

## STUDIES ON THE INTERACTION BETWEEN $\text{Cu}^{++}$ WITH DL-ALANINE

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### ABSTRACT

The formation of complex of copper (II) with DL-alanine have been studied at 25, 30, 35, 40 and 45°C and different ionic strengths (0.07, 0.12, 0.17, 0.22 and 0.32 M.). The thermodynamic equilibrium constants and the thermodynamic parameters  $\Delta G^\circ$ ,  $\Delta H^\circ$  and  $\Delta S^\circ$  for copper (II) complexes of DL-alanine were calculated.

### INTRODUCTION

In recent years there has been considerable interest in the elucidation of the structures of the complex species formed in aqueous solutions of metal peptides because of their biological significance in enzyme reactions. The copper complexes of the alanine and polyglycines are of particular importance since dissociation of the peptide hydrogen atoms is facilitated in which takes place in the physiological pH range Freeman, *et al.*, (1965), Freeman, *et al.*, (1964), Freeman, (1966), Strandberg, *et al.*, (1961). In solutions, however, there has been considerable disagreement as to the nature of the ligand atoms involved in coordination with the copper ion.

In a series of interesting studies Kober and Surgiura Kober, *et al.*, (1912), and Kober and Haw Kober, *et al.*, (1916), showed that cupric ion forms with monocarboxylic-amino acids compounds of the type  $\text{CuA}_2$  where A refers of the amino acid molecule; and with glutamic acid, isoserine, and all polypeptides, compounds of the type  $\text{CuA}$ .

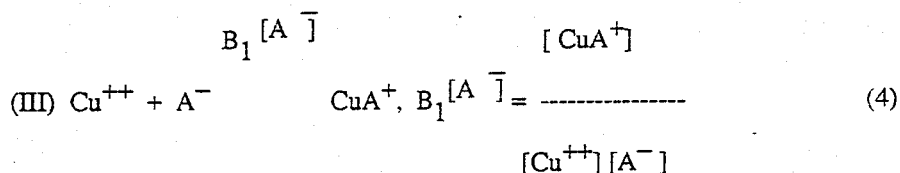
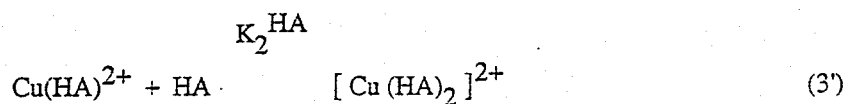
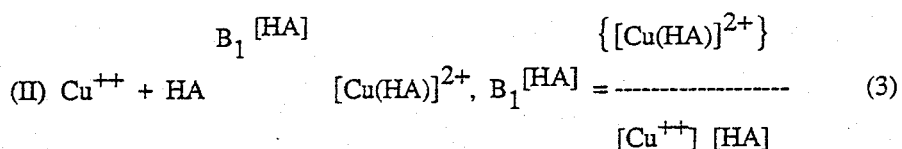
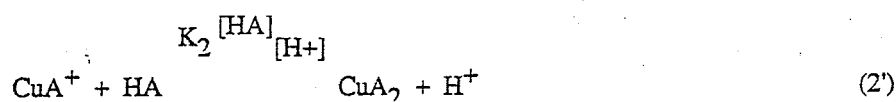
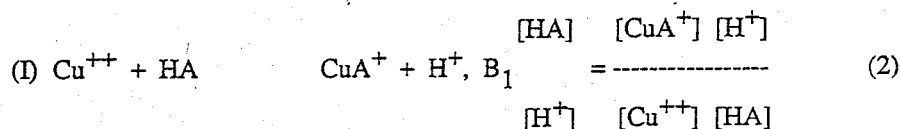
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In the present study, potentiometric measurements have been made for the formation of complex between the DI-alanine and copper (II) ions using Bjerrum's method Bjerrum (1941, 1957). The ionization constants of the pure DI-alanine are evaluated Emara, *et al.*, (1990).

### THEORETICAL CONSIDERATIONS

The calculated value for the stability constants depends on the proposed equilibrium reaction, and hence on the assumption of which of the species is involved in complex formation.

There are three possible reactions could take place :



The degree of formation of ligand number ( $\bar{n}$ ) has been defined Irving, *et al.*, (1953), as the average number of ligands bound per metal ion present in whatever form :

$$\bar{n} = \frac{L_{(\text{bound})}}{C_M} = \frac{L_{\text{tot.}} - L_{\text{free}}}{C_M} \quad (5)$$

The values of  $\bar{n}$  and  $[L]$  have been evaluated by any one of several graphical or numerical methods Rossotti, *et al.*, (1961), Beck (1970), Hartly, *et al.*, (1980).

