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Kinetics of Multidentate Ligand Substitution Reactions. VI. The Substitution Reaction of Diethylenetriaminepentaacetic Acid with the Nitrilotriacetato Nickelate(II) Chelate

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The kinetics of the substitution reaction of diethylenetriaminepentaacetic acid (DTPA) with the nitrilotriacetato nickelate(II) chelate have been studied polarographically in both acid and alkaline media. The reaction was found to be first-order with respect to DTPA and also first-order with respect to the nitrilotriacetato nickelate(II) chelate with 1-to-1 composition. In an acid solution the reaction proceeds mainly through tervalent and quadrivalent DTPA anions. On the other hand, in an alkaline solution the reaction proceeds through quadrivalent and quinquevalent DTPA anions. The heat of activation and the entropy of activation for the three elementary reactions were estimated, and the effect of the protonation of the quinquevalent DTPA anion on the reaction rate was discussed.

In previous investigations,[1-4] kinetic studies of the nucleophilic substitution reactions between Eriochrom Black T (BT) and cobalt(II)- and nickel(II)-aminopolycarboxylate chelates were carried out spectrophotometrically. From a comparison of the rate constants of the reactions with chelates of *N*-(2-hydroxyethyl)-ethylenediamine, *N,N′,N′*-triacetic acid (EDTA-OH), cyclohexanediaminetetraacetic acid (CyDTA), and diethylenetriaminepentaacetic acid (DTPA) with those of the corresponding reactions involving EDTA chelates, a detailed reaction mechanism was formulated, and the steric effect was quantitatively discussed on the basis of the proposed reaction intermediates.

It now seems to be important and necessary to extend the study to the investigation of the effect of various ligands on the reaction mechanism and the rate of the nucleophilic substitution reaction involving the metal(II) aminopolycarboxylate chelate. This paper will describe a polarographic study of the kinetics on the reaction of diethylenetriaminepentaacetic acid with the nitrilotriacetato nickelate(II) chelate.

Experimental

Reagents. The nickel (II) nitrate solution was prepared by dissolving a known amount of metallic nickel (99.99% pure) in dilute nitric acid (1+1) and by removing the excess nitric acid by distillation under reduced pressure. The standardization of the concentration of nickel (II) solution was described in a previous paper.[2] The recrystallization of nitrilotriacetic acid (NTA) and DTPA and the preparation of their solutions were also described previously.[2,4] The other reagents were of analytical-reagent grades and were used without further purification.

Apparatus and Experimental Procedure. All the polarograms and the current-time curves were obtained with a Yanagimoto PA-102 pen-recording polarograph, using a dropping mercury electrode which had an *m* value of 0.837 mg/sec and a drop time of 4.02 sec in an air-free acetate buffer solution (total concentration of acetate ions=0.10M, $\mu=0.20$) with a pH of 4.80 at 25°C at −0.50 V *vs.* SCE at the mercury height of 75 cm. The experimental procedures were the same as have previously been described by Tanaka, Kato and Tamamushi.[5] In this study, all the measurements were conducted in solutions with an ionic strength of 0.20 ($NaClO_4$). In the pH range from 4.50 to 5.80, an acetate buffer was employed. In the alkaline region ($8.50<pH<10.00$), however, no buffer reagent was used, for sample solutions contained a large excess of uncomplexed NTA and so had a sufficient buffer capacity already. Uncomplexed DTPA develops a well-defined anodic wave over the entire pH range covered,[6] so the rate of the reaction was followed by measuring the change in the diffusion current of DTPA with the time. In the potential range where the anodic wave due to the uncomplexed DTPA can be observed, nickel (II)-DTPA and NTA chelates are non-reactive in the polarographic electrolysis. Therefore, neither nickel (II) chelate has any effect on the determination of the concentration

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

[2] M. Kodama, C. Sasaki and M. Murata, *ibid.*, **41**, 1333 (1968).

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

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

[5] N. Tanaka, K. Kato and R. Tamamushi, This Bulletin, **31**, 283 (1958).

