

Ternary Complexes of Copper(II) Containing Some Similar Types of Amino Acids

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The stability constants of CuAB types of complexes in six ternary systems, Cu(II)-DL-alanine or β -alanine (A)-DL-2-aminobutyric acid (2-aba), DL-3-aminobutyric acid (3-aba), and 4-aminobutyric acid (4-aba) (B) have been determined pH-metrically at 37°C and $I=0.15$ (NaClO₄) in aqueous perchlorate medium. The auxiliary data like the acid dissociation constants of these ligands and the stability constants of their binary chelates with Cu(II) have also been obtained under identical conditions. The stability constant data are discussed in terms of statistical effects, steric factors and ring size influence upon chelation. In the ternary systems studied, no marked stabilization is observed compared to the statistical case. The results indicate the preferred formation of Cu(II) ternary chelates containing five and six membered rings rather than those with two rings of same size.

STUDIES of Cu(II) binary and ternary complexes containing amino acid ligands have been extensively reviewed in recent times¹⁻⁶. A number of reports⁷⁻⁹ are available on Cu(II) ternary complexes containing amino acid (A) and dipeptides, imidazoles or carboxylic acids (B). However, there have been relatively few publications dealing with the stability constant data on Cu(II) ternary complexes containing similar types of ligands. We have previously reported^{10,11} some ternary complex systems of this type, where no marked stability for ternary complex formation, compared to the statistical case, was observed. The present investigation deals with the stability constant determination of the six ternary systems, Cu(II)-DL-alanine or β -alanine (A)-DL-2-aminobutyric acid (2-aba), DL-3-aminobutyric acid (3-aba), and 4-aminobutyric acid (4-aba) (B) in aqueous perchlorate medium at 37°C and $I=0.15$ (NaClO₄) by pH-titrimetry. The amino acids employed may be classified into three groups: (i) α -amino acids (DL-alanine and 2-aba; capable of forming five-membered chelate rings); (ii) β -amino acids (β -alanine and 3-aba; capable of forming six-membered chelates) and (iii) γ -amino acid (4-aba; capable of forming seven-membered chelate ring). Thus, the ternary systems reported in this paper are expected to form ternary chelates containing five-five, six-five, seven-six, six-six and five-seven membered rings. The auxiliary data like the acid dissociation constants of these amino acids and the stability constants of their binary chelates with Cu(II) have been also evaluated under identical conditions.

Materials and Methods

All the ligands except β -alanine were obtained from Fluka. β -Alanine was of chempure sample.

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Cu(ClO₄)₂ and other reagents were prepared and standardised as described earlier¹⁰⁻¹³.

pH titrations were carried out as described earlier¹⁰⁻¹³ at 37°C and at an ionic strength of 0.15 (NaClO₄) under N₂ atmosphere using a digital pH-meter (M/s. Bhagyanagar Electronics, Hyderabad; accuracy ± 0.01 pH units) having glass and electrode assembly. The electrode system was calibrated in terms of [H⁺].

Calculations were restricted to systems below pH 7 and were made with the aid of the computer program¹⁴ MINIQUAD-75 on an IBM-370 computer. The pK_w value of 13.62 was used in the calculations. The charges for all the complex species reported in this paper were neglected for clarity.

Results and Discussion

Stability of binary complexes—In addition to HA and H₂A species, the Cu(II) binary complex species with the presently studied α - and β -amino acids (A) were found to be of the type CuA and CuA₂, while the Cu(II)- γ -amino acid (A) system gave only CuA complex. It may be mentioned that CuAH types of amino acid complexes have also been reported in literature^{7,15}. Child and Perrin¹⁵ reported a stability constant value of 1.53 for the coordination of the glycine zwitterion through the carboxylate group with Cu(II). This value is very small compared to those reported for other Cu(II)-amino acid complexes and hence in the present study, the protoacid species were not considered. Actually, Letter and Bauman¹⁶ could not find any evidence for the complex formation between Cu(II) and amino acid zwitterion.

