

THE INFRARED SPECTROSCOPIC COMPARISON OF METAL
COMPLEXES OF IMIDAZOLE AND STRUCTURALLY RELATED COMPOUNDS

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INTRODUCTION

It has been established that the basic structure of the imidazole molecule is very important biologically. It has been included in the structure of many biologically important compounds, such as, histidine and histamine. Other heterocyclic nitrogen-containing compounds similar to imidazole have also proven to be biologically important. Their importance has been derived from the ability of the nitrogen atoms to complex with metal ions. (28)

Simple amines, polyamines, peptides, aminopolycarboxylic acids and a wide variety of heterocyclic nitrogen compounds have been studied in their reactions with various metal ions. In the past few years, a distinct change in emphasis has occurred in the research on coordination compounds by focusing on the quantitative measurement of the equilibria involved in complexation and chelation. Among the more commonly employed techniques used in the study of complexes have been absorption spectra measurements, optical rotation measurements, polarographic measurements, potentiometric titration data, transference studies, electromotive force measurements, conductance studies, and ion exchange studies. The greatest contributions to complex formation data and other thermodynamic values have been derived from potentiometric titration studies and from absorption spectra. (1,3,8,9,10,33,35,39,48,49,50)

However, by far the largest part of these investigations have been accomplished in solutions. Isolation of these complexes from solution has usually been ignored due to the difficulties involved in their preparation and analysis. Therefore, investigation of the solid state has, up to this

time, received only minor attention. That was the reason this research had been undertaken. It was thought by the author that further investigation in this field could not but help to eventually aid in the understanding of these compounds and their significance in various biological functions.

TABLE 1

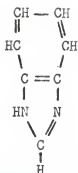
Chemical structures of ligands studied.



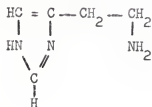
Imidazole



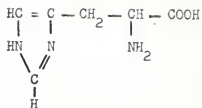
Pyrazole



Benzimidazole



Histamine



Histidine

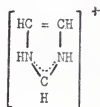
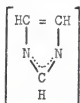
REVIEW OF LITERATURE

Imidazole

Imidazole is a five membered ring containing two nitrogens and three carbons. By convention (36), the secondary amine nitrogen atom has been designated as the "pyrrole" nitrogen while the tertiary amine nitrogen atom has been termed the "pyridine" nitrogen. Imidazole is considered to be a moderately strong Lewis base. The proton attached to the pyridine nitrogen of the protonated species has a pK_a value of 7.09 (28). The proton attached to the pyrrole nitrogen has a pK_a value of 14.52 (54).

It has been shown that the imidazole group in several larger biologically important molecules is capable of complexing very strongly with metal ions. Imidazole groups in bovine serum albumin, for example, have been shown to be the principal sites for metal interaction (52). Evidence has been given which indicates that the imidazole nucleus of dimethylbenzimidazole provided one of the five nitrogen atoms coordinated to Co (III) in vitamin B_{12} . It provided a site for similar interactions with hemoglobin, myoglobin, cytochrome C, and histidine (24).

The first investigation of imidazole by infrared spectra was undertaken by Otting (47). His study of imidazole spectra in both the solid state and in chloroform solution led him to postulate the structure of imidazole as best being represented by two ionic structures:



These structures both possess C_{2v} symmetry. Therefore, it may be assumed that the molecule would also exhibit C_{2v} symmetry.

Zimmerman investigated the infrared spectrum of imidazole in the solid state and in non-polar solvents (58). He concluded that imidazole existed in a highly associated form due to the amount of intermolecular hydrogen bridges between the pyrrole nitrogen of one imidazole molecule and the pyridine nitrogen of another.

More recently, X-ray studies by Lundberg (37) have also shown a high degree of intermolecular hydrogen bridge bonding between nitrogen atoms of adjacent molecules in solid imidazole. The N-H ---N distance was reported to be 2.7 Å.

Raman spectra have been reported for imidazole, imidazolium chloride, and the N-deuterated analogs in aqueous solution (22). Assignments were tentatively proposed for a few of the bands. A normal coordinate analysis was made for the imidazole molecule assuming it as a ten-body structure having C_{2v} symmetry (13). All modes of vibration were assigned as well as overtones and combination bands.

Metal-imidazole complexes in aqueous solution have been investigated extensively by using polarographic and various titrimetric techniques. Andrews and Romary (2) have determined the successive stability constants of Cd (II) complexes by polarography. Edsall and co-workers (19) have determined the successive formation constants for the Cu(II) and Zn(II) imidazole complexes from potentiometric titration work. From this work, they concluded that the maximum coordination number shown by Cu(II) and Zn(II) toward imidazole in solution was four. Id and co-workers (36) determined the formation constants for the Cd(II)-imidazole and the Cd(II)-1-methylimidazole

complexes from polarographic data. They concluded that the highest ordered complex obtained with either ligand was the 4 to 1 complex. These authors also observed that the formation constants of the imidazole and 1-methylimidazole complexes were nearly equal. They concluded, therefore, that, due to the fact that the pyrrole nitrogen was substituted in the latter complex, the bonding must have occurred through the pyridine nitrogen.

The successive formation constants of the Mn(II) and Co(II)-imidazole complexes have been determined by Martin and Edsall (38). White and co-workers (56) measured the magnetic moment of the Co(II)-imidazole complex in aqueous solution and concluded from the high spin of the complex that the bonding was predominantly ionic. The maximum coordination number for the Co(II)-imidazole complex was reported to be six. Li and co-workers (34) have determined the successive formation constants for the Ni(II)-imidazole complex by potentiometric and polarographic methods. Again the maximum coordination number was found to be six. The same investigators measured the magnetic moment of the hexacoordinated Ni(II)-imidazole complex and obtained a value of 3.24 BM. This was consistent with an octahedral configuration which contained two unpaired electrons.

The thermodynamic functions of the Cu(II), Ni(II), Zn(II), and Ag(I) complexes of imidazole have been determined by Bauman and Wang (5) using calorimetric techniques. Identical values were obtained for the heats of formation of the Ag(I) complexes of imidazole and 1-methylimidazole. Therefore, they, too, concluded that the pyridine nitrogen was responsible for the bonding which formed the complexes.

Bauman and Wang (5) have also investigated the infrared spectra of the solid imidazolato complexes of Ni(II), Cu(II), Zn(II), Cd(II), and Ag(I).

In these complexes, the ionization of the pyrrole hydrogen produced the anionic imidazole ring which served as the coordinating ligand. Unlike the monodentate imidazole ligand, the imidazolate anion was capable of coordination at both nitrogen positions. However, due to the proximity of the binding sites, the ligand could not form a bidentate complex. Instead, the sites were utilized to form imidazole bridges in a polymeric metal complex structure.

Histamine

Histamine, 4(or 5) - (2-aminoethyl) imidazole, is one of the many biologically important compounds found to contain the basic imidazole ring. The physiological action of the compound has been summarized by Sir Henry Dale (15). The resemblance between the effects of histamine and many of the effects caused by anaphylactic shock has been noted by Dale. Histamine has been known to be a stimulator of the plain muscle. Asthmatic reactions of the allergies are considered to be a result of the bronchiole-constrictive properties of histamine. Rashes and urticarial reactions of the allergies are believed to be caused by the capillary - dilatant action of histamine.

As a result of many isolated animal experiments with histamine, much speculation concerning the uncertainty about the mechanisms of histamine formation, release, and production of the biological response has been related to lack of understanding of the histamine responsive sites within the tissues.

To ascribe all allergic manifestations to the reaction of histamine producing a direct response has probably been an over-simplification of the mechanism. Histamine is now considered to be probably only one of the active agents which causes allergy. Another unidentified agent may also be involved. There has been so little information available concerned with the nature of the

histamine bonding sites that any information of a positive nature may prove to be of significant value. A study of the more simple reactions of histamine should eventually enable workers to better understand the more complex reactions involving histamine in the tissues of the body.

Certain generalizations have been made from a review on the activity of histamine as a function of its molecular structure (28). It may be noted from these generalizations that requirements which promoted highest biological activity also tend to promote the complexing ability of the molecule.

A. The presence of a basic side chain nitrogen has been shown to be essential. N-alkylation of the histamine primary amino group reduced activity in proportion to the size and number of the attached groups. For instance, N, N-dibenzylhistamine possessed no histaminic activity. Acylation or benzoylation of the side chain nitrogen also deprives the molecule of its normal biological activity.

Substitution of the primary amino hydrogens would also be expected to result in a negative effect upon the ability of the molecule to form a bidentate complex because such a complex would utilize the primary amino nitrogen.

B. The number of carbon atoms between the imidazole nucleus and the primary amino nitrogen was shown to be critical. The 2-aminoethyl side chain produced maximum activity when attached at the 4 (or 5) position of imidazole. Any variation from this number of carbons diminished the biological activity of the molecule.

When histamine forms a bidentate complex the two carbons on the side chain, the carbon from the imidazole ring, the two nitrogens, and the complexing metal can form a six-membered ring. This is considered most favorable for chelate stability. Therefore, any variation from the two carbon side

chain would probably diminish the complexing ability of the molecule.

C. The position at which the side chain is attached was also important. It had to be attached at the 4 (or 5) position of imidazole or its biological activity would be diminished. Both 1-(2-aminoethyl)-imidazole and 2-(2-aminoethyl)-imidazole are inactive. This requirement is also necessary for the formation of the six-membered ring upon complexation.

