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Kinetics of Multidentate Ligand Substitution Reactions. XVII.* Substitution Reactions of Diethylenetriaminepentaacetate (DTPA) with Aminopolycarboxylate Complexes of Nickel(II) and Cobalt(II)

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The kinetics of the substitution reactions of DTPA with *N*-(2-hydroxyethyl)iminodiacetate (HIDA) and *N*-(2-hydroxyethyl)ethylenediamine-*N,N′,N′*-triacetate (EDTA-OH) complexes of nickel(II) and EDTA-OH and 2,2′-ethylenedioxydi(ethylamine)-*N,N,N′,N′*-tetraacetate (GEDTA) complexes of cobalt(II) were studied systematically by employing the polarographic technique. The reaction of ethylenediaminetetraacetate (EDTA) with the nitrilotriacetate (NTA) complex of nickel(II) in an alkaline medium was also studied. All the substitution reactions were found to have a common reaction mechanism. They were first-order with respect to DTPA or EDTA and also first-order with respect to the 1 : 1 ratio metal(II) complex of HIDA, NTA, EDTA-OH, or GEDTA. From a comparison of the observed rate constants with those estimated on the basis of the proposed reaction intermediate, the detailed reaction mechanism and the steric effect of the DTPA anion on the reaction rates were studied. The DTPA anion had practically no effect on the rates of the substitution reactions of the aminopolycarboxylate complexes of metal (II) ions.

Previously,[1)] the present author studied the kinetics of the substitution reaction of DTPA with the nickel(II)–NTA complex and discussed the effect of the protonation of the DTPA anion on its reaction rate. However, no detailed reaction mechanism was investigated in that paper. He also studied the kinetics of the substitution reactions of cyclohexane-1,2-diamine-*N,N,N′,N′*-tetraacetate(CyDTA) with the aminopolycarboxylate complexes of zinc(II) and cobalt(II), and discussed the nature of the steric effect of the CyDTA anion on their reaction rates.[2)] Consequently, in order to understand more precisely the nature of the steric effect of the entering group on the rate of the substitution reaction involving an aminopolycarboxylate complex, it seems to be necessary and important to conduct a kinetic study of the substitution reaction involving DTPA. This paper will describe a kinetic study of the substitution reactions of DTPA with the nickel(II)–HIDA and –EDTA-OH and cobalt(II)–EDTA-OH and –GEDTA complexes, using the polarographic technique. The substitution reaction of EDTA with the nickel(II)–NTA complex in an alkaline solution will also be studied in this paper, and its reaction rate will be compared with those of the DTPA reactions.

Experimental

Reagents. The methods of preparing and standardizing the nickel(II) and cobalt(II) nitrate solutions were given previously.[3)] The EDTA, DTPA, EDTA-OH, and GEDTA used in this study were recrystallized as their acids from their aqueous solutions. The preparation and recrystallization of the acid form of HIDA were also given previously.[4)] All the other chemicals used were of an analytical reagent grade and were used without further purification.

Apparatus and Experimental Procedures. The apparatus and experimental procedures employed were the same as those given previously.[2)] In this study, no buffer reagent was used, because all the sample solutions always contained a large excess of uncomplexed HIDA, NTA, EDTA-OH, or GEDTA, and had enough buffer capacity over the entire pH range covered ($8.30<\mathrm{pH}<9.00$ in the HIDA system, $9.00<\mathrm{pH}<10.00$ in the NTA system, $9.00<\mathrm{pH}<10.40$ in the EDTA-OH system, and $9.40<\mathrm{pH}<10.40$ in the GEDTA system). All the kinetic measurements were conducted under experimental conditions where all the reactions could be treated as pseudo first-order reactions. The rate of the substitution reaction was determined by measuring the change in the dissolution wave-height due to the uncomplexed DTPA or EDTA. The ionic strength of the sample solution was adjusted to 0.30 by adding an appropriate amount of $NaClO_4$.

Results and Discussion

The substitution reactions of DTPA with the nickel(II)–HIDA and cobalt(II)–GEDTA complexes and the reaction of EDTA with the nickel(II)–NTA complex showed kinetic behavior quite similar to that of the reaction of DTPA with the nickel(II)–NTA complex.[1)] This fact suggests that the reaction mechanism for the above reactions can be formulated as:

$$\mathrm{MX}_2^{(2-2m)+} \rightleftarrows \mathrm{MX}^{(2-m)+} + \mathrm{X}^{m-} \quad \text{(a) in a rapid equil.}$$

$$\mathrm{MX}^{(2-m)+} + \begin{cases} \mathrm{HY}^{1-n} \overset{k_\mathrm{H}}{\rightleftarrows} \mathrm{MY}^{2-n} + \mathrm{HX}^{1-m} & \text{(b)} \\ \mathrm{Y}^{n-} \overset{k_0}{\rightleftarrows} \mathrm{MY}^{2-n} + \mathrm{X}^{m-} & \text{(c)} \end{cases} \quad \text{rds}$$

