Inorganica Chimica Acta, 92 (1984) 199–201

Study of Copper(II) Ternary Complexes Involving Tertiary Amines and Histidine

VIBHA K. PATEL and PABITRA K. BHATTACHARYA*

Department of Chemistry, Faculty of Science, M.S. University of Baroda, Baroda - 390 002, India

Received December 9, 1983

Histidine is a biochemically important ligand having an ambidentate nature. It has three coordinating sites, amino nitrogen, imidazole nitrogen and carboxyl oxygen. In the mixed ligand complexes [MAL] where A is a tertiary amine, it is known that [MA] discriminates between N–N and N–O⁻ coordinating ligands. The present study of the formation constants and the electronic spectra of the mixed-ligand complexes involving tertiary amines and histidine shows that histidine coordinates with [CuA] from the N–O⁻ site like amino-acid in the lower pH range and from the N–N site like histamine in the higher pH range.

Introduction

In recent years considerable attention has been paid to the investigation of copper(II) binary and ternary complexes containing imidazole and its derivatives, histamine or histidine as ligands, since they are important ligands for copper(II) binding in many biological systems [1–6]. Imidazole is unidentate and histamine is bidentate, coordinating through one imidazole nitrogen and the other amino nitrogen. However, the Cu(II) histidine system is of considerable interest because of the ambidentate nature of histidine, having three coordinating sites, imidazole N, amino N and the carboxyl O atom. In the Cu–histidine binary systems, due to the strong preference of copper(II) for square planar or grossly distorted octahedral complexes, there is the possibility of two types of Cu(II)–histidine complexes, $[Cu(HL)]^{2+}$ and $[CuL]^{+}$, in whicn only two binding sites are attached to the metal ion.

It was suggested earlier that in the species $[Cu(LH)]^{2+}$ coordination is from the imidazole nitrogen and carboxyl oxygen, the amino proton remaining undissociated [7]. However, this will give rise to a less stable seven membered ring. A crystal structure [8] study of the $[Cu(LH)_2]$ complex has shown that the coordination is from amino N and carboxyl O as in amino acids and the imidazole N remains protonated. It has been further confirmed by Pettit and coworkers by the determination of formation constants in solution [9]. In the species $[CuL]^{+}$, coordination is from amino N and imidazole N [2, 3]. There may be a weak coordination of carboxyl O also. The formation constants of various possible binary species such as [CuLH], [CuL], $[CuL_2H]$ and $[CuL_2]$ have been reported by several workers [3, 5, 9].

The study of the ternary complexes involving tertiary amines (A) is gaining importance because of the statistical stabilization of the ternary complexes due to M → A π interaction [10–12]. It has been further observed that $[MA]^{2+}$ complexes discriminate between secondary ligands (L) with different coordinating sites in the order $O^{-}–O^{-} > O^{-}–N > N–N$ [11–14].

In order to see if histidine coordinates with CuA^{2+} from the N–N end or the O^{-}–N end and to compare the stabilities of the resulting ternary complexes, it was thought of interest to study [CuAL] complexes where A = 2,2′-bipyridyl (A^1) or 1,10-phenanthroline (A^2) and L = histidine (L^1). Such a study is useful because tertiary amines and histidine are compounds of biological importance. In order to ascertain the coordination sites in [CuA], histidine formation constants of the ternary complexes $[CuAL_2]$, L^2 = histamine, have also been redetermined [15] under identical conditions.

Experimental

All reagents used were of A.R. grade and the titrations were carried out using the digital pH meter with an accuracy of ±0.01. The proton–ligand formation constants of histidine LH_3, LH_2, LH and the formation constants of the binary complexes [CuLH], [CuL], $[CuL_2H]$ and $[CuL_2]$ were determined in aqueous medium and 0.2 mol dm^{-3} ($Na[ClO_4]$) at 30 °C using the SCOGS computer program [16] (charges on the species have been omitted for simplicity). In the case of histamine, proton–ligand formation constants of the species LH_2, LH and formation constants of the binary complexes [CuL] and $[CuL_2]$ were also refined under identical condi-

*Author to whom correspondence should be addressed.

0020-1693/84/$3.00

TABLE I. Proton–Ligand and Binary Cu(II) Ligand Formation Constants in Aqueous Medium I = 0.2 mol dm^{-3} ($Na[ClO_4]$) at 30 °C. Standard deviations are given in parentheses.

