

Kinetics of Complexation of Nickel (II) by L-Tyrosine

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Received 28 December 1984; revised 2 September 1985; rerevised and accepted 1 October 1985

The kinetics of complexation of nickel (II) by L-tyrosine has been studied by stopped flow method in the pH range of 6.10-7.50 under pseudo-first order conditions, $[\text{Ni(II)}] \gg [\text{L-tyrosine}]$. The values of k'_{obs} for the reaction vary from 0.06-5.00 s^{-1} . The detailed kinetic study has shown that initial complexing with Ni(II) is by the carboxylate group of the zwitterion; the overall rate constant has been resolved into specific rate constants. There is a good agreement between calculated values and the experimentally obtained values for k'_{obs} for the formation of mono complex of Ni(II) at various pH values. The values of energy of activation and entropy of activation for the overall reaction have also been evaluated.

Complexation reactions have received considerable attention due to the wide range of processes in which metal ions participate. The kinetic data from such studies can yield information about the detailed mechanism by which the ligand enters the first coordination sphere of the metal ion.

Letter and Jordan¹ studied the kinetics of complexation of Ni(II) by tyrosine over the pH range 6.40-6.90 and interpreted their kinetic data on the basis of Eq. (1).

$$k'_{\text{obs}} = k_{\text{obs}}[\text{Ni}^{2+}] = \frac{k'_3[\text{Ni}^{2+}]}{K_a + [\text{H}^+]} + k'_{-3} \quad \dots (1)$$

This equation suggests that in this pH range, 70-85% of the tyrosine remains uncomplexed and the system may be treated as one coming to equilibrium. Equation (1) appears over simplified since it shows a simply linear dependence of variables. It is, however, not the case as shown by the results of kinetic studies²⁻⁴ of other amino acids. Further, it is doubtful that Eq. (1), which is based on results in a narrow pH range, will hold good for the reaction at high pH also. Letter and Jordan¹ also did not make any attempt to resolve the overall rate constant into specific rate constants corresponding to different steps of the overall process, and the results were interpreted in terms of only two specific rate constants k'_3 and k'_{-3} .

It was, therefore, thought desirable to have a quantitative and comprehensive kinetic study of complexing of L-tyrosine by nickel (II) over a wide range of pH 6.0-7.5. The significance of the present work is that instead of a simplified kinetic equation, an overall kinetic equation encompassing specific rate constants for all possible steps has been suggested to interpret the data and specific rate constants have also been evaluated.

The results of a number of kinetic studies¹⁻⁴ of

complexation of amino acid by Ni(II) have indicated that initially amino acid dissociates into a uninegative ion (carboxylate ion) which probably complexes with Ni(II). This possibility has also been re-examined in the present investigation, since the micro dissociation constants for the three functional groups of tyrosine are known⁵. The pK values for these functional groups are 9.21 ($-\text{COOH}$), 9.63 ($-\text{OH}$) and 9.20 ($-\text{NH}$). Therefore, it is quite interesting to study this system because it is very certain that phenolic group being weakly dissociated as compared to $-\text{COOH}$ and $-\text{NH}$ groups, does not participate in the complexation reaction and only $-\text{COOH}$ and $-\text{NH}$ groups of tyrosine are involved.

Materials and Methods

L-Tyrosine (Koch-Light) was recrystallized from aq. ethanol and dried *in vacuo*. 2,6-Lutidine (Merck-Schuchardt), potassium nitrate (AR) and bromothymol blue (BDH) were used as such. Stock solution of Ni(II) was prepared from reagent grade nickel nitrate and standardised by EDTA titration.

Doubly distilled water was used for preparing all solutions. The ionic strength of all reaction mixtures was kept constant at 0.2 by adding KNO_3 . The concentration of tyrosine in solution was determined spectrophotometrically.

Stopped flow kinetic measurements

Kinetic measurements were made on a standard Aminco-Morrow stopped flow system. The temperature of the reaction system could be controlled to within $\pm 0.05^\circ\text{C}$. The reactions were followed spectrophotometrically at 617nm by pH indicator method using bromothymol blue. The total absorbance change was kept small so that the relative voltage change (ΔV) could be observed on the oscilloscope ($\Delta V \propto \Delta A$).

All the reactions were carried out in 0.2 mol dm^{-3} KNO_3 and the effects of metal ion ($< 1 \times 10^{-2} \text{ mol dm}^{-3}$) on ionic strength was neglected. All kinetic runs were made under pseudo-first order conditions using ten-fold molar excess of Ni(II) over the ligand.

Blank experiments in which indicator and Ni(II) solutions or indicator and ligand solutions were mixed showed no absorbance change of a magnitude in the time scale such as to interfere with the results.