The stabilities for the CuA complexes (Table 1) decrease in the order: α -amino acids > β -amino acids > γ -amino acids, though $\log \beta_{H_2A}$ values for these ligands are in the reverse order i.e. the stability of the Cu(II) binary chelates decreases with the ring size order: 5 > 6 > 7. Again, the stability constants

TABLE 1 — STABILITY CONSTANTS FOR PARENT BINARY Cu(II)-AMINO ACID (A) SYSTEMS

 [Temp. = 37°C; $I = 0.15$ (NaClO₄)]

Results	Amino Acids, A				
	α -Amino acids		β -Amino acids		γ -Amino acid
	DL-Alanine	2-aba	β -alanine	3-aba	4-aba
$\log \beta_{HA}$ ($pK_{NH_3^+}$)	9.55(2)	9.43(1)	9.91(1)	9.95(1)	10.15(1)
$\log \beta_{H_2A}$	11.81(3)	11.54(1)	13.49(1)	13.30(1)	14.24(1)
$\log \beta_{CuA}$ ($\log K_{CuA}^{Cu}$)	8.16(2)	8.10(2)	7.12(2)	7.16(2)	6.07(9)
$\log \beta_{CuA_2}$	15.03(3)	15.13(4)	12.86(6)	12.90(5)	—
pK_{COOH}	2.26	2.11	3.58	3.35	4.09
$\log K_{CuA_2}^{CuA}$	6.87	7.03	5.74	5.74	—

Standard deviations are given in parentheses.

 TABLE 2 — STABILITY CONSTANTS FOR Cu(II)-DL-ALANINE OR β -ALANINE (A)-SECONDARY LIGAND (B) SYSTEMS

 [Temp. = 37°C; $I = 0.15$ (NaClO₄)]

Parameter	DL-Alanine (A) and secondary ligands(B)			β -Alanine (A) and secondary ligands (B)		
	2-aba	3-aba	4-aba	2-aba	3-aba	4-aba
$\log \beta_{CuAB}$	14.83(15)	14.44(4)	13.80(15)	14.31(6)	13.25(6)	11.36(2.02)
$\log K_{CuA}^{CuA}$	6.67	6.28	5.64	7.19	6.13	—
$\log K_{CuAB}^{CuB}$	6.73	7.29	7.73	6.21	6.10	—
$\Delta \log K$	-1.43	-0.87	-0.43	-0.91	-1.02	—
$\log X$	-0.50	0.95	—	0.63	0.74	—
$\log \beta_{CuAB}(\text{calc.})$	15.38	14.26	13.88	14.30	13.18	12.80
$\Delta \log \beta$	-0.55	0.18	-0.08	0.01	0.07	—

Standard deviations are given in parentheses.

for the CuA₂ when A is α - and β -amino acids (Table 1) show that Cu(II) binary chelates with two five-membered rings are more stable than those with two six-membered rings. The absence of the CuA₂ species in the Cu(II)-4-aba (A) system may be attributed to the steric factors associated with two seven-membered rings. However, Takenaka and coworkers¹⁷ achieved in isolating bis(4-aba) copper(II) complex, where these two 4-aba ligands bind monodentately through their N-amino groups.

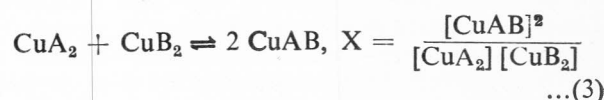
Figure 1 represents the pH-dependence of the concentration distribution of the complexes formed in the Cu(II)-2-aba, 3-aba and 4-aba (A) systems. The other α - and β -amino acid systems in this study showed almost the same qualitative features.