[6] M. Kodama and A. Kimura, *ibid.*, **40**, 1639 (1967).

of uncomplexed DTPA.[6] As the reaction rate was determined in this study by measuring the wave height of the uncomplexed DTPA, DTPA is also consumed by the polarographic electrolysis. However, the amount of DTPA consumed by the polarographic electrolysis is negligibly small as compared with that consumed by the substitution reaction with the nickel (II)-NTA chelate. The contribution of the polarographic electrolysis to the whole DTPA concentration change is only 0.05%, even under the experimental conditions where the present reaction proceeds at its slowest rate. In the polarographic electrolysis, a small amount of the mercury(II)-DTPA chelate is also formed at the electrode surface. However, the formation of the mercury(II)-DTPA chelate may be expected to give no effect on the rate of the substitution reaction, because the amount of mercury(II)-DTPA chelate formed is negligible as compared with those of the chemical species involved in the substitution reaction, and also because its stability constant is much greater than that of the nickel(II)-DTPA chelate.[7] This prediction was also confirmed experimentally by adding a small amount of the mercury-(II)-DTPA chelate (2×10^{-6}M). The presence of the mercury(II)-DTPA chelate had no effect on the rate of reaction.

Results and Discussion

All the exchange reactions were studied in solutions containing a large excess of complexed and uncomplexed NTA. Therefore, the exchange reaction (Reaction (1)) can be treated as a pseudo-first-order reaction.

$$\mathrm{H}_n\mathrm{Z}^{n-5} \underset{k^-}{\overset{k^+}{\rightleftarrows}} \begin{cases}\mathrm{NiZ}^{3-} + n\mathrm{H}^+ \\ \mathrm{NiHZ}^{2-}\end{cases}$$

where $\mathrm{H}_n\mathrm{Z}^{n-5}$ denotes the incompletely-deprotonated DTPA anion and NiZ^{3-} and NiHZ,$^{2-}$ normal and protonated nickel(II)-DTPA chelates respectively.

The stability constants of nickel(II)-DTPA chelates are much greater than those of the corresponding nickel(II)-NTA chelates.[7] Therefore, the apparent rate constant of the forward reaction, k^+, must be much greater than that of the backward reaction, k^-, hence, it seemed that rate of the backward reaction may be neglected as compared with that of the forward reaction. This theory was examined experimentally. The presence of the 10.0 mM nickel(II)-DTPA chelate was found to have no effect on the rate of the substitution reaction of DTPA with the nickel(II)-NTA chelate. Consequently, if the present reaction proceeds through simultaneous reaction pathways which involve the dissociation of the nickel(II)-NTA chelate as well as the second-order nucleophilic substitution reactions involving completely- and incompletely-dissociated DTPA anions, the rate of the disappearance of uncomplexed DTPA should be a function of the uncomplexed DTPA concentration and the apparent rate constant, k^+, in a solution of a given pH and with given concentrations of the nickel(II)-NTA chelate and uncomplexed NTA will be given by:

$$k^+ = k_\alpha + \frac{k_\beta}{[\mathrm{DTPA}]_f} \tag{2}$$

where $[\mathrm{DTPA}]_f$ indicates the concentration of uncomplexed DTPA and where the k's are constants.

Consequently, the rate law for the disappearance of uncomplexed DTPA can be expressed as:

$$-\frac{\mathrm{d}[\mathrm{DTPA}]_f}{\mathrm{d}t} = k^+[\mathrm{DTPA}]_f = k_\alpha[\mathrm{DTPA}]_f + k_\beta \tag{3}$$

By integrating Eq. (3), we obtain:

$$-\ln\left([\mathrm{DTPA}]_f + \frac{k_\beta}{k_\alpha}\right) = -k_\alpha\cdot t - \ln\left([\mathrm{DTPA}]_f^0 + \frac{k_\beta}{k_\alpha}\right) \tag{4}$$

where $[\mathrm{DTPA}]_f^0$ and $[\mathrm{DTPA}]_f$ are the concentrations of uncomplexed DTPA at time=0 and t respectively.

