expected to be stronger in the hydroxy species than in the aquo species because of the negative charge of the hydroxy ligand. In either a D or an I_d mechanism, the strength of this iron–oxygen bond would affect the rate of dissociation of the pentacyanoaquoferrate(II) ion.

A study[9] of $\Delta V^{\ddagger}$ for the reaction of $Fe(CN)_5X^{3-} + Y$ has resulted in the conclusion that the reaction proceeds by a D mechanism. Correlations of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ in an isokinetic plot (line B in Figure 7) are consistent with this mechanism for other reactions of closely related pentacyanoferrate(II) complexes with nitrogen- and sulfur-donor ligands. It is of interest, however, that for comparable reactions of both the aquo and hydroxy complexes, the values of $\Delta H^{\ddagger}$ are significantly lower (by ~5–6 kcal mol^{-1}) and lie on a separate line (A in Figure 7), in an isokinetic plot. One interpretation of this finding is that there is a change in mechanism from a D to an I_d process in the case of these oxygen donors. The I_d mechanism has been postulated[22] for dissociation reactions of $Fe(CN)_5X^{3-}$ especially in the case where X is H_2O.

Acknowledgment. D.H.M. wishes to thank the University of Victoria for a Graduate Fellowship. Assistance from the National Research Council of Canada is also acknowledged.

Registry No. Sodium pentacyanoammineferrate(II), 14099-05-9; TU, 62-56-6; ATU, 109-57-9; DMTU, 534-13-4; $Fe(CN)_5OH_2^{3-}$, 18497-51-3; $Fe(CN)_5OH^{4-}$, 42859-22-3; $HFe(CN)_5OH^{2-}$, 70912-43-5.

Supplementary Material Available: A more complete table of kinetic data (5 pages). Ordering information is given on any current masthead page.

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Kinetics of Complexing of a Tridendate Nickel(II) Complex by Histidine Derivatives and Glycine

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The kinetics of complexing of the nickel(II) tridendate Schiff-base complex triaquo(tribenzo[b,f,j][1,5,9]triazacyclododecine)nickel(II) {(TRI)Ni$(OH_2)_3^{2+}$} by histidine, 3-methylhistidine, histamine, histidine methyl ester, and glycine have been studied. For the first three ligands the observed pseudo-first-order rate constant is given by $k_{expt} = \{A[\text{total ligand}]/(K_a + (H^+)) + B(H^+)\}/(C(H^+) + 1)$. This is shown to be consistent with the mechanism

$$Ni + HL \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} Ni{-}LH \underset{k_{32}(H^+)}{\overset{k_{23}}{\rightleftharpoons}} Ni{-}L \underset{k_{53}}{\overset{k_{35}}{\rightleftharpoons}} Ni{=}L$$

with $A = k_{12}K_{a_1}$, $B = k_{21}k_{53}/k_{35}K_{23}$, and $C = k_{21}/k_{35}K_{23}$ where $K_{23} = k_{23}(H^+)/k_{32}$. Further work shows that the $Ni(OH_2)_6^{2+}$–histidine system conforms to the same rate law. The rate law with the other ligands is found to be simpler, and analysis indicates this is the case because of the higher acidity of the ester and unfavorable equilibrium for complexing of the carboxylate group for glycine.

The reactions of monodendate ligands with hexaaquonickel(II) are thought generally to proceed by a dissociative ion-pair mechanism.[1,2] This information can be used to elucidate the details of reaction pathways for complexing by multidendate ligands such as the amino acids. For this family of ligands earlier work[2] had assumed that initial bond formation between the amino acid and metal ion was rate limiting and concluded that only the anionic form of an α-amino acid is reactive. A recent reanalysis[3] has shown that the kinetics are equally consistent with a reaction scheme which essentially involves monodendate intermediate complex formation in a rapid preequilibrium, followed by rate-controlling chelate ring closure. It has been shown[4] that with two pyridine-2-carboxylic acids the mechanism changes rate-controlling steps as the pH changes from 2.5 to 6.5. In addition, the variation in rate constant for various α-amino acid–$Ni(OH_2)_6^{2+}$ systems can be explained in terms of steric effects on dissociation of the monodendate intermediate.[4]

The present work was designed to further explore the reaction pathways and reactivities of amino acid–nickel(II) systems by studying a tridendate Schiff-base complex of nickel(II) [(TRI)Ni$(OH_2)_3^{2+}$, Figure 1] reacting with histidine and its derivatives. The TRI complex was chosen for several reasons: (i) it exists as two resolvable, stable optical isomers so that stereoselectivity can be studied; (ii) its water-exchange rate[5] is almost the same as that of $Ni(OH_2)_6^{2+}$, so that a dissociative mechanism should yield similar rates for the two systems, and differences will reflect steric effects of the (TRI) ligand and probability effects because there are half the reactive sites present compared with $Ni(OH_2)_6^{2+}$.

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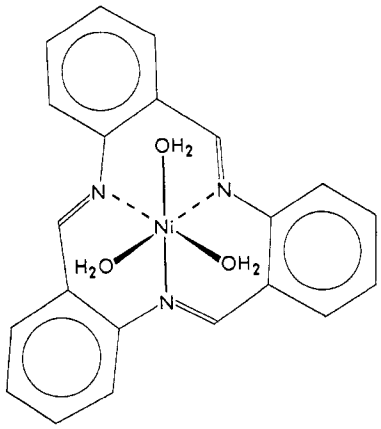


Figure 1. Structure of $(TRI)Ni(OH_2)_3^{2+}$.

The $(TRI)Ni(OH_2)_3^{2+}$ system presents some practical advantages as well. It is a strong chromophore in the near-ultraviolet region so that the reaction can be studied directly as well as by the usual indicator method. Since TRI is not displaced by histidine, the reaction can be studied under pseudo-first-order conditions in the ligand concentration without the problem of bis-complex formation.

