

SYNTHESIS AND CHARACTERIZATION OF MIXED LIGAND COPPER(II) COMPLEXES OF HISTIDINE AND HIPPURIC ACID

G. KUMAR

University of Botswana, BOTSWANA

Abstract. Mixed ligand copper(II) complexes,

$[\text{Cu}_2(\text{C}_6\text{H}_8\text{N}_3\text{O}_2)_2 - \mu\text{-(C}_6\text{H}_5\text{CONHCH}_2\text{COO)}(\text{H}_2\text{O})_2] \cdot 2\text{H}_2\text{O}$ and

$[\text{Cu}_2(\text{C}_6\text{H}_8\text{N}_3\text{O}_2)_2 - \mu\text{-(C}_6\text{H}_5\text{CONHCH}_2\text{COO)}(\text{H}_2\text{O})_2]$ formed with histidine and

hippuric acid have been synthesized and characterized by their elemental analysis, magneto chemical measurements and spectral (IR and electronic) studies. Histidine in these complexes acts as a tridentate ligand, coordinating through the two nitrogen atoms of imidazole ring and the amino group and carboxylate oxygen whereas hippuric acid shows a bidentate nature and the coordination occurs through the carboxylate oxygen and the nitrogen of the amido group. Water molecules satisfy the remaining coordination positions. The complexes have been suggested to show a bi nuclear penta coordinated (possibly square pyramidal) structure.

Keywords: Cu(II) complexes, histidine, hippuric acid, synthesis, characterization, structure

Introduction

Histidine is a basic amino acid, containing weakly basic imidazole group (Fig. 1). It is well known for its biological importance being an essential amino acid. Its exceptional ability to bind the metal ions is ascribed to the formation of six membered rings in which the metal is attached to an imidazole nitrogen atom and the α -amino group. Coordination may also occur from the carboxylate oxygen and thus on the whole it may show tridentate behavior. Thus in 1:1 metal histidine complex, sufficient number

of coordination sites remain available, which may be satisfied by secondary ligands to result into mixed complexes.

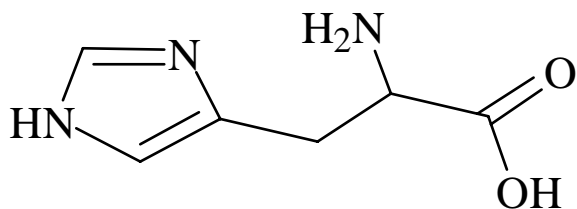


Figure 1: Structure of Histidine

Hippuric acid is an α -amido acid (Fig. 2) containing an acidic COOH, basic NH and a substituent benzoyl group. It is thus capable of forming metal chelates. It has a special biological importance as it is found in the urine of camel. Its alkali, calcium and magnesium salts have also been used as solubilizers in the preparation of aqueous solution of some sparingly soluble medicinal compounds [1].

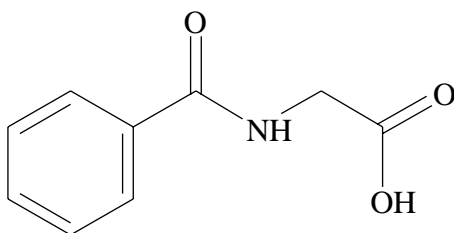


Figure 2: Structure of Hippuric Acid

Cu(II) amino acids complexes, in recent years have been receiving much attention due to their useful antibacterial agents. Copper-histidine treatment has been used for Menkes disease [2]. The formation and characterization of Al(III), Be(II) and Cu(II) complexes of histidine in solution and their characterization by Potentiometric and spectroscopic studies have been done [3-5]. Kinetics and mechanism of thermal decomposition of o-vanilline-L-histidine complexes of some transition metal ions in which histidine acts as a tridentate ligand and an octahedral structure for the complexes has been reported [6]. Synthesis, structural, coordination and thermal stability studies of mixed ligand complexes of histidine with other ligands (adenine/guanine, ethylenediamine, diethylenetriamine or N,N,N',N'',N'''-pentamethyldiethylenetriamine, glycine or L-alanine, histamine and diethylglyoxime) [7-11] have also been carried out. In

earlier publications [12-14], the synthesis and characterization of mixed ligand Cu(II), Ni(II) and Co(II) complexes of hippuric acid and nitrilotriacetic acid/ iminodiacetic/ histidine have been reported. Literature reveals that no studies on the synthesis and structural studies of mixed ligand Cu(II) complexes of histidine and hippuric acid have been carried out. Hence the present paper reports the synthesis and characterization of new mixed ligand Cu(II) complexes formed with histidine and hippuric acid.

