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Kinetics of Multidentate Ligand Substitution Reactions. VIII. Substitution Reactions of Diethylenetriaminepentaacetic Acid with Nickel(II) Iminodiacetate and Aspartate Chelates and of Cyclohexane-1,2-diamine-*N*,*N*,*N*′,*N*′-tetraacetic Acid with the Nickel(II) Aspartate Chelate

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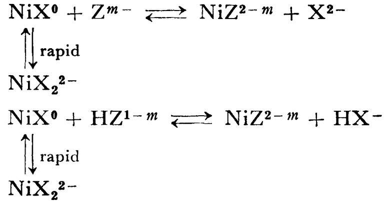
The substitution reactions of diethylenetriaminepentaacetic acid (DTPA) with nickel(II) chelates of iminodiacetic acid (IDA) and aspartic acid (Asp) and of cyclohexane-1,2-diamine-*N*,*N*,*N*′*N*′-tetraacetic acid (CyDTA) with the nickel(II) chelate of aspartic acid were studied by employing the polarographic method. All the reactions studied were found to proceed through the following two simultaneous reaction paths:



i)
$$\begin{tikzcd} \mathrm{NiX^0} + \mathrm{Z}^{m-} \arrow[r, shift left] \arrow[d, shift left, "\text{rapid}"] & \mathrm{NiZ}^{2-m} + \mathrm{X}^{2-} \arrow[l, shift left] \\ \mathrm{NiX_2}^{2-} \arrow[u, shift left] & \end{tikzcd}$$

ii)
$$\begin{tikzcd} \mathrm{NiX^0} + \mathrm{HZ}^{1-m} \arrow[r, shift left] \arrow[d, shift left, "\text{rapid}"] & \mathrm{NiZ}^{2-m} + \mathrm{HX}^{-} \arrow[l, shift left] \\ \mathrm{NiX_2}^{2-} \arrow[u, shift left] & \end{tikzcd}$$

where $\mathrm{NiX^0}$ and $\mathrm{NiX_2}^{2-}$ denote nickel(II)-IDA or Asp chelates of 1-to-1 and 1-to-2 compositions respectively, and where Z^{m-} indicates a completely-deprotonated DTPA or CyDTA anion. From a comparison of the rate constants of substitution reactions involving the nickel(II)-aspartate chelate with the corresponding rate constants of substitution reactions involving the nickel(II)-iminodiacetate chelate, the six-membered ring of the nickel(II)-aspartate chelate, as compared with its five-membered ring, was concluded to be more labile in the substitution reaction.

In our laboratory, a series of substitution reactions involving nickel(II)- and cobalt(II)-aminopolycarboxylate chelates have been studied kinetically.[1-4] In the substitution reaction involving Eriochrom Black T (BT), from a comparison of the rate constants the reaction intermediate was found to have the structure in which the leaving aminopolycarboxylate anion forms a five-membered ring with the metal ion through one nitrogen group and one oxygen group (Glycinate mechanism).[2]

Diethylenetriaminepentaacetic acid (DTPA) and cyclohexane-2,2′-diamine-*N*,*N*,*N*′,*N*′-tetraacetic acid (CyDTA) were found to displace aspartate and iminodiacetate anions from their nickel(II) chelates at measureable rates. Although both aspartic acid (Asp) and iminodiacetic acid (IDA) have one nitrogen group and two carboxylate groups, the former can form chelates which have one five-membered ring and one six-membered ring with metal ions, while the latter forms chelates which have two five-membered rings. Therefore, by comparing the rate constants for the substitution reactions of the nickel(II)-aspartate chelate with those of the nickel(II)-iminodiacetate chelate, one can determine which of the above two nickel(II) chelates is substitution-inert. In this connection, it would be worthwhile to conduct a kinetic study of the substitution reactions of nickel(II)-aspartate and iminodiacetate chelates with DTPA and CyDTA. This investigation will also provide further important information about the nature of the reaction intermediate in the substitution reaction involving the metal-aminopolycarboxylate chelate. In this paper, the kinetics of the substitution reactions of DTPA with nickel(II)-Asp and IDA chelates and of CyDTA with the nickel(II)-Asp chelate were investigated systematically.

