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Multidentate Ligand Substitution Reactions. XII. Substitution Reactions of the Nickel(II)-nitrilotriacetate Complex with Diethylenetriaminepentaacetic Acid in the Presence of Ethylenediamine and of the Nickel(II)-*N*-(2-hydroxyethyl)-iminodiacetate Complex with Ethylenediaminetetraacetic Acid and Cyclohexane-1,2-diamine-*N*,*N*,*N'*,*N'*-tetraacetic Acid

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The substitution reactions of the nickel(II)-nitrilotriacetate complex with diethylenetriaminepentaacetic acid in the presence of ethylenediamine and of the nickel(II)-*N*-(2-hydroxyethyl)-iminodiacetate complex with ethylenediaminetetraacetic acid and cyclohexane-1,2-diamine-*N*,*N*,*N'*,*N'*-tetraacetic acid were studied by employing the polarographic method. In the presence of ethylenediamine, the reaction of the nickel(II)-nitrilotriacetate complex with diethylenetriaminepentaacetic acid was found to proceed through the following four pathways:

$$\mathrm{NiX_2}^{4-} \xrightleftharpoons{\text{rapid}} \mathrm{NiXA}^- \begin{array}{l} \overset{\text{rapid}}{\nearrow\swarrow}\ \mathrm{NiX}^- + \left\{\begin{array}{l} \mathrm{Z}^{5-} \xrightleftharpoons{k_1^+} \mathrm{NiZ}^{3-} + \mathrm{X}^{3-} \\ \mathrm{HZ}^{4-} \xrightleftharpoons{k_2^+} \mathrm{NiZ}^{3-} + \mathrm{HX}^{2-} \end{array}\right. \\ \underset{\text{rapid}}{\searrow\nwarrow}\ \mathrm{NiA}^{2+} + \left\{\begin{array}{l} \mathrm{Z}^{5-} \xrightleftharpoons{k_3^+} \mathrm{NiZ}^{3-} + \mathrm{A}^{0} \\ \mathrm{HZ}^{4-} \xrightleftharpoons{k_4^+} \mathrm{NiZ}^{3-} + \mathrm{HA}^{+} \end{array}\right. \end{array}$$

where X^{3-} and Z^{5-} denote completely-deprotonated nitrilotriacetate and diethylenetriaminepentaacetate anions respectively, and A°, ethylenediamine. By comparing the rate constants of the substitution reactions of the nickel(II)-nitrilotriacetate and ethylenediamine complexes with their dissociation rate constants, the structure of the reaction intermediate was determined. From the concentration dependence of the reaction rate, the reactions of the nickel(II)-*N*-(2-hydroxyethyl)-iminodiacetate complex with ethylenediaminetetraacetic acid and with cyclohexane-1,2-diamine-*N*,*N*,*N'*,*N'*-tetraacetic acid were concluded to proceed through the following two reaction pathways:

$$\text{i)}\quad \begin{array}{l} \mathrm{NiX_2}^{2-} \\ \quad \downarrow\uparrow \text{rapid} \\ \mathrm{NiX}^{0} + \mathrm{Y}^{4-} \xrightleftharpoons{k_1^+} \mathrm{NiY}^{2-} + \mathrm{X}^{2-} \end{array}$$

$$\text{ii)}\quad \begin{array}{l} \mathrm{NiX_2}^{2-} \\ \quad \downarrow\uparrow \text{rapid} \\ \mathrm{NiX}^{0} + \mathrm{HY}^{3-} \xrightleftharpoons{k_2^+} \mathrm{NiY}^{2-} + \mathrm{HX}^{-} \end{array}$$

where X^{2-} and Y^{4-} mean completely-deprotonated *N*-(2-hydroxyethyl)-iminodiacetate and ethylenediaminetetraacetate or cyclohexane-1,2-diamine-*N*,*N*,*N'*,*N'*-tetraacetate anions. From a comparison of the rate constants for the reaction of the *N*-(2-hydroxyethyl)-iminodiacetate complex with those for the corresponding reaction of the iminodiacetate complex, it was found that the hydroxyethyl group in the *N*-(2-hydroxyethyl)-iminodiacetate anion rather accelerates the dissociation of the *N*-(2-hydroxyethyl)-iminodiacetate anion from the nickel(II) ion.

In previous papers,[1,2] we studied the substitution reaction of the nickel(II)-ethylenediaminetetraacetate (EDTA) complex with Eriochrome Black T (BT). In those papers, we mentioned that in the presence of the ammonia or thiocyanate anion the nickel(II)-EDTA

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[1] M. Kodama, C. Sasaki, and M. Murata, This Bulletin, **41**, 1333 (1968).

[2] M. Kodama and K. Miyamoto, *ibid.*, **42**, 833 (1969).

complex shows the same kinetic behavior as in its absence, but the rate of the reaction was reducd, appreciably by increasing the concentration of the ammonia or thiocyanate anion. This was ascribed to the fact that, although the reaction proceeds only through the normal nickel(II)-EDTA complex, even in the presence of the ammonia or thiocyanate ion, its concentration is reduced by the formation of a mixed ligand complex with an ammonia or thiocyanate ion. Diethylenetriaminepentaacetic acid (DTPA) also reacts with the nickel(II)-nitrilotriacetate (NTA) complex at a measurable rate and displaces the NTA anion from its nickel(II) complex.[3] This reaction was found to proceed only through the 1:1-ratio nickel(II)-NTA complex. In the presence of ethylenediamine (EN), contrary to the observation of the effect of ammonia on the substitution reaction of nickel(II)-EDTA with BT, the substitution reaction of DTPA with the nickel(II)-NTA complex proceeds not only through the nickel(II)-NTA complex with a 1:1 ratio, but also through the nickel(II)-EN complex with a 1:1 ratio. We also studied the steric effect of the leaving group on the rate of the substitution reactions of nickel(II)-aminopolycarboxylate complexes with BT and demonstrated that the cyclohexane ring of cyclohexane-1, 2-diamine-*N,N,N′,N′*,-tetraacetate(CyDTA) anion slows the reaction considerably.[4] As in the case of the nickel(II)-iminodiacetate (IDA) complex,[5] the nickel(II)-*N*-(2-hydroxyethyl)-iminodiacetate (HIDA) complex also reacts with EDTA and CyDTA. Although the HIDA has the hydroxyethyl group, the reactions of the nickel(II)-HIDA complex with EDTA and CyDTA proceed much faster than would be expected for a simple glycinate mechanism. In this paper, first, we will study the substitution reaction of the nickel(II)-NTA complex with DTPA in the presence of EN and will determine the detailed reaction mechanism and rate constants. Secondly, we will deal with the substitution reactions of the nickel(II)-HIDA complex with EDTA and CyDTA, and will discuss the effect of the hydroxyethyl group of the HIDA ion on the rate of the substitution reaction.

