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Kinetics of complexation of Ni(II) with DL-2-Amino butanoic acid and Acetyl –L-histidine

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Abstract

Kinetics of the complexation of Ni(II) with DL-2-Amino butanoic acid and Acetyl L-histidine was studied in the pH range 6.03-7.18 at 620 nm using bromothymol blue as indicator, under first order conditions. The overall rate constant was resolved into stepwise rate constant and corresponding activation parameters were also determined. Negative value of entropy of activation predicts associatively activated mechanism. These amino acids are excreted in urine in certain genetic disorders. Chelation with metal ions may open new avenues for detecting these metabolic disorders.

Keywords: Kinetics, chelation, binding sites, specific rate constant, activation parameters.

1. Introduction

DL-2-Amino butanoic acid (Dent *et al.*, 1947; Waley, 1956; Walker, 1952) ^[1, 2, 3] is present in animal tissues, eye lens and potato extract. Incertain genetic disorders (Dent, 1947) ^[4], where thereis defective reabsorption of amino acids like of DL-2-Amino butanoic acid, by the kidney, it appears in large quantities in the urine. This excessive excretion is detected by chelation ofDL-2-Amino butanoic acid with suitable metal ion. Similarly, excessive Acetyl L-histidine appears inurine of patients with a genetic disorder histidenemia which is due to the deficiency of enzyme histidase (Cotran *et al.*, 1989) ^[5]. The normal catabolic pathway of histidine is disturbed and retained histidineis converted into acetyl histidine which is excreted in urine. In this disorder, patients show physical and intellectual retardation. Speech is also defective. Dietary restriction ofhistidine also does not help the patients. Chelation with metal ions may open new avenues for detecting this metabolic disorder.

In order to understand the exact mechanism of binding, it is desired to know about the available active sites, overall rate constants, stepwise rate constants corresponding to the interaction of various forms of the ligand with the metal ion.

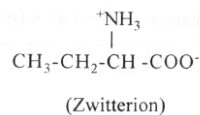
Keeping this in mind, a comprehensive kinetic study of Ni (II) with DL-2-Ainmo butanoic acid and Acetyl-L-histidine was carried out. The obtained kinetic data was resolved into stepwise rate constants. Activation parameters corresponding to different steps were also calculated.

Methodology

The kinetics of the complexation of Ni (II) with DL-2-Aminobutanoic acid and Acetyl L-histidine was studied in the pH range 6.03-7.18. The study was restricted in this range to avoid the hydrolysis of Ni (II) to Ni(OH)⁺. The ionic strength of the reaction mixture was maintained at 0.1 M with KNO₃. The temperatures of investigations were 25, 30, 35 and 40 (±0.05)°C. The study was done under first order conditions i.e. large excess of metal ion over the ligand. Transmittance changes were monitored at 620 am using bromothymol blue as an indicator. Plots of concentration change versus time were utilized to obtain the value of first order constants (k'obs) and second order rate constant (kobs).

Result and Discussion

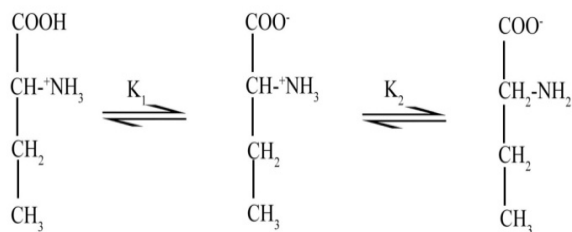
The predominant form of DL-2-Amino butanoic acid in solution is:

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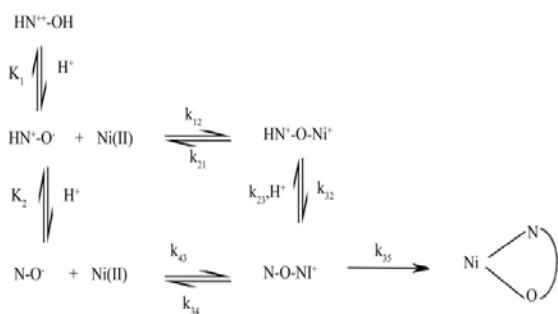
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It has two coordinating groups i.e. a carboxylic and an amino group. Values of dissociation constants (Martell *et al.*, 1974) indicate that these two groups participate in the complexation with metal ions.

Different equilibrium existing among various forms of DL-2-Amino butanoic acid are:



Diprotonated (HN⁺ - OH), monoprotonated (HN⁺ - O⁻) and deprotonated (N-O⁻) forms were found to react with Ni(II) in the following manner (Scheme 1). This suggested scheme was found to give the best fit with our kinetic data.



