Indian Journal of chemistry
Vol. 31A, April 1992, pp. 256-259

Studies on biologically relevant ternary metal complexes: Part VI—Stability of ternary Co(II), Ni(II), Cu(II) and Zn(II) complexes involving aminopolycarboxylic acids and amino acids

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Received 16 April 1991; revised and accepted 21 December 1991

Ternary metal complexes of the type MLA, where M = Co(II), Ni(II), Cu(II) and Zn(II); L = iminodiacetic acid (IMDA) or nitrilotriacetic acid (NTA) and A = glycine, alanine, valine, leucine, norleucine, phenylalanine, tryptophan, serine, threonine, methionine, aspartic acid, ethylenediamine or pyrocatechol have been investigated potentiometrically at 35°C and $\mu = 0.2\ M$ (KNO_3). The stabilities of the ternary complexes have been quantitatively compared with the stabilities of the corresponding binary metal complexes (MA) determined under identical experimental conditions. Ternary complexes containing IMDA are found to be more stable than the corresponding complexes containing NTA. With respect to ligand L, the stability of ternary complexes increases in the order: pyrocatechol ($^-O-O^-$ donor) < bidentate amino acid ($N-O^-$ donor) < ethylenediamine ($N-N$ donor). Cu(II) ternary complexes are found to be less stable than the corresponding Co(II), Ni(II) or Zn(II) complexes. Ternary Cu(II) complexes containing bis(imidazol-2-yl)methane are more stable than the corresponding complexes containing IMDA or NTA. Various factors leading to differences in the relative stabilities of the ternary complexes are discussed.

In our earlier studies of ternary metal complexes the effect of imidazole and its derivatives such as bis(imidazol-2-yl)methane (BIM) and bis(imidazol-2-yl)nitromethane (NBIM) on the stability of various ternary complexes was investigated[1-5]. In the present investigation the formation and stability of ternary Co(II), Ni(II), Cu(II) and Zn(II) complexes (MLA) involving the aminopolycarboxylic acids (L), i.e., iminodiacetic acid (IMDA) or nitrilotriacetic acid (NTA) and various ligands (A) containing $N-O^-$, $^-O-O^-$ or $N-N$ donor atoms have been investigated by *p*H-metric methods at 35°C and $\mu = 0.2M$ (KNO_3). The stabilities of these ternary complexes have been quantitatively compared with those of the corresponding binary metal complexes determined by us earlier under identical experimental conditions[5,8,9]. The relative ability of the imidazole derivative (BIM) and the aminopolycarboxylic acids in influencing the stability of the ternary Cu(II) metal complexes has been compared.

Materials and Methods

The amino acids glycine (Gly), DL-alanine (Ala), valine (Val), leucine (Leu), phenylalanine (Phe), tryptophan (Trypt), methionine (Met), serine (Ser), threonine (Thr), aspartic acid (Asp), ethylenediamine dihydrochloride (En) and pyrocatechol (Pyr) were obtained from Sigma Chemical Co., USA. Iminodiacetic acid (IMDA), nitrilotriacetic acid (NTA), ethylenediaminetetraacetic acid (EDTA), potassium hydrogen pthalate, potassium nitrate, metal nitrates and sodium hydroxide were BDH reagents of Analar grade. Stock solutions (0.02 *M*) of Co(II), Cu(II), Ni(II) and Zn(II) were prepared and standardised by complexometric titration with EDTA[6]. Carbonate-free NaOH was prepared and standardized by titrating with potassium hydrogen pthalate.

Formation constants of ternary complexes were determined by potentiometric titration of solutions containing a 1:1:1 molar ratio of ligand L, metal ion and ligand A, with standard carbonate-free NaOH. IMDA, bidentate amino acids, En and Pyr were used in diprotonated form while NTA and Asp were used in triprotonated form. The potentiometric titrations were carried out in a double walled titration cell maintained at 35°C ± 0.2. The ionic strength was maintained effectively constant at 0.2 by suitable addition of reagent grade KNO_3. Further details of the experimental procedure are given in our earlier papers[3,8,9].