Although the aspects listed above have provided interesting scope for analyses, the major result of this work came as an initially unpleasant surprise. The pH dependence of the rate coefficients was more complex than that previously observed with $Ni(OH_2)_6^{2+}$–histidine and analogous systems.[2,5-7] The explanation of this complexity provides a further indication that chelate ring closing is rate controlling in some cases and has added new information on the kinetics of chelate formation.

Experimental Section

Materials. The nickel complex triaquo(tribenzo[*b,f,j*][1,5,9]-triazacycloduodecine)nickel(II) nitrate, commonly designated as $(TRI)Ni(OH_2)_3(NO_3)_2$, was prepared as described by Taylor, Vergez and Busch.[8] The perchlorate salt was prepared by dissolving 1.5 g of the nitrate in 100 mL of warm water, adding 10 mL of 3 M $NaClO_4$, and cooling the solution in ice for several hours. The product was recrystallized analogously, collected by filtration, washed with cold water, and dried in vacuo over calcium sulfate. Anal. Calcd for $(TRI)Ni(OH_2)_3(ClO_4)_2$: C, 40.62; H, 3.41; N, 6.78. Found: C, 40.75; H, 2.79; N, 6.85.

The electronic spectrum of $(TRI)Ni(OH_2)_3^{2+}$ in 0.01 M $HClO_4$ shows maxima (with molar absorption coefficients in parentheses) at 315 (1.18×10^4 dm^3 mol^{-1} cm^{-1}) and 275 nm (4.10×10^4 dm^3 mol^{-1} cm^{-1}) in good agreement with previous results.[9] Solutions of $(TRI)Ni(OH_2)_3^{2+}$ showed no change in electronic spectrum at pH ≤ 7 over periods of at least 3 days.

The ligands D-histidine, DL-histidine, and L-3-methylhistidine[10] were used as supplied by Sigma Chemical Co. The L-histidine (Nutritional Biochemicals Corp.) was recrystallized from 50% aqueous ethanol and dried in vacuo over $CaSO_4$. Anal. Calcd for $C_6H_9N_3O_2$: C, 46.5; H, 5.81; N, 27.1. Found: C, 46.9; H, 5.83; N, 27.5. Histamine was used as supplied (Matheson Coleman and Bell) after drying in vacuo over calcium sulfate. Anal. Calcd for $C_5H_8N_3$: C, 54.0; H, 8.11; N, 37.8. Found: C, 53.4; H, 8.07; N, 38.2.

The L-histidine methyl ester dihydrochloride (Aldrich) was used as supplied. Anal. Calcd for $C_7H_{13}N_3O_2Cl_2$: C, 34.7; H, 5.41; N, 17.4. Found: C, 34.4; H, 5.32; N, 17.4. Samples for kinetic runs were converted to the perchlorate salt by treatment with the appropriate amount of silver perchlorate. The AgCl was separated from the solution by centrifugation.

Buffer solutions of MES (2,2-(*N*-morpholino)ethanesulfonic acid)) and PIPES (1,4-piperazinebis(ethanesulfonic acid)) were prepared from products as supplied (Polysciences). Stock solutions (5×10^{-4} M) of bromothymol blue and bromocresol purple (Matheson Coleman and Bell) were prepared by dissolving the commercial product in water containing an equivalent amount of sodium hydroxide. Solutions of lithium perchlorate, perchloric acid, and sodium hydroxide were standardized by standard methods, and all solutions for kinetic studies were prepared in doubly distilled deionized water.

Kinetic Measurements. An Aminco-Morrow stopped-flow system described previously[4,7] was used. The transmittance–time curves were recorded photographically, digitalized manually, and analyzed by least-squares methods after conversion of transmittance to absorbance. The reaction was followed at 620 nm (bromothymol blue), at 590 nm (bromocresol purple) or at 275 nm with no indicator added. Blank experiments with indicator in both drive syringes showed no transmittance change unless $(TRI)Ni(OH_2)_3^{2+}$ and the desired ligand were mixed in the stopped-flow apparatus.

Table I. Kinetic Results for the Reaction of $(TRI)Ni(OH_2)_3^{2+}$ with Histidine[a]

pH	$10^4 \times$ [histidine], M	k_{exptl}, s^{-1} obsd	k_{exptl}, s^{-1} calcd[b]	conditions[c]
5.55	33.3	0.601 ± 0.04	0.613	iv, vi
5.56	30.5	0.690 ± 0.02	0.598	ii, vi
5.56	31.5	0.788 ± 0.02	0.607	i, vi
5.56	23.3	0.460 ± 0.02	0.530	i, vi
5.84	23.3	0.923 ± 0.04	0.879	i, vi
5.87	33.3	1.21 ± 0.08	1.22	i, vi
5.87	38.6	1.38 ± 0.06	1.37	i, vi
5.87	47.2	1.63 ± 0.04	1.62	i, vi
5.89	75.3	2.30 ± 0.2	2.56	i, vi
6.00	10.3	0.613 ± 0.05	0.695	i, vii
6.15	3.03	0.362 ± 0.01	0.424	iii, viii
6.15	23.3	1.70 ± 0.12	1.75	i, vi
6.16	30.3	2.27 ± 0.09	2.26	iii, viii
6.16	9.95	0.824 ± 0.05	0.893	iii, viii
6.17	4.97	0.490 ± 0.05	0.564	iii, viii
6.18	49.9	3.94 ± 0.1	3.75	iii, viii
6.18	33.3	2.35 ± 0.1	2.58	i, vi
6.20	10.3	1.00 ± 0.04	0.983	i, vii
6.20	9.59	0.954 ± 0.07	0.930	i, vii
6.21	30.5	2.71 ± 0.1	2.54	iv, vii
6.21	31.5	2.96 ± 0.1	2.62	ii, vii
6.28	9.47	1.19 ± 0.09	1.05	v, vii
6.32	5.15	0.610 ± 0.05	0.699	iii, viii
6.46	9.47	1.47 ± 0.09	1.40	v, vii
6.60	5.15	0.910 ± 0.03	0.983	iii, viii
6.60	5.48	0.920 ± 0.05	1.04	iii, viii
6.70	9.59	2.00 ± 0.1	1.93	i, vii
6.77	9.36	1.82 ± 0.03	2.03	iii, vii
6.79	18.7	3.53 ± 0.10	4.03	iii, vii
6.80	5.48	1.14 ± 0.05	1.26	iii, viii
6.91	9.40	2.48 ± 0.2	2.31	i, vii
6.94	9.59	2.59 ± 0.1	2.40	v, vii
7.01	9.59	2.60 ± 0.2	2.53	v, vii
7.10	9.40	2.58 ± 0.1	2.62	i, vii
7.11	9.71	2.85 ± 0.2	2.71	v, vii
7.21	9.71	2.90 ± 0.2	2.85	v, vii
7.21	9.71	2.97 ± 0.2	2.74	v, vii