Experimental

Reagents. The standard nickel(II) nitrate solution was prepared by dissolving a known amount of metallic nickel (99.99 %) in dilute nitric acid (1+1) and by then removing the excess nitric acid by distillation under reduced pressure. NTA, EDTA, CyDTA, and DTPA were recrystallized from their aqueous solutions by adding pure ethanol and hydrochloric acid. Their standard solutions were prepared by dissolving them in doubly-distilled water. In this study, EN purified by distillation under reduced pressure was used. The other chemicals were of analytical reagent grades and were used without further purification.

Apparatus and Experimental Procedures. All the d.c. polarograms and current-time curves were recorded by means of a Yanagimoto pen-recording polarograph, PA-102. The characteristic features of the dropping mercury electrode (DME) used in this study have been described previously.[3] For all the spectrophotometric measurements, a Hitachi EPS-3 recording spectrophotometer with a pair of 1-cm quartz cells was used. The pH was measured with a glass electrode pH-meter (a Hitachi-Horiba F-5). The rate of the substitution reaction was determined by measuring the change in the diffusion current of the anodic wave due to the decrease in the uncomplexed EDTA, CyDTA, or DTPA concentration with the time. In the kinetic study, all the measurements were conducted in solutions with an ionic strength of 0.30 ($NaClO_4$) and containing large excesses of complexed and uncomplexed EN, NTA, or HIDA over EDTA, CyDTA, or DTPA at 25°C. Therefore, all the substitution reactions could be treated as pseudo-first-order reactions. In this study, no buffer reagent was required to keep the solution's pH constant over the entire pH range covered ($7.50<pH<9.00$), because all the solutions contained a large excess of uncomplexed EN, NTA, or HIDA. All the experimental procedures employed in the kinetic study were the same as have previously been described.[3] In the spectrophotometric determination of the solution equilibrium, sample solutions with an ionic strength of 0.50 were used.

Results and Discussion

Spectrophotometric Determination of Solution Equilibria between the Nickel(II)-Nitrilotriacetate Complex and Ethylenediamine. Thermodynamically, when the product of the conditional formation constant of a 1:1 nickel(II)-NTA complex, K_{NiX}' $(=K_{\mathrm{NiX}}/(\alpha_H)_X)$, and the total concentration of the nickel(II) ion is larger than 1.0×10^6, the nickel(II) ion in the solution containing an equimolar NTA can be expected to exist exclusively in the form of NiX^-. Furthermore, when the concentration of the nickel(II)-NTA complex is nearly equal to that of uncomplexed EN and the $K_{\mathrm{NiX}}'/(1+K_{\mathrm{NiA_2}}^{\mathrm{A}'}[\mathrm{A}]_f)K_{\mathrm{NiA}}'$ value is larger than 1.0×10^4, EN can not displace the NTA anion from its nickel(II) complex. Here, K_{NiA}' and $K_{\mathrm{NiA_2}}^{\mathrm{A}'}$ mean conditional first and second formation constants of nickel(II)-EN complex, and $[\mathrm{A}]_f$, the concentration of the uncomplexed EN. Therefore, if the above conditions are fulfilled, the addition of EN to the nickel(II)-NTA complex solution will necessarily result in the formation of a mixed nickel (II)-NTA-EN complex according to the following equation:

$$\mathrm{NiX^-} + \mathrm{A^0} = \mathrm{NiXA^-}; \quad K_{\mathrm{NiX}}^{\mathrm{A}} = \frac{[\mathrm{NiXA^-}]}{[\mathrm{NiX^-}]\cdot[\mathrm{A_0}]} \tag{1}$$

The nickel(II)-NTA complex in an aqueous solution gives an absorption spectrum with two absorption maxima, at 395 and at 635 mμ. By the addition of EN to the nickel(II)-NTA solution, its absorbance was increased remarkably and the absorption curve's maxima were shifted to shorter wavelengths (365 and 585 $m\mu$). These facts can be interpreted in terms of the formation of a mixed ligand complex involving an EN. As was discussed in the spectrophotometric determination of the formation constants of nickel(II)-ethylenediaminemonoacetate complexes, the following relation can be derived for the above solution equilibrium:[6]

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[3] M. Kodama, This Bulletin, **42**, 2532 (1969).

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

[5] M. Kodama, *ibid.*, **42**, 3330 (1969).

[6] M. Kodama, Y. Fujii, and T. Ueda, This Bulletin, **43**, 2085 (1970).

$$\log \frac{1}{[\mathrm{A}]_t - \dfrac{A - A_{\mathrm{NiX}}}{\varepsilon_{\mathrm{NiXA}} - \varepsilon_{\mathrm{NiX}}}} = \log \frac{A_{\mathrm{NiXA}} - A}{A - A_{\mathrm{NiX}}} + \log \frac{K^{\mathrm{A}}_{\mathrm{NiX}}}{(\alpha_H)_A} \qquad (2)$$

where ε's and $[\mathrm{A}]_t$ mean the molar extinction coefficients and the total concentration of EN, and where A, A_{NiXA}, and A_{NiX} are, respectively, the absorbance of the solutions in which NiX$^-$ and NiXA$^-$ coexist, in which all the nickel(II)-NTA complex exists in the form of NiXA$^-$ and in which there is no EN. With the aid of Eq. (2), the experimental data were analyzed. The results obtained are reproduced in Fig. 1. From the $\log [1/([\mathrm{A}]_t - (A - A_{\mathrm{NiX}})/(\varepsilon_{\mathrm{NiXA}} - \varepsilon_{\mathrm{NiX}}))]$ value at $\log [(A_{\mathrm{NiXA}} - A)/(A - A_{\mathrm{NiX}})] = $ zero, the $\log K^{\mathrm{A}}_{\mathrm{NiXA}}/(\alpha_H)_A$ value was estimated to be 1.84. This corresponds to the $\log K^{\mathrm{A}}_{\mathrm{NiXA}}$ value of 5.84.