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1) M. Kodama, This Bulletin, **40**, 2575 (1967).

2) M. Kodama, C. Sasaki and T. Noda, *ibid.*, **41**, 2033 (1968).

3) M. Kodama, C. Sasaki and K. Miyamoto, *ibid.*, **42**, 163 (1969).

4) M. Kodama, *ibid.*, **42**, 2532 (1969).

Experimental

Reagents. The preparation of the standard nickel(II) nitrate solution was described in a previous paper.[4] The methods of purifying CyDTA and DTPA and preparing their standard solutions have also been given previously.[3] L-Aspartic acid and iminodiacetic acid were recrystallized from their aqueous solutions. The standard solutions were prepared by dissolving known amounts of recrystallized Asp and IDA in redistilled water. All the other chemicals used were of an analytical-reagent grade and were used without further purification.

Apparatus and Experimental Procedures. All the d.c. polarograms and current-time curves were recorded automatically by employing a Yanagimoto pen-recording polarograph PA–102 or a Hitachi recorder QPD–54. The dropping mercury electrode (DME) used in this study was also described previously.[5] All the experimental procedures were the same as these employed previously.[4] All the current-time curves were measured in the pH range from 9.00 to 10.50 in solutions with an ionic strength of 0.20 and containing a large excess of complexed and un-complexed Asp or IDA over DTPA or CyDTA. Therefore, all the substitution reactions could be treated as pseudo first-order reactions. In this study, no buffer reagent was used because all the sample solutions contained un-complexed aspartic acid or iminodiacetic acid, which has enough of a buffer capacity to maintain the solution pH constant over the entire pH range covered.

Results and Discussion

As was found in the substitution reaction of the nickel(II)-NTA chelate with DTPA,[4] in all the substitution reactions studied the plot of $\log(i_0/i_t)$ against time, t, give linear relations which pass through the point of origin, provided that all the other experimental conditions are kept constant (Fig. 1). Here, i_0 and i_t mean the wave-heights of DTPA or CyDTA at time $t=0$ or t respectively.[4] When the other experimental conditions were kept constant, the slope of the above linear relation was not influenced by the addition of a nickel(II)-DTPA or -CyDTA chelate, and it was independent of the initial concentration of DTPA or CyDTA. However, it was exactly proportional to the concentration of the nickel(II)-Asp or -IDA chelate with a 1-to-1 composition, $[\mathrm{NiX}]_t/(1+K_2[\mathrm{X}]_f/(\alpha_\mathrm{H})_\mathrm{X})$. Here, $[\mathrm{NiX}]_t$, $[\mathrm{X}]_f$, and $(\alpha_\mathrm{H})_\mathrm{X}$ mean the total concentration of the nickel(II)-Asp or -IDA chelate, the concentration of uncomplexed Asp or IDA, and the (α_H) value of Asp or IDA respectively. K_2 is the second successive formation constant of the nickel(II)-Asp or -IDA chelate. Typical results are shown in Tables 1, 2, and 3. As is illustrated in Figs. 2 and 3, the product of the log-plot slope and $2.303\cdot(\alpha_\mathrm{H})_\mathrm{Z}\cdot(1+K_2[\mathrm{X}]_f/(\alpha_\mathrm{H})_\mathrm{X})/[\mathrm{NiX}]_t$ was a linear function of the hydrogen ion concentration,

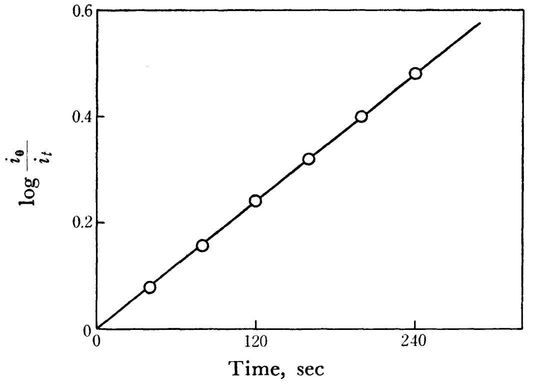

Fig. 1. The plot of $\log(i_0/i_t)$ against time.
Here, i_0 and i_t mean the anodic wave-heights of CyDTA at time $t=0$ and t, respectively.
Ionic strength = 0.20, 1.0°C
Initial concentration of CyDTA = 0.40 mM
Total concentration of Ni(II)-Asp chelate = 8.0 mM
Concentration of uncomplexed Asp = 34.0 mM