Formation constants of ternary complexes

Stability constants for ternary complexes formed according to equilibrium (1)

$$ML + A \overset{K^{ML}_{MLA}}{\rightleftharpoons} MLA \qquad \ldots (1)$$

where

$$K^{ML}_{MLA} = \frac{[MLA]}{[ML][A]} \qquad \ldots (2)$$

were calculated from the *p*H-metric data using the appropriate mass balance equations given in our earlier papers[8,9]. The ternary constants were further refined with the computer program SCOGS[10].

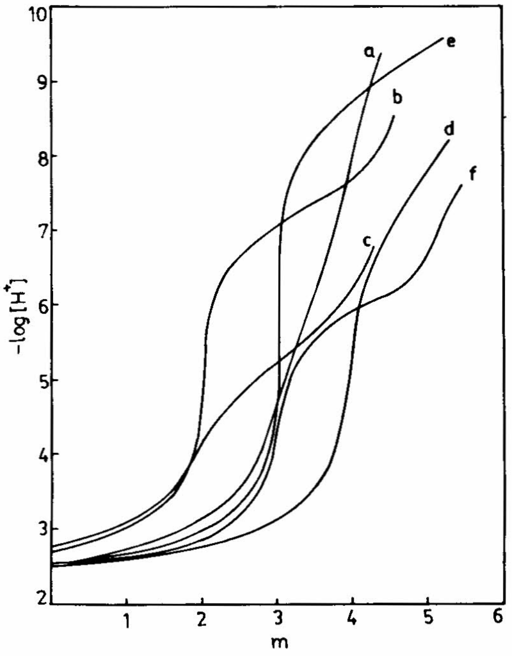

Fig. 1—Potentiometric titration curves for ternary systems containing IMDA or NTA(L), Cu(II) [M] and Ala/Trypt/Pyr/En in a 1:1:1 molar ratio [Curve a = IMDA-Cu(II)-Trypt; b = IMDA-Cu(II)-Pyr; c = IMDA-Cu(II)-En; d = NTA-Cu(II)-Ala; e = NTA-Cu(II)-Pyr; and f = NTA-Cu(II)-En. $T_L = T_M = T_A = 1.00 \times 10^{-3}$ *M*, t = 35°C; $\mu = 0.2$ *M* (KNO_3), m = mol of base added per mole of metal ion]

Results and Discussion

Representative potentiometric titration curves for ternary systems containing IMDA or NTA, Cu(II) and Ala/Trypt/Pyr/En in a 1:1:1 molar ratio are shown in Fig. 1. Formation constants (Eq. 2) were calculated from the potentiometric data and are listed in Tables 1 and 2. The stabilities of the various ternary complexes have been quantitatively compared with the stabilities of the corresponding binary complexes (determined by us earlier, under identical experimental conditions[8,9]) in terms of the parameter Δlog *K*, given by the expression

$$\Delta \log K = \log K^{ML}_{MLA} - \log K^{M}_{MA} \qquad \ldots (3)$$

These values are also listed in Tables 1 and 2. The parameter Δlog *K* is a quantitative measure of the extent to which the two ligands (L and A) in coordination sphere of the metal ion mutually influence each other. The statistical ratio for the coordination of a bidentate ligand with an octahedral [M(II)-IMDA] binary complex [M = Co, Ni or Zn] relative to the octahedrtal aquo metal ion is 3/12; hence Δlog *K* = −0.6.

The data in Table 1 show that the Δlog *K* values for ternary Co(II), Ni(II) and Zn(II) complexes in-

Table 1—Stability constants* of ternary complexes of Co(II), Ni(II) and Zn(II) containing iminodiacetic acid {Temp. = 35°C; $\mu = 0.2$ *M*(KNO_3)}

