BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 3330—3333 (1969)

Kinetics of Multidentate Ligand Substitution Reactions. VII. Substitution Reactions of the Nickel(II)-Iminodiacetate Chelate with Ethylenediaminetetraacetic Acid and 1,2-Diaminocyclohexanetetraacetic Acid and of the Cobalt(II)-Nitrilotriacetate with 1,2-Diaminocyclohexanetetraacetic Acid

Mutsuo KODAMA

Department of Chemistry, Ibaraki University, Bunkyo-cho, Mito

(Received March 10, 1969)

In the previous paper,[1] the kinetics of the substitution reaction between the nickel(II)-nitrilotriacetate chelate and diethylenetriaminepentaacetic acid (DTPA) were investigated systematically by the polarographic method. The reaction proceeded mainly through tervalent, quadrivalent, and quinquivalent DTPA anions. In an acid medium, the contribution of the quinquivalent DTPA anion reaction was negligible. The activation parameters, $\Delta H^{\neq}$ and $\Delta S^{\neq}$, for the three elementary reactions were also determined. In the two elementary reactions which proceed through tervalent and quinquivalent DTPA anions, the $\Delta S^{\neq}$ values were negative. The reaction which involves the quadrivalent DTPA anion, however, had a positive entropy of activation. This was ascribed to the fact that in the quadrivalent DTPA anion, intramolecular hydrogen bonding among hydrogen-ion and nitrogen groups places the DTPA anion in a favorable position to from a mixed ligand reaction intermediate; thus, less freedom was lost in the formation of the intermediate. In the nucleophilic substitution reaction involving 1,2-diaminocyclohexanetetraacetic acid (CyDTA), the CyDTA anion would be placed in a favorable position to react with metal. Therefore, even the reaction involving the completely-deprotonated CyDTA anion will give a positive entropy of activation. In this paper, the substitution reactions of CyDTA with nickel(II)-iminodiacetate and cobalt(II)-nitrilotriacetate chelates were studied by observing the change in the anodic wave-height of uncomplexed CyDTA. The exchange reaction between ethylenediaminetetraacetic acid (EDTA) and the nickel(II)-iminodiacetate chelate was compared with the reaction of CyDTA with the nickel(II)-iminodiacetate chelate.

Experimental

Reagents. The ways of preparing and standardizing the nickel(II) nitrate and cobalt(II) perchlorate solutions were given in previous papers.[1,2] Iminodiacetic acid (IDA) was recrystallized three times from an aqueous solution by adding pure ethanol, and a known amount was dissolved in doubly-distilled water. The recrystallization of nitrilotriacetic acid (NTA), EDTA, and CyDTA and the preparation of their solutions have also been described previously.[3,4] Other reagents were of an analytical reagent grade and were used without further purification.

Apparatus and Experimental Procedure. All the apparatus (Pen-recording polarograph and the dropping mercury electrode) and experimental procedures were the same as have been described previously.[1] All the measurements were conducted in solutions with the ionic strength of 0.20 ($NaClO_4$) in the pH range from 8.50 to 10.00. Since the sample solutions contained a large excess of uncomplexed NTA or IDA, no buffer reagent was used. The reaction rate was followed by recording automatically the change in the anodic wave-height of uncomplexed CyDTA or EDTA with the time.

Results and Discussion

The reaction of the nickel(II)-IDA chelate with EDTA and that with CyDTA were studied at 25 and 33°C respectively. The reaction beween the cobalt(II)-NTA chelate and CyDTA was studied at 18°C. All the substitution reactions investigated in solutions containing a large excess of complexed and uncomplexed IDA or NTA in the pH range from 8.50 to 10.00. Therefore, the reaction could be treated as pseude first-order reaction. In this study, the concentration of the metal(II)-IDA or -NTA chelate, $[MX]_t$, ranged from 8.50 to 20.00 mM and that of uncomplexed IDA or NTA, $[X]_f$, from 7.0 to 25.0 mM. As had been observed in the reaction of DTPA with the nickel(II)-NTA chelate,[1] the plot of $\log(i_0/i_t)$ aginst t invariably gave a straight line passing through the point of origin (Fig. 1). When the

---

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

[2] M. Kodama, *ibid.*, **40**, 2575 (1967).