Ligand	K_1^H	K_2^H	K_3^H	$\log K_{CuLH}^{Cu}$	$\log K_{CuL}^{Cu}$	$\log K_{CuL_2}^{CuL}$
Histidine (L^1)	9.05	6.23	2.42	8.23	10.16	7.51
	(0.02)	(0.03)	(0.04)	(0.1)	(0.1)	(0.1)
Histamine (L^2)	9.78	6.25	–	–	9.79	6.98
	(0.01)	(0.02)			(0.07)	(0.07)

TABLE II. Formation Constants of Mixed-ligand Complexes and Δ logK in Aqueous Medium, I = 0.2 mol dm^{-3} ($Na[ClO_4]$) at 30 °C. Standard deviations are given in parentheses.

Ligands	A^1				A^2			
	$\log K_{CuA^1LH}^{CuA^1}$	$\log K_{CuA^1L}^{CuA^1}$	Δ log K		$\log K_{CuA^2LH}^{CuA^2}$	$\log K_{CuA^2L}^{CuA^2}$	Δ log K	
			I	II			I	II
L^1	7.54	8.36	−0.66	−1.66	7.46	8.00	−0.77	−2.16
	(0.2)	(0.1)			(0.2)	(0.2)		
L^2	–	8.00	–	−1.79	–	8.13	–	−1.66
		(0.07)				(0.1)		

$$\Delta \log K\ I = \log K_{CuALH}^{CuA} - \log K_{CuLH}^{Cu}$$

$$\Delta \log K\ II = \log K_{CuAL}^{CuA} - \log K_{CuL}^{Cu}$$

TABLE III. Visible Spectra of Mixed-ligand Complexes in Aqueous Medium at Different pH.

Complex	pH	cm^{-1}
CuA^1L^1	6.5	15,000
CuA^1L^2	6.5	15,000

tions. The values have been tabulated in Table I. They are in agreement with the values reported earlier [3–5, 9, 15]. These refined values were used as fixed parameters for the refinement of the formation constants of the mixed-ligand complexes involving histidine [CuALH] and [CuAL]) using the computer method in two ways:

(1) by considering the complete formation of CuA and the species present in the solution to be LH_3, LH_2, LH, L, CuA, CuAL and CuALH.

(2) by taking into account all possible species present in solution, *i.e.* AH_2, AH, A, LH_3, LH_2, LH, L, [CuA], [CuA_2], [CuLH], [CuL], [CuL_2H], [CuAL] and [CuALH].

In the case of histamine, the species considered were LH_2, LH, L, [CuA] and [CuAL] in the first computer method and AH_2, AH, A, LH_2, LH, L, [CuA], [CuA_2], [CuL], [CuL_2] and [CuAL] in the second computer method.

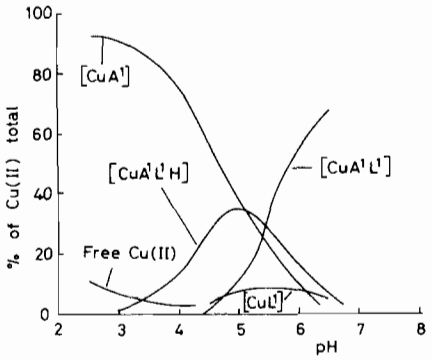

Fig. 1. Variation of concentration of different species with pH: Cu(II) + dipy (A^1) + histidine (L^1) system in aqueous medium.

Results and Discussion

It is observed that the values obtained by both computer methods are in close agreement. This shows that the presumption in the first method, that the formation is in steps, *i.e.* [CuA] is first formed and then the formation of the species [CuALH] or [CuAL] takes place, is correct. In the second method, where all possible species have been considered, the plot of concentration of the species against pH (Fig. 1) shows that in the lower pH range (pH 1.8–3)

[CuA] is formed and then the co-ordination of histidine takes place.