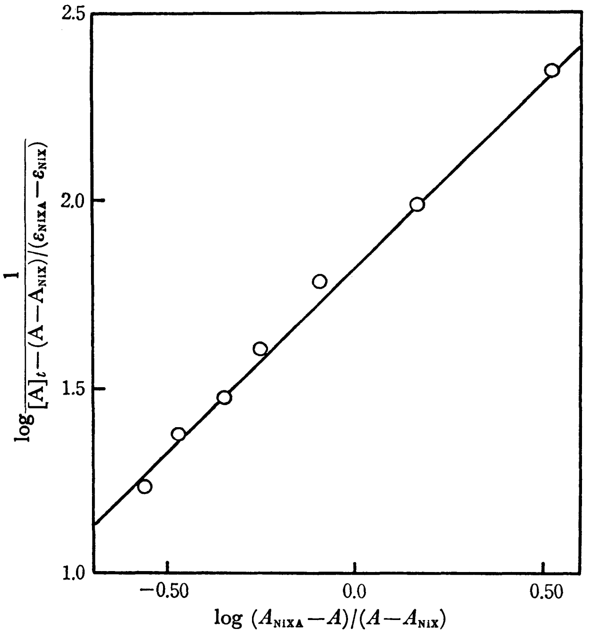


Fig. 1. The relation between $\log [1/[[\mathrm{A}]_t - (A - A_{\mathrm{NiX}})/(\varepsilon_{\mathrm{NiXA}} - \varepsilon_{\mathrm{NiX}})]]$ and $\log (A_{\mathrm{NiXA}} - A)/(A - A_{\mathrm{NiX}})$.
The concentration of Ni(II)-NTA complex = 24.0 mM
pH = 6.50, $\mu = 0.50$, $\lambda = 550$ mμ
The EN concentration ranged from 30 to 300 mM

The Kinetic Study of the Substitution Reaction of the Nickel(II)-Nitrilotriacetate Complex with Diethylenetriaminepentaacetic Acid in the Presence of Ethylenediamine. As was found in the substitution reaction of the nickel(II)-NTA complex with DTPA in the absence of EN,[3] a linear relation passing through the point of origin could be obtained by plotting the $\log (i_0/i_t)$ against the time, t, in the present substitution reaction (the results are not shown here). Here, i_0 and i_t denote the wave heights of DTPA at times $t=0$ and $t=t$ respectively. When the other experimental conditions were kept constant, the slope of the above linear relation was not influenced by the addition of the nickel(II)-DTPA complex and was independent of the initial concentration of DTPA (Table 1). These facts clearly indicate that the forward reaction is much faster than the backward reaction, and that the dissociation of the nickel(II)-NTA complex is not involved in the present reaction. Therefore, the log-plot slope multiplied by 2.303 should be equal to the apparent rate constant of the forward reaction, k^+_{ap}. Furthermore, the log-plot slope was found to be exactly proportional to the total concentration of the nickel(II) ion (Table 2). As was shown in Fig. 2, the substitution reaction of the nickel(II)-NTA complex with DTPA in the presence of EN gave the linear relation between the log-plot slope multiplied by $(1 + K^{\mathrm{X}'}_{\mathrm{NiX}_2}[\mathrm{X}]_f / K^{\mathrm{A}'}_{\mathrm{NiXA}}[\mathrm{A}]_f)$ and the reciprocal of the uncomplexed EN concentration, $[\mathrm{A}]_f^{-1}$. Here, $K^{\mathrm{X}}_{\mathrm{NiX}_2}$ denotes the second successive formation constant of the nickel(II)-NTA complex. By plotting the intercept of the above linear relation multiplied by the $(\alpha_H)_Z K^{\mathrm{X}'}_{\mathrm{NiAX}}[\mathrm{X}]_f/[\mathrm{Ni}]_t$ value or the slope multiplied by the $(\alpha_H)_Z K^{\mathrm{A}'}_{\mathrm{NiXA}}/[\mathrm{Ni}]_t$ value against the hydrogen ion concentration, we could also obtain the straight line with the intercept of a finite value. The linear relations thus obtained are shown in Figs. 3 and 4. These facts

Table 1. THE DEPENDENCE OF LOG-PLOT SLOPE ON THE CONCENTRATION OF DTPA

Total Ni(II) concentration = 10.0 mM, pH 7.92
Uncomplexed NTA concentration = 20.0 mM, Uncomplexed EN concentration = 50.0 mM

Initial concentration of DTPA, mM	Log-plot slope sec^{-1}
0.125	2.66×10^{-3}
0.250	2.71×10^{-3}
0.375	2.65×10^{-3}
0.500	2.63×10^{-3}
0.625	2.62×10^{-3}

Table 2. THE DEPENDENCE OF LOG-PLOT SLOPE ON THE CONCENTRATION OF NICKEL(II) ION

Initial concentration of DTPA = 0.50 mM, pH = 7.73
Uncomplexed NTA concentration = 20.0 mM, Uncomplexed EN concentration = 60.0 mM

Concentration of nickel(II) ion mM	Log-plot slope sec^{-1}	Concentraion ratio	Slope ratio
6.0	1.64×10^{-3}	1.00	1.00
10.0	2.77×10^{-3}	1.67	1.69
14.0	3.92×10^{-3}	2.33	2.39
18.0	4.95×10^{-3}	3.00	3.02
22.0	6.05×10^{-3}	3.67	3.69

