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Equilibrium Study of the Mixed Ligand Complexes of Copper(II)–Amino Acids and 2,2'-Bipyridyl with Thiodicarboxylic and Pyridine Dicarboxylic Acids

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Recently there has been an increase in the importance of mixed ligand complexes in biological systems. The role of metal ions, particularly copper ion, in biological systems has been thoroughly reviewed by Sigel [1]. The mixed-ligand chelates of Cu(II)–amino acids with 2,2'-bipyridyl, peptides and amino acids have been studied extensively [2–5]. A study of the complexing ability of thiodicarboxylic acids with Cu(II)–2,2'-bipyridyl and amino acid binary complexes and distribution of their complexes as a function of pH is worthwhile since thiocompounds of Cu(II) are used as biological active substances [6].

Our previous work on mixed-ligand chelates of uranyl ion with thiodicarboxylic and pyridine dicarboxylic acids showed that the coordination takes place through O–O and N–O donor atoms respectively [7]. In view of a recent article by Rayford [8] on a Cr(III) complex of dipicolinic (pyridine-2-6-dicarboxylic acid) and its structure and the series of papers by Edwards *et al.* [9] on fluoride crystal structures in which they describe the tridentate nature of dipicolinic acid with Mo(VI) from X-ray diffractometer data, we undertook this study to examine the coordination tendency of these ligands with copper ion and to draw conclusions about possible equilibria and the mode of bonding in the complex species involved.

Experimental

The measurements were carried out as described previously and the procedure of calculation was used [10, 11]. The stock solution of copper perchlorate was prepared and its concentration was estimated by EDTA titrations. The ligands were obtained from Fluka (Germany) and B.D.H. (AnalaR), India, and the purity was checked by their melting points. All solutions were prepared in doubly distilled water. The mixed-ligand stabilities and other equilibrium constants were evaluated by the method of Ramamoorthy and Manning [12] using an IBM 370/155 computer at the Indian Institute of Technology, Madras.

Results and Discussion

When a metal ion is in equilibrium with two different ligands, X and Y, both of which can form bis complexes with the metal ion, equilibria [1–7] forming simple non-protonated complexes will be present:

$$K_{MX_1} = K(M + X \rightleftharpoons MX) \quad (1)$$

$$K_{MX_2} = K(M + X \rightleftharpoons MX_2) \quad (2)$$

$$K_{2XY} = K(MX + Y \rightleftharpoons MXY) \quad (3)$$

$$K_{MY_1} = K(M + Y \rightleftharpoons MY) \quad (4)$$

$$K_{MY_2} = K(MY + Y \rightleftharpoons MY_2) \quad (5)$$

$$K_{2YX} = K(MY + X \rightleftharpoons MXY) \quad (6)$$

$$\beta_{XY} = K(M + X + Y \rightleftharpoons MXY) \quad (7)$$

The two equilibrium constants involving the ternary complex are defined by Sigel [13], ΔlogK (equation 8)

$$\Delta\log K = \log K_{2XY} - \log K_{MY_1} = \log K_{2YX} - \log K_{MX_1} \quad (8)$$

The disproportionation constant is given by the reaction $K_{DXY} = K(MX_2 + MY_2 \rightleftharpoons 2MXY)$. Thus ΔlogK is a measure of the affinity that Y has for bonding to the aquated metal ion and to the complex (MX). Since more coordination sites are available for bonding the first ligand to a metal ion than for the second ligand, ΔlogK should, in general, be negative. K_{DXY} is a disproportionation constant and a value of 0.6 log units is to be expected statistically. The value of K_{DXY} is clearly dependent on the stabilities of the binary bis complexes since these complexes are not intermediates in the formation of ternary complexes.

Metal complex formation constants for the binary complexes studied in this work are reported in Table I and measured values for the formation constants for the ternary complexes are in Table II. Cu(II) forms 1:1 and 1:2 complexes with all the ligands except thiodipropionic acid. In most cases the formation constants are close to comparable values reported in the literature but the values differ for different experimental conditions.

In the present investigation, aspartic, glutamic and 2,2'-bipyridyl can be considered as primary ligands and thiodiglycolic, thiodipropionic, quinolinic, dipicolinic (which can form eight, ten, five and five membered rings) as secondary ligands respectively. A comparison of the values for stability constants in

TABLE I. Complex Formation Constants (logK) for the Parent Binary Complexes of Copper(II) at 30 °C and μ = 0.1 M ($NaClO_4$). Standard deviations are given in parentheses.

Ligand/acids	$\log K_1$	$\log K_2$
2,2′-Bipyridyl	8.10(2) 8.10[a] 8.15[b]	5.34(3) 5.34[a] 5.50[b]
Glutamic	7.85(4) 7.87[b] 7.74[b] 8.27[c]	6.30(2) 6.29[b] 6.30[b] 6.47[c]
Aspartic	8.40(1) 8.40[b] 8.80[c]	6.75(3) 6.78[b] 6.96[c]
Dipicolinic	6.15(2) 6.30[b]	4.32(2)
Quinolinic	5.29(4)	2.86(3)
Thiodiglycolic	4.58(3) 4.57[b]	3.20(2) 3.18[b]
Thiodipropionic	2.55(2) 2.53[b]	

[a] Ref. 15. [b] Ref. 19. [c] Ref. 2 and 3.

