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Ternary Coordination Complex Formation between Glycylglycine Copper(II) & DL-4-Aminobutyric Acid

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Received 3 July 1981; accepted 10 September 1981.

Computer based analysis of the potentiometric data obtained at 37°C and I = 0.15 M; (NaClO₄) for the Cu(II)-glycylglycine (A)-0.-4-minobutyric acid (B) system indicates the presence of two ternary complexes (CuAB and CuABHL₁) in addition to the binary complex species (HA, H₂A, CuA, CuAHL₁, HB, H₂B, and CuB). The results suggest that the five and seven-membered chelate rings in the CuAB complex is less favoured. It appears that the amide-deprotonated glycylglycine in the CuABHL₁ complex species is tridentate similar to that in the CuAHL₁ glycylglycine binary complex.

STUDIES on Cu(II)-dipeptide-amino acid ternary complex systems, though intermittent, have directed for a better understanding of the metal ionenzyme-substrate complexes1'2. It is generally agreed 1-0 that initial complex formation between Cu(II) and a dipeptide results in a five-membered chelate ring involving N-amino and O-peptido donor groups in both the binary and ternary systems. At higher pH, the dipeptide undergoes deprotonation at the amide group and becomet tridentate via N-amino, N-peptido and O-carboxylategroups in the Cu(II)-dipeptide binary systems. However, in the Cu(II)-dipeptide (A)-secondary ligand(B) ternary systems where B is bidentate or tridentate, 317-9, several workers favour the bidentate binding of amidedeprotonated dipeptides via N-amino and N-peptido groups, while others 5,10 favourits tridentate binding as is the case with CuAH-1 dipeptide binary complex. Nair et al.11 recently reported that amide-deprotonated dipeptide is tridentate in the presence of a monodentate ligand like imidazole in the Cu(II) ternary systems. The present communication deals with the coordination behaviour of a dipeptide, viz. glycylglycine (glgl) with Cu(II) in the presence of DL-4-aminobutyric acid (4-aba).

The potentiometric studies were carried out at 37°C and I = 0.15 M (NaClO₄) with the apparatus and procedure described previously^{12'13}. Both glgl and 4-aba were obtained from Fluka. Cu(ClO₄)₂ and other reagents were prepared and estimated as described earlier¹⁴.

Analysis of the potentiometric data in the pH range 3.00—8.00 in the Cu(II)-glgl(A)-4-aba(B) ternary system in this study using MINIQUAD-75 computer program¹⁵ on an IBM-370 computer showed the presence of two ternary complexes (CuAB and CuABH₋₁) in addition to the binary species⁶⁻¹⁶ (HA, H₂A, CuA, CuAH₋₁, CuA₂H₋₁, HB, H₂B and

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Table 1 - Stability Constants for Cu(ii) gigl(A) - I ab 1 (B)

 $[I = 0.15 M (NaClO_1); temp. = 37^{\circ}]$

Constant	Value	Constant	Value
log: BCuAB	12.29(10)	pK_{CuAB}^{H}	5.65
log BCuABH_1	6.64(4)	log KCuAll	5.02
log KCuAB	6.59		0.57
log KCuB	6.22	∆log KCuABH_1	1.05
Alog KCuAB	+0.52		

Stability constants of proton and binary complexes of gigl (ref. 6) and 4-aba (ref. 16) with Cu(II) used for the calculation of the above constants have been taken from our earlier published work.

CuB). The charges of all these complexes are neglected for clarity.

It appears that complex formation between glgl(A) and Cu(II) in the CuAB species involves the formation of a five-membered chelate ring as is the case with CuA-glgl complex, because $\log K_{\text{CuAB}}^{\text{CuB}}$ (Table 1) and $\log K_{\text{CuA}}^{\text{Cu}}$ values are comparable. Similarly comparison of the $\log K_{\text{CuAB}}^{\text{CuA}}$ (Table 1) and $\log K_{\text{CuB}}^{\text{Cu}}$ values (B) forms a seven-membered chelate ring in the CuAB complex species. Thu the CuAB species would contain five-and seven-membered chelate rings. Since more coordination positions are available for binding the first ligand to a given multivalent metal ion than for the second ligand, negative values for $\Delta \log K_{\text{CuAB}}$ (Eqs. 1 and 2) are expected. But this parameter for the title system

$$CuA + CuB \rightleftharpoons CuAB + Cu$$
 ...(1)

$$\Delta \log K_{\text{CuAB}} = \log \beta_{\text{CuAB}} = (\log \beta_{\text{CuA}} + \log \beta_{\text{CuB}}) \dots (2)$$

is positive (Table 1). It indicates that 4-aba (B) ligand prefers to add on to CuA glgl binary complex rather than to aquated Cu(II). Also, the positive Alog Keuan value suggests that the formation of ternary complex, CuAB is preferred over the binary complexes, CuA or CuB. However, the maximum amount of the total Cu(II) present in CuAB complex is only 7.5% (Fig. 1), while the statistically expected value is 50% indicating that the CuAB formation is less favoured. This may be atributed to the steries factors associated with the five- and seven-membered chelate rings in this species.

Previously, Nair and coworkers^{8*0} reported that amide-deprotonated glgl (AH₋₁) is bidentate in the CuABH₋₁, when B is a bidentate ligand like DL-2-aminobutyric acid, 3-aminobutyric acid, histamine or glycinamide; or a tridentate ligand like L-histiding, DL-2,3-diaminopropionic acid, DL-2,4-diaminobutyric acid or DL-ornithine. This conclusion was arrived at by considering (i) log $K_{\text{CuAB}}^{\text{CuA}}$ and log $K_{\text{CuABH}-1}^{\text{CuAH}}$, (ii) $\triangle \log K_{\text{CuAHH}-1}^{\text{CuAH}}$ (Eqs 3 and 4) and (iii) $pK_{\text{CuAH}}^{\text{CuAH}}$ values in the Cu(II)-glgl(A)-B and Cu(II)-glycinamide (A)-B ternary systems.

