Stability and Structure of some Binary and Mixed-ligand Complexes of Zinc(II)

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The stability and structure of ZnBH, ZnB, ZnB_2H_2, ZnB_2H, or ZnB_2 types of binary complexes in the Zn^{II}–DL-2,3-diaminopropionic acid (dapa), –DL-2,4-diaminobutyric acid (daba), and –DL-ornithine (Orn) (B); and $ZnABH_2$, ZnABH, or ZnAB types of mixed-ligand complexes in the Zn^{II}–histamine/L-histidine (A)–dapa,–daba, and –Orn (B) systems are discussed from the computer-based analysis of the pH titration data at 37 °C and I = 0.15 mol dm^{-3} ($NaClO_4$). In both the binary and mixed-ligand systems, dapa, daba, and Orn (B) appear to be tridentate. The results clearly demonstrate that in the ZnBH, ZnB_2H_2, and ZnB_2H binary complexes and ZnABH mixed species the site of protonation is the terminal amino-group of ligand B. In the $ZnABH_2$ complexes, one proton is attached to the ligand A and other to the ligand B. In the Zn^{II}–histidine (A)–dapa,–daba, and – Orn (B) systems, the results suggest the histamine-like mode of binding for L-histidine (A). More than the statistical order of stabilities was observed for most of the mixed-ligand complex species detected in the present investigation.

Considerable attention has been paid in recent years to the investigation of the complex forming properties of potentially tridentate ligands such as histidine, serine, threonine, tryptophan, tyrosine, and diaminocarboxylic acids because such studies are closely connected with peptide and complex chemistry.[1–4] Since the third donor group in the diaminocarboxylic acids of general formula $NH_2(CH_2)_nCH(NH_2)COOH$, where n = 1 (2,3-diaminopropionic acid), n = 2 (2,4-diaminobutyric acid), n = 3 (ornithine), and n = 4 (lysine), is the nitrogen atom which is able to co-ordinate with hydrogen ions at intermediate pH values, there is often significant competition between hydrogen and metal ions for co-ordinating with the third donor group, resulting in a number of complex equilibria. Thus investigations on the metal complexes of diaminocarboxylic acids have been carried out by several workers.[3,5–10] The first reports on these lines were made by Albert.[5] Copper(II) complexes of diaminocarboxylic acids have been well studied.[6–8] Brookes and Pettit[6] investigated the diaminocarboxylic acid complexes of Co^{II} and Ni^{II} also. However, no detailed studies have been carried out on the Zn^{II} binary complexes of diaminocarboxylic acids. The present paper deals with the stability and structure of Zn^{II} complexes with three diaminocarboxylic acids, namely DL-2,3-diaminopropionic acid (dapa), DL-2,4-diaminobutyric acid (daba), and DL-ornithine (Orn). Again, bearing in mind the outstanding biological significance of the metal complexes containing imidazole and its derivatives, the Zn^{II}–A–B mixed-ligand systems [A = L-histidine, histamine, or imidazole; B = dapa, daba, or Orn] were also investigated by pH titrimetry at 37 °C and at I = 0.15 mol dm^{-3} ($NaClO_4$).

Experimental

The methods of preparation and determination of $Zn(ClO_4)_2$ and of other reagents are described earlier.[8–12] All the ligands used were obtained from Fluka. Doubly-distilled water was used for the preparation of all the solutions. The pH titrations were carried out at 37 °C under a nitrogen atmosphere (freed from oxygen and CO_2) with the apparatus and procedure described elsewhere.[8–12] A constant ionic strength of 0.15 mol dm^{-3} was maintained by the addition of sodium perchlorate.

Table 1. Values of protonation constants (ref. 14) for histamine and L-histidine ligands and their parent binary stability constants with Zn^{II} at 37 °C and I = 0.15 mol dm^{-3} ($NaClO_4$). Standard deviations are given in parentheses

	A	
Parameter	Histamine	L-Histidine
log β_{HA}	9.39(8)	8.96(3)
log β_{H_2A}	15.34(1)	14.96(5)
log β_{H_3A}	—	17.37(9)
log β_{ZnAH}	11.91(5)	—
log β_{ZnA}	5.39(3)	6.41(2)
log $\beta_{ZnA_2H_2}$	—	22.80(12)
log β_{ZnA_2H}	—	17.47(9)
log β_{ZnA_2}	10.45(4)	11.74(2)
log $K^{ZnA}_{ZnA_2}$	5.06	5.33

Table 2. Stability constants for the parent binary Zn^{II}–dapa,–daba, and –Orn (B) systems at 37 °C and I = 0.15 mol dm^{-3} ($NaClO_4$). Standard deviations are given in parentheses

	B		
Parameter	dapa	daba	Orn
log β_{HB} *	9.37(2)	9.93(2)	10.22(1)
log β_{H_2B} *	15.98(3)	18.02(4)	18.85(2)
log β_{H_3B} *	17.37(5)	19.88(6)	20.99(4)
log β_{ZnBH}	13.61(4)	14.22(4)	14.56(2)
log β_{ZnB}	—	—	6.69(3)
log $\beta_{ZnB_2H_2}$	25.70(3)	27.04(16)	27.83(11)
log β_{ZnB_2H}	—	21.47(4)	—
log β_{ZnB_2}	13.70(2)	13.44(4)	—
log P	4.24	4.29	4.34
log P'	6.96	7.18	7.39
log $K^{ZnBH}_{ZnB_2H}$	—	7.05	—
pK^{H}_{ZnBH}	—	—	7.87

* From ref. 8.