corresponding to Relation (1):

$$k_{\mathrm{ap}}^{+} = \frac{[\mathrm{Me(II)}] \times \left(k_0 + k_\mathrm{H} \cdot \frac{[\mathrm{H}^+]}{K_\mathrm{n}}\right)}{(\alpha_\mathrm{H})_\mathrm{Y} \cdot \left(1 + \frac{K_2 \cdot [\mathrm{X}]_\mathrm{f}}{(\alpha_\mathrm{H})_\mathrm{X}}\right)} \tag{1}$$

where k_{ap}, [Me(II)], and K_n are, respectively, the pseudo first-order rate constant, the metal(II) concentration, and the fifth dissociation constant of diethylenetriaminepentaacetic acid or the fourth dissociation constant of ethylenediaminetetraacetic acid; all the other symbols used have their usual meanings.[2)] The k_0 and k_H values for the above reactions were determined from the intercepts and slopes of the linear relations between $k_{\mathrm{ap}}^{+} \times (1+K_2 \cdot [\mathrm{X}]_\mathrm{f}/(\alpha_\mathrm{H})_\mathrm{X})(\alpha_\mathrm{H})_\mathrm{Y}/[\mathrm{Me(II)}]$ and [H+]; they are listed in Tables 1 and 2.

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* Part XVI: M. Kodama, This Bulletin, **47**, 1430 (1974).

TABLE 1. SUBSTITUTION RATE CONSTANTS OF Ni(II) COMPLEXES
$\mu=0.30$, 25°C

System	Rate constant		Log rate constant ratio		
			Obsd		
	k_0	k_H	k_0	k_H	Calcd[a)]
NTA[7)]	3×10^{-5}	—	-7.76	—	-7.58
NTA–EDTA	1.5×10^{3}	2.33×10^{2}	0	0	0
NTA–DTPA[1)]	9.1×10^{2}	3.06×10^{2}	-0.22	$+0.12$	0
HIDA–DTPA	1.1×10^{5}	1.50×10^{4}	1.87	1.81	2.08
EDTA-OH–DTPA	2.3×10^{-3}	3.76×10^{-3}	-4.82	-4.80	-5.14

a) Calculated on the basis of the Gly reaction mechanism.

TABLE 2. SUBSTITUTION RATE CONSTANTS OF Co(II) COMPLEXES
$\mu=0.30$, 25°C

System	Rate constant		Log rate constant ratio		
			Obsd		
	k_0	k_H	k_0	k_H	Calcd[a)]
EDTA-OH	2.1×10^{1}	3.8	0	0	0
GEDTA	1.0×10^{4} [b)]	2.0×10^{3}	2.70	2.72	2.60

a) Calculated on the basis of the Gly reaction mechanism. b) Less accurate.

In the substitution reactions involving metal (II)–EDTA-OH complexes, the pseudo first-order rate constant, k_{ap}^{+}, was 1) proportional to the metal(II) concentration, 2) independent of the initial concentration of DTPA, and also 3) independent of the concentration of uncomplexed EDTA-OH. Furthermore, the plot of the k_{ap}^{+} value multiplied by $(\alpha_H)_Y/[Me(II)]$ against $[H^+]$ gave a linear relation with an intercept of a finite value (Fig. 1). These facts imply that the substitution reactions of DTPA with the metal(II)–EDTA-OH complexes proceed through (b) and (c), corresponding to Relation (2):

$$k_{ap}^{+} = \frac{[Me(II)]}{(\alpha_H)_Y}\cdot\left(k_0+k_H\cdot\frac{[H^+]}{K_n}\right) \tag{2}$$

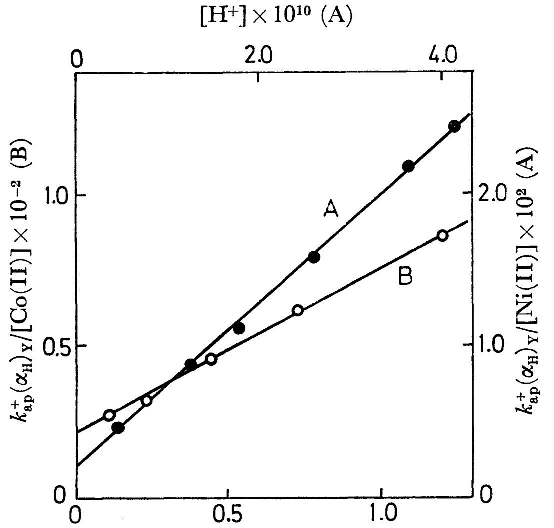

Fig. 1. The plot of $k_{ap}^{+}\times(\alpha_H)_Y/[Me(II)]$ against $[H^+]$
$\mu=0.30$, 25 °C
A) Ni(II) system
$[Ni(II)]=18.2$ mM, $[EDTA\text{-}OH]_f=18.2$ mM, $[DTPA]_i=1.82$ mM
B) Co(II) system
$[Co(II)]=6.37$ mM, $[EDTA\text{-}OH]_f=21.0$ mM, $[DTPA]_i=0.546$ mM

Therefore, the k_0 and k_H values were estimated from the intercepts and slopes of the straight lines in Fig. 1; they are listed in Tables 1 and 2.