The reaction can be shown to take place in the following steps.

$$[CuA] + LH \rightleftharpoons [CuALH] \quad (1)$$

$$[CuA] + L \rightleftharpoons [CuAL] \quad (2)$$

In the lower pH range ($3 \approx 5$) there is formation of [CuALH] due to coordination from amino N and carboxyl O, the imidazole N remaining protonated. It is observed in the plot of the concentration of species (Fig. 1) that [CuALH] is maximum (35.0%) at pH 5.0. [CuAL] formation starts at higher pH 4.8 due to coordination from imidazole N and amino N. As the pH is increased the percentage concentration of [CuAL] increases and reaches 70% at pH 6.5.

The fact that in the species [CuALH] coordination is from amino N and carboxyl O is confirmed by the observation that the value of log K_{CuALH}^{CuA} (7.54) is comparable with that of log $K_{CuA\ phenylalanine}^{CuA}$ (7.49). The formation constant of the species [CuAL] (log K_{CuAL}^{CuA} = 8.36) is comparable to the formation constant of the ternary complex species [CuA histamine] (log $K_{CuA\ histamine}^{CuA}$ = 8.00), showing that the coordination in [CuAL] is from the imidazole and amino nitrogens of histidine, as in the case of histamine (Table II).

The site of coordination of histidine in [CuAL] in the higher pH range is confirmed by observing that at pH 6.5 the spectrum of [CuAL] shows a band at 15 000 cm^{-1} comparable to that of [CuA histamine] (15 000 cm^{-1}). This shows that coordination of histidine in [CuAL] is from the histamine end, the carboxylate part remaining free, as Cu(II) does not prefer axial coordination (Table III).

Thus, just as Cu(II) prefers to coordinate with histidine from the O^-—N end in the lower pH range and from the imidazole and amino nitrogen end in the higher pH range in the binary complex, [CuA] also coordinates with histidine from the O^-—N end in the lower pH range forming [CuALH] and from the N–N end in the higher pH range forming [CuAL]. As expected [12, 17], Δ logK for N–N coordination (log k_{CuAL}^{CuA} – log K_{CuL}^{Cu}) is more negative (–1.66). Δ log K for O^-–N coordination (log K_{CuALH}^{CuA} – log K_{CuLH}^{Cu}) is less negative (–0.69), as in the case of other amino acids.

Acknowledgement

We are thankful to CSIR for financial support to the scheme under which this work was carried out.

References

1 'Metal Ions in Biological System', Ed. H. Sigel, Marcel Dekker, New York, *2* (1973).
2 D. D. Perrin and V. S. Sharma, *J. Chem. Soc. (A)*, 724 (1967).
3 M. S. Nair, M. Santappa and P. Natarajan, *J. Chem. Soc. Dalton Trans.*, 1312 (1980).
4 L. G. Sillen and A. E. Martell, 'Stability Constants of Metal Ion Complexes', Spec. Publ., The Chemical Soc., London, *17* and *25* (1964, 1971).
5 D. R. Williams, *J. Chem. Soc. Dalton Trans.*, 790 (1972).
6 E. W. Wilson, M. H. Kasperian and R. B. Martin, *J. Am. Chem. Soc., 92,* 5365 (1970).
7 'Inorganic Biochemistry', Ed. Eichhorn, Amsterdam, Oxford, New York, *1*, 146 (1973).
8 B. Evertson, *Acta Cryst., B25,* 30 (1969).
9 L. D. Pettit and J. L. M. Swash, *J. Chem. Soc., Dalton Trans.*, 588 (1976).
10 G. A. L'Heurex and A. E. Martell, *J. Inorg. Nucl. Chem., 28,* 481 (1966).
11 H. Sigel, *Chimia, 21,* 489 (1967).
12 R. Griesser and H. Sigel, *Inorg. Chem., 9,* 1238 (1970).
13 P. J. Patel, V. K. Patel and P. K. Bhattacharya, *Indian J. Chem., 21,* 590 (1982).
14 H. Sigel, B. E. Fischer and B. Prijs, *J. Am. Chem. Soc., 99,* 4489 (1977).
15 M. S. Mohan, D. Bancraft and E. H. Abbott, *Inorg. Chem., 18,* 344 (1979).
16 a) I. G. Sayce, *Talanta, 15,* 1397 (1968).
b) I. G. Sayce, *Talanta, 18,* 653 (1971).
c) I. G. Sayce and V. S. Sharma, *Talanta, 19,* 831 (1972).
17 H. Sigel, R. Caraco and B. Prijs, *Inorg. Chem., 13,* 462 (1974).