As was reported previously,[6] the limiting current of the anodic wave due to uncomplexed DTPA is proportional to the concentration of uncomplexed DTPA over the entire pH range studied. Therefore, Eq. (4) can be rewritten as:

$$-\log\left(i_t + \frac{k_\beta\cdot k}{k_\alpha}\right) = \frac{k_\alpha}{2.303} - \log\left(i_0 + \frac{k_\beta\cdot k}{k_\alpha}\right) \tag{5}$$

where i_0 and i_t are the wave heights of DTPA at $t=0$ and $t=t$ respectively and where k is the constant,

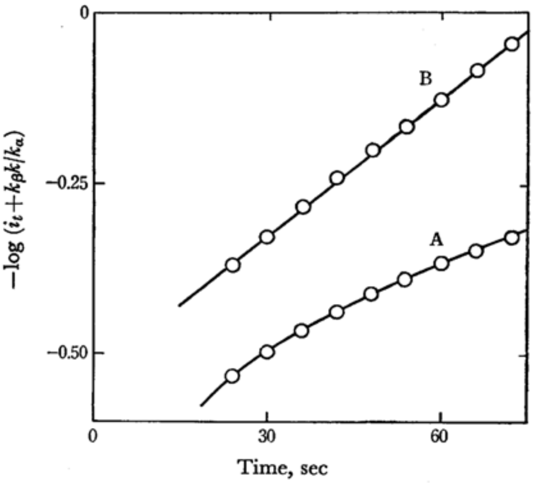

Fig. 1. The plot of $-\log(i_t+k_\beta k/k_\alpha)$ against t.
Concentration of Ni(II)-NTA chelate=6.90 mM
Concentration of uncomplexed NTA=9.53 mM
Concentration of acetate ion=9.15×10^{-2}M
Initial concentration of DTPA=0.453 mM
pH=5.00, μ=0.20, at 25°C
A. $k_\beta k/k_\alpha=1.00$, B. $k_\beta k/k_\alpha=0$

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[7] L. G. Sillen and A. E. Martell, "Stability Constants of Metal-Ion Complexes," The Chemical Society, London (1964), pp. 507, 693.

defined as $i=k\cdot[\mathrm{DTPA}]_f$.

If the present reaction mechanism does not involve the dissociation of the nickel(II)-NTA chelate, $k_\beta\cdot k/k_\alpha$ in Eq. (5) should be zero. Equation (5) was examined by using typical experimental data. As is illustrated in Fig. 1, the log-plot gave a linear relationship only when $k_\beta\cdot k/k_\alpha$ was zero over the entire pH range covered in this study. This fact clearly indicates that the reaction of DTPA with the nickel(II)-NTA chelate does not involve the dissociation of the nitrilotriacetato nickelate(II) chelate. This conclusion could also be confirmed by the fact that the k_α value determined from the slope of the linear relationship of $-\log i_t$ *versus* t was independent of the concentration of uncomplexed DTPA. The results obtained in the acid media (acetate buffer) are shown in Table 1.

TABLE 1. DEPENDENCE OF THE SLOPE ON THE DTPA CONCENTRATION

Concentration of uncomplexed NTA=9.53 mM
Concentration of nickel(II)-NTA chelate=6.90 mM
Concentration of acetate ion=9.15×10^{-2}M
μ=0.20, 25°C, pH=5.00

Initial concentration of DTPA, mM	Slope sec^{-1}
0.275	6.12×10^{-3}
0.453	6.12×10^{-3}
0.641	6.10×10^{-3}

With regard to the k_α value estimated from the above linear relationship, the following facts can also be established in acid media (4.50<pH<5.80):

1) In solutions of a given pH and with given concentrations of acetate ion and uncomplexed NTA, k_α is proportional to the concentration of the nickel(II)-NTA chelate (Table 2).

TABLE 2. DEPENDENCE OF THE SLOPE ON THE CONCENTRATION OF NICKEL(II)-NTA CHELATE

Concentration of uncomplexed NTA=9.53 mM
Initial concentration of DTPA=0.453 mM
Concentration of acetate ion=9.15×10^{-2}M
μ=0.20, 25°C, pH=5.00

Concn. of Ni(II)-NTA, mM	Slope sec^{-1}	Concn. ratio	Slope ratio
6.90	6.12×10^{-3}	1.00	1.00
10.35	9.10×10^{-3}	1.50	1.49
13.80	$12.2_5\times10^{-3}$	2.00	2.00

2) In solutions of a given pH and with given concentrations of uncomplexed and complexed NTA, k_α is independent of the concentration of the acetate ion (Table 3).