D. Ring substitution has been shown to reduce histaminic potency. Methylation of the imidazole ring at the 2-carbon caused the least decrease in activity. 1-methyl-4-(2-aminoethyl)-imidazole exhibits only slight activity while 1-methyl-5-(2-aminoethyl)-imidazole showed no activity at all.

E. Other aromatic nuclei have been used to replace that of imidazole (i.e. pyridine). However, activity depended upon the existence of a tertiary amine nitrogen as part of the aromatic system. The nuclei also had to be small and unsubstituted. For imidazole complexes, the tertiary amine nitrogen has been shown to be the one which was involved in complexation with the metal ion. Therefore, its existence in the histamine molecule would be expected to be crucial in order for the molecule to complex with metal ions. These structural restrictions upon histaminic activity suggested an enzyme-like specificity in the production of the histamine responses. The possession of active polar centers has been found to be characteristic of enzyme systems.

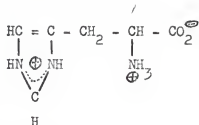
The activity of many enzyme systems has been shown to be dependent upon the presence of specific metal ions. Klotz and Loh Ming (30) confirmed the postulate that metal ions may serve as a bridge between proteins and small organic molecules. Mediation, by the binding of Hg(II), Cu(II), Ag(I), Ni(II), Au(II), Co(II), and Mn(II) ions has also been demonstrated. Mickel and Andrews (43, 44) studied histamine-metal complexes titrimetrically. They

suggested that the molecule was a bidentate ligand. The two binding sites were the tertiary nitrogen in the imidazole ring and the primary amine nitrogen on the side chain. The secondary amine nitrogen plays no part in the complexation of the ligand to a metal ion.

Very little work has been reported of histamine-metal complexes in the solid state.

Histidine

Histidine, an amino acid, is the precursor of histamine. Histamine was first synthesized by the decarboxylation of histidine. Histidine has also been very important from a biological point of view because it is one of the strongest coordinating ligands among the amino acids. X-ray data (16) have shown that histidine-hydrochloride exists in the solid state as a "zwitter" ion with the following structure:



The structure of histidine in aqueous solution has been found to be a function of pH. Its acid dissociation constants in water are 1.81, 6.11, and 9.20 for proton ionization from the carboxyl, imidazole, and amino groups, respectively (28). The histidine molecule contains an asymmetric carbon. Therefore, it is capable of exhibiting the optically active dextro and levo isometric forms.

The nujol mull spectrum of histidine-hydrochloride has been investigated in the region of 650 to 5000 cm^{-1} by Larsson (31). He made general assignments

for some of the bands appearing in the spectrum. The Raman spectra of histidine in aqueous solution as an anion and as both a doubly and singly charged cation has been investigated by Garfinkel and Edsall (22). They, too, have suggested general assignments based upon comparison with corresponding spectra for imidazole and 4-methylimidazole.

As in the case of imidazole, there has been a large amount of literature available concerning formation constants for histidine-metal complexes in solution. Li and co-workers (53) have determined the formation constants of the Cu(II) and Ni(II) complexes of histidine by pH titration and have assumed the bonding site of histidine to be the amino group and the pyridine nitrogen of the imidazole ring.

Doran and co-workers (17) have investigated the Cu(II) complex of histidine and concluded that the ligand probably functions as a tridentate ligand in the complex. Leberman and Rabin (32) have deduced from potentiometric work that histidine was coordinated as a tridentate ligand in the complexes of Co(II), Ni(II), and Zn(II). Earnshaw and Larkworthy (18) have proposed an octahedral structure for the solid Co(II)-histidine complex. They assumed that the histidine molecule behaved as a tridentate ligand. They based their argument on the magnetic moment of the bis-Co(II) histidine complex which was found to be 5.16 BM. This value agreed well with that expected for Co(II) octahedral complexes. Nortia (45) has concluded, on the basis of spectrophotometric and magnetic studies, that the solid bis-Ni(II)-histidine complex had an octahedral configuration with histidine acting as a tridentate ligand. The crystal structure of the bis-Zn(II)-histidine complex has been determined by Harding and Cole (26). Their work has indicated that Zn(II) is coordinated by two amino nitrogens and by two imidazole nitrogens.

with two carboxylate oxygens near enough to be considered loosely coordinated.

Weitzel (55) has reported the solid state IR spectrum of the bis-Zn(II) histidine complex. However, detailed investigation of the chelates, including general assignment of absorption bands has, as yet, not been undertaken.

McDonald and Phillips (40) have reported NMR investigation of the structure of the paramagnetic Co(II)-histidine complex in aqueous solution as a function of pH. From the observed NMR contact shifts, these workers were able to distinguish four Co(II)-histidine complexes. At pH values of less than 4 a weak 1:1 metal to ligand complex formed in which only the histidine carboxylate group was bonded to the metal ion. At pH values of 4 to 10 strong 1:1 and 1:2 metal to ligand complexes were formed in which the histidine behaved as a tridentate ligand. At pH values above 11 a tetrahedral 1:2 Co(II)-histidine complex was formed in which histidine was bound to Co(II)- through the amino group and an imidazole nitrogen.

Benzimidazole

Benzimidazole is a disubstituted imidazole. The 4 and 5 positions have been substituted by the fused benzene ring. The benzimidazoles have been found to be predominantly basic compounds due to the ability of the pyridine nitrogen to accept protons. The pK_a of benzimidazole has been found to be 5.5. This value is significantly lower than the pK_a of 7.1 for imidazole (28).

This compound is not of the biological significance of the previous ligands. Its importance here lies in its similarity to imidazole. In spite of its comparatively low basicity, metal complexes of the compound have been isolated by Goodgame and Cotton (24). These authors also reported the ultraviolet spectra and performed ligand field calculations for the complexes.

Pyrazole

Pyrazole is a structural isomer of imidazole. The difference in structure is the position of the two nitrogen atoms. They are adjacent in the purazole molecule, while they are separated by a carbon atom in the imidazole ring. This has the effect of considerably lowering the dipole moment and dissociation constant for pyrazole (28).

TABLE 2

The dipole moment and pK_a of imidazole and pyrazole.

	Dipole Moment	pK_a
Pyrazole	1.57	2.53
Imidazole	3.84	7.1

There has been little literature data concerning pyrazole as a ligand either in solution or in the solid state.

EXPERIMENTAL

Definition of Terms and Symbols

Throughout the rest of the text certain terms, symbols and abbreviations will be frequently used. In order to avoid possible confusion they have been collected and listed as follows:

Im - imidazole

Py - pyrazole

Bz - benzimidazole

Hm - histamine

Hd - histidine

ligand - A molecule or ion which is bound in a complex to a central ion.

complex - The product which results when a metal ion combines with an electron donor.

chelate - The complex which is formed by the combination of a metal ion with a ligand having two or more electron pair donating groups. This produces a ring structure.

bidentate - A ligand which contributes two electron pair donating groups when combining with a metal ion to produce a chelate.

The following abbreviations are found in tables containing infrared spectra:

VS - very strong

S - strong

M - medium

W - weak

br - broad

Sh - shoulder

Instruments

All infrared spectra were obtained using a Perkin-Elmer 457 Model Spectrophotometer. This instrument was equipped to permit scale expansion if desired and provided three scanning speeds. With this instrument, it was possible to scan the region from 4000 cm^{-1} to 250 cm^{-1} . Cesium bromide optics were used for the 600 cm^{-1} to 250 cm^{-1} region. Some of the infrared spectra were obtained as nujol mulls pressed between sodium chloride plates. However, most of the spectra were obtained by means of pressed potassium bromide pellets. These pellets were prepared by means of a Pellet Press and Holder which was purchased from Wilks Scientific Corporation.

Glove Bags were purchased from Instruments for Research and Industry. They were utilized in the preparation and handling of some of the complexes which proved to be either water or oxygen sensitive.

The polarograms determined for analysis purposes were obtained by the use of a Sargent Polarograph Model XXI.

Materials

Imidazole was purchased from K & K Laboratories, Plainview, New York. It was then purified by vacuum sublimation and recrystallization from benzene. In the purified form the imidazole existed as long, needle-like, white crystals. It had a melting point of 90°C . This was identical with the literature value.

Pyrazole was purchased from Eastman Organic Chemicals, Rochester, New York. It was purified by vacuum sublimation. The white crystals which were collected had a melting point of 70° . This was identical with the literature value.

Benzimidazole was purchased from Eastman Organic Chemicals. The white

crystals had a melting point of 170° . No further purification was attempted.

Histidine was purchased from Nutritional Biochemicals Corporation. The white, finely divided crystals melted at 287° . No further purification was necessary.

Histamine free base was purchased from Eastman Organic Chemicals. The crystals were light yellow in color. The melting point was 83° . It was used without further purification.

All metal (II) perchlorate hydrated salts were purchased from G. Frederick Smith Chemical Company, Columbus, Ohio.

Deuterium oxide was purchased from Merck and Company Inc., St. Louis, Mo. The isotopic purity of this compound was guaranteed to be at least 99.7% by the distributor.

Procedures

N-deuterated imidazole was prepared by dissolving one gram of imidazole in 10 ml. of D_2O . The solution was then evaporated to dryness in a vacuum over P_2O_5 . This procedure was repeated twice more to assure adequate exchange in the 1-position of imidazole. Exactly the same procedure was employed to prepare N-deuterated pyrazole and N-deuterated benzimidazole.

