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Metal-containing Complexes of Lactams, Imidazoles, and Benzimidazoles and Their Biological Activity

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The results of the latest investigations of the problem of the synthesis of metal-containing complexes of lactams, imidazoles, and benzimidazoles, their structure, and their stability in solutions are surveyed. Some data on their biological activity (pesticide and pharmacological) and the mechanism of their physiological action are presented.
The bibliography includes 190 references.

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I. INTRODUCTION

One of the aspects of the use of coordination compounds of transition metals is their application as biologically active substances. The involvement of metal ions and their complexes in biological processes has been described in a number of monographs.[1-4] Recently the attention of investigators has been attracted increasingly by biocoordination compounds which can be used as biologically active preparations in medicine and agriculture.[5-11] The employment of complexes of microelements with biologically active substances such as vitamins, hormones, nucleic acids, etc. is of interest in medical practice. Many medicinal drugs behave as ligands which interact specifically with the ions of a particular metal or group of metals. A series of preparations with anticancer, antibacterial, and antiviral activities have been obtained in recent years on the basis of metal complexes; some of these are used in clinical and experimental medicine.

In view of their toxicity and high phytocidal activity inorganic salts of microelements have not found extensive application in agriculture. However, complexes containing microelements and organic compounds are as a rule more active biologically and less toxic. In the assortment of chemical plant protecting agents available throughout the world, metal-containing compounds occupy an important place.[12] Thus, one of the groups of fungicides consists of various copper compounds which are widely employed in the fight against plant diseases; in some of these diseases, the copper compounds cannot be replaced by other preparations.

The complexes proposed for use in agriculture are as a rule more effective even at lower concentrations than metal ions and organic molecules which enter into their composition. They provide the microelements lacking by the plants, are not phytotoxic, have a broad spectrum of activity, are resistant to the action of light and heat, and, what is most important, are not toxic to warm blooded animals or their toxicity is low. The complexes make it possible to combine in one molecule several biometals or several different molecules with biological activity and acting synergistically, which results in an appreciable enhancement of the overall effect. The complexes act more slowly than salts, but their activity is more prolonged and involves no risk for agricultural crops.

Preparations based on complexes greatly improve the pesticidal qualities of polymeric materials and compositions based on them. The use of complexes and salts mixed with other pesticides to prepare biocidal paints for the coating of the bottoms of ships and other underwater constructions is effective.[13]

The rapid development of biocoordination chemistry is directly related also to the study of the role of metal complexes in processes important in living organisms. One of such problems involves the study of the mechanism of the action of physiologically active substances on biological membranes, enzymes, etc. Here membrane-active compounds, promoting the selective transfer of metal ions through biological and artificial membranes, which is basically related to the complex formation process, are of considerable importance.

Among the various classes of biologically active coordination compounds, complexes with nitrogen-containing heterocycles as ligands have attracted attention.[14] The metal-containing complexes of lactams and azoles, which play an important role in biological processes and have also found applications in pharmocological preparations and as effective plant protecting agents, are promising in this sense.

The present review is devoted to the latest advances in the field of complexes of transition metal salts with certain nitrogen-containing heterocyles—lactams, imidazoles, and benzimidazoles. It describes the current data on the synthesis, structure, and biological activity of these complexes.

II. COMPLEXES OF LACTAMS

The complexes of lactams with heavy metal salts (I) were first obtained in the 1950's.[15]

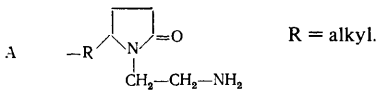
$$MX_m \cdot nA \quad \text{(I)}$$

M = Fe, Co, Ni, Cu;
X = halogen;
$m = 2$;
$n = 3.8$;
A = amide, lactam.

Compounds (I) are readily formed from the initial reactants on heating to 40–160 °C in the presence of a solvent [tetrahydrofuran (THF), methanol, and ethanol] or in the presence of an excess of the initial amide.[15-17] As a rule, between 3 and 10 moles of the amide are used per mole of the metal salt.

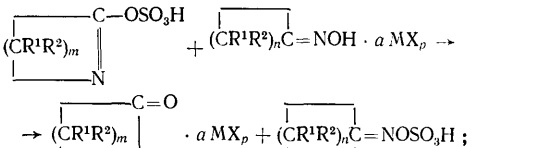
Madan and co-workers[18-20] proposed a method of synthesis of copper-containing complexes of lactams by the interaction of the latter with copper(I) chloride subjected to preliminary dehydration by boiling in 2,2-dimethoxypropane for 2 h. A series of metal complexes of butyrolactam and ε-caprolactam were synthesised in this way. The complexes of 8-caprolactam with cobalt salts have been described.[21] They are obtained in solution in orthoformic ester (tri-isopropoxymethane).

The complexes of 5-alkyl-1-(β-aminoethyl)-2-pyrrolidinones with platinum and palladium salts[22] having the formula (I) with M = Pt or Pd, X = Cl or Br, and $m = n = 2$ have also been synthesised:



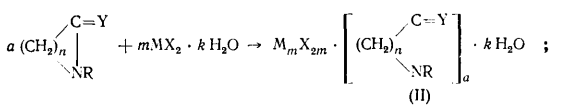
R = alkyl.

Another method of synthesis of metal complexes of lactams[23,24] consists in the reaction between lactam *O*-sulphates and complexes of alicyclic ketoximes with metal halides (Lewis acids):



$m, n = 3—11$, R^1, R^2 = H, alkyl, alkenyl;
M = Cu (II), Zn, Al, Sn (II), Sb (III), B, Zr (IV), Fe (III), Ni (II).

The complexes of unsubstituted and *N*-substituted lactams and thiolactams with heavy metal salts having the general formula (II) have been described.[35-38] They are obtained by the reaction of the corresponding lactams with heavy metal salts in absolute ethanol at room temperature or on boiling:



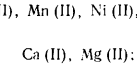
(II)

$a = 1—4$; $n = 3,5$; $m = 1,2$; $k = 0—2$;
M = Cu (II), Zn, Mn (II), Hg (II), Ni (II), Y = O, S;
X = Cl, Br, NO_3; R = H, Ph, CH_3, —CHCCl₃ (OH).

Complexes of a similar type, where the complex-formation reaction proceeds without the elimination of a mobile hydrogen atom, are usually crystalline compounds which contain water of crystallisation derived from the solvent or from the surrounding medium. They can be converted into anhydrous complexes by recrystallisation from an anhydrous solvent such as THF. The complexes (I) are as a rule soluble in water and many organic solvents. The solutions produced are usually stable, but sometimes the complex decomposes on heating into the initial amides and heavy metal salts. Heating of the complexes above the melting point can also lead to decomposition into the initial components. Compounds (I) can be employed as catalysts of the carbonylation reaction and in many instances their catalytic activity is higher than that of the simple salts.[15] The complexes described[18-20] are stable under normal conditions and do not undergo photochemical decomposition and decomposition on heating to 120 °C. All the caprolactam complexes investigated behave as powerful electrolytes.

Recently numerous studies devoted to the determination of the structure and stability of the lactam complexes have appeared in the literature.[39-44] As a rule, infrared and ultraviolet spectroscopy, NMR, EPR, X-ray diffraction, and X-ray spectroscopy are used for the determination of the structures. The infrared spectroscopic and NMR methods make it possible to determine reliably the type of coordination in the complexes of lactams. Coordination to the complex-forming agent takes place as a rule via the oxygen atom, which is demonstrated by the bathochromic shift of the carbonyl group frequency by 30—40 cm^{-1} compared with the free lactam. The small changes in the NH stretching vibration frequencies in the infrared spectra indicate merely a general rearrangement of the ligand molecule in the course of the complex formation process. Lactams behave as monodentate ligands. The stability constants of the complexes are determined as a rule polarographically and by potentiometric titration. Certain physicochemical properties of the metal complexes of lactams have been investigated.[42-44] The number of molecules of water of crystallisation has been determined by the derivatographic method and the molar conductance of the melts and solutions of these complexes has been investigated.

The physicochemical properties of the lactam complexes have been studied in greatest detail by Madan and co-workers.[18-20] It has been shown that the coordination of the ligand to the transition metal is via the carbonyl oxygen atom of the ligand. The perchlorates of these complexes have the general formula

$[MA_6]^{n+}(ClO_4^-)_n$ M = Cr (III), Al (III), Fe (III), Co (II), Mn (II), Ni (II), Cu (II), Cd (II), Zn (II), Ca (II), Mg (II); A = ;

$n = 2.3$; R = H, CH_3.

However, the halogen-containing complexes of Co^{2+}, Cu^{2+}, Mn^{2+}, and Fe^{3+} exhibit appreciable structural differences in relation to the perchlorate complexes. An octahedral structure of the cation and a tetrahedral structure of the anion are characteristic of the cobalt complexes $[CoA_6]^{2+}[CoX_4]^{2-}$, where X = Cl, Br, I, or NCS. The copper and manganese complexes incorporate one or two molecules of the ligand A: MA_2Cl_2 and $MACl_2$. The iron chloride complex has the formula $[FeA_4Cl_2][FeCl_4]$. All these complexes have been characterised by the infrared and electronic spectra and their electrical conductivities and magnetic susceptibilities have been studied.

The coordination compounds of zinc complexes of lactams have been investigated.[45] The compounds obtained were identified by infrared spectroscopy and some of their properties were studied: molar conductance and thermal stability, which is important in connection with the use of such compounds as lactam polymerisation activators. It has been shown that the bond between the zinc atom and the lactam is formed via the oxygen atom. All these complexes contain neither water nor a solvent. The enlargement of the lactam ring on passing from caprolactam to caprylolactam in the case of chloride and bromide complexes does not affect the molecular structure. In the iodide- and thiocyanate-containing complexes the enlargement of the lactam ring entails the coordination of a smaller number of molecules. The complex cation $[ZnA_6]^{2+}$ is not formed in the presence of these anions. The greatest thermal stability is shown by bromides and then by the chlorides.

Complexes of tervalent chromium salts with pyrrolidinone and caprolactam have been described.[48] Their structure has been demonstrated with the aid of infrared spectra. The composition and structure of complexes of 5-alkyl-1-(β-aminoethyl)-2-pyrrolidinones with platinum and palladium salts have been established.[22] Comparison of the infrared spectra of the complexes and the initial ligands reveals an appreciable bathochromic shift of the $\nu(NH_2)$ bands, which indicates the involvement of the amino-nitrogen atom in coordination to the metal. The presence in the spectra of the initial ligands of a broad band associated with the stretching vibrations of the NH_2 group at 3400—3300 cm^{-1} and the fairly low stretching vibration frequency of the carbonyl group (1705—1709 cm^{-1}) indicate the presence of an intramolecular hydrogen bond in the ligands. Complex formation involves the rupture of the

hydrogen bond, which is demonstrated by the increase of $\nu(C{=}O)$ to 1722 cm^{-1}. The latter finding is also confirmed by the fact that the C=O group of the ligand does not participate in coordination (otherwise its frequency in the spectrum of the complex would have been lower than that of the free ligand). The nitrogen atom of the heterocycle is also not involved in complex formation, which can be accounted for by the presence of the mesomeric effect, which reduces the electron density at the ring nitrogen atom.