Experimental

Solutions of hippuric acid (Fluka) and histidine (Fluka) were prepared by dissolving them in one equivalent of sodium hydroxide. The solution of copper(II) chloride dihydrate (BDH) was prepared in one equivalent of hydrochloric acid. To prepare the metal complex, the two ligands were mixed with 0.1M metal ion solution in 1:1:1 molar ratio at room temperature and the pH of the solution was adjusted to ~ 5.03 by adding sodium hydroxide solution. The resulting dark blue solution was then concentrated over a steam bath and allowed to crystallize overnight. The dark brown product was then filtered and washed first with 50% ethanol - water mixture followed by acetone and dried in a vacuum desiccator. On heating the dark brown crystalline product in an air oven at 100-110°C for about two hours, the colour of the complex changed to black indicating the loss of water molecules from the complex.

The IR spectra of the ligands and Cu(II) complexes were recorded on a Perkin-Elmer FTIR-2000 spectrophotometer in 4000-400 cm^{-1} range on KBr discs. The magnetic susceptibility of the complexes was measured at room temperature using Johnson Matthew Alfa Product magnetic susceptibility balance. The electronic spectra of the complexes were recorded on Shimadzu UV vis 2501 PC spectrophotometer model TCC-240A in methanol in 190-1100 nm range. The Vario EL CHNO/S elemental analyzer was used to carry out the elemental (CHN) analysis and the metal content in the complexes was determined using Atomic Absorption Spectrophotometer 220FS.

Results and discussion

Elemental Analysis

Analytical data are as follows:

1. [Bis(histidino) - μ -(hippurato)(diaqua)dicopper].dihydrate. Anal. calcd. for $[\text{Cu}_2(\text{C}_6\text{H}_8\text{N}_3\text{O}_2)_2 - \mu\text{-(C}_6\text{H}_5\text{CONHCH}_2\text{COO)}(\text{H}_2\text{O})_2].2\text{H}_2\text{O}$: Cu = 18.54% ; C = 36.78% ; H = 4.71% ; N = 14.30% , Found : Cu = 19.04% ; C = 37.01% ; H = 4.54% ; N = 14.01% .

2. [Bis(histidino) - μ -(hippurato)(diaqua)dicopper] Anal. calcd. for $[\text{Cu}_2(\text{C}_6\text{H}_8\text{N}_3\text{O}_2)_2 - \mu\text{-(C}_6\text{H}_5\text{CONHCH}_2\text{COO)}(\text{H}_2\text{O})_2]$: Cu = 19.57% ; C = 38.82% ; H = 4.35% ; N = 15.08% ; Found Cu = 20.01% ; C = 38.62% ; H = 3.92% ; N=15.29%.

NOTE: In further discussion in the text for convenience the two complexes are referred to as tetrahydrate and dihydrate respectively.

