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Complexation of Co(II) and Cu(II) with L-2-Amino 4-methyl mercaptobutanoic acid: A Kinetic Study

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Abstract
Methionine is a sulphur containing essential amino acid and cannot be synthesised in living beings. In deficiency state of methionine, the formation of creatinine would be reduced giving a false impression of depressed kidney function. Therefore, a comprehensive kinetic study was carried out to study its interaction with metal ions Co (II) and Cu(II). Rate constants corresponding to the binding steps, outer sphere complex formation reaction (K_{os}), rate constant of water exchange (k_o) were computed. The proposed mechanism is supported by the computation of activation parameters corresponding to stepwise rate constants.

Keywords: Kinetic studies, complexation, specific rate constant, activation parameters

Introduction
L-2-Amino 4-methyl mercaptobutanoic acid (Methionine) is a sulphur containing essential amino acid and cannot be synthesized in living beings. It is the biological precursor of Vitamin B (Harington *et al*., 1939) [1]. Its presence also increases the rate of formation of creatinine. The elimination of creatinine by kidney called creatinine clearance is used as an acceptable measure of kidney function. In deficiency state of methionine the formation of creatinine would be reduced giving a false impression of depressed kidney function.

In addition, L-2 Amino 4-methyl mercapto butanoic acid acts as a methyl donor to promote myelination of nervous system. This is the process by which nervous system attains structural and functional maturity. Its deficiency results in tingling sensation and numbness of limbs (Cotran *et al*., 1989) [2].

Deficiency of L-2 Amino 4-methyl mercapto butanoic acid may give rise to fatty liver, known as lipotropic action. It is an essential amino acid that can fulfill the requirements of cystine as well.

Because of the immense significance of L-2-Amino 4-methyl butanoic acid, a comprehensive kinetic study was carried out to study its interaction with metal ions like Co(II) and Cu(II). Rate constants corresponding to the binding steps, outer sphere complex formation constant (K_{os}), rate constant of water exchange (k_o) were computed.

To support the proposed mechanism, activation parameters corresponding to the stepwise rate constants were also calculated.

Methodology
The complexation of Co(II) with L-2-Amino 4-methyl mercapto butanoic acid, under first order conditions, i.e. [Co(II)] >>[L-2-Amino 4-methyl mercapto butanoic acid], was studied in the pH range 5.92-7.05. The study was restricted in this pH range to avoid hydrolysis of Co(II). The studies were carried out at 20, 25, 30 and 35 ($\pm$ 0.05)^{o}C. Oscilloscope traces of concentration change versus time were taken to calculate firs order rate constants. The complexation reaction was monitored at 620 nm using pH indicator method.

The complexation of Cu(ll) L-2-Amino 4-methyl mercapto butanoic acid was investigated in the pH range 2.23-2.93 at temperatures 25,30 and 35 (±0.05)°C. The ionic strength of the reaction mixture was maintained at 0.1 M with KNO_3. The reaction was studied at 600 nm under first order conditions i.e. [Cu(II]>> [L-2-Amino 4-methyl mercapto butanoic acid]. No indicator was used as the transmittance changes were large enough to be monitored directly.

Result and Discussion
Predominant form of L-2-Anino 4-methyl mercapto butanoic acid in aqueous solution is

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Different equilibria existing among the various forms of L-2-   Amino 4-methyl mercapto butanoic acid are:
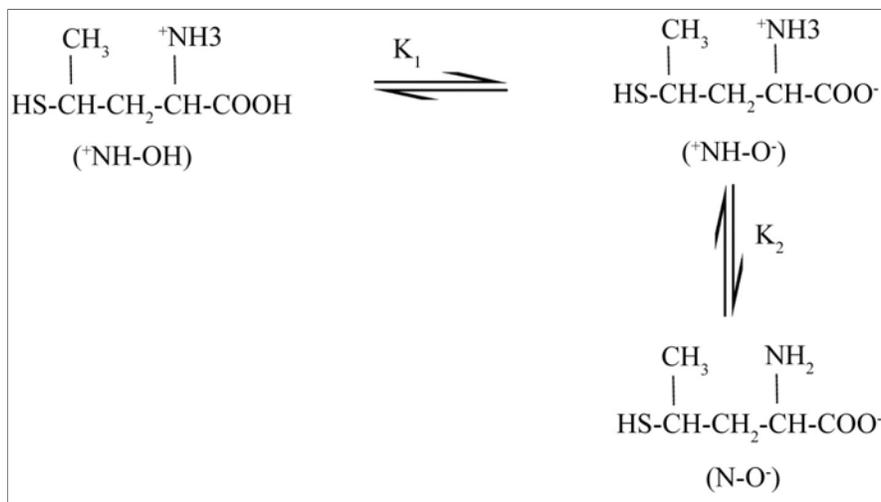
where ($^+$NH - OH), ($^+$NH - O$^-$) and (N - O$^-$) are the diprotonated, monoprotonated and deprotonated forms respectively of L-2-Amino 4-methyl mercaptobutanoic acid.The values (Martell *et al*., 1974) of K_1 and K_2 at 25°C are 2.20 and 9.05 respectively. These values were corrected for other temperatures of investigations using equation.