Thus analysis of the physicochemical data of various workers (mainly infrared spectroscopic data) permits the conclusion that in the complexes of unsubstituted and *N*-alkyl-substituted lactams the ligand is coordinated to the metal via the oxygen atom, while in the complexes of 1-(β-aminoethyl)-substituted lactams coordination is via the amino-nitrogen. The nitrogen atom of the heterocycle is not involved in complex formation.

The structure of compound (II), described in a number of patents,[35-38] has been demonstrated with the aid of infrared spectra; the presence of molecules of water of crystallisation has been confirmed by the derivatographic method and the molar conductances of the complexes have also been investigated.

Compounds (II), namely dipyrrolidinocopper(II) dichloride and tricaprolactamocopper(II) dichloride monohydrate, have been investigated by X-ray diffraction and X-ray spectroscopy.[51-52] The structure of the single crystal of $Cu(P)_2Cl_2$, where P = pyrrolidinone, has been described and is illustrated in Fig. 1. The molecules in the crystal are combined into dimers with highly asymmetric Cu...Cl...Cu bridges. The

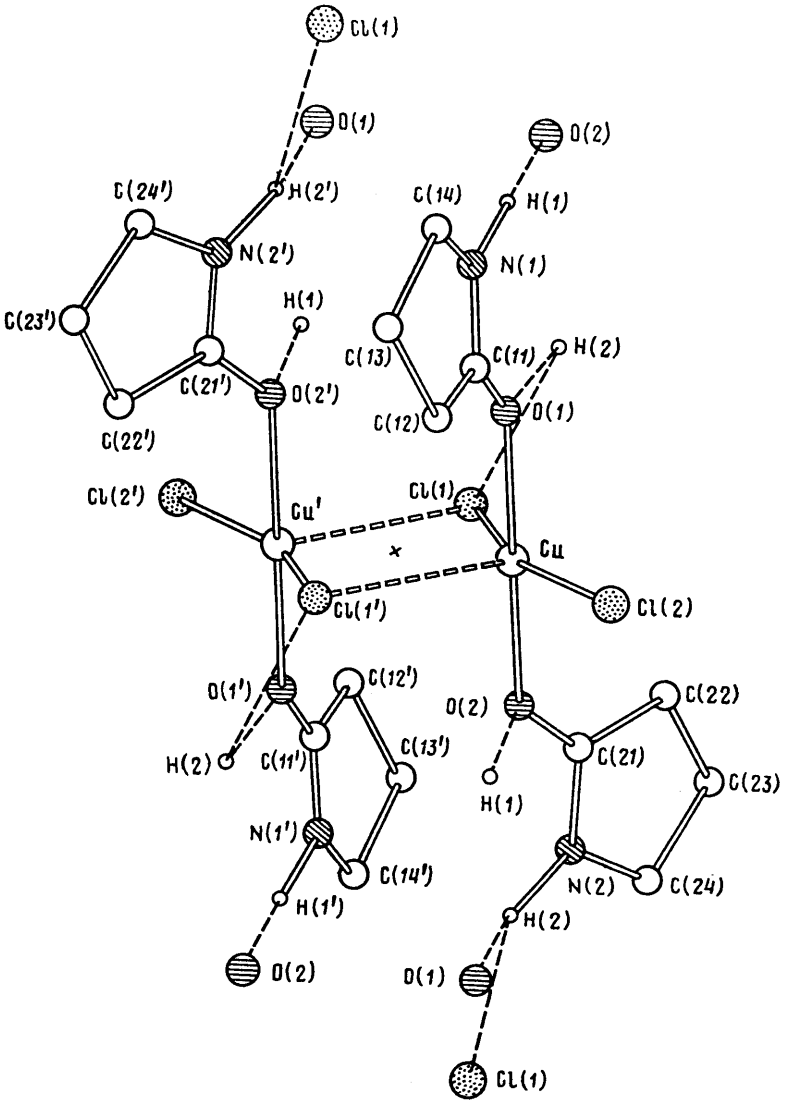


Figure 1. The structure of the dimer in the crystal structure of the $CuCl_2$ complex of 2-pyrrolidinone; the H atoms of the CH_2 groups are not shown.[51]

coordination of the copper atom is intermediate between square and trigonal-bipyramidal (with the ligand atoms in the axial positions). The free coordination site in the *trans*-position relative to the chlorine atom is not completely shielded (<159°).

A different picture obtains for the complex with caprolactam. The structure of tricaprolactamocopper(II) dichloride monohydrate is ionic (Fig.2). The complex is made up of the $[Cu(CL)_6]^{2+}$ cations (CL = caprolactam), which possess crystallographic symmetry with the Cu^{2+} ion at the centre of symmetry, and the anions $[CuCl_3(CL)]^-$, whose number is twice as great. Thus the complex has the formula $[Cu(CL)_6]^{2+}[CuCl_3(CL)]_2^-$. The molecule of water of crystallisation is evidently split off at the instant of the growing of the single crystal. Like pyrrolidinone, caprolactam is a monodentate ligand and is coordinated to the copper atom via the oxygen atom.

The copper atom in the anion has a coordination number of 4 (three Cu–Cl bonds and one Cu...O bond). On the other hand, in the cation copper has a coordination of 4 + 2, i.e. four normal coordinate bonds and two weakened Cu–O(4) and Cu–O(4′) bonds. They correspond to extremely weak metal–oxygen interactions. The caprolactam has in all cases the chair configuration, which is also characteristic of free caprolactam. The cations and anions are combined via hydrogen bonds into an infinite puckered layer.

Analysis of the infrared spectra of compounds (II) has shown that the vibration frequencies of the carbonyl group are reduced by 40–45 cm^{-1} compared with the free ligands. The involvement of the oxygen atom in complex formation cannot fail to alter the lactam system and displacements are therefore observed in the region of the ν(NH) stretching vibration frequencies, but the M – N bond is not formed. It follows from the foregoing that the lactam complexes have

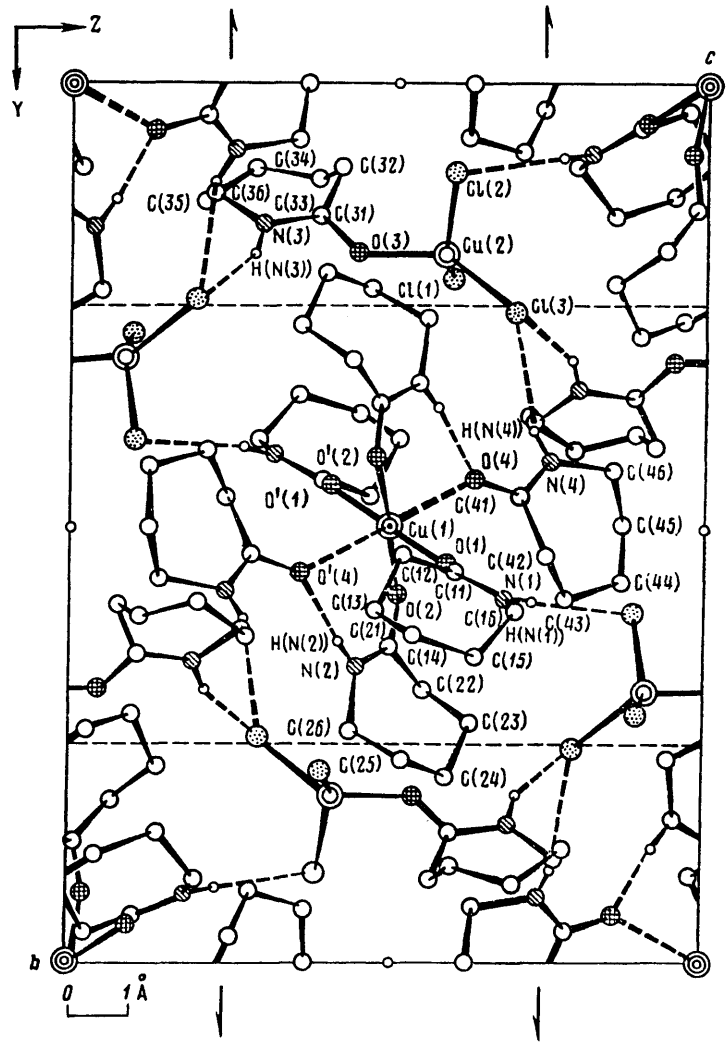


Figure 2. The structure of the $CuCl_2$ complex of caprolactam projected along the a axis (the H atoms of the CH_2 groups are not shown); the dashed lines represent the hydrogen bonds and the additional coordination interactions.[52]

completely different structures depending on the size of the lactam ring. The pyrrolidinone complex has a covalent structure and is dimeric in the crystalline state, while the caprolactam complex has an ionic structure and consists of a polymer.

Analysis of the literature quoted in this Section shows that all the lactam complexes with heavy metal salts are readily soluble in water and polar organic solvents and sparingly soluble in non-polar solvents; they are stable under normal conditions and behave like strong electrolytes.[18-20]

The complexes may or may not contain molecules of water of crystallisation. The most convenient methods of their synthesis are based on the direct interaction of the ligand with heavy metal salts in a polar solvent.

Modern physicochemical methods are used to establish their structures: infrared and ultraviolet spectroscopy, NMR, EPR, and determinations of electronic conductivity and magnetic susceptibility. However, the most reliable methods, which unambiguously establish the structure of the complex and the spatial disposition of the atoms in the molecule, are X-ray diffraction and X-ray spectroscopy.

Unfortunately these methods cannot be used to determine the structures of all complexes, as X-ray diffraction involves the growing of a single crystal and this cannot be achieved in all cases.

III. METAL COMPLEXES OF IMIDAZOLES AND BENZIMIDAZOLES

The early studies on the chemistry of coordination compounds of imidazoles and benzimidazoles were described in the review of Garnovskii et al.[61] A paper on the synthesis and structure of complexes of azoles with metal halides was published later.[62]

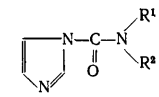
The complexes of azoles are usually obtained by the interaction of the components on heating in organic solvents or by fusing azoles together with metal halides.[63-72] These methods of synthesis frequently lead to compounds containing a large number of solvent molecules. In order to obtain complexes with low coordination numbers, the decomposition of their solvates *in vacuo* at 80–150 °C is therefore employed. In certain cases the presence of solvents leads to the formation of solvolysis and substitution products.