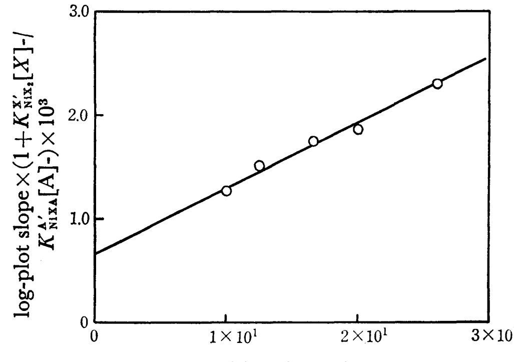


Fig. 2. The plot of log-plot slope $\times (1 + K^{\mathrm{X}'}_{\mathrm{NiX}_2}[\mathrm{X}]_f / K^{\mathrm{A}'}_{\mathrm{NiXA}}[\mathrm{A}]_f)$ against the reciprocal of the EN concentration.
The concentration of uncomplexed NTA = 20.0 mM
The Ni(II) concentration = 10.0 mM
pH = 8.12, $\mu = 0.30$, 25°C

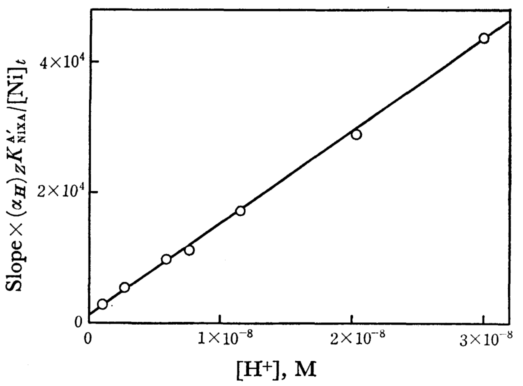


Fig. 3. The relation between the slope×$(\alpha_H)_Z K^{A'}_{NiXA}/[Ni]_t$ and the hydrogen ion concentration.
The concentration of uncomplexed NTA =20.0 mM
The Ni(II) concentration =10.0 mM
$\mu=0.30$, 25°C

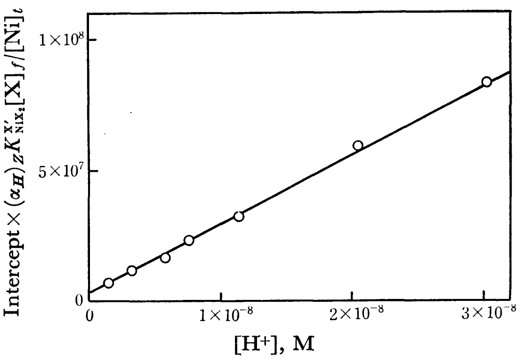
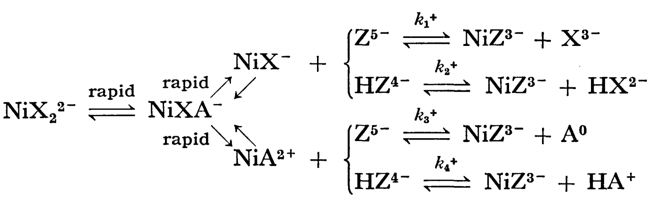


Fig. 4. The relation between the intercept×$(\alpha_H)_Z K^{X'}_{NiX_2}[X]_f/[Ni]_t$ and the hydrogen ion concentration.
The concentration of uncomplexed NTA=20.0 mM
The Ni(II) concentration=10.0 mM
$\mu=0.30$, 25°C

evidently imply that the substitution reaction of the nickel(II)-NTA complex with DTPA in the presence of EN proceeds through the following four reaction pathways:



For the above reaction mechanism, k_{ap}^+ is given by this relation (3):

$$k_{ap}^+ = \left(\frac{k_X{}^+}{K^{A'}_{NiXA}[A]_f} + \frac{k_A{}^+}{K^{X'}_{NiXA}[X]_f}\right) \times \frac{[Ni]_t}{(\alpha_H)_Z \cdot \left(1 + \dfrac{K^{X'}_{NiX_2}[X]_f}{K^{A'}_{NiXA}[A]_f}\right)} \tag{3}$$

Here, k_X^+ and k_A^+ are given by (4a) and (4b) respectively.

$$k_X{}^+ = k_1{}^+ + k_2{}^+ \frac{[H^+]}{K_5} \tag{4a}$$

$$k_A{}^+ = k_3{}^+ + k_4{}^+ \frac{[H^+]}{K_5} \tag{4b}$$

where K_5 means the fifth dissociation constant of DTPA.

TABLE 3. RATE CONSTANTS (μ=0.30, 25°C) AND THE SLOPE AND INTERCEPT OF THE LINEAR RELATION BETWEEN $(1+K^{X'}_{NiX_2}[X]_f/K^{A'}_{NiXA}[A]_f)$×LOG-PLOT SLOPE AND THE RECIPROCAL OF THE UNCOMPLEXED NTA CONCENTRATION

i) Rate constant (M^{-1} sec^{-1})

Rate constant	
$k_1{}^+$	2×10^3
$k_2{}^+$	2.4×10^2
$k_3{}^+$	3×10^6
$k_4{}^+$	4.7×10^5
k_d^{EN} 8)	0.14

ii) Slope and Intercept
Ni(II) concentration=10.0 mM, pH=8.98
Uncomplexed EN concentration=15.7 mM

Slope		Intercept	
Calcd	Obsd	Calcd	Obsd
4.3×10^{-6}	4.4×10^{-6}	$1._3\times10^{-3}$	$1._5\times10^{-3}$