An investigation of the literature has revealed that a number of methods have been devised to prepare metal complexes of imidazole. Carlson (8) prepared the solid imidazole complexes of Cu(II), Ni(II), Mn(II), Fe(II), and Co(II) by dissolving the chloride salt of the metal ion in H_2O and reducing the pH of the solution to approximately three with HCl. An excess of imidazole was added and the complex immediately precipitated out of solution. The crystals were then filtered, washed and dried under vacuum without further purification.

Bauman and Wang(5), however, preferred to prepare the complex by adding NaOH to a solution containing the metal ion and an excess of imidazole. The precipitate which formed was then filtered and dried under vacuum. Other methods have been suggested (7), but have all been similar to the two aforementioned methods. If the preparation involved a base, the product was generally polymeric in nature as was Bauman's. However, if the preparation utilized a neutral or acidic media, monomeric complexes resulted. Therefore, a procedure was devised in which slightly acid solutions were used.

The mole ratio of metal to imidazole was one to six. The metal perchlorate was dissolved in a 50% ethanol - 50% water mixture at about 80 degrees C. The imidazole was also dissolved in a similar mixture of hot ethanol-water. The solution containing the ligand was then neutralized by dilute HClO_4 . The two hot, concentrated solutions were combined and allowed to cool. The crystals which were formed were collected and recrystallized from ethanol. The purified crystals were filtered, dried, and kept in a vacuum desiccator at 5°. After this research had begun other workers have prepared similar complexes by much the same method, (20, 21, 25).

The metal complexes with the other ligands were prepared by the same method. The mole ratio of metal ion to pyrazole was one to six. The mole ratio of metal ion to benzimidazole was one to six. The mole ratio of metal ion to histidine was one to three. The mole ratio of metal ion to histamine was one to three.

All the Cd(II) complexes formed white, needle-like crystals which seemed stable to air and water. All the Zn(II) complexes were also white and remained stable in air. The Cu(II) complexes with imidazole and pyrazole were blue in color. The Cu(II) complex with benzimidazole was violet in color. The

histidine and histamine complexes of Cu(II) were a deep blue. All the Cu(II) complexes were stable to air and water. The Ni(II) complex with benzimidazole was yellow. The Ni(II) complexes with histamine and histidine were violet. All the Ni(II) complexes were air and water stable. The Co(II) complexes with imidazole and histidine were pink in color. The Co(II) complex with benzimidazole was blue. The Co(II) complexes with pyrazole and histamine were light orange. All the Co(II) complexes were air and water stable.

Fe(II) and Mn(II) formed white complexes with all five ligands. However, they presented a problem in their preparation and handling because they were all easily oxidized and therefore air sensitive. They were handled as much as possible in a nitrogen atmosphere. The Cr(II) ion did not form stable complexes with imidazole and pyrazole. The Cr(II) complexes with benzimidazole and histamine were white. The Cr(II) complex with histidine was pink in color. These complexes were hygroscopic as well as air sensitive. They, too, were handled in an atmosphere of nitrogen.

The analysis of all complexes was determined by polarography (2, 41). It was first determined that the complex could be dissociated completely so that an analysis for the metal ion could be undertaken. It was found that all the complexes dissociated completely in an acid solution. However, an adequate polarogram could not be obtained from the acid media. KClO_4 was then tried as the supporting electrolyte. It served well in that capacity. A procedure was then devised for the analysis of metal ions in the complexes using KClO_4 as the supporting electrolyte.

Standard solutions of the metal ion from the perchlorate salt were made up in 0.1 N KClO_4 . Approximately 0.1 gram of the complex was weighed accurately and dissolved in 20 ml. of 0.25 N HClO_4 . After the complex was dissolved,

it was neutralized by 0.25 N KOH. Two drops of acid were then added to insure slight acidity and the solution was diluted to 50 ml. This procedure resulted in the same concentration of KClO_4 in the sample solution as in the standard solutions. The polarograms of the standards and samples were then determined. From the polarograms of the standards, a graph of diffusion current versus concentration of the metal ion was prepared. By means of the graph, the diffusion currents from the polarograms of the samples were converted to concentration. From this value, a per cent of metal in the sample was calculated. Theoretical percentages for the metal were then calculated for all possible complexes. The percentage from the sample was then compared with the theoretical percentages and the coordination number for the metal in that particular complex was thereby determined.

RESULTS AND DISCUSSION

Analysis of Complexes

The results of the polarographic analysis of the complexes to determine coordination number are shown in Table 3.

Table 3

Analysis results for the metal complexes .

<u>Compound</u>	<u>Theoretical % of metal</u>	<u>% found</u>
$\text{Cd}(\text{Im})_6(\text{ClO}_4)_2$	15.58	15.53
$\text{Cd}(\text{Py})_6(\text{ClO}_4)_2$	15.58	15.44
$\text{Cd}(\text{Bz})_4(\text{ClO}_4)_2$	14.3	14.0
$\text{Cd}(\text{Hd})_2(\text{ClO}_4)_2$	18.03	17.1
$\text{Cd}(\text{Hm})_2(\text{ClO}_4)_2$	21.01	20.8
$\text{Zn}(\text{Im})_6(\text{ClO}_4)_2$	9.67	9.32
$\text{Zn}(\text{Py})_6(\text{ClO}_4)_2$	9.67	9.17
$\text{Zn}(\text{Bz})_4(\text{ClO}_4)_2$	8.83	8.90
$\text{Zn}(\text{Hd})_2(\text{ClO}_4)_2$	11.3	10.7
$\text{Zn}(\text{Hm})_2(\text{ClO}_4)_2$	13.4	13.3
$\text{Cu}(\text{Im})_4(\text{ClO}_4)_2$	11.88	11.7
$\text{Cu}(\text{Py})_6(\text{ClO}_4)_2$	9.47	9.72
$\text{Cu}(\text{Bz})_4(\text{ClO}_4)_2$	8.65	8.05
$\text{Cu}(\text{Hd})_2(\text{ClO}_4)_2$	11.1	10.8
$\text{Cu}(\text{Hm})_2(\text{ClO}_4)_2$	13.1	12.6
$\text{Ni}(\text{Im})_6(\text{ClO}_4)_2$	8.82	8.62

Table 3 -- continued

<u>Compound</u>	<u>Theoretical % of metal</u>	<u>% found</u>
Ni(Py) ₆ (ClO ₄) ₂	8.82	8.83
Ni(Bz) ₄ (ClO ₄) ₂	8.04	7.9
Ni(Hd) ₂ (ClO ₄) ₂	10.34	10.0
Ni(Hm) ₂ (ClO ₄) ₂	12.24	11.6
Co(Im) ₆ (ClO ₄) ₂	8.85	8.6
Co(Py) ₆ (ClO ₄) ₂	8.85	8.4
Co(Bz) ₄ (ClO ₄)	8.07	7.7
Co(Hd) ₂ (ClO ₄) ₂	10.37	10.6
Co(Hm) ₂ (ClO ₄) ₂	12.27	11.9
Fe(Im) ₆ (ClO ₄) ₂	8.43	
Fe(Py) ₆ (ClO ₄) ₂	8.43	8.1
Fe(Bz) ₄ (ClO ₄) ₂	7.68	7.76
Fe(Hd) ₂ (ClO ₄) ₂	9.89	10.04
Fe(Hm) ₂ (ClO ₄) ₂	11.71	
Mn(Im) ₄ (ClO ₄) ₂	10.45	9.7
Mn(Py) ₄ (ClO ₄) ₂	10.45	9.9
Mn(Bz) ₄ (ClO ₄) ₂	7.57	7.7
Mn(Hd) ₂ (ClO ₄) ₂	9.74	9.27
Mn(Hm) ₂ (ClO ₄) ₂	11.54	
Cr(Bz) ₄ (ClO ₄) ₂	7.19	
Cr(Hd) ₂ (ClO ₄) ₂	12.81	12.53
Cr(Hm) ₂ (ClO ₄) ₂	10.99	10.2

Imidazole Complexes

The infrared spectrum of imidazole has been obtained and assigned by Cordes and Walter (13). The work done by the author was initiated by an

infrared study of the imidazole free ligand in the solid state. The spectra which were obtained compared quite well with that of Cordes. Assignments of the principle bands were made on the basis of Cordes work. The spectrum and assignments are listed in Table 4.

The effect of coordination upon the ligand has been of prime interest in this work. To determine this effect, one must have first determined which infrared bands were the most sensitive to coordination. Other workers (4, 11, 46) have found that metal-nitrogen absorption bands served well in that capacity. Harkins and co-workers (27) have indicated that the nitrogen-hydrogen band can also be sensitive to small electron shifts in a ligand which occur upon coordination.

Corsin and co-workers (14) helped assign the spectra of pyridine complexes by comparing the spectra of the free ligand to that of the deuterated analog. A similar project was undertaken in this work to verify the spectral assignments, especially those for N-H modes. The amine hydrogen of imidazole was deuterated and the spectrum determined for the product. This spectrum has been shown in Table 4 and Plate 1. Splitting occurred for several imidazole peaks, but the appearance of three new peaks was particularly significant. These were the peaks at 1349 cm^{-1} , 955 cm^{-1} , and 557 cm^{-1} . They were attributed to the N-D bending mode. This helped establish the accuracy of the original assignments because the bands at 1535 cm^{-1} , 1145 cm^{-1} , and 621 cm^{-1} would be expected to be shifted downfield as was observed.

