Kinetics of Ternary Complex Formation with the (Nitrilotriacetato)copper(II) Complex

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Ligand substitution reactions of the (nitrilotriacetato)copper(II) complex ($CuNTA^-$) with simple mono- and bidentate ligands (L) have been investigated by making use of the temperature-jump relaxation technique. At 25 °C, the forward rate constants for reaction $CuNTA^- + L = CuNTA(L)^-$ are as follows: L = NH_3, 1.5×10^8 M^{-1} s^{-1}; L = CH_3NH_2, 3.4×10^7 M^{-1} s^{-1}; L = glycinate, 1.1×10^8 M^{-1} s^{-1}; L = α-alaninate, 4.9×10^7 M^{-1} s^{-1}; L = β-alaninate, 3.8×10^7 M^{-1} s^{-1}; L = 2,2′-bipyridine, 1.2×10^6 M^{-1} s^{-1}; L = 1,10-phenanthroline, 2.2×10^5 M^{-1} s^{-1}. The rate constants for the reactions of the zwitterion form of glycine and α-alanine, $CuNTA^- + HL^{\pm} = CuNTA(L)^{2-} + H^+$, are 1.6×10^3 M^{-1} s^{-1} and 1.8×10^3 M^{-1} s^{-1}, respectively. It was concluded that the reactions of the aliphatic ligands proceed through a dissociative interchange mechanism in which the axial coordination of the entering ligand is the rate-determining step. The unusually slow reactions with the aromatic ligands have been interpreted in terms of steric interference between the coordinated and entering ligands.

Introduction

Ligand substitution reactions of copper(II) have been the subject of intensive kinetic studies since the early sixties. The formation of mono complexes with simple mono- and bidentate ligands is typically fast, the corresponding forward rate constants fall in the range of 10^8–5×10^9 M^{-1} s^{-1}.[1] The extreme lability was attributed to the strong tetragonal distortion of the octahedral ligand field around the metal ion. It makes possible a very rapid coordination via the axial positions.[2,3] With a few exceptions, the rate constants were interpreted in terms of the dissociative interchange mechanism proposed by Wilkins and Eigen.[4]

The mechanisms for the coordination of additional ligands seem to be less straightforward. The observed trends in the rate constants were interpreted by taking into account statistical and electrostatic factors,[5-8] suggesting a shift in the rate-determining step[9-12] or proposing a mechanistic changeover from I_d to I_a.[13-15] The two latter possibilities imply that the coordinated ligand(s) significantly alter the kinetic feature of the metal ion center.

The inborn difficulty with the confirmation of the mechanism is that interactions between the already coordinated and entering ligands also may strongly affect the complex formation kinetics. Also, because of the extreme lability of copper(II), no direct experimental information is attainable for the individual steps of the overall reaction. Thus, the selection of proper model systems is crucial in terms of developing the intrinsic mechanism for these ligand substitution reactions.

In the present study, the complexation reactions of ammonia, methylamine, glycinate (gly^-), α-alaninate (α-ala^-), β-alaninate (β-ala^-), 2,2′-bipyridine (bpy), and 1,10-phenanthroline (phen) with the $CuNTA^-$ complex (NTA^{3-} = nitrilotriacetate ion) were investigated by the temperature-jump method. Nitrilotriacetate is a relatively simple aliphatic ligand with flexible carboxylic arms. In the $CuNTA^-$ complex, it presumably occupies four adjacent positions leaving open two cis-octahedral sites for further ligands.[16,17] Specific interactions and steric effects due to the coordinated ligand are expected to be of marginal kinetic importance in the studied reactions. Moreover, with the exceptions of bpy and phen, ligand substitution reactions of the entering ligands were classified as "normal". Therefore, the present study may provide novel kinetic information for ternary complex formation reactions of copper(II) in the absence of specific steric effects.

