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Amidine: *Structure*, Reactivity and Complexation Behaviour

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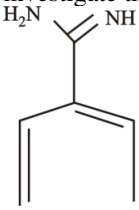
Abstract : The present review discuss about the structure, reactivity of various amidines. The complexation behavior of amidine especially aryl benzamidine with different metal ions has been discussed. This review article is useful for inorganic and bioinorganic chemist.

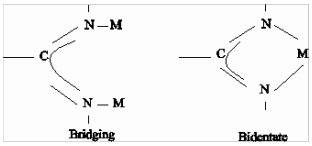
Introduction

The chemistry of amidines has been the subject of two comprehensive monographs [1,2]. Amidines, the dinitrogen analogs of carboxylic acids and esters, display a rich chemistry conferred by their unique structure and diverse binding properties. They combine the properties of an azomethine like C-N double bond with an amide like C-N single bond having some partial double bond character. These compounds are very interesting because of their basicity[3,4], biological activity[5] and their use as intermediates in the synthesis of some metallocyclic complexes[6] as well as heterocyclic complexes[7]. Recently chiral amidine-phosphine hybrid ligands with enantio-discrimnating properties have been reported [8]. Amidines as strong lewis bases react with boron trihalides to form amidine-mixed boron trihalide adduct system [4].

Recently research papers concerning the structure of amidines[9,10] reflecting the widespread interest in pharmaceutical binding and their biological importance. This structural investigation was undertaken to investigate the effect of diaryl substitution on the central



benzamidine fragment,the possibility of hydrogen bonding and to examine the structural changes which occur to an amidine upon complexation with a transition metal to form an important pseudoallyl group.



Scheme 1: Amidino bonding modes

In order to design selective, high affinity ligands to target protein, it is advantageous to understand the structural determinants for protein-ligand complex formation at the molecular level [11, 12]. In a model system; it successively mapped the factor Xa binding site onto trypsin, showing that certain mutations influence both protein structure and inhibitor specificity [12]. A new strategy for structure- based drug design that combines high quality docking with data from existing ligand-protein cocrystal x-ray structures [11, 13]. Docking accuracy can be improved by the effective utilization of the existing x-ray structures of ligands cocrystallised with the target proteins[13].

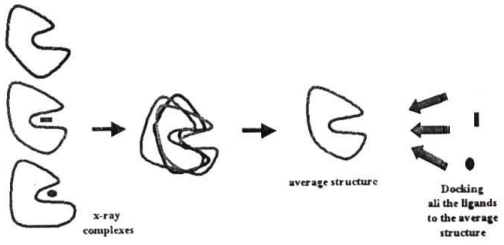


Fig.1: Average protein structure selection [11]

The strategy of combining docking with 3D similarity function implemented in new alogrithum SDOCKER proved to be effective in three different systems, namely thrombin, CDK2 and HIV-1 protease [11]. SDOCKER represents a very promising and important direction in the development of tools utilizing structural genomic information [14].It has been reported

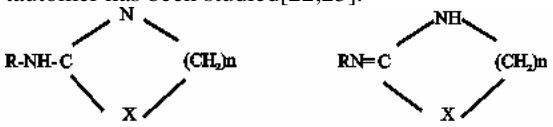
that the results obtained from a structure based NMR screening approach to factor Xa lead generation[15]. The small molecule screening collection was specifically designed to include both diverse fragments from known drugs and targeted fragments from known factor Xa inhibitors[15] of all the proteins involved in the coagulation cascade, factor Xa is a prime target in cardiovascular drug discovery[16,17]. Factor Xa is a trypsin like serine protease that converts prothrombin to catalytically active thrombin, the protein at the center of events in the coagulation process and is therefore key to several of the process necessary to form stable clots. A such, factor Xa is an attractive target for new anticoagulant agents[16].

An improved preparation of safer and highly purified autologous plasmin and to demonstrate its clinical applications, has been found that benzamidine used for suppression of protein denaturation[18]. Synthetic inhibitors of benzamidine type have been found to be inhibiting effects on arginine specific cystein proteinases of P. gingivalis[19]. In vitro effects of the synthetic inhibitors of cystein proteinases on virulence of P. gingivalis were observed further in vitro tests concerning immunomodulatory effects should be done before these substances are used for therapy in clinical controlled studies [19].

Bis-benzamidine can inhibit lgE-dependent tryptase release from human tonsil mast cells [20]. Therfore, it seems likely that this inhibitor of tryptase is a novel promising mast cell stablising drug for treating and preventing allergic inflammation or other mast cell associated diseases [20].

Conformation of Cyclic Amidines

Many compounds containing an amidine moiety are known to possess interesting biological properties, particularly as antihypertensive agents[21]. A general method is developed using ^{1}H, ^{13}C NMR chemical shifts to determine unambiguously the predominant tautomeric forms of many known cyclic amidines, two different tautomer has been studied[22,23].



Scheme 2 : Different tautomer of amidines

^{15}N NMR spectra shows just two hydrogenated nitrogen atoms, which confirm that the amino form is the most stable tautomer, but the observation of a sharp signal and two broad signals(^{15}N decoupled spectra) and the corresponding broad signal for the $=C-NH_2$ protons, indicates the occurance of tautomerism between the amino and imino form, observable for some of the studied benzamidine[23]. Theoretical calculations lead to the conclusion that these compounds occur mostly as the amino tautomer with Z configuration as the most stable diastereoisomer, which is stablised by hydrogen bonding[23].

The binding free energy of benzamidine trypsin complexes has been calculated and the association constant has been measured[24]. The linear interaction energy(LIE) approximation to examine the inhibitory activity of a series of substituted benzamidines against the serine protease trypsin[24,25]. The fundamental premise of the LIE approximation is that the binding free energy of ligands to proteins can be calculated as a linear combination of ligand environment interaction differences between the bound and unbound states. Monte Carlo(MC) sampling is employed to calculate the ensemble averaged electrostatic and vanderwaals interactions between the benzamidines and their respective environments in the two physical states[24].

Structure and Reactivity

Most fundamental aspects in chemical and biochemical studies are the concepts of structure, energetic and reactivity as well as their inter-relationships. In most chemical reactions, there are disruption and formation of chemical bonds, being essential, to establish databases with experimental reliable data of bond dissociation energies (BDEs) as a direct information of the strength of chemical bonds[26]. Chemical species containing the N-H bond form an important class of compounds with a large variety of applications, from pharmaceutical agents[27-29] to toxic substances[30,31]. These compounds may be found in the building blocks of bio-molecules as well as in a large number of chemical industry products. In fact, not only are they relevant in life process but also can have different roles in industry acting as antioxidants[28,32,33] complexing agents[34] or in the manufacture of herbicides, surfactants, dyes, pigment, rubber, polymers and several biological materials[28]. The N-H bonds play a crucial role in many biological mechanism as, for example in the proton- transfer enzymatic reaction catalyzed by acetylcholinesterase, where N-H bonds are cleaved and formed at the imidazole ring from the Glu327- His440-Ser200 catalytic triad[29]. Also they are important in the antioxidant activity of phenothiazine and related compounds to prevent premature polymerization or oxidation of plastics, lubricating oils, foods or cosmetics [28,35] and are equally relevant in free radical reactions[36].

Structure reactivity relationship has always attracted the attention of chemists. Hammett [37] looking for quantitative models of similarity, proposed equation (1) describes

$$\text{Log K(or k)} = \log K^{0}(\text{or } k^{0}) + \rho\sigma \quad \text{----------(1)}$$

The relationship between the equilibrium or rate constant for substituted (K or k) and unsubstituted (K^0 or k^0) derivatives in a reaction series, the reaction constant(ρ) and the substituted constant(σ)[3,37]. In amidine, only a few σ – type values for the amidine group have been proposed[38-40]. The first estimates of σ_I and σ^{o}_{R} for

the N=CH-NMe_2 group was carried out by shorter[39] on the basis of the ^{13}C chemical shifts obtained. The proposed σ_1 and σ^o_R values, when compared with the literature data for the NMe_2 group(Table 1).