When the imidazole ligand was coordinated by a metal ion a considerable shift of electrons within the ligand occurred. This was reflected by the frequency shifts in the infrared spectra. Coordination induced an electron flow into the ring from each of the ring protons. Therefore, absorption bands

TABLE 4

Infrared frequencies (cm^{-1}) of imidazole and d-imidazole.

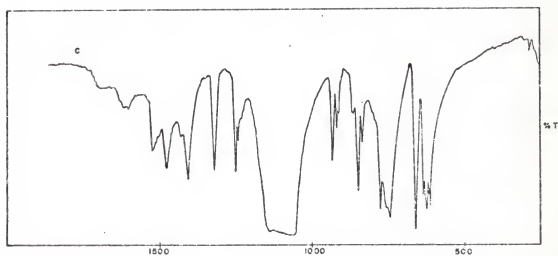
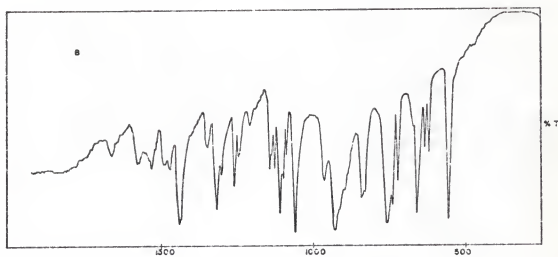
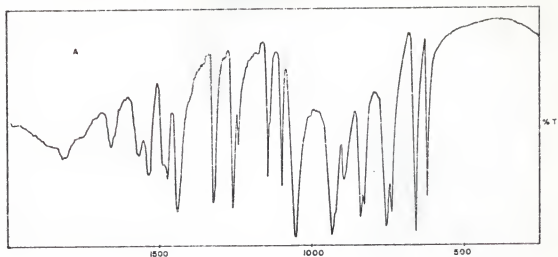
<u>Imidazole</u>	<u>d-Imidazole</u>	<u>Assignments</u>
1815 m *		overtone
1662 s	1664 m	overtone
	1579 m	
1569 s		Ring stretch
1535 s	1533 m	N-H band + C = C stretch
	1490 m	
1476 s	1472 m	Ring stretch + N-H bend
1440 s	1441 s	Ring stretch + N-H bend
	1349 m	N-D bend
1323 s	1318 s	C-H bend
	1303 m	C-H bend
1260 s	1261 s	Ring breathe
1242 m	1248 m	combination
	1210 w	
1145 s	1144 m	Ring stretch + N-H bend
	1138 sh	
	1128 m	
	1112 s	
1100 s	1099 s	C-H bend
	1089 m	
1054 vs	1059 s	C-H bend
	965 m	N-D bend
934 vs	930 s	C-H bend
893 m		Ring bend
841 s	841 s	
830 m	831 s	
756 s	758 s	C-H bend out of plane
739 s	742 s	C-H bend out of plane
	723 s	
660 s	662 s	Torsion
	635 m	
621 s	623 m	N-H bend out of plane
	557 s	N-D bend out of plane

* See explanation - page 14.

EXPLANATION OF PLATE I

- A. Infrared Spectrum of Imidazole.
- B. Infrared Spectrum of N-deuterated Imidazole.
- C. Infrared Spectrum of $\text{Fe}(\text{Im})_6(\text{ClO}_4)_2$.

PLATE I



assigned to various ring vibrations underwent the largest shifts.

An increase in the ring frequencies upon coordination was expected for two reasons. First, a simple inductive effect was expected because the bonding occurred with a positive metal ion. Second, a $d_{\pi}-p_{\pi}$ interaction may have occurred to provide a mechanism by which the metal ion may dissipate excess negative charge to prevent a negative charge accumulation on itself.

In both cases, the stronger coordinating metal would be expected to produce a higher electron density in the ring system of the ligand. Therefore, the energy of the ring bonds and the frequency of the infrared bands assigned to ring vibrations served as a means to measure the extent of the metal - imidazole interaction. The stronger metal - imidazole bond was expected to produce a higher ring frequency.

The infrared spectra of all the metal - imidazole complexes were listed in Table 5. All the spectra were quite similar, but trends which reflected the degree of interaction or bond strength between the metal and imidazole were apparent. The bands at about 1530 cm^{-1} , 1480 cm^{-1} , 1410 cm^{-1} , and 1251 cm^{-1} all reflected the amount of electron density in the ring system. The ring stretching frequencies increased in the following order: $\text{Cd(II)} \sim \text{Fe(II)} < \text{Co(II)} < \text{Mn(II)} < \text{Ni(II)} < \text{Zn(II)} < \text{Cu(II)}$. The bands at about 250 cm^{-1} have been assigned to the metal-nitrogen bond vibration. The trend exhibited by this band placed Mn(II) equivalent with Cd(II) and Fe(II). This was in good agreement with the Irving-Williams order of stability of transition metal complexes with nitrogen containing ligands. The Mn(II) had been coordinated to only four imidazole ligands. Therefore, the inductive effect caused by the positive Mn(II) was slightly larger than would have occurred with six ligands attached to the metal ion. This increased inductive effect

TABLE 5

Infrared spectra of metal-imidazole complexations in cm^{-1} .

$\text{Mn}(\text{Im})_4$	$\text{Fe}(\text{Im})_6$	$\text{Co}(\text{Im})_6$	$\text{Ni}(\text{Im})_6$	$\text{Cu}(\text{Im})_4$	$\text{Zn}(\text{Im})_6$	$\text{Ca}(\text{Im})_6$
1527 s	1524 s	1524 s	1528 s	1529 m	1527 s	1522 s
1481 s	1478 s	1481 s	1481 s	1485 m	1484 s	1490 s
1408 s	1406 s	1409 s	1409 s	1422 s	1420 m	1409 s
1321 s	1320 s	1321 s	1322 s	1325 s	1325 s	1323 s
1251 s	1251 s	1252 s	1253 s	1258 s	1260 s	1252 s
1244 w	1244 m	1243 s	1247 m	1238 sh		1241 m
933 s	933 s	935 s	938 s	941 s	939 s	933 s
919 s	919 w	920 m	920 s	919 m	920 m	915 s
848 s	850 s	850 s	850 s	850 s	850 s	854 s
833 m	835 s	835 m	835 s	824 s	831 br	
776 s	776 s	778 s	778 s	777 s	765 vs	758 s
744 s	745 s	746 s	745 s	747 s	745 s	745 s
660 vs	661 s	662 s	665 s	660 vs	656 s	658 s
624 s	626 s	622 m	626 s	620 s	625 s	625 s
250 m	250 m	260 m	266 m	285 s	273 m	238 m

was reflected in the ring frequencies, but did not seem to be quite as large a factor in determining the metal - nitrogen frequencies. Therefore, if ring frequencies had been used to determine the order of stability $Mn(II)$ would have been misplaced. The metal - nitrogen frequencies proved valuable in resolving the question.

Pyrazole Complexes

Some work has been done on the infrared spectrum of the pyrazole ligand in the solid state (57). Although the work was by no means conclusive, it was used as the basis from which assignments of the pyrazole spectrum were made. As with imidazole, assignments were verified by comparing the spectra of solid pyrazole and the nitrogen-deuterated analog. These spectra are shown in Table 6 and Plate II. Again, as with imidazole, a large amount of splitting of the original pyrazole vibrational bands was observed. However, only one band in the spectrum of the deuterated pyrazole was considered to be due to a nitrogen-deuterium bond. This band was observed at 969 cm^{-1} . This substantiated the assignment of the 1148 cm^{-1} and 1134 cm^{-1} bands in the spectrum of the free pyrazole ligand to a mode of vibration due to the nitrogen-hydrogen bond. The shift observed was similar to that observed in the imidazole and deuterated imidazole spectra.

The splitting of the higher vibrational frequencies of 1460 cm^{-1} , 1391 cm^{-1} , and 1353 cm^{-1} upon deuteration provided additional evidence to substantiate the assignments. When the amino hydrogen was replaced by a deuterium the symmetry of the ring was decreased. The expected result would be that the vibrational bands due to ring stretching would be split.

The complexes of pyrazole, as well as the complexes of all the other ligands, were prepared from metal perchlorate salts. The perchlorate anion

TABLE 6

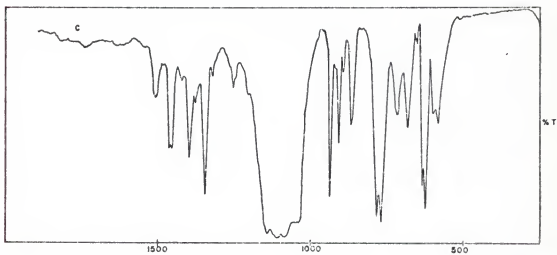
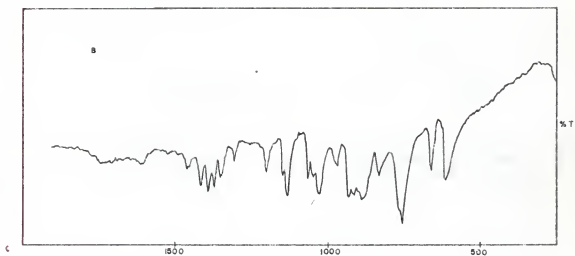
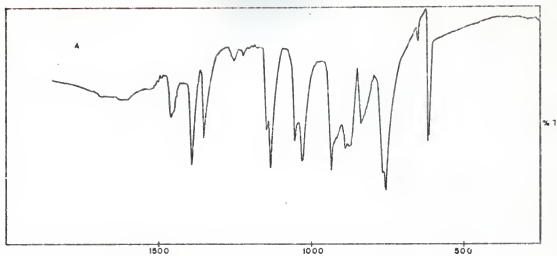
Infrared frequencies (cm^{-1}) of pyrazole and d-pyrazole.