In the case of sparingly soluble metal salts, the ligand exchange method is used. For this purpose, one obtains initially relatively unstable and readily soluble complexes of the salts MX_n (X = halogen), for example, with ethers or acetonitrile, and they are then used in reactions with solutions in imidazole or benzimidazoles. In particular, such a method has been used to synthesise copper(I) complexes. The ligand exchange reaction is carried out in an inert atmosphere.[73-76]

The complexes synthesised can contain between one and six ligand molecules. The number of coordinated groups depends little on the basicity of the imidazole derivatives, but basicity is important in the synthesis of compounds with benzimidazole and its usbstituted derivatives. Thus, imidazole (pK_a = 7) complexes containing from one to six azole molecules have been isolated,[65-70] while only compounds having the composition $MX_2.4HA$ are readily obtained from benzimidazole (pK_a = 5.53).[74,75]

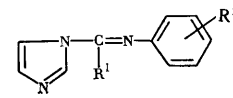
It is important to note that the introduction of bulky substituents into the ligand molecule frequently diminishes the number of coordinated groups. However, when the substituents are remote from the coordination centre, the composition of the complexes is the same as for the unsubstituted molecule. Thus *N*-alkylimidazoles form complexes having the composition MX_2A_6 even in the presence of the butyl substituent, while compounds containing not more than four ligand molecules can be isolated for 2-methyl- and 1,2-dimethyl-imidazoles.[66-69]

The same phenomenon occurs in the synthesis of imidazole complexes with pesticidal activity. Thus the complexes of Cu^{2+}, Mn^{2+}, Fe^{2+}, Ni^{2+}, Ca^{2+}, and Mg^{2+} chlorides with carbamoyl imidazoles contain between two and four ligand molecules:



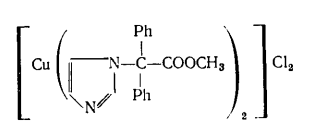
R^1 = alkyl; R^2 = phenoxyalkyl.

On the other hand, the interaction in an inert organic solvent of imidazole derivatives of the type

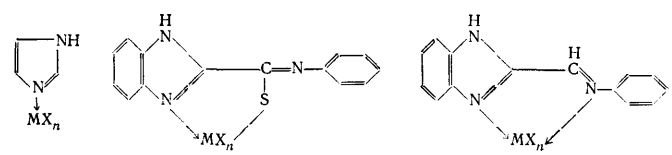


(R^1 = alkyl, alkoxy-group, or $PhCH_2$; R^2 = Cl or CF_3) with Cu^{2+}, Zn^{2+}, Mn^{2+}, Co^{2+}, Fe^{2+}, and Al^{2+} sulphates, chlorides, acetates, and nitrates leads to the formation of complexes containing only two or three ligand molecules.[160-166]

The nature of the metal has little influence on the composition of the complexes. Only copper salts, for which it is not always possible to isolate complexes containing six molecules of azole ligands, are an exception. Thus, the copper complex of methyl diphenylimidazole-1-acetate, which is obtained by the reaction of the ligand and $CuCl_2$ in an alcoholic medium, contains only two molecules of the imidazole derivative:[167]



The question of the location of the coordinate bond is important for imidazoles, benzimidazoles, and their substituted derivatives. Depending on the type of molecule, the metal, and the conditions of synthesis, the coordinate bond can be located at the "pyridine" N(3) atom, or at another heteroatom (O or S) present in the substituted molecule, or in the π-electron system:



According to the literature data discussed by Garnovskii and co-workers,[61,62] coordination takes place predominantly via the nitrogen atom of the "pyridine" type. In this case the molecules of imidazoles and benzimidazoles play the role of monodentate ligands.

The same conculsion concerning the location of the bond in imidazole *N*-ethylimidazole, and *N*-propylimidazole biologically active complexes of Mn^{2+}, Pt^{2+}, and Pd^{2+} was arrived at by other investigators.[77-82]

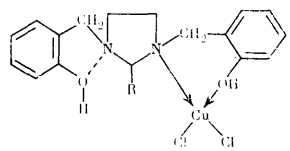
A number of studied have been devoted to metal complexes with 1-vinylimidazoles (A), including those exhibiting biological activity.[83-85] It has been shown by ^{13}C NMR that the coordination of the ligand in the complexes of vinylimidazoles with tin halides $R_{4-n}SnX_n.nA$ (R = alkyl; *n* and *m* = 1 and 2) takes place via the "pyridine" nitrogen atom, which

can entail a change in the mutual orientation of the vinyl group and the heterocycle. The same mode of addition of the ligand obtains in the complexes $MX_n.2A$ and $MX_n.4A$, where MX_n represents Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, and Al^{3+} halides. However, Shchelokov et al,[86] who investigated the Pt^{2+} and Pd^{2+} complexes with 1-vinylimidazole, reached the conclusion, on the basis of infrared spectra, that the vinyl group can be involved in the formation of a bond with the central atom.

2-Hydroxymethyl-1-vinylimidazole, 1-vinyl-2-vinyloxymethylimidazole, 1-ethyl-2-vinyloxymethylimidazole, as well as their benzimidazole analogues have been used as ligands.[87,88] Complexes with the halides, sulphates, and acetates of a series of transition metals have been isolated. Their composition ranges form 1:1 to 1:4 (M:A). The chlorides and acetates show respectively the highest and lowest coordinating capacities. The presence of a substituent in the 2-position in the imidazole ring leads to the formation of complexes in which the metal is coordinated to a smaller number of ligands than in the case of unsubstituted 1-vinylimidazole.

Spectroscopic data have shown that the hydroxymethylimidazoles are coordinated via the nitrogen atom in the 3-position in the imidazole ring. The coordination interaction involves also the π-electron system of the heterocylce and the vinyl group.

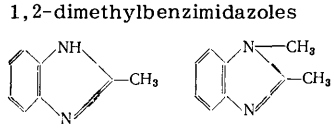
Metal complexes with imidazolidine derivatives have been described.[89,90] Compounds containing not more than two ligand molecules, whose bonds with the central atom are formed via a nitrogen atom as well as the atoms of other functional groups present in the molecule, are produced, for example:



R = Ph, $C_6H_4OCH_3$, CH_3.

In surveying the studies of recent years on the synthesis and properties of complexes of benzimidazole and its substituted derivatives,[91-96] one may note the rarely encountered case where the bond between the benzimidazole ligands and the complex-forming agent in the mixed copper(II) carboxylate complexes with benzimidazole $CuZ.HA.H_2O$ (HA = Benzimidazole and Z = residues of malonic, succinic, malic, or maleic acid) is believed[91] to be formed via the nitrogen atom of the NH group, whose stretching vibration frequency undergoes a bathochromic shift on coordination.

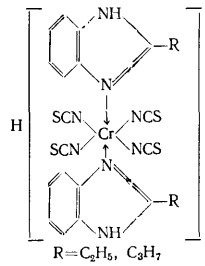
On the basis of the bathochromic shift of the ν(CN) stretching vibration frequency of the imidazole ring on coordination, it has been concluded that the molecules of benzimidazole derivatives in the complexes of bivalent zinc and manganese with 2-methyl- or 1,2-dimethylbenzimidazoles



(HA) (A')

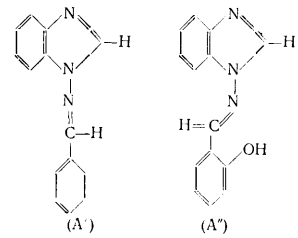
having the compositions $MX_2.HA$ and $MX_2.2A'$ (X = Cl, Br, I, NO_3, CH_3COO, or $1/2SO_4$) add to the zinc(II) and manganese(II) ions via the nitrogen atom in the 3-position in the imidazole ring. The spectra of the complexes can also contain bands characteristic of the acid residues present in the inner sphere.

In the chromium(III) complexes of 2-ethyl and 2-propylbenzimidazoles which have been isolated, the *N*-coordination of the thiocyanate groups has also been indicated:



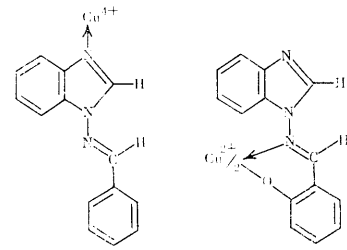
$R = C_2H_5$, C_3H_7

After the interaction of copper(I) halides and acetates with benzylidene-1-aminobenzimidazole (A') and salicylidene-1-amino-benzimidazole (A"),



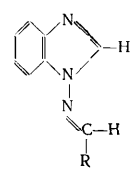
(A') (A")

complexes of two types were isolated: the molecular adducts $CuX.A'$, $2CuAc_2.3A'$, $CuX.A"$, and $CuX.3A"$, as well as the inner complex $Cu(A" - H)_2$, where X = Br or I. It has been shown by infrared spectroscopy that the azomethines are coordinated to the copper(I) atom via the nitrogen atom of the "pyridine" type in the benzimidazole ring in the molecular adducts and via the azomethine group in the inner complex, for example:



A study of the EPR spectra of the complexes obtained has shown that the interaction of the azomethines (A') and (A") with copper(I) halides is not accompanied by a change in the valence state of copper in the case where complexes of the type of adducts are formed. The interaction involving the formation of the inner complex leads to the formation of bivalent copper complexes and CuBr is oxidised more readily than CuI.[97]

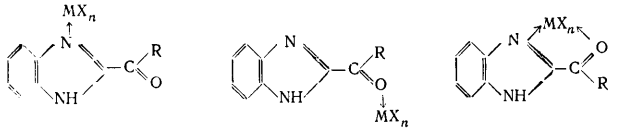
The complex-forming properties of the azomethines of 1-aminobenzimidazoles are determined by the specific features of the steric and electronic structures of the ligand. It has been established that the coordination interaction of the azomethines of 1-aminobenzimidazoles with metal salts proceeds in the first place via the N-donor centre of the hetero-fragment and not via the azomethine bond $-N = C\lesssim$:[98]



R = Ph, $C_{10}H_7$, $3\text{-}IC_6H_4$, $3\text{-}NO_2C_6H_4$, $4\text{-}NO_2C_6H_4$, $2\text{-}HOC_6H_4$, $3\text{-}BrC_6H_4$, $5\text{-}BrC_6H_4$, $4\text{-}HOC_6H_4$.