Table 1: Comparision of the σ values of the amidine

Group	σ_1	$-\sigma^o_R$	$-\sigma^o_P$	$-\sigma^o_M$	$-\sigma^+_M$	σ_F	σ_α
N=CH-NMe_2	0.03[a]	0.29[a]	0.25[b]	0.03[b]	1.0[b]	0.05[b]	0.40[b]

[a][39], [b][3]

The application of σ together with the structure – basicity relationships in the prediction of microscopic basicties for individual sites in bifunctional compounds enables the explanation and estimation of additional effects,e.g. internal solvation or the formation of a three centered complex[3].

The gas-phase hemolytic N-H bond dissociation enthalpy (BDE) was investigated for a large series of molecules containing at least one N-H bond by means of accurate- density functional theory calculations [26]. The computed value for the R=NH bond in benzamidine is 404.4KJ/mole. The effect of substituent in the aromatic ring of substituted benzamidine plays a key role. The effects due to the presence of electron donating or electron withdrawing groups vary largely with the position considered i.e, ortho, meta and para. In substituted benzamidine electron donar destabilize the parent substituted molecules and hence there is a decrease in the N-H bond dissociation enthalpy when compared with the computed values for benzamidine. Electron withdrawing group stabilizes the neutral substituted molecule and therefore, the N-H BDE increases with respect to benzamidine solvent effects were also taken in account and rather significant differences are found among N-H BDEs computed in the gas phase and in other polar and non polar solvents[26].

Complexation Behaviour

The interaction of aryl amidine(Benzamidine) with various metal ions have been studied groupwise.

Group 4 metal complexes

New novel ligands has been designed as principal chelating units based on iminohydroxamic acids and their derivatives for aluminoxane-cocatalysed olefin insertion polymerization with group 4 metals(titanium, zirconium) as the active metal sites[41]. Various anionic and neutral[N,O] and [N,N] ligand systems are easily accessible by a modular synthetic sequence of imidoyl chlorides with substituted hydroxyl amines.Steric protection of the metal coordination site, a necessary requirement for suppression of chain termination pathway of non-metallocene catalyst, is brought about by bulky aryl substituents on the imino nitrogen atoms[41]. Some new synthesized titanium and zirconium complexes are diamagnetic and are yellow to orange in color.

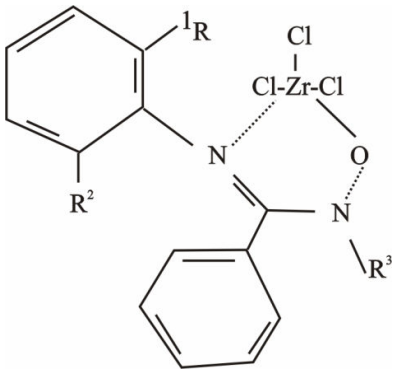


Fig.2a: $^1R = {}^2R$ =i-Pr, ^3R = Me
Fig.2b: $^1R = {}^2R = {}^3R$ = Me
Fig.2c: ^1R =Ph, ^2R =H, ^3R = Me
Fig.2d: $^1R = {}^2R$ =H, ^3R = Me
Fig.2e: $^1R = {}^2R = {}^3R$ = i-Pr
Fig.2f: $^1R = {}^2R$ =i-Pr, ^3R = p-tol

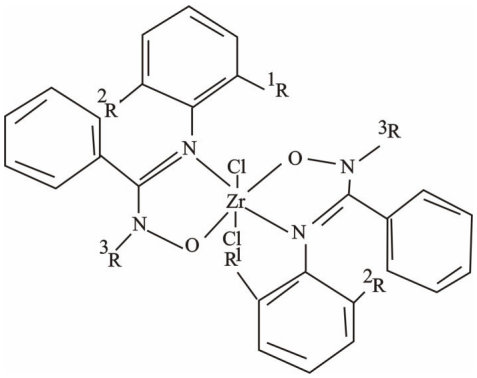


Fig3: $^1R = {}^2R$ = i-Pr, ^3R = Me[41]

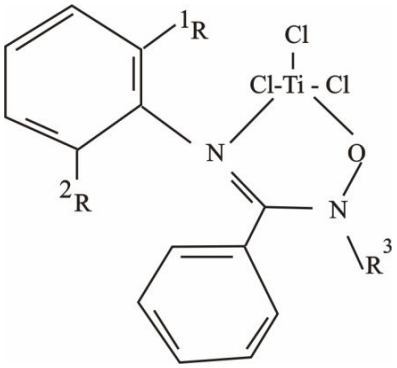


Fig.4:$^1R = {}^2R = {}^3R$ = Me[41]

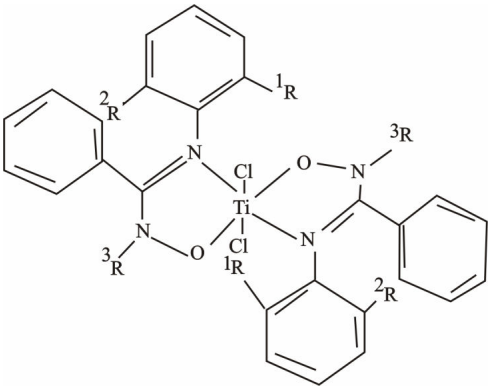


Fig 5a: ^{1}R = ^{2}R = ^{3}R = Me

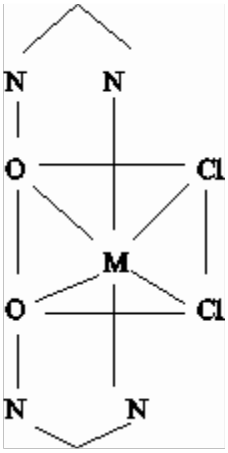


Fig. 5b: Cis Isomer

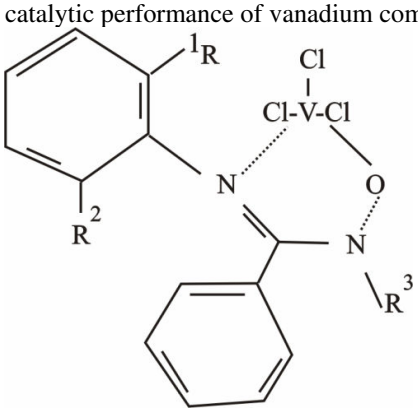
Scheme 3: Metal complexes of [N,O] and [N,N] iminohyroxamato ligands

The ^{1}H and ^{13}C NMR spectra clearly shows that the [N,O]$ZrCl_3$ mono complexes(Fig. 2a) exist predominantly as mixture of isomers containing THF as an additional neutral ligand in an octahedral coordination environment. In principle, four pairs of chiral diastereoisomers are possible with these heterotropic [N,O] chelate ligands in combination with three chloride ions and one THF ligand. Mono Zirconium complexes containing the N-(2,6-diisopropyl phenyl) substituent exist as one isomer(2a, 2e.2f), whereas those with sterically less demanding N-aryl groups give rise to the observation of two distereoisomers(2b,2c,2d) according to their NMR spectra[41]. In contrast to the [N,O]$ZrCl_3$ complexes(2a-2f), no coordinated THF was present in the titanium complex (fig4) most likely due to the smaller size of the lighter transition metal atom. Also complex fig 3 with two chelating [N,O] ligands had no coordinated THF.

Unexpectedly the structure corresponds to the $[N,O]_2$-$TiCl_2$ bis complex fig 5a which must have been formed from the[N,O] $TiCl_2$ (mono) complex fig 4 by ligand scrambling. The stereochemistry of fig5a corresponds to isomer(fig5b) with cis oriented chloro ligands and trans oriented imino donar sites of the heterotropic iminohydroxamato ligands. To evaluate the catalytic performance of these above complexes a standard polymerization procedure was applied. In term of activity, all [N,O] and [N,N] zirconium showed a moderate activity. The bis(complex) $[N,O]_2$ $ZrCl_2$(fig3) had the lowest activity of all zirconium complexes clearly indicates that one ligand per metal center[N,O]$ZrCl_2$ is superior to a 2:1 ratio. Changing the metal to titanium resulted in a significantly reduced activity with either the [N,O] or [N,N] ligand architecture.