Calculations were made with the aid of the MINIQUAD-75 computer program[13] on an IBM-370 computer. Various models were fitted to the data and the model selected was that which gave the best statistical fit, consistent with chemical logic,

Table 3. Stability constants for the Zn^{II}–histamine (A)–dapa,–daba, and –Orn (B) mixed systems at 37 °C and I = 0.15 mol dm^{-3} ($NaClO_4$). Standard deviations are given in parentheses

	B		
Parameter	dapa	daba	Orn
$\log \beta_{ZnAB}$	—	12.87(8)	11.56(3)
$\log \beta_{ZnABH}$	—	19.65(15)	19.33(3)
$\log \beta_{ZnABH_2}$	25.44(8)	26.22(14)	26.59(7)
$\log K^{ZnA}_{ZnAB}$	—	7.48	6.17
$\log K^{ZnB}_{ZnAB}$	—	—	4.87
$\Delta \log K_{ZnAB}$	—	—	−0.52
$\log X_{ZnAB}$	—	1.85	—
pK^{H}_{ZnABH}	—	6.78	7.77
$\log K^{ZnA}_{ZnABH}$	—	14.26	13.94
$\Delta \log K_{ZnABH}$	—	−0.04	−0.62
$\log X_{ZnABH}$	—	1.81	0.38
$\log K^{ZnAH}_{ZnABH_2}$	13.53	14.31	14.68
$\log K^{ZnBH}_{ZnABH_2}$	11.83	12.00	12.03
$\Delta \log K_{ZnABH_2}$	−0.08	+0.09	+0.12

Table 4. Stability constants for the Zn^{II}–L-histidine (A)–dapa,–daba, and –Orn (B) mixed systems at 37 °C and I = 0.15 mol dm^{-3} ($NaClO_4$). Standard deviations are given in parentheses

	B		
Parameter	dapa	daba	Orn
$\log \beta_{ZnAB}$	—	—	11.69(15)
$\log \beta_{ZnABH}$	19.03(2)	—	20.30(2)
$\log \beta_{ZnABH_2}$	25.66(16)	26.81(15)	27.10(2)
$\log K^{ZnA}_{ZnAB}$	—	—	5.28
$\log K^{ZnB}_{ZnAB}$	—	—	5.00
$\Delta \log K_{ZnAB}$	—	—	−1.41
$\log K^{ZnA}_{ZnABH}$	12.62	—	13.89
$\log K^{ZnBH}_{ZnABH}$	5.42	—	5.74
$\Delta \log K_{ZnABH}$	−0.99	—	−0.67
$\log X_{ZnABH}$	0.62	—	1.03
$\log K^{ZnBH}_{ZnABH_2}$	12.05	12.59	12.54
$pK^{H}_{ZnABH_2}$	6.63	—	6.80
$\log X_{ZnABH_2}$	2.82	3.78	3.57

to the range of titration data without giving any systematic drifts in the magnitudes of various residuals. At high pH values, hydroxo-complexes were often present. Since these data could not be fitted satisfactorily to any simple model, points above the onset of a systematic drift in residuals were omitted. The results obtained are reported in Tables 2—4. Though the binary stability constant data of Zn^{II}–histamine and –L-histidine (A) systems have been reported previously,[14] they have been included in Table 1 as these constants have been used in the present study for the computation of mixed-ligand stability constant data. The species distribution plots obtained for the binary systems and two mixed-ligand systems are given in Figures 1—3. The charges of all the complex species reported in this paper are omitted for clarity.

Results and Discussion

Binary Complexes of Zinc(II) *with dapa, daba, and Orn.*—Our results from the detailed titration studies indicate that the Zn^{II}–dapa (B) system contains ZnBH, ZnB_2H_2, and ZnB_2 as the major species, while the Zn^{II}–daba (B) system showed the presence of ZnBH, ZnB_2H_2, ZnB_2H, and ZnB_2 complexes in addition to the species HB, H_2B, and H_3B. In the Zn^{II}–Orn (B) system, the species HB, H_2B, and H_3B along with the complexes