Δlog Kchabn-1 = log βομαθη-1 - (log βchan-1 log Boun)

...(3)

One may expect the same type of binding of the ligand B in both CuAB and CuABH_, complexes and thus log KCuAB and log KCuAH-1 values must be comparable. This trend was seen in the Cu(II)-glycina-mide(A)-B systems, but in the Cu(II)-glgl (A)-B systems the log Kouabna-1 values were lower than log KCUAB values by ~3 log units. This was explainedby considering the bidentate binding of AH-1 glgl in CuABH-1 unlike its tridentate binding in the CuAH-1. Similar arguments have been put forward. to explain the negative \triangle lo $K_{\text{cuabre-1}}$ values (Eq. 4) with high magnitude in the case of Cu(II)-glgl(A)-B systems, while the \(\Delta\log K_{cun-1}\) values in the Cu(II)glycinamide-B systems are in the order of statistically expected values. The bidentate mode of binding of AH_1 glgl in the ternary complex systems is further confirmed by the fact that pKHCUAB values in all the Cu(II)-glgl-B systems studied are nearly identical within the limits of experimental error to the corresponding Cu(II)-glycinamide-B systems. Sigel3 also reported the bidentate binding of AH-, glgl in the Cu(II)-glgl-2,2'-bipyridyl ternary system. For finding out the mode of coordination of AH-1 glgl in presently studied Cu(II)-glgl-4-aba system, the Cu(II) glycianmide-4-aba system was also investigated, but no appreciable complexing seems to have been revealed. If one compares the log KCuAB and log KCuABH-1 values in Table 1 for the title system, it may be noted that the latter parameter is lower than the former by only ~1.5 log units and its $\triangle \log K_{\text{Ouadh}_{H-1}}$ value is in the order of statistically expected values. Both these values suggest that the AH₋₁ glgl is tridentate in CuABH₋₁ as in the case in CuAH₋₁ glgl binary com-

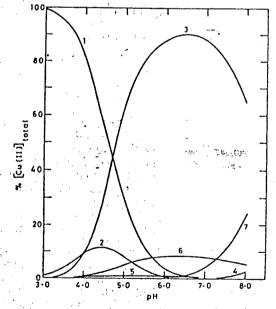


Fig. 1 — Species distribution for the Cu(II)-glgl(A)-4-aba(B) system at a metal-A-B ratio of 1:1:1 [(1) unbound Cu(II); (2) CuA; (3) CuAH₋₁; (4) CuA₂H₋₁; (5) CuB; (6) CuAB; and (7) CuABH₋₁].

plex. Thus in the CuABH₋₁ species three equatorial coordination sites would be occupied by ΛH_{-1} glgl, while the 4-aba (B) would occupy one equatorial and one axial position. This sturcture is similar to that of the Cu(AH_1)A glgl complex6, the difference is that the second glgl ligand is replaced by the 4-aba (B) ligand in the ternary system.

This tridentate binding of AH_1 glgl in the title system is surprising, because 4-aba(B) is also a bidentate ligand like DL-2-aminobutyric acid or 3aminobutyric acid, under whose presence All-1 glgl is found to be bidentate. This may probably be accounted for by considering the fact that if AH-, glgl binds in a bidentate manner, then the CuABILspecies in the title system would have five- and seven membered chelate rings, possibly less favoured due to steric reasons. The strain due to the seven-membered ring of 4-aba (B) would get reduced by its coordination in one equatorial position and one axial position at a greater distance. This is possible only by the

coordination of AH-, glgl in a tridentate manner, i.e. by occupying three equatorial sites similar to its binding in the CuAH-1 glgl binary complex. The difference in the log $K_{\text{CuAH}}^{\text{CuA}}$ and log $K_{\text{CuAH}-1}^{\text{CuAH}-1}$ values of ~1.5 log units in the title system may thus be accounted for by the fact that in the CuAB complex, 4-aba (B) occupies two equatorial positions while in the CuABH_1 complex, it occupies one equatorial and one axial position.

Thus, the present investigation shows that the coordination behaviour of amide-deprotonated dipentide in the ternary Cu(II) complex systems is highly influenced by the chelate ring size-due to the secondary ligand, B. The CuABH_1 complex species is favoured above pH 6.5 and there is a steady increase in its concentration with rise in pH as shown in Fig. 1. At pH 8.0, about 24% of the total metal was found to be present in the form of CuABH_, species.

- 1. FREEMAN, H. C., Inorganic biochemistry, Vol. I, Chapter IV, edited by G. L. Eichhorn, (Elsevier, New York), 1973.
- Sigel, H., Metal ions in biological systems, Vol. II (Marcel Dekker, New York), 1973.
- SIGEL, H., Islorg. Chem., 14 (1975), 1535.
 BROOKES, G. & PETTIT, L. D., J. chem. Soc. Dalton Trans., (1975), 2112.
- GERGELY, A. & NAGYPAL, I., J. chem. Soc. Dalton Trans., (1977), 1109.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., Indian J. Chem., 19A (1980), 672.
 MARTIN, R. P., MOSANI, L. & SARKAR, B., J. blol. Chem., 246 (1971), 5944.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., J. chem. Soc. Dalton Trans., (1980), 2138.
 NAIR M. S., J. chem. Soc., Dalton Trans., (1982), 561.
 Lim, M. C., Sinn, E. & Martin, R. B., Inorg. Chem., 15 (1976), 807.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., Inorg. chim. Acta, 41 (1980), 7.
 NAIR, M. S. & SANTAPPA, M., J. chem. Soc. Dalton Trans., (1981), 992; Indian J. Chem., 21A (1982), 58.
 NAIR, M. S., SANTAPPA, M. & MURUGAN, P. K., Inorg. Chem., 21 (1982), 142.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., J. chem. GERGELY, A. & NAGYPAL, I., J. chem. Soc. Dalton Trans.,

- NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., J. chem. Soc. Dalton Trans., (1980), 1312; Indian J. Chem., 19A (1980), 1105.
- 15. GANS, P., VACCA, A. & SABALINA, ...,
 18 (1976), 237.
 16 NAIR, M. S. & SANTAPPA, M., Indian J. Chem., 20A

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STUDIES on Cu(II)-dipeptide-amino acid ternary complex systems, though intermittent, directed for a better understanding of the metal ionenzyme-substrate complexes112. It is generally agreed 1-6 that initial complex formation between Cu(II) and a dipeptide results in a five-membered chelate ring involving N-amino and O-peptido donor groups in both the binary and ternary systems. At higher pH, the dipeptide undergoes deprotonation at the amide group and become¹⁻⁶ tridentate via N-amino, N-peptido and O-carboxylategroups in the Cu(II)-dipeptide binary systems. However, in the Cu(II)-dipeptide (A)-secondary ligand(B) ternary systems where B is bidentate or tridentate, 317-9. several workers favour the bidentate binding of amidedeprotonated dipeptides via N-amino and N-peptido groups, while others 6:10 favour its tridentate binding as is the case with CuAH-, dipeptide binary complex. Nair et al.11 recently reported that amide-deprotonated dipeptide is tridentate in the presence of a monodentate ligand like imidazole in the Cu(II) ternary systems. The present communication deals with the coordination behaviour of a dipeptide, viz. glycylglycine (glgl) with Cu(II) in the presence of DL-4-aminobutyric acid (4-aba).

The 'potentiometric studies were carried out at 37°C and I = 0.15 M (NaClO₄) with the apparatus and procedure described previously 12'13. Both glgl and 4-aba were obtained from Fluka. Cu(CIG4)2 and other reagents were prepared and estimated as described carlier14.

Analysis of the potentiometric data in the pH range 3.00-8.00 in the Cu(II)-glgl(A)-4-aba(B) ternary system in this study using MINIQUAD-75 computer program¹⁵ on an IBM-370 computer showed the presence of two ternary complexes (CuAB and CuABH-1) in addition to the binary species 6.16 (HA, H_2A , CuA, CuA H_{-1} , CuA $_2H_{-1}$, HB, H_2B and

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Table 1 -- Sparing Constants for Cufff algh(A) dealer (B) TERNARY SYSTEM

 $[I = 0.15 \ M \text{ (NaClO}_3); \text{ temp.} = 37 \text{ }]$

Constant	Value	Constant	Value
log BCuAB	12.29(10)	$ ho K_{ m CoAB}^{ m H}$	5.65
log βCuABII_1	6.64(4)	log A'CoAH	5.03
log KCuAB	6.59	log K ^{Cull} CoABH 1	0.5%
log KCuAB	6.23 .	Alog KCGAIII.	1.05
∆log KCuAn	+0.52		

Stability constants of proton and binary completes of 1814 (ref. 6) and 4-abn (ref. 16) with Cu(II) used for the calculation of the above constants have been taken from our earlier published work.

CuB). The charges of all these complexes are needed ed for clarity.

It appears that complex formation between gleich. and Cu(II) in the CuAB species involves the formation of a five-membered chelate ring as is the case with CuA-glgl complex, because log K_CuB (Table 1) and log KCuA values are comparable. Similarly comparison of the log $K_{\text{CuAn}}^{\text{CuAn}}$ (Table 1) and log $K_{\text{cuan}}^{\text{CuAn}}$ values to clearly indicate that 4-aba (B) forms a sevenmembered chelate ring in the CuAB complex species. Thu the CuAB species would contain five-and sevenmembered chelate rings. Since more coordination. positions are available for binding the first ligand to a given multivalent metal ion than for the second ligand, negative values for $\triangle \log K_{\text{cuth}}$ (Eqs. 1 and 2) are expected. But this parameter for the title system

$$CuA + CuB \rightleftharpoons CuAB + Cu$$
 ...(i)

$$\triangle \log K_{\text{CuAB}} = \log \beta_{\text{CuAB}} = (\log \beta_{\text{CuA}} + \log \beta_{\text{CuB}}) \dots (2)$$

is positive (Table 1). It indicates that 4-aba (B) ligand prefers to add on to CuA glgl binary complex rather than to aquated Cu(II). Also, the DOSITIVE $\triangle \log K_{\text{curfi}}$ value suggests that the formation of ternary complex, CuAB is preferred over the binary complexes, CuA or CuB. However, the maximum amount of the total Cu(II) present in CuAB complex is only 7.5% (Fig. 1), while the statistically expected value is 50% indicating that the CuAB formation is less favoured. This may be attributed to the storic factors associated with the five- and seven-membered chelate rings in this species.