Group 5 metal complexes

N'- Hydroxy –N^1, N^2- diaryl benzamidines, a new type of monobasic and bidentate chelating agents possessing the function R_3-C(R_1NOH)=N-R_2 react with vanadium(V) to form coloured 1:2 (Metal:ligand) complexes[42].The newly synthesized reagents were tested for their potentialities towards spectrophotometric determination of Vanadium(V) using Beer's law. The compounds reacted with vanadium in presence of adduct- forming substances in a similar manner with only slight variation in the value of λ_{max} and ε. The substitution of N^1-phenyl group(R_1) or N^2- phenyl group(R_2) with aryl groups has only slight bathochromic effect whereas, p-chlorophenyl causes highest hypochromic shift, when attached to hydroxyl amine nitrogen atom[42]. The selectivity and sensitivity of these reagents has been analyzed using various commercial samples[43]. To evaluate the catalytic performance of vanadium complexes, a



Where ^{1}R = ^{2}R = ^{3}R = Me[41]

Fig 6: Vanadium complexes of [N,O] iminohyroxamato ligand

standard polymerization procedure was applied[41]. The new families of hydroxamate based N- substituted benzamidine are easily available for complexation with

vanadium to formed dark green complex (Fig 6) which is strongly paramagnetic[41].

Group 6 metal complexes

A newly synthesized monobasic and bidentate chelating agent N^1-hydroxy-N^1-p-tolyl-N^2-(3,4-dimethylphenyl) benzamidine(Hhtdb) is found to be selective chromogenic reagent for extractive photometric determination of molybdenum(V)-thiocynate complex into benzene(using ascorbic acid) as reducing agent[44]. Various optimization constants and nature of complex separation from diverse ions and its application to the analysis of ore and alloys has been studied. The overall extraction equilibrium may be expressed as follows:

$MoO^{3+} + 2SCN^- + 2Hhtdbo \leftrightarrow MoO(SCN)_2OC_{22}H_{21}N_2(HOC_{22}H_{21}N_2)_o + H^+$

where $HOC_{22}H_{21}N_2$ denotes hydroxyamidine and subscript o, the organic phase. The absorption spectra showed the formation of 1:2:2(Metal:reagent:thiocynate) mixed complex in benzene[44].

N, N'- bis(2,6-diisopropyl phenyl) trifluoroacetamidine reacts with $Mo(CO)_6$ to produce a coordinated complex with $Mo(CO)_3$ in which the ligand is in Z-anti geometry[45]. The metal is η6- coordinated to the imino-2, 6-diisopropyl phenyl ring and the amino N-H unit is directed towards the metal determined by single crystal x-ray structure. The high steric bulk of this superamidine ligand apparently prevents the formation of a metal-meta bonded $Mo(Amidinate)_4$ as observed in a redox reaction between N, N'- diphenylbenzamidine and $Mo(CO)_6$ under similar thermal reaction condition[45].

The newly synthesized ligand N',N"–bis(3–carboxy-1–oxoprop–2-enyl) 2-Amino- N–arylbenzamidine forms octahedral complex (fig 7), in which nitrate anion are attached with .

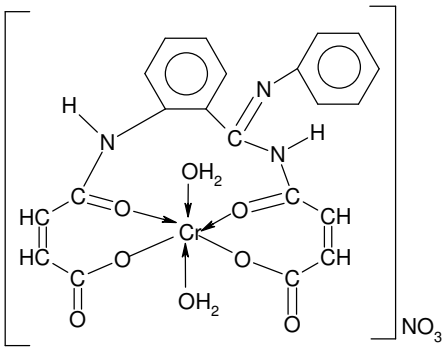


Fig. 7: Chromium complex of aryl benzamidine[46]

chromium metal ion by primary valency[46]. The complex was synthesized and characterized by various spectral techniques with thermal studies. The mode of interaction of the ligand with chromium complex is well explained. Powder diffraction technique has determined triclinic crystal system with P_1 space group(fig 8).

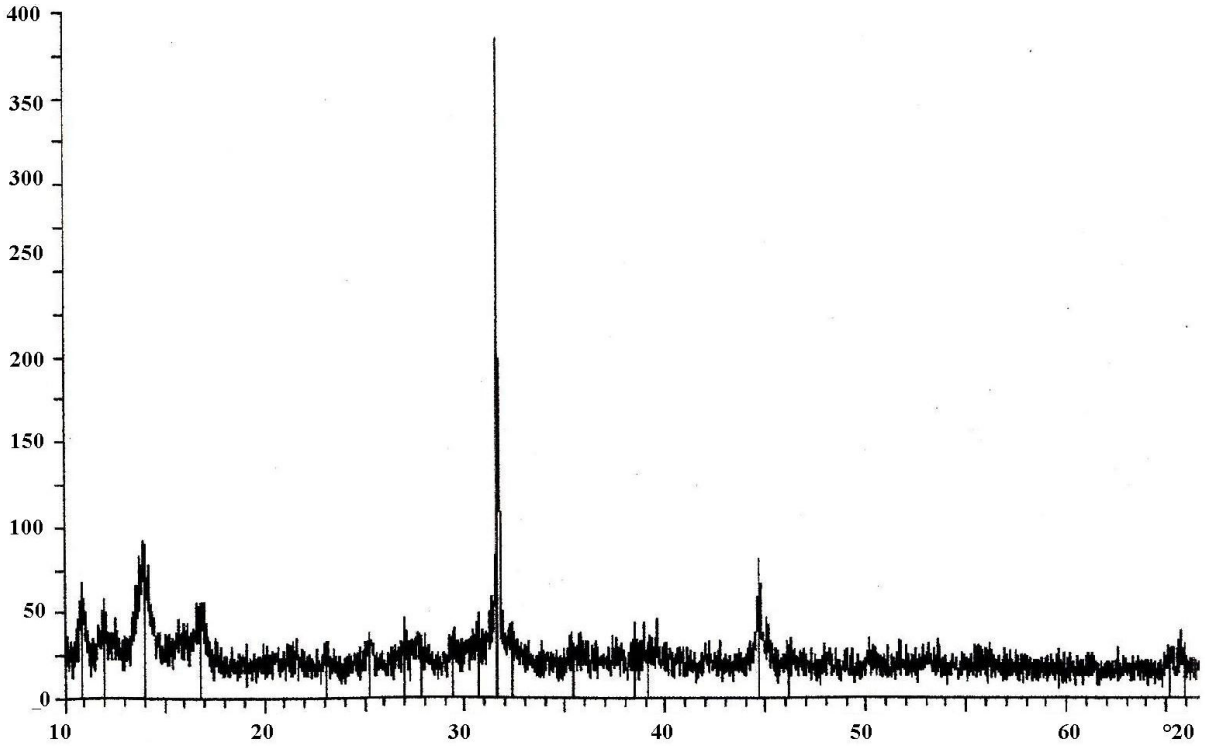


Fig 8 : XRPD spectra of chromium – aryl benzamidine complex[46]

The reaction of alkynyl alkoxy metal (Chromium, Tungustan) carbene complexes with 1, 3 dinitrogen system (amidines) has been studied. The main product obtained corresponds to the cycloadduct, whose cyclic structure may be related to dinitrogen systems. The complexes can be oxidatively or reductively demetallated [47]. The synthesis and crystal structure of unsymmetrical chromium – benzamidine complexes $[Cr_3(PhNC(Ph)NPy)_4Cl_2]$ has been studied[48]. The Cr_3 chain in $[Cr_3(PhNC(Ph)NPy)_4Cl_2]$ is unsymmetrical with Cr-Cr distances of 2.269(1) and 2.513(1)[48]. A simple and selective spectrophotometric method for determination of Cr(VI) with hydroxyamidine to water samples has been analysed[49]. The molar extinction coefficient of the complexes of Cr(VI) with different hydroxyamidines lie in the range of (1.30-1.52)×10^4Lmol^{-1}cm^{-1} at λ_{max} 390-400nm(Detection limit 0.1µg Cr /cm^3)[49].