Stability of the ternary complexes — The ternary systems in the present study showed the presence of the CuAB types of ternary complexes in addition to HA, H₂A, CuA, CuA₂, HB, H₂B, CuB and CuB₂ complex species. The parameters generally used for indicating the stabilisation of the ternary complexes with respect to the binary ones, viz. (i) $\Delta \log K$, the difference between the stabilities of the binary and ternary complexes, (ii) $\log X$, the disproportionation constant, and (iii) $\Delta \log \beta$, the stabilization constant were calculated using Eqs (2), (4) and (5) for the equilibrium reactions (1) and (3).

Ternary complexes CuAB and CuBA (Eq. 2) are identical with respect to labile species in solution.



$$\begin{aligned} \Delta \log K &= \log K_{CuAB}^{CuA} - \log K_{CuB}^{Cu} \\ &= \log K_{CuBA}^{CuB} - \log K_{CuA}^{Cu} \quad \dots (2) \end{aligned}$$



$$\log X = 2 \log \beta_{CuAB} - (\log \beta_{CuA_2} + \log \beta_{CuB_2}) \quad \dots (4)$$

$$\Delta \log \beta = \log \beta_{CuAB} (\text{expl.}) - \log \beta_{CuAB} (\text{calc.}) \quad (5)$$

$$\Delta \log \beta_{CuAB} (\text{calc.}) = \frac{1}{2} (\log \beta_{CuA_2} + \log \beta_{CuB_2} + \log 4) \quad \dots (6)$$

Since more coordination sites are available for bonding the first ligand to a metal ion than for the second ligand, $\Delta \log K$ should, in general, be negative. With Cu(II) usually having a coordination number of four, the expected value for $\Delta \log K$ is -0.6 and that for $\log X$ it is 0.6. Thus the values of $\Delta \log K > -0.6$, $\log X > 0.6$ and $\Delta \log \beta$ to be positive suggest

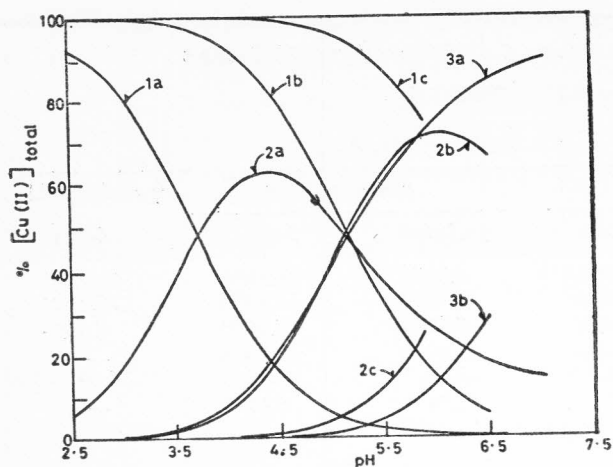


Fig. 1 — Species distribution for the Cu(II) binary complexes of 2-aba (a), 3-aba (b) and 4-aba (c) (A) at a Cu-A ratio of 1:2 [Species : (1) Free Cu(II), (2) CuA, and (3) CuA₂].

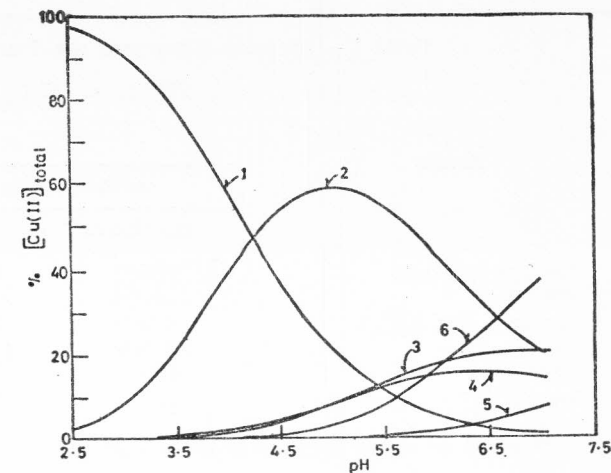


Fig. 2 — Distribution diagram for the Cu(II)-DL-alanine (A)-3-aba (B) system at a Cu-A-B ratio of 1:1:1 [Species : (1) Free Cu(II), (2) CuA, (3) CuA₂, (4) CuB, (5) CuB₂, and (6) CuAB].

the marked stabilisation of the ternary complexes compared to the binary ones.