<u>Pyrazole</u>	<u>d-Pyrazole</u>	<u>Assignments</u>
1460 s	1463 m	ring stretch
	1455 m	
	1417 s	
1391 s	1392 s	ring stretch
	1372 s	ring stretch
1353 s	1354 s	
	1349 s	
	1307 m	C-H bend + ring
1254 m		
1225 w		
	1201 s	ring stretch + N-H bend
1148 s	1148 s	
1134 s	1133 s	
	1065 s	C-H bend
1052 s	1049 m	
1031 s	1029 s	
	969 m	N-D bend
934 s	931 s	ring bend in plane
	913 s	
	890 s	
890 m		C-H bend out of plane
875 m		
837 s	832 s	
757 s	756 s	ring bend out of plane
652 w	660 s	
618 s	613 s	

EXPLANATION OF PLATE II

- A. Infrared Spectrum of Pyrazole.
- B. Infrared Spectrum of N-deuterated pyrazole.
- C. Infrared Spectrum of $\text{Mn(Py)}_4(\text{ClO}_4)_2$.

PLATE II



was, therefore, present in all of the metal complexes. This anion also contributed its own vibrational bands to the spectra produced by the metal complexes. These bands occurred at 626 cm^{-1} , 940 cm^{-1} , and in a broad area from about 1000 cm^{-1} to about 1200 cm^{-1} . These bands interfered very little with the bands of interest in the imidazole complexes. However, such was not the case with the pyrazole complexes. The two bands which contained nitrogen-hydrogen bending modes were completely obscured by the broad perchlorate band.

However, bands of higher frequencies were found to be quite useful in determining electron density shifts in the ligand upon coordination. The three bands observed were at about 1460 cm^{-1} , 1400 cm^{-1} , and 1350 cm^{-1} . The first and third of these bands were generally lowered with respect to the frequency of the same band in the spectrum of the free ligand. The second band was raised with respect to its position in the free ligand spectrum. These bands were shown with the spectra of the metal-pyrazole complexes in Table 7.

* Imidazole and pyrazole proved to be quite similar in their electron shifts upon coordination with a metal cation. There was a general withdrawal of electrons from bonds attached to the ring. This was due simply to the attraction from the positive ion. The electrons were withdrawn through the ring for the same reason. The point to which the electrons were attracted was the bond between the nitrogen and the metal. Since this occurred with each ligand, the result was that the metal ion had attracted more negative charge than it could tolerate by the principle of electroneutrality. Therefore, the metal ion utilized a $d_{\pi} - p_{\pi}$ mechanism to place excess negative charge back on the ligand. This mechanism is known as "back-bonding". It places electron density in the pi bonding system of the ring. Hence, the

TABLE 7

Infrared spectra of metal-pyrazole complex cations in cm^{-1} .

Mn(Py)_4^{++}	Fe(Py)_4^{++}	Co(Py)_6^{++}	Ni(Py)_6^{++}	Cu(PyP)_6^{++}	Zn(Py)_6^{++}	Cd(Py)_6^{++}
1456 s	1454 s	1460 s	1457 s	1464 s	1460 s	1461 s
1398 s	1398 s	1402 s	1401 s	1401 s	1400 s	1398 s
1348 s	1345 s	1350 s	1349 s	1352 s	1350 s	1350 s
1256 m	1255 w	1260 m	1259 m	1253 m	1259 m	1255 s
1041 s	1040 s	1045 s	1046 s	1049 s	1042 s	1040 s
940 s	939 s	942 s	941 s	943 s	940 s	938 s
912 s	909 s	912 s	911 s	911 s	910 s	909 s
897 m	895 w	890 m	894 m	896 m	898 w	892 m
871 s	860 m	863 m	869 m	865 s	861 m	861 m
						858 m
786 s	784 s	787 s	782 s	791 s	785 s	783 s
773 s	771 s	774 s	770 s	776 s	772 s	769 s
720 s	720 m	722 s	725 m		725 m	725 s
684 s	684 s	690 s	685 s	697 s	684 s	679 s
639 s	637 s	639 s	637 s	637 s	636 s	636 s
628 s	625 s	628 s	626 s	627 s	626 s	626 s
602 s	600 s	603 m	600 m	612 s	600 m	599 s
585 s	588 s	589 s	593 s	593 s	589 s	581 s

increase of the ring frequencies was actually a reflection of the "back-bonding" process.

Each of the frequencies is determined by the vibrational modes of a combination of sigma and pi bonds within the ring. The sigma bonds experience a general withdrawal of electrons while the pi bonds gain electron density. Therefore, the bands which were shifted to a lower frequency were due to a combination of vibrational modes due primarily to sigma bonds. The band which shifted to a higher frequency was primarily due to the pi bonds in the ring.

The ring frequencies also provided a reasonable measure of the ability of the metal ion to coordinate with the ligand. However, some of the bands in the region between 600 cm^{-1} and 250 cm^{-1} were also useful. The pyrazole complexes all contained a band in the region of 590 cm^{-1} . This band exhibited a trend which again compared favorably with the Irving-Williams order of stability. The same trend determined on the basis of ring frequencies would have placed Co(II) higher than Ni(II). The greater inductive effect of Mn(II) on the ligand due to its lower coordination number was again taken into consideration as with the Mn(II)-imidazole complex.

Benzimidazole Complexes

Benzimidazole has been used to form stable tetrahedral complexes (24, 42). However, very little work has been published concerning the assignment of the infrared spectrum of solid benzimidazole. The spectrum is considerably more complex than the spectrum of solid imidazole. This was expected due to the fact that the benzimidazole spectrum contained absorption bands from the fused benzene ring as well as the principle absorption bands due to the imidazole ring. Therefore, assignment of all the absorption bands in the spectrum was not attempted. Interest was centered only on absorption bands

produced by the imidazole ring. The location of those bands was facilitated by deuteration of the amine hydrogen on benzimidazole and comparison of the infrared spectra of benzimidazole and the nitrogen-deuterated analog. These spectra are shown in Table 8 and Plate III. It was found that deuteration produced a downfield shift for one band and a considerable amount of splitting of other bands found in the benzimidazole spectrum. Using this data, it was possible to deduce which absorption bands had been produced by the imidazole ring.

The band at 1132 cm^{-1} was shifted to 955 cm^{-1} . The band at 1451 cm^{-1} was split and shifted slightly downfield. The bands at 1270 cm^{-1} and 1241 cm^{-1} were also split upon deuteration. Therefore, the bands at 1451 cm^{-1} , 1401 cm^{-1} , 2170 cm^{-1} , and 1241 cm^{-1} were expected to be dependent upon the imidazole ring vibration. The spectra produced by the benzimidazole metal complexes indicated this was true. The spectra are shown in Table 8. The two higher bands, 1451 cm^{-1} and 1401 cm^{-1} , experienced a shift to a higher frequency in the spectra of the metal complex. Therefore, the two bands resulted primarily from vibrations due to bonds related to the pi bonding system within the imidazole ring. The two lower bands experienced a shift to a lower frequency. This indicated that the bands were produced from vibrational modes consisting of bonds in or near the imidazole ring, but primarily not concerned with the pi bonding in the ring.

The frequency shifts found for the benzimidazole complexes were generally smaller than the shifts found in the spectra of the imidazole and pyrazole complexes. This was explained by the presence of the fused benzene ring on the ligand. The pi system from the benzene ring and that from the imidazole ring interacted. The benzene ring was then able to serve as an electron

reservoir which could easily accept or donate electron density to the pi system of the imidazole ring. Electronic changes in the imidazole ring due to complexation would be diminished due to that mechanism.

TABLE 8

Infrared spectra of benzimidazole and d-benzimidazole in cm^{-1} .

<u>Benzimidazole</u>	<u>d-Benzimidazole</u>
1764 s	1761 m
1614 m	
1596 w	
1582 s	1582 s
1490 sh	1492 w
1472 s	1471 s
1451 s	1447 s
	1425 s
1401 vs	1402 s
1360 s	1358 s
1341 m	1338 s
	1323 s
1296 s	1298 s
	1280 s
1270 s	1270 s
	1259 s
1241 s	1246 s
	1234 s
	1219 s
1199 s	1191 w

Table 8 - continued

Benzimidazoled-benzimidazole

1184 sh	1175 w
1158 m	1158 m
1132 s	
1111 m	1110 s
1001 s	1002 sh
	995 s
957 s	949 s
931 m	920 sh
895 sh	
886 s	887 s
846 m	845 w
769 s	769 s
	756 sh
750 s	749 s
744 s	741 s
634 s	
627 s	628 s
618 s	613 s
	584 s
578 m	555 m
542 m	539 m
422 s	421 s
419 s	412 s
	405 s
270 m	268 m

EXPLANATION OF PLATE III

- A. Infrared Spectrum of Benzimidazole.
- B. Infrared Spectrum of N-deuterated Benzimidazole.
- C. Infrared Spectrum of $\text{Cd}(\text{Bz})_4(\text{ClO}_4)_2$.