[a] At 25 °C and $I = 0.30$ M ($LiClO_4$). The k_{exptl} reported is the average of ten runs, and error limits are 1 standard deviation. The results are quoted to one extra figure as they were used in least-squares analysis to avoid round-off problems. The $[(TRI)Ni(OH_2)_3(ClO_4)_2]$ was $<< 0.1 \times$ [histidine] and was in the range $(0.5\text{-}3.0) \times 10^{-4}$ M. [b] Calculated from a least-squares fit to eq 7. [c] Key: i, racemic $(TRI)Ni(OH_2)_3^{2+}$ and L-histidine; ii, $(+)_{436}$-$(TRI)Ni(OH_2)_3^{2+}$ and L-histidine; iii, $(-)_{436}$-$(TRI)Ni(OH_2)_3^{2+}$ and L-histidine; iv, $(+)_{436}$-$(TRI)Ni(OH_2)_3^{2+}$ and D-histidine; v, racemic $(TRI)Ni(OH_2)_3^{2+}$ and racemic histidine; vi, bromocresol purple indicator, 2.5×10^{-5} M; vii, bromothymol blue indicator, 2.5×10^{-5} M; vii, bromothymol blue indicator, 2.5×10^{-5} M; viii, direct observation at 275 nm.

Results and Analysis

Histidine and $(TRI)Ni(OH_2)_3^{2+}$. The kinetics of this reaction have been studied at pH 5.5–7.2, with histidine in excess at concentrations of $(3\text{–}75) \times 10^{-4}$ M. The results are given in Table I, where k_{exptl} is the experimental pseudo-first-order rate constant.

A preliminary examination of runs under very similar concentration conditions indicates that k_{exptl} is independent of the experimental method. Similarly, it appears that k_{exptl}

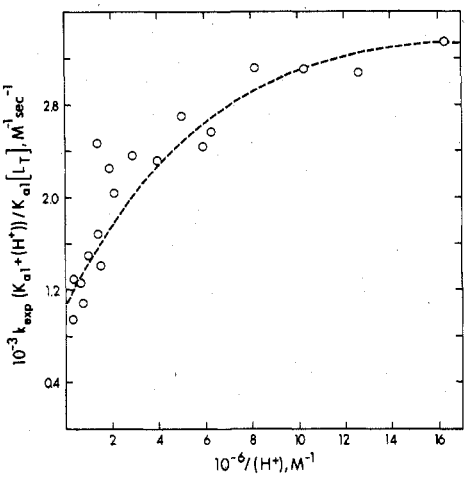


Figure 2. Variation of $k_{exptl}(K_{a_1} + (H^+))/K_{a_1}[L_T]$ with $(H^+)^{-1}$ for $(TRI)Ni(OH_2)_3^{2+}$ + histidine at 25 °C in 0.3 M $LiClO_4$. About half the data are plotted, and the line drawn is an eye-guide only.

is independent, within experimental uncertainty, of the ligand or metal complex stereoisomer used, as can be seen from results at about pH 5.6, 6.15, and 6.21 in Table I. This failure to detect kinetic stereoselectivity was disappointing since it has been found that histidine can be used to resolve $(TRI)Ni(OH_2)_3^{2+}$.[11]

In previous studies[2,5,6,7] on the reaction of histidine and its derivatives with $Ni(OH_2)_6^{2+}$ it was found that the results were consistent with the simple reaction scheme in eq 1.

$$\begin{array}{ccc} & H_2L^+ & \\ & \uparrow\downarrow & \\ H^+ + HL + Ni^{2+} & \overset{k_1}{\rightleftharpoons} & NiL^+ + H^+ \\ & \uparrow\downarrow & \\ H^+ + L^- + Ni^{2+} & \overset{k_0}{\rightleftharpoons} & NiL^+ \end{array} \qquad (1)$$

The pseudo-first-order rate constant for this reaction scheme is[7] given in eq 2, where $[L_T] \equiv [H_2L^+] + [HL] + [L^-]$. Since

$$k_{exptl} = \frac{k_1K_{a_1}(H^+) + k_0K_{a_1}K_{a_2}}{(H^+)^2 + K_{a_1}(H^+) + K_{a_1}K_{a_2}}[L_T] \qquad (2)$$

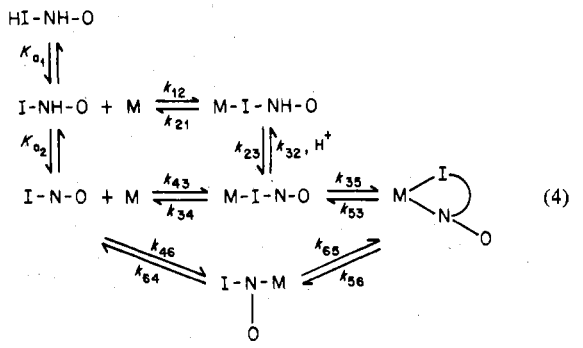
$K_{a_2} \ll (H^+)$ for histidine under the conditions of this study, then eq 2 predicts that a plot of $k_{exptl}(K_{a_1} + (H^+))/K_{a_1}[L_T]$ vs. $(H^+)^{-1}$ should be linear. Such a plot is shown in Figure 2 for the reaction of $(TRI)Ni(OH_2)_3^{2+}$ with histidine. The plot is clearly not linear, and the reaction scheme in eq 1 does not describe the results presented here.