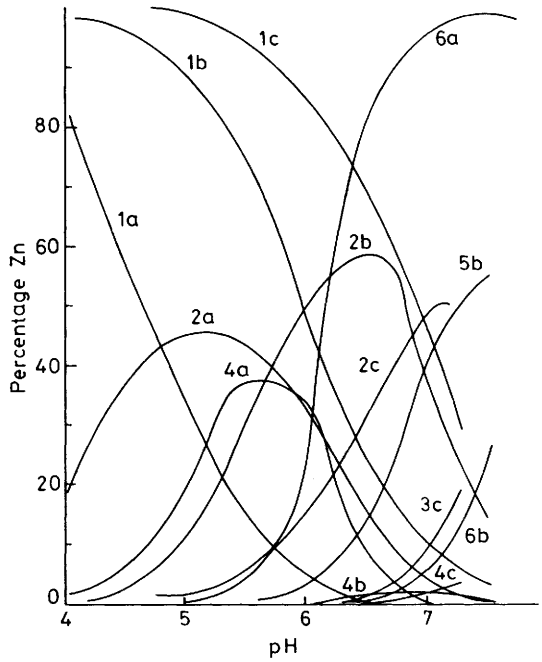

Figure 1. Distribution diagram for the Zn^{II}–B (1:2) systems: (a) dapa, (b) daba, (c) Orn. (1) Unbound Zn, (2) ZnBH, (3) ZnB, (4) ZnB_2H_2, (5) ZnB_2H, and (6) ZnB_2

ZnBH, ZnB, and ZnB_2H_2 were detected. The ZnBH species in all the above systems were found to be favoured at low pH (Figure 1), indicating that the extra proton in this complex species can attach to any one of the two amino-groups, preferably to the terminal amino-group of the ligand B. In order to characterise the metal–ligand binding, the parameter log P was computed using equation (1). The value obtained in all the

$$\log P = \log \beta_{ZnBH} - \log \beta_{HB} \quad (1)$$

three systems (Table 2) compares favourably with the value of the overall formation constant for the ZnA glycine complex.[3] This clearly suggests that an α-amino-carboxylate chelation is involved resulting in a five-membered chelate ring in the ZnBH (B = dapa, daba, or Orn) complexes with the proton residing on the respective terminal amino-groups.

Of the several complex species that contain Zn^{II} and dapa, daba, or Orn ligands (B) in the ratio 1:2, ZnB_2H_2 is the one formed at the lowest pH values, accounting for a maximum of *ca.* 38% at pH 5.5 in the Zn^{II}–dapa system, *ca.* 3% at pH 4.3 in the Zn^{II}–daba system, and *ca.* 4.5 in the Zn^{II}–Orn system (Figure 1). Here it may be mentioned that since the percentage of Zn^{II} in the form of ZnB_2H_2 in the Zn^{II}–daba and –Orn (B) systems was found to be very low, the chemical models excluding these complex species were also tested. However, for obtaining the best-fit statistical model the inclusion of these complex species was found to be essential. The less preference for the formation of ZnB_2H_2 species in the systems with B = daba or Orn is also evident from the values of their formation constants (Table 2) with very high standard deviations. As discussed above, since the extra proton in the ZnBH (B = dapa, daba, or Orn) complexes is attached to the corresponding terminal amino-groups of the ligand, it may be easily concluded that in the $Zn(BH)_2$ complex also, the protonation sites are the terminal amino-groups of the two ligands. This becomes clearer if it is noted that the log P' values in Table 1 derived from equation (2) are comparable to the values of the overall formation constants

for the ZnA_2 glycine complex.[3] Thus in the ZnB_2H_2 (B = dapa, daba, or Orn) complexes, the two ligands bind the metal in a

$$\log P' = \log \beta_{ZnB_2H_2} - 2 \log \beta_{HB} \quad (2)$$

glycine-like mode resulting in two five-membered chelate rings with the two protons residing on their terminal amino-groups.

Only in the Zn^{II}–daba system, the best-fit model contained ZnB_2H species, accounting for *ca.* 55% of the total metal at pH 7.5. Since the site of protonation is the terminal amino-group of daba in its ZnBH complex, it may be concluded that in its ZnB_2H complex also the proton is attached to the terminal amino-group of one among the two daba ligands. The log $K^{ZnBH}_{ZnB_2H}$ value of 7.05 is of the order expected for the tridentate binding of B^- in the Zn(BH)B complex. Thus in the ZnB_2H (B = daba) complex, one among the two ligands binds the metal with all three donor groups and the other ligand binds the metal in glycine-like mode with its terminal amino-group being protonated.

It is surprising to note that the Zn^{II}–Orn system showed the presence of ZnB species, while the ZnB_2 complex was not detected. The reverse was the case in the Zn^{II}–dapa and –daba (B) systems. About 20% of the total metal was found to be present in the form of ZnB in the Zn^{II}–Orn system. Albert[5] reported a value of 4.10 log units at 25 °C for the ZnB–Orn complex and concluded that Orn binds Zn^{II} in a glycine-like mode. But the present investigation gives a value of 6.69 log units, indicating the possibility of the binding of Orn in a tridentate manner though it would involve one seven- and one five-membered chelate rings. However, it is not surprising because in the Ni^{II} and Co^{II} complexes containing the potentially tridentate ligands such as Orn, lysine, or arginine also, these ligands at high pH range bind the metal with all the three co-ordination groups, although the chelate rings formed by the two nitrogen donors would be abnormally large.[6] However, in the Cu^{II}–Orn, –lysine, or –arginine binary systems these ligands bind the metal in a glycine-like mode.[6–8] In the Zn^{II}–Orn system in the present investigation the ZnB complex was found to be favoured at high pH (Figure 1). Thus, analogous to the NiB and CoB (B = Orn) complexes, it is justified that Orn binds Zn^{II} in a tridentate manner. Since Orn is tridentate in its ZnB complex involving one five- and one seven-membered chelate ring, one would expect the ZnB_2 (B = Orn) complex species to contain two five- and two seven-membered chelate rings which must be less favoured due to steric reasons.