If one complex is formed, then :

$$\frac{\bar{n}}{(1-\bar{n})} = B_1 [L] \quad (6)$$

A plot of  $\frac{\bar{n}}{(1-\bar{n})}$  versus  $[L]$  will yield a straight line of slope  $B_1$ .

If two complexes are formed equation (6) take form :

$$\frac{\bar{n}}{(1-\bar{n}) [L]} = B_1 + B_2 \cdot \frac{(2-\bar{n}) [L]}{(1-\bar{n})} \quad (7)$$

Here once more a plot of  $\frac{\bar{n}}{(1-\bar{n}) [L]}$  versus  $\frac{(2-\bar{n}) [L]}{(1-\bar{n})}$  gives a straight line with a slope of  $B_2$  and an intercept  $B_1$ .

If the reaction proceeds as (I),  $\bar{n}$  can be expressed in the following manner using equation (5):

$$\bar{n} = \frac{[CuA^+] + 2 [CuA_2]}{[Cu^{++}] + [CuA^+] + [CuA_2]} \quad (8)$$

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$$\text{Since : } \text{CuA}^+ = B_1 \frac{[\text{HA}][\text{Cu}^{++}]}{[\text{H}^+]}$$

$$\text{CuA}_2 = B_2 \frac{[\text{HA}]^2}{[\text{H}^+]^2} \cdot \text{Cu}^{++}$$

By substituting in equation (7)

$$n = \frac{B_1 \frac{[\text{HA}]}{[\text{H}^+]} \cdot [\text{Cu}^{++}] \frac{[\text{HA}]}{[\text{H}^+]} + 2B_2 \frac{[\text{HA}]^2}{[\text{H}^+]^2} [\text{Cu}^{++}] \frac{[\text{HA}]}{[\text{H}^+]}}{[\text{Cu}^{++}] + B_1 \frac{[\text{HA}]}{[\text{H}^+]} \cdot [\text{Cu}^{++}] \frac{[\text{HA}]}{[\text{H}^+]} + B_2 \frac{[\text{HA}]^2}{[\text{H}^+]^2} [\text{Cu}^{++}] \frac{[\text{HA}]}{[\text{H}^+]}} \quad (9)$$

On rearrangement equation (9) and considering the formation of only up to (1 : 2) complexes we obtain :

$$\frac{n}{(1-n)} = \frac{B_1 \frac{[\text{HA}]}{[\text{H}^+]} + B_2 \frac{[\text{HA}]^2}{[\text{H}^+]^2} \cdot \frac{(2-n)[\text{HA}]}{(1-n)[\text{H}^+]}}{(1-n)[\text{H}^+]}} \quad (10)$$

A plot of  $\frac{n}{(1-n)} \frac{[\text{H}^+]}{[\text{HA}]}$  versus  $\frac{(2-n)[\text{HA}]}{(1-n)[\text{H}^+]}$  gives intercept as  $B_1 \frac{[\text{HA}]}{[\text{H}^+]}$

and slope as  $B_2 \frac{[\text{HA}]}{[\text{H}^+]}$ .

Similar calculations for reaction (II) and (III) lead respectively to the following equations :

$$\frac{n}{(1-n)[\text{HA}]} = B_1 \frac{[\text{HA}]}{[\text{H}^+]} + B_2 \frac{[\text{HA}]^2}{[\text{H}^+]^2} \cdot \frac{(2-n)[\text{HA}]}{(1-n)} \quad (11)$$

$$\text{and } \frac{n}{(1-n)[A^-]} = B_1[A^-] + B_2[A^-] \frac{(2-n)[A^-]}{(1-n)} \quad (12)$$

From which the constants  $B_1^{[HA]}$ ,  $B_1^{[A^-]}$  and  $B_2^{[HA]}$ ,  $B_2^{[A^-]}$  are obtained as intercepts and slopes respectively.

The stability constants  $B_1^{[HA]}_{[H^+]}$  and  $B_1^{[A^-]}$  are related by the equation :

$$B_1^{[HA]}_{[H^+]} = B_1^{[A^-]} \cdot K_2 \quad (13)$$

where  $K_2$  is the second dissociation constant of DL-alanine.