Table 1. THE RELATION BETWEEN THE LOG-PLOT SLOPE AND THE INITIAL CONCENTRATION OF CyDTA OR DTPA
ionic strength = 0.20

A) Ni(II)-Asp CyDTA system

Concentration of CyDTA, mM	Slope, sec^{-1}
0.30	2.02×10^{-3}
0.40	2.00×10^{-3}
0.60	2.02×10^{-3}

pH = 9.56, 25°C
Concentration of uncomplexed aspartate = 34.0 mM
Total concentration of Ni(II)-Asp chelate = 8.0 mM

B) Ni(II)-Asp DTPA system

Concentration of DTPA, mM	Slope, sec^{-1}
0.30	2.26×10^{-3}
0.40	2.30×10^{-3}
0.60	2.30×10^{-3}

pH = 10.50, 1.0°C
Concentration of uncomplexed aspartate = 34.0 mM
Total concentration of Ni(II)-Asp chelate = 8.0 mM

C) Ni(II)-IDA DTPA system

Concentration of DTPA, mM	Slope, sec^{-1}
0.366	3.10×10^{-3}
0.610	3.13×10^{-3}
0.854	3.08×10^{-3}

pH = 9.30, 25°C
Concentration of uncomplexed iminodiacetate = 10.14 mM
Total concentration of Ni(II)-IDA chelate = 8.63 mM

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5) M. Kodama and A. Kimura, This Bulletin, **40**, 1639 (1967).

TABLE 2. THE RELATION BETWEEN THE LOG-PLOT SLOPE AND THE CONCENTRATION OF UNCOMPLEXED Asp OR IDA
ionic strength=0.20

A) Ni(II)-Asp CyDTA system

Concentration of uncomplexed Asp $[X]_f$, mM	Slope sec^{-1}	Slope×$[X]_f$ sec^{-1} mM
24.0	2.83×10^{-3}	6.80×10^{-2}
34.0	2.00×10^{-3}	6.80×10^{-2}
44.0	1.56×10^{-3}	6.80×10^{-2}

pH=9.56, 25°C
Initial concentration of CyDTA=0.40 mM
Total concentration of Ni(II)-Asp = 8.0 mM

B) Ni(II)-Asp DTPA system

Concentration of uncomplexed Asp $[X]_f$, mM	Slope sec^{-1}	Slope×$[X]_f$ sec^{-1} mM
24.0	3.38×10^{-3}	8.10×10^{-2}
34.0	2.30×10^{-3}	7.85×10^{-2}
44.0	1.88×10^{-3}	8.25×10^{-2}

pH=10.50, 1.0°C
Initial concentration of DTPA=0.40 mM
Total concentration of Ni(II)-Asp=8.0 mM

C) Ni(II)-IDA DTPA system

Concentration of uncomplexed Asp $[X]_f$, mM	Slope sec^{-1}	Slope×$[X]_f$ sec^{-1} mM
10.14	3.13×10^{-3}	3.18×10^{-2}
19.34	1.65×10^{-3}	3.19×10^{-2}
28.44	1.10×10^{-3}	3.14×10^{-2}

pH=9.30, 25°C
Initial concentration of DTPA=0.61 mM
Total concentration of Ni(II)-IDA=8.63 mM

TABLE 3. THE RELATION BETWEEN THE LOG-PLOT SLOPE AND THE TOTAL CONCENTRATION OF NICKEL(II)-Asp OR -IDA CHELATE
ionic strength=0.20

A) Ni(II)-Asp CyDTA system

Concentration of Ni(II)-Asp mM	Slope sec^{-1}	Concentration ratio	Slope ratio
6.0	1.50×10^{-3}	1.00	1.00
8.0	2.00×10^{-3}	1.33	1.33
10.0	2.52×10^{-3}	1.67	1.68

pH=9.56, 25°C
Concentration of uncomplexed Asp=34.0 mM
Initial concentration of CyDTA=0.40 mM