From the slopes and intercepts of the linear relations in Figs. 3 and 4, k_1^+, k_2^+, k_3^+, and k_4^+ were determined; they are listed in Table 3. Although the precision is not satisfactory, the k_3^+ and k_4^+ values determined in this study agree well with those obtained in the kinetic study of the substitution reaction of the nickel(II)-EN complex with DTPA (μ=0.30, $k_3^+=4\times10^6$, $k_4^+=3.5\times10^5$).[7] If the substitution reaction of the nickel(II)-NTA complex with DTPA in the presence of EN proceeds through the above four reaction pathways, the k_1^+, k_2^+, k_3^+, and k_4^+ values obtained in this study should explain satisfactorily the effect of the concentration of the uncomplexed NTA on the reaction rate. Equation (3) clearly indicates that, provided that the other experimental conditions are kept constant, a plot of the log-plot slope multiplied by the $(1+K^{X'}_{NiX_2}[X]_f/K^{A'}_{NiXA}[A]_f)$ value against the reciprocal of the uncomplexed NTA concentration, $[X]_f^{-1}$, should yield a straight line, the slope and the intercept of which are $2.303\times k_A^+[Ni]_t/$

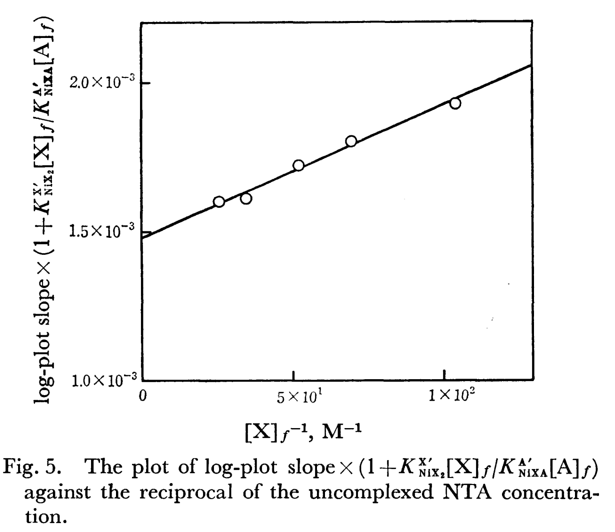


Fig. 5. The plot of log-plot slope×$(1+K^{X'}_{NiX_2}[X]_f/K^{A'}_{NiXA}[A]_f)$ against the reciprocal of the uncomplexed NTA concentration.
The concentration of uncomplexed EN=15.7 mM
The Ni(II) concentration=10.0 mM
pH=8.98, μ=0.30, 25°C

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[7] The details will be described in a future report.

Table 4. The dependence of log-plot slope on the concentration of nickel(II)-HIDA complex
$\mu=0.30$, 25°C

System	Concentration of Ni(II)-HIDA complex mM	Log-plot slope sec^{-1}	Concentration ratio	slope ratio	
EDTA	5.85	1.40×10^{-2}	1.00	1.00	Concentration of uncomplexed HIDA=18.0 mM
	9.74	2.31×10^{-2}	1.67	1.65	Initial concentration of EDTA=0.52 mM
	13.65	3.12×10^{-2}	2.33	2.23	pH=9.48
CyDTA	9.75	0.625×10^{-4}	1.00	1.00	Concentration of uncomplexed HIDA=10.0 mM
	14.6_0	1.00×10^{-4}	1.50	1.60	Initial concentration of CyDTA=0.49 mM
	19.5_0	1.26×10^{-4}	2.00	2.01	pH=8.44

$K^{X'}_{NiXA}(\alpha_H)_Z$ and $2.303\times k_A^+[Ni]_t/K^{A'}_{NiXA}[A]_f(\alpha_H)_Z$ respectively. A typical linear relation between the product of the log-plot slope and the $(1+K^{X'}_{NiX_2}[X]_f/K^{A'}_{NiXA}[A]_f)$ and the reciprocal of the concentration of uncomplexed NTA is reproduced in Fig. 5. The slope and intercept of the above linear relation were compared with those calculated with the aid of Eq. (3) by using the k_1^+, k_2^+, k_3^+, and k_4^+ values listed in Table 3. The calculated values agreed well with those obtained (Table 3). This agreement strongly supports the reaction mechanism proposed by the present authors.

*The Kinetic Study of Substitution Reactions of the Nickel(II)-*N*-(2-Hydroxyethyl)-Iminodiacetate Complex with Ethylenediaminetetraacetic Acid and with Cyclohexane-1,2-diamine-*N,N,N′,N′*-tetraacetic Acid.* In the substitution reaction of the nickel(II)-HIDA complex, quite similar results to those obtained in the substitution reactions of the nickel(II)-iminodiacetate (IDA) complex with EDTA and CyDTA were obtained. The plot of log(i_0/i_t) against t invariably gave a straight line passing through the point of origin. Its slope was independent of the initial concentration of EDTA or CyDTA and was not influenced by the addition of the nickel(II)-EDTA or CyDTA complex (the results will not be given here). It was also found that the log-plot slope is exactly proportional to the concentration of the 1:1 nickel(II)-HIDA complex in solutions of a given pH (Table 4), and that the plot of the product of the log-plot slope and $2.303\times(\alpha_H)_Y(1+K^{X'}_{NiX_2}[X]_f)/[Ni]_t$ against the concentration of the hydrogen ion gives a linear relation (Fig. 6) corresponding to the following relation:

$$\frac{k_{ap}^+(\alpha_H)_Y(1+K^{X'}_{NiX_2}[X]_f)}{[Ni]_t}=k_\alpha{}^+ + k_\beta{}^+[H^+] \qquad (5)$$

where $(\alpha_H)_Y$ denotes the (α_H) value of EDTA or CyDTA, $K^{X'}_{NiX_2}$, the conditional second successive formation constant of the nickel(II)-HIDA complex, and $[X]_f$, the concentration of the uncomplexed HIDA. Therefore, we can safely propose the following reaction mechanism for the substitution reaction of the nickel(II)-HIDA complex with EDTA or CyDTA.