Also,  $B_1^{[HA]}_{[H^+]}$  and  $B_2^{[A^-]}$  are related by the equation :

$$B_2^{[HA]}_{[H^+]} = B_2^{[A^-]} \cdot K_2 \quad (14)$$

## EXPERIMENTAL

The pH measurements were made with a Radiometer model PH-M 62 digital pH-mV meter equipped with a glass pH electrode model GK 2301 C-QL, which was immersed in a double jacketed cell thermostated at the correct temperature by LKB-BROMMA model 2209 MULTI TEMP.

All materials used were analytical reagents. The solvent used in this study is deionized distilled water. Copper perchlorate was prepared by dissolving copper carbonate in boiling perchloric acid using a slight excess of the former. The ligand solution was prepared by adding 16 ml. NaOH 0.5 M to 0.7128 gram DL-alanine, then completed to 20 ml. with deionized distilled water. Stock solutions of the other required materials were prepared.

Different concentrations were prepared by taking the required aliquot of the stock solutions, and dilutions were done just before the pH measurements. Sodium perchlorate was used to fix the ionic strength. Several measurements at ionic

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strengths (0.07, 0.12, 0.17, 0.22 and 0.32 M) were carried out to give an average value for the stoichiometric constants. The measurements at 25, 30, 35, 40 and 45°C were carried out. The pH of the meter is first adjusted using buffer 7, followed by buffer 4 and 9.

In most equilibrium studies on metal complex formation, the equilibrium constant is evaluated from measurements in solutions containing varying concentrations of metal and ligand. Such varying concentrations will produce changes in ionic strength and consequently in the formation constants values, so that the ionic strength should be kept constant by addition of a non-reacting salt.

The experiment can be carried out in one of two ways, either, the change of pH can be measured as a function of ligand concentration Bjerrum (1941, 1957).

OR, the pH can be measured as a function of the concentration of acid or alkali added to constant metal and total ligand concentration Irving *et al.* (1953).

As we mentioned above we used Bjerrum's method in this study as follows: A 200 ml. solution containing  $5 \times 10^{-3}$  M of  $\text{Cu}(\text{ClO}_4)_2$ ,  $5 \times 10^{-3}$  M of mineral acid ( $\text{HClO}_4$ ) and sufficient amount of 1M  $\text{NaClO}_4$  to adjust the required ionic strength, and thermostated at the desired temperature. The solution was then titrated with 0.4 M sodium alanate and the pH was measured after each addition of the titrant.

## RESULTS AND DISCUSSION

Having completed the calculations for the ionization constants of the pure Dl-alanine in our previous study Emara, *et al.*, (1990), we now make use of these data for calculating the stability constants of Cu (II) ions with Dl-alanine. Using the Bjerrum's technique. The Dl-alanine can exist in several forms in the solutions, namely diprotonated ( $\text{H}_2\text{A}^+$ ), monoprotonated (HA), unprotonated ( $\text{A}^-$ ), where  $\text{A}^-$  represents the alaninate species; Each of these species can act as a ligand in the solution. Also, there is possibility of forming mono or bidentate complexes in some of these ligands.

In our calculations we assume that each of the above mentioned ligand species  $A^-$ ,  $HA$  and  $H_2A^+$  is available to react with the metal ion present. We also assume the possibility of forming  $(CuA^+ \text{ or } CuA_2)$  and  $[Cu(HA)^{2+} \text{ or } Cu(HA)_2^{2+}]$  and  $[Cu(H_2A)^{+++} \text{ or } Cu(H_2A)_2^{++++}]$  depending on the scheme suggested for possible interactions.

Although each of these species at least in theory could act as the ligation species, the  $H_2A^+$  species was eliminated based on the fact that in the pH range at which it is the predominant species ( $pH < 6$ ) on complexation was observed from the results of ( $n$ ) values for Cu (II) DL-alanine complexes. We now discuss each scheme separately.

#### Scheme I :

The  $HA$  acts as a bidentate ligand via the carboxylic oxygen and the amino nitrogen, a release of the proton of the Zwitter ion ammonium group takes place with complexation according to the suggested equilibrium in this scheme.