$$\text{Log } K_a^{T2} = \log K_a^{T1} + \frac{\Delta H (T_2 - T_1)}{4.576/T_1 T_2}$$

Following Scheme 1 for the interaction of various forms of the ligand with Co(II) was suggested and found to be in conformity with our kinetic data.
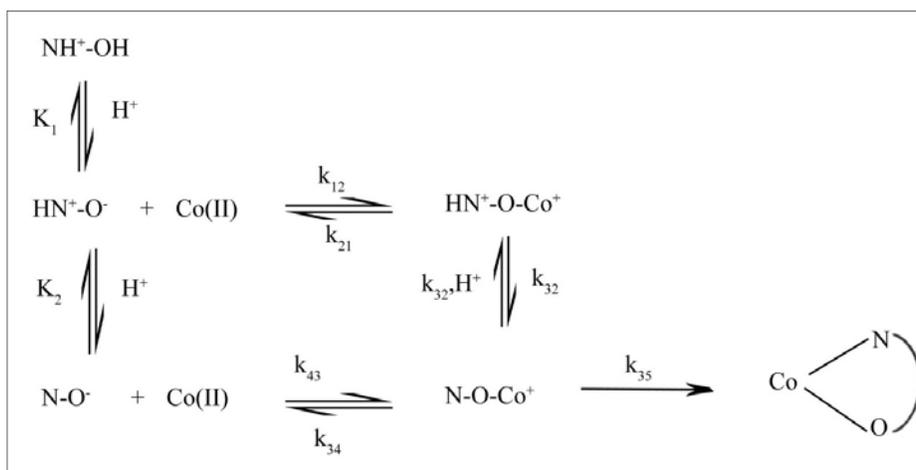
Scheme 1: Based on Scheme 1 rate of the reaction is:

Rate = k_{35} [N- O– Co$^+$]   (3)

Applying steady state approximation to non - chelating species (HN$^+$ -O - Co$^+$) and (N - O –Co$^+$) we have:
Applying the approximation that $k_{35} \gg k_{34}$ ($\because$the reaction goes toward completion) and at high pH's,

K_{23} (k_{14} +k_{35})$\gg k_{21} k_{32}$ [H$^+$], we get:

$$\frac{k_{obs} \{[H^+]^2 + K_1[H^+]\, K_1 K_2\}}{K_1[H^+]} = k_{12} + k_{43} \frac{K_2}{[H^+]}$$ (4)

The above equation predicts a linear, plot for k_{obs} $\{[H^+]$ +K_1 $K_2\}/K_1[H_+]\}$ versus [H$^+$] and this is what was actually observed. The plots for Co(II)- L-2-Amino 4-methyl mercapto
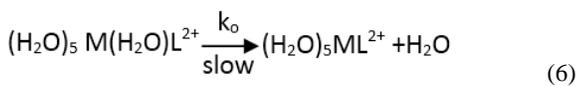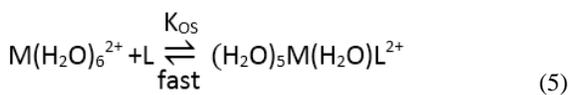
butanoic acid system are shown in Fig. 1. The values of specific rate constants k_{12} and k_{43} from were calculated from the intercept and slope respectively of these plots (Table 1). Average values of energies of activation were calculated from the linear plots of log k versus 1/T while those of enthalpies and entropies of activation were evaluated from the slopes and intercepts respectively of log k / T versus 1/T. These values are given in Table 1.