Group 7 metal complexes

The use of amidinato ligands of the type RNC(R')NR$^-$ has met with considerable success for the preparation of manganese complexes[50]. Synthesis and characterization of new $MCl_2(amidine)_2$ compounds i.e, $[MCl_2(HDPhF)_2]_2$ (Where DPhF = diphenyl formamidinato) has been carried out. The molecular structure is shown in fig 9. The manganese atoms are bound to five groups,namely two neutral HDPhF molecules, one terminal and two bridging chloride ions.

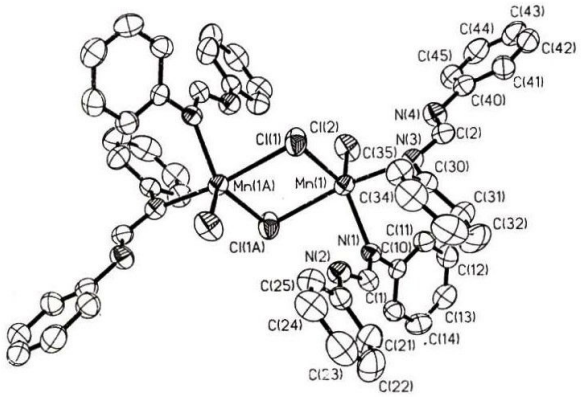


Fig 9 : Thermal ellipsoid plot of the dinuclear compound $MCl_2(HDPhF)_2]_2$[50]

A long metal – metal separation [3.798(2) Å] and a magnetic moment which corresponds to five unpaired electrons preclude the existence of any type of manganese- manganese bond. The dinuclear molecule is internally stabilized by the presence of short(3.11 Å) contacts between N(4) and Cl(2) due to an intermolecular hydrogen bond[50]. The Mn-N(3) bond, where N(3) is almost trans to Cl(1A), is 0.12 Å longer than the Mn-N(1) bond. The bond asymmetry is also observed for the bridging chloride ions. The Mn-Cl(1) bond distance is 0.26 Å shorter than that of Mn(1A)-Cl(1). As it is frequently encountered in compounds which contain both terminal and bridging groups, the former bond is slightly shorter [50].

Synthesis, characterization and fungitoxicity of bidentate high-spin coordinated manganese complexes with N-(5-phenyl-1, 3, 4 thiadiazol-2-yl) benzamidine has been studied[51]. The corrected magnetic moments for the Mn(II) complex is 5.94BM quite typical of six coordinated complexes, whereas electronic spectrum exhibits two d-d bands, and a charge transfer band. The two d-d transition bands in this complex may be assigned as $^6A_{1g} \rightarrow {}^4T_{1g}(G), {}^4E_g(G)$ and $^6A_{1g} \rightarrow {}^4T_{2g}(G), {}^4T_{1g}(G)$. Fungicidal screening data clearly indicate that the complexes are more fungitoxic than the free ligand[51]. Manganese(II) complex with N',N"–bis(3–carboxy-1–oxoprop–2-enyl) 2-Amino- N–arylbenzamidine was synthesized and characterized by various spectral techniques with thermal studies and forms tetrahedral geometry[46]. The manganese complex(figure 10) show intense absorption at >25000 cm^{-1} assigned to ligand centered transition while two weak transitions are observed at 22472 cm^{-1} & 21413 cm^{-1} may be referred to a combination of

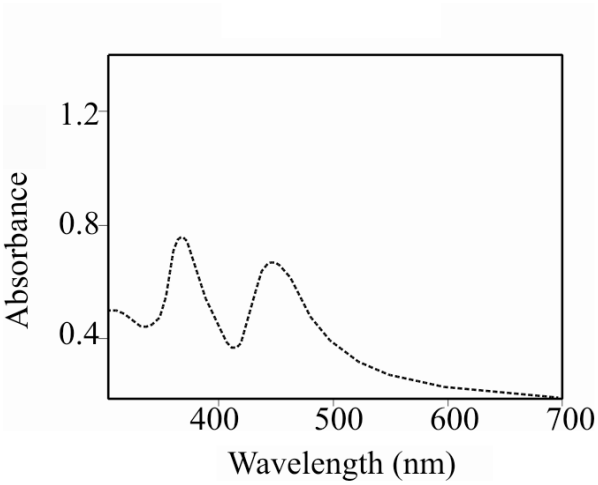


Fig 10: Electronic spectra of manganese(II)-arylbenzamidine complex[46]

MLCT and d-d transition($^2A_1 \rightarrow {}^4T_1$), suggesting tetrahedral geometry of the complex. The magnetic moment value of the complex is 5.90BM, may have tetrahedral/ octahedral geometry. The tetrahedral geometry suggested by electronic spectra of manganese(II) complex supported magnetic moment, a high spin tetrahedral complex.

Only few Rhenium complexes of benzamidine are known and the structures of the complexes were ascertained [52].

Group 8 metal complexes

N-hydroxy, N-meta chlorophenyl N'-(2,3dimethyl) phenyl benzamidine have been found to be potential analytical reagent for the spectrophotometric estimation

of iron(III) in the presence of thiocynate and azide[53]. This method has a wider working range of reagent concentration and has been applied for the determination of iron in drugs [53]. The overall reaction can be expressed as follows:

$Fe^{3+} + 2X^- + HOAm_o \leftrightarrow [FeOAm(X)_2]_o + H^+$

Where X^- = SCN^- or N^{3-}, HOAm = Hydroxyamidine, o = organic phase

The ratio of chelating extractant and azide or thiocynate to metal in mixed complex is found to be 1:1:2(Fe:HOAm:N_3^-/SCN) in benzene. The molar absorbances of azido and thiocynato mixed complexes are 4000 and 12000 l $m^{-1}cm^{-1}$ at 520 and 460nm respectively.The thiocyanato mixed complex can be extracted quantitatively from 0.1 to 0.4 M HCl[53].

Group 9 metal complexes

Cobalt complexes

F. A. Cotton and its coworker prepared $CoCl_2(DTolF)_2$ (DTolF = di-p-tolylformamidinato) by a melt reaction using $CoCl_2$ and DTolF[50]. They found that such reactions-sometimes yield a product that is slightly oily and therefore purification steps are sometimes needed. If the reagents are refluxed in toluene the reaction proceeds more clearly and in higher yields. They suggested the latter procedure as well as the use of an excess of $CoCl_2$ for the preparation of $CoCl_2$(HDPhBz)(DPhBz = diphenylbenzamidinato) displays the characteristics blue colour of tetrahedral Co(II) compounds[50]. Its reactivity is similar to that of its HDPhF analogue. The structure is illustrated in fig.11 and is very similar to the previously described $CoCl_2(DTolF)_2$.

The two chloride ions and a nitrogen atom of each HDPhBz group complete the pseudo-tetrahedral coordination sphere. In MCl_2 (amidine)$_2$ compounds, there are N-N-----Cl hydrogen bonds whose help stabilize the molecule. In $CoCl_2$(HDPhBz), Cl(1) and N(4), Cl(2) and N(2) have separations of 3.25 and 3.19Å respectively[50]. Presumably the presence of hydrogen bonds contributes significantly to the observed chemical stability of the crystalline samples.Some dinuclear complexes of cobalt from $CoCl_2(HDPhBz)_2$ has also been studied.