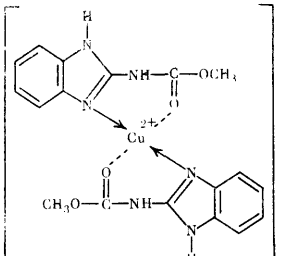
Transition metal complexes with 2-(2-hydroxyphenyl)- and 2-(2-aminophenyl)benzimidazoles contain one or two ligand molecules. It has been shown by infrared spectroscopy that the aminophenyl derivative of benzimidazole is coordinated via the amino-group of the aniline residue and the tertiary N(3) atom of the imidazole ring. In the complexes of 2-pyridylbenzimidazoles with lanthanides and molybdenum(III) coordination is achieved via the nitrogen atom of the pyridine ring and the N(3) atom of the imidazole ring.[99-106]

In the complexes with carbonylbenzimidazoles the coordinate bond is located predominantly at the nitrogen atom of the heterocycle and complex formation proceeds via the oxygen atoms only in the case of the "hardest" Lewis acids:[61]



R = H, alkyl .

Copper(II) complexes with methyl benzimidazole-2-carbamate (HA) have been described.[107] A product having the composition $CuX_2.2HA$ (X = Cl or Br) was obtained. The infrared spectrum of the ligand contains in the region of the stretching vibrations of the NH group a single band at 3300 cm^{-1}. The stretching vibration band of the carbonyl group is at 1710 cm^{-1} and $\nu(C=N)$ is at 1630 cm^{-1}. There is hardly any change in the position of the 3300 cm^{-1} NH vibration band in the spectrum of the complex, although its intensity is appreciably reduced. The vibration bands of the carbonyl and C = N groups are at 1735 and 1645 cm^{-1}. On this basis, it has been suggested that the bond with the metal ion in the complex is formed via the tertiary nitrogen atom and the carbonyl oxygen atom:



As stated in previously published reviews,[61,62] the type of polyhedra formed in the complexes with azoles depends on a series of factors: the coordination number and the electronic configuration of the complex-forming agent, the character of the anion, the nature of the ligand, and in some cases also the state of aggregation of the system. The configuration of the complexes with imidazoles and benzimidazoles was usually determined from magnetic susceptibility and spectroscopic data. Studies on the X-ray diffraction of such compounds are more rarely encountered.

It has been shown on the basis of the observed effective magnetic moments at different temperatures, spectroscopic data, and electrical conductivity in methanol that the complexes with 4-methylimidazole (HA) having the composition $[M(HA)_6]X_2$ [M = Co(II) or Ni(II)] and also $[Ni(HA)_6].[HgCl_4]$, $[Ni(HA)_2(NCS)_4]^{2-}$ and $[Ni(HA)_4(NCS)_2]$ have an octahedral or distroted octahedral configuration, while the complexes $[Ni(HA)_2Cl_2]$ and $[Ni(HA)_4X_2]$ have a tetrahedral configuration. The thiocyanate group in the inner sphere is present in the form of an ion coordinated to the nitrogen atom, which plays the role of a bridge.[108] An X-ray diffraction study of the compound CoA_2Q_2, where A = 1-methylimidazole and Q = 2,4,6-trichlorophenol, showed that Co^{2+} is located in a distorted tetrahedral environment made up of the nitrogen atoms of the two A ligands and the oxygen atoms of the two Q ligands. In view of the bond between the metal ion and one of the chlorine atoms of the Q ligand, the environment of the metal becomes of the distorted square-pyramidal type with one of the nitrogen atoms at the apex of the pyramid. The structure is stabilised by two intramolecular hydrogen bonds C–H...Cl between a carbon atom of A and a chlorine atom of Q. For the same ligands in the Co^{2+}, Zn^{2+}, and Ni^{2+} complexes, it has been found by spectrophotometric and EPR methods that the Q anion in MQ_2A_n is linked to the central atom and the complexes have the configuration of a distorted tetrahedron or a distorted octahedron.[109,110]

The structure of $[CuA_4(AcO)_4].6H_2O$ consists of centrosymmetric dimers linked by acetate bridges. The copper atom is involved in a tetragonal-pyramidal coordination with one bridging acetate ligand at the apex of the pyramid and with the nitrogen atoms in the two methylimidazole ligands and the oxygen atoms of the acetate ions at the base of the pyramid. Water molecules form a system of hydrogen bonds.[111]

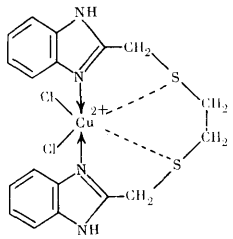
On the basis of X-ray diffraction data and the results obtained by other physical research techniques, it has been established that the copper complexes of 1-methylimidazole and substituted iminoacids have a square-planar structure. The copper atom is located at the centre of symmetry and is surrounded by the two oxygen atoms of the carbonyl groups and two nitrogen atoms of the substituted imidazole. On coordination of two water molecules, the complex has a distorted octahedral configuration.[112,113]

Rhodium complexes containing imidazole (HA^1), benzimidazole (HA^2), and 2-methylbenzimidazole (HA^3) with the compositions $[Rh(HA^1)_4Cl_2]Cl$, $[Rh(HA^2)_4Cl_2]Cl$, $[Rh(A^2)_3].3H_2O$, and $[Rh(HA^3)_4(H_2O)_2]Cl_3$, as well as the iridium compounds $[Ir(HA^2)X_3(H_2O)_2]I$ (X = Cl, Br, or I) and $[Ir(HA^2)_4X]X$ (X = Br, I, NO_2, or NCS), have a polymeric octahedral structure with bridging groups. On the other hand, the complexes $[Pt(HA^3)_4]Cl_2$, $[Pt(HA^1)_2Cl_2]$, $[Pt(HA^2)_2Cl_2]$, and $[Pt(HA^3)_2Cl_2]$, as well as compounds in which the chloride ion has been replaced by the Br^-, I^-, and NO_3^- ions are monomeric and have a planar *trans*- or *cis*-configuration.[114]

The complexes coordinating between four and six 2-methylbenzimidazole molecules have a distorted tetrahedral configuration for Cu^{2+}, a tetrahedral configuration for Co^{2+}, and an octahedral or tetrahedral configuration for Ni^{2+} and Fe^{3+}.[115] The nickel compounds $[Ni(HA)_4]X_2$ (X = Cl, Br, or NO_3 and HA = benzimidazole and its derivatives) have a square-planar structure. On heating, the chloride, bromide, and nitrate complexes are converted into $[Ni(HA)_4]X_2$ and the values of μ_{eff} indicate the formation of a distorted octahedral configuration. The replacement of the benzimidazole derivative by the unsubstituted ligand makes it possible to achieve such a transition also for the iodide compounds.[116]

X-Ray diffraction and electronic spectroscopic data as well as measurements of the magnetic susceptibility have shown that the Co^{2+}, Ni^{2+}, and Cu^{2+} complexes of 5-nitrobenzimidazole have pseudotetrahedral and distorted octahedral structures. The cobalt and halogen-containing nickel compounds with 3,4-dihydro-1-phenyl-1*H*-1,4-oxazino[4,3*a*]benzimidazole have a tetrahedral configuration. On the other hand, the nickel(II) thiocyanate complex is square planar. In all the compounds indicated the ligand is coordinated via the N(3) atom of the benzimidazole ring. In the copper complexes of

tris(2-benzylimidazolymethylamine) there is a trigonalbipyramidal or distorted octahedral configuration. The study of the structure of the complex



showed that the copper atoms are located in a distorted trigonal-bipyramidal environment with the N(3) atom of the ligand in the axial position and also with two S atoms and Cl^- ions in the equatorial plane.[117-120]

The stability of the complexes of azoles had not been the subject of systematic study previously. There were only isolated investigations of the stability of imidazole compounds. The stability of the complexes is directly related to their biological activity. It follows from Azizov's study[5] that complexes with an average stability constant $\lg \beta \cong 8-9$ exhibits the highest bioactivity. Numerous publications devoted to the investigation of the thermodynamic and kinetic stabilities of coordination compounds with imidazole, benzimidazole, and their substituted derivatives have appeared recently. Thus the relative basicities of imidazole and its substituted derivatives have been estimated[121-125] and studies have been made of the complex formation reactions of cobalt(II), copper(II), and nickel(II) salts with the above ligands. It follows from the values of pK_B found for the ligands in benzyl and n-butyl alcohols that the electron-accepting properties of the imidazoles become more pronounced with enhancement of the acid properties of the alcohols. In DMSO, acetonitrile, and acetone the differences between the proton-accepting properties of the ligands in each solvent depend mainly on the inductive effect of the substituent, on which steric effects associated with the number, size, and degree of branching of the substituents in the imidazole molecule may be superimposed. When electron-donating substituents are introduced into the ligand molecule, an increase of the stability of the Co^{2+} and Cu^{2+} complexes is observed, while the introduction of the electron-accepting substituents entails some decrease of the stability of the complexes. The study of the complex formation reaction between Ni^{2+} and imidazoles demonstrated a decrease of the rate of formation of the complex in the presence of small amounts of added acetone, which can be accounted for by the specific solvation of the ligand and by a change in the dielectric constant of the medium.

The presence of the hydroxide ion influences the formation of complexes by the Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, and Hg^{2+} salts with imidazole (HA). At low ligand concentrations the complex $M(OH)_2.HA$ is formed, while at high concentrations the complex $M(HA)_n$ ($n = 1-4$) is formed stepwise.[126-130]

The study of the formation of mixed complexes with imidazole and aminoacids showed that Zn^{2+} reacts with imidazole, histamine (H_2R), and histidine (H_3Q) to form the complexes $[Zn(HA)_n]^{2+}$ ($n = 1-4$) and also $[Zn(HA)_nR]$ ($n = 1$ or 2) and $[Zn(HR)Q]^{2-}$ and $[Zn(H_2R)Q]^-$. The composition of the complexes shows that imidazole is coordinated as a monodentate ligand without the elimination of a proton while histamine and histidine are coordinated as bi- and tri-dentate ligands with abstraction of one, two, or three protons.[131-134]

The dissociation constants of the ligands and the stepwise stability constants of the Cu^{2+}, Co^{2+}, Ni^{2+}, and Zn^{2+} complexes with 4-methylimidazole (HA) have been determined. In the case of Co^{2+} in aqueous solution there is an equilibrium between the octahedral complexes $[Co(H_2O)_{6-n}(HA)_n]^{2+}$ and the tetrahedral compounds $[Co(H_2O)_{4-n}(HA)_n]^{2+}$. The dependence of the formation constants K_n on the number of coordinated ethylimidazole molecules n for Cu^{2+} and Zn^{2+} is anomalous in the case of K_3 and K_4. In this case the logarithms of the constants are equal to the sums of the corresponding quantities for the complexes $[M(HA)_4]^{2+}$, $[M(H_2O)_2(HA)_2]^{2+}$, and $[M(H_2O)(HA)_3]^{2+}$ formed simultaneously in solution.