At pH 7.5, the respective amounts of the total Zn^{II} present in the form of ZnB_2 species in the Zn^{II}–dapa and –daba systems are 99 and 26%. The log β_{ZnB_2} values of 13.70 and 13.44 respectively in the above two systems (Table 2) are higher than those values expected for the bidentate binding of both ligands, indicating that both the ligands must be tridentate in their respective ZnB_2 complexes. However, since the log β_{H_3B} value of 19.88 for daba is higher than that of 17.37 for dapa, one should expect a higher log β value for the ZnB_2 (B = daba) complex than that for the dapa complex. However, the results in Table 2 indicate the opposite trend. This may probably be accounted for by considering the steric factors associated with the two six- and two five-membered chelate rings in the ZnB_2 (B = daba) complex in comparison with the four five-membered chelate rings in the ZnB_2 (B = dapa) complex.

Mixed-ligand Systems of Zinc(II).—Six mixed-ligand systems, namely Zn^{II}–histamine (A)–dapa, –daba, or –Orn (B) and Zn^{II}–L-histidine (A)–dapa,–daba, or –Orn (B) are discussed in this section (see Tables 3 and 4 and Figures 2 and 3). The Zn^{II}–imidazole (A)–dapa,–daba, or –Orn (B) systems were also studied, but no appreciable complexing was revealed. The Zn^{II}–histamine (A)–daba or –Orn (B) mixed-ligand systems showed

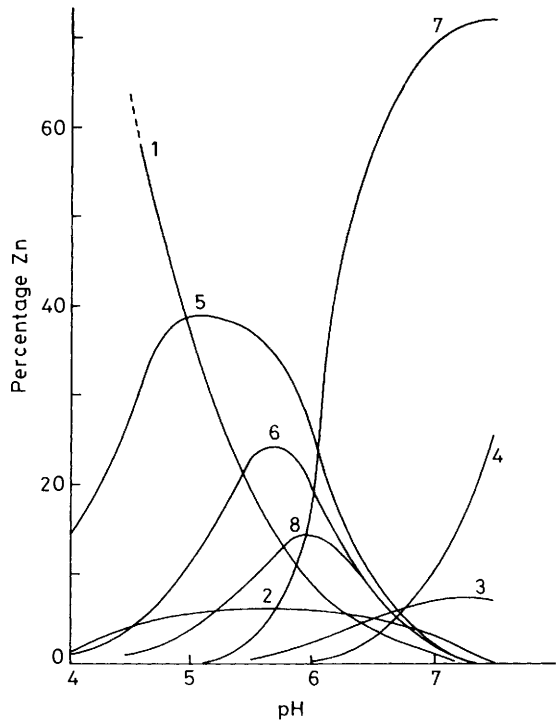

Figure 2. Distribution diagram for the Zn^{II}–histamine (A)–dapa (B) system ($C_M = 2.948 \times 10^{-3}$, $C_A = 4.492 \times 10^{-3}$, $C_B = 4.484 \times 10^{-3}$ mol dm^{-3}). (1) Unbound Zn, (2) ZnAH, (3) ZnA, (4) ZnA_2, (5) ZnBH, (6) ZnB_2H_2, (7) ZnB_2, and (8) $ZnABH_2$

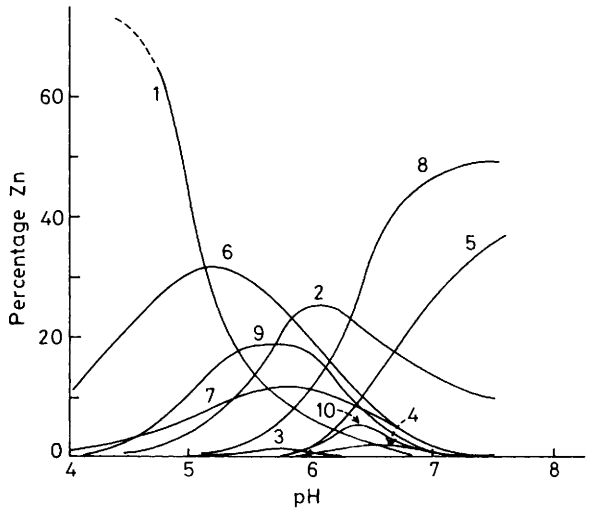

Figure 3. Distribution diagram for the Zn^{II}–L-histidine (A)–dapa (B) system ($C_M = 2.948 \times 10^{-3}$, $C_A = 3.054 \times 10^{-3}$, $C_B = 2.988 \times 10^{-3}$ mol dm^{-3}). (1) Unbound metal, (2) ZnA, (3) ZnA_2H_2, (4) ZnA_2H, (5) ZnA_2, (6) ZnBH, (7) ZnB_2H_2, (8) ZnB_2, (9) $ZnABH_2$, and (10) ZnABH