Experimental Section

Reagents. Stock solutions were prepared from reagent grade $CuCl_2 \cdot 2H_2O$, H_3NTA, NH_4Cl, Hgly, bpy, phen, KCl (Merck), Hα-ala and Hβ-ala (Fluka) without further purification. $CH_3NH_2 \cdot HCl$ (Merck) was recrystallized from methanol before use. The solubility of bpy and phen was improved by adding equivalent amount of HCl (Baker Chemicals) to the stock solution. For the preparation of the NTA stock solution, the ligand was weighted in H_3NTA form and two protons were neutralized by adding appropriate amount of KOH solution (Baker Chemicals). Chlorophenol red (CPR) (Merck) and bromothymol blue (BTB) (Fluka) stock solutions were prepared by dissolving the indicators in equivalent amount of KOH. In order to solubilize CPR, methanol also was added in 1%. All solutions were freshly prepared in triply distilled water.

The pH of the samples was adjusted to ±0.01 unit by dropwise addition of 1.0 M HCl or KOH solutions. The ionic strength was adjusted to 2.0 M (NH_4Cl), 1.0 M ($CH_3NH_2 \cdot HCl$) and 0.5 M (KCl) for the other ligands. In the case of the first two ligands, the higher ionic strength was chosen in order to obtain sufficiently high free ligand concentration in a pH region where the formation of hydroxo complexes is negligible.

Methods. The pH of the samples was measured with a Radiometer PHM 52 digital pH meter equipped with a Metrohm EA 125 combined electrode. The electrode calibration procedure was described elsewhere.[18]

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Table I. Experimental Conditions for the Kinetic Studies on the $CuNTA^- + L = CuNTA(L)^-$ Reactions

ligand (L)	$10^4C_{Cu^{2+}}$ (M)	10^4C_{NTA} (M)	C_I (M)	pH	τ (μs)	no of pts
NH_3[a]	5.0–50.0	5.1–50.1	2.0	5.51–5.95	3.5–10.6	17
CH_3NH_2[b]	2.0–10.0	3.2–11.0	1.0	6.09–6.98	47–137	9
gly [a]	0.6–10.0	3.7–36.0	0.05–0.15	5.34–6.81	104–632	22
α-ala [a]	2.5–10.0	5.9–20.0	0.05–0.10	5.45–6.68	177–505	9
β-ala [b]	1.2–5.0	2.0–6.2	0.025–0.10	6.73–7.60	99–359	19
bpy	0.5–1.0	0.5–4.0	(4.4–22) × 10^{-5}	6.90	3.9–15.7[c]	5
phen	0.3–2.0	3.9–5.7	(2.6–18) × 10^{-5}	7.20	68–182[c]	9

[a] Indicator: CPR, $C_{Ind} = (2.0–8.0) \times 10^{-5}$ M. [b] Indicator: BTB, $C_{Ind} = (2.0–8.0) \times 10^{-5}$ M. [c] τ in ms.

The pH refers to $-\log[H^+]$ throughout this paper. In the equilibrium studies the spectra were recorded on a Carry 118 spectrophotometer.

Kinetic experiments were made by using the temperature-jump relaxation technique with spectrophotometric detection. The applied conventional[19] and cable T-jump apparatus,[20] the details of the relaxation measurements and the evaluation of the relaxation time(s) (τ) from the experimental relaxation curves have been described elsewhere.[21] Each relaxation time was determined from the average of at least 5 replicate kinetic runs. The reproducibility of the relaxation time for a single exponential trace was 8%. In the $CuNTA^- + NH_3$ system two partly overlapping relaxation effects were observed. Because of the opposite amplitudes, the two relaxation times could be determined within an error of 15%. The pH of the samples were checked both prior and after the T-jump experiments.

In the case of NH_3 and the aliphatic ligands, the shift in the complex equilibria did not generate measurable relaxation effects. Thus, chlorophenol red (with NH_3, gly^- and α-ala^-) or bromothymol blue (with CH_3NH_2 and β-ala^-) were used as coupled indicators and the kinetic curves were monitored at their characteristic absorbancy band (λ = 550–600 nm). Typically two relaxation effects were observed. Based on blank experiments in the absence of the $CuNTA^-$ complex, the faster relaxation process was assigned to proton transfer reactions between the indicator and the entering ligand. Kinetic runs in the absence of the ligand showed no relaxation effects. In the reactions of bpy and phen the relaxation curves were recorded at the UV absorption band of the aromatic ligand and complexes, at 305–310 nm. The experimental conditions are summarized in Table I.