Previously, Nair and coworkers8'9 reported that amide-deprotonated glgl (AH-1) is bidentate in the CuABH₁, when B is a bidentate ligand like DL-2aminobutyric acid, 3-aminobutyric acid, histamine or glycinamide; or a tridentate ligand like L-histidine, DL-2,3-diaminopropionic acid, DL-2,4-diaminobutyric acid or DL-ornithine. This conclusion was arrived at by considering (i) $\log K_{\text{CuAB}}^{\text{CuAB}}$ and $\log K_{\text{CuABH}-1}^{\text{CuAH}-1}$, (ii) △log KcuABH-1 (Eqs 3 and 4) and (iii) pKCuAB values in the Cu(II)-glgl(A)-B and Cu(II)-glycinamide (A)-B ternary systems.

 $\triangle \log K_{\text{CHABH-1}} = \log \beta_{\text{CHABH-1}} - (\log \beta_{\text{CHABH-1}}$ log βcuB)

...(3)

One may expect the same type of binding of the ligand B in both CuAB and CuABH_1 complexes and thus log KCuAB and log KCuABH_1 values must be comparable. This trend was seen in the Cu(II)-glycinamide(A)-B systems, but in the Cu(II)-glgl (A)-B systems the log Kouabna-1 values were lower than log KCUAR values by ~3 log units. This was explainedby considering the bidentate binding of AH₋₁ glgl in CuABH₋₁ unlike its tridentate binding in the CuAH_1. Similar arguments have been put forwardo to explain the negative \triangle lo $K_{\text{cuabil}-1}$ values (Eq. 4) with high magnitude in the case of Cu(II)-glgl(A)-B systems, while the $\triangle \log K_{0uH-1}$ values in the Cu(II)glycinamide-B systems are in the order of statistically expected values. The bidentate mode of binding of AH_1 glgl in the ternary complex systems is further confirmed by the fact that pK_{CuAB}^H values in all the Cu(II)-glgl-B systems studied are nearly identical within the limits of experimental error to the corresponding Cu(II)-glycinamide-B systems. Sigel³ also reported the bidentate binding of AH₋₁ glgl in the Cu(II)-glgl-2,2'-bipyridyl ternary system. For finding out the mode of coordination of AH-1 glgl in presently studied Cu(II)-glgl-4-aba system, the Cu(II) glycianmide-4-aba system was also investigated, but no appreciable complexing seems to have been revealed. If one compares the log KCuAB and log KCuABI-1 values in Table I for the title system, it may be noted that the latter parameter is lower than the former by only ~1.5 log units and its \(\text{log } Koundary \) value is in the order of statistically expected values. Both these values suggest that the AH₋₁ glgl is tridentate in CuABH₋₁ as in the case in CuAH₋₁ glgl binary com-

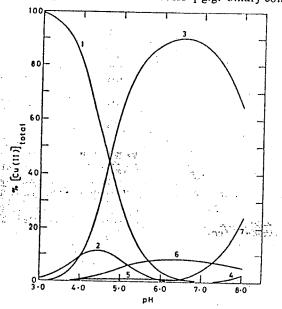


Fig. 1 — Species distribution for the Cu(II)-glgl(A)-4-aba(B) system at a metal-A-B ratio of 1:1:1 ((1) unbound Cu(II); (2) CuA; (3) CuAH_1; (4) CuA₁H_1; (5) CuB; (6) CuAB; and (7) CuABH_1].

plex. Thus in the CuABH-1 species three equatorial coordination sites would be occupied by AHglgl, while the 4-aba (B) would occupy one equatorial and one axial position. This sturcture is similar to that of the Cu(AH_1)A glgl complex⁶, the difference is that the second glgl ligand is replaced by the 4-aba

(B) ligand in the ternary system.

This tridentate binding of AH-1 glgl in the title system is surprising, because 4-aba(B) is also a bidentate ligand like DL-2-aminobutyric acid or 3-aminobutyric acid, under whose presence AH-1 glgl is found to be bidentate. This may probably accounted for by considering the fact that if AH_{-1} glgl binds in a bidentate manner, then the CuABH-1 species in the title system would have five- and seven membered chelate rings, possibly less favoured due to steric reasons. The strain due to the seven-membered ring of 4-aba (B) would get reduced by its coordination in one equatorial position and one axial position at a greater distance. This is possible only by the coordination of AII-1 glgl in a tridentate manner, i.e. by occupying three equatorial sites similar to its binding in the CuAH-, glgl binary complex. The difference in the log $K_{\text{CuAB}}^{\text{CuAB}}$ and log $K_{\text{CuABH}-1}^{\text{CuABH}-1}$ values of ~1.5 log units in the title system may thus be accounted for by the fact that in the CuAB complex, 4-aba (B) occupies two equatorial positions while in the CuABH_1 complex, it occupies one equatorial and one axial position.

Thus, the present investigation shows that the coordination behaviour of amide-deprotonated dipeptide in the ternary Cu(II) complex systems is highly influenced by the chelate ring size-due to the secondary ligand, B. The CuABH_1 complex species is favoured above pH 6.5 and there is a steady increase in its concentration with rise in pH as shown in Fig. 1. At pH 8.0, about 24% of the total metal was found to be present in the form of CuABH_1 species.

- FREEMAN, H. C., Inorganic biochemistry, Vol. I, Chapter IV, edited by G. L. Eichhorn, (Elsevier, New York), 1973.

- Sigel, H., Metal ions in biological systems, Vol. II (Marcel Dekker, New York), 1973.
 Sigel, H., Intarg. Chem., 14 (1975), 1535.
 BROOKES, G. & PETTIT, L. D., J. chem. Soc. Dalton Trans., (1975), 2112.
- (1975), 2112.
 GERGELY, A. & NAGYPAL, I., J. chem. Soc. Dalton Trans., (1977), 1109.
 NAIR, M. S., SANFAPPA, M. & NATARAJAN, P., Indian J. Chem., 19A (1980), 672.