3) In solutions of a given pH and with given concentrations of the acetate ion and the nickel(II)-NTA chelate, k_α is independent of the concentration of uncomplexed NTA (Table 4).

TABLE 3. DEPENDENCE OF THE SLOPE ON THE CONCENTRATION OF ACETATE ION

Concentration of uncomplexed NTA=9.53 mM
Concentration of nickel(II)-NTA chelate=6.90 mM
Initial concentration of DTPA=0.453 mM
μ=0.20, 25°C, pH=5.00

Concentration of acetate, ion, M	Slope, sec^{-1}
4.57×10^{-2}	6.12×10^{-3}
9.15×10^{-2}	6.12×10^{-3}
1.32×10^{-1}	6.15×10^{-3}

TABLE 4. DEPENDENCE OF THE SLOPE ON THE CONCENTRATION OF UNCOMPLEXED NTA

Concentration of nickel(II)-NTA chelate=6.90 mM
Concentration of acetate ion=9.15×10^{-2}M
Initial concentration of DTPA=0.453 mM
μ=0.20, 25°C, pH=5.00

Concentration of NTA, mM	Slope, sec^{-1}
9.53	6.12×10^{-3}
14.30	6.10×10^{-3}
19.10	6.10×10^{-3}

4) In solutions with given concentrations of the acetate ion and complexed and uncomplexed NTA, the plot of $k_\alpha\cdot(\alpha_H)_Z/[\mathrm{H}^+]$ against $[\mathrm{H}^+]$ gives a linear relationship (Fig. 2). Here, $(\alpha_H)_Z$ is the (α_H) value of DTPA.

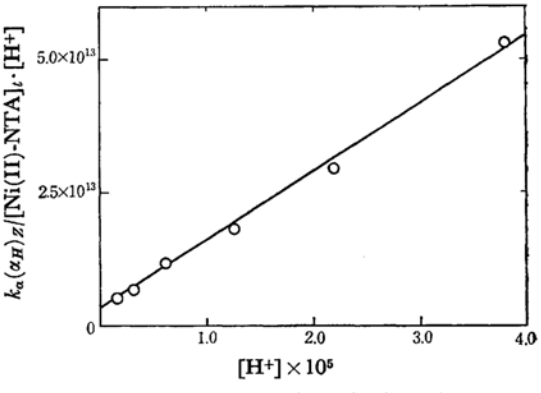

Fig. 2. The plot of $k_\alpha(\alpha_H)_Z/[\mathrm{Ni(II)\text{-}NTA}]_t\cdot[\mathrm{H}^+]$ against $[\mathrm{H}^+]$
Concentration of Ni(II)-NTA chelate=6.90 mM
Concentration of uncomplexed NTA=9.53 mM
Concentration of acetate ion=9.15×10^{-2}M
Initial concentration of DTPA=0.453 mM
μ=0.20, at 25°C

Thermodynamic calculation reveals that nickel (II) ions in solutions with pH's from 4.50 to 5.80 containing 10 mM uncomplexed NTA form only the chelate with a 1-to-1 composition, that the predominant uncomplexed DTPA species are tervalent and quadrivalent anions, and that their concentrations are given by $[\mathrm{DTPA}]_f[\mathrm{H}^+]^2/k_5\cdot k_4$ and $[\mathrm{DTPA}]_f[\mathrm{H}^+]/k_5$ respectively. Here, k_4 and k_5 denote the fourth and fifth dissociation constants of DTPA. Therefore, the above facts indicate that the present substitution reaction proceeds mainly through the following two simultaneous reaction pathways in the pH range from 4.50 to 5.80:

$$\begin{tikzcd} \text{i) } \mathrm{NiX}^- + \mathrm{H_2Z}^{3-} \arrow[r, shift left, "k_1^+"] & \mathrm{NiZ}^{3-} + \mathrm{H}^+ + \mathrm{HX}^{2-} \arrow[l, shift left] \arrow[d, shift left, "\text{rapid}"] \\ & \mathrm{NiHZ}^{2-} \arrow[u, shift left] \end{tikzcd}$$