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

[4] M. Kodama and H. Ebine, *ibid.*, **40**, 1857 (1967).

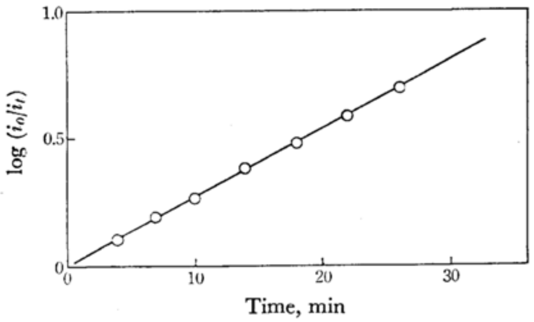

Fig. 1. log i_o/i_t *vs.* time plot for the exchange reaction of nickel (II)-IDA chelate with CyDTA

pH=9.05, μ=0.20, 33°C
Initial concentration of CyDTA=0.610 mM
Concentration of nickel(II)-IDA chelate =10.24 mM
Concentration of uncomplexed IDA=6.92 mM

other experimental conditions were kept constant, its slope was independent of the initial concentration of CyDTA or EDTA. The presence of the metal(II)-CyDTA or -EDTA chelate had no effect on the slope of the linear relation. Therefore, as was discussed in the substitution reaction of DTPA with the nickel(II)-NTA chelate,[1] it can be concluded that, practically, the rate of the backward reaction of the present substitution reaction is negligible compared with that of the forward reaction, and that all the three substitution reactions studied here proceed through simultaneous reaction pathways which involve only direct second-order nucleophilic substitution reactions of the metal(II)-IDA or -NTA chelate with the CyDTA or EDTA anion. The slope of the linear relation between $-\log i_t$ and t was also proportional to the concentration of the metal(II)-IDA or -NTA chelate and inversely proportional to the value of $1+K_{\mathrm{MX_2}}^{\mathrm{X}}\cdot[\mathrm{X}]_f/(\alpha_\mathrm{H})_x$, provided that the other experimental conditions were kept constant (Tables 1 and 2). All the symbols used here have the same meanings as previously.[1] These two facts clearly indicate that the slope is exactly proportional to the concentration of the metal(II)-IDA or -NTA chelate with a 1-to-1 composition. In the solutions with given concentrations of the complexed and uncomplexed IDA, or NTA, and with a given initial con-

TABLE 1. DEPENDENCE OF THE SLOPE ON THE CONCENTRATION OF NICKEL(II) - IDA OR COBALT(II) - NTA CHELATE

1) Nickel(II)-IDA chelate-EDTA system

μ=0.20 pH=9.23 [EDTA]=0.610 mM
$[\mathrm{IDA}]_f$=10.14 mM 25°C

Concentration of Ni(II)-IDA chelate, $[\mathrm{NiX}]_t$, mM	Slope sec^{-1}	Concentration ratio	Slope ratio
8.63	2.50×10^{-3}	1.00	1.00
12.95	3.73×10^{-3}	1.50	1.49
17.26	5.10×10^{-3}	2.00	2.04

2) Nickel(II)-IDA-CyDTA system

μ=0.20 pH=8.90 [CyDTA]=0.610 mM
$[\mathrm{IDA}]_f$=6.92 mM 33°C

Concentration of Ni(II)-IDA chelate, $[\mathrm{NiX}]_t$, mM	Slope sec^{-1}	Concentration ratio	Slope ratio
10.24	6.29×10^{-4}	1.00	1.00
20.48	1.26×10^{-3}	2.00	2.00

3) Cobalt(II)-NTA-CyDTA system

μ=0.20 pH=9.65 [CyDTA]=0.610 mM
$[\mathrm{NTA}]_f$=9.55 mM 18°C

Concentration of Co(II)-NTA chelate, $[\mathrm{CoX}]_t$, mM	Slope sec^{-1}	Concentration ratio	Slope ratio
9.15	2.21×10^{-4}	1.00	1.00
11.40	2.72×10^{-4}	1.25	1.23
16.80	3.97×10^{-4}	1.84	1.80