Calculation of Water Exchange Rate Constant
A general mechanism (Eigen *et al*., 1962) for complexation involves an outer sphere complex formation between the metal ion and ligand followed by the loss of a water molecule from the inner coordination sphere of the metal ion and an attack by the ligand. This is represented as:
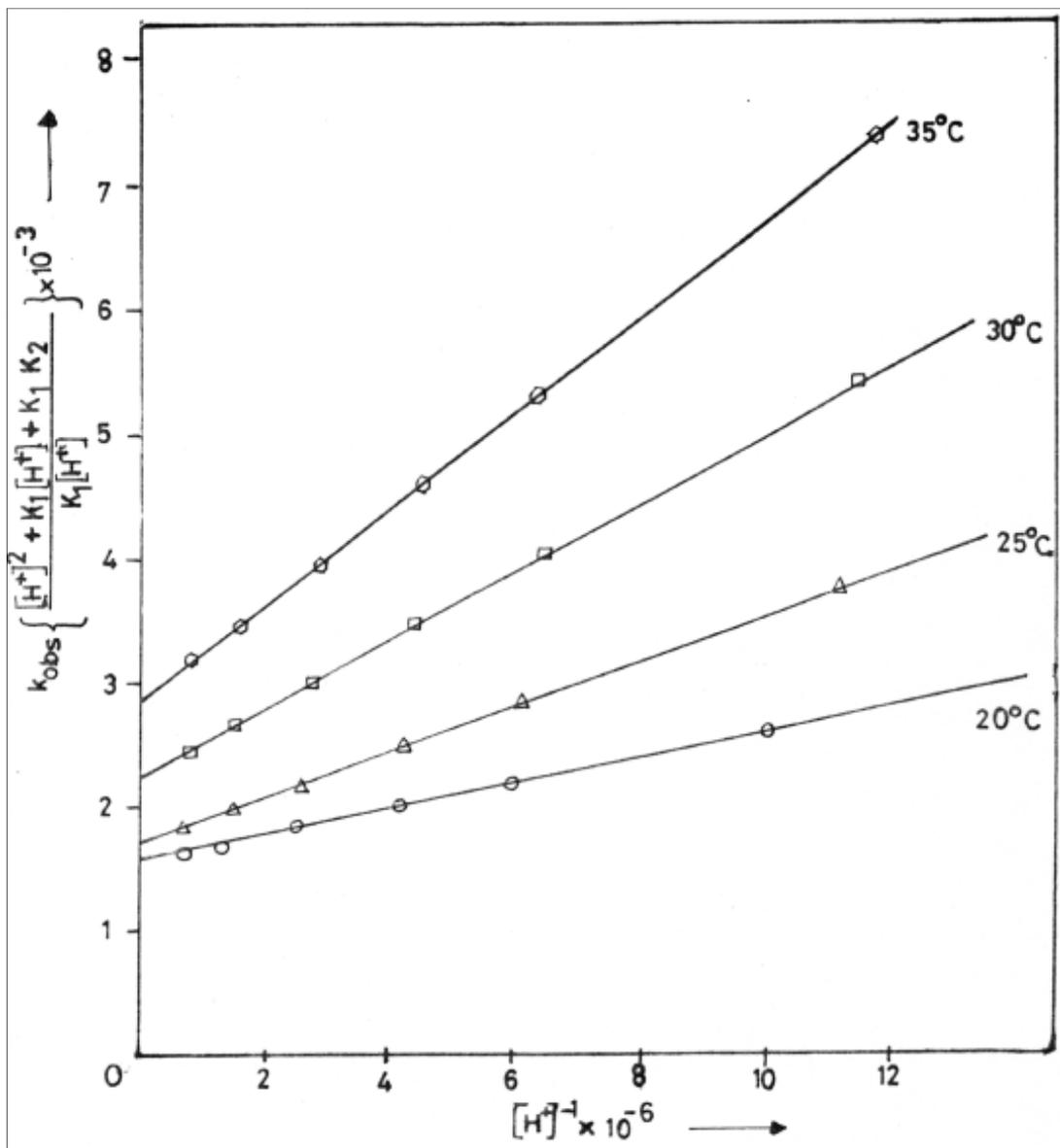
Fig 1: Plots of $k_{obs}\{[H^+]^2 + K_1[H^+] + K_1 K_2 / K_1 [H^+]$ versus $[H^+]^{-1}$ for Co(II)-L-2-Amino 4-methyl mercapto butanoic acid complexation at different temperatures

$$M(H_2O)_6^{2+} + L \underset{fast}{\overset{K_{OS}}{\rightleftharpoons}} (H_2O)_5 M(H_2O)L^{2+} \qquad (5)$$

$$(H_2O)_5 M(H_2O)L^{2+} \xrightarrow[slow]{k_o} (H_2O)_5 ML^{2+} + H_2O \qquad (6)$$