B) Ni(II)-Asp DTPA system

Concentration of Ni(II)-Asp mM	Slope sec^{-1}	Concentration ratio	Slope ratio
6.0	1.80×10^{-3}	1.00	1.00
8.0	2.30×10^{-3}	1.33	1.28
10.0	3.02×10^{-3}	1.67	1.68

pH=10.50, 1.0°C
Concentration of uncomplexed Asp=34.0 mM
Initial concentration of DTPA=0.40 mM

C) Ni(II)-IDA DTPA system

Concentration of Ni(II)-IDA mM	Slope sec^{-1}	Concentration ratio	Slope ratio
8.63	3.13×10^{-3}	1.00	1.00
13.00	4.52×10^{-3}	1.50	1.45
17.30	6.40×10^{-3}	2.00	2.04

pH=9.30, 25°C
Concentration of uncomplexed IDA=10.14 mM
Initial concentration of DTPA=0.61 mM

and the log-plot slope is given by:

$$\text{log-plot slope} = (k_i + k_{ii}[\mathrm{H}^+]) \times \frac{[\mathrm{NiX}]_t}{2.303\cdot(\alpha_H)_Z\cdot\left(1 + \dfrac{K_2\cdot[\mathrm{X}]_f}{(\alpha_\mathrm{H})_\mathrm{X}}\right)} \tag{1}$$

where $1+K_2\cdot[\mathrm{X}]_f/(\alpha_\mathrm{H})_\mathrm{X}$ is practically identical with $K_2\cdot[\mathrm{X}]_f/(\alpha_\mathrm{H})_\mathrm{X}$ under the present experimental conditions. Therefore, all the substitution reactions studied can be concluded to proceed through the following two simultaneous reaction pathways and, therefore, k_i and k_{ii} in Eq. (1) can be equated with k_1^+ and k_2^+/k_d respectively (here, k_d denotes the k_4 of CyDTA or k_5 of DTPA):

$$\text{i)}\quad \begin{array}{l} \mathrm{NiX^0} + \mathrm{Z}^{m-} \overset{k_1^+}{\rightleftarrows} \mathrm{NiZ}^{2-m} + \mathrm{X}^{2-} \\ \quad \Big\updownarrow \text{rapid} \\ \mathrm{NiX_2}^{2-} \end{array}$$

$$\text{ii)}\quad \begin{array}{l} \mathrm{NiX^0} + \mathrm{HZ}^{1-m} \overset{k_2^+}{\rightleftarrows} \mathrm{Ni}^{2-m} + \mathrm{HX}^- \\ \quad \Big\updownarrow \text{rapid} \\ \mathrm{NiX_2}^{2-} \end{array}$$

where $\mathrm{NiX^0}$ and $\mathrm{NiX_2}^{2-}$ denote a nickel(II)-Asp or -IDA chelate with a 1-to-1 or a 1-to-2 composition respectively, and where Z^{m-} means a completely-deprotonated DTPA or CyDTA anion.

From the linear relations shown in Figs. 2 and 3, the k_1^+ and k_2^+ values were determined. These values are listed together with the k_1^+ and k_2^+ values for the substitution reaction of the nickel(II)-IDA chelate with CyDTA,⁶⁾ in Table 4. Since the

TABLE 4. k_1^+ AND k_2^+ VALUES
ionic strength=0.20

System	k_1^+ M$^{-1}\cdot$sec^{-1}	k_2^+ M$^{-1}\cdot$sec^{-1}	Temperature °C
Ni(II)-IDA CyDTA⁶⁾	1.7×10^4	3.30×10^2	25
Ni(II)-Asp CyDTA	0	2.50×10^3	25
Ni(II)-IDA DTPA	3.8×10^4	6.13×10^3	25
	$1.3_4\times10^4$	8.26×10^2	1.0
Ni(II)-Asp DTPA	3.0×10^4	6.85×10^3	1.0

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6) M. Kodama, This Bulletin, **42**, 3330 (1969).