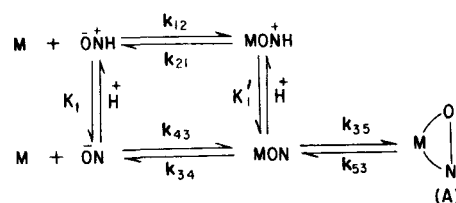
Results and Discussion

The mechanism of complexation of amino acid by metal ion can be represented as shown in Scheme 1, where O and N represent the carboxylate and amino moieties of the amino acid, respectively. Since, equilibrium steps corresponding to constants K_1 and K'_1 are rapid in comparison to other steps, the concentration changes are exponential¹ and represented by two time constants γ_+ and γ_- , γ_+ being smaller time constant determines the rate of the reaction. The value of γ_+ has been determined¹ by Eq. (2).

$$\gamma_+ = \frac{\{(k_{12}[\text{H}^+] + k_{43}K_1)/K_1 + [\text{H}^+]\}}{k_{21}[\text{H}^+] + K'_1(k_{34} + k_{35}) + k_{53}(K'_1 + [\text{H}^+])} \dots (2)$$

The study of complexation^{6,7} of tyrosine by Ni(II) has shown that the predominant product ($> 90\%$) is in the form of mono complex. That is why only the kinetics of the formation of the mono complex of Ni(II) with tyrosine have been studied in the present work. Similar study done by Weber and Simeon⁸ indicates that in the complex formation of tyrosine with Ni(II), only 15-30% of the tyrosine is complexed and the rest remains uncomplexed because of least favourable experimental conditions. It means that reaction does not go to completion. Therefore, k_{53} in Eq. (2) cannot be zero.

In order to have a total kinetic equation to interpret the results of complexing of L-tyrosine by Ni^{2+} , we have simplified the denominator of Eq. (2) using the approximation; $k_{21}[\text{H}^+] \gg K'_1(k_{34} + k_{35})$. This is justified since the value⁹ of K'_1 is of the order of $\sim 10^{-9} \text{ mol dm}^{-3}$. Hoffmann¹⁰ has shown that k_{21} is of the order of 10^4 for amino acids reacting with metal ions. Since the water exchange rate is of the order of $\sim 10^4$, k_{35} cannot have a value more than that of water exchange rate, otherwise the ring closure reaction would have taken place by an associative process. Moreover, it may be thought that the coordinated amino acid has a strong labilizing effect on the dissociation of a water molecule from Ni(II). Hoffmann¹⁰ observed the value of k_{34} to be of the



Scheme 1

order of $\sim 10^3$. Since the values of k_{34} and k_{35} are comparable^{3,4}, the value of $(k_{34} + k_{35})$ will be of the order of $\sim 10^3$. On multiplying this by K'_1 , i.e. 10^{-9} we get the value of $K'_1(k_{34} + k_{35})$ to be $\sim 10^{-6}$. On the other hand, in our experimental conditions, $[\text{H}^+]$ varies from 10^{-8} to 10^{-9} . Therefore, $k_{21}[\text{H}^+] \approx 10^4 \times 10^{-8} \approx 10^{-4} \text{ s}^{-1}$. This indicates that $k_{21}[\text{H}^+] \gg K'_1(k_{34} + k_{35})$ and hence $K'_1(k_{34} + k_{35})$ can be neglected in the denominator of Eq. (2). Second approximation which simplifies the denominator of Eq. (2) is: $k_{21}[\text{H}^+] \gg k_{53}(K'_1 + [\text{H}^+])$. By way of justification for this approximation, we can say that in Scheme 1, MONH species is less stable than the metal chelate (A). Therefore, the dissociation of MONH into M^{2+} and ONH^- is more favourable than the cleavage of (A) into MON. Moreover, the relative basicity of the leaving group indicates that $k_{21} \gg k_{53}$. Since, $[\text{H}^+] > K'_1$ we can justify that $k_{21}[\text{H}^+] > k_{53}(K'_1 + [\text{H}^+])$. Using these two approximations, Eq. (2) is reduced to Eq. (3):

$$\gamma_+ = \frac{\{(k_{12}k_{35}K'_1[\text{H}^+][\text{M}] + k_{43}K'_1k_{35}K_1[\text{M}]) / (K_1 + [\text{H}^+]) + k_{53}k_{21}[\text{H}^+] + k_{53}k_{34}K'_1\}}{k_{21}[\text{H}^+]} \dots (3)$$

The formation constant of the complex is related to the constants in Scheme 1 by

$$K_f = \left(\frac{k_{43}}{k_{34}}\right) \left(\frac{k_{35}}{k_{53}}\right) \dots (4)$$