PLATE III

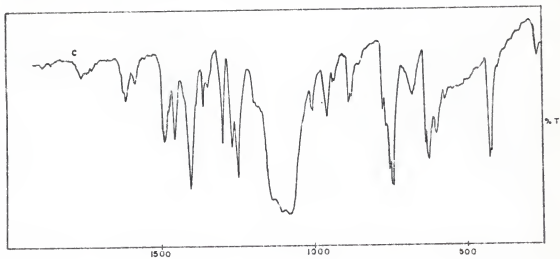
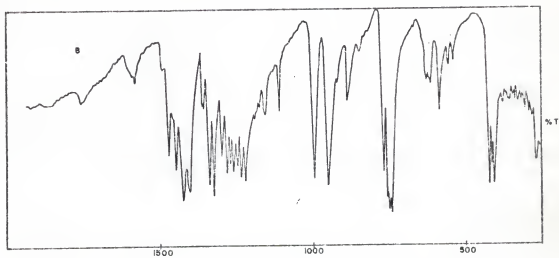
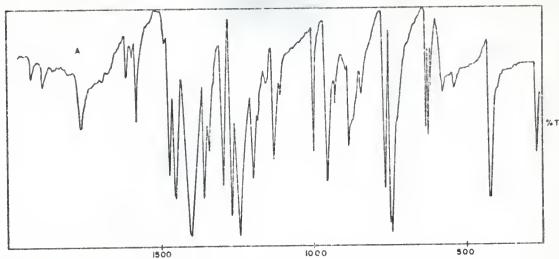


TABLE 9

Infrared spectra of metal-benzimidazole complex cations in cm^{-1} .

$\text{Cr}(\text{Bz})_4^{++}$	$\text{Mn}(\text{Bz})_4^{++}$	$\text{Fe}(\text{Bz})_4^{++}$	$\text{Co}(\text{Bz})_4^{++}$	$\text{Ni}(\text{Bz})_4^{++}$	$\text{Cu}(\text{Bz})_4^{++}$	$\text{Zn}(\text{Bz})_4^{++}$	$\text{Cd}(\text{Bz})_4^{++}$
1611 m	1618 m	1614 s		1612 s	1618 m	1613 s	1618 s
1584 w	1583 m	1586 w	1594 s	1593 s	1593 s	1595 s	1583 m
1478 s	1489 s	1490 s	1490 s	1490 s	1491 s	1492 s	1490 s
1449 s	1452 s	1450 s	1450-60br	1456 s	1463 s	1452 m	1457 s
1409 s	1402 vs	1402 s	1403 s	1405 s	1410 s	1406 s	1404 s
1360 m	1361 m	1362 m	1360 sh	1361 m	1362 sh	1361 sh	1362 m
1345 m	1340 sh	1347 w	1343 m	1349 m	1349 m	1346 m	1349 sh
1298 s	1298 s	1298 s	1294 s	1304 s	1203 s	1298 s	1300 s
1261 sh	1264 s	1265 s	1268 s	1270 s	1269 s	1270 s	1269 s
1240 s	1243 s	1239 s	1234 s	1245 s	1251 s	1242 s	1244 s
1005 s	1009 m	1004 m	1003 m	1009 s	1010 m	1004 s	1002 m
949 s	954 s	949 s	972 m	458 s	976 s	973 s	957 m
929 sh	930 m		928 m	930 m	931 s	927 m	933 w
881 w	884 s	873 m	883 m	887 s	888 m	885 m	886 m
768 s	773 s	781 m	771 s	776 s	775 s	773 s	773 m
757 sh	765 s	767 s	761 w	762 m	763 s		751 s
742 vs	740 vs	741 vs	740 vs	741 vs	737 vs	740 vs	740 s
624 w	625 s	625 s	620 s	626 s	623 sh	620 s	625 s
540 m	540 w	540 m	551 m	550 m	550 m	552 m	571 w
421 vs	423 vs	421 vs	423 vs	425 s	429 s	429 s	424 s
269 m	279 m			268 w	261 s	280 s	270 m

reservoir which could easily accept or donate electron density to the pi system of the imidazole ring. Electronic changes in the imidazole ring due to complexation would be diminished due to that mechanism.

The benzimidazole ligand itself contained absorption bands in the region 500 cm^{-1} to 250 cm^{-1} . These bands also occurred in the spectra for the metal complexes thereby obscuring any absorption bands due to a metal-nitrogen bond which may have been present. However, the trend established by the ring absorption bands compared favorably with the Irving-Williams order of stability for transition metal ions.

Histidine Complexes

Little previous work has been undertaken to establish assignments for the infrared spectrum of histidine free base. Deuteration of this ligand would have been of little value due to the fact that the amine protons and the acid proton would also undergo exchange. This would have produced a very complicated spectrum which would have been of little aid in interpreting the histidine spectrum.

Intra-molecular bonding obscured a large portion of the spectrum of the free ligand from 1360 cm^{-1} to 1650 cm^{-1} . Therefore, the absorption bands in the spectra of the metal-histidine complexes which were due to imidazole ring vibrations were determined by comparison with the spectra of the metal complexes of the previously discussed ligands. Absorption bands at about 1370 cm^{-1} and 1260 cm^{-1} were assigned to vibrational modes of the imidazole ring contained in the histidine molecule. The band at about 290 cm^{-1} was assigned to the metal-nitrogen bond. The spectra are shown on Table 10 and Plate IV. The trends exhibited by these bands are again consistent with the Irving-Williams order of stability.

TABLE 10

Infrared spectra of histidine free base
and metal-histidine complex cations in cm^{-1} .

Hd	Cr(Hd)_2^{++}	Mn(Hd)_2^{++}	Fe(Hd)_2^{++}	Co(Hd)_2^{++}	Ni(Hd)_2^{++}	Cu(Hd)_2^{++}	Zn(Hd)_2^{++}	Cd(Hd)_2^{++}
	1569 m	1574 m	1571 s		1578 s		1576 m	1570 m
	1487 s	1482 m	1486 s	1496 m	1481 s			1487 s
		1429 m	1428 m	1430 s	1429 s	1430 m	1429 m	1428 m
1403 s	1402 s	1404 s	1400 m	1394 s	1385 s	1403 s	1405 s	
1363 w	1365 w	1364 w	1364 s	1384 s	1385 s	1363 w		
1336 s	1332 s	1335 s	1333 s	1345 m	1331 s	1345 m	1335 s	1331 s
	1282 m	1282 m	1282 s	1299 s	1281 w	1302 m	1280 m	1282 m
1248 s	1258 s	1259 w	1259 m	1267 s	1266 m	1268 m	1258 w	1258 s
1219 m	1231 s	1230 s	1232 m		1221 w		1230 m	1229 w
1167 m								
1141 w								
1110 s								
10835 s								
1961 s	987 w		985 w	990 m	988 w	984 m		
963 s	959 m		959 s		958 m		957 w	958 w
917 s	940 w	940 m	939 m	929 m	939 m	938 w	940 w	940 w
850 sh	863 s	858 s	862 s	839 s	863 m	865 m	856 m	862 m
832 s	820 s	820 m	819 m	819 m	819 m	822 m	819 m	820 m
904 m	804 m	804 w	802 m	797 s	803 s	803 m	803 m	803 m
792 w								
775 s	780 s	782 s	780 s	775 s	780 s	780 s	780 s	778 s
731 s	711 s	711 s	711 s	710 m	712 s	719 m	712 s	712 m

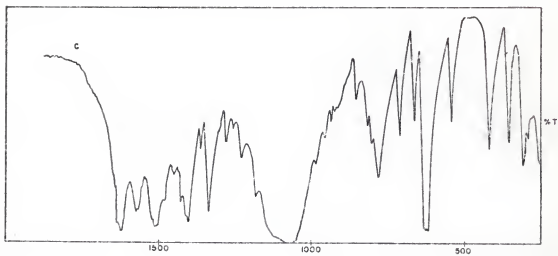
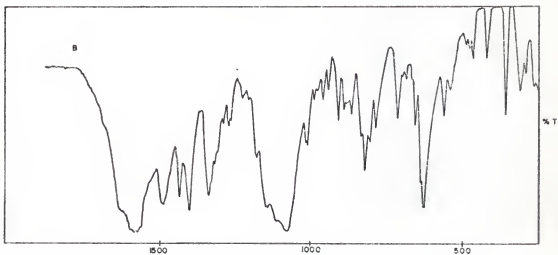
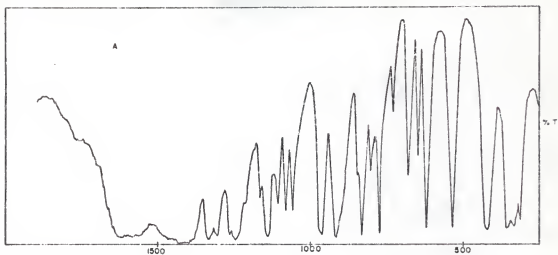
Table 10 -- continued

Hd	Cr(Hd) ₂ ⁺⁺	Mn(Hd) ₂ ⁺⁺	Fe(Hd) ₂ ⁺⁺	Co(Hd) ₂ ⁺⁺	Ni(Hd) ₂ ⁺⁺	Cu(Hd) ₂ ⁺⁺	Zn(Hd) ₂ ⁺⁺	Cd(Hd) ₂ ⁺⁺
683 s								
651 s	665 s	665 s	665 s	688 m	652 s	675 m	665 s	664 m
622 s	627 s	628 s	628 s	626 s	625 s	625 s	625 s	625 s
536 s	540 s	542 s	540 s	530 s	541 m	542 m	541 s	540 s
424 s	418 s	420 s	417 s	423 w	420 s	409 w	419 s	420 s
360 s	353 s	357 s	355 s	360 d	359 s	368 w	356 s	352 s
335 s								
315 s	305 s	310 s	303 s	302 w	310 s	304 m	309 s	302 s
		281 m	290 s	292 m	291 m	295 m	291 m	390 m

EXPLANATION OF PLATE IV

- A. Infrared Spectrum of Histidine.
- B. Infrared Spectrum of $\text{Ni}(\text{Hd})_2(\text{ClO}_4)_2$.
- C. Infrared Spectrum of $\text{Zn}(\text{Hd})_2(\text{ClO}_4)_2$.