$$\begin{tikzcd} \text{ii) } \mathrm{NiX}^- + \mathrm{HZ}^{4-} \arrow[r, shift left, "k_2^+"] & \mathrm{NiZ}^{3-} + \mathrm{HX}^{2-} \arrow[l, shift left] \arrow[d, shift left, "\text{rapid}"] \\ & \mathrm{NiHZ}^{2-} \arrow[u, shift left] \end{tikzcd}$$

where NiX^- is the nickel(II)-NTA chelate with a 1-to-1 composition; HZ^{4-} and $\mathrm{H_2Z}^{3-}$, quadrivalent and tervalent DTPA anions respectively, and HX^{2-}, the doubly-deprotonated NTA anion. On the basis of the above reaction mechanism, k_α in an acid medium can be written as:

$$k_\alpha = \left(\frac{k_2^+[\mathrm{H}^+]}{k_5} + \frac{k_1^+\cdot[\mathrm{H}^+]^2}{k_4\cdot k_5}\right)\frac{[\mathrm{Ni(II)\text{-}NTA}]_t}{(\alpha_H)_Z} \tag{6}$$

In an alkaline medium (8.50<pH<10.00), as is illustrated by Tables 5 and 6, the k_α value determined from the linear relationship between $\log i_t$ and t was also found to be proportional to the total concentration of the nickel(II)-NTA chelate, but to be inversely proportional to the value of $1+k_{\mathrm{NiX_2}}\cdot[\mathrm{X}]_f/(\alpha_H)_X$, provided that the other experimental conditions are kept constant. Here, $K_{\mathrm{NiX_2}}$, $(\alpha_H)_X$ and $[\mathrm{X}]_f$ have the same meanings as have been used previously.[2] The above facts clearly indicate that the k_α value is linearly proportional to the concentration of the nickel(II)-NTA chelate with a 1-to-1 composition. $[\mathrm{X}]_f$ was calculated from the total concentrations of NTA and nickel(II) ions with the aid of Eq. (2) of Ref. 2. As was found in the acid medium, k_α was also independent of the DTPA concentration (these results are not shown here). This fact clearly indicates that, in the pH range from 8.50 to 10.00, the substitution reaction of DTPA with the nitrilotriacetato nickelate(II) chelate does not proceed through the reaction pathway in which the dissociation of the nickel(II)-NTA chelate is involved.

TABLE 5. DEPENDENCE OF THE SLOPE ON THE TOTAL CONCENTRATION OF NICKEL (II)-NTA CHELATE

Concentration of uncomplexed NTA=11.7 mM
Initial concentration of DTPA=0.453 mM
μ=0.20, 25°C, pH=9.50

Total concn. of Ni(II)-NTA, mM	Slope, sec^{-1}	Concn. ratio	Slope ratio
6.90	8.50×10^{-3}	1.00	1.00
10.35	$12.8\ \times10^{-3}$	1.50	1.51
13.80	$16.7\ \times10^{-3}$	2.00	1.97

TABLE 6. DEPENDENCE OF THE SLOPE ON THE $[1+K_{\mathrm{NiX_2}}[\mathrm{X}]_f/(\alpha_H)_X]$ VALUE

Initial concentration of DTPA=0.453 mM
Total concentration of nickel(II)-NTA chelate=6.90 mM
μ=0.20, 25°C, pH=9.50

Concn. of uncomplexed NTA, mM	Slope, sec^{-1}	Slope$\times[1+K_{\mathrm{NiX_2}}[\mathrm{X}]_f/(\alpha_H)_X]$
11.70	8.50×10^{-3}	1.19
27.3	3.58×10^{-3}	1.25
37.7	2.68×10^{-3}	1.21

The k_α value was also a function of the hydrogen ion concentration, and there was a linear relationship between $k_\alpha\cdot(\alpha_H)_Z[1+k_{\mathrm{NiX_2}}\cdot[\mathrm{X}]_f/(\alpha_H)_X]/[\mathrm{Ni(II)NTA}]_t$ and the hydrogen ion concentration, $[\mathrm{H}^+]$ (Fig. 3). Here, $[\mathrm{Ni(II)NTA}]_t$ indicates the total concentrations of nickel(II)-NTA chelates. All the facts stated above clearly indicate that, in an alkaline solution, the present reaction mainly proceeds through the following two reaction pathways.