The simplest rate law which has been found to be consistent with the histidine results is given in eq 3. The values of A, B, and C determined by a nonlinear least-squares analysis are $(2.39 \pm 0.07) \times 10^{-3}$ M^{-1} s^{-1}, $(8.5 \pm 2.1) \times 10^5$ M^{-1} s^{-1}, and $(2.4 \pm 0.2) \times 10^6$ M^{-1}, respectively.[12]

$$k_{exptl} = \frac{\dfrac{A[L_T]}{K_{a_1} + (H^+)} + B(H^+)}{C(H^+) + 1} \qquad (3)$$

This rate law is consistent with the reaction scheme in eq 4 where the imidazole, amino, and carboxylate functions of histidine are represented by I–N–O.

The rate law for this scheme has been developed by the method used previously for the slightly simpler scheme in which the k_{46} path was omitted. The rate constants for proton transfer (k_{23}, k_{32}) are defined as before[13] and are related to the acid dissociation constant K_{23} by $K_{23} = k_{23}(H^+)/k_{32}$. After due consideration of the probable rates of proton transfer[13,14] and substitution[3,15] it was found that the general solution simplifies to eq 5, where K_f is the formation constant for the complex and $K_f = k_{43}k_{35}/k_{34}k_{53}$.



(4)

$$k_{exptl} = \left(\frac{k_{12}(H^+) + (k_{43} + k_{46})K_{a_2}}{(k_{21}(H^+)/k_{35}K_{23}) + 1}\right) \times \left(\frac{K_{a_1}[L_T]}{K_{a_1}K_{a_2} + K_{a_1}(H^+) + (H^+)^2} + \frac{1}{K_fK_{a_2}}\right) \qquad (5)$$

In the case of histidine $K_{a_2} \ll (H^+)$ so that eq 5 reduces to eq 3 if $k_{12}(H^+) \gg (k_{43} + k_{46})K_{a_2}$. Then $A = k_{12}K_{a_1}$, $B = k_{12}/K_fK_{a_2}$, and $C = k_{21}/k_{35}K_{23}$. The application of detailed balancing to eq 4 shows that

$$C = \left(\frac{k_{12}}{K_{a_2}}\right)\left(\frac{k_{34}}{k_{43}k_{35}}\right) \qquad B/C = k_{53} \qquad (6)$$

and the kinetic results can be used to evaluate $k_{12} = 3.6 \times 10^3$ M^{-1} s^{-1}, $k_{43}k_{35}/k_{34} = 2.5 \times 10^6$ M^{-1} s^{-1}, $k_{53} = 0.35$ s^{-1}, and $K_f = 7 \times 10^6$ M^{-1}.

3-Methylhistidine and $(TRI)Ni(OH_2)_3^{2+}$. This system has been studied at 18 ligand concentrations between 9.2×10^{-4} and 68×10^{-4} M and at $(TRI)Ni(OH_2)_3^{2+}$ concentrations between 0.8×10^{-4} and 2×10^{-4} M over the pH range 5.6–7.0. The results are given in Table IB[16] and are compared to values calculated from a least-squares fit to eq 3. The values of A, B, and C are $(6.5 \pm 0.5) \times 10^{-3}$ s^{-1}, $(1.0 \pm 0.35) \times 10^6$ M^{-1} s^{-1}, and $(2.4 \pm 0.45) \times 10^6$ M^{-1}, respectively. Analysis in terms of eq 4, 5, and 6 gives $k_{12} = 4 \times 10^3$ M^{-1} s^{-1}, $k_{43}k_{35}/k_{34} = 4.2 \times 10^6$ M^{-1} s^{-1}, $k_{53} = 0.53$ s^{-1}, and $K_f = 8.0 \times 10^6$ M^{-1}.

Histamine and $(TRI)Ni(OH_2)_3^{2+}$. In the pH range 5.8–6.9, 24 ligand concentrations were studied between 2.14×10^{-3} and 8.25×10^{-3} M. The results are given in Table IC.[16] The least-squares best-fit parameters to eq 3 are $A = 0.88 \times 10^{-3}$ s^{-1}, $B = (10.4 \pm 0.4) \times 10^6$ M^{-1} s^{-1}, and $C = (9.6 \pm 0.4) \times 10^6$ M^{-1}. The values of k_{12}, $k_{43}k_{35}/k_{34}$, k_{53}, and K_f are 1.4×10^3 M^{-1} s^{-1}, 1.4×10^6 M^{-1} s^{-1}, 1 s^{-1}, and 1.4×10^6 M^{-1}, respectively.

Histidine Methyl Ester and $(TRI)Ni(OH_2)_3^{2+}$. This system was studied in the pH range 5.25–6.87 at ligand concentrations of $(1.04–6.29) \times 10^{-3}$ M. The results are given in Table ID.[16]

The rate law for this system is consistent with eq 5 if $k_{21}(H^+)/k_{35}K_{23} \ll 1$. This difference from histidine and histamine is easily understood when it is realized that the amino group of the ester is more acidic ($pK_{a_2} = 7.36$) than that of histidine ($pK_{a_2} = 9.22$) or histamine ($pK_{a_2} = 9.97$). Since K_{23} should parallel K_{a_2}, the larger K_{23} with the ester makes $k_{21}(H^+)/k_{35}K_{23}$ about 10^2 times smaller. This factor also makes the $(k_{43} + k_{46})K_{a_2}$ term in the numerator of eq 5 of the same magnitude as $k_{21}(H^+)$.