Scheme 1

The values of K₁ and K₂ at 25 °C were taken from the literature and corrected for other temperatures of our study using the thermodynamic relation:

$$\text{pK}_a^{T_2} = \{\Delta H (T_2 - T_1) / 4.576 T_1 T_2\} + \text{pK}_a^{T_1}$$

According to above scheme, the overall differential equation for Ni (II) –DL- 2-Amino butanoic acid complexation:

$$\text{Rate} = -d [\text{Ni (II)}] = -d [\text{DL-2-Amino butanoic acid}] \quad (1)$$

$$= k_{\text{obs}}[\text{Ni(II)}] \{ [\text{HN}^+-\text{OH}] + [\text{HN}^+-\text{O}^-] + [\text{N} - \text{O}^-] \} \quad (2)$$

$$= k'_{\text{obs}} \{ [\text{HN}^+-\text{OH}] + [\text{HN}^+-\text{O}^-] + [\text{N-O}^-] \} \quad (3)$$

Applying steady rate approximation to various intermediates we obtained:

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

Linear plots of k_{obs} {[H⁺]² + K₁ [H⁺] + K₁ K₂} / K₁ [H⁺] versus [H⁺]⁻¹ are shown in Fig. 1. The value of k₁₂ and k₄₃ were calculated from the intercept and slopes respectively of Fig. 1 and are reported in Table I. The values of enthalpies of activation and entropies of activation corresponding to k₁₂ and k₄₃ were evaluated from the slopes and intercepts respectively of the linear plots of log k/T versus 1/T equation and is given in Table 1.

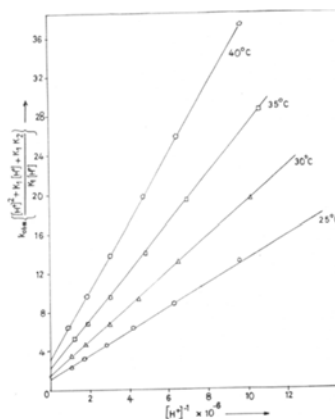


Fig 1: Plots of k_{obs} {[H⁺]² + K₁ [H⁺] + K₁ K₂} / K₁ [H⁺] versus [H⁺]⁻¹ for Ni(II)-DL-2-Amino butanoic acid complexation at different temperatures.

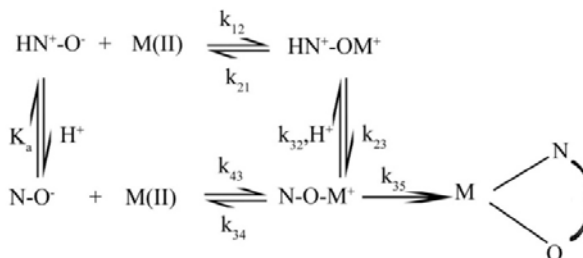
Table 1: Values of specific rate constants at different temperatures and their activation parameters for the complexation of Ni(II) with DL-2-Amino butanoic acid

Temperature (+ 0.05)°C	k ₁₂ (M ⁻¹ s ⁻¹)	k ₄₃ × 10 ⁻² (M ⁻¹ s ⁻¹)
25	1.20	5.19
30	1.60	5.60
35	2.20	5.93
40	3.00	6.28
ΔH (kJ mol ⁻¹)	53.17 ± 2.60	7.88 ± 0.25
ΔS (J K ⁻¹ mol ⁻¹)	-38.67 ± 1.61	-183.14 ± 4.11

Ni(II)- Acetyl L-Histidine complexation

Histidine is a tridentate ligand. The three active sites are: an amino group, an imidazole nitrogen and a carboxyl oxygen. It has been found that because of strong intramolecular hydrogen bonding between protonated amino and carboxylate group, the activity of both these groups is blocked to larger extent. As a result, the nitrogen of imidazole having a non-bonding pair of electron participate first in bond formation with metal ions. In case of acetyl histidine, there is no such hydrogen bonding and it is expected that carboxylate and the nitrogen of imidazole both participate in bond formation.