the presence of three mixed complexes ($ZnABH_2$, ZnABH, and ZnAB), while in the Zn^{II}–histamine (A)–dapa (B) system only the $ZnABH_2$ species was detected. In all the three mixed-ligand systems with histidine as the primary ligand (A), the $ZnABH_2$ type of mixed species was detected. In addition to this species, the system with B = dapa showed the presence of ZnABH species while in the system with B = Orn, ZnABH and ZnAB were also detected. During the computation of mixed-ligand

complex stability, the stability constants for the binary complexes of zinc(II) with the ligands A and B estimated under identical conditions (Tables 1 and 2) were treated as non-refinable parameters.

Stability and Structure of ZnAB *Mixed Complexes.*—The ZnAB complexes in the Zn^{II}–histamine (A)–daba and –Orn (B) systems and Zn^{II}–histidine (A)–Orn (B) systems were found to be favoured above pH 6.5 and there is a steady increase in their formation with rise in pH. The log β_{ZnAB} values of 11.56 and 11.69 respectively in the systems Zn^{II}–histamine (A)–Orn (B) and Zn^{II}–histidine (A)–Orn (B) are comparable within the limits of experimental error. This indicates that histidine in its ZnAB species binds in a histamine-like manner. This is also reflected in the log K^{ZnB}_{ZnAB} and log K^{ZnA}_{ZnAB} values in Table 4 for the Zn^{II}–histidine (A)–Orn (B) system. If histidine were tridentate in the ZnAB species also, as is the case with the ZnA histidine binary species,[14] one should expect the log K^{ZnB}_{ZnAB} and log β_{ZnA} values to be comparable. However, the log K^{ZnB}_{ZnAB} value of 5.00 is *ca.* 1.4 log units less than the log β_{ZnA} value for the Zn^{II}–histidine system (Tables 1 and 4). This clearly indicates a difference in the bonding of histidine in the mixed and binary complex species. The log K^{ZnB}_{ZnAB} value of 5.00 is nearly identical to the log β value of 5.39 for the ZnA histamine complex. Therefore it can be concluded that in the ZnAB mixed species in the Zn^{II}–histidine (A)–Orn (B) system, histidine binds in a histamine-like manner. The same conclusion may further be confirmed from the fact that the log K^{ZnA}_{ZnAB} value of 5.28 is lower than the log K^{Zn}_{ZnB} value in the Zn^{II}–Orn (B) binary system by *ca.* 1.4 log units. This is because, for the computation of log K^{ZnA}_{ZnAB}, equation (3), the value of log β_{ZnA} used was

$$\log K^{ZnB}_{ZnAB} = \log \beta_{ZnAB} - \log \beta_{ZnA} \quad (3)$$

that for the tridentate binding of histidine (A) in its ZnA binary complex, though it is bidentate in the ZnAB mixed species. If the allowance for this difference in binding of histidine in its binary and mixed complex species is made, then the log K^{ZnA}_{ZnAB} value in Table 4 clearly demonstrates that Orn is tridentate in the ZnAB species in the Zn^{II}–histidine (A)–Orn (B) system. Again, the log K^{ZnA}_{ZnAB} values of 7.48 and 6.17 respectively in the Zn^{II}–histamine (A)–daba and –Orn (B) systems (Table 3) are very close to those expected for the tridentate binding of daba and Orn. The log K^{ZnB}_{ZnAB} value of 4.87 in the system with B = Orn is of the order expected for the bidentate binding of histamine (A) in its ZnAB complex. This parameter could not be computed for the system where B = daba because the stability constant datum for the ZnB (B = daba) complex could not be obtained in the present investigation (Table 2). However, comparison of the log β_{ZnAB} value of 12.87 in this system with the value (11.56) obtained in the Zn^{II}–histamine (A)–Orn (B) system clearly suggests that histamine is bidentate in the former system also. Since the log β_{H_3B} values are in the order Orn > daba (Table 2), one should expect a higher log β_{ZnAB} (or log K^{ZnA}_{ZnAB}) value for the Zn^{II}–histamine (A)–Orn (B) system compared to that for the Zn^{II}–histamine (A)–daba (B) system. The opposite trend (Table 3) observed may be accounted for by steric factors since one five-, one six-, and one seven-membered chelate ring are present in the ZnAB species in the ternary system with B = Orn compared to the one five- and two six-membered chelate rings in the ZnAB species in the system with B = daba. Thus the results on the ZnAB complexes in the Zn^{II}–histamine (A)–daba and –Orn (B) systems and Zn^{II}–histidine (A)–Orn (B) system show that this complex species would have an octahedral structure with one of its faces being occupied by the secondary ligand (B), two other sites of the other face would be occupied by the histamine or histidine (A) ligand, and the third site of this face would be completed by the solvent water molecule.