A nonlinear least-squares analysis of the appropriately modified form of eq 5 yields $k_{12} = (1.30 \pm 0.04) \times 10^3$ M^{-1} s^{-1}, $k_{43} + k_{46} = (5.05 \pm 0.27) \times 10^3$ M^{-1} s^{-1}, and $K_f = (5.6 \pm 4) \times 10^5$ M^{-1}.

Histidine and $Ni(OH_2)_6^{2+}$. It was of some concern that the rate law found here for histidine + $(TRI)Ni(OH_2)_3^{2+}$ was more complex than that observed in two previous studies[6,7] with

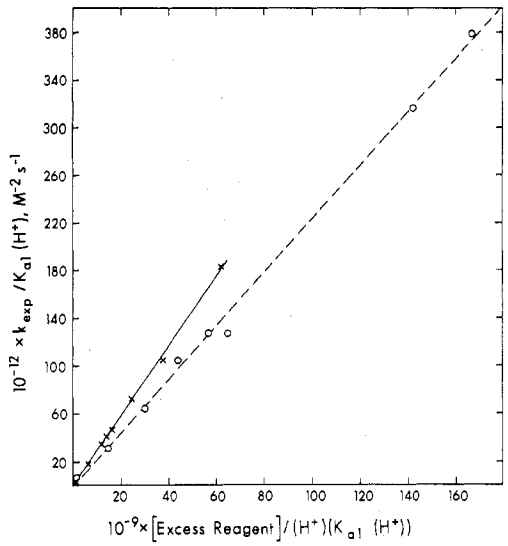


Figure 3. Variation of $k_{exptl}/K_{a_1}(H^+)$ with [excess reagent]/$(H^+)(K_{a_1} + (H^+))$ for $Ni(OH_2)_6^{2+}$ and histidine: (×) this study, histidine in excess, 25 °C, 0.3 M $LiClO_4$; (○) ref 9, $Ni(OH_2)_6^{2+}$ in excess, 23.7 °C, 0.1 M KNO_3. Several points near the origin from this study have been omitted for clarity, but full results are given in Table II.

Table II. Kinetic Results for the Reaction of $Ni(OH_2)_6^{2+}$ with Histidine[a]

pH	10^{-3} × [histidine], M	k_{exptl}, s^{-1} obsd	calcd[b] eq 7	calcd[b] eq 5
5.88[c]	0.948	0.639 ± 0.04	0.836	0.637
6.08[c]	0.948	0.963 ± 0.04	1.10	0.965
6.31[c]	0.948	1.36 ± 0.05	1.42	1.40
6.52	1.90	3.75 ± 0.1	3.39	3.57
6.53	4.74	8.99 ± 0.5	8.51	8.99
6.73	1.93	4.35 ± 0.1	3.91	4.31
6.78	1.90	4.44 ± 0.2	3.94	4.38
6.81	4.74	10.8 ± 0.6	9.96	11.1
6.99	1.90	4.85 ± 0.2	4.27	4.87
7.00	4.74	12.1 ± 0.4	10.7	12.2

[a] At 25 °C and I = 0.30 M ($LiClO_4$). The value of k_{exptl} is the average of at least ten runs, and error limits are 1 standard deviation. The reagents are L-histidine, $Ni(OH_2)_6(ClO_4)_2$ (8×10^{-5} M), bromothymol blue indicator (1.3×10^{-5} M), and PIPES buffer (2×10^{-3} M) unless otherwise indicated. [b] Obtained from least-squares fit to the equation from the text as noted, with K_f, K_{a_1}, and K_{a_2} values of 4.7×10^8 M^{-1}, 6.6×10^{-7} M, and 6.0×10^{-10} M, respectively. For eq 7 $k_{12}K_{a_1} = 2.04 \times 10^{-3}$ s^{-1}, and parameters for eq 3 are given in the text. [c] MES buffer (2×10^{-3} M).

$Ni(OH_2)_6^{2+}$. An examination of the earlier work indicated that there could have been insufficient data at low enough pH to clearly show the $k_{21}(H^+)/k_{35}K_{23}$ term in eq 5. In order to extend the earlier work to lower pH while maintaining ionic strength and obtaining significant complexing it was necessary to work with [histidine] ≫ $[Ni(OH_2)_6^{2+}]$. It is recognized that this adds the complication of bis(histidine) complex formation; however, it is believed that this is not a problem because no biphasic behavior was observed, and the results are in reasonable agreement with an earlier study,[7] considering differences in temperature and ionic strength.

The rate law used previously[6,7] for the $Ni(OH_2)_6^{2+}$–histidine system can be derived from eq 5, if, as above, $K_{a_2} \ll (H^+)$, $(k_{43} + k_{46})K_{a_2} \ll k_{12}(H^+)$, and, in addition, $k_{21}(H^+)/k_{35}K_{23} \ll 1$. Then eq 5 simplifies to eq 7. The kinetic results are

$$k_{exptl} = \frac{k_{12}K_{a_1}[L_T]}{K_{a_1} + (H^+)} + \frac{k_{12}K_{a_1}(H^+)}{K_f K_{a_1} K_{a_2}} \qquad (7)$$