Starting material	Dinuclear compound formed	M- M separation	Ref.
$CoCl_2(HDPh)_2$	$Co_2(DPhF)_3$	2.385(1)	54
$CoCl_2(HDPh)_2$	$Co_2(DPhF)_4$	2.3735(9)	55
$CoCl_2(HDPhBz)_2$	$Co_2(DPhBz)_3$	2.320(1)	54
$CoCl_2(HDPhBz)_2$	$Co_2(DPhBz)_4$	2.298(2)	55

Cobalt(II) complexes of N-arylbenzamidine complexes were isolated and characterized by spectroscopic, thermal and powder diffraction studies[56]. Cobalt (II) complexes were found to be monomer and involved coordination through carboxylate oxygen of the amide ligands along with two water molecules giving octahedral geometry. In the TOF- MS spectra of complexes, the isotopic profile observed at 236/238 in the spectrum is in good agreement with that calculated for $[C_{14}H_{12}N_3O]^+$ species, which could be the result of demetallation and subsequently a partial intra molecular hydrogen bonding(fig12).

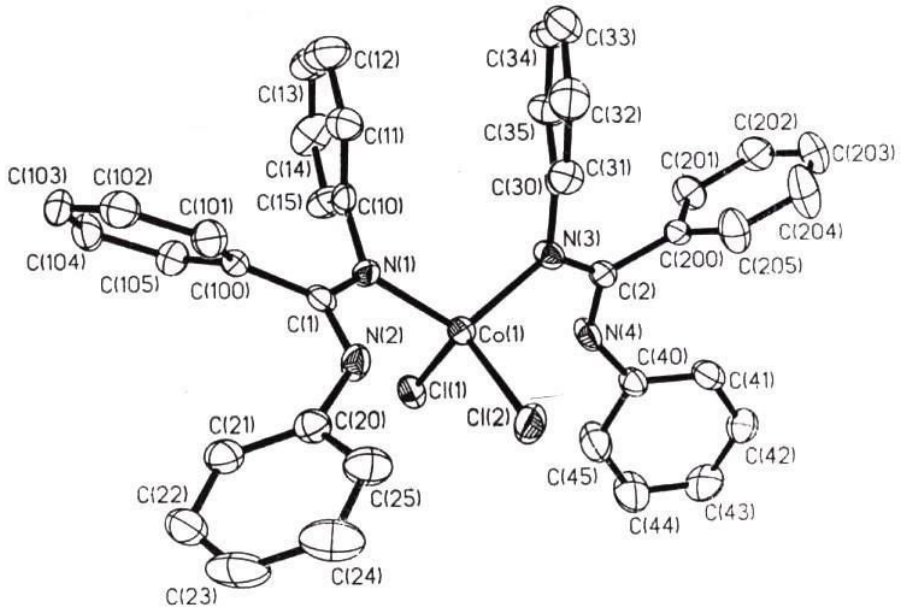


Fig 11 : Structural representation of $CoCl_2$(HDPhBz)[50]

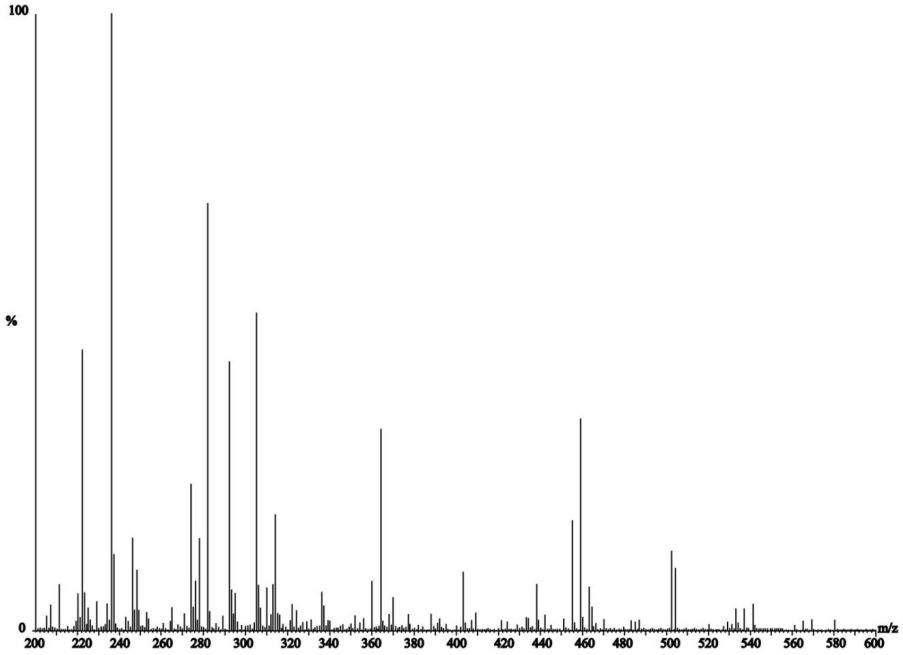


Fig 12 : TOF-MS spectrum of the Co-arylbenzamidine complex[56]

Vibrational spectra indicate the presence of H_2O molecule in the complexes that has been supported by TG/DTA. Kinetic parameter shows that the decomposition follows first order kinetics and proceeds in Two-step decomposition. The thermal behaviour of complexes shows that water molecule is removed in first step – followed by decomposition of the ligand molecule in the second step. Magnetic susceptibility measurements and electronic spectra also support octahedral coordination geometry around the Cobalt (II) ions. The complex crystallizes in the cubic/ hexagonal/ tetragonal crystal system[56].

Rhodium complexes

Several nitrogen-donor ligands containing N-C-N units such as acetamidine[57] or formamidine[58] have proved to be versatile ligands towards rhodium. They can attach to the metals in a unidentate, chelating or bridging mode.Some new binuclear and mononuclear benzamidinato and benzamidine rhodium complexes and the determination of its crystal structure are the first reported crystal structures of amidinatorhodium(I) complexes[59].

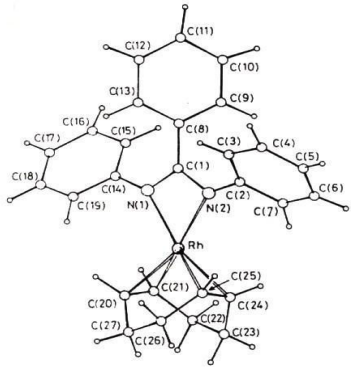


Fig 13:[Rh{CPh(NPh)$_2$}(cod)][59]

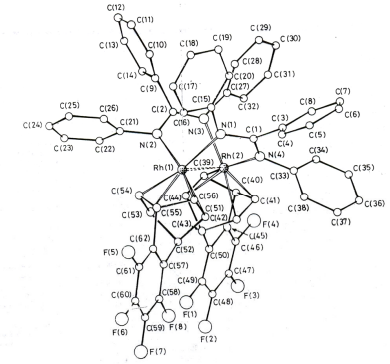


Fig 14: [Rh{μ-CPh(NPh)$_2$(tfbb)$_2$][59]

The crystal structure of $[Rh\{CPh(NPh)_2\}(Cod)]_2$(complexI)(fig13) and $[Rh_2\{\mu\text{-}CPh(NPh)_2\}_2(tfbb)_2]$ (complex II)(fig14) has been studied[59]. Complex I crystallizes in the monoclinic space group $P_{21/n}$ with a =10.315(2), b = 19.507(3),c = 11.429(3)Å, β = 103.62(1)˚ and Z = 4. But the complex II are monoclinic, space group $P_{21/c}$ with Z = 4 and a unit cell of dimensions a = 21.692(2), b = 12.512(2), c = 19.969(2) Å and β = 107.90(1)˚. Both crystal structures were solved by Patterson and Fourier methods and refined by Full-matrix least squares to R 0.040 and 0.047 respectively. The structure of compound I is mononuclear with the N,N'-diphenyl benzamidinate acting as a chelating ligand, through the nitrogen atoms. In contrast, complexII is binuclear with the benzamidinate ligand bridging two rhodium atoms[Rh-----Rh 2.982(3)Å].