- J. Chem., 19A (1980), 672.

 7. MARTIN, R. P., MOSANI, L. & SARKAR, B., J. biol. Chem., 246 (1971), 594.

 8. NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., J. chem. Soc., Dalton Trans., (1980), 2138.

 9. NAIRM, S., J. chem. Soc., Dalton Trans., (1982), 561.

 10. Lim, M. C., Sinn, E. & Martin, R. B., Inorg. Chem., 15 (1976), 807.

 11. NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., Inorg. chim. Acta, 41 (1980), 7.

 12. NAIR, M.S. & SANTAPPA, M., J. chem. Soc. Dalton Trans., (1981), 992; Indian J. Chem., 21A (1982), 58.

 13. NAIR, M. S., SANTAPPA, M. & MURUGAN, P. K., Inorg. Chem., 21 (1982), 142.

 14. NAIR, M. S., SANTAPPA, M. & NATARAJAN, P. J. chem.

- NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., J. chem. Soc. Dalion Trans., (1980), 1312; Indian J. Chem., 19A
- (1930), 1105. 15. Gans, P., Vacca, A. & Sabatini, A., Inorg. chim. Acta, 18 (1976), 237. 16. Nair., M. S. & Santappa, M., Indian J. Chem., 20A
- JAIR, M. S (1981), 990.

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Table 1 -- Stability Constants for Cu(H) glgi(A) [5-a]) (4)
Ternary System

 $[I = 0.15 \ M \text{ (NaClO}_1); \text{ temp.} = 37^{\circ}]$

Constant	Value	Constant	Value
log BCUAB	12.29(10)	" $ ho K_{\mathrm{CoAB}}^{\mathrm{H}}$	5,65
log BCuABU-1	6.63(3)	bg KCGAH	5.00
log KCuAB	6.59	log KCuB CuAUR-1	0.57
log KCuAB	6.23	Δlog KCaABH_1	1.05
∆log KCuAB	+0.52		

Stability constants of proton and binary complexes of gigl (ref. 6) and 6 aba (ref. 16) with Cu(II) used for the calculation of the above constants have been taken from our earlier published work.

CuB). The charges of all these complexes are neglected for clarity.

It appears that complex formation between glei(A) and Cu(H) in the CuAB species involves the formation of a five-membered chelatering as is the case with CuA-glgl complex, because $\log K_{\rm GuAB}^{\rm CuB}$ (Table 1) and $\log K_{\rm GuA}^{\rm Cu}$ values are comparable. Similarly comparison of the $\log K_{\rm GuAB}^{\rm CuA}$ (Table 1) and $\log K_{\rm GuAB}^{\rm CuB}$ values clearly indicate that 4-aba (B) forms a person membered chelatering in the CuAB complex species. Thu the CuAB species would contain five-and seven membered chelaterings. Since more coordination positions are available for binding the first ligand tora given multivalent metal ion than for the second-ligand, negative values for $\Delta \log K_{\rm CuAB}$ (Eq. 1 and 2) are expected. But this parameter for the title system

$$CuA + CuB \rightleftharpoons CuAB + Cu$$
 ...(1)

 $\triangle \log K_{\text{cuan}} = \log \beta_{\text{cuan}} = (\log \beta_{\text{cuan}} + \log \beta_{\text{cun}}) \dots (2)$

is positive (Table 1). It indicates that 4-aba (B) ligand prefers to add on to CuA glgl binary complex rather than to aquated Cu(II). Also, the positive Alog Kenan value suggests that the formation of ternary complex, CuAB is preferred over the binary complexes, CuA or CuB. However, the maximum amount of the total Cu(II) present in CuAB complex is only 7.5% (Fig. 1), while the statistically expected value is 50% indicating that the CuAB formation is less favoured. This may be atributed to the steric factors associated with the five- and seven-membered chelate rings in this species.

Previously, Nair and coworkers^{8'9} reported that amide-deprotonated glgl (AH₋₁) is bidentate in the CuABH₋₁, when B is a bidentate ligand like DL-2-aminobutyric acid, 3-aminobutyric acid, histamine or glycinamide; or a tridentate ligand like L-histidine, DL-2,3-diaminopropionic acid, DL-2,4-diaminobutyric acid or DL-ornithine. This conclusion was arrived at by considering (i) log $K_{\text{CuAB}}^{\text{CuAB}}$ and log $K_{\text{CuABH}-1}^{\text{CuAH}-1}$, (ii) $\Delta \log K_{\text{CuAnn}-1}$ (Eqs 3 and 4) and (iii) $pK_{\text{CuAB}}^{\text{H}}$ values in the Cu(II)-glgl(A)-B and Cu(II)-glycinamide (A)-B ternary systems.