Table III. Kinetic Results for the Reaction of $(TRI)Ni(OH_2)_3^{2+}$ with Glycine[a]

pH	10^2 [glycine], M	k_{exptl}, s^{-1} obsd	calcd[b]
6.20	10.0	0.634 ± 0.03	0.569
6.20	7.0	0.454 ± 0.01	0.413
6.21	7.38	0.457 ± 0.01	0.442
6.21	3.00	0.221 ± 0.02	0.205
6.22	5.87	0.394 ± 0.02	0.367
6.23	3.03	0.217 ± 0.01	0.215
6.42	3.00	0.315 ± 0.03	0.306
6.61	3.00	0.465 ± 0.01	0.450
6.71[c]	3.00	0.533 ± 0.05	0.555
6.86[c]	1.00	0.234 ± 0.01	0.284
6.86[c]	3.00	0.749 ± 0.04	0.767
6.98[c]	1.00	0.355 ± 0.02	0.361
7.00[c]	3.00	0.984 ± 0.03	1.04

[a] At 25 °C and I = 0.30 M ($LiClO_4$). Each k_{exptl} reported is the average of at least eight runs, and error limits are 1 standard deviation. The reagents were racemic $(TRI)Ni(OH_2)_3^{2+}$ (2.0×10^{-4} M), bromothymol blue (2.5×10^{-5} M), and MES buffer (4.0×10^{-3} M) unless otherwise stated. [b] Calculated from a least-squares fit to eq 21. [c] PIPES buffer (4.0×10^{-3} M).

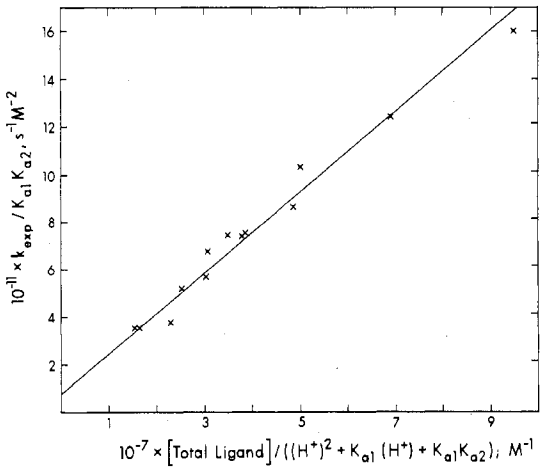


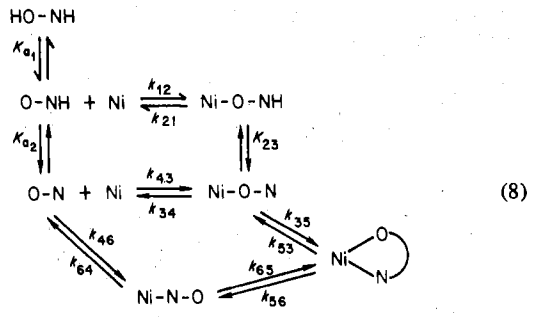
Figure 4. Variation of $k_{exptl}/K_{a_1}K_{a_2}$ with [total ligand]/$((H^+)^2 + K_{a_1}(H^+) + K_{a_1}K_{a_2})$ for glycine.

given in Table II and plotted in Figure 3 in a way which should produce a straight line according to eq 7. In fact the plot appears linear, but it has obscured significant deviations at low pH as can be seen from a comparison of the fitted (to eq 7) and experimental values in Table II. On the other hand the data are well fitted by eq 5 with the previous assumption that $(k_{43} + k_{46})K_{a_2} \ll k_{12}(H^+)$, with the known value of $K_f = 4.7 \times 10^8$ M^{-1}.[17] The observed and calculated values are compared in Table II, and the least-squares fit gives $k_{12}K_{a_1} = (2.04 \pm 0.08) \times 10^{-3}$ s^{-1} and $k_{21}/k_{35}K_{23} = (4.25 \pm 0.9) \times 10^5$ M^{-1}. These values can be used to calculate $k_{12} = 3.1 \times 10^3$ M^{-1} s^{-1}, $k_{43}k_{35}/k_{34} = 1.2 \times 10^7$ M^{-1} s^{-1}, and $k_{53} = 0.025$ s^{-1}.

Glycine and $(TRI)Ni(OH_2)_3^{2+}$. The kinetic results for this system are given in Table III. The pH dependence of k_{exptl} is essentially consistent with eq 2 if $k_1 = 0$, as shown by the appropriate plot in Figure 4. The only inconsistency is that the plot has a positive intercept while eq 2 predicts a zero intercept, but this can be accounted for if the reaction is reversible as shown in the analysis below.

If glycine is represented by HO–NH, O–NH, and O–N for the cation, zwitterion, and anion forms, respectively, then a reasonable reaction scheme is given in eq 8, where $K_{23} = k_{23}(H^+)/k_{32}$ as in eq 4.

This scheme was analyzed by assuming a steady state for the mondendate intermediates in the same way that eq 4 was



(8)

analyzed.[3] The systems are different, however, in that results on the dissociation rates of substituted acetate ligands[18] indicate that $k_{21} > k_{23}$. Further considerations show that $k_{32} \gg k_{34}$ and k_{35} and that $k_{64} \gg k_{46}$. With these conditions, and noting that $k_{12}K_{23}/k_{21} = k_{43}K_{a_2}/k_{34}$, it is found that

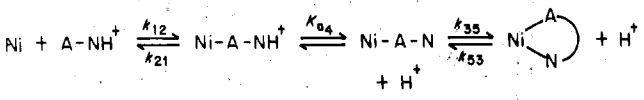
$$k_{\text{exptl}} = \left(\frac{k_{43}k_{35}}{k_{34}} + k_{46}\right)\left(\frac{K_{a_1}K_{a_2}[L_T]}{(H^+)^2 + K_{a_1}(H^+) + K_{a_1}K_{a_2}} + \frac{1}{K_f}\right) \quad (9)$$

A least-squares fit of the results to eq 9 gives $((k_{43}k_{35}/k_{34}) + k_{46}) = (1.71 \pm 0.15) \times 10^4\ M^{-1}\ s^{-1}$ and $K_f = (4.0 \pm 0.7) \times 10^5\ M^{-1}$. The observed and calculated values are compared in Table III.