By taking into account the $\log K_{\text{CuAB}}^{\text{CuB}}$ and \log

$K_{\text{CuAB}}^{\text{CuA}}$ values in Table 2 for the Cu(II)-DL-alanine

(A)- 2-aba, 3-aba or 4-aba (B) systems, one may easily draw the conclusion that these three ternary systems, respectively, involve five and five-, five and six-, and five and seven-membered chelate rings. Again the results for the Cu(II)- β -alanine (A)-2-aba or 3-aba (B) systems (Table 2) indicate that the CuAB complexes in these systems contain six and five-, and six and six-membered chelate rings. The $\log \beta_{\text{CuAB}}$ value of 11.36 ± 2.06 reported in Table 2 for the Cu(II)- β -alanine (A)-4-aba (B) systems where one expects six and seven-membered chelate rings seems to be highly inaccurate as is evident from its high standard deviation. Only below 1% of the total Cu(II) was found to be present in the form of CuAB ternary species in this system. Again, no appreciable complexation was revealed for the five and seven-membered ternary chelate rings in the Cu(II)-DL-alanine (A)-4-aba (B) system where only 8% of the total metal was present in the form of CuAB. Thus, the lesser ternary complexation tendency for the five and seven- and six and seven-membered chelate rings may be due to (i) absence of steric hindrance in the binary complex due to 4-aba (B), where the CuB₂ complex was not forming and (ii) presence of steric hindrance in the corresponding CuAB ternary complex species.

The values in Table 2 for all the ternary systems under study for (i) $\Delta \log K$ (Eqs 1 and 2) are considerably more negative compared to the statistically expected value of -0.6 , (ii) $\log X$ (Eqs 3 and 4) do not deviate much from the statistically expected value of 0.6 and (iii) $\Delta \log \beta$ (Eq. 5) are almost zero. All these results clearly indicate that there is no marked stabilization in the ternary complex formation. The same results are also reflected in the concentration

distribution diagrams i.e. while on statistical grounds 50% of the total metal was expected in the form of the ternary complex¹⁸ in none of the systems under study this trend was found, the maximum concentration being 39%, that too only in the Cu(II)-DL-alanine (A)-3-aba (B) system (Fig. 1). This may be ascribed to the mutual interactions between the primary (A) and secondary (B) ligands as both are amino acids of similar types. If we take into account the $\Delta \log K$, $\log X$ and $\Delta \log \beta$ values (Table 2) for the Cu(II)-DL-alanine or β -alanine (A)-2-aba, 3-aba (B) systems, it becomes clear that the Cu(II) ternary systems containing five and six-membered rings [Cu(II)-DL-alanine (A)-3-aba (B) and Cu(II)- β -alanine (A)-2-aba (B) systems] are more stable than those with two five- [Cu(II)-DL-alanine (A)-2-aba (B) system] or two six- [Cu(II)- β -alanine (A)-3-aba (B) system] membered rings. This may be attributed to the fact that the rings of different sizes bring in more of ligand field asymmetry and stabilise the ternary complexes. Again, the observation that Cu(II) binary chelates containing two five-membered rings are more stable than those with two six-membered, one may expect the same trend for the Cu(II) ternary chelates also containing two five or two six-membered rings. But from the $\Delta \log K$ and $\log X$ values (Table 2) for the Cu(II)-DL-alanine (A)-2-aba (B) and Cu(II)- β -alanine (A)-3-aba (B) systems, it appears that the two five-membered chelate rings in the former system are less stable than the two six-membered rings in the latter. Sigel *et al.*^{5,18} also observed this type of higher stability for the Cu(II) ternary chelates containing two six-membered rings than those with two five-membered rings. Thus, in general it may be concluded that Cu(II) ternary chelates containing five and six-membered rings are preferred more than those containing two rings of equal sizes. This is in conformity with 39%, 19% and 17% of the total metal bound in the form of the CuAB complex species in the five and six-, five- and five-, and six and six-membered chelate ring systems respectively.