Ligand (A)	Co(II)			Ni(II)			Zn(II)		
	$\log K^{ML}_{MLA}$	$\log K^{M}_{MA}$	Δlog *K*	$\log K^{ML}_{MLA}$	$\log K^{M}_{MA}$	Δlog *K*	$\log K^{ML}_{MLA}$	$\log K^{M}_{MA}$	Δlog *K*
Glycine	3.84	4.62	−0.78	5.01	5.90	−0.89	4.02	4.86	−0.84
Alanine	3.48	4.35	−0.87	4.65	5.60	−0.95	3.93	4.80	−0.87
Valine	3.31	4.24	−0.93	4.90	5.70	−0.80	3.91	4.70	−0.79
Leucine	3.51	4.27	−0.76	4.56	5.47	−0.91	3.90	4.69	−0.79
Phenylalanine	3.05	3.90	−0.85	4.12	5.13	−1.01	3-73	4.61	−0.88
Tryptophan	3.19	4.10	−0.91	4.32	5.25	−0.93	3.57	4.59	−1.02
Serine	3.25	4.19	−0.94	4.53	5.42	−0.89	3.73	4.66	−0.93
Threonine	3.32	4.13	−0.81	4.64	5.52	−0.88	3.93	4.69	−0.76
Methionine	3.09	3.98	−0.89	4.35	5.32	−0.97	3.56	4.37	−0.81
Aspartic acid	4.49	5.78	−1.29	5.84	7.17	−1.33	3.80	5.23	−1.43
Ethylenediamine	5.18	5.81	−0.63	6.80	7.46	−0.66	5.57	6.25	−0.68
Pyrocatechol	6.55	7.69	−1.14	6.52	7.60	−1.08	6.92	8.11	−1.19

*Constants accurate to ±0.02. Binary constants K^{M}_{MA} are taken from ref. 5.

Table 2—Stability constants* of ternary Cu(II) complexes containing IMDA, NTA or BIM
{Temp. = 35.0°C; $\mu = 0.2\ M(KNO_3)$}

		IMDA		NTA		BIM†	
Ligand (A)	$\log K^{M}_{MA}$	$\log K^{ML}_{MLA}$	$\Delta\log K$	$\log K^{ML}_{MLA}$	$\Delta\log K$	$\log K^{ML}_{MLA}$	$\Delta\log K$
Glycine	8.00	6.14	−1.86	5.35	−2.65	7.25	−0.75
Alanine	7.94	5.95	−1.99	4.96	−2.98	7.29	−0.65
Valine	8.08	6.30	−1.78	5.24	−2.84	7.39	−0.69
Leucine	8.04	6.09	−1.95	5.40	−2.64	7.29	−0.75
Phenylalanine	7.64	5.84	−1.80	5.05	−2.59	7.45	−0.19
Tryptophan	7.96	6.25	−1.71	5.28	−2.68	8.15	+0.19
Serine	7.80	5.84	−1.96	5.10	−2.70		
Threonine	7.90	5.89	−2.01	5.34	−2.56		
Methionine	7.70	5.81	−1.89	5.05	−2.65	7.10	−0.60
Aspartic acid	8.38	5.79	−2.59	5.20	−3.18		
Ethylenediamine	10.32	9.32	−1.00	8.25	−2.07	9.35	−0.97
Pyrocatechol	13.64	11.28	−2.36	10.64	−3.00	13.35	−0.29

*Constants accurate to ±0.02. Binary constants K^{M}_{MA} are taken from refs 8 & 9.
†Values from ref. 4.

volving IMDA and bidentate amino acids Gly, Ala, Val, Leu, Phe, Trypt, Ser, Thr or Met are slightly more negative than expected on statistical grounds alone. The extra destabilization results from electrostatic repulsion between the negative charges on IMDA and the amino acid anion. Electrostatic repulsion between IMDA and Pyr (both of which bear two negative charges each) result in further destabilization of ternary complexes containing these two ligands. The Δlog *K* values for ternary systems containing Asp are more negative than those observed for all other systems. Asp is tridentate and dinegative and hence both statistical and electrostatic effects lead to loss of stability. Since En is a neutral molecule, the Δlog *K* values are of the statistically expected magnitiude. *p*H-Metal complex species distribution profiles for (IMDA-Ni-Ala), (IMDA-Ni-Pyr) and (IMDA-Ni-En) ternary systems were computed from the protonation and stability constant data using the computer programme Complex[11]. Typical curves are given in Fig. 2 for the IMDA-Ni(II)-En system. These plots showed that the pecentage of the ternary complex (MLA) was 88, 60 and 28, respectively, for the ligands, En, Ala and Pyr. Similar trends were observed for ternary systems containing Co(II) and Zn(II). Hence, with respect to the nature of the donor atoms on ligand A, the stability of the ternary complexes containing IMDA increase in the order: $^{-}O-O^{-} < N-O^{-} < N-N$.

