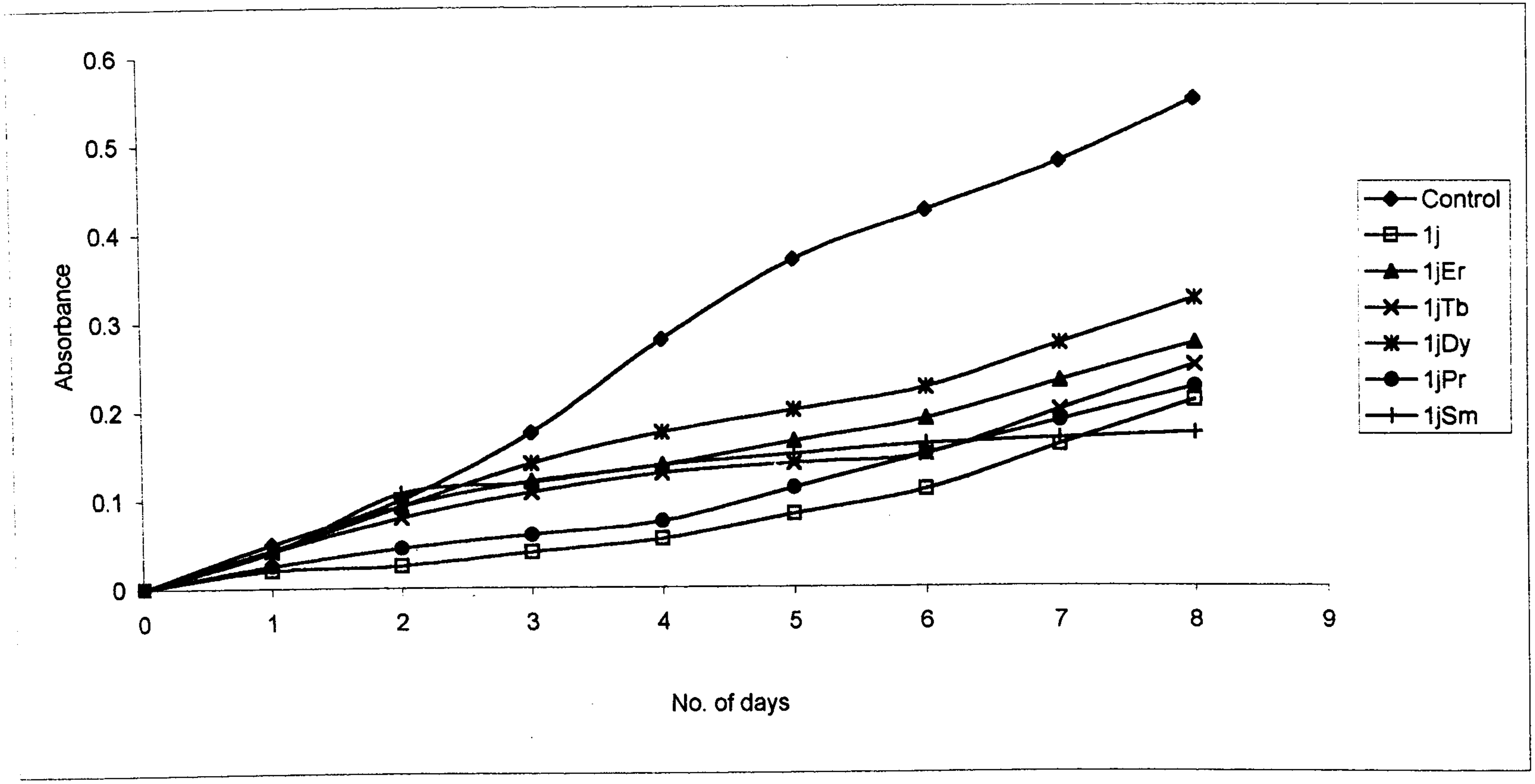


Fig. 48 Antioxidant assay of **1j** and its complexes

However, the antioxidant activity of the curcuminoids increased on complexation with aluminium(III). The observed data of tris aluminium chelates of curcuminoids considered in chapter 3 are given in figures 49 & 50. The figures clearly demonstrates that appreciable increase in activity of the aluminium chelates. No reasonable explanation can be suggested for this observation from the available data except the small size of the Al^{3+} ion. It is to be pointed out that turmeric powder is a common ingredient in many food preparation of the subcontinent and it is traditionally believed that cooking in earthernware (clay) vessels is good for human health. This may be due to the formation of some kind of complexes of aluminium with the curcuminoids. Although no definite conclusion can be arrived at from the data available in the study.