In order to characterize the stability of the ZnAB mixed species with respect to the corresponding binary analogues, the parameters Δ log K_{ZnAB} [equations (4) and (5)] and log X_{ZnAB} [equations (6) and (7)] are computed. On statistical

$$ZnA + ZnB \rightleftharpoons ZnAB + Zn \quad (4)$$

$$\Delta \log K_{ZnAB} = \log \beta_{ZnAB} - (\log \beta_{ZnA} + \log \beta_{ZnB}) \quad (5)$$

$$ZnA_2 + ZnB_2 \rightleftharpoons 2\ ZnAB \quad (6)$$

$$\log X_{ZnAB} = 2 \log \beta_{ZnAB} - (\log \beta_{ZnA_2} + \log \beta_{ZnB_2}) \quad (7)$$

grounds,[1,15] in general considerably less negative Δ log K and more positive log X values indicate the marked stabilities of the mixed complexes. The values expected[1,15] statistically for these two parameters for Zn^{II} mixed-ligand complexes are −0.6 and +0.6 respectively. The Δ log K_{ZnAB} value of −0.52 for the Zn^{II}–histamine (A)–Orn (B) system falls within the statistical order. The value of log X_{ZnAB} could not be calculated in this system as log β for the ZnB_2 (B = Orn) complex could not be obtained in the present investigation. The log X_{ZnAB} value of 1.85 for the Zn^{II}–histamine (A)–daba (B) system is very much higher than that statistically expected[1,15] (+0.6) indicating the preference for the formation of ZnAB ternary complexes compared to the formation of ZnA_2 or ZnB_2 binary complexes. The Δ log K_{ZnAB} value could not be computed in this system as the stability constant datum for the ZnB (B = daba) complex could not be obtained (Table 2). The value of −1.41 for Δ log K_{ZnAB} for the Zn^{II}–histidine (A)–Orn (B) system is very highly negative. This may probably be accounted for by considering the fact that for the computation of this parameter [equation (5)], the log β_{ZnA} value used was that for the tridentate binding of histidine, though it is bidentate in the ZnAB mixed species as discussed earlier. If allowance is made for this difference in binding of histidine in the binary and mixed species, one can easily conclude from the Δ log K_{ZnAB} value that the ZnAB mixed species in this system is markedly stabilized.

Stability and Structure of ZnABH *Mixed Complexes.*—The ZnABH species in the Zn^{II}–histamine (A)–daba and–Orn (B) and Zn^{II}–histidine (A)–dapa and –Orn (B) systems were found to be favoured above pH 5.5. With regard to the site of protonation in these ZnABH species, it seems that the proton is attached to the secondary ligand, B, possibly to its terminal amino-group as is the case with ZnBH or ZnB_2H_2 (B = dapa, daba, or Orn) complexes. This would become more apparent if a comparison is made between the pK^{H}_{ZnABH} and pK^{H}_{ZnBH} values. For example, in the Zn^{II}–histamine (A)–Orn (B) system the pK^{H}_{ZnABH} value of 7.77 compares favourably with the pK^{H}_{ZnBH} value of 7.87. In the system with B = daba, since the pK^{H}_{ZnBH} value is not available (Table 2), the same type of comparison is not possible. However, if the log K^{ZnA}_{ZnABH} value of 14.26 for this system is compared with the log β_{ZnBH} value of 14.22, it becomes clear that in both the mixed and binary species the same type of protonation site is involved which means that as in the case of ZnBH (B = daba) in the ZnABH mixed species also the proton is attached to the terminal amino-group of daba (B). The log K^{ZnA}_{ZnABH} values in the Zn^{II}–histidine (A) –dapa and –Orn (B) systems (Table 3) follow the trend of log β_{ZnBH} values in Table 2, demonstrating that the extra proton in the ZnABH complex species in these two ternary systems is attached to the secondary ligand (B), possibly to its terminal amino-group. The log K^{ZnBH}_{ZnABH} values of 5.42 and 5.74 respectively in the above two systems are slightly greater than the log β value of 5.39 for the ZnA (A = histamine) complex,

but far less than the log β value of 6.41 in the ZnA (A = histidine) complex. This indicates that the most probable mode of binding of histidine (A) in the ZnABH complexes in the above two systems is histamine-like. We now consider how to account for the slightly higher log K^{ZnBH}_{ZnABH} values compared to that expected for the histamine-like mode of binding of histidine. In the light of the discussion given above, the electrostatic interaction between the free $-COO^-$ group of the histidine (A) ligand and the protonated terminal amino group, $-NH_3^+$ of the dapa or Orn (B) ligands in the ZnABH complexes would certainly give additional stabilization to these complexes and thus high log K^{ZnBH}_{ZnABH} values. The log K^{ZnA}_{ZnABH} values [equation (8)] in the Zn^{II}–histidine (A)–dapa