Rate expressed as

$$Rate = \frac{d[ML^{2+}]}{dt} = K_{OS} k_o [M(H_2O)_6^{2+}][L] \qquad (7)$$

According to Scheme 1 water exchange takes place via k_{12} and k_{43} steps, therefore, rate of the reaction is written as:

$$Rate = k_{12}[HN^+ - O^-][Co(II)] + k_{43}[N - O^-][Co(II)] \qquad (8)$$

From Table 1 $k_{43} \gg k_{12}$, therefore, above equation reduces to:

$$Rate = k_{43}[N - O^-][Co(II)] \qquad (9)$$

Comparing equation (112) and (114) we have,

$$k_{43} = k_o K_{os} \qquad (10)$$

knowing k_{43} and K_{os}, the value of k_o was calculated (Fuoss, 1958). The value of k_o at 25°C was found to be 1.04×10^5 s^{-1}. The values at other temperatures of investigation are reported in Table 1.
The value of $\Delta H_{43}^{\#}$ is found to be smaller than $\Delta H_{12}^{\#}$, confirming the higher reactivity of deprotonated form of the ligand. Negative value of entropy of activation suggests that the reaction is between oppositely charged tons and proceeds via associative path way.
The values of first order rate constant (k'_{obs}) were evaluated from the plots of concentration change versus time. These values are reported in Table 1.

Table 1: Values of specific rate constants and their activation parameters for the interaction of Co(II) and Cu(II) with L-2-Amino 4-methyl mercapto butanoic acid

Temperature (± 0.05) °C	Co(II) – Ligand			Cu(II) – Ligand		
	$K_{12} \times 10^{-3}$ $(M^{-1}s^{-1})$	$K_{43} \times 10^{-5}$ $(M^{-1}s^{-1})$	$k_o \times 10^{-5}$ (s^{-1})	$K_{12} \times 10^{-3}$ $(M^{-1}s^{-1})$	$K_{43} \times 10^{-9}$ $(M^{-1}s^{-1})$	$k_o \times 10^{-9}$ (s^{-1})
20	1.55	1.69	0.85	-	-	-
25	1.70	2.07	1.04	3.35	6.26	3.16
30	2.25	2.25	1.14	4.15	6.88	3.47
35	2.85	2.49	1.26	5.00	7.48	3.77
$\Delta H^{\#}$ (kJ mol^{-1})	31.35 +2.77	17.30 + 0.83	-	27.94 + 0.20	11.58 + 0.11	-
$\Delta S^{\#}$ (J k^{-1} mol^{-1})	-94.18 + 2.35	-95.59 + 2.74	-	-100.28 + 7.41	-35.18 + 3.16	-

The plots of $k_{obs}\{$ $[H^+]^2+ K_1 [H^+] +K_1K_2\}/K_1[H^+]$ versus $[H^+]^{-1}$ were found to be linear (Fig. 1). This suggested that the mode of interaction of various forms of L-2-Amino 4-methylmercaptobutanoic acid with Cu(II) was in according with Scheme 1. The values of specific rate constants (Table 1) were obtained from the plots by following the procedure described for Co(II)-L-2-Amino 4-methyl mercapto butanoic acid system. The values of activation parameters corresponding to specific rate constants were calculated from the plots of log k and log k/T versus 1/T. These values are given in Table 1. The value of water exchange rate constant (k_o) at different temperatures of investigation is also given in Table 1. The obtained value of k_o was found to be in excellent agreement with that obtained from NMR studies (Swift *et al.*, 1962).

The value of k_{43} is found to be much larger than of k_{12}, indicating that the deprotonated form is more reactive than the mono protonated form. The reactivity of both the forms increase with rise in temperature. Higher reactivity of deprotonated form is in conformity with the obtained values of activation parameters. The energy and enthalpy of activation corresponding to k_{43} is found to be smaller than that for k_{12} step. Negative values of entropy of activation indicate that the reaction is between two oppositely charged species.

Comparison of data indicates that in both the systems deprotonated form is more reactive than the mono protonated form but the reaction is faster in case of Copper (II) system. This is explained on the basis of difference in crystal field stabilization energy. The loss of water molecule changes the geometry from Octahedral to Trigonal bipyramidal.

The difference in CFSE (Oh-TBP) are 2.55 and 1.09 for Co(II) and Cu(II) respectively. The lower value in case of Cu(II) is responsible for the larger value of k_{43}. This theoretical explanation is supported by the calculated values of activation parameters. The value of enthalpy of activation for k_{43} step is 19.30 kJ mol^{-1} and 11.58 kJ mol^{-1} for Co(II) and Cu(II) respectively. The lower value of $\Delta H_{43}^{\#}$ for Cu(II) is responsible for higher rate of complexation of Cu(II) with deprotonated form of L-2-Amino 4-methyl mercapto butanoic acid.

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