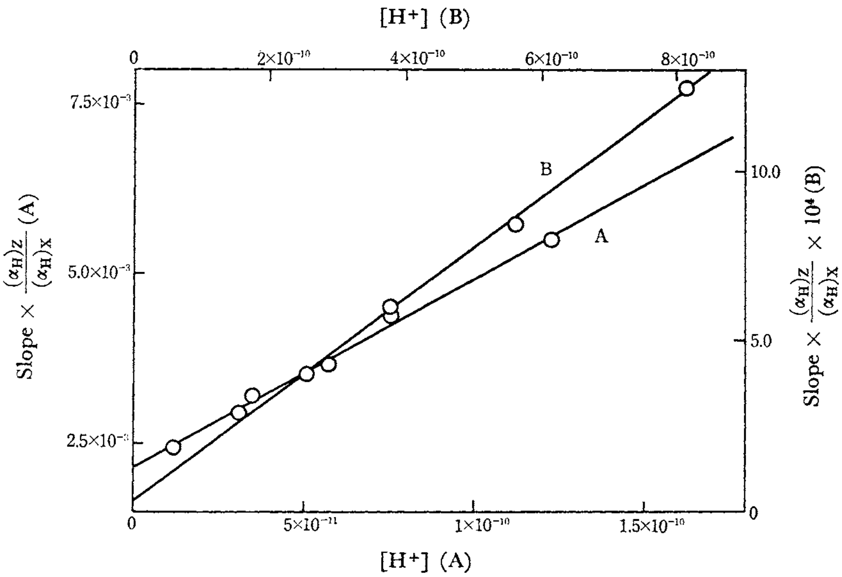

Fig. 2. The plot of log-plot slope$\times(\alpha_H)_Z/(\alpha_H)_X$ against the hydrogen ion concentration.
Ionic strength = 0.20, 1.0°C
Initial concentration of DTPA = 0.40 mM
A) Total concentration of Ni(II)-Asp chelate = 8.0 mM
Concentration of uncomplexed Asp = 34.0 mM
B) Total concentration of Ni(II)-IDA chelate = 10.0 mM
Concentration of uncomplexed IDA = 20.0 mM

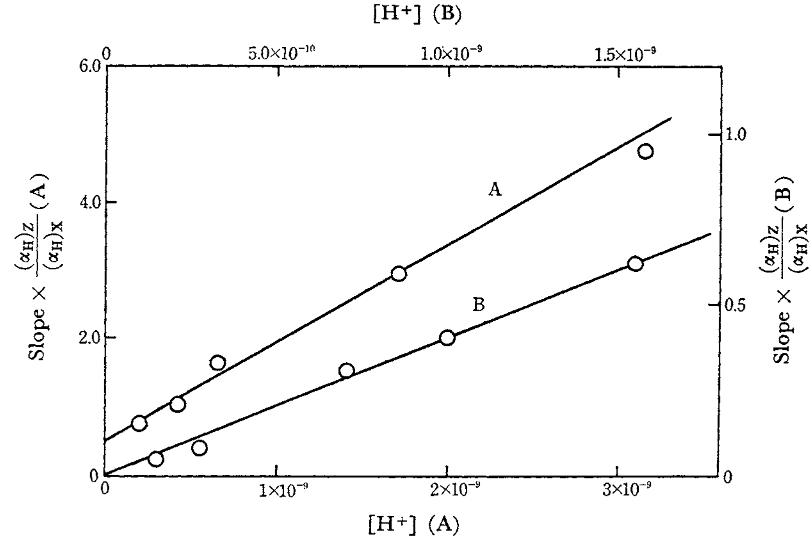

Fig. 3. The plot of log-plot slope$\times(\alpha_H)_Z/(\alpha_H)_X$ against the hydrogen ion concentration.
Ionic strength = 0.20, 25°C
A) Initial concentration of DTPA = 0.40 mM
Total concentration of Ni(II)-IDA chelate = 8.63 mM
Concentration of uncomplexed IDA = 10.14 mM
B) Initial concentration of CyDTA = 0.40 mM
Total concentration of Ni(II)-Asp chelate = 8.0 mM
Concentration of uncomplexed Asp = 34.0 mM