The rate constants were obtained by fitting the appropriate expressions for the reciprocals of the relaxation times ($r = 1/\tau$) to the measured values by minimizing the relative deviations, $\sum[(r_{calc,i} - r_{exp,i})/r_{exp,i}]^2$, with a nonlinear least-squares fitting algorithm.[22] The stability of the regression method was tested by repeating the calculations with randomly varied initial estimates for the fitted parameters. The sensitivity of the data for the calculated parameters were checked by changing one of the rate constants by 20% and refitting the remaining ones. The reported error limits represent one standard deviation. The results are given for 25 °C.

Equilibrium Constants. The speciation in the studied systems was calculated on the basis of the equilibrium constants listed in Table II.

Reliable stability constants for the ternary complexes of the aromatic ligands are not available from the literature. These data were determined by spectrophotometric titrations in the present study. Solutions of Cu^{2+} and NTA^{3-} were titrated with solutions of the aromatic ligand at practically constant pH (~7.00). These experiments were optimized for the formation of the ternary complex. In the titrated solutions, the NTA^{3-} concentration and pH was adjusted such that the $CuNTA^-$ complex was the dominant species. The total concentration of the metal ion was in the range of 2×10^{-5}–1×10^{-4} M (bpy) and 6×10^{-6}–5×10^{-5} M (phen). The concentration ratio of the aromatic ligand to the total metal ion was increased up to 12:1 (bpy) and 20:1 (phen). Under the applied conditions, at least 60–70% of the observed spectral effect is due to the formation of the ternary complex.

Table II. Stability Constants for the Complexes Formed in the Cu^{2+}–NTA^-–L Ternary Systems

reacn	log K	ref
$NTA^{3-} + H^+ = HNTA^{2-}$	9.32	23
$HNTA^{2-} + H^+ = H_2NTA^-$	2.27	23
$H_2NTA^- + H^+ = H_3NTA$	1.79	23
$Cu^{2+} + NTA^{3-} = CuNTA^-$	13.00	24
$CuNTA^- + NTA^{3-} = Cu(NTA)_2^{3-}$	4.14	23
$NH_3 + H^+ = NH_4^+$	9.53	25
$CuNTA^- + NH_3 = CuNTA(NH_3)^-$	3.74	23
$CH_3NH_2 + H^+ = CH_3NH_3^+$	10.96	23
$CuNTA^- + CH_3NH_2 = CuNTA(CH_3NH_2)^-$	4.09	23
$gly^- + H^+ = Hgly$	9.63	23
$Hgly + H^+ = H_2gly^+$	2.50	23
$Cu^{2+} + gly^- = Cu(gly)^+$	8.20	24
$Cu(gly)^+ + gly^- = Cu(gly)_2$	6.90	24
$CuNTA^- + gly^- = CuNTA(gly)^{2-}$	5.39	23
α-$ala^- + H^+ = H\alpha$-ala	9.83	24
$H\alpha$-ala $+ H^+ = H_2\alpha$-ala^+	2.40	24
$Cu^{2+} + \alpha$-$ala^- = Cu(\alpha$-$ala)^+$	8.21	24
$Cu(\alpha$-$ala)^+ + \alpha$-$ala^- = Cu(\alpha$-$ala)_2$	6.79	24
$CuNTA^- + \alpha$-$ala^- = CuNTA(\alpha$-$ala)^{2-}$	5.42	26
β-$ala^- + H^+ = H\beta$-ala	10.35	26
$H\beta$-ala $+ H^+ = H_2\beta$-ala^+	3.55	26
$Cu^{2+} + \beta$-$ala^- = Cu(\beta$-$ala)^+$	7.26	11
$Cu(\beta$-$ala)^+ + \beta$-$ala^- = Cu(\beta$-$ala)_2$	5.63	11
$CuNTA^- + \beta$-$ala^- = CuNTA(\beta$-$ala)^{2-}$	4.56	26
$bpy + H^+ = Hbpy^+$	4.54	27
$Cu^{2+} + bpy = Cu(bpy)^{2+}$	8.88	28
$Cu(bpy)^{2+} + bpy = Cu(bpy)_2^{2+}$	5.78	28
$Cu(bpy)_2^{2+} + bpy = Cu(bpy)_3^{2+}$	3.25	29
$CuNTA^- + bpy = CuNTA(bpy)^-$	4.82 ± 0.05	a
$phen + H^+ = Hphen^+$	5.03	30
$Cu^{2+} + phen = Cu(phen)^{2+}$	9.20	24
$Cu(phen)^{2+} + phen = Cu(phen)_2^{2+}$	6.70	24
$Cu(phen)_2^{2+} + phen = Cu(phen)_3^{2+}$	5.20	24
$CuNTA^- + phen = CuNTA(phen)^-$	5.3 ± 0.1	a

[a] This work.