IR Studies

In amino acids, νNH_3^+ appears in 3130-3030 cm^{-1} region [15]. In the IR spectra of histidine it appears at $\sim 3082 \text{ cm}^{-1}$, but overlaps with other vibrations such as $\nu(\text{NH})$ (imidazole group) and $\nu(\text{CN})$ (heterocyclic + νCH_2 group $\sim 3016 \text{ cm}^{-1}$). Theoretically νNH_3^+ should vanish on coordination. In metal complexes however, some broad band appears at $\sim 3399 \text{ cm}^{-1}$, which must be arising from other vibrations appearing in this region. In histidine, δNH_3^+ appears at 1560 cm^{-1} which vanishes in the metal complexes. The $\nu_{\text{as}}\text{COO}^-$ and $\nu_{\text{s}}\text{COO}^-$ absorptions in histidine appear at 1633 and 1418 cm^{-1} respectively [16]. In imidazole [17], the νNH absorption appears at 3125 cm^{-1} . In histidine, it gets mixed with other absorptions in this region and a broad band at $3082 - 2866 \text{ cm}^{-1}$ is visible. In case of metal complexes it is absent since no band is observed in this region. Hippuric acid shows characteristic $\nu(\text{C}=\text{O})$ absorption bands for the COOH group at 1750 cm^{-1} which vanishes in case of copper(II) complexes. Instead, asymmetric and symmetric COO^- stretching frequencies are obtained. In tetrahydrate complex, $\nu_{\text{as}}\text{COO}^-$ and $\nu_{\text{s}}\text{COO}^-$ frequencies are observed at 1607 and 1395 cm^{-1} respectively whereas in dihydrate complex these vibrations are observed at 1611 and 1393 cm^{-1} respectively. The $\nu(\text{NH})$ absorptions in hippuric acid are observed at 3343 cm^{-1} which in complexes is mixed with $\nu(\text{OH})$ and is observed at $\sim 3399 \text{ cm}^{-1}$. Hippuric acid shows amide I ($\nu\text{C}=\text{O}$) band at 1608 cm^{-1} , amide II [$\delta(\text{NH}) + \nu(\text{CN})$] band with benzene ring vibrations in $1559-1412 \text{ cm}^{-1}$ range, amide III [$\nu(\text{CN}) + \delta(\text{NH})$] band at 1310 cm^{-1} . In tetrahydrate and dihydrate complexes, amide I band together with $\nu_{\text{as}}\text{COO}^-$ is obtained at 1607 and 1611 cm^{-1} respectively. Amide II band along with benzene ring and $\nu_{\text{s}}\text{COO}^-$ vibrations are obtained at 1395 and 1393 cm^{-1} in tetrahydrate and dihydrate complexes respectively. In tetrahydrate complex amide III band with νCN vibrations is obtained at 1324 cm^{-1} whereas in dihydrate complex this band is obtained at 1321 cm^{-1} . The greater difference (Δ) in the positions of $\nu_{\text{as}}\text{COO}^-$ and $\nu_{\text{s}}\text{COO}^-$ stretching frequencies of the free ligands and the complexes indicate the monodentate coordination of the carboxyl group [18-19]. Besides, both the complexes show additional bands at $\sim 3399 \text{ cm}^{-1}$ attributable to water molecules [17]. The appearance of the rocking ρ (HOH) frequency (20) at 705 and 709 cm^{-1} in case of tetrahydrate and dihydrate complexes respectively shows the presence of coordinated water molecules. The IR frequencies of the ligands and the metal complexes are given in Table 1. Thus the IR studies suggest that in Cu(II) complexes, histidine coordinates through the carboxylate oxygen and two nitrogens from imidazole and $-\text{NH}_2$ groups, hence acts as a tridentate ligand. Hippuric acid shows bidentate behavior, coordinating through the carboxylate oxygen atom and the nitrogen of the amido group.

Magnetic measurements and electronic spectra

Copper(II) complexes show subnormal magnetic moments,

$[\text{Cu}_2(\text{C}_6\text{H}_8\text{N}_3\text{O}_2)_2 - \mu-(\text{C}_6\text{H}_5\text{CONHCH}_2\text{COO})(\text{H}_2\text{O})_2].2\text{H}_2\text{O}$: $\mu_{\text{eff}} = 1.52$ BM and $[\text{Cu}_2(\text{C}_6\text{H}_8\text{N}_3\text{O}_2)_2 - \mu-(\text{C}_6\text{H}_5\text{CONHCH}_2\text{COO})(\text{H}_2\text{O})_2]$: $\mu_{\text{eff}} = 1.57$ BM suggesting their dimeric nature [20]. The magnetic measurements are given in Table 2. Both the complexes show the following absorption bands.

1. $[\text{Cu}_2(\text{C}_6\text{H}_8\text{N}_3\text{O}_2)_2 - \mu-(\text{C}_6\text{H}_5\text{CONHCH}_2\text{COO})(\text{H}_2\text{O})_2].2\text{H}_2\text{O}$ 3316,15649,17730, 43871, 50761 cm^{-1}
2. $[\text{Cu}_2(\text{C}_6\text{H}_8\text{N}_3\text{O}_2)_2 - \mu-(\text{C}_6\text{H}_5\text{CONHCH}_2\text{COO})(\text{H}_2\text{O})_2]$ 13927, 15798, 17730, 50251 cm^{-1}

Table 1. IR Frequencies (cm^{-1}) of histidine, hippuric acid and their mixed copper(II) complexes