The stability constants ($\lg \beta_n$) show that the stability of the complexes of methylimidazole is somewhat lower than that of the corresponding compounds of the butyl derivative as a consequence of the lower basicity of methylimidazole. The stability of the complexes of Co^{2+}, Ni^{2+}, and other transition metals with 1-methyl-, 2,2-dimethyl-, 2-ethyl-, 1-methyl-, 2-ethyl-, 1,2,4-trimethyl-, 1-propyl-, and 1-butyl-imidazoles diminishes with increase in the size of the substituent in the imidazole molecule. In the complex formation reaction of the transition metals with imidazole derivatives having involved substituents, 1:1 complexes are formed as a rule. Thus 2-[(2-carboxyphenyl)azo]-4,5-diphenylimidazole reacts with Th^{4+}, UO_2^{2+}, and Ce^{3+} ions in ethanol to form compounds with the composition indicated and stability constants, $\lg \beta$, 7.17, 6.91, and 6.68 respectively for these ions.[135-143]

A number of studies have been devoted to the complex formation reactions of transition metals with benzimidazole and its substituted derivatives. It has been noted[144-146] that the formation of complexes by copper(II) and cobalt(II) chlorides and nitrates in non-aqueous solutions is influenced by the nature of the solvent and to a lesser extent by the size and character of the substituent in the benzimidazole molecule. In the case of cadmium(II) carboxylates the stability of the complex with benzimidazole depends on the charge of the complex species. The addition of the first benzimidazole molecule to the complex cation is less favourable than the interaction with the uncharged species. This is associated with the change in the strength of the dative $d-\pi^*$ bond between the metal carboxylate and benzimidazole. A π-dative interaction has been noted in the formation of complexes by substituted benzimidazoles with Co^{2+}, Zr^{2+}, Ni^{2+}, and Mn^{2+}. Benzimidazole and 4-azobenzimidazole form the complexes $[M(H_2O)_{6-n}(HA)_n]^{2+}$, while 2-hydroxymethylbenzimidazole forms the complexes $[M(HA)_4]^{2+}$.[147-149]

Summarising the literature data presented for the metal complexes of imidazoles and benzimidazoles, one may conclude that the azole complexes isolated from solutions or melts contain between one and six ligand molecules. The coordinate bond is as a rule located at the "pyridine" nitrogen atom and other heteroatoms in the substituted azole molecule and is involved in complex formation only in the case of "hard" Lewis acids.

The type of polyhedra of the transition metal complexes of imidazole, benzimidazole, and their derivatives depends on a number of factors. The data presented lead to the conclusion that the geometrical configuration of the complexes with azoles varies from distorted octahedral to square planar. The nature of the complex-forming agent and the ligand as well as the character of the anion of the metal salt are very important in this instance.

In considering the stability of the complexes of azoles in solution, one may note its decrease with increase in the size of the substituent in the ligand molecule. The stability is influenced by the inductive and steric effects of the substituents in the azole molecule and also by the nature of the organic solvent (the majority of studies on the formation of complexes by imidazoles and benzimidazoles have been performed in a non-aqueous medium). In the series of benzimidazole complexes the stability is influenced also by the π-dative

interaction involving the *d* electrons of the metal and the antibonding π* orbitals of the ligand molecule.

IV. BIOLOGICAL ACTIVITY OF COMPLEXES OF LACTAMS, IMIDAZOLES, AND BENZIMIDAZOLES

The study of the biological activity of complexes is important for medicine and agriculture. Investigation of the properties of these substances in biological cycles of toxic elements and in the first place in their interaction with various organisms in the environment (bacteria, fungi, higher plants, and animals) plays an important role.

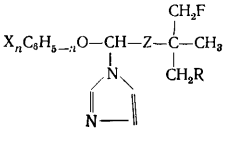
The use of biocoordination compounds in medicine is based on the fact that the concentration of biometals in various tissues for the normally functioning organism must be maintained at vigorously specified levels by regulating them with the aid of the system of appropriate proteins and hormones. In some cases it is necessary to resort to special preparations containing the particular bioelement in a form assimilable by the organism.[2]

Biocoordination compounds as chemical plant protecting agents have been attracting increasing attention in the agricultural industry. This is because the metal-containing organic compounds exhibit a high activity against a broad spectrum of pathogens and are as a rule safe for the environment.

The question of the physiological activity of coordination compounds of lactams and azoles has been inadequately investigated. The metal complexes of azoles play an important role in biological objects and processes.[150-152] The imidazole group enters into the composition of the most important enzymes: creatine kinase, chymotrypsin, carboxypeptidase A, carboanhydrase B, and others. The imidazole group is very important in phosphorylation systems. Haemoproteins fulfil an important biological role. The involvement of the imidazole group of histidine in the binding of oxygen by haemoglobin and myoglobin has been postulated.

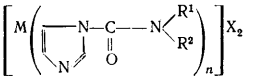
Metal complexes with imidazole, benzimidazole, and their derivatives possess pharmacological activity. Stimulators of antitumour protection, preparations with antimicrobial activity, etc. have been found among them.[81,85]

Such compounds include platinum(II) and palladium(II) complexes of 1-ethyl- and 1-propyl-imidazoles having the composition MX_2A_2 and MX_2A_4 (X = Cl, Br, or I). The complexes of many transition metals with imidazole derivatives having the general formula

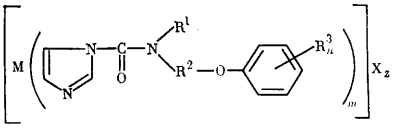


where Z = CO or CH(OH), R = H or F, X = halogen, alkyl, NO_2, CN, alkoxycarbonyl, substituted phenyl, or unsubstituted phenyl, and n = 0–3 can be used in medicine and veterinary practice for the treatment of dermatomycoses and systemic mycoses. The cobalt(II) and nickel(II) complexes containing two or four molecules of 3,4-dihydro-1-phenyl-1*H*-oxazino[4,3*a*]benzimidazole possess antiviral properties.[153-156] There are some data concerning the pharmacological activity of the metal complexes of lactams.[157-160] Thus, certain 1,5-disubstituted pyrrolidinones and their salts exhibit vasodilating, antiulcer, and hypotensive activities. Lactam derivatives, in particular silylated lactams, have attracted attention as valuable physiologically active substances. They function as mediators in the inhibition of the nervous system and posses anticonvulsant, [illegible]

Many metal complexes with imidazole, benzimidazole, and lactams exhibit a pesticidal activity. Thus carbamoylimidazoles and their complexes with copper(II), manganese(II), iron(II), calcium(II), nickel(II), and magnesium(II) salts are active fungicides:

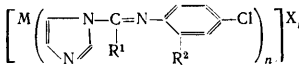


(R^1 = alkyl, R^2 = phenoxyalkyl, X = univalent anion, and n = 2–4) and



(R^1 = alkyl, R^2 = branched alkylene, R^3 = alkyl or halogen, n = 0–5, m = 2 or 4, and X = univalent anion). At a concentration of 1 g litre^{-1} the preparations inhibit the development of *Botrytis cinerea* and *Erysiphe graminis*.[160-162]

The copper(II), zinc(II), manganese(II), cobalt(II), iron(III), and aluminium(III) compounds

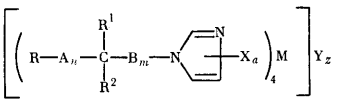


(R^1 = alkyl, alkoxyalkyl, or $PhCH_2$, R^2 = Cl or CF_3, n = 2 or 3, X = univalent anion, and m = 2 or 3) exhibit a broad spectrum fungicidal activity.

The complexes and the ligands entering into their composition can also possess plant growth stimulating properties, apart from their fungicidal activity. At a concentration of 4 g litre^{-1}, they influence the growth of soya, tomatoes, the cottonplant, etc., they intensify the green colour of leaves and bushing out, and inhibit apical tissues.[163-166]

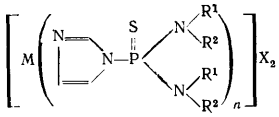
The copper complex of methyl diphenylimidazole-1-acetate (A) $[Cu(A)_2]Cl_2$ is a fungicidal preparation (especially active against powdery mildew fungi). At a concentration of 1.2×10^{-4}–1×10^{-9}% the preparation greatly reduces the infection of barley by the fungus *Erysiphe graminis*, the infection of the apple tree by *Podosphaera lencotricha*, and of cucumbers by *Erysiphe cichoreaclarum*.[167]

The calcium(II), magnesium(II), manganese(II), copper(II), zinc(II), nickel(II), cobalt(II), tin(II), cadmium(II), chromium(III), and iron(III) complexes of 1-arylalkylimidazoles possess fungicidal activity:[168-171]



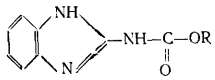
(R = aryl or substituted aryl, R^1 and R^2 = alkyl, alkenyl arylakyl, substituted arylakyl, phenyl, substituted phenyl, etc., A and B = alkylene, X = alkyl, halogen, or NO_2, a = 0–3, n and m = 0 or 1, and Y = anion). In contrast to the free imidazoles, the complexes are not phytotoxic, can be used to treat green plants, and also can serve as seed pickling agents. They suppress the development of phytopathogenic fungi and are effective against barley *helminthosporiosis*, the grey mould and mildew of the leguminous plants, tomatoes, and the grape vines, phytophtorosis of tomatoes, piriculariosis of rice, and the stem and grey rust in wheat

The cobalt(II), cadmium(II), iron(II), nickel(II), manganese(II), and zinc(II) complexes of imidazolylphosphonothioic diamide, i.e.

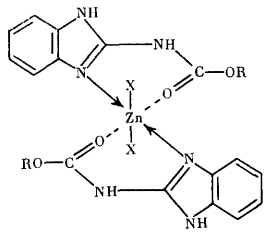


where R^1 and R^2 = alkyl, Ph, CH_2CHCH_2, CH_2Ph, or furfuryl, X = non-phytotoxic anion, and n = 1–4, possess fungicidal activity. The compounds can be used as bactericides for the protection of plants and also various materials (polymers, fabrics, and paper).[172–174] At a concentration of 24–100 mg litre^{-1}, the complexes induce 75–100% destruction of *Phytophtora infestans*, *Venturia inaequalis*, and other fungi.