If it is assumed that various forms of the ligand react with metal ion in accordance with Scheme 2, where the metal ion attacks the carboxylate end of the amino acid because of electrostatic interaction



Scheme 2

The plots of k_{obs} {1 + K_a / [H⁺]} versus [H⁺]⁻¹ are expected to be linear. However these plots at the temperatures of our investigations were found to be non-linear (Fig. 2). To explain the nonlinearity of these plots, an alternative Scheme 3 was suggested, which was found to give the best fit with our kinetic data

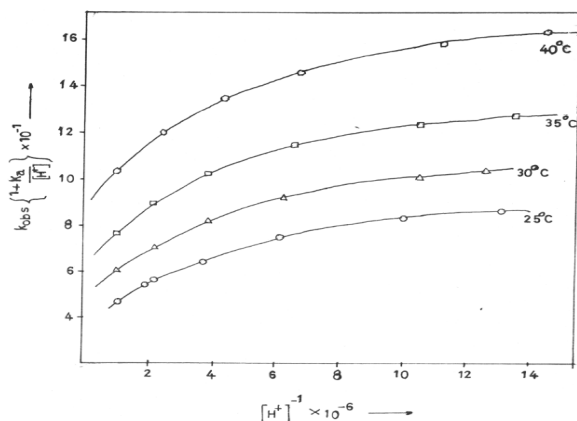
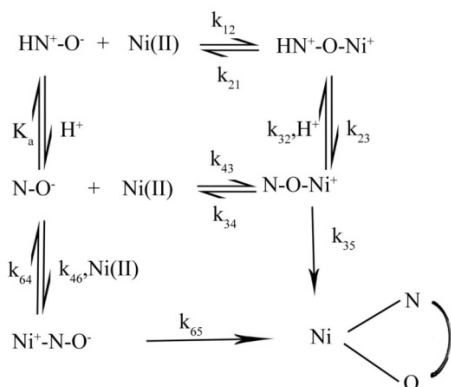


Fig 2: Plots of $k_{\text{obs}} \{1 + K_a/[H^+]\}$ versus $[H^+]^{-1} \text{Ni(II)-L-2-Acetyl-L-histidine}$ complexation at different temperatures.

Scheme 3

According to Scheme 3 overall reaction rate is:

$$\text{Rate} = k_{35}[\text{N}-\text{O}-\text{Ni}^+] + k_{65}[\text{Ni}^+-\text{N}-\text{O}^-] \quad (5)$$

Applying steady state approximation for unstable intermediates

($\text{HN}^+-\text{O}-\text{Ni}^+$), ($\text{N}-\text{O}-\text{Ni}^+$) and ($\text{Ni}^+-\text{N}-\text{O}^-$) we get:

$$k_{\text{obs}} = \frac{A + B/[H^+]}{C/[H^+] + 1} \times \frac{1}{\{K_a + [H^+]\}} \quad (6)$$

Where $A = (k_{43} + k_{46}) K_a$

$B = k_{12}$

$C = k_{21} k_{32} / k_{23} k_{35}$

The values of A, B and C were evaluated by carrying out a non-linear regression analysis. The values of $(k_{43} + k_{46})$, k_{12} and $k_{21} k_{32} / k_{23} k_{35}$ were calculated from the values of A, B and C. Average values of activation parameters corresponding to k_{12} and $(k_{43} + k_{46})$ were calculated from the linear plots of $\log k$ and $\log k/T$ versus $1/T$. These values are reported in Table 2.

The values of $(k_{43} + k_{46})$ show that the deprotonated form will react more rapidly with Ni(II) as compared to the zwitterionic form. Because of electrostatic forces of attraction between the positive charge of Ni(II) and the negative charge of carboxylate group, it is inferred that k_{43} is greater than k_{46} . Activation parameters corresponding to k_{12} and $(k_{43} + k_{46})$ (Table 2), further confirm that k_{12} is slow as compared to $(k_{43} + k_{46})$. Also, the values of second order rate constants calculated on the basis of Scheme 3 are in good agreement with the experimental values. Thus, the overall mechanism is in conformity with our kinetic result. Negative value of the entropy of activation suggests an associatively activation mechanism.

Table 2: Values of specific rate constants at different temperatures and corresponding activation parameters for the complexation of Ni(II) with Acetyl L-histidine

Temperature (± 0.05) $^{\circ}\text{C}$	$k_{12} \times 10^{-1}$	$(k_{12} \times k_{46}) \times 10^{-2}$	$k_{21} k_{32} / k_{23} k_{35} \times 10^{-5}$
25	7.00	1.05	6.07
30	9.01	1.12	5.39
35	10.50	1.43	4.60
40	12.00	1.81	2.31
ΔH^{\ddagger} (kJ mol $^{-1}$)	26.23 ± 0.54	25.34 ± 0.13	
ΔS^{\ddagger} (J K $^{-1}$ mol $^{-1}$)	-137.77 ± 1.96	-138.90 ± 1.18	

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