...(3) $\triangle \log K_{\text{Cuari-1}} = \log \beta_{\text{Cuari-1}} - (\log \beta_{\text{Cuari-1}})$ log Boun)

One may expect the same type of binding of the ligand B in both GuAB and CuABH_, complexes and thus log $K_{C_uAB}^{C_uA}$ and log $K_{C_uABH_1}^{C_uAH_1}$ values must be comparable. This trend was seen in the Cu(II)-glycinamide(A)-B systems, but in the Cu(II)-glgl (A)-B systems the log Kouabna-1 values were lower than log KeuAn values by ~3 log units. This was explainedby considering the bidentate binding of AH-1 glgl in CuABH-, unlike its tridentate binding in the CuAH-1. Similar arguments have been put forward? to explain the negative \(\Delta \) lo $K_{\text{cuann-1}}$ values (Eq. 4) with high magnitude in the case of Cu(II)-glgl(A)-B systems, while the $\triangle \log K_{0uH-1}$ values in the Cu(II)glycinamide-B systems are in the order of statistically expected values. The bidentate mode of binding of AH₋₁ glgl in the ternary complex systems is further confirmed by the fact that $pK_{\text{CuAB}}^{\text{H}}$ values in all the Cu(II)-glgl-B systems studied are nearly identical within the limits of experimental error to the corresponding Cu(II)-glycinamide-B systems. Sigel3 also reported the bidentate binding of AH₋₁ glgl in the Cu(II)-glgl-2,2'-bipyridyl ternary system. For finding out the mode of coordination of AH₋₁ glgl in presently studied Cu(II)-glgl-4-aba system, the Cu(II) glycianmide-4-aba system was also investigated, but no appreciable complexing seems to have been revealed. If one compares the log KCuAB and log KCuABI-1 values in Table I for the title system, it may be noted that the latter parameter is lower than the former by only ~1.5 log units and its \(\text{log } Kc_{\text{nABH}-1} \) value is in the order of statistically expected values. Both these values suggest that the AH-, glgl is tridentate in CuABH_1 as in the case in CuAH_1 glgl binary com-

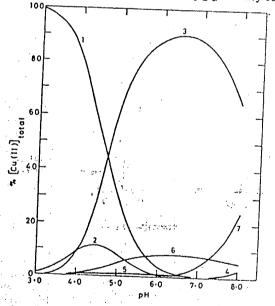


Fig. 1 — Species distribution for the Cu(II)-glgl(A)-4-aba(B) system at a metal-A-B ratio of 1:1:1 ((1) unbound Cu(II); (2) CuA; (3) CuAH_1; (4) CuA₂H_1; (5) CuB; (6) CuAB; and (7) CuABH_1].

plex. Thus in the CuABH₋₁ species three equatorial coordination sites would be occupied by AH₋₁ glgl, while the 4-aba (B) would occupy one equatorial and one axial position. This sturcture is similar to that of the Cu(AH_1)A glgl complex, the difference is that the second glgl ligand is replaced by the 4-aba (B) figand in the ternary system.

This tridentate binding of AH-, glgl in the title system is surprising, because 4-aba(B) is also a bidentate ligand like DL-2-aminobutyric acid or 3aminobutyric acid, under whose presence AIL glgl is found to be bidentate. This may probably be accounted for by considering the fact that if Allglgl binds in a bidentate manner, then the CuABIIspecies in the title system would have five- and seven membered chelate rings, possibly less favoured due to steric reasons. The strain due to the seven-membered ring of 4-aba (B) would get reduced by its coordination in one equatorial position and one axial position at a greater distance. This is possible only by the coordination of AH-1 glgl in a tridentate manner, i.e. by occupying three equatorial sites similar to its binding in the CuAH₋₁ glgl binary complex. The difference in the log K^{CuAH}_{cuAH} and log K^{CuAH}_{cuAH} values of ~1.5 log units in the title system may thus be accounted for by the fact that in the CuAB complex, 4-aba (B) occupies two equatorial positions while in the CuABH, complex, it occupies one equatorial and one axial position.

Thus, the present investigation shows that the coordination behaviour of amide-deprotonated dipeptide in the ternary Cu(II) complex systems is highly influenced by the chelate ring size-due to the secondary ligand, B. The CuABH_1 complex species is favoured above pH 6.5 and there is a steady increase in its concentration with rise in pH as shown in Fig. 1. At pl 1 8.0, about 24% of the total metal was found to

be present in the form of CuABH-1 species.

- FREEMAN, H. C., Inorganic biochemistry, Vol. I, Chapter IV, edited by G. L. Eichhorn, (Elsevier, New York), 1973.
- SIGEL, H., Metal ions in biological systems, Vol. II (Marcel Dekker, New York), 1973.
 SIGEL, H., Interg. Chem., 14 (1975), 1535.
 BROOKES, G. & PETTIT, L. D., J. chem. Soc. Dalton Trans., (1975), 2112.

- 5. GERGELY, A. & NAGYPAL, I., J. chem. Soc. Dulton Trans., (1977), 110). 6. NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., Indian J. Chem., 19A (1980), 672.

- J. Chem., 19A (1930), 672.
 MARTIN, R. P., MOSANI, L. & SARKAR, B., J. biol. Chem., 246 (1971), 5924.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., J. chem., Soc. Dalton Trans., (1980), 2138.
 NAIRM, S., J. chem. Soc., Dalton Trans., (1982), 561.
 LIM, M. C., SINN, E. & MARTIN, R. B., Juorg. Chem., 15 (1970), 807.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., Inorg. chim. Acta, 41 (1980), 7.
 NAIR, M. S. & SANTAPPA, M., J. chem. Soc. Dalton Trans., (1931), 992.; Indian J. Chem., 21A (1982), 58.
 NAIR, M. S., SANTAPPA, M. & MURUGAN, P. K., Inorg. Chem., 21 (1982), 142.

- NAIR, M. S., SANTAPPA, M. & MURUGAN, P. K., Inorg. Chem., 21 (1982), 142.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., J. Chem., Soc. Dalton Trans., (1980), 1312; Indian J. Chem., 19A
- Soc. Dation Frans., (1930), 1930, 1930, 1930, 1930, 1955.