It cannot be decided with certainty which component is dominant in the first term in eq 9. However, it seems reasonable that $k_{43} > k_{46}$ because of the negative charge on the carboxylate group. Results with picolinic acid[4] indicate that $k_{35} \approx k_{34}$, so that probably $(k_{43}k_{35}/k_{34}) > k_{46}$. If this is the case, then one can calculate that $k_{53} \approx 0.043\ s^{-1}$.

Discussion

The variety of rate laws and rate constants which have been determined from the different systems studied here can be rationalized in a straightforward way. All of the ligands studied have as the dominant species the general form A–NH, where A is an imidazole nitrogen for all the histidine derivatives and a carboxylate oxygen for glycine. The general mechanism can be formulated as



If one assumes a dissociative ion-pair mechanism for ligand complexing, then k_{12} and k_{35} will be controlled by the rate of water exchange from the metal ion, with k_{12} somewhat smaller because it is really a product of an ion-pair formation constant and the water-exchange rate constant. In any case k_{12} and k_{35} should be relatively independent of the ligand. The value of K_{a_4} should parallel the corresponding ionization constant of the free ligand. Values of k_{21} and k_{53} will depend on the basicity of the A or N atom.

With these ideas in mind it is possible to construct qualitative reaction profiles for the reaction with various ligands as shown in Figure 5. It should be noted that the position of the equilibrium described by K_{a_4} actually depends on the pH and that the diagrams assume pH 6 where the undissociated species is dominant for the systems studied here. For histidine, histamine, and 3-methylhistidine A is a moderately basic imidazole nitrogen, k_{21} is small, and the first valley on the diagram is low followed by the unfavorable K_{a_4} equilibrium with the second valley high followed by the k_{35} step. The diagram clearly shows how the rate-limiting step is k_{35}, the chelate ring closing.

These systems differ from the ester in that K_{a_4} is more favorable with the ester, and, although k_{35} has the same magnitude, this step is no longer rate limiting because the second valley is lower. Thus the ester is "normal", in a historical sense, in that first bond formation (k_{12}) is rate limiting for complex formation with nickel(II).

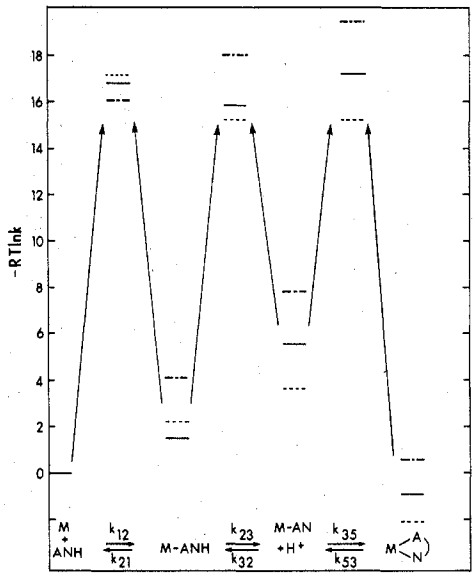


Figure 5. Reaction profile for the complexing of histidine (—), histidine methyl ester (- - -), and glycine (-·-) by $(TRI)Ni(OH_2)_3^{2+}$. The calculations are for [total ligand] = 10^{-3} M and pH 6 and are based on kinetic data discussed in the text.

Glycine differs from the above systems in that the first bond is formed with a poor base, the carboxylate oxygen. Therefore, k_{21} is much larger, and the first valley is higher than in the cases discussed above. Subsequent steps are analogous to those with histidine and histamine, and chelate ring closure becomes rate limiting because of the unfavorable preequilibrium.

The results charted in Figure 5 can be used to understand the kinetic complexity found for histidine, histamine, and histidine methyl ester. This complexity is caused by the $k_{21}(H^+)/k_{35}K_{a_4}$ term in the denominator of eq 5. In the limiting case where $k_{21}(H^+)/k_{35}K_{a_4} \gg 1$, the measured formation rate constant is $k_{12}k_{35}K_{a_4}/k_{21}$; i.e., k_{35} is rate limiting as shown by Figure 5. However, if the pH is increased, the second valley in Figure 5 becomes lower, and, since k_{35} is the same, the third peak will lower as well and could fall below the first peak, as it does for histidine at pH 7. In eq 5 this corresponds to $k_{21}(H^+)/k_{34}K_{a_4} \ll 1$, and k_{12} is determined experimentally, and the first bond formation is rate limiting. The latter condition applies more generally with $Ni(OH_2)_6^{2+}$ than with $(TRI)Ni(OH_2)_3^{2+}$. This can be rationalized if the TRI ligand has some steric influence and makes k_{21} larger than with $Ni(OH_2)_6^{2+}$. Thus one must examine results such as those in Table II rather carefully to find some evidence for the $k_{12}/k_{35}K_{a_4}$ term with $Ni(OH_2)_6^{2+}$.

One of the original goals of this work was to investigate kinetic stereoselectivity in the reaction of $(TRI)Ni(OH_2)_3^{2+}$ and histidine. In fact, no definitive evidence for such an effect has been found. The first two runs in Table I and two runs at pH 6.21 might indicate that the rate coefficient for $(+)_{436}$-$(TRI)Ni(OH_2)_3^{2+}$ is larger with L-histidine than with D-histidine. However, the differences are not outstanding, and $(-)_{436}$-$(TRI)Ni(OH_2)_3^{2+}$ does not seem to react consistently more slowly with L-histidine. With the rate law and reaction sequence now determined one can see in retrospect that if stereoselectivity lies in the rate constants for dissociation, the effect could best be demonstrated at low pH and low ligand concentration where the k_{21} and k_{53} terms are most significant in eq 5.