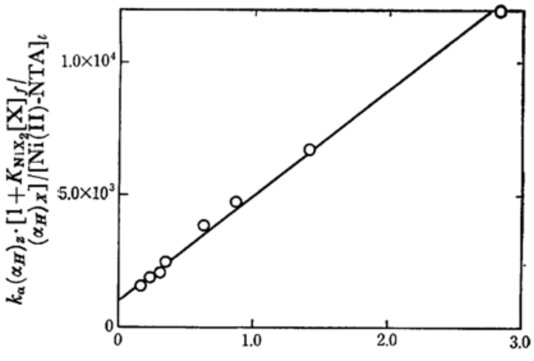

Fig. 3. The plot of $k_\alpha(\alpha_H)_z\cdot[1+K_{\mathrm{NiX_2}}([\mathrm{X}]_f/(\alpha_H)_X]/[\mathrm{Ni(II)\text{-}NTA}]_t$ against $[\mathrm{H}^+]$
Total concentration of nickel(II)-NTA chelate=6.90 mM
Total concentration of NTA=28.0 mM
Initial concentration of DTPA=0.453 mM
μ=0.20, at 25°C

$$\begin{tikzcd} \text{ii) } \mathrm{NiX}^- + \mathrm{HZ}^{4-} \arrow[r, shift left, "k_2^+"] \arrow[d, shift left, "\text{rapid}"] & \mathrm{NiZ}^{3-} + \mathrm{HX}^{2-} \arrow[l, shift left] \\ \mathrm{NiX_2}^{4-} \arrow[u, shift left] & \end{tikzcd}$$

$$\begin{tikzcd} \text{iii) } \mathrm{NiX}^- + \mathrm{Z}^{5-} \arrow[r, shift left, "k_3^+"] \arrow[d, shift left, "\text{rapid}"] & \mathrm{NiZ}^{3-} + \mathrm{X}^{3-} \arrow[l, shift left] \\ \mathrm{NiX_2}^{4-} \arrow[u, shift left] & \end{tikzcd}$$

where NiX_2^{4-} indicates the nickel(II)-NTA chelate with a 1-to-2 composition. Therefore, k_a in Eq. (5) can be written as:

$$k_a = \left(k_3{}^+ + k_2{}^+ \cdot \frac{[\mathrm{H}^+]}{k_5}\right) \times \frac{[\mathrm{Ni(II)\text{-}NTA}]_t}{(\alpha_H)_Z \cdot [1 + K_{\mathrm{NiX_2}} \cdot [\mathrm{X}]_f/(\alpha_H)_X]} \tag{7}$$

From the slopes and intercepts shown in Figs. 2 and 3, $k_1{}^+$, $k_2{}^+$ and $k_3{}^+$ were determined at 25°C. The $k_2{}^+$ value determined from the slope in Fig. 3 agreed well with that obtained from the intercept in Fig. 2. This agreement strongly supports the proposed reaction mechanism.

Similar results were also obtained in the experiments at 18°C and 9°C. The k^+ value determined at 18°C and 9°C are given in Table 7, along with the results obtained at 25°C. Linear relationships were found between the log k^+ value and $1/T$ for three elementary reactions, i), ii) and iii); this made it possible to calculate the heat and entropy of activation. The results are given in Table 7. The k^+ values given in Table 7 are much greater than the corresponding rate constants for the reaction of the nickel(II)-NTA chelate with EDTA-OH,[8] lending strong support to the present author's conclusion that the exchange reaction of DTPA with the nickel(II)-NTA chelate proceeds predominantly through three simultaneous reaction pathways, all of which involve a second-order nucleophilic substitution reaction without any dissociation of the nickel(II)-NTA chelate. The greater rate constants probably mean that the present exchange reaction proceeds by a mechanism which involves a reaction intermediate more stable than that for the nickel-(II)-NTA-EDTA-OH reaction.