When this scheme was considered and the data were fitted to equation (10) using a computer program, we recorded the results of :

$$B_1 \frac{[HA]}{[H^+]} \text{ and } K_2 \frac{[HA]}{[H^+]}$$

The stoichiometric  $K_1 \frac{[HA]}{[H^+]}$  and  $K_2 \frac{[HA]}{[H^+]}$  values at the various ionic strengths are extrapolated to the zero ionic strength at the corresponding temperature while thermodynamic values  $K_2^*$  are evaluated at 25, 30, 35; 40 and 45°C. Figures (1) and (2) show the plot of  $\log K_1 \frac{[HA]}{[H^+]}$  and  $\log K_2 \frac{[HA]}{[H^+]}$  against  $(1/T)$  respectively. Linear behaviour is observed. It was possible to obtain some thermodynamic parameters such as:  $\Delta H^\circ$ ,  $\Delta S^\circ$ , and  $\Delta G^\circ$ .

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Table (1) Complex formation constants and Thermodynamic parameters for complexes of DL-alanine with Cu<sup>2+</sup> assuming that :

$$B_1 \frac{[HA]}{[H^+]}$$

$$Cu^{2+} + HA \rightleftharpoons CuA^+ + H^+$$

Temperature °C	$10^2 K_1 \frac{[HA]}{[H^+]}$	$\Delta G^\circ$ K. J. mole <sup>-1</sup>	$\Delta H^\circ$ K.J. mole <sup>-1</sup>	$\Delta S^\circ$ J. deg <sup>-1</sup> mole <sup>-1</sup>
25	5.55	7.16	30.75	79.18
30	7.20	6.62	30.75	79.63
35	14.40	4.96	30.75	83.75
40	3.40	8.79	30.75	70.16
45	7.70	6.77	30.75	75.40

Table (2) Complex Formation constants and thermodynamic parameters for complexes of DL-alanine with Cu<sup>2+</sup> assuming that :

$$K_2 \frac{[HA]}{[H^+]}$$

$$CuA^+ + HA \rightleftharpoons CuA_2 + H^+$$

Temperature °C	$10^4 K_2 \frac{HA}{H^+}$	$\Delta G^\circ$ K. J. mole <sup>-1</sup>	$\Delta H^\circ$ K.J. mole <sup>-1</sup>	$\Delta S^\circ$ J. deg <sup>-1</sup> mole <sup>-1</sup>
25	3.00	20.08	-11.03	-104.40
30	0.0003	43.60	-11.03	-180.30
35	3.30	20.51	-11.03	-102.41
40	1.35	23.17	-11.03	-109.26
45	1.90	22.64	-11.03	-105.87

**Scheme II :**

Here HA acts as a monodentate ligand, coordinating, via the carboxylic group, giving rise to the above equilibria. This reaction was considered and the data were fitted to equation (II). However, the final results for  $B_1 \frac{[HA]}{[H^]}$  are negative values or zero.

The fact that the values for  $B_1$  and  $B_2$  are negative values or zero simply excludes the possibility of existence of such scheme, under the present experimental conditions.



It is worth noting that such scheme reaction is unlikely, due to the fact that the carboxylic group is weakly chelating group.

**Scheme III :**

Here the alaninate anion  $A^-$  where both carboxylic and amino groups are deprotonated, could act as the ligating species, equation (12) is used to calculate  $B_1[A^-]$  and  $B_2[A^-]$  for this scheme.

Also, the plots of these results of  $\log K_1[A^-]$  and  $\log K_2[A^-]$  against  $(1/T)$  are shown in figures (3) and (4) respectively. It is shown here that only  $B_1[A^-]$  is obtained and on  $B_2[A^-]$  values could be evaluated.

In all the above three schemes thermodynamic equilibrium constants are obtained by extrapolating the stoichiometric stability constants to zero ionic strength.

Table (3) Complex formation constants and thermodynamic parameters for complexes of DL-alanine with  $Cu^{2+}$  assuming that :

		$B_1[A^-]$		
		$Cu^{2+} + A^-$	$CuA^+$	
Temperature		$\Delta G^\circ$	$\Delta H^\circ$	$\Delta S^\circ$
°C	$10^{-8} K_1[A^-]$	K. J. mole <sup>-1</sup>	K.J. mole <sup>-1</sup>	J. deg <sup>-1</sup> mole <sup>-1</sup>
25	4.00	-49.03	24.69	247.38
30	5.95	-50.86	24.69	249.31
35	8.50	-52.61	24.69	250.95
40	5.40	-52.28	24.69	245.90
45	2.90	-51.47	24.69	239.50