Group 10 metal complexes

Nickel complexes

Nickel is one of the most toxic elements of transition metals[60]. Allergic contact dermatitis(nickel itch) is the most frequent effect of exposure to nickel(II). Nickel(II) metal compounds also cause eczema. Nickel hypersensitivity may also cause pulmonary asthma, conjunctivitis and reactions around nickel containing implants and prostheses. Respiratory disorders including bronchitis and asthama have been observed among workers exposed to nickel dusts and aerosols in nickel refineries, welding shops and electroplating industries. Due to this exposure a considerable amount of nickel(II) found in urine and other biological samples of the workers working in these industries. Therefore the determination of nickel(II) in biological fluid is very important[60,61].

In electroanalytical chemistry, adsorptive stripping voltammetry is widely recognized as one of the most sensitive methods[61-63]. It has been shown that adsorption of metal chelates can be used as a preconcentration step to improve the detection limit of electroanalytical determination [61]. The strength of adsorption of metal-ligand complex is determined both by electrostatic as well as pi-orbital interactions. N-2-pyridylbenzamidine(NPBA) is used as the ligand and possesses both aromatic as well as >C=N and $-NH_2$ group. Therefore, the high adsorption by the present ligand helps to improve the detection limit of determination of nickel(II)[61].

Synthesis of new $NiCl_2$(HDTolF){ DtolF = di-p-tolyl formamidinato}as well as that of the dinuclear complexes $Ni_2(DPhF)_4${ DPhF = diphenyl formamidinato) and characterized by X-ray crystallography[64].The structure of $NiCl_2(HDTolF)_2$ is shown in fig. 15. The average Ni-Cl and

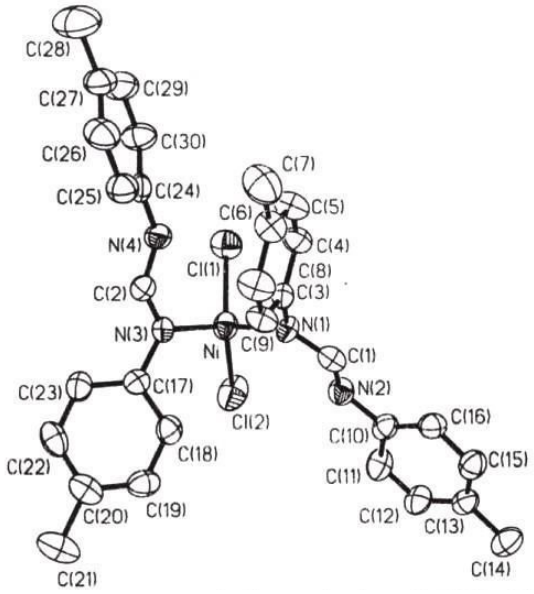


Fig 15: A plot of molecular structure of $NiCl_2(HDTolF)_2$[64]

Ni-N bond lengths are 2.249(2) and 2.005(1) Å respectively. Short distances between the chloride ions and the protonated nitrogen atoms of the HDTolF molecules are a clear indication of the presence of hydrogen bonds. The Cl(1)- N(4) distance is 3.11Å and the Cl(2)-N(2) separation is 3.20Å. The general, the trend of slightly shorter C-N(imido) as compared with C-N(amine) bond distances observed in other complexed and uncomplexed neutral amidines[64]

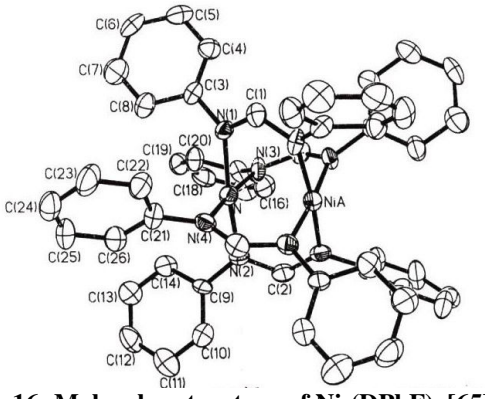


Fig 16: Molecular structure of $Ni_2(DPhF)_4$ [65]

The action of strong base on the HDPhF(DPhF= diphenyl formamidinato) of $NiCl_2(HDTolF)_2$(fig15) yields crystal of $Ni_2(DPhF)_4$ (fig.16) which is in all important respects identical with the previously reported $Ni_2(DTolF)_4$[65]. The long Ni-Ni separation [2.490(3)Å] is consistent with the absence of a bond, four amidinato group form bridges between the metal atoms, which have an essentially square planar coordination. The main interest in the preparation of $Ni_2(DPhF)_4$ was shown that

there exists a general pathway to the synthesis of dinuclear amidinato compounds from species of the type $MCl_2(amidine)_2$.

Complexes of Ni(II) with ligands N', N" – bis (3 – carboxy-1–oxoprop–2-enyl) 2- Amino–N–arylbenzamidine, N', N" – bis (3 – carboxy- 1 – oxopropanyl) 2- Amino–N–arylbenzamidine and N', N" – bis (3–carboxy-1– oxophenelenyl) 2-Amino–N–arylbenzamidine have been synthesized and characterized by various physico-chemical techniques[66]. Molecular structure of the complexes have been optimized by MM2 calculations and supported octahedral geometry around nickel (II) ions. Results of semi-empirical quantum chemical calculations performed to explain the bonding mode of the ligands. The thermal decomposition mechanism has been proposed for metal complexes. The final product of decomposition is the formation of NiO, which has been confirmed by comparing the observed/estimated and the calculated mass of the pyrolysis product [66].

Newly synthesized nickel complexes were evaluated for their performance as olefin polymerization catalyst[41]. Treatment with $NiBr_2$ in dichloromethane at room temperature overnight afforded the corresponding [N,O]$NiBr_2$ complexes and [N,N]Br_2 complexes(Fig 17-19) in good yield(Scheme 4).

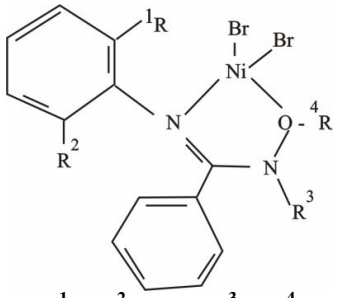


Fig.17a: $^1R = {}^2R$ = i-Pr,$^3R = {}^4R$ = Me
Fig. 17b: $^1R = {}^2R = {}^3R = {}^4R$ = Me
Fig. 17c: ^1R =Ph, ^2R = H, $^3R = {}^4R$ = Me
Fig. 17d: $^1R = {}^2R$ = H, $^3R = {}^4R$ = Me

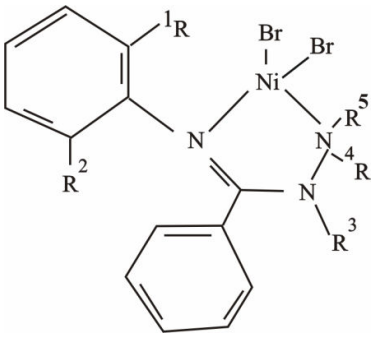


Fig. 18a: $^1R = {}^2R$ = i-Pr,$^3R = {}^4R$ = Me,^5R =H
Fig. 18b: $^1R = {}^2R$ = i-Pr,^3R =H, $^4R = {}^5R$ =Me

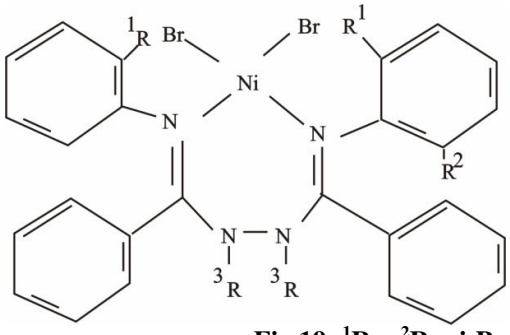


Fig 19: $^1R = {}^2R$ = i-Pr,$^3R = {}^4R$ = Me

Scheme 4: Nickel complexes of [N,O] and [N,N] iminohyroxamato ligands

With the exception of fig 19, which is a seven membered chelate in contrast to all other complexes, all the Ni-complexes are dark green of brown, air sensitive and paramagnetic. Broad and shifted signals were observed in the ^{1}H NMR spectra and signal intensities in the ^{13}C NMR spectra. The paramagnetism of the complexes clearly indicates nonquadratic, nonpolar coordination geometry and these compounds exist either as four-coordinate tetrahedrally distorted monomers or as bromo-bridged five coordinate dimmers.