And from Scheme 1, it can easily be shown that

$$K'_1k_{12}k_{34} = K_1k_{21}k_{43} \dots (5)$$

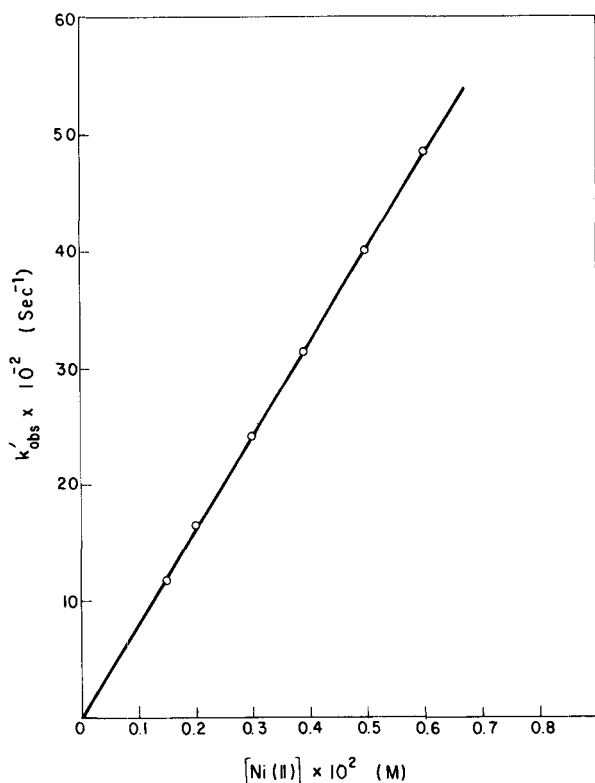
This on rearrangement gives

$$\frac{k_{43}}{k_{34}} = \left(\frac{K'_1}{K_1}\right) \left(\frac{k_{12}}{k_{21}}\right) \dots (6)$$

Substituting Eq. (6) in Eq. (4) we get

$$K_f = \left(\frac{K'_1}{K_1}\right) \left(\frac{k_{12}}{k_{21}}\right) \left(\frac{k_{35}}{k_{53}}\right) \dots (7)$$

Barr and Kustin⁶ found $\log K_f = 5.14$. Since $pK_1 = 9.2$, $K_1K_f = 8.7 \times 10^{-5}$. Substituting this value in Eq. (7) and rearranging we get,

Fig. 1—Plot of k'_{obs} versus $[\text{Ni(II)}]$ at pH 7.26

$$\frac{K'_1}{k_{21}} = \frac{8.7 \times 10^{-5} k_{53}}{k_{12} k_{35}} \quad \dots (8)$$

Equation (3) is now converted into Eq. (9) by substituting Eqs (5) and (7) in Eq. (3).

$$k'_{\text{obs}} = k_{\text{obs}}[\text{M}^{2+}] = k_{43} \frac{k_{35}}{k_{34}} \frac{K_1 [\text{M}^{2+}]}{K_1 + [\text{H}^+]} + \frac{8.7 \times 10^{-5} k_{53} k_{43} K_1 [\text{M}^{2+}]}{k_{12} [\text{H}^+] (K_1 + [\text{H}^+])} + k_{53} + \frac{8.7 \times 10^{-5} k_{53}}{k_{12} (k_{35}/k_{34}) [\text{H}^+]} \quad \dots (9)$$

Equation (9) is taken into account to interpret the kinetic results for the complexing of Ni(II) by tyrosine.

Evaluation of overall and step rate constants

The kinetic data of the tyrosine-nickel (II) reaction at a given pH for a large excess of Ni(II) are consistent with the differential rate expression (10), which is for a pseudo-first order reaction.

$$-\frac{d[\text{tyrosine}]}{dt} = k'_{\text{obs}}[\text{tyrosine}] \quad \dots (10)$$

The values of k'_{obs} are obtained graphically as usual and these values are reported in Table 1. k'_{obs} is related to k_{obs} by the relation:

Table 1—Kinetic Data for Formation of Mono Complex of Nickel (II) with L-Tyrosine

$[\text{L-Tyrosine}] = 1 \times 10^{-4} \text{ mol dm}^{-3}$; temp. = $30 \pm 0.05^\circ \text{C}$; $I = 0.20 \text{ mol dm}^{-3} (\text{KNO}_3)$