PLATE IV



Histamine Complexes

Much the same procedure was used in the investigation of the histamine-metal complexes as was used with the histidine complexes. Deuteration was not utilized because the primary amine hydrogen would have also exchanged with the deuterium. The spectrum of the resulting deuterated histamine would have been of little use in assigning the absorption bands of histamine to specific vibrational modes.

Absorption bands due to the imidazole ring vibrations were again located by comparison of the spectra of metal-histamine complexes with the metal complexes of the other ligands. The histamine absorption bands at 1462 cm^{-1} , 1454 cm^{-1} , and 1247 cm^{-1} were assigned to vibrational modes of the imidazole ring of the histamine molecule. The bands at about 280 cm^{-1} were assigned to metal-nitrogen bonds. The spectra are shown on Table 11 and Plate V. Again all trends proved to be consistent with the Irving-Williams order of stability.

TABLE 11

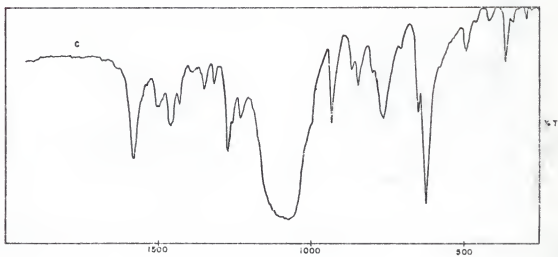
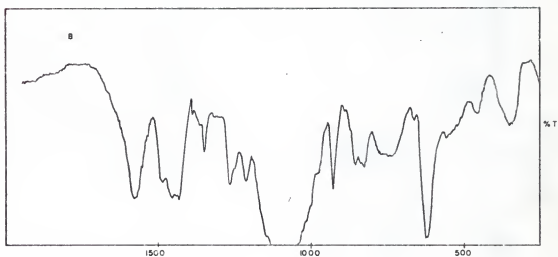
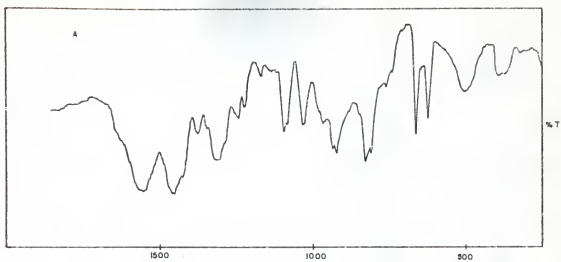
Infrared spectra of histamine free base and
metal-histamine complex cations in cm^{-1} .

Histamine	Cr(Hm)_2^{++}	Mn(Hm)_2^{++}	Co(Hm)_2^{++}	Ni(Hm)_2^{++}	Cu(Hm)_2^{++}	Zn(Hm)_2^{++}	Cd(Hm)_2^{++}
1560 br	1564 s	1563 s	1589 s	1570 s	1583 s	1579 s	1569 s
1462 s	1488 s	1482 s	1489 s	1491 s	1500 m	1492 m	1488 s
1454 s	1454 s		1455 s	1459 s	1460 s	1476	
1428 sh	1438 s		1433 s	1429 s	1430 m	1430 s	
1379 m	1381 m		1385 w	1386 m			1382 w
		1351 s	1350 m	1351 s	1350 m	1350 m	
1351 s	1318 m	1316 w		1307 m	1318 m	1324 w	1318 m
1247 m	1241 s	1262 s	1266 s	1269 s	1272 s	1270 m	1269 m
1228 m							
1098 s							
1033 s							
938 s							
923 s		928 m	928 s	926 s	931 s	928 s	921 w
	848 s	853 s	855 s	861 s	867 m	851 s	845 s
830 s	802 m		827 s	835 m	846 m	841 s	
811 s							
762 w	762 s	761 m			761 s		762 s
740 w	740 s	739 w		735 br			740 s
665 s							
	636 sh	634 sh		642 s	649 s		636 s
624 s	623 s	625 s	623 s	622 s	621 s	623 s	622 s
506 br	496 w		453 m	475 m	491 m	485 m	
395 br	365 s	345 m	351 s	360 s	362 s		363 s
	268 m	268 m	285 m	290 w	295 w	291 m	270 m

EXPLANATION OF PLATE V

- A. Infrared Spectrum of Histamine.
- B. Infrared Spectrum of $\text{Co(Hm)}_2(\text{ClO}_4)_2$.
- C. Infrared Spectrum of $\text{Cu(Hm)}_2(\text{ClO}_4)_2$.

PLATE V



SUMMARY

The transition metal complexes of five similar ligands, imidazole, pyrazole, benzimidazole, histidine, and histamine were prepared by adding together hot, concentrated solutions of the metal perchlorate and the ligand. This proved to be a more successful method of preparing the complexes than had been used in the past. Since the work began, others have used the same method in the preparation of the complexes (20, 21).

The resulting complexes were analyzed for metal ion content by polarographic methods. The per cent metal ion in the complex was then calculated from diffusion current and compared with the theoretical per cent of metal in complexes of various coordination numbers. In this way, the coordination number for the complexes was determined.

Assignments of some of the spectral bands was accomplished by deuteration of the amino hydrogen and analysis of the resulting spectra or by comparison with spectra for which the assignments had previously been determined.

The order of stability for complexes of nitrogen containing ligands with the transition metals has been determined by Irving-Williams to be as follows: $Mn(II) < Fe(II) < Co(II) < Ni(II) < Cu(II) > Zn(II)$. The complexes of each of the five ligands agreed favorably with that trend.

The results of the investigation revealed the changes which occurred in the electron densities within the ligand upon complexation. There was a correlation between the strength of the metal-ligand bond and the frequencies of the absorption bands due to vibrational modes of the imidazole ring. This

was an indication that as the sigma bond strength between the metal and ligand increased, the back-bonding between metal d orbitals and unoccupied nitrogen orbitals also increased. This strengthened the metal-nitrogen bond even more while increasing the electron density in the imidazole ring.

The absorption bands in the region of 250 cm^{-1} to 300 cm^{-1} were assigned to the bond between the metal and the 3-nitrogen in the imidazole ring. From those bands, an order of stability may be constructed for the five ligands to reflect their ability to form stable complexes with metal ions. The bands for the histidine complexes were of slightly higher frequencies than the corresponding bands for the histamine complexes. Imidazole formed the most stable monodentate complexes. Benzimidazole and pyrazole formed the least stable complexes as they showed no evidence of a band above 250 cm^{-1} which could have been assigned to a metal-nitrogen bond. The order of bonding strength for the ligands would be as follows: histidine > histamine > imidazole > benzimidazole ~ pyrazole.

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REFERENCES

1. Andrews, A. C. and E. W. Grundemeier
Effects of metal chelation on introligand bonds.
J. Inorg. Nucl. Chem., 28, 455 (1966)
2. Andrews, A. C. and J. K. Romary
Stability constants of Cd^{++} complexes by polarography.
J. Chem. Soc. 405 (1964)
3. Andrews, A. C., T. D. Lyons and T. D. O'Brien
Stability constants by potentiometry.
J. Chem. Soc. 1776 (1962)
4. Barrow, Kruegar and Basolo
Nitrogen-metal bonds in IR spectra of ammine complexes.
J. Inorg. Nucl. Chem. 2, 340 (1956)
5. Baumann, J. E. Jr. and J. C. Wang
Preparation of metal complexes with imidazole as ligand.
Inorg. Chem. 3, 368 (1964)
6. Brooks, P. and N. Davidson
Imidazole and histidine complexes with $\text{Hg}(\text{ClO}_4)_2$.
JACS 82, 2118 (1960)
7. Brown, G. P. and S. Aftergut
Preparation of Zn, Co, and Cu complexes with imidazole.
J. Polymer Sci., Pt. A 2(4) 1839 (1964)
8. Carlson, R. H.
Structures of imidazole and histidine are studied as a
function of pH.
Ph. D. Dissertation Thesis. University of Illinois (1964)
9. Carlson, R. H. and T. L. Brown
Spectra of imidazole and histidine complexes in solution.
Inorg. Chem. 5, 268 (1966)
10. Chawla, I. D.
Thermodynamic values of imidazole complexes by potentiometry.
Ph. D. Dissertation. Kansas State University, 1962