i) $NiX_2{}^{2-}$

$$\Downarrow\!\Uparrow \text{rapid}$$

$$NiX^0 + Y^{4-} \xrightleftharpoons{k_1{}^+} NiY^{2-} + X^{2-}$$

ii) $NiX_2{}^{2-}$

$$\Downarrow\!\Uparrow \text{rapid}$$

$$NiX^0 + HY^{3-} \xrightleftharpoons{k_2{}^+} NiY^{2-} + HX^-$$

where Y^{4-} denotes the completely-deprotonated EDTA or CyDTA anion, and X^{2-}, the completely-deprotonated HIDA anion. If the reaction of the nickel(II)-HIDA complex with EDTA or CyDTA has the above reaction mechanism, k_α^+ and k_β^+ in Eq. (5) should be equal to k_1^+ and k_2^+/K_4 respectively. Here, K_4 corresponds to the fourth dissociation constant of EDTA or CyDTA. Thus, we can determine the k_1^+ and k_2^+ values for the reactions of the nickel(II)-HIDA complex with EDTA and CyDTA from the intercepts and slopes of the linear relations in Fig. 6. The k_1^+ and k_2^+ values thus determined are listed in Table 5, together with the k_1^+ and k_2^+ values of the substitution reactions of the nickel(II)-IDA complex with EDTA and CyDTA.⁵⁾

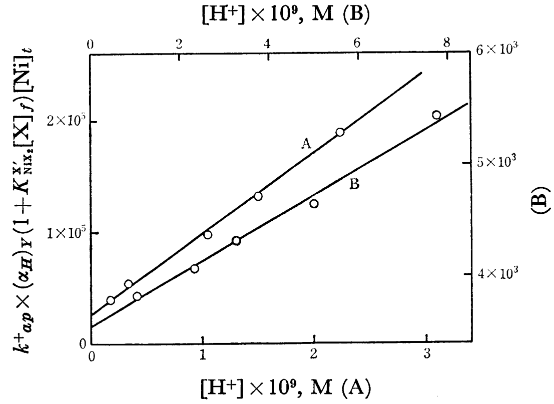

Fig. 6. The relation between $K^+{}_{ap}\cdot(\alpha_H)_Y(1+K^{X'}_{NiX_2}[X]_f)/[Ni]_t$ and the hydrogen ion concentration.
$\mu=0.30$, 25°C
A) Ni(II)-HIDA—EDTA reaction
The concentration of uncomplexed HIDA=18.0 mM
The Ni(II) concentration=10.0 mM
Initial concentration of EDTA=0.52 mM
B) Ni(II)-HIDA—CyDTA reaction
The concentration of uncomplexed HIDA=10.0 mM
The Ni(II) concentration=10.0 mM
Initial concentration of CyDTA=0.49 mM

We can mention here that the rate for the substitu-

Table 5. Rate constants ($\mu=0.30$, 25°C)
i) Substitution reaction

System	Rate constant M^{-1} sec^{-1}	EDTA	CyDTA
HIDA	$k_1{}^+$	1.7×10^4	3.7×10^3
	$k_2{}^+$	$7.3_5\times10^3$	0.94
IDA⁵⁾	$k_1{}^+$	2.1×10^4	1.7×10^4
	$k_2{}^+$	$7.3_3\times10^3$	$3.3_3\times10^2$

ii) Dissociation reaction

Ni(II)-IDA complex¹⁷⁾	$k_d=2.8\times10^4$ ($\mu=0.10$, 25°C)

tion reaction of the nickel(II)-EN complex with DTPA is much larger than that for the dissociation of the nickel(II)-EN complex.[8] This can be explained in terms of the formation of the mixed ligand complex reaction intermediate involving the DTPA anion.[1,9] As was attempted in the substitution reaction of the nickel(II)-EDMA complex with DTPA,[6] we can also estimate the structure of the reaction intermediate in the substitution reaction of the nickel(II)-EN complex with DTPA by comparing its rate constant with that for the dissociation of the nickel(II)-EN complex. If the reaction of the nickel(II)-EN complex proceeds through the reaction intermediate I_a, the rate constant, k_3^+, should be about 3×10^7 times larger than the dissociation constant of a 1 : 1 ratio nickel(II)-EN complex. Here, we used the nickel(II)-*N*-ethyl-glycinate complex as a model. In the estimation of the relative rate constant, the electrostatic contribution to the stability of the reaction intermediate, K_{elec}, and the statistical factor were also taken into account. Similarly, when the reaction intermediate is given by I_b or I_c (Fig. 7), the ratio of the rate constant, k_3^+, to the dissociation rate constant of a 1 : 1 nickel(II)-EN complex should be 3×10^9 or 1×10^9. The k_3^+ and k_d^{EN} values in Table 3 clearly indicate that the reaction intermediate I_a fits best. From a comparison of the k_1^+ value with the dissociation rate constant of a 1 : 1 ratio nickel(II)-NTA complex, we can also estimate the structure of the reaction intermediate in the reaction of the nickel(II)-NTA complex with DTPA. The rate constant for the dissociation of a 1 : 1 nickel(II)-NTA complex was reported by Kimura (3.0×10^{-5} sec^{-1}, $\mu=0.10$, 25°C).[10]

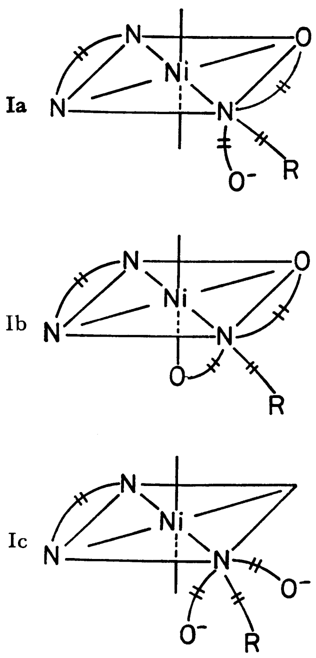

Fig. 7. Reaction intermediates for the substitution reaction of nickel(II)-EN complex with DTPA.