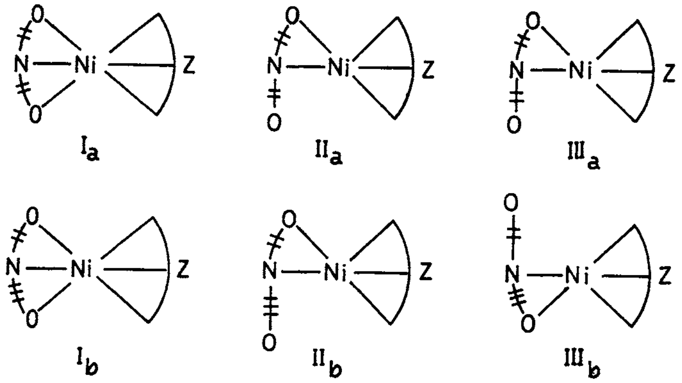

Fig. 4. Reaction intermediates.

substitution reaction of the nickel(II)-Asp chelate with DTPA proceeded too rapidly for us to determine the rate accurately at room temperature, the current-time curves were measured at 1.0°C. The rate constants for the substitution reaction of the nickel(II)-IDA chelate with DTPA determined at 1.0°C are also listed in Table 4.

As is shown in Table 4, the k_2^+ values of the nickel(II)-Asp chelate systems are about seven times as large as those of the nickel(II)-IDA chelate systems. Since the k_1^+ values could be determined less accurately, only the k_2^+ values were used for the comparison of the rate constants. From the above results and discussion, it might be expected that the substitution reaction involving the nickel(II)-Asp chelate proceeds through a mixed ligand reaction intermediate (activated complex) similar to that in the substitution reaction of the nickel(II)-IDA chelate. As was discussed previously,[2)] we can estimate the structure of the reaction intermediate by comparing the rate constant calculated on the basis of the proposed reaction intermediate and the observed rate constant. If the Ni(II)-DTPA or -CyDTA segments in the reaction intermediates of both substitution reactions have the same structure, and if the Ni(II)-Asp and Ni(II)-IDA segments in the reaction intermediate have the I_a and I_b structures respectively, the k_2^+ value for the reaction of the nickel(II)-Asp chelate must be equal to that for the reaction of the nickel(II)-IDA chelate, because the rates of dissociation of aspartate and iminodiacetate anions from the reaction intermediate are considered to be identical. If both aspartate and IDA anions in the reaction intermediate form only one five-membered ring with a nickel(II) ion (II_a and II_b), the k_2^+ value for the substitution reaction of the nickel(II)-Asp chelate must be about six times as large as that for the reaction of the nickel(II)-IDA chelate, because the stability constant ratio corrected for the statistical factor between nickel(II)-IDA and -Asp chelates of a 1-to-1 composition[7)] is estimated to be 6.0. On the other hand, if the Ni(II)-Asp segment in the reaction intermediate has the six-membered ring and the Ni(II)-IDA segment, a five-membered ring (III_a and III_b), the k_2^+ value for the reaction of the nickel(II)-IDA chelate should be three times as large as that for the reaction of the nickel(II)-Asp chelate. Here, nickel(II) chelates of α-aninate and β-alaninate were used as models. For the reaction intermediates where nickel(II)-IDA and -Asp segment include only one nitrogen bond, the k_2^+ value for the reaction of nickel(II)-Asp must be twelve times as large as that for the reaction of the nickel(II)-IDA chelate.

As is shown in Table 4, the k_2^+ values for the substitution reactions of the nickel(II)-Asp chelate with both DTPA and CyDTA are almost seven times as large as those for the reactions of the nickel(II)-IDA chelate. This fact clearly indicates that all the present substitution reactions also proceed through the glycinate reaction intermediate (II_a and II_b), as in the case of the substitution reaction of BT.[2)] With metal ions, the aspartate anion can form the chelate with five- and six-membered rings. Therefore, the finding that the reaction of the nickel(II)-Asp chelate proceeds through the reaction intermediate II_b clearly shows that the five-membered ring, as compared with the six-membered ring, is more inert in the substitution reaction.

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[7)] L. G. Sillen and A. E. Martell, "Stability Constants of Metal-Ion Complexes," The Chemical Society, London (1964).