TABLE 2. DEPENDENCE OF THE SLOPE ON THE CONCENTRATION OF UNCOMPLEXED IDA OR NTA

1) Nickel(II)-IDA-EDTA system
μ=0.20 pH=9.23 [EDTA]=0.610 mM
$[\mathrm{NiX}]_t$=8.63 mM 25°C

Concentration of uncomplexed IDA, $[\mathrm{X}]_f$, mM	Slope sec^{-1}	Slope$\times[1+K_{\mathrm{NiX_2}}^{X}\times[\mathrm{X}]_f/(\alpha_\mathrm{H})_x]$
10.14	2.50×10^{-3}	56.9
19.34	1.33×10^{-3}	57.6
28.44	8.83×10^{-4}	56.2

2) Nickel(II)-IDA-CyDTA system
μ=0.20 pH=8.90 [CyDTA]=0.610 mM
$[\mathrm{NiX}]_t$=10.24 mM 33°C

Concentration of uncomplexed IDA, $[\mathrm{X}]_f$, mM	Slope sec^{-1}	Slope$\times[1+K_{\mathrm{NiX_2}}^{X}\times[\mathrm{X}]_f/(\alpha_\mathrm{H})_x]$
6.92	6.29×10^{-4}	9.77
16.07	2.76×10^{-4}	9.95
25.22	1.75×10^{-4}	9.90

3) Cobalt(II)-NTA-CyDTA system
μ=0.20 pH=9.65 [CyDTA]=0.610 mM
$[\mathrm{CoX}]_t$=9.15 mM 18°C

Concentration of uncomplexed NTA, $[\mathrm{X}]_f$, mM	Slope sec^{-1}	Slope$\times[1+K_{\mathrm{CoX_2}}^{X}\times[\mathrm{X}]_f/(\alpha_\mathrm{H})_x]$
9.55	2.21×10^{-4}	5.03×10^{-3}
13.10	1.69×10^{-4}	5.19×10^{-3}
17.10	1.29×10^{-4}	5.13×10^{-3}

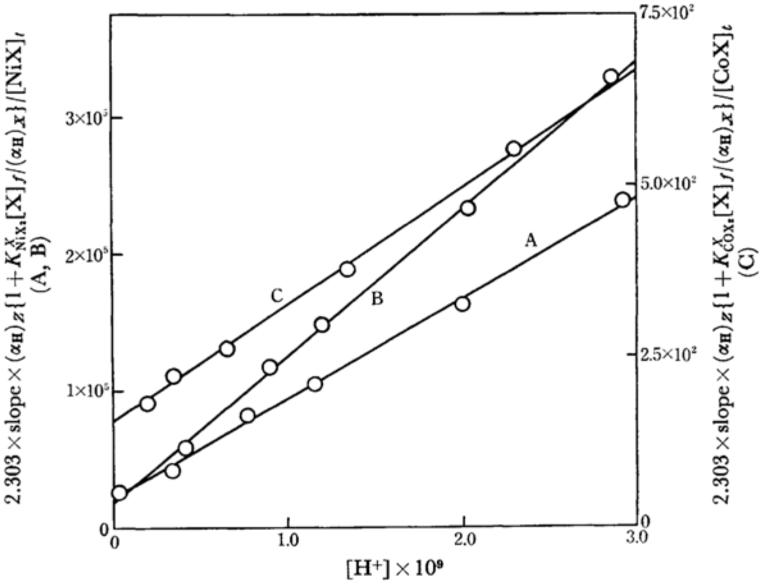

Fig. 2. The plot of $2.303\times\text{slope}\times(\alpha_H)_Z[1+K^X_{MX_2}[X]_f/(\alpha_H)_Z]/[NiX]_t$ against $[H^+]$