$10^2[\text{Ni(II)}]$ (mol dm^{-3})	pH	$10^2 k'_{\text{obs}}$ (s^{-1})	k_{obs} ($\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$)
0.50	6.10	6.37	12.74
0.50	6.20	6.99	13.98
0.50	6.32	7.94	15.80
0.50	6.42	8.96	17.92
0.47	6.50	9.64	20.51
0.45	6.60	10.81	24.02
0.45	6.70	12.60	28.00
0.43	6.84	15.40	35.81
0.43	6.92	17.70	41.16
0.40	7.04	20.94	52.35
0.40	7.16	26.40	66.00
0.38	7.26	31.30	82.36
0.38	7.36	37.60	96.94
0.38	7.44	45.40	119.47
0.38	7.50	50.50	132.89
1.00	6.90	99.00	99.00

$$k'_{\text{obs}} = k_{\text{obs}}[\text{Ni(II)}] \quad \dots (11)$$

The plot of k'_{obs} versus Ni(II) at constant pH of 7.26, shown in Fig. 1, is linear passing through the origin, the slope giving the second order rate constant (k_{obs}). The values of k_{obs} at different pH values are given in Table 1. Interpretation of kinetic data on the basis of Eq. (9) and the evaluation of specific rate constants were done as follows:

The dependence of k'_{obs} on $[\text{M}^{2+}]/K_1 + [\text{H}^+]$ can be interpreted on the basis of Eq. (9). At low pH, we can neglect second and fourth terms in Eq. (9) in comparison to first and third terms. Eq. (9) is then reduced to Eq. (12).

$$k'_{\text{obs}} = \frac{k_{43} k_{35} K_1}{k_{34}} \frac{[\text{M}^{2+}]}{(K_1 + [\text{H}^+])} + k_{53} \quad \dots (12)$$

Eq. (12) can be written as

$$k'_{\text{obs}} = k'_1 \frac{[\text{M}^{2+}]}{(K_1 + [\text{H}^+])} + k'_{-1} \quad \dots (13)$$

where $k'_1 = k_{43} k_{35} K_1 / k_{34}$ and $k'_{-1} = k_{53}$

Eq. (13) predicts the plot between k'_{obs} and $[\text{M}^{2+}]/\{K_1 + [\text{H}^+]\}$ to be linear with a slope equal to k'_1 and intercept equal to k'_{-1} . But Eq. (13) can be valid at comparatively low pH ($\text{pH} \leq 7$). At high pH, the plot of k'_{obs} versus $[\text{M}^{2+}]/\{K_1 + [\text{H}^+]\}$ is not linear. The reason for this behaviour is that the variable $[\text{H}^+]$ is mixed in the denominator of Eq. (9). Therefore, it is concluded that in order to predict the behaviour of the reaction at high pH, we cannot consider the simplified Eq. (13) and we have to consider the total kinetic Eq. (9) to interpret the results.

Table 2—Variation of Overall Rate Constant (k_{obs}) at Different Temperatures

pH = 6.90; $[\text{Ni(II)}] = 1.00 \times 10^{-2} \text{ mol dm}^{-3}$; $[\text{L-Tyrosine}] = 1.00 \times 10^{-3} \text{ mol dm}^{-3}$

Sl No.	T (± 0.05 °C)	k_{obs} ($\text{dm}^3 \text{mol}^{-1} \text{s}^{-1}$)
1	30.0	99
2	40.5	126
3	47.0	160
4	50.0	198
5	55.0	224
6	60.0	277

$E_a = 33.4 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -99.0 \text{ JK}^{-1} \text{mol}^{-1}$.

The main objective of the present work was to resolve the overall rate constant into specific step rate constants. In order to evaluate specific step rate constants, a non-linear last square analysis of the data of Table 1 as per Eq. (9) was made which provided values of k_{43} , k_{12} , k_{53} and k_{34}/k_{35} as $(1.6 \pm 0.2) \times 10^4$, $(8.20 \pm 2) \times 10^3 \text{ dm}^3 \text{mol}^{-1} \text{s}^{-1}$, $0.05 \pm 0.001 \text{ s}^{-1}$ and 2.28 ± 0.3 respectively.

In order to evaluate the values of the activation parameters for the overall reaction, the kinetic runs were carried out at six different temperatures (30–60°C)

and values of overall rate constants (k) at these temperatures are reported in Table 2. From the plot $\log k/T$ versus $1/T$, the values of E_a , and $\Delta S^\ddagger$ were evaluated and these are also given in Table 2.

An evidence in support of our suggested kinetic Eq. (10) comes from the value of formation constant of the complex, K_f given by Eq. (4). Substituting our experimental values of k_{43} , k_{34}/k_{35} and k_{53} in Eq. (4), the value of K_f comes out to be $1.4 \times 10^5 M$ which compares well with the reported⁷ value of $1.38 \times 10^5 M$.

Acknowledgement

One of the authors (J P) is thankful to the CSIR, New Delhi for the award of a research fellowship.

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