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Table (4) Complex formation constants and thermodynamic parameters for complexes of Dl-alanine with Cu<sup>2+</sup> assuming that :

$$B_2 [A^-] \text{ CuA}^+ + A^- \rightleftharpoons \text{CuA}_2$$

Temperature		$\Delta G^\circ$	$\Delta H^\circ$	$\Delta S^\circ$
°C	$10^{-5} K_2 [A^-]$	K. J. mole <sup>-1</sup>	K.J. mole <sup>-1</sup>	J. deg <sup>-1</sup> mole <sup>-1</sup>
25	9.10	-33.97	-26.44	25.26
30	0.07	-22.29	-26.44	-13.72
35	4.50	-33.31	-26.44	22.29
40	3.30	-33.04	-26.44	21.08
45	1.84	-32.02	-26.44	17.56

Inspecting the thermodynamic parameters of the two schemes for copper complexes, we observe that CuA<sup>+</sup> is the most favored complex than CuA<sub>2</sub>, followed by (CuA<sup>+</sup> + H<sup>+</sup>) or (CuA<sub>2</sub> + H<sup>+</sup>).

This of course is understandable from both statistical as well as energy point of view. The data of B<sub>1</sub> for CuA<sup>+</sup> showed that the tendency of copper for complexation is good which is reflected by B<sub>1</sub> [A<sup>-</sup>] values and the  $\Delta G^\circ$  values.

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*M. M. Emar, et. al.,*

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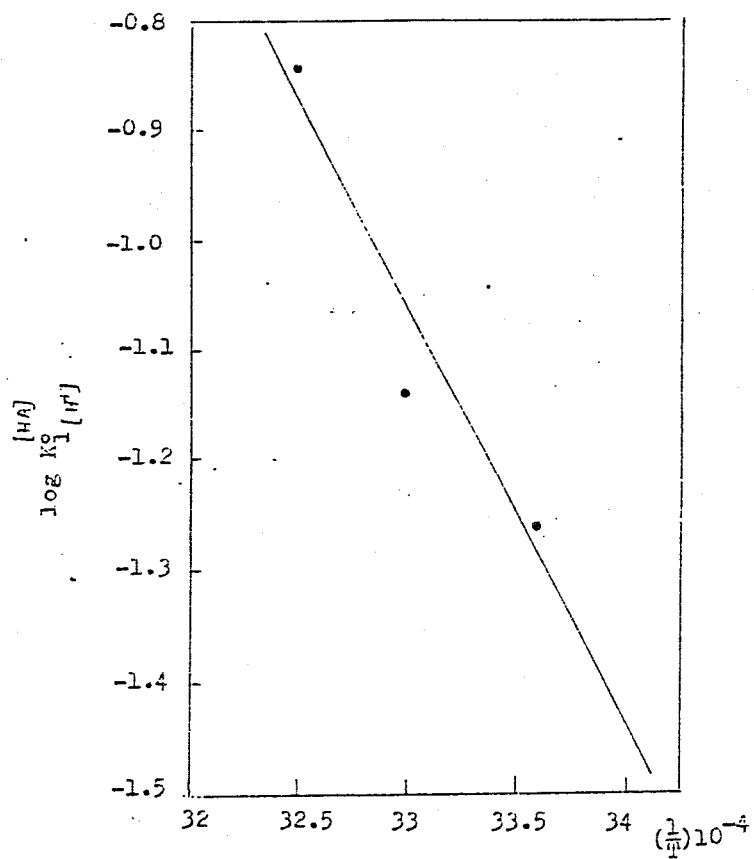


Fig. (1):  $\log K_1 \frac{[HA]}{[H^+]}$  against  $(\frac{1}{T}) 10^{-4}$  for the reaction between  $\text{Cu(II)}$  and DI-alaninate ion.