67

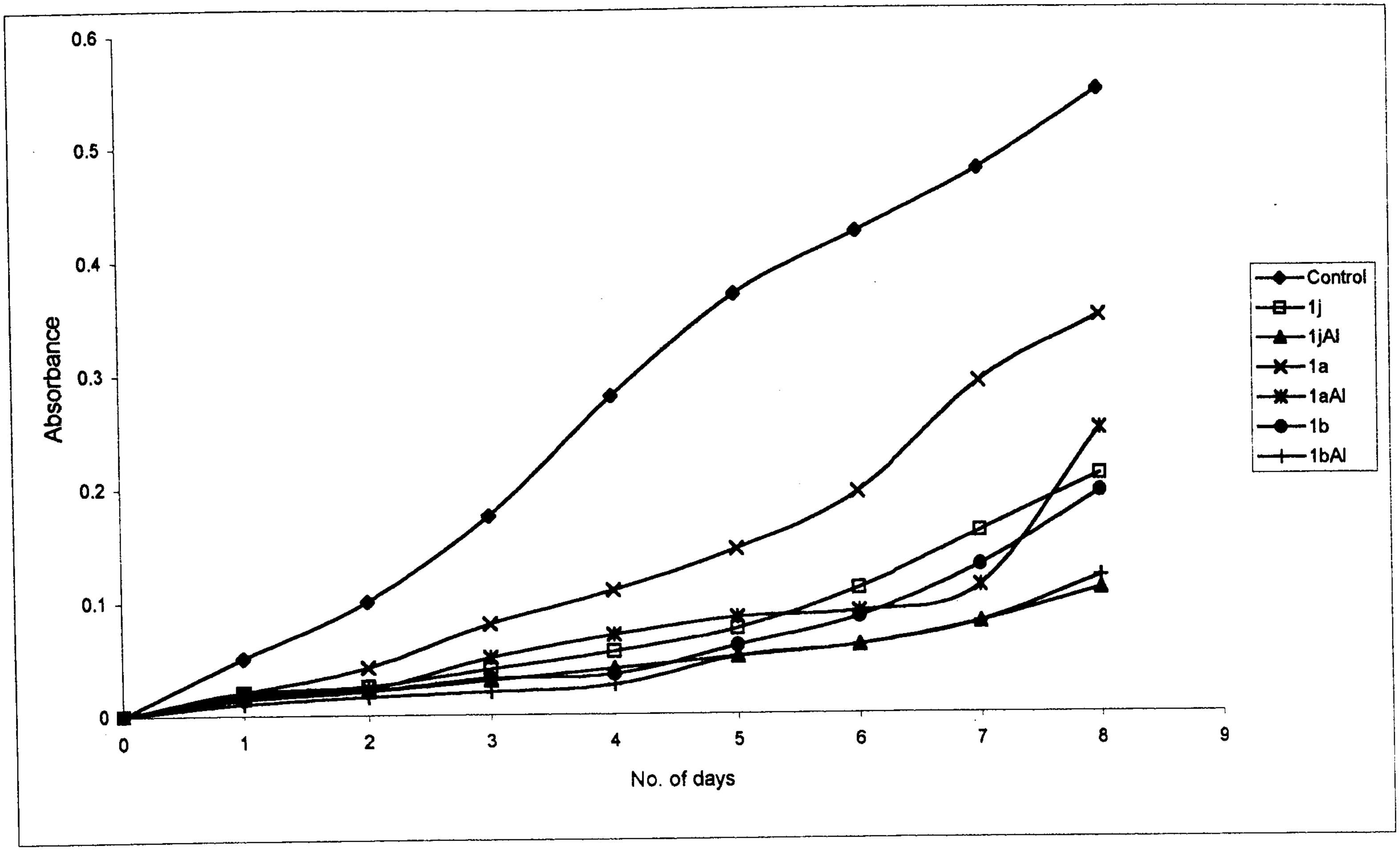


Fig. 49 Antioxidant assay of **1a, 1b, 1j** and their Aluminium(III) complexes

68

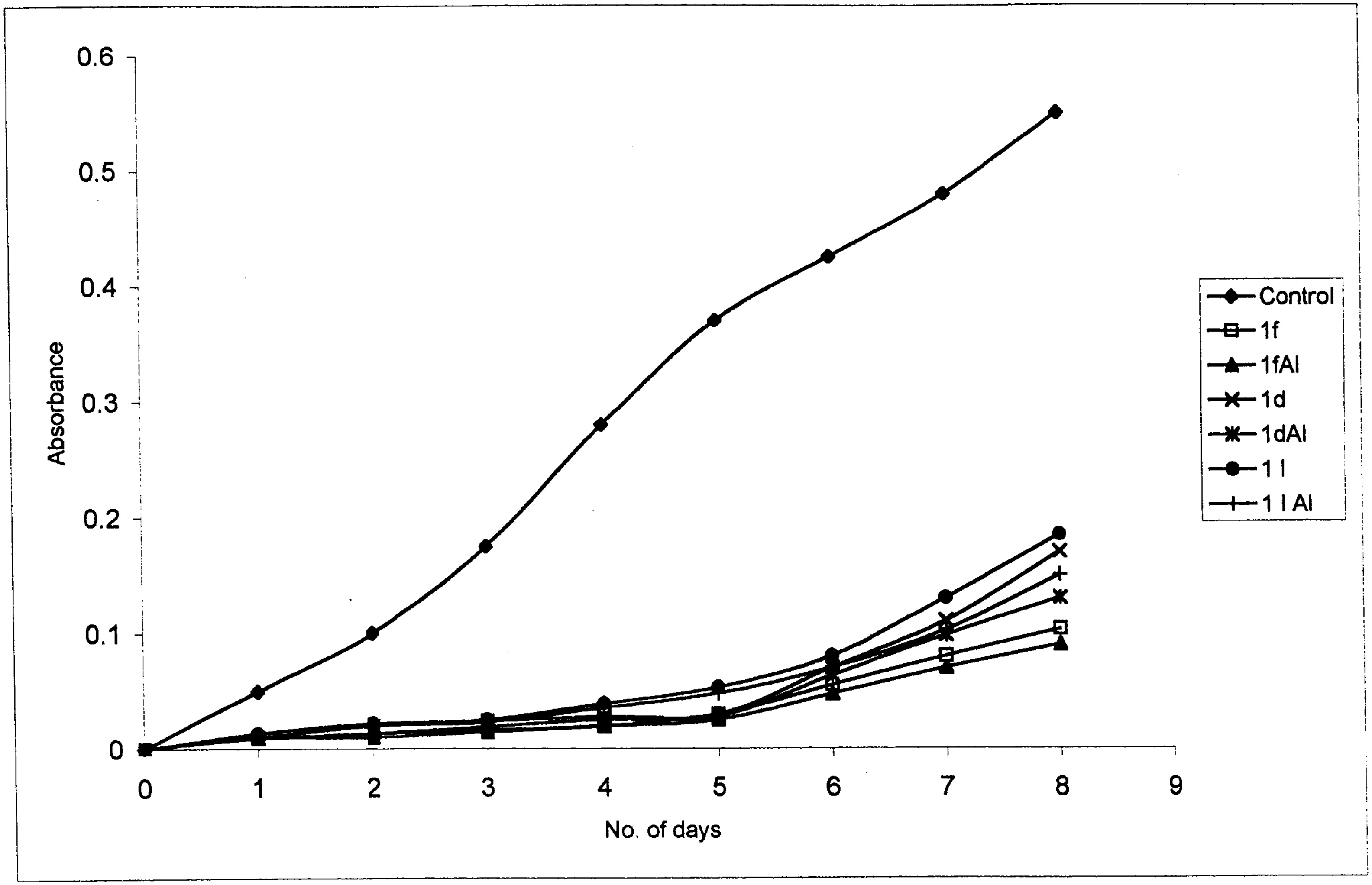


Fig. 50 Antioxidant assay of **1f, 1d, 1l** and their Aluminium (III) complexes

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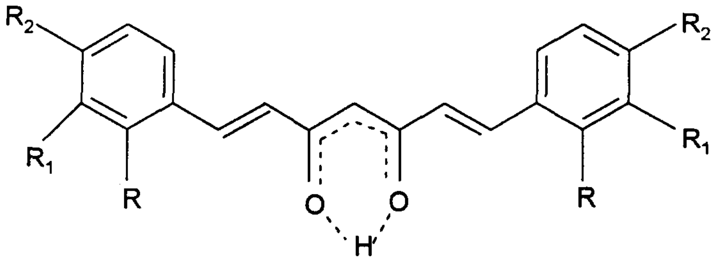
JULY 2004