Transition metal complexes of benzimidazole derivatives have been investigated as effective fungicides. The zinc(II) and copper(II) complexes of urethanes

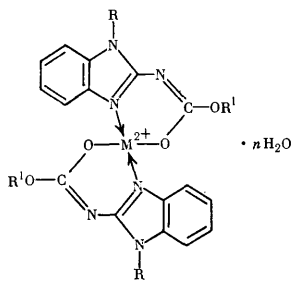


where R = lower alkyl, have been described in patents,[175–178] for example:



The complexes exhibit protective and eradicating fungicidal activities. At a concentration of 16–80 mg litre^{-1} they are active against apple scab and powdery mildew. A number of transition metal complexes of methyl benzimidazole-2-carbamate exhibit a broad spectrum of fungicidal activities, are non-toxic to man, and their fungicidal activity persists for a long time. The preparation can be used for the protection of plastics and leather.

Fungicidal and acaricidal activities are shown by the cadmium(II), zinc(II), copper(II), nickel(II), manganese(II), and cobalt(II) complexes having the general formula

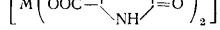


where R = $-\overset{O}{\overset{\|}{C}}-NHR^2$; $-\overset{O}{\overset{\|}{C}}-R^3$, $-\overset{S}{\overset{\|}{C}}-CCl_3$ (R^1 = alkyl, R^2 = alkyl or substituted alkyl, etc. R^3 = H, alkyl, alkenyl, cycloalkyl, phenyl, etc., n = 0–3[179,180]). Dehydration of the compounds leads to an increase of their fungicidal activity and also to an appreciable improvement of stability on storage.

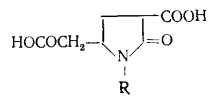
Mixtures exhibiting a synergistic effect are also employed as fungicidal preparations. They contain zinc salts and methyl 1-butylcarbamoylbenzimidazole-2-carbamate. They readily penetrate plants and exhibit a prolonged protective activity. Fungicidal preparations containing a mixture of methyl benzimidazole-2-carbamate and the manganese or zinc salt of ethylenebisdithiocarbamic acid in proportions ranging from 1:1 to 1:20 (1:10 are the preferred proportions).[181]

Less information is available in the literature about the pesticidal activity of lactam complexes. The use of coordination compounds of lactams agains plant pathogens has been reported.[182–186] The substances proved to be effective inhibitors of the growth of certain phytopathogenic bacteria inducing diseases of the grapevine and certain melon crops. In particular, they inhibit the growth of *Bacterium tumefaciens*, *Pactobacterium aroideae*, and *Xanthomonas campestris*.

Complexes based on 5-alkyl-1-(β-aminoethyl)-2-pyrrolidinones, described by Sedavkina and Shebaldova,[22] exhibit antimicrobial and antiphage activities. The parmacological and pesticida' activities of pyrrolidinonecarboxylic acids have been mentioned.[53–60] The zinc(II), copper(II), and calcium(II) complexes



show an antifungal effect. The zinc salt shows a greater inhibiting activity against dermatophytes than the copper salt. On the other hand, the calcium salt influences protein metabolism in bony and skin tissues. Fungicidal preparations containing only the copper salt of the amidodicarboxylic acid



(R = H, alkyl, or cycloalkyl) are especially effective against phytophtorosis and the genuine powdery mildew of cucumbers.[58]

Among the lactam complexes of transition metal salts, the preparation "Kartotsid" [Cartocide?] the copper(II) complex of ε-caprolactam exhibiting a broad spectrum of fungicidal acitivity and safe for the environment, is promising.[187] It can replace the familiar fungicidal preparations, namely copper oxide chloride and Khomezin—in sugar beet and potato plantations, vineyards, and orchards, and also makes it possible to reduce appreciably the consumption of copper.[188] Furthermore, the preparation has a low toxicity (LD_{50} = 1200 mg kg^{-1}) for warm blooded animals.

When biologically active metal complexes are used, it is very important to investigate the mechanism of their action on living cells. The character of the action of biocoordination compounds is at present by no means always clear. There exist at least three possible mechanisms of their action: (1) the activity is manifested by the ligand and the role of the metal reduces to creating a suitable transport form; (2) the metal ion itself exhibits an activity and the complex is necessary for the transport of the metal ion across the cell membrane; (3) the active species, namely the complex ions, can interact with cell centres important for vital activity.[2]

The majority of the theories of the mechanism of the action of copper-containing preparations are based on the adsorption capacity of the fungal cell protoplasm. It is known that a deposit of the copper-containing fungicides on the plant is not absolutely insoluble in water—a certain microamount of copper is present in solution. According to the cumulative theory, the copper present in solution is absorbed by the spores, which disturbs the equilibrium and fresh portions of copper dissolve. The process continues until the sport accumulates a toxic dose of copper.[189]

In certain cases the fungicidal properties of copper complexes can be explained by their structure. Thus the free coordination site in the *trans*-position relative to the chlorine atom is not fully shielded in the compound having formula(II) and described in patents[35-38] (see above), where the ligand is caprolactam and the inorganic salt is $CuCl_2$. Precisely this fact can explain the high biological activity of the compound. Probably owing to the imperfection of the coordination environment of the copper atom, the latter interacts with the sulphhydryl groups of enzymes and coenzymes, since the latter are especially sensitive to the action of heavy metals. This leads to the precipitation of the protein substance, as a result of which the fungus is destroyed. However, the available data about the behaviour of complexes in bio-objects are as yet inadequate for an unambiguous solution of the problem of the mechanism of the action of these complexes.

In order to determine the mechanism of the action of the fungicidal preparation "Kartotsid", a study has been made of its interaction with two-layer phospholipid membranes,[190] since transfer across a two-layer membrane is decisive in the action of any physiologically active susbstance. It is known that two-layer lipid membranes are effective models of cell membranes. Measurements of the membrane potential, electrical resistance, and electrical capacitance of lipid two-layer membranes as a function of the "Kartotsid" concentration suggested that the primary mechanism of its fungicidal action is associated with the increase of conductivity and with the breakdown of the structural organisation of the cell membrane. The increase of the membrane conductivity is caused by the lipophilic properties of the membrane-active form of "Kartotsid". The molecules of the preparation in living organisms apparently act not only on the surface regions of the cell membranes but also penetrate into the interior of the cell.

As a result of their penetration into the cell, the copper ions inactivate enzymes, forming chelate complexes. The activity of many enzymes is known to diminish following the substitution of the active metal of the enzyme complex (for example, magnesium) by heavy metals such as copper or mercury. Thus the role of the lactam molecules in the complex with the copper ion probably reduces to facilitating the transmembrane transfer of Cu^{2+} ions into the interior of the cell.

Summarising the data presented concerning the physiological activity of imidazole, benzimidazole, and lactam complexes, one may conclude that at present they have not as yet found a wide-scale application in the national economy, although much work is already being done along these lines. Evidently many transition metal complexes of the above ligands possess pesticidal and pharmacological activities. In most instances the activity of the complexes is higher than that of their constituent organic molecules. Furthermore, the complexes are always less toxic for warm blooded animals than the coordinated physiologically active ligands. It has been shown in relation to the preparation "Kartotsid" that bio-coordination compounds contain less toxic copper than the preparations based on simple copper salts used at present which is extremely important from the ecological standpoint. All these factors make one confident that physiologically active metal complexes will find more extensive applications in agriculture in the immediate future.

REFERENCES

1. M.N.Hughes, "The Inorganic Chemistry of Biological Processes" (Translated into Russian), Izd.Mir, Moscow, 1983, p.74.
2. K.B.Yatsimirskii, "Vvednie v Bioneorganicheskuyu Khimiyu" (Introduction to Bioinorganic Chemistry), Izd.Naukova Dumka, Kiev, 1976, p.85.
3. D.R.Williams, "The Metals of Life: the Solution Chemistry of Metal Ions in Biological Systems" (Translated into Russian), Izd.Mir, Moscow, 1975, p.21.
4. K.B.Yatsimirskii (Editor), "Biologicheskie Aspekty Koordinatsionnoi Khimii" (Biological Apsects of Coordination Chemistry), Izd.Naukova Dumka, Kiev, 1977, p.3.
5. M.A.Azizov, "O Kompleksnykh Soedineniyakh Nekotorykh Mikroelementov s Bioaktivnymi Veshchestvami" (Complexes of Certain Microelements with Bioactive Substances), Izd.Meditsina, Tashkent, 1969, p.5.
6. Kh.Kh.Khakimov, "Naprav ennyi Sintez Biologicheski Aktivnykh Soedinenii" (Specific Synthesis of Biologically Active Compounds), Izd.Nauka, Moscow, 1976, p.128.
7. B.A.Bovykin, Farmatsiya, 1979, (6), 62.
8. M.G.Bezrukov, A.M.Belousova, and V.A.Sergeev, Uspekhi Khim., 1982, **51**, 696 [Russ.Chem.Rev., 1982(4)].
9. V.V.Lukachina, Koord.Khim., 1982, **8**, 419.
10. N.A.Parpiev, A.Kushakbaev, and M.M.Azizov, "Koordinatsionnye Soedineniya Metallov s Lekarstvennymi Preparatami" (Coordination Compounds of Metals with Medicinal Drugs), Izd.Fan, Tashkent, 1982.
11. A.I.Stetsenko, M.A.Presnov, and A.L.Konovalova, Uspekhi Khim., 1981, **50**, 688 [Russ.Chem.Rev., 1981(4)].
12. E.A.Bovykin, S.S.Kukalenko, and S.I.Shestakova, "Biokoordinatsionnaya Khimiya na Sluzhbe Narodnogo Khozyaistva" (Biocoordination Chemistry at the Service of the National Economy), Izd.NIITEKhim, Moscow, 1984, No.1.
13. US P.4092441 (1978).
14. G.A.Modnikova and I.S.Musatova, "Poisk Biologicheski Aktivnykh Soedinenii v Ryadu Azot- i Kislorodsoderzhashchikh Geterotsiklov. Sbornik Nauchnykh Trudov" (Symposium. The Search for Biologically Active Compounds among Nitrogen- and Oxygen-containing Heterocycles), Izd.VINIKhFI, Moscow, 1980, No.8, p.9.
15. B.P.774956 (1957).
16. B.P.138745 (1972).
17. B.P. 1294559 (1970).
18. S.K.Madan and H.H.Denk, J.Inorg.Nuclear Chem., 1965, **27**, 1049.
19. S.K.Madan and J.A.Sturr, J.Inorg.Nuclear Chem., 1967, **29**, 1669.
20. S.K.Madan and H.H.Denk, Inorg.Chem., 1967, **6**, 421.
21. F.Kutek, Coll.Czech., 1978, **43**, 2250.
22. V.A.Sedavkina and A.D.Shebaldova, Khim.Farm. Zhur., 1982, (1), 65.
23. US P.3687938 (1972).
24. US P.3828028 (1974).
25. R.I.Niedzielski and G.Znider, Canad.J.Chem., 1965, **43**, 2618.
26. D.P.Wyman, J.Org.Chem., 1964, **29**, 1956.
27. BRD Appl.2221497 (1972); Chem.Abs., 1973, **78**, 29273.
28. Japanese Appl.46-42657 (1971); Chem.Abs., 1973, **78**, 97142.
29. M.Masaki and K.Fukui, Bull.Chem.Soc.Japan., 1973, **46**, 3179.