Histidine	Band Assignment	Hip- puric Acid	Band Assignment	[[Cu ₂ -His - HA}. 2H ₂ O]. 29H ₂ O]	[[Cu ₂ -His- HA}. 2H ₂ O]	Band Assignment
3082-2866	v(NH) (imidazole) + vCH (Heterocyclic) +v NH ₃ ⁺ + vCH(-CH ₂)	1750	v (C=O) Carboxylic group	3399	3399	v (OH) water molecules mixed with v(NH)
1633	v _{as} COO ⁻	3085	v (CH)	3141	3134	v(NH) + v(CH)
1418	v _s COO ⁻	3343	v(NH)	1607	1611	v _{as} COO ⁻ + v (C=O) amide I
1560	δNH ₃ ⁺	1608	v(C=O) amide I	1395	1393	v _s COO ⁻ + benzene ring + δNH+vCN) amide II
1457	Ring Structure (imidazole)	1559, 1487, 1412	Benzene ring +(δNH+vCN) amide II	1324	1321	vCN+(vCN+δNH) amide III
1336	vCN	1310	(vCN + δ NH) amide III	705	709	P _f (HOH) Coordinated water molecule

* His and HA stand for anion of histidine and hippuric acid respectively

Table 2. Magnetic measurements of copper(II) complexes

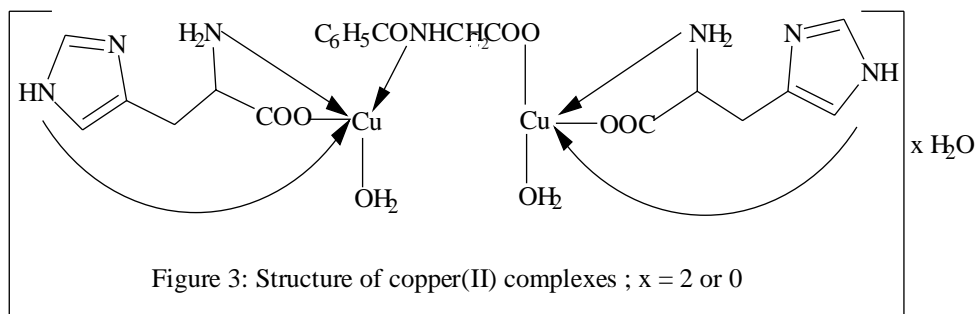
Compound	Temp (K)	$\chi_g \times 10^{-6}$ c.g.s	$\chi_M \times 10^{-6}$ c.g.s	$\chi_M' \times 10^{-6}$ c.g.s	μ_{eff} (BM)
$[\{\text{Cu}_2\text{-His-HA}\} \cdot 2\text{H}_2\text{O}] \cdot 2\text{H}_2\text{O}$	290	2.5955	889.78	997.37	1.52
$[\{\text{Cu}_2\text{-His-HA}\} \cdot 2\text{H}_2\text{O}]$	292	2.9260	950.36	1057.95	1.57

* His and HA stand for anion of histidine and hippuric acid respectively.

The bands at 13316 and 13927 cm^{-1} are the main d-d transition bands in tetrahydrate and dihydrate complexes respectively, whereas bands at 17730 cm^{-1} in both the complexes is indicative of their tetragonally distorted nature [21] as observed in square planar Cu(II) complexes. The bands at 15649 and 15798 cm^{-1} in tetrahydrate and dihydrate complexes respectively are in support of their square pyramidal structure [22-23]. The bands at 43871 and 50251 cm^{-1} (tetrahydrate) and 50251 (dihydrate) cm^{-1} can be regarded as charge transfer bands. It may thus be concluded that Cu(II) complexes are binuclear penta coordinated (possibly square pyramidal) complexes as is borne out from their analytical and subnormal magnetic moments, but somehow in both the complexes the band at $\sim 27000 \text{ cm}^{-1}$ usually observed in binuclear Cu(II) carboxylate is not observed [24].

Conclusion

Thus the evidences obtained from the above studies suggest a penta coordinated (possibly square pyramidal) structure for copper(II) complexes in which histidine acts as a tridentate ligand and hippuric acid shows a bidentate behavior. Water molecules satisfy the other coordination positions (Fig. 3).



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✉ **Dr. G. Kumar,**
Department of Chemistry,
University of Botswana,
P/Bag UB 704, Gabarone, BOTSWANA
E-Mail: kumarg@mopipi.ub.bw