The Δlog *K* values in Tables 1 and 2 show that the stabilities of ternary Cu(II) complexes containing IMDA are lower than those of the corresponding

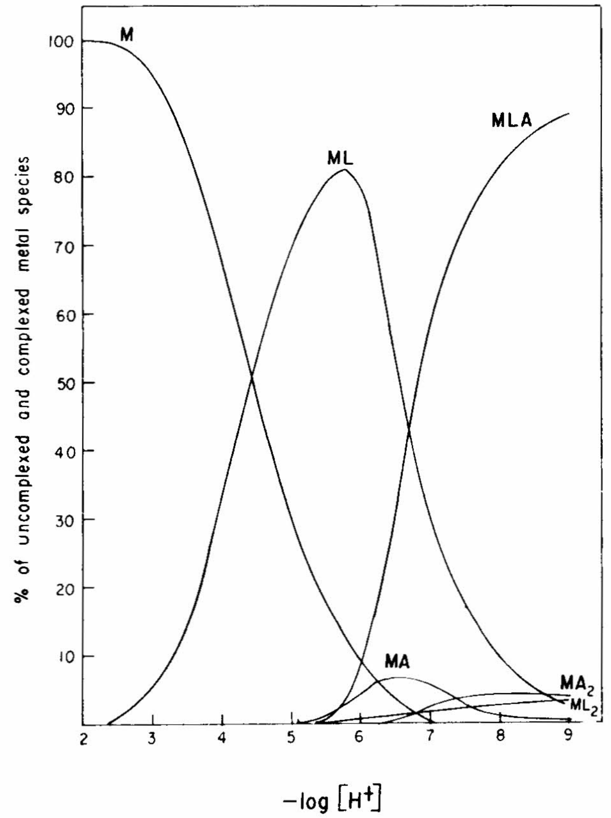

Fig. 2—*p*H-species distribution profile for the ternary 1:1:1 IMDA-Ni(II)-En system. Ordinate represents the percentage of a given metal complex species as a function of the total metal concentration {M = Ni, L = IMDA, A = ethylenediamine; [M] = [L] = [A] = 0.001 *M* each, temp. = 35°C, $\mu = 0.2\ M(KNO_3)$}

Co(II) or Zn(II) complexes. The greater destabilization could result from the fact that Cu(II) is tetragonally distorted with only four strong equitorial binding sites and two weak axial sites. It is worthwhile to compare the relative stabilities of ternary Cu(II) complexes containing IMDA, NTA and BIM. The $\Delta\log K$ values (Table 2) for ternary complexes involving BIM and amino acids without an aromatic side chain (Gly, Ala, Val, Leu, Ser, Thr and Met) are more positive relative to the corresponding complexes containing IMDA or NTA. The greater stability of BIM containing complexes may be attributed to (a) favourable statistical factor for binding the second ligand, since BIM occupies only two sites on the metal ion, whereas IMDA and NTA bind to 3 or 4 sites respectively, (b) favourable electrostatic interaction between the positively charged $(\text{Cu-BIM})^{2+}$ complex and the mononegative amino acid anion (similar stabilization does not occur with neutral (Cu-IMDA) or negative $(\text{Cu-NTA})^-$ complexes), and (c) metal-ligand back-bonding in binary $(\text{Cu-BIM})^{2+}$ complexes causing the metal centre to become more positive and hence favouring the interaction with anionic amino acids and Pyr. In binary (Cu-IMDA) and $(\text{Cu-NTA})^-$ complexes the absence of such back-bonding effects allows electron density to build up on the metal centre and interaction with ligand A is not favoured.

Ternary Cu(II) complexes containing BIM and the amino acids Phe and Trypt (which possess aromatic side chains) are considerably stabilised due to intramolecular metal ion mediated stacking interactions between the aromatic moieties of the two ligands. Due to the aliphatic nature of IMDA or NTA, such stabilizing stacking interactions do not occur. In ternary complexes containing En the stability of the complexes with respect to ligand L increases in the order NTA < IMDA < BIM. Since En is a neutral ligand the above order may primarily be consequence of a favourable statistical factor resulting from the increasing number of binding sites on the binary ML complexes. The present investigation emphasizes the important role of statistical, electrostatic, metal-ligand back-bonding and metal ion mediated stacking interactions in stabilizing ternary complexes.

Acknowledgement

A K R and G N R thank the CSIR, New Delhi for providing research fellowships.

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