Palladium and Platinum complexes

In recent years there has been considerable interest concerning the coordination chemistry of chalcogen-nitrogen ligands with the platinum group metals. Much of this work has focused on complexes of S-N ligands[67], while the coordination chemistry of the corresponding Se-N system is less well developed. Chalcogen substituted diazenes are versatile polydentate ligand because of the variety of hetroatom available for coordination. The fig 20 shows the diazene and the fig 21 shows the platinum or palladium complex unexpectedly produces the divalent tridentate azine metallocycles[68](Scheme 5).

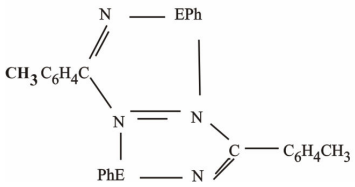


Fig 20: E = S, Se[68]

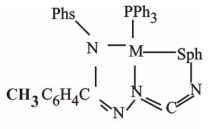


Fig. 21: M= Pd, Pt[68]

Scheme 5: Substituted diazenes and its group 10 metal complexes[68]

X-ray structure determinations have revealed that the coordination sites of the approximately square planar metal complexes [69]. Platinum$(Am)_2${Am = N^1,N^2-diphenyl benzamidine complexes has also been studied[10].

Group 11 metal complexes

The determination of the structure of N^1,N^2 diphenyl benzamidine has allowed the comparison of an amidine ligand in its coordinated and non-coordinated forms for the first time[70]. On complexation with copper the C-N bond becomes shorter and the C=N bond longer to yield a C-N bond indicative of the delocalization which occurs on complexation. The N-C-N angle is seen to be sensitive to be bonding mode adopted[70].

Complex	C-N(Å)	N-C-N(˚)
Bonding mode		
$Cu_2(Am)_2$	1.328(7)	120.0(5)
Bridging	1.334(8)	

Complexes of Cu(II) with bioactive ligands N', N" – bis (3 – carboxy-1–oxoprop–2-enyl) 2- Amino–N–arylbenzamidine, N', N" – bis (3 – carboxy- 1 – oxopropanyl) 2- Amino–N–arylbenzamidine and N', N" – bis (3–carboxy-1– oxophenelenyl) 2-Amino–N–arylbenzamidine have been synthesized and characterized by various physico-chemical techniques[71]. Mass spectrum explains the successive degradation of the molecular species in solution and justifies ML complexes(fig. 22).

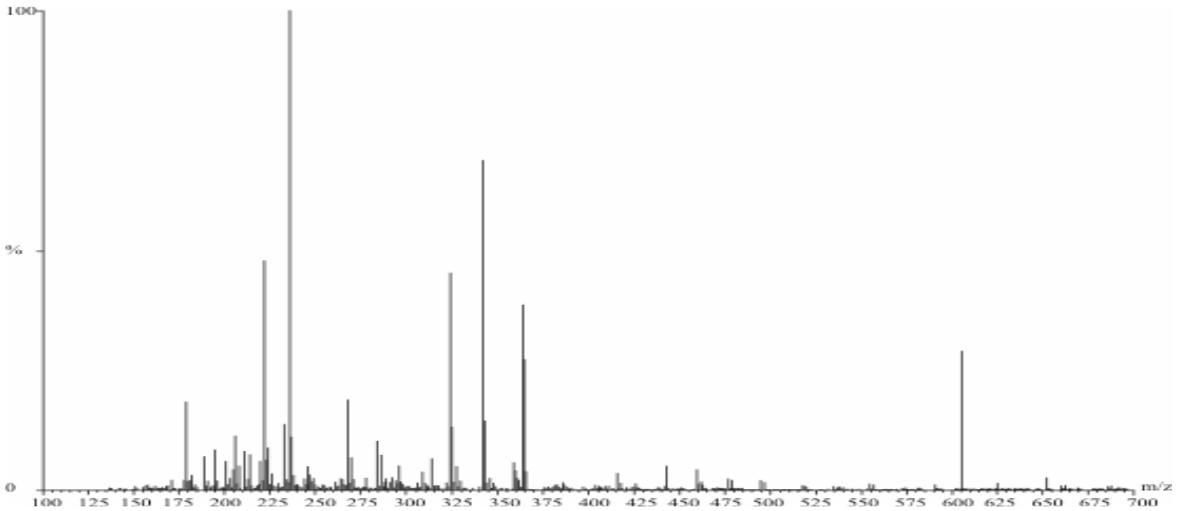


Fig. 22: TOF-MS spectrum of copper- benzamidine complex[71]

Vibrational spectra indicate coordination of amide and carboxylate oxygen of the ligands along with water molecules. Electronic spectra and magnetic susceptibility measurements reveal octahedral geometry for Cu(II) complexes. The EPR of the reported complex show $g_{\parallel} > g_{\perp} > 2.0023$ and G value within the range 2.08-4.49 are consistent with $dx^2–y^2$ ground state in an octahedral geometry(fig.23). The geometric parameter G, which is a measure of the exchange interaction between the copper centers in the polycrystalline compound, is calculated using the equation: $G = (g_{\parallel}–2.0023)/(g_{\perp}–2.0023)$ for axial spectra and for rhombic spectra $G = (g_3–2)/(g_{\perp}–2)$ and $g_{\perp}=(g_1+g_2)/2$. If G > 4, exchange interaction is negligible if it is less than 4; considerable exchange interaction is indicated in the solid complex[71].

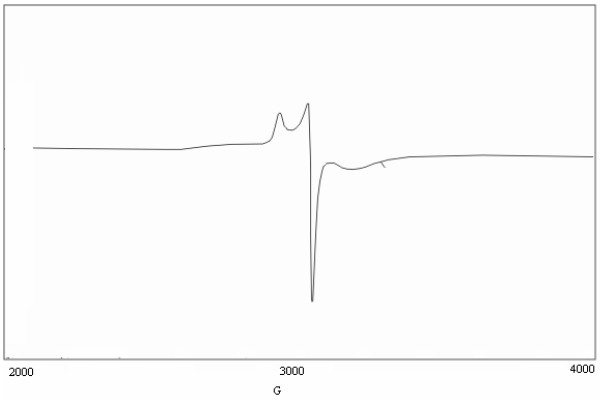


Fig 23 : EPR spectrum of copper-benzamidine complex[71]

The voltammogram of the copper(II) complex shows a quasi-reversible redox process and a simple one electron process assignable to the Cu(II)/Cu(I) couple(fig. 24).

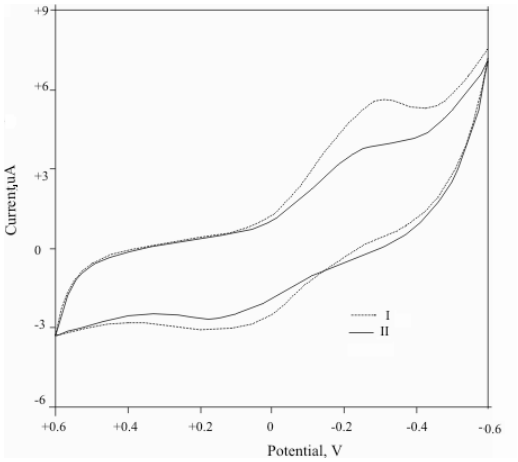


Fig. 24: Cyclic voltammogram of the copper benzamidine complexes[71]

Kinetic and thermodynamic parameters were computed from the thermal data using Coats and Redfern method, which confirm first order kinetics. The bio-efficacy of the ligands and its copper complexes have been examined against the growth of bacteria and pathogenic fungi *in vitro* to evaluate their anti-microbial potential. The free ligands and its copper complexes were screened against *Rhizopus sp.* and *Aspergillus niger* fungi and *Escherchia coli* & *S.aureus* bacteria to asses their potential antimicrobial activity. The results are quite promising. The antimicrobial data reveal that the complexes are more bioactive than the free ligands. The results indicate that the ligand and its metal complexes possess notable antimicrobial properties[71]. The x-ray diffraction pattern reveals the crystalline nature of the complexes, giving triclinic crystal system with P_1 space group for the copper complexes(fig25).