 15. Gans, P., Vacca, A. & Sabatini, A., Inorg. chim. Acta, 18 (1975), 237.

 16. Nair, M. S. & Santappa, M., Indian J. Chem., 20A

Ternary Coordination Complex Formation between Glycylglycine, Copper(II) & DL-4-Aminobutyric Acid

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Received 3 July 1981; accepted 10 September 1981

Computer based analysis of the potentiometric data—obtained at 37°C and I=0.15~M—(NaClO₄) for the Cu(II)-glycylglycine (A)-DL-4-aminobutyric acid (B) system indicates the presence of two ternary complexes (CuAB and CuABH₋₁) in addition to the binary complex species (HA, H₂A, CuA, CuAH₋₁, HB, H₂B, and CuB). The results suggest that the five and seven-membered chelate rings in the CuAB complex is less favoured. It appears that the amide-deprotonated glycylglycine in the CuABH₋₁ complex species is tridentate similar to that in the CuAH₋₁ glycylglycine binary complex.

STUDIES on Cu(II)-dipeptide-amino acid ternary complex systems, though intermittent, directed for a better understanding of the metal ionenzyme-substrate complexes^{1/2}. It is generally agreed¹⁻⁶ that initial complex formation between Cu(II) and a dipeptide results in a five-membered chelate ring involving N-amino and O-peptido donor groups in both the binary and ternary systems. At higher pH, the dipeptide undergoes deprotonation at the amide group and become1-6 tridentate via N-amino, N-peptido and O carboxylategroups in the Cu(II)-dipeptide binary systems. However, in the Cu(II)-dipeptide (A)-secondary ligand(B) ternary systems where B is bidentate or tridentate, 27-9, several workers favour the bidentate binding of amidedeprotonated dipeptides via N-amino and N-peptido groups, while others 10 favour its tridentate binding as is the case with CuAH_, dipeptide binary complex. Nair et al. " recently reported that amide-deprotonated dipeptide is tridentate in the presence of a monodentate ligand like imidazole in the Cu(II) ternary systems. The present communication deals with the coordination behaviour of a dipeptide, viz. glycylglycine (glgl) with Cu(II) in the presence of DL-4-aminobutyric acid (4-aba).

The 'potentiometric studies were carried out at 37°C and I = 0.15 M (NaClO₄) with the apparatus and procedure described previously^{12'13}. Both glgl and 4-aba were obtained from Fluka. Cu(ClG₄)₂ and other reagents were prepared and estimated as described earlier¹⁴.

Analysis of the potentiometric data in the pH range 3.00—8:00 in the Cu(II)-glgl(A)-4-aba(B) ternary system in this study using MINIQUAD-75 computer program¹⁵ on an IBM-370 computer showed the presence of two ternary complexes (CuAB and CuABH₋₁) in addition to the binary species⁶⁺¹⁶ (HA, H₂A, CuA, CuAH₋₁, CuA₂H₋₁, HB, H₂B and

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Table 1 -- Stability Co stants for Cu(II) glgl(A) 4-a5a (B)
Ternary System

$[I = 0.15 M \text{ (NaClO}_{4}); \text{ temp.} = 37^{2}]$				
Constant	Value	Constant	Value	
log BCuAD .	12.29(10)	pK_{CuAB}^{14}	5.65	
log βCuABII_1	6.63(4)	log K Cuall	5.00	
log KCuAB	6.59	log KCuAliffer	0.57	
log KCuAB	6.22	∆log KC0ABH_1	- 1.05	
∆log KCUAB	+0.52			

Stability constants of proton and binary complexes of add (ref. 6) and Saba (ref. 16) with Cu(II) used for the extention of the above constants have been taken from our earlier published work.

CuB). The charges of all these complexes are neglected for clarity.

It appears that complex formation between glgl(Δ) and Cu(II) in the CuAB species involves the formation of a five-membered chelate ring as is the case with CuA-glgl complex, because $\log K_{\rm CuAB}^{\rm CuB}$ (Table I) and $\log K_{\rm CuA}^{\rm CuB}$ values are comparable. Similarly comparison of the $\log K_{\rm CuAB}^{\rm CuB}$ (Table I) and $\log K_{\rm CuB}^{\rm CuB}$ values clearly indicate that 4-aba (B) forms a seven-membered chelate ring in the CuAB complex species. Thu the CuAB species would contain five-and seven-membered chelate rings. Since more coordination positions are available for binding the first ligand to A given multivalent metal ion than for the responding ligand, negative values for Δ log $K_{\rm CuAB}$ (Eqs. 1 and 2) are expected. But this parameter for the title system

$$CuA + CuB \rightleftharpoons CuAB + Cu$$
 ...(1)

 $\triangle \log K_{\text{cuan}} = \log \beta_{\text{cuan}} = (\log \beta_{\text{cuan}} + \log \beta_{\text{cunn}}) = (2)$

is positive (Table 1). It indicates that 4-aba (B) ligand prefers to add on to CuA glgl binary according rather than to aquated Cu(II). Also, the positive Alog Keuan value suggests that the formation of ternary complex, CuAB is preferred over the binary complexes, CuA or CuB. However, the maximum amount of the total Cu(II) present in CuAB complex is only 7.5% (Fig. 1), while the statistically expected value is 50% indicating that the CuAB formation is less favoured. This may be atributed to the statisfactors associated with the five- and seven-membered chelate rings in this species.