The distribution of the various binary and ternary complex species in all the ternary systems in the present study were obtained in terms of the percentage bound Cu(II) as a function of pH and all of them show the same qualitative changes, viz. a progressive increase, with pH, in the amounts of ternary and bis-complexes, tending to limiting values, accompanied by corresponding decrease in the concentration of free metal ion and the 1 : 1 complexes. In order to show these trends, the curves obtained for the Cu(II)-DL-alanine (A)-3-aba (B) system in a 1 : 1 : 1 solution is shown in Fig. 2.

Finally it is interesting to classify the ternary systems reported in this paper into two different groups on the basis of the difference in basicities of the two ligands A and B involved in complexation. In the first type, two ligands have comparable basicity and thus compete equally for the metal ion, i.e. the two ligands may complex simultaneously in a single step or one ligand may gradually replace the other in a 1 : 2 binary complexes in several successive steps to form the ternary complexes. The Cu(II)-DL-alanine (A)-2-aba (B) and Cu(II)- β -alanine (A)-3-aba (B) ternary systems in the present study fall in this category. In the second type, the two ligands differ much in their basicity and thus one of the complexes, say CuA is considerably more stable than CuB and the ligand exchange does not occur between CuA and the ligand B. The ternary complex is formed in two distinct steps. The Cu(II)-DL-alanine (A)-3-aba or 4-aba (B) and Cu(II)- β -alanine (A)-2-aba or 4-aba (B) systems belong to second category.

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References

1. SIGEL, H., *Metal ions in biological systems*, Vol. 1-9 (Marcel Dekker, New York), 1973-79.
2. PRATT, J. M., *Inorganic chemistry of vitamin B₁₂* (Academic Press, London), 1972.
3. SARKAR, B. & KRUCK, T. P. A., *The biochemistry of copper*, edited by J. Peisach, P. Aisen & W. E. Blumberg (Academic Press, New York), 1966.
4. MARTIN, R. B. & PRADOS, R., *J. inorg. nucl. Chem.*, **36** (1974), 1665.
5. SIGEL, H., *Angew. Chem. Int. Edn*, **14** (1975), 394.
6. CHOW, S. T. & MCAULIFFE, *Progress in inorganic chemistry*, Vol. 19, edited by S. J. Lippard (Wiley, New York), 1975, 51-105.
7. *Stability constants of metal-ion complexes* (Special publication) edited by L. G. Sillen & A. E. Martell (The Chemical Society, London), N. 17, 1964; No. 25, 1971.
8. NAIR, M. S., *Ph. D. thesis*, University of Madras, Madras, 1979.
9. BROOKES, G. & PETTIT, L. D., *J. chem. Soc. Dalton*, (1977), 1918.
10. NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., *J. chem. Soc. Dalton*, (1980), 1312.
11. NAIR, M. S. & SANTAPPA, M., *J. chem. Soc. Dalton*, (1981), 992.
12. NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., *Inorg. chim. Acta*, **41** (1980), 7.
13. NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., *Indian J. Chem.*, **19A** (1980), 1106.
14. GANS, P., VACCA, A. & SABATINI, A., *Inorg. chim. Acta*, **18** (1976), 237.
15. CHILD, C. W. & PERRIN, D. D., *J. chem. Soc.*, (1969), 1039.
16. LETTER, J. E. & BAUMEN, J. E., *J. Am. chem. Soc.*, **90** (1968), 858.
17. TAKENAKA, A., OSHIMA, E., YAMADA, S. & WATANABLE, T., *Acta Crystallogr.*, **B 29** (1973), 503.
18. SIGEL, H., CARACO, R. & PRIJS, B., *Inorg. Chem.*, **13** (1974), 462.