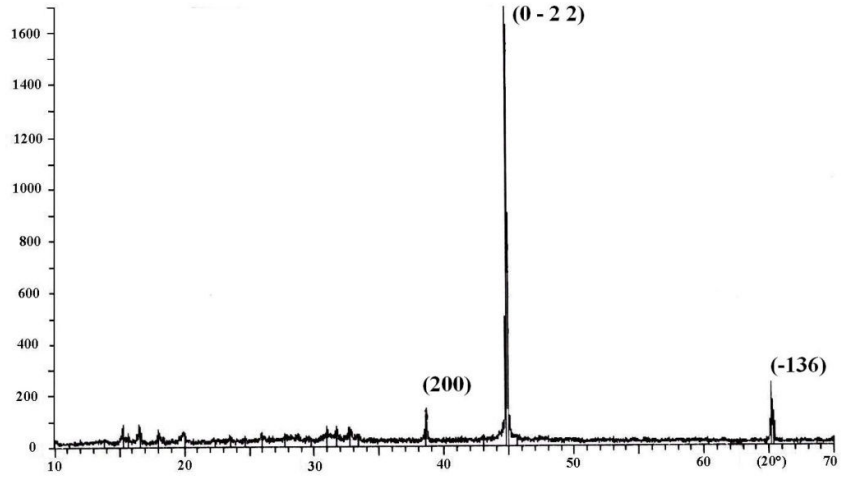


Fig 25: X-ray diffraction of the copper – benzamidine complex[71]

Group 12 metal complexes

Only few research articles deals group 12 metals with amidines.Synthesis and spectrothermal studies of group 12 metals with ligands N', N" – bis (3 – carboxy-1–oxoprop–2-enyl) 2- Amino–N–arylbenzamidine, N', N" – bis (3 – carboxy- 1 – oxopropanyl) 2- Amino–N–arylbenzamidine and N', N" – bis (3–carboxy-1–oxophenelenyl) 2-Amino–N–arylbenzamidine have been synthesized and characterized by various physico-chemical techniques[72]. The infrared and ^{1}H NMR spectral data are in agreement with coordination of amide and carboxylate oxygen of the ligands giving a MO_4 tetrahedral chromophore. The elemental analyses and mass spectral data have justified the ML complexes. The thermal behaviour of complexes shows that water molecule is removed in first step—followed by decomposition of the rest of the molecule in the next steps. Kinetic and thermodynamic parameters were computed from the thermal data using Coats and Redfern method, which confirm first order kinetics(fig 26)[72].

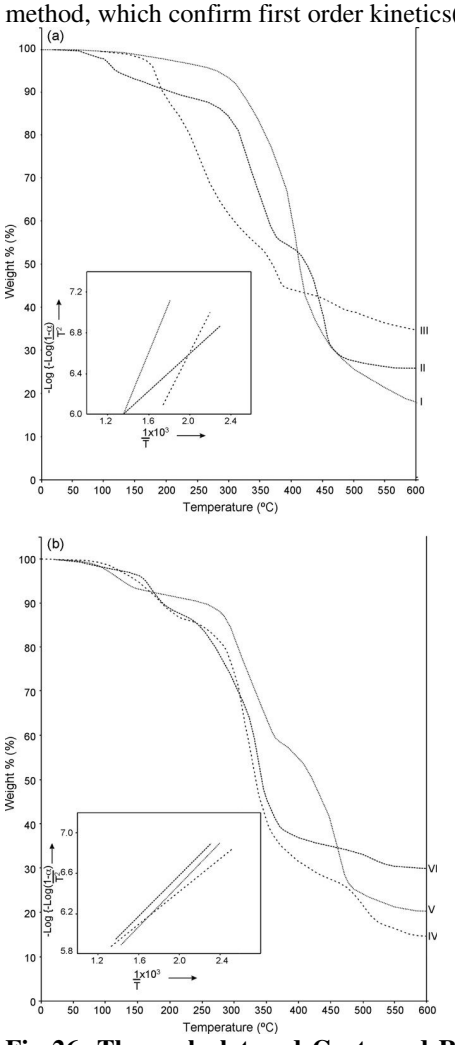


Fig 26: Thermal plot and Coats and Redfern plot of group 12 metal – benzamidine complexes[72]

Molecular structures of the complexes have been optimized by MM2 calculations and supported tetrahedral geometry(fig 27).

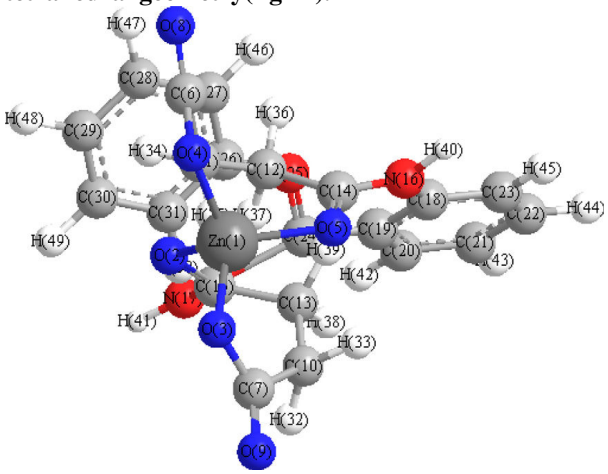
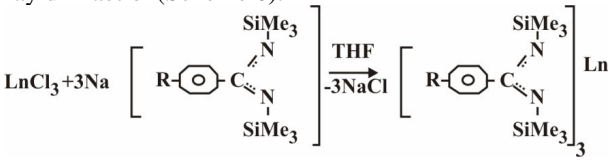


Fig 27: Optimized structure of the Zn(II) – benzamidine complexes[72]

Lanthanide complexes

Only few research papers on lanthanide-benzamidine complexes are available.Using a sterically demanding amidinate auxillary ligand and an in-situ alkylation procedure, neutral mono(amidinate)monoalkyl complexes were prepared[73]. For spanning the full size range of the lanthanide metals,structures were established by single crystal x-ray analysis. The catalytic activity of the cationic alkyl species in ethane polymerization was found to vary by over two orders of magnitude depending on the metal ionic radius, the intermediate metal sizes being found to be the most effective[73].

Anhydrous lanthanide trichloride react with N-silylated sodium benzamidinates Na[4-$RC_6H_4C(NSiMe_3)_2$] to give the monomeric, hemleptic, lanthanide(III) benzamidinates [4-$RC_6H_4C(NSiMe_3)_2]_3Ln$ (R=H,MeO, CF_3,Ph)[100]. The molecular structure of [4-$RMeOC_6H_4C(NSiMe_3)_2]_3Pr$ has been determined by x-ray diffraction(Scheme 6).



Scheme 6 : Lanthanide complex of N-silylated benzamidinates

Absorption and emission measurements reveal that the three benzamidinate ligands produce an unusually large crystal field[74]. Rare earth chelates of N-hydroxy, N-phenyl, N'-p-anisyl benzamidine(HPAB) has been isolated and characterized by various physio-chemical technique and rare earth ions is attributed to the presence of – N(OH)-C=N[75].

Acknowledgement

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