Table 7. Rate constants, heat of activation and entropy of activation for reactions i), ii) and iii)

k^+ value	Temperature, °C			ΔH^{++} kcal/mol	ΔS^{++} e.u.
	9.0	18.0	25.0		
$k_1{}^+$	0.499	0.175	1.78	12.2	−16.5
$k_2{}^+$	2.77×10^1	7.24×10^1	3.06×10^2	19.3	20.5
$k_3{}^+$	3.1×10^2	7.0×10^2	9.1×10^2	10.0	−11.2

On the basis of the conclusion reached by Rorabacher and Margerum concerning the reaction of nickel(II)-polyamine complexes with EDTA,[9] the reaction intermediate expected for the present exchange reaction may involve the DTPA anion, all three nitrogen groups of which are coordinated to the nickel(II) ion, as well as the tervalent NTA anion. If the DTPA anion in the reaction intermediate forms only two nickel(II)-nitrogen bonds or less, the k^+ values of the present reaction should be smaller than the corresponding rate constants for the nickel(II)-NTA–EDTA-OH reaction, because the less stable reaction intermediate due to the larger steric effect of DTPA would make the reaction more sluggish.

It is also interesting to note that the heat of activation for the elementary reaction ii) is much larger than those for i) and iii) reactions, and that the entropy of activation for the ii) reaction is positive, whereas those for the i) and iii) reactions are negative. Generally, the entropy of activation for a second-order nucleophilic substitution reaction involving a multidentate ligand may be expected to be negative, because the conformational, translational, and rotational freedom of an entering multidentate ligand would be lost in the formation of a mixed ligand intermediate chelate. The negative entropy for the elementary reaction iii) may be responsible for this effect. An NMR study of the protonation of the quinquevalent DTPA anion (Fig. 4) in an aqueous solution[10] gave the conclusion that, after the addition of one proton equivalent, the terminal nitrogen groups, (1) and (3), are each protonated 26% of the time each; the central nitrogen group (2) is protonated 41% of the time, and the central acetate group (4) is protonated 7% of the time, while the terminal acetate groups are not protonated to any detectable extent. On the other hand, when a second proton equivalent is added, the two terminal nitrogen groups are each protonated 85% of the time, the central nitrogen group (2) is protonated only 15% of the time, and four terminal acetate groups are protonated 4% of the time. The fact that the first proton is almost equally bonded among the three nitrogen groups of the DTPA anion probably indicates that the intramolecular hydrogen bonding arranges the DTPA anion in a favorable position to form the reaction intermediate. Thus, less conformational and rotational freedom is lost in the formation of the mixed ligand intermediate chelate, corresponding to the positive entropy of activation for the elementary reaction ii). The tervalent DTPA anion, H_2Z^{3-}, where the two terminal nitrogen groups are almost completely-protonated and where the central nitrogen group is protonated only 15% of the time, may have a conformation less favor-

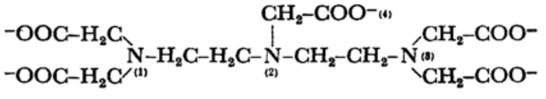

Fig. 4. Quinquevalent DTP Aanion.

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[8] M. Kimura, *Nippon Kagaku Zasshi* (*J. Chem. Soc. Japan, Pure Chem. Sect.*), **89**, 1209 (1968).

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

[10] J. L. Sudmeier and C. N. Reilley, *Anal. Chem.*, **36**, 1698 (1964).

able to the formation of the reaction intermediate, because the electrostatic repulsion between the positively-protonated sites would prevent the DTPA anion from having a favorable conformation to react with the nickel(II)-NTA chelate. Thus, a remarkable decrease in entropy for the elementary reaction i) can be expected.

Finally, it can also be mentioned that, with an increase in the extent of the protonation of the central nitrogen and acetate groups, the heat of activation becomes greater. This probably suggests that the deprotonation of these groups is inherently required for the formation of a mixed ligand chelate intermediate, through which the exchange reaction of the nickel(II)-NTA chelate with DTPA proceeds. The importance of the conformation of the attacking group will be discussed in a subsequent paper.

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