25°C, $\mu=0.20$

A : Ni(II)-IDA-EDTA system
Initial concentration of EDTA=0.610 mM
Concentration of nickel(II)-IDA chelate=8.63 mM
Total concentration of IDA=27.4 mM

B : Ni(II)-IDA-CyDTA system
Initial concentration of CyDTA=0.610 mM
Concentration of nickel(II)-IDA chelate=10.24 mM
Total concentration of IDA=27.4 mM

C : Co(II)-NTA-CyDTA system
Initial concentration of CyDTA=0.610 mM
Concentration of cobalt(II)-NTA chelate=9.15 mM
Total concentration of NTA=27.4 mM

centration of CyDTA or EDTA, the plot of slope $\times(\alpha_H)_Z$ *vs.* $[H^+]$ gave a linear relation (Fig. 2). Here, $(\alpha_H)_Z$ is the (α_H) value of CyDTA or EDTA.

From the above experimental facts and discussion, it can be safely concluded that all the three exchange reactions proceed mainly through the following two simultaneous reaction pathways:

$$\begin{array}{ll} \text{i)} & MX^{2-m} + Z^{4-} \overset{k_1^+}{\rightleftarrows} MZ^{2-} + X^{m-} \\ & \quad\big\updownarrow \text{rapid} \\ & MX_2{}^{2-2m} \\ \text{ii)} & MX^{2-m} + HZ^{3-} \overset{k_2^+}{\rightleftarrows} MZ^{2-} + HX^{1-m} \\ & \quad\big\updownarrow \text{rapid} \\ & MX_2{}^{2-2m} \end{array}$$

where MX^{2-m} and MX_2^{2-2m} mean the metal (II)-IDA or -NTA chelates with 1-to-1 and 1-to-2 compositions respectively; X^{m-}, the completley-deprotonated IDA or NTA anion, and Z^{4-}, the completely-deprotonated CyDTA or EDTA anion. On the basis of the above reaction mechanism, the slope of the linear relation between $-\log i_t$ and t can be expressed as:

$$\text{slope} = \frac{1}{2.303}\left(k_1{}^+ + \frac{k_2{}^+\cdot[H]^+}{k_4}\right) \times \frac{[MX]_t}{(\alpha_H)_Z\left[1+\dfrac{K^X_{MX_2}\cdot[X]_f}{(\alpha_H)_X}\right]} \qquad (1)$$

where k_4 is the fourth dissociation constant of CyDTA or EDTA.

The $k_1{}^+$ and $k_2{}^+$ values determined from the slope and the intercept of the linear relation between slope $\times$ 2.303 $\times$ $(\alpha_H)_Z[1+K^X_{MX_2}[X]_f/(\alpha_H)_X]/[MX]_t$ and $[H^+]$ are given in Table 3. Similar results were also obtained in the experiments carried out at the other two temperatures. The rate constants for the two elementary reactions determined at the other two temperatures are also listed in Table 3. In all cases, linear relations were found between $\log k_i{}^+$ and $1/T$ for both elementary reactions; these made it possible to calculate the heats and entropies of activation. The heats and the entropies of activation determined from the linear

TABLE 3. RATE CONSTANTS, HEAT OF ACTIVATION AND ENTROPY OF ACTIVATION FOR REACTIONS (i) AND (ii)

1) Nickel(II)-IDA-EDTA reaction

k^+ value M^{-1} sec^{-1}	Temperature, °C 18	25	33	$\Delta H^{\neq}$ kcal	$\Delta S^{\neq}$ e.u.
k_1^+	1.5×10^4	2.1×10^4	4.5×10^4	8.4	−10.4
k_2^+	3.35×10^3	7.33×10^3	1.38×10^4	13.9	5.6

2) Nickel(II)-IDA-CyDTA reaction

k^+ value M^{-1} sec^{-1}	Temperature, °C 18	25	33	$\Delta H^{\neq}$ kcal	$\Delta S^{\neq}$ e.u.
k_1^+	9.0×10^3	1.7×10^4	4.1×10^4	16.6	16.9
k_2^+	1.86×10^2	3.33×10^2	7.48×10^2	16.1	7.5