$$\log K^{ZnA}_{ZnABH} = \log \beta_{ZnABH} - \log \beta_{ZnA} \quad (8)$$

and –Orn (B) systems also suggest a different mode of binding of histidine in the ZnABH mixed complexes and in the ZnA histidine binary complex. If histidine were tridentate in the ZnABH mixed complexes also as in the ZnA histidine binary complex, one should expect comparable values of log β_{ZnBH} and log K^{ZnA}_{ZnABH} (Tables 2 and 4). However the former parameter, in both the systems under discussion, is *ca.* 1 log unit less than the latter suggesting a difference in binding of histidine (A) in the ZnA binary species and ZnABH mixed species; in the light of the above discussion, it can be easily concluded that histidine should be histamine-like in the ZnABH complexes, while it is tridentate in the ZnA binary species.[14]

In order to define the parameters Δ log *K* and log *X* in the case of ZnABH, the exact protonated ligand species must be taken into consideration. From the foregoing discussion, it can be seen that the above parameters can be defined by equations (9)—(12). The Δ log K_{ZnABH} value of −0.04 and log X_{ZnABH} values of

$$ZnA + ZnBH \rightleftharpoons ZnABH + Zn \quad (9)$$

$$\Delta \log K_{ZnABH} = \log \beta_{ZnABH} - (\log \beta_{ZnA} + \log \beta_{ZnBH}) \quad (10)$$

$$\log X_{ZnABH} = 2 \log \beta_{ZnABH} - (\log \beta_{ZnA_2} + \log \beta_{ZnB_2H_2}) \quad (11)$$

$$ZnA_2 + ZnB_2H_2 \rightleftharpoons 2\ ZnABH \quad (12)$$

1.81 in the Zn^{II}–histamine (A)–daba (B) system are higher than the respective statistically expected values[1,15] demonstrating the marked stabilities for the mixed complexes. However, in the Zn^{II}–histamine (A)–Orn (B) system, the Δ log K_{ZnABH} value of −0.62 and log X_{ZnABH} value of 0.38 do not deviate much from their corresponding statistically expected values. The Δ log K_{ZnABH} values in the Zn^{II}–histidine (A)–dapa and –Orn (B) systems (Table 4) are highly negative. This may again be accounted for by considering the same factors as described above for explaining the highly negative Δ log K_{ZnAB} values in the Zn^{II}–histidine (A)–Orn (B) system.

Stability and Structure of $ZnABH_2$ *Mixed Complexes.*—The $ZnABH_2$ complexes in the Zn^{II}–histamine/histidine (A)–dapa,–daba, and –Orn (B) systems were found to be favoured above pH 4.00. Regarding their solution structures, it may be predicted with a fair amount of certainty that of the two protons therein, one would be attached to the histamine/histidine (A) ligand and the other to the dapa, daba, or Orn (B) ligand. This becomes more obvious if a comparison is made between log $K^{ZnBH}_{ZnABH_2}$ and log β_{ZnAH} and also between log $K^{ZnAH}_{ZnABH_2}$ and log β_{ZnBH}. For example, the log $K^{ZnBH}_{ZnABH_2}$ values in Table 3 in all the Zn^{II}–histamine (A)–dapa,–daba, or –Orn (B) systems (the respective values are 11.83, 12.00, and 12.03) compare favourably with the log β_{ZnAH} value of 11.91 in the Zn^{II}–histamine (A) system. Again the log $K^{ZnAH}_{ZnABH_2}$ values of 13.53, 14.31, and 14.68 (Table 3) in the mixed systems with B = dapa, daba, or Orn are nearly identical to the corresponding log β_{ZnBH} values of 13.61, 14.22, and 14.56 in the Zn^{II}–dapa,–daba, and –Orn (B) binary systems (Table 2). As set out in the introduction, the extra proton in the ZnAH (A = histamine) complex is attached to the primary amino-group and the extra proton in the ZnBH (B = dapa, daba, or Orn) complexes is attached to their terminal amino-groups. The same structural characteristics can be assigned to the $ZnABH_2$ complexes in the Zn^{II}–histamine (A)–dapa,–daba, or –Orn (B) systems also. Regarding the site of protonation in the $ZnABH_2$ complexes in the Zn^{II}–histidine (A)–dapa,–daba, or –Orn (B) systems, the log $K^{ZnBH}_{ZnABH_2}$ values in Table 4 are nearly identical to each other in all the three systems suggesting that one proton must be attached to the histidine (A) ligand. A natural consequence is that the other proton must be attached to the dapa, daba, or Orn (B) ligand, possibly to their terminal amino-group as is the case with the ZnBH or ZnB_2H_2 (B = dapa, daba, or Orn) complexes as described in the introduction. However, this type of binding cannot be confirmed by comparing the log $K^{ZnAH}_{ZnABH_2}$ values because log β values for the ZnAH complex are not available (Table 1). It has already been reported[14] that in the ZnA_2H and ZnA_2H_2 (A = histidine) complexes, only the imidazole nitrogen of the histidine is involved in co-ordination with the metal with the carboxyl groups of the ligands remaining free, the extra protons attaching to the primary amino-groups. The same type of binding of histidine may be assigned for the $ZnABH_2$ species in the mixed systems with A = histidine also. These structural characteristics would be preferred because of the electrostatic interaction between the $-NH_3^+$ groups in the histidine (A) or dapa, daba, or Orn (B) ligands and the $-COO^-$ group in the histidine (A) ligand. This unidentate binding of the protonated histidine ligand may further be confirmed by noting that the log β_{ZnABH_2} values in the Zn^{II}–histamine (A) –dapa, –daba, or –Orn (B) systems (Table 3) differ from those values in Zn^{II}–histidine (A)–dapa,–daba, or –Orn (B) systems (Table 4) only by 0.2—0.4 log units. These slightly higher log β_{ZnABH_2} values in the systems with A = histidine compared to those in the corresponding systems with A = histamine may be accounted for by considering the additional stabilization for the $ZnABH_2$ complexes in the former systems due to the electrostatic interaction as discussed above.