30. BRD Appl.2043378 (1979); Auszuge aus den Auslegenschrift, 1979 (15).
31. Japanese Appl.55-3346 (1980); Tokkyo Koho, 1980, (3–84).
32. Japanese Appl.50-84589 (1975); Chem.Abs., 1976 **84**, 43336.
33. Krizo and B.Casensky, Chem.Prum., 1978, **28**(2), 176.
34. Japanese Appl.46-42189 (1971); Chem.Abs., 1973, **78**, 135698.
35. USSR P.704067 (1978); Byul.Izobret., 1983, (27), 246.
36. USSR P.732350 (1979); Byul.Izobret., 1983, (26), 230.
37. USSR P.681779 (1978); Byul.Izobret., 1983, (26), 230.
38. French Appl.2485010 (1981); Bulletin officiel de la propriete industrielle, 1981, (52).
39. N.J.Biedermann, Z.Naturforsch., 1974, **29b**, 65.
40. B.Roninson and K.Lempton, Electrochem.Method Anal., 1970, (3), 91.
41. P.Deni and J.S.Bart, Inorg.Chim.Acta, 1976, **17**, 97.
42. B.Dusek and F.Kutek, Coll.Czech.Chem.Comm., 1975, **40**, 2569.
43. R.Choukroun and D.Gervais, Inorg.Chim.Acta., 1978, **26**, 17.
44. Yu.G.Eremin and T.I.Martishova, Zhur.Neorg.Khim., 1970, **15**, 350 [Russ.J.Inorg.Chem., 1970(2)].
45. B.Dusek and F.Kutek, Zhur.Neorg.Khim., 1980, **25**, 2926 [Russ.J.Inorg.Chem., 1980(11)].
46. D.M.Hart and B.I.Davis, J.Inorg.Nuclear Chem., 1968, **30**, 2263.
47. S.K.Madan and W.V.Miller, J.Inorg.Nuclear Chem., 1968, **30**, 3287.
48. C.A.Rollinson and R.C.White, Inorg.Chem., 1962, **1**, 281.
49. O.Bohunovsky and S.C.Jain, Canad.J.Chem., 1969, **47**, 1689.
50. R.J.Niedzielski and G.Znider, Canad.J.Chem., 1965, **43**, 2618.
51. S.S.Kukalenko, Yu.T.Struchkov, S.I.Shestakova, A.S.Batsanov, and A.G.Tsybulevskii, Koord.Khim., 1983, **9**, 306.
52. S.S.Kukalenko, Yu.T.Struchkov, S.I.Shestakova, A.S.Batsanov, and A.G.Tsybulevskii, Koord.Khim., 1983, **9**, 312.
53. Japanese Appl.56-39051 (1981); Chem.Abs., 1981, 95, 42384.
54. M.Kotoucec and V.Springer, Acta Fac.Farm.Univ. Comenianse, 1978, **32**, 111.
55. P.Rogli and H.Monnier, Trav.Soc.Pharm.Montpellier, 1978, **38**, 135.
56. E.Moczaz and B.Phen Denh Fuy, Rhumateloque (Paris), 1979, **8**(2), 71.
57. US P.4025525 (1977).
58. Japanese Appl.52-24343 (1978); Ref.Zhur.Khim., 1979, 16O340.
59. B.P.1294559 (1970).
60. USSR P.726099 (1978); Byul.Izobret., 1980, (13), 18.
61. A.D.Garnovskii, O.A.Osipov, L.I.Kuznetsova, and N.N.Bogdashev, Uspekhi Khim., 1973, **42**, 177 [Russ.Chem.Rev., 1973(2)].
62. A.D.Garnovskii, O.A.Osipov, and V.N.Sheinker, Koord.Khim., 1980, **6**, 3.
63. W.M.Davis, I.Dewan, and S.Lippard, J.Inorg.Chem., 1981, **20**, 2928.
64. L.Antolini, L.P.Battaglia, A.B.Cotradi, G.Marcotrigiano, L.Menabue, G.C.Pellacani, and M.Saladini, J.Inorg.Chem., 1982, **21**, 1381.
65. S.Sano and V.Sugiura, Chem.Comm., 1982, 750.
66. M.I.Drew and S.M.Nelson, J.Chem.Soc., Dalton Trans., 1981, 1868.
67. R.Quinn, M.Nappa, and I.S.Valentine, J.Amer. Chem.Soc., 1982, **104**, 2588.
68. R.N.Shchelokov, G.S.Muraveiskaya, V.N.Voropaev, G.G.Skvortsova, and E.S.Domnina, Koord.Khim., 1982, **8**, 51.
69. E.S.Domnina, Yu.N.Ivlev, N.I.Shergina, N.N.Chinanina, D.A.Belousova, Yu.L.Frolova, and G.G.Skvortsova, Zhur.Obshch.Khim., 1971, **41**, 1102.
70. N.I.Shergina, N.N.Chinanina, Yu.N.Ivlev, E.S.Domnina, and G.G.Skvortsova, Zhur.Prikl. Spektrosk., 1972, **27**(1), 176.
71. O.Yu.Ryabukhina, T.A.Yusman, Yu.I.Ryabukhin, A.D.Garnovskii, and G.N.Dorofeenko, Koord.Khim., 1980, **6**, 1186.
72. V.I.Ovcharenko, S.V.Larionov, R.A.Sadykov, R.Z.Sagdeev, I.A.Grigor'ev, and L.B.Volodarskii, Koord.Khim., 1977, **3**, 1559.
73. G.R.Chaudhury and K.C.Dask, Inorg.Nuclear Chem., 1981, **43**, 2189.
74. A.T.Marcelis, C.G.van Kralingen, I.Opschoor, and I.Reedijk, Rec.Trav.chim., 1980, **99**, 198.
75. A.M.Handriks and I.J.Reedijk, Inorg.Chim.Acta., 1979, **37**, 15.
76. P.D.Singh and L.K.Mishra, J.Indian Chem.Soc., 1981, **58**, 434.
77. P.L.Birker, A.I.Schierbeek, G.C.Verchoor, and I.Reedijk, Chem.Comm., 1981, 1124.
78. R.Uson and I.Gimeno, J.Organometal.Chem., 1981, **220**, 173.
79. R.Uson, I.Gimeno, and L.A.Oro, Transit.Metal. Chem., 1981, **6**, 103.
80. M.Micolini, F.Braga, and G.Pinto, Inorg.Chim.Acta., 1979, **34**, 295.
81. E.K.D'yachenko, K.N.Lyubomirova, and N.A.Ostankevich, Zhur.Obshch.Khim., 1981, **51**, 2531.
82. G.K.Chandhury and K.C.Dash, J.Indian Chem.Soc., 1979, **56**, 87.
83. V.K.Voronov, T.E.Moskovskaya, V.I.Glukhikh, N.M.Vitkovskaya, Yu.N.Ivlev, E.S.Domina, G.G.Skvortsova, and M.G.Voronkov, Koord.Khim., 1978, **4**, 388.
84. A.A.Kashaev, E.A.Zel'bet, M.P.Demidov, Yu.L.Frolov, N.N.Chinanina, E.S.Domnina, and G.G.Skvortsova, Koord.Khim., 1978, **4**, 785.
85. V.I.Sokol, M.A.Porai-Koshits, V.P.Nikolaev, E.S.Domnina, L.V.Baikalova, G.G.Skvortsova, and L.A.Butman, Koord.Khim., 1979, **5**, 1725.
86. R.N.Shchelokov, G.S.Muraveiskaya, V.N.Voropaev, G.G.Skvortsova, and E.S.Domnina, Koord.Khim., 1980, **6**, 613.
87. E.S.Domnina, L.V.Baikalov, L.E.Protasova, N.M.Deriglazov, N.N.Chinanina, V.I.Skorobogatova, and G.G.Skvortsova, Koord.Khim., 1979, **5**, 14.
88. L.V.Baikalova, E.S.Domnina, G.G.Skvortsova, L.E.Protasova, N.N.Chinanina, and V.K.Voronov, Koord.Khim., 1982, **8**, 1035.
89. E.N.D'yatchenko, N.N.Lyubomirova, V.E.Ivashova, and N.A.Shtankevich, Zhur.Obshch.Khim., 1981, **51**, 2531.