11. Clark, R. J. H. and C. S. Williams
Metal chloride complexes of pyridine are studied to investigate metal-ligand bond in IR.
Inorg. Chem. 4, 350 (1965)
12. Coates, G. E.M., L. H. Green, P. Powell and K. Wade
"Principles of Organometallic Chemistry"
London: Methuen and Co. Ltd. (1968)
13. Cordes, M. and J. L. Walter
Assignment of infrared bands for imidazole.
Spectrochim. Acta., Vol. 24 A 237 (1968)
14. Corsin, Fax and Lord
Assignment of pyridine and pyridine-d₅ spectra.
J. Chem. Phys. 21, 1170 (1953)
15. Dale, Henry
Pharmacology of histamine.
Ann. New York State Acad. Sci. 50(9), 1017 (1950)
16. Donohue, J. L., R. Lavine and J. S. Rollett
X-ray data of histidine hydrochloride.
Acta. Cryst., 2, 655 (1956)
17. Doran, M. A., S. Chaberek and A. E. Martell
Histidine shown to be a tridentate ligand.
JACS 86, 2129 (1964)
18. Earnshaw, A. and L. F. Larkworthy
Co-histidine complex shown to be octahedral.
Nature 192, 1068 (1961)
19. Edsall, J. T., G. Felsenfeld, D. S. Goodmsn, F. R. N. Gurd.
Association constants for Cu(II) and Zn(II) imidazole complexes.
JACS 75, 434 (1953)
20. Eilbeck, W. J., F. Holmes, C. E. Taylor, A. E. Underhill
Solid metal-imidazole complexes are prepared.
J. Chem. Soc. A 128 (1968)
21. Eilbeck, W. J., F. Holmes, A. E. Underhill
Absorption spectra of metal-imidazole complexes assigned.
J. Chem. Soc. A. 757 (1967)
22. Garfinkel, D., J. T. Edsall
IR and Raman Spectra of imidazole complexes.
JACS 80, 3807 (1958)
23. Gillespie, R. J., J. H. Ridd, R. F. M. White
N. M. R. study of selectivity of imidazole deuteration.
J. Chem. Soc. 3228 (1958)

24. Goodgame, M., F. A. Cotton
Ligand field calculations for benzimidazole complexes.
JACS 84, 1543 (1962)
25. Goodgame, D. M. L., M. Goodgame, P. J. Hayward, G. W. Rayner-Canham
Preparation of solid complexes of imidazole with Cu(II), Ni(II),
Co(II) and Zn(II).
Inorg. Chem. 1, 2447 (1968)
26. Harding, M. M. and S. J. Cole
Crystal Structure of bis-Zn(II) histidine complex.
Proc. Chem. Soc. 178 (1962)
27. Harkins, T. R., J. L. Walters, O. E. Harris, and Freiser
N-H vibrational modes used to determine degree of coordination.
JACS 78, 260 (1956)
28. Hofmann, Klaus
"Imidazole and Its Derivatives"
New York: Interscience Publishers (1953)
29. Irving, H., and R. J. P. Williams
Complex stability of transition metals determined.
J. Chem. Soc. 3192 (1953)
30. Klotz, I. M. and W. C. Loh Ming
Mediation by metals of the binding of small molecules by proteins.
JACS, 76, 805 (1954)
31. Larsson, L.
I R spectrum of histidine hydrochloride.
Acta. Chem. Scand. 4, 31 (1950)
32. Leberman, R. and B. R. Rabin
Histidine shown to form octahedral complex.
Trans. Farad. Soc. 55, 1660 (1959)
33. Li, N. C., Br. G. Doody, and J. M. White
Potentiometric investigation of imidazole complexes.
JACS 79, 5859 (1957)
34. Li, N. C., T. L. Chu, C. T. Faju, and J. M. White
Ultraviolet spectra of imidazole complexes.
JACS 77, 859 (1955)
35. Li, N. C., P. Tang and R. Mathur
Polarographic investigation of imidazole complexes in D₂O.
J. Phys. Chem. 65, 1074 (1961)
36. Li, N. C., J. M. White and E. Doody
Stability constants of imidazole complexes determined.
JACS 76, 6219 (1954)

37. Lundberg, B. K. S.
Structure of Zn-imidazole complex.
Acta Crystallogr. 21 (6) 901 (1966)
38. Martin, R. B. and J. T. Edsall
Stability constants for imidazole complexes with Mn(II) and Co(II).
JACS 80, 5033 (1958)
39. Mathur, R. and H. Lal
Stability constants of histamine and histidine complexes with Co(II).
J. Phys. Chem., 63, 439 (1959)
40. McDonald, C. C. and W. D. Phillips
NMR study of histidine complexes.
JACS, 85, 3736 (1963)
41. Meites, Louis
"Polarographic Techniques"
New York: Interscience Publishers (1965)
42. Melson, G. A. and R. H. Nuttall
Metal complexes with benzimidazole are tetrahedral.
J. Mol. Struct., 1, (6), 405 (1968)
43. Mickel, B. L. and A. C. Andrews
Complexes of histamine with Co(II), Ni(II), and Cu(II).
JACS 77, 323 (1955)
44. Mickel, B. L. and A. C. Andrews
Stability of the histamine chelates.
JACS 77, 5291 (1955)
45. Nortia, T.
Stability of histamine and histidine complexes with Co(II) and Ni(II).
Suomen Kera B 32 245 (1959)
46. Nuttall, Gill, Scaife and Sharp
IR of pyridine complexes.
J. Inorg. Nuc. Chem. 18, 79 (1961)
47. Otting, Walter
Properties of five-membered nitrogen heterocycles.
Chem. Ber. 89, 2887 (1956)
48. Rao, M. S. N. and Hira Lal
Ultraviolet spectra of metal complexes of imidazole and proteins.
J. Chem. Soc. 3228 (1958)
49. Rao, G. N. and N. C. Li
Coordination numbers of Cd(II) and Ni(II) is found to be six.
Can. J. Chem. 44 (14) 1637 (1966)

50. Schubert, J., E. L. Lind, W. M. Westfall, R. Pflieger, N. C. Li
Ion Exchange work with ^{60}Co and ^{65}Zn imidazole complexes.
JACS 80, 4799 (1958)
51. Silva, M., Rocha E.
Histamine; its role in anaphylaxis and allergy.
Springfield: Charles C. Thomas (1955)
52. Tanford, C.
Nitrogen is complexing site for metals on proteins.
JACS 74, 211 (1952)
53. Tanford, C. and M. L. Wagner
Stability constants for Cd(II) imidazole complex.
JACS 75, 434 (1953)
54. Walba, H. and R. W. Isensee
Ultraviolet investigation of imidazole.
J. Org. Chem. 21 702 (1956)
55. Weitzel, G. F. Schneider, A. M. Fretzdorff and H. E. Heyke
IR spectra of solid Zn-histidine complex.
Z. Physiol. Chem., 307 14 (1957)
56. White, J. M., T. J. Weismann and N. C. Li
Magnetic moment measurements of Co(II)-imidazole complexes.
J. Phys Chem., 61, 126 (1957)
57. Zecchina, A. L., Cerruti, S. Coluccia and E. Barello
IR of pyrazole assigned.
J. Chem. Soc. B (12), 1363 (1967)
58. Zimmerman, H.
IR of solid imidazole.
Z. Electrochem., 65, 821 (1961)

THE INFRARED SPECTROSCOPIC COMPARISON OF METAL
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by

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Over the years it has been established that the basic structure of the imidazole molecule is very important biologically. It has been included in the structure of a great many biologically important compounds, such as, histidine and histamine. Other heterocyclic nitrogen-containing compounds similar to imidazole have also proven to be biologically important. Their importance has been derived in part at least, from the ability of the nitrogen atoms to complex with metal ions.

Complexes of ligands containing the imidazole ring with certain metal ions have been the center of extensive research in the past few years. However, most of the work investigated the complexes in solution. The present work has dealt with the complexes in the solid state.

The complexes were prepared by adding together hot, concentrated solutions of the metal perchlorate and the ligand. The resulting complexes were then analyzed for metal ion content by polarographic methods. The complexes were then investigated by means of infrared spectroscopy. Assignment of the spectra was verified by comparing spectra of the free ligand with that of the N-deuterated analogs. In the case of the ligands for which that method was impossible, assignments were determined by comparing the unknown spectra with the spectra of other ligands which had previously been assigned.

Irving and Williams have determined the order of stability for complexes of nitrogen containing ligands with transition metals to be as follows:
 $Mn(II) < Fe(II) < Co(II) < Ni(II) < Cu(II) > Zn(II)$. The complexes of all five ligands compared favorably with that trend.

The results of this investigation revealed the changes which occurred in the electron densities within the ligand as it changed from a free ligand to a complexed species. There was a definite correlation between the strength of the metal - ligand bond and the frequencies of the absorption bands due to vibrational modes of the imidazole ring. This was an indication that as the strength of the sigma bond between the metal and ligand increased, the back-bonding between metal d orbitals and unoccupied nitrogen orbitals also increased. This strengthened the metal-nitrogen bond while increasing the electron density in the imidazole ring.

The absorption bands in the region of 250 cm^{-1} to 300 cm^{-1} were assigned to the bond between the metal and the 3-nitrogen in the imidazole ring. This bond strength was a direct indication of the stability of the complexes. Therefore, from those bands, an order of stability was constructed for the five ligands which reflected their ability to form stable complexes with metal ions. The order is as follows: histidine > histamine > imidazole > benzimidazole \sim pyrazole.