As was discussed in connection with the dissociation[5)] and substitution reactions[6)] of the ethylenediaminemonoacetate (EDMA) complex of nickel(II), the entering group in the ligand substitution reaction just assists the dissociation of the leaving group without effecting any change in the detailed dissociation mechanism. Previously,[3)] the present author established that the nickel(II)–NTA complex dissociates through the Gly reaction intermediate, in which the leaving NTA anion is bonded to the nickel(II) ion through the glycinate chelate ring (Gly mechanism). Therefore, it is natural to believe that the substitution reaction of the nickel(II)–NTA complex with EDTA also proceeds through a Gly mechanism.[2,7,8)] If the Gly mechanism can be assumed for the reaction of the nickel(II)–NTA complex with EDTA, the rate constant ratio between the dissociation reaction of the nickel(II)–NTA complex,[9)] and its substitution reaction with EDTA should be 1: $10^{7.58}$. The above rate constant ratio was calculated with the aid of the $k=k_{rds}K_AK_LK_{st}K_{elec}/K_{MX}$ relation[2,10)] by using the K_A value of $10^{9.27}$, the K_{st} ratio of 2, and the K_{elec} ratio of $10^{2.0}$. The observed ratio was 1: $10^{7.76}$ (Table 1). The good agreement between the observed and calculated ratios supports the above Gly-mechanism explanation, suggesting that the EDTA anion had practically no steric effect on its substitution reaction with the nickel(II)–NTA complex. As is illustrated in Table 1, the k_0 and k_H values for the reaction of DTPA with the nickel(II)–NTA complex can also be understood in terms of a simple

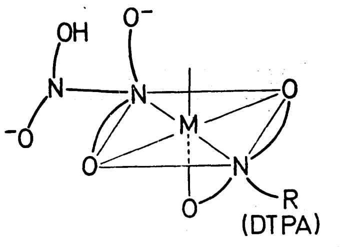

Fig. 2. A possible intermediate for the substitution reaction of DTPA with metal(II)-EDTA-OH complex, [Me^{II} (EDTA-OH) (DTPA)]$^{-n}$

Gly mechanism. The k_0 and k_H values of the substitution reaction of DTPA with the nickel(II)–HIDA complex can also be understood by assuming the Gly mechanism. The rate constant ratio between the DTPA reactions with the nickel(II)–HIDA and –NTA complexes estimated on the basis of the Gly mechanism was 1: $10^{2.08}$, and the good agreement with the observed k_0 ratio of 1: $10^{1.87}$ or the k_H ratio of 1: $10^{1.82}$ (Table 1). Similarly, the k_0 and k_H values of the reaction of DTPA with the nickel(II)–EDTA-OH complex could also be understood by assuming the Gly reaction mechanism (the reaction intermediate in Fig. 2). The rate constant ratio between the nickel(II)–NTA and –EDTA-OH systems, as calculated on the basis of the proposed reaction mechanism, was 1: $10^{-5.14}$. The observed k_0 and k_H ratios were 1: $10^{-4.80}$ and 1: $10^{-4.81}$ respectively. The agreement between the observed and calculated ratios can be regarded as satisfactory. As was mentioned above, the rates of the DTPA reactions studied could be understood by assuming the Gly reaction mechanism. This evidently implies that, irrespective of its large molecular size, the entering DTPA anion exerts practically no steric effect on the rate of its substitution reaction with the aminopolycarboxylate complex of nickel(II). The result obtained in the kinetic study of the DTPA substitution reactions of cobalt(II)–EDTA-OH and –GEDTA complexes proved the above conclusion to be true. Since the cobalt(II) complex shows kinetic behavior quite similar to that of the nickel(II) complex,[11] one can safely assume the Gly reaction mechanism for the DTPA reactions of the cobalt(II)–EDTA-OH and –GEDTA complexes. On the basis of the Gly mechanism, the rate constant ratio between the EDTA-OH and GEDTA systems could be estimated to be 1: $10^{2.60}$. The observed k_0 and k_H ratios were 1: $10^{2.70}$ and 1: $10^{2.72}$ respectively. The agreement between the calculated and observed ratios can be regarded as satisfactory (Table 2). The conclusion that the DTPA anion has no practical effect on its substitution reaction rates could also be confirmed by an examination of the molecular model. A close examination of the molecular model revealed that, for all the DTPA system, the glycinate reaction intermediate in which the leaving aminopolycarboxylate and entering DTPA anions are, respectively, bonded to the metal(II) ion through the glycinate and iminodiacetate chelate rings could be formed without any difficulty. This can be ascribed chiefly to the free bond rotation of the DTPA and aminopolycarboxylate anions involved in the substitution reactions.

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