90. V.I.Ovcharenko, S.V.Larionov, R.Z.Sagdeev, and L.B.Volodarskii, Izv.Sibir.Otd.Akad.Nauk SSSR, Ser.Khim., 1978, **7**, 79.
91. R.I.Kharitonova, V.M.Bolotov, and G.V.Kharitonov, Koord.Khim., 1976, **2**, 1547.
92. M.Haga, Inorg.Chim.Acta, 1980, **45**, L183.
93. A.Mishra and J.P.Singh, Curr.Sci.(India), 1980, **49**, 194.
94. K.F.Slyusarenko, M.V.Artemenko, M.V.Pokhodnya, and O.N.Kononenko, Ukrain.Khim., Zhur., 1978, **44**, 687.
95. K.F.Slyusarenko, M.V.Artemenko, and V.A.Pokhodnya, Ukrain.Khim., Zhur., 1982, **48**, 121.
96. K.F.Slyusarenko, M.V.Artemenko, D.I.Lapina, V.A.Pokhodnya, and N.I.Zakharenko, Ukrain.Khim., Zhur., 1982, **48**, 235.
97. L.I.Kuznetsova, A.D.Garnovskii, O.A.Osipov, V.G.Zaletov, Yu.V.Kolodyazhnyi, and O.A.Volotskaya, Koord.Khim., 1982, **8**, 1054.
98. L.I.Kuznetsova, Yu.V.Kolodyazhnyi, O.A.Volotskaya, N.L.Chikina, V.V.Kuz'menko, and A.D.Garnovskii, Koord.Khim., 1982, **8**, 445.
99. L.K.Thompson, B.S.Ramaswamy, and R.D.Dawe, Canad.J.Chem., 1978, **56**, 1311.
100. H.Grefohning and E.Gagliardi, Microchim.Acta., 1982, 2(1), 9.
101. P.T.Joseph et al., Transit.Metal.Chem., 1978, **3**(5), 586.
102. A.Mishra and V.K.Singh, J.Indian Chem.Soc., 1981, **58**, 1197.
103. A.Mishra, M.P.Singh, and J.K.Singh, J.Indian Chem.Soc., 1980, **52**, 249.
104. A.Mishra, V.K.Singh, and M.P.Singh, J.Indian Chem.Soc., 1982, **59**, 622.
105. K.C.Dash and N.J.Mohanta, J.Inorg.Nuclear Chem., 1978, **40**, 499.
106. S.P.Chosii and H.M.Prasad, J.Indian Chem.Soc., 1979, **56**, 660.
107. A.M.Aminov, A.A.Atakuziev, A.M.Kats, S.S.Kasymova, and Ch.Sh.Kadyrov, Uzbek.Khim., Zhur., 1981, (5), 58.
108. K.C.Dash and P.Pujari, J.Inorg.Nuclear Chem., 1977, **39**, 2167.
109. M.B.Cingi, L.A.Manotti, A.Tiripicehio, K.I.Reedij, and R.C.Van Landschoot, Inorg.Chim.Acta., 1980, **39**, 181.
110. R.C.Van Landschoot, I.A.Van Hest, and I.Reedijk, Inorg.Chim.Acta., 1980, **46**, 41.
111. I.Buukari, A.Busnot, F.Bunot, A.Leclarie, and M.A.Bernard, Acta Cryst., 1982, **B38**, 2458.
112. I.Nakao, W.Mori, T.Sakurai, and A.Nakahara, Inorg. Chim.Acta, 1981, **55**, 103.
113. L.P.Battaglia, A.B.Corradi, L.Menabue, G.C.Pellacani, P.Prampolini, and M.Saladini, J.Chem. Soc., Dalton Trans., 1982, 781.
114. S.P.Ghosh, K.Bhattacherjee, L.Dubey, and L.K.Mishra, J.Indian Chem.Soc., 1977, **54**, 230.
115. T.Sakurai, H.Kaji, and A.Nakahara, Inorg.Chim. Acta, 1982, **67**, 1.
116. J.Ihara and R.Tsuchuya, Bull.Chem.Soc.Japan., 1980, **53**, 1614.
117. L.K.Mishra, J.Indian Chem.Soc., 1982, **59**, 795.
118. M.Goodgame, B.Piggott, and S.D.Thorpe, Inorg. Chim.Acta., 1982, **67**, 91.
119. A.W.Addison et al., Inorg.Chem., 1981, **20**, 103.
120. J.H.Paul et al., Inorg.Chem., 1982, **21**, 357.
121. V.I.Dulova and A.P.Myagchenko, Zhur.Fiz.Khim., 1980, **54**, 511 [Russ.J.Phys.Chem., 1980(2)].
122. V.I.Dulova, A.P.Myagchenko, and A.A.Kochanova, Ukrain.Khim.Zhur., 1981, **47**, 1300.
123. V.I.Dulova, A.P.Myagchenko, V.D.Kolotyuk, and K.Yu.Chotii, Koord.Khim., 1982, **8**, 1103.
124. M.C.Navarro Ranninger et al., J.Therm.Anal., 1978, **14**, 281.
125. V.A.Shormanov, N.I.Pimenova, G.A.Krestov, and G.S.Bykova, Zhur.Neorg.Khim., 1978, **23**, 438 [Russ.J.Inorg.Chem., 1978(2)].
126. I.Granberg and S.Sjöberg, Acta Chem.Scand., 1981, **A35**, 193.
127. W.Forsling, Acta Chem.Scand., 1979, **A33**, 641.
128. S.Sjöberg, Acta Chem.Scand., 1977, **A31**, 718.
129. S.Sjöberg, Acta Chem.Scand., 1977, **A31**, 729.
130. W.Forsling, Acta Chem.Scand., 1977, **A31**, 759.
131. A.Marzotto and H.Kozlowskii, Inorg.Chim.Acta, 1982, **67**, 87.
132. M.S.Nair, K.Venkatachalapathi, and M.Santappa, J.Chem.Soc., Dalton.Trans., 1982, 555.
133. M.S.Mohan, D.Sancraft, and E.H.Albott, Inorg. Chem., 1979, **18**, 1527.
134. M.S.Nair, M.Santappa, and P.K.Murugan, Inorg. Chem., 1982, **21**, 142.
135. B.Lenarcik and K.K.Obla, Rocz.Chem., 1977, **51**, 2079.
136. B.Lenarcik and B.Barsczc, Rocz.Chem., 1977, **51**, 1849.
137. K.C.Dash and P.J.Pajari, J.Inorg.Nuclear Chem., **40**, 1173.
138. B.Lenarcik and K.Kurdziel, Pol.J.Chem., 1982, **55**, 737.
139. M.Güntensperger and A.D.Zuberbühler, Helv.Chim. Acta, 1977, **60**, 2584.
140. B.Lenarcik and B.Barszez, Pol.J.Chem., 1979, **53**, 963.
141. B.Lenarcik, B.Barszez, and J.Kulig, Rocz.Chem., 1977, **51**, 1315.
142. R.C.Van Landschoot, J.A.M.Van Hest, and J.Reedijh, J.Inorg.Nuclear Chem., 1976, **38**, 185.
143. A.N.Hamman, J.Indian Electrochem.Soc., 1979, **28**(4), 217.
144. G.V.Kharitonov, V.M.Bolotov, and R.I.Kharitonova, Koord.Khim., 1980, **6**, 1190.
145. V.I.Dulova, O.P.Golosova, and I.L.Gulivets, in "Problemy Sol'vatsii i Kompleksoobrazovaniya" (Problems of Solvation and Complex Formation), Ivanovo, 1980, p.94.
146. V.I.Dulova and O.P.Golosova, Ukrain.Khim., Zhur., 1982, **48**, 350.
147. B.Lenarcik and W.Maciejewski, Pol.J.Chem., 1981, **55**, 31.
148. K.S.Patel, I.M.Bhatt, and D.P.Dani, J.Indian Chem. Soc., 1977, **54**, 1007.
149. T.M.Chernovalova, M.S.Chernov'yants, and K.N.Bagdasarov, Zhur.Obshch.Khim., 1978, **48**, 1843.
150. G.L.Eichhorn (Editor), "Inorganic Biochemistry" (Translated into Russian), Izd.Mir, Moscow, 1978, p.711.
151. A.D.Garnovskii, Doctoral Thesis in Chemical Sciences, Rostov State University, Rostov-on-Don, 1972.
152. G.L.Eichhorn, "The Chemistry of Coordination Compounds" (Translated into Russian), Inostr.Lit., Moscow, 1960.
153. US P.3562282 (1971).
154. US P.4060625 (1977).
155. BRD Appl.2918897 (1980); Ref.Zhur.Khim.,1981,22091.

156. M.Goodgame, B.Piggott, and S.D.Thorpe, Inorg. Chim.Acta, 1982, **67**, 91.
157. L.M.Khananashvili, D.Sh.Akhobadze, and L.K.Dzhainashvili, Khim.Farm.Zhur., 1982, **16**, 560.
158. V.A.Sedavkina, N.A.Morozova, and V.F.Chulkov, Khim.Farm.Zhur., 1982, **16**, 54.
159. US P.4311512 (1982).
160. G.R.Chaudhury and K.C.Dash, Indian J.Chem., 1979, **A17**, 364.
161. B.P.1567521 (1980).
162. B.P.1586998 (1981).
163. Japanese Appl.54-119461 (1979): Ref.Zhur.Khim., 1980, 12O293.
164. B.P.1555576 (1979).
165. British Appl.2013175 (1979); Ref.Zhur.Khim., 1980, 13O379.
166. BRD Appl.2739352 (1979); Ref.Zhur.Khim., 1980, 15O330.
167. BRD Appl.2503337 (1976); Ref.Zhur.Khim., 1977, 16O337.
168. US P.4237158 (1980).
169. US P.4105762 (1978).
170. US P.4085209 (1978).
171. US P.4143173 (1979).
172. BRD P.1951996 (1973).
173. US P.3632755 (1972).
174. French P.2063428 (1971).
175. US P.3705939 (1972).
176. Australian P.417616 (1971).
177. US P.3595870 (1971).
178. Japanese Appl.49-48433 (1974): Ref.Zhur.Khim., 1975, 20O350.
179. Japanese Appl.55-44800 (1980); Ref.Zhur.Khim., 1981, 15O307.
180. Japanese Appl.54-145216 (1979): Ref.Zhur.Khim., 1980, 21O324.
181. US P.3789122 (1974).
182. EPV 39788 (1982); Chem.Abs., 1982, **96**, 181340 [sic].
183. K.C.Jupta and P.A.Sengh, Pesticides, 1980, **14**(10), 35.
184. U.Thust and H.Wegert, Chem.Techn., 1977, **29**, 671.
185. D.Weisbrod, Toxicol.Anal.Probl.Loesungsmittelexpo, 1979 (publ.1980), 55; Chem.Abs., 1982, **96**, 80872.
186. US P.4177346 (1979).
187. B.A.Bovykin, S.S.Kukalenko, and S.I.Shestakova, "Tezisy Dokladov Nauchno-Tekhnicheskogo Soveshchaniya po Obsuzhdeniyu Aktual'nykh Napravlenii v Plane Poiska, Razrabotki i Primeneniya Khimicheskikh Sredstv Zashchita Rastenii" (Abstracts of Reports at the Scientific and Technical Conference on Current Trends in the Search, Development, and Applications of Chemical Plant Protecting Agents), Tallin, 1982, p.52.
188. S.S.Kukalenko, V.A.Udovenko, S.I.Shestakova, and E.I.Andreeva, "Tezisy Dokladov na Vsesoyuznoi Konferentsii po Khimicheskim Sredstvam Zashchity Rastenii" (Abstracts of Reports at the All-Union Conference on Chemical Plant Protecting Agents), Ufa, 1982, p.152.
189. N.M.Golyshin, in "Fungitsidy v Sel'skom Khozyaistve" (Fungicides in Agriculture), Izd.Kolos, Moscow, 1970, p.108.
190. A.M.Omel'chenko, B.A.Bovykin, S.S.Kukalenko, S.I.Shestakova, and A.V.Plakhotnik, Sel'skokhozyaistvennaya Biologiya, 1984, (5), 75.

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