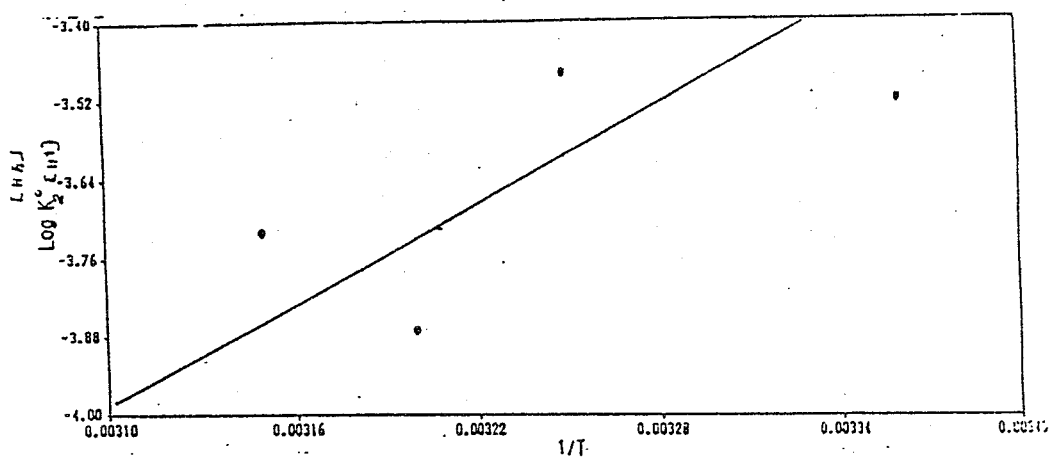


Fig. (2):  $\text{Log } K_2^{\frac{[\text{HA}]}{[\text{H}^+]}}$  against  $(1/T)$  for the reaction between Cu(II) and DI-alaninate ion.

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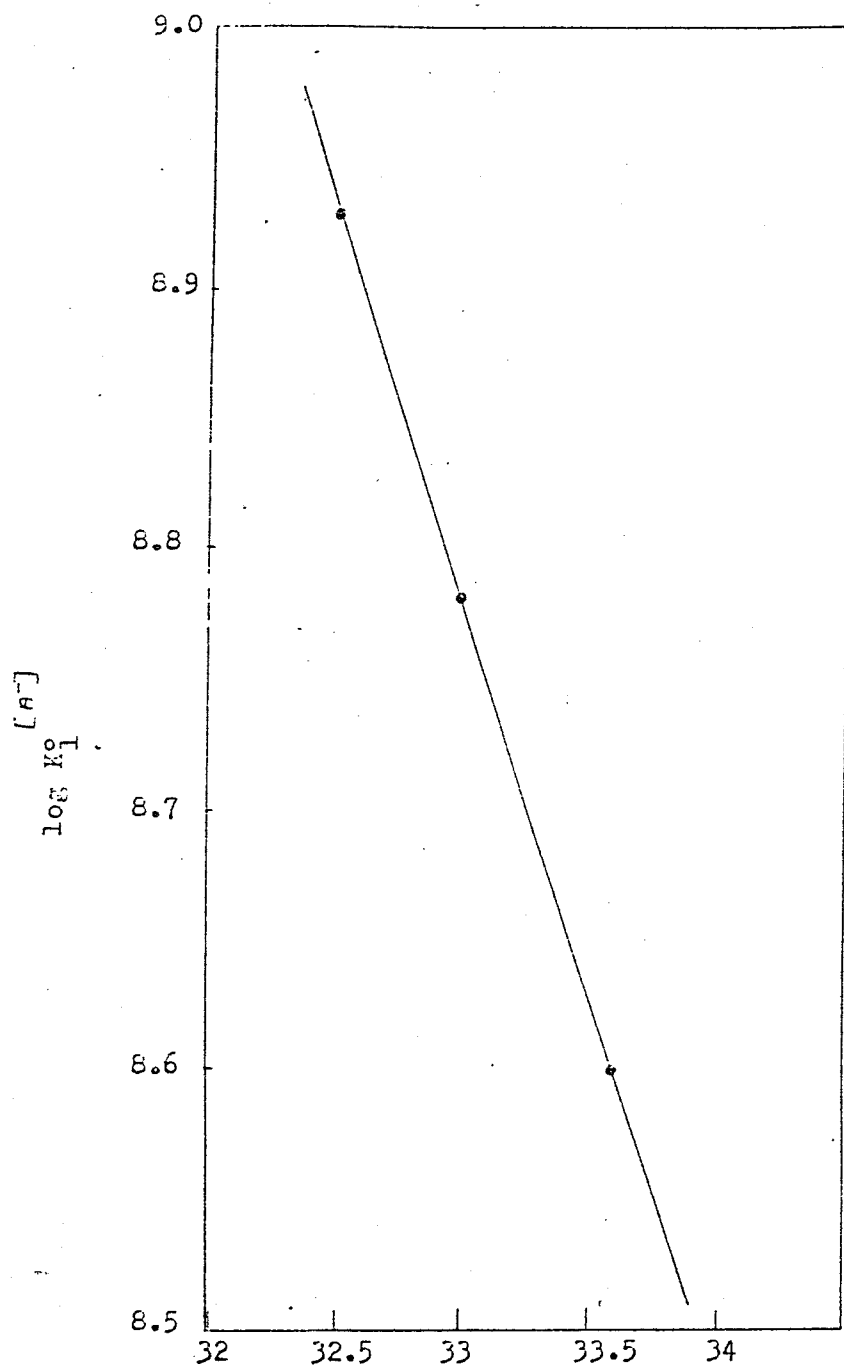