3) Cobalt(II)-NTA-CyDTA reaction

k^+ value M^{-1} sec^{-1}	Temperature, °C 18	25	33	$\Delta H^{\neq}$ kcal	$\Delta S^{\neq}$ e.u.
k_1^+	3.4×10^1	6.5×10^1	1.55×10^2	15.5	3.4
k_2^+	1.33×10^{-1}	3.42×10^{-1}	6.50×10^{-1}	20.6	5.2

TABLE 4. NUMERICAL VALUES*

1) pK values (mixed constants)[11]

	pK_1	pK_2	pK_3	pK_4
IDA	—	9.34		
NTA	—	—	9.60	
EDTA	—	—	6.03	10.00
CyDTA	—	—	5.99	11.42

2) log $K^X_{MX_2}$ values[11]

	log $K^X_{MX_2}$
Ni(II)-IDA chelate	6.35
Co(II)-NTA chelate	3.63

* These values are calculated from the related constants in solutions of ionic strength 0.10 and the activity coefficients of the ions calculated by means of Davies equation.[12]

relation between log k_i^+ and $1/T$ are also given in Table 3. The numerical values used in the calculation of (α_H)'s, $[X]_f$, and k_2^+ are listed in Table 4. The way of calculating $[X]_f$ was given in previous paper.[3]

As is shown in Table 3, both elementary reactions gave positive entropies of activation in the substitution reactions involving CyDTA. In the NMR study of the conformation of the CyDTA anion, Reilley *et al.*[5,6] concluded that, in tervalent and quadrivalent CyDTA anions, two iminodiacetate groups occupy nearly diequatorial positions on the cyclohexane ring because of the steric effect of the cyclohexane ring. The preorientation of the CyDTA anion by the cyclohexane ring probably places the CyDTA anion in a favorable position to react with metal ion. Thus, less conformational and rotational freedom will be lost in the chelate formation reaction of CyDTA. This prediction has been confirmed by several authors[7–9] in their thermodynamic study of the chelate formation reaction. The entropies of the reaction of CyDTA chelates are always greater than those of the corresponding EDTA chelates. The experimental evidence that, in the substitution reactions involving CyDTA, both elementary reactions gave positive entropies of activation may also be ascribed to the preorientated diequatorial conformation of the CyDTA anion. Thus, these facts support the present author's explanation of the effect of the protonation of the CyDTA anion on the heat of activation given in a previous paper.[1] The positive entropy of activation for the elementary reaction (ii) in the reaction of EDTA with the nickel(II)-IDA chelate can also be attributed to the conformation of the tervalent EDTA anion, which is similar to that of the chelated EDTA anion.[6]

Finally, it can also be mentioned that the k_2^+ value for the reaction of EDTA with the nickel(II)-IDA chelate is about 1000 times greater than that with the nickel(II)-NTA chelate.[10] The k_2^+ ratio between the nickel(II)-IDA and nickel(II)-NTA systems agrees well with the ratio of the stability constants of the chelates with the 1-to-1 composition.[11] This agreement probably means that the reaction of EDTA with nickel(II)-IDA proceeds through the same reaction intermediate as that for the reaction with the nickel(II)-NTA chelate.

The present author wishes to express his hearty thanks to Mr. Tomohiko Noda and Miss Yayoe Tominaga for their help during this research.

---

[5] J. L. Sudmeier and C. N. Reilley, *Anal. Chem.*, **36**, 1707 (1964).

[6] Y. Fujiwara and C. N. Reilley, *ibid.*, **40**, 890 (1968).

[7] D. L. Wright, J. H. Holloway and C. N. Reilley, *ibid.*, **37**, 883 (1965).

[8] G. Anderegg, *Helv. Chim. Acta*, **46**, 1833 (1963).

[9] T. Moeller and T. M. Hseu, *J. Inorg. Nucl. Chem.*, **24**, 1635 (1962).

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

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

[12] J. N. Butler, "Ionic Equilibrium," Addison-Wesley Publishing Co., Reading, Massachusetts (1964), p. 437.