Table I suggests that glutamic acid bonds glycine-like whereas aspartic acid must be tridentate, as confirmed the findings of other workers [14, 15]. The coordination in Cu(II)–quinolinic acid can take place in two ways: the chelation through O–O donor atoms would give a seven membered ring whereas a five membered ring is formed when the nitrogen of the pyridine ring is involved in the chelation. The geometry of pyridine 2-6-dicarboxylate ligands is unremarkable [9] and the Cu–N and Cu–O coordination is possible by displacement of the water molecules from the equatorial plane, and ligand acid must be tridentate. More recently, similar coordination of this ligand has been reported [8, 9] on the basis of X-ray diffraction data and equilibrium constants for molybdenum and chromium complexes respectively. In the case of thiodiglycolic and thiodipropionic acids, if only the carboxylate ions were bonding [16], one would except smaller formation constants and this type of coordination is recorded for uranyl complexes [17]. In the present study, observed values of equilibrium constants lead to the conclusion that the coordination occurs through sulphur and oxygens of carboxylate ions in thiodiglycolic, and through O–O donor atoms for thiodipropionic acid.

The negative ΔlogK (Table II) show the preferential formation of ternary complexes to the binary ones. However, a positive ΔlogK is observed in the 2,2′-bipyridyl–thiodipropionic acid system. A literature search revealed that positive ΔlogK is obtained when one ligand is N–N donor and the other O–O donor atoms, in agreement with the earlier finding of Sigel [1, 5]. Additionally, in this system the mixed-ligand is formed by the disproportionation reaction $MX + MY_2 \rightleftharpoons MXY + MY$. The tendency of mixed-ligand chelate formation is the same in the case of glutamic–dipicolinic, aspartic–thiodiglycolic, aspartic–dipicolinic and 2,2′-bipyridyl–thiodiglycolic; ΔlogK = –0.79, –0.72, –0.71 and –0.74 respectively.

In all the cases in Table II, the values of K_{DXY} are significantly greater than 0.6, suggesting that the ternary complexes are very stable relative to their binary analogues. A comparison of K_{2YX} values with K_{MX_2} and K_{2XY} with K_{MY_2} indicates the ternary complexes are much more stable than the binary. In the systems involving 2,2′-bipyridyl as a primary ligand the mixed complexes are stable as compared to their binary complexes, due to the neutralisation of the charge of mixed complexes [18],

$$MY_2^{2+} + MX_2^{2-} \rightleftharpoons 2MXY^{\circ}$$

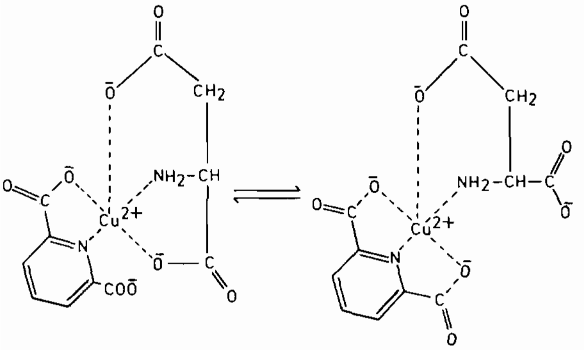
In addition to this, it is seen that when a mixed ligand chelate can be formed from a neutral and negative

TABLE II. Complex Formation Constants for the Ternary Complexes of Cu(II)-amino Acids and 2,2′-Bipyridyl with Some Dicarboxylic Acid at 30 °C and μ = 0.1 M ($NaClO_4$). Standard deviations are given in parentheses.

System/acid	β_{XY}	K_{DXY}	K_{2XY}	K_{2YX}	ΔlogK
Glutamic–thiodiglycolic	11.87(2)	1.81	7.29	4.02	–0.56
Glutamic–thiodipropionic	9.46(1)	0.61	6.93	1.61	–0.92
Glutamic–quinolinic	11.56(1)	0.82	6.27	3.71	–1.58
Glutamic–dipicolinic	13.21(3)	1.80	7.06	5.36	–0.79
Aspartic–thiodiglycolic	12.26(4)	1.59	7.68	3.86	–0.72
Aspartic–thiodipropionic	10.34(2)	1.04	7.81	1.94	–0.61
Aspartic–quinolinic	12.32(3)	1.35	7.03	3.92	–1.37
Aspartic–dipicolinic	13.84(1)	2.05	7.69	5.44	–0.71
2,2′-Bipyridyl–thiodiglycolic	11.94(2)	2.66	7.36	3.84	–0.74
2,2′-Bipyridyl–thiodipropionic	10.99(2)	3.10	8.44	2.89	+0.34
2,2′-Bipyridyl–dipicolinic	12.91(3)	1.91	6.76	4.81	–1.34

ligand both enthalpy and entropy effects favour the mixed ligand chelate over the disproportionation products.

Aspartic acid forms mixed complexes of exceptionally high stability with all the four dicarboxylic acids, due to the fact that this ligand is capable of both glycine- and β-alanine-like coordination. The increase in stability constant is associated with the higher number of coordination possibilities. The significantly higher value, *i.e.* 2.05 of K_{DXY} for the aspartic–dipicolinic acid system accompanied by the highest stability of ternary complex may be due to the tridentate nature of these ligands. For dipicolinic acid, assuming equatorial coordination, there is also the possibility of the $-COO^-$ group displacing the α-COO^- group of the aspartic acid from the coordination sphere to a certain extent, with the formation of a mixed complex as a result of the subsequent structural rearrangement. The ternary complex in which equatorial and equatorial–axial coordination of dipicolinic and aspartic acids respectively take place is much more stable than the other.



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