Fig. (3):  $\log K_1 [A^-]$  against  $(1/T) \cdot 10^{-4}$  for the reaction between  $\text{Cu(II)}$  and  
270 DI-alaninate ion.

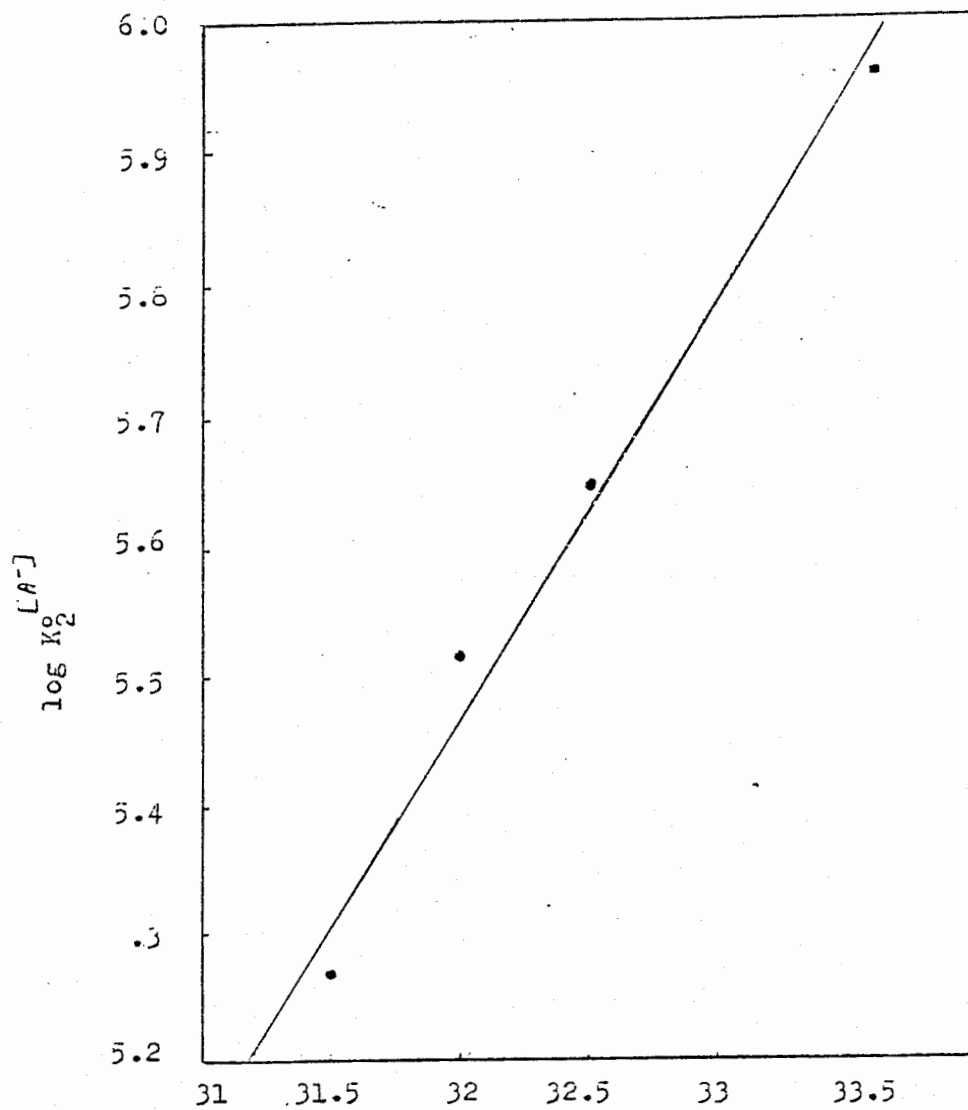


Fig. (4):  $\log K_2 [A^-]$  against  $(1/T) \cdot 10^{-4}$  for the reaction between Cu(II) and DI-alaninate ion.