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 $\triangle \log K_{\text{CHABH}-1} = \log \beta_{\text{CHABH}-1} - (\log \beta_{\text{CHAB}-1} + \frac{1}{2})$ log βcun)

...(3)

One may expect the same type of binding of the ligand B in both CuAB and CuABH_1 complexes and thus log K_{GuAB}^{GuA} and log $K_{GuABH_1}^{GuABH_1}$ values must be comparable. This trend was seen in the Cu(II)-glycinamide(A)-B systems, but in the Cu(II)-glg1 (A)-B systems the log Kouanna-1 values were lower than log K_{CuAn}^{CuA} values by ~ 3 log units. This was explainedby considering the bidentate binding of AH-1 glgl in CuABH-1 unlike its tridentate binding in the CuAH-i. Similar arguments have been put forward? to explain the negative \triangle lo $K_{\text{CuABH}-1}$ values (Eq. 4) with high magnitude in the case of Cu(II)-glgl(A)-Bsystems, while the $\triangle \log K_{cun-1}$ values in the Cu(II)glycinamide-B systems are in the order of statistically expected values. The bidentate mode of binding of AH-1 glgl in the ternary complex systems is further confirmed by the fact that $pK_{\text{CuAB}}^{\text{II}}$ values in all the Cu(II)-glgl-B systems studied are nearly identical within the limits of experimental error to the corresponding Cu(II)-glycinamide-B systems. Sigel3 also reported the bidentate binding of AH-1 glgl in the Cu(II)-glgl-2,2'-bipyridyl ternary system. For finding out the mode of coordination of AH-1 glgl in presently studied Cu(II)-glgl-4-aba system, the Cu(II) glycianmide-4-aba system was also investigated, but no appreciable complexing seems to have been revealed. If one compares the log $K_{\text{CuAB}}^{\text{CuA}}$ and log $K_{\text{CuABH}-1}^{\text{CuAH}-1}$ values in Table I for the title system, it may be noted that the latter parameter is lower than the former by only ~1:5 log units and its Alog Konani-1 value is in the order of statistically expected values. Both these values suggest that the AH₋₁, glgl is tridentate in CuABH₋₁ as in the case in CuAH₋₁ glgl binary com-

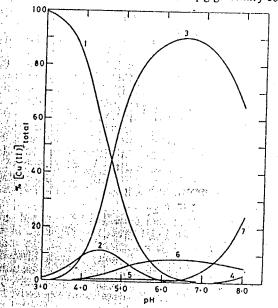


Fig. 1— Species distribution for the Cu(II) glgl(A)-4-aba(B) system at a metal-A-B ratio of 1:1:1 [(1) unbound Cu(II); (2) CuA; (3) CuAH_1; (4) CuA₂H_1; (5) CuB; (6) CuAB; and (7) CuABH_1].

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This tridentate binding of AH-, glgl in the title system is surprising, because 4-aba(B) is also a bidentate ligand like DL-2-aninobutyric acid or 3aminobutyric acid, under whose presence AH_, glgl is found to be bidentate. This may probably be accounted for by considering the fact that if ΛH_{-1} glgl binds in a bidentate manner, then the CuABH-1 species in the title system would have five- and seven membered chelate rings, possibly less favoured due to steric reasons. The strain due to the seven-membered ring of 4-aba (B) would get reduced by its coordination in one equatorial position and one axial position at a greater distance. This is possible only by the coordination of AH-1 glgl in a tridentate manner, i.e. by occupying three equatorial sites similar to its binding in the CuAH-1 glgl binary complex. The difference in the log KCuAn and log KCuAni-1 values of ~1.5 log units in the title system may thus be accounted for by the fact that in the CuAB complex, 4-aba (B) occupies two equatorial positions while in the CuABH₁ complex, it occupies one equatorial and one axial position.

Thus, the present investigation shows that the coordination behaviour of amide-deprotonated dipeptide in the ternary Cu(II) complex systems is highly influenced by the chelate ring size due to the secondary ligand, B. The CuABH_1 complex species is favoured above pH 6.5 and there is a steady increase in its concentration with rise in pH as shown in Fig. 1. At pH 8.0, about 24% of the total metal was found to be present in the form of CuABH-1 species.

- FREEMAN, H. C., Inorganic biochemistry, Vol. I, Chapter IV, edited by G. L. Eichhorn, (Elsevier, New York).
- 2. Sigel, H., Metal ions in biological systems, Vol. II (Marcel Dekker, New York), 1973
- 3. Sigel, H., Istorg. Chem., 14 (1975), 1535.
 4. Brookes, G. & Pettit, L. D., J. chem. Soc. Dalton Trans., (1975), 2112
- GERGELY, A. & NAGYPAL, I., J. chem. Soc. Dalton Trans., (1977), 1102.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., Indian J. Chem., 19A (1980), 672.
 MARTIN, R. P., MOSANI, L. & SARKAR, B., J. biol. Chem., 246 (1971), 59-44.
 NAIR M. S. SANTAPPA, M. & NAIRAMAN, P., Indian S. SANTAPPA, M. S. NAIRAMAN, P. S. NAIRA

- NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., J. chem. Soc. Dalton Trans., (1980), 2138.
 NAIR, M. S., J. chem. Soc., Dalton Trans., (1982), 561.
 LIM, M. C., SINN, E. & MARTIN, R. B., Inorg. Chem., 15-(1976), 807.
 NAIR M. S. SANTAPPA M. & NATARAJAN P. Juge.
- NAIR, M. S., SANTAPPA, M. & NATARAJAN, P., Inorg. chim. Acta, 41 (1980), 7.
 NAIR, M. S. & SANTAPPA, M., J. chem. Soc. Dalton Trans., (1981), 992; Indian J. Chem., 21A (1982), 58.
 NAIR, M. S., SANTAPPA, M. & MURUGAN, P. K., Inorg. Chem., 21 (1982), 142.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P. J. chem.
 NAIR, M. S., SANTAPPA, M. & NATARAJAN, P. J. chem.

- S. & SANTAPPA, M., Indian J. Chem., 20A