Table IV. Summary of Kinetic Results

ligand	metal complex	$10^{-3}k_{12}$, M^{-1} s^{-1}	$10^{-6}k_{21}/k_{35}K_{a_4}$	k_{53}, s^{-1}	$10^{-3}(k_{43} + k_{46})$, M^{-1} s^{-1}	$10^{-6}K_f$, M^{-1}
histidine	$(TRI)Ni(OH_2)_3^{2+}$	3.6	2.4	0.35		7
	$Ni(OH_2)_6^{2+}$	3.1	0.425	0.028		47[a]
	$Ni(OH_2)_6^{2+}$ [b]	2.2				
3-methylhistidine	$(TRI)Ni(OH_2)_3^{2+}$	4	2.4	0.42		8
	$Ni(OH_2)_6^{2+}$ [c]	2.1				
histamine	$(TRI)Ni(OH_2)_3^{2+}$	1.4	9.6	1.1		1.4
	$Ni(OH_2)_6^{2+}$ [d]	1	2.5	0.11		6
histidine methyl ester	$(TRI)Ni(OH_2)_3^{2+}$	1.3		(~1.6)	5	0.56
	$Ni(OH_2)_6^{2+}$ [b]	0.6			2.6	
glycine	$(TRI)Ni(OH_2)_3^{2+}$			(0.043)	17[f]	0.4
	$Ni(OH_2)_6^{2+}$ [e]			(0.033)	22[f]	0.6[a]

[a] Reference 17. [b] Reference 7. [c] Reference 15. [d] On the basis of a reanalysis of the results of ref 16. [e] Reference 2a. [f] Value of $(k_{43}k_{35}/k_{34} + k_{46})$.

The kinetic results are summarized in Table IV along with values for $Ni(OH_2)_6^{2+}$ for comparison. The formation rate constants (k_{12} or $k_{43} + k_{46}$) show the parallel with ligand charge expected for the dissociative ion-pair mechanism. Thus the rate constants for the cationic forms of histamine and histidine methyl ester have rate constants about 3 times less than those for the neutral forms of histidine, 3-methylhistidine, and histidine methyl ester, which in turn are about 4 times less than for the glycine anion (the latter may not be a simple rate constant however).

A comparison of the k_{12} values for $(TRI)Ni(OH_2)_3^{2+}$ and $Ni(OH_2)_6^{2+}$ shows that they are somewhat ($\lesssim$ 2 times) smaller for the latter with all the histidine derivatives. Although the water-exchange rate on $(TRI)Ni(OH_2)_3^{2+}$ is slightly (~15%) larger, the reduced number of reaction sites and the bulk of the TRI ligand could easily have led to a prediction that $Ni(OH_2)_6^{2+}$ would have larger rate constants. In fact, this is the case with glycine. Possibly there is some interaction between the imidazole substituent of histidine and the benzene ring of TRI which makes "ion-pair" formation more favorable in the histidine systems.

The values of k_{53} are about 10 times smaller for histidine and histamine with $(TRI)Ni(OH_2)_3^{2+}$ than those with $Ni(OH_2)_6^{2+}$. This may reflect a steric effect of the TRI ligand. The difference is much less with glycine, but this is consistent with a steric argument since there are no bulky substituents present on glycine.

It is interesting to note that the k_{53} values for the two ligands without a carboxylate group (histamine and the ester) are similar but larger than the values for histidine and 3-methylhistidine. This could be attributed to carboxylate chelation in which case k_{53} is really the rate constant for amino group dissociation divided by the equilibrium constant for carboxylate chelate formation. If this is the case, the much smaller k_{53} value for $Ni(OH_2)_6^{2+}$–histidine would indicate that carboxylate coordination is more significant here than in the case with $(TRI)Ni(OH_2)_2^{3+}$ and histidine.

It is more difficult to analyze the composite constant $k_{43}k_{35}/k_{34}$. The values are significantly smaller for $(TRI)Ni(OH_2)_3^{2+}$ in the two cases where comparisons can be made. If k_{43} parallels k_{12}, then $k_{43}k_{35}/k_{34}$ should be larger with $(TRI)Ni(OH_2)_3^{2+}$, but this is not the case. However, steric effects may make k_{34} larger with $(TRI)Ni(OH_2)_3^{2+}$ causing $k_{43}k_{35}/k_{34}$ to be smaller than with $Ni(OH_2)_6^{2+}$.

In summary, it has been found that the kinetics of the complexing of $Ni(OH_2)_6^{2+}$ and $(TRI)Ni(OH_2)_3^{2+}$ by histidine and its derivatives can be controlled by first bond formation or chelate ring closing depending on the type of ligand and the experimental conditions. The nonreacting TRI ligand does not seem to have any substantial steric or probability effects on the rate of bond formation, and the kinetic differences with $Ni(OH_2)_6^{2+}$ can be understood on the basis of steric acceleration of bond-breaking reactions with the histidine ligands.

Registry No. $(TRI)Ni(OH_2)_3(ClO_4)_2$, 36609-58-2; $(+)_{436}$-$(TRI)Ni(OH_2)_3^{2+}$, 18660-65-6; $(-)_{436}$-$(TRI)Ni(OH_2)_3^{2+}$, 18660-66-7; L-histidine, 71-00-1; D-histidine, 351-50-8; DL-histidine, 4998-57-6; $Ni(OH_2)_6^{2+}$, 15365-79-4; glycine, 56-40-6; L-3-methylhistidine, 368-16-1; histamine, 51-45-6; L-histidine methyl ester, 1499-46-3.

Supplementary Material Available: Kinetic results for the reaction of $(TRI)Ni(OH_2)_3^{2+}$ with 3-methylhistidine (Table IB), histamine (Table IC), and L-histidine methyl ester (Table ID) (3 pages). Ordering information is given on any current masthead page.

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