SUMMARY

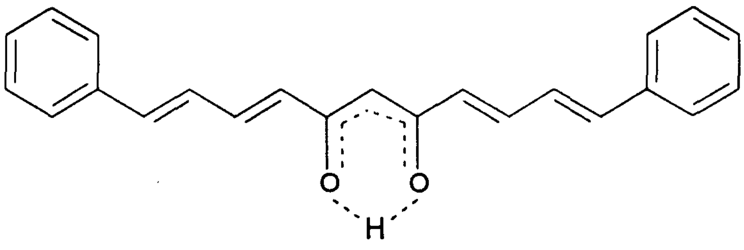
The eleven 1,7-diarylheptanoids (synthetic analogues of natural curcuminoids present in the herbaceous medicinal plant turmeric) given below formed well defined complexes with the various lanthanide ions.

Type 1



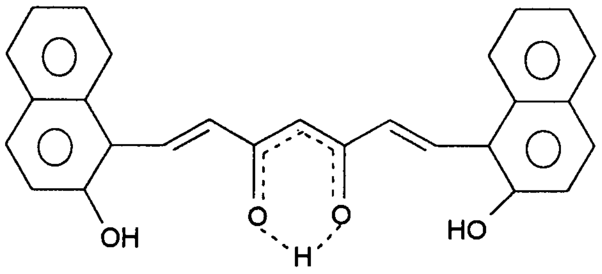
Compound	R	R_1	R_2
1a	H	H	H
1d	OH	H	H
1e	Cl	H	H
1g	H	H	OCH_3
1h	H	H	OH
1i	H	H	$N(CH_3)_2$
1j	H	OCH_3	OH
1k	H	OCH_3	OCH_3

Type 2



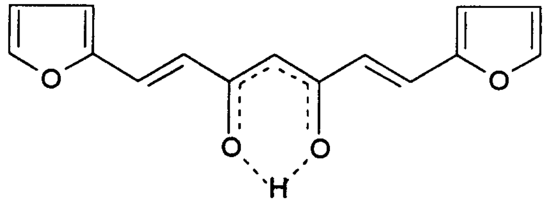
1b

Type 3



1f

Type 4



1c

On the basis of analytical and spectral data, the lanthanide complexes can be conveniently classified into the following types.

1. $[LnL_2X(H_2O)_2]$ $X = Cl^-$ or NO_3^-
2. $[TbL_2(NO_3)_2(H_2O)_2]$
3. $[LnL_3(H_2O)_2]$

where L is the deprotonated 1,7-diarylheptanoid HL.

Electronic, ir, nmr and mass spectral data of the complexes unequivocally support the monobasic bidentate nature of the diarylheptanoids. In all the complexes, only the diketo oxygens are involved in bonding with the metal ion with the formation of a stable six-membered C_3O_2Ln chelate ring. The spectral data clearly suggest that aryl substituents such as –OH and $-OCH_3$ are not involved in bonding with the metal ion. Thermograms of some of the complexes revealed the complexes are not volatile unlike lanthanide complexes of many β-diketones. Fluorescence spectra of the compounds have been explained on the basis of electronic effects of aryl substituents.

From the actinide series, dioxouranium(VI) yielded complexes of the type [UO_2L_2]. These complexes were characterised on the basis of ir, nmr and mass spectral data.

Aluminium(III) formed [AlL_3] type complexes with the 1,7-diarylheptanoids. The ir, nmr and mass spectral data of the complexes are in conflrmity with the monobasic bidentate coordination of the ligands in the tris aluminium(III) chelates.

The anti-oxidant activity of turmeric and natural curcuminoids are well established. Therefore, the antioxidant properties of the 1,7-diarylheptanoids and their metal complexes were studied. The data showed that all the compounds possess antioxidant activity. However, complexation decreased the activity except in the case of the aluminium chelates. The activity of the curcuminoids strongly depends on the nature of the aryl substituents. The anti-oxidant activity of compounds has been compared with the antitumour activity of the compounds.

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