The Δ log K_{ZnABH_2} values calculated *via* equations (13) and (14) in the Zn^{II}–histamine (A)–dapa, –daba, or –Orn systems

$$ZnAH + ZnBH \rightleftharpoons ZnABH_2 + Zn \quad (13)$$

$$\Delta \log K_{ZnABH_2} = \log \beta_{ZnABH_2} - (\log \beta_{ZnAH} + \log \beta_{ZnBH}) \quad (14)$$

(Table 3) are much less negative suggesting enhanced stabilities for the $ZnABH_2$ complexes in all these systems. However, this parameter could not be calculated for the mixed systems with A = histidine as the stability constant for the ZnAH (A = histidine) complex is not available (Table 1). However, the parameter log X_{ZnABH_2} was calculated for all the three systems with A = histidine [equations (15) and (16)] and is

$$ZnA_2H_2 + ZnB_2H_2 \rightleftharpoons 2\ ZnABH_2 \quad (15)$$

$$\log X_{ZnABH_2} = 2 \log \beta_{ZnABH_2} - (\log \beta_{ZnA_2H_2} + \log \beta_{ZnB_2H_2}) \quad (16)$$

very much higher than the corresponding statistically expected value[1,15] of +0.6, indicating the marked stabilities of the $ZnABH_2$ complexes. However, this parameter could not be calculated for the $ZnABH_2$ species in the systems with A = histamine because the stability constant for the ZnA_2H_2 species is not available (Table 1).

The distribution of various binary and mixed complexes (as percentages of total metal) as a function of pH has been calculated for all the mixed-ligand systems under study and such plots obtained for Zn^{II}–histamine (A)–dapa (B) and Zn^{II}–histidine (A)–dapa (B) are given in Figures 2 and 3 respectively. Though marked stabilities compared to the statistical case were observed for most of the mixed species detected, in none of them did the maximum amount of total Zn^{II} found in the form of mixed complex species exceed the statistically expected [1,15] 50% with regard to the parent binary species. Of course this is not surprising because usually the amount of mixed species with zinc never exceeds 50% and more often it is nearer 30%. Now it appears to be more appropriate to compare the mixed-ligand complex formation tendency of Cu^{II} and Zn^{II} in the presence of histamine/histidine (A) and dapa, daba, or Orn (B) ligands. The data available in the literature [10] on Cu^{II}–histamine/histidine (A)–dapa,–daba, or –Orn (B) mixed systems show that the $CuABH_2$, CuABH, and CuAB types of complexes in these systems have very high stabilities compared to the binary complexes and their formation was found to be appreciable in most of the systems, accounting for more than 60% of the total metal. However, the results on similar Zn^{II} mixed-ligand systems reported in this paper show that the statistical stability of the $ZnABH_2$, ZnABH, and ZnAB complexes is not that much higher than in the corresponding Cu^{II} complexes. Also the extent of Zn^{II} mixed-ligand complex formation is not appreciable when compared with the corresponding Cu^{II} mixed-ligand systems. These show that Zn^{II} mixed-ligand complex formation in the presence of the histamine/histidine primary ligand (A) is less important compared with similar Cu^{II} mixed-ligand formation. This probably can be accounted for by considering the fact that in the Zn^{II}–histamine/histidine (A) binary systems, the complex formation is favoured by the π-acceptor property of the imidazole group in both the ZnA and ZnA_2 complexes, unlike that for the similar Cu^{II} systems where this property appears only in the CuA and for steric reasons not in the CuA_2 complexes.[7,14] So, in the Cu^{II}–histamine/histidine (A)–secondary ligand (B) systems, generally there would be extensive mixed-ligand complex formation while in the Zn^{II} mixed systems containing histamine/histidine primary ligand (A), the formation of mixed complexes is less favoured and the formation of bis-complexes due to histamine/histidine ligands would be predominant.

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