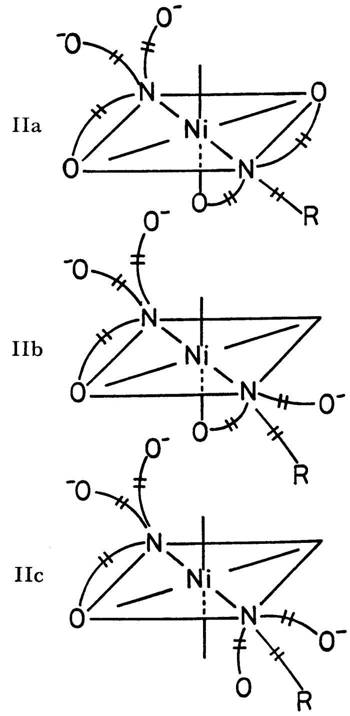

Fig. 8. Reaction intermediates for the substitution reaction of nickel(II)-NTA complex with DTPA.

As was discussed in connection with the dissociation of nickel(II)-aspartate complex,[11] by comparing this value with the rate constant calculated on the basis of the reaction intermediate proposed, we can determine the detailed structure of the reaction intermediate. The rate constant reported by Kimura agrees well only with that calculated on the basis of a glycinate reaction intermediate.[12] Consequently, the following are considered to be the possible reaction intermediate in the substitution reaction of the nickel(II)-NTA complex with DTPA (Fig. 8). The k_1^+ value determined in this study is $7._7\times10^7$ times larger than the dissociation rate constant of the nickel(II)-NTA complex. As is shown in Fig. 8, the rate constant ratio estimated on the basis of the reaction intermediate, II_a, agreed best with that determined experimentally. In general, the substitution reaction of the nickel(II)-aminopolycarboxylate complex proceeds through the reaction intermediate in which the attacking aminopolycarboxylate anion is bonded to the nickel(II) ion through the iminodiacetate chelate ring. Therefore, the above conclusion must be reasonable.

Previously,[2] we had reported that even in the presence of ammonia the substitution reaction of nickel(II)-EDTA complex with BT proceeds only through the normal nickel(II)-EDTA complex, NiY^{2-}. Theo-

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8) A. K. S. Ahmed and R. G. Wilkins, *J. Chem. Soc.*, **1959**, 3700.

9) D. B. Rorabacher and D. W. Margerum, *Inorg. Chem.*, **3**, 382 (1964).

10) M. Kimura, *Nippon Kagaku Zasshi*, **89**, 1209 (1968).

11) M. Kodama, H. Nunokawa, and N. Oyama, This Bulletin, **44**, in Press.

12) The glycinate reaction intermediate means the reaction intermediate in which the leaving NTA anion is bonded to the nickel(II) ion through a glycinate chelate ring. The rate constant calculated with the aid of Eq. (16) in Ref. (11) was 1.6×10^{-5} sec^{-1}. In the calculation, the electrostatic contribution to the stability of the reaction intermediate and the statistical factor were also taken into consideration.

retically, the substitution reaction of the nickel(II)-EDTA complex with BT in the presence of ammonia can be expected to proceed also through the nickel(II)-ammonia complex. However, the reaction pathway which involves a mixed-ligand 1:1:1 ratio ammonia, EDTA nickel(II) complex, $\mathrm{NiY(NH_3)^{2-}}$, is unlikely, because the mixed-ligand complex is much less favorable for the formation of a reaction intermediate, which is essentially a mixed-ligand complex involving a BT anion. On the basis of the reaction intermediate, we can estimate the contribution of the reaction pathway involving the nickel(II)-ammonia complex to the whole reaction. If we apply Eq. (5) in Ref. (13) or Eq. (17) in Ref. (9) to the substitution reaction of the nickel(II)-EDTA complex with BT, the contribution ratio of the reaction pathway involving the ammonia complex to that involving the EDTA complex can be calculated approximately by using the following relation:

$$\text{Ratio} = \frac{k_d^{\mathrm{NH_3}} \cdot K_{\mathrm{Ni(NH_3)}} \cdot (\alpha_H)_Y \cdot [\mathrm{NH_3}]_f}{4 \cdot k_d^{\mathrm{gly}} \cdot K_{\mathrm{Ni\text{-}gly}} \cdot (\alpha_H)_{\mathrm{NH_3}} \cdot [\mathrm{Y}]_f}$$

where $k_d^{\mathrm{NH_3}}$ (14) and k_d^{gly} (15) are the rate constants for the dissociation of ammonia and glycinate anions respectively from the nickel(II) ion in the reaction intermediate, $[\mathrm{NH_3}]_f$ and $[\mathrm{Y}]_f$, the concentrations of uncomplexed ammonia and of uncomplexed EDTA, and $K_{\mathrm{Ni(NH_3)}}$ and $K_{\mathrm{Ni\text{-}gly}}$, the formation constants of 1 : 1-ratio nickel(II)-ammonia and -glycinate complexes respectively, and where the (α_H)'s indicate the (α_H) values of ammonia and EDTA, and 4, the statistical factor for the formation of a nickel(II)-glycinate chelate ring between the nickel(II) ion and the tetravalent EDTA anion. In the derivation of the above equation, we assumed that the nickel(II)-BT segments in the reaction intermediates of both reaction pathways have the same structure and that the reaction pathway involving the nickel(II)-EDTA complex proceeds via a glycinate reaction intermediate.(13) With the aid of the above relation, the ratio was calculated to be about 0.01 by using the reported numerical values. This small contribution ratio clearly supports the present author's explanation that the substitution reaction of the nickel(II)-EDTA complex with BT in the presence of ammonia proceeds exclusively through the normal nickel(II)-EDTA complex, $\mathrm{NiY^{2-}}$. Similarly, on the basis of the proposed reaction intermediates, we can also estimate the contribution of the reaction pathway involving the normal nickel(II)-NTA complex to the whole reaction. If the reaction pathway involving the nickel(II)-EN complex proceeds through the reaction intermediate I_a, and that involving the nickel(II)-NTA complex, through II_a, under the conditions where the concentration of the uncomplexed EN is nearly identical with that of the uncomplexed NTA, the ratio of the contribution of the former reaction pathway to that of the latter reaction pathway will be given by the following relation:

$$\text{Ratio} = \frac{4 \times k_d^{\mathrm{EN}} K'_{\mathrm{Ni\text{-}EN}}}{6 \times k_d^{\mathrm{gly}} K_{\mathrm{Ni\text{-}IDA}}}$$

where 4 and 6 are statistical factors; k_d^{EN} the rate constant for the dissociation of the nickel(II)-EN complex with a 1 : 1 ratio,(8) and $K_{\mathrm{Ni-EN}}$ and $K_{\mathrm{Ni-IDA}}$, the formation constants of 1: 1-ratio nickel(II)-EN and -IDA complexes. The ratio calculated with the aid of the above relation was nearly equal to unity. This also supports the reaction mechanism proposed by the present authors for the substitution of the nickel(II)-NTA complex with DTPA in the presence of ethylenediamine.

As is clear from the data shown in Table 5, the $k_1^{\dagger}$ and $k_2^{\dagger}$ values for the substitution reaction of the nickel(II)-HIDA complex with EDTA are nearly identical with those for the corresponding substitution reaction of the nickel(II)-IDA complex. If the above two substitution reactions proceed through the reaction intermediates in which both HIDA and IDA anions are bonded to the nickel(II) ion through one nitrogen and two oxygen atoms, the $k_1^{\dagger}$ value for the former reaction should be nearly equal to the $k_1^{\dagger}$ value for the latter reaction, for the relative stabilities of the reaction intermediates for both reactions must be the same. Already, we have established that the substitution reaction of the nickel(II)-IDA complex with DTPA has the glycinate mechanism,(16) and also that the rate constants for the reaction of the nickel(II)-IDA complex with DTPA are nearly identical with those for the reaction with EDTA.(5) These facts clearly imply that the reaction of the nickel(II)-IDA complex with EDTA also proceeds through the reaction intermediate in which the displaced IDA anion is bonded to the nickel(II) ion through one nitrogen and one oxygen atoms (the glycinate mechanism). Thus, in the substitution reaction of the nickel(II)-IDA complex with EDTA, the reaction intermediate in which the displaced IDA anion is bonded to the nickel(II) ion through one nitrogen and two oxygey atoms should be eliminated. If the reactions of both nickel(II)-IDA and -HIDA complex with EDTA have the glycinate mechanism, the rate constant for the substitution reaction of the nickel(II)-HIDA complex should be approximately 17 times smaller than that for the reaction involving the nickel(II)-IDA complex, because the formation constant of the nickel(II)-HIDA complex with a 1 : 1 ratio is 17 times larger than that of the 1: 1 nickel(II)-IDA complex. Therefore, the finding that the $k_1^{\dagger}$ and $k_2^{\dagger}$ values for the reaction of the nickel(II)-HIDA complex are nearly equal to those for the reaction of the nickel(II)-IDA complex should be ascribed to the fact that the hydroxyethyl group in the HIDA anion effectively helps the dissociation of the HIDA anion from the nickel(II) ion in the reaction intermediate. Furthermore, the $k_1^{\dagger}$ value for the substitution reaction of the nickel(II)-IDA complex with EDTA is about 1×10^8 times larger than the rate constant for the dissociation of a 1: 1-ratio nickel(II)-IDA complex.(11,17)

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13) M. Kodama, C. Sasaki, and T. Noda, This Bulletin, **41**, 2033 (1968).

14) G. G. Hummes and J. I. Steinfeld, *J. Amer. Chem. Soc.*, **84**, 4639 (1962).

15) D. W. Margerum, D. B. Rorabacher, and J. F. G. Clarke, Jr., *Inorg. Chem.*, **2**, 667 (1963).

16) M. Kodama and T. Ueda, This Bulletin, **43**, 419 (1970).

17) T. J. Bydalek and A. H. Constant, *Inorg. Chem.*, **4**, 833 (1965).

If the reaction of the nickel(II)-IDA complex with EDTA proceeds through the reaction intermediate in which the EDTA anion is bonded to the nickel(II) ion through the iminodiacetate chelate ring, the ratio of the rate constant between the substitution and dissociation reactions of the nickel(II)-IDA complex should be 2.1×10^8. Here, we used the nickel(II)-HIDA complex as a model of the nickel(II)-EDTA segment. In the above calculations, the statistical factor and the electrostatic contribution were also taken into account. The rate-constant ratio calculated on the basis of the reaction intermediate in which the EDTA anion is bonded to the nickel(II) ion through the iminodiacetate chelate ring agreed well with that observed. From the above results and the discussion of them, we can safely conclude that the substitution reaction of the nickel(II)-HIDA complex with EDTA proceeds through the following reaction intermediate (Fig. 9). As is shown in Table 5, the $k_1^\ddagger$ and $k_2^\ddagger$ values for the substitution reaction of the nickel(II)-HIDA complex with CyDTA are appreciably smaller than those of the other substitution reactions studied. This may be attributed mainly to the steric hindrance resulting from the interaction between the cyclohexane ring of CyDTA anion and the hydroxyethyl group of the HIDA anion. Finally, it should be noted that the $k_2^\ddagger$ value, especially, for the reaction with CyDTA is much smaller than the $k_1^\ddagger$ value. Since the protonation of the CyDTA anion bonded to the nickel(II) ion will reduce the electrostatic repulsion between the un-coordinated carboylate groups, and will stabilize the reaction intermediate, the above fact suggests the importance of the deprotonation of the attacking group in the formation of the reaction intermediate. In order to describe the precise nature of the effect of the protonation of the attacking group, a further, systematic investigation is necessary

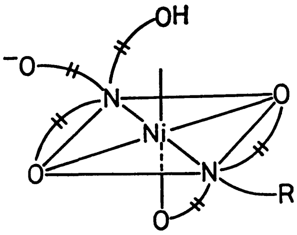

Fig. 9. Reaction intermediate for the substitution reaction of nickel(II)-HIDA complex with EDTA.