The experimental data from the UV region of the spectra were evaluated by using the program PSEQUAD.[31] The formation constant of the ternary complex and the spectra of $CuNTA(bpy)^-$ and bpy were fitted at 21 wavelengths in the range of 215–325 nm. In the other system, the stability constant and the spectra of $CuNTA(phen)^-$, phen and $Cu(phen)_3^{2+}$ were calculated at 17 wavelengths (240–320 nm). The stability constants and spectra of the other species were included as known parameters. The calculated spectra of the free ligands and $Cu(phen)_3^{2+}$ were statistically identical with those determined in the absence of the $CuNTA^-$ complex. The equilibrium constants are listed in Table II.

The pK_a's of the indicators were determined by using spectrophotometry. The corresponding values are 5.92 (2.0 M NH_4Cl), 5.91 (0.5 M KCl) for CPR and 7.07 (1.0 M CH_3NH_2·HCl), 7.09 (0.5 M KCl) for BTB.

Results

Proton Transfer Reactions. Reactions between the entering ligands (L = NH_3, CH_3NH_2, gly^- β-ala^-) and the indicators (In) were investigated in order to estimate the relaxation effects of the coupled proton transfer processes. The general mechanism for these reactions includes a protolytic (eqs 1a and 2a), a hydrolytic (eqs 1b and 2b) and a direct pathway (eq 3).[32] (For the sake of

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Table III. Rate Constants for Proton Transfer Reactions

indicator	ligand	$10^{-8}k_3$ (M^{-1} s^{-1})	$10^{-10}k_{1a}$ (M^{-1} s^{-1})	$10^{-10}k_{2a}$ (M^{-1} s^{-1})
CPR	NH_3	4.9 ± 0.3	4.3[a]	4.9 ± 1.1
CPR	glycine	10.5 ± 0.7	5.9 ± 1.2	3.5 ± 0.9
BTB	CH_3NH_2	2.9 ± 0.2		
BTB	β-alanine	<6.0		

[a] From ref 33.

Table IV. Rate Constants for the Formation of Ternary CuNTA(L) Complexes: $CuNTA^- + L = CuNTA(L)^-$

reacn	k_+ (M^{-1} s^{-1})	k (s^{-1})
$CuNTA + NH_3 = CuNTA(NH_3)$	$(1.5 \pm 0.1) \times 10^8$ 2.1×10^8 [a]	3.0×10^4
$CuNTA + CH_3NH_2 = CuNTA(CH_3NH_2)$	$(3.4 \pm 0.4) \times 10^7$ $\sim 5.5 \times 10^7$ [a]	$(1.7 \pm 0.4) \times 10^3$
$CuNTA + gly = CuNTA(gly)^-$	$(1.1 \pm 0.1) \times 10^8$	$(2.5 \pm 1.1) \times 10^2$
$CuNTA + \alpha\text{-ala} = CuNTA(\alpha\text{-ala})^-$	$(4.9 \pm 0.4) \times 10^7$	1.9×10^2
$CuNTA + \beta\text{-ala} = CuNTA(\beta\text{-ala})^-$	$(3.8 \pm 0.4) \times 10^7$	1.1×10^3
$CuNTA + Hgly^\pm = CuNTA(gly)^- + H^+$	$(1.6 \pm 0.7) \times 10^3$	2.7×10^7 [b]
$CuNTA + H\alpha\text{-ala}^\pm = CuNTA(\alpha\text{-ala})^- + H^+$	$(1.8 \pm 0.3) \times 10^3$	4.5×10^7 [b]
CuNTA + bpy = CuNTA(bpy)	$(1.2 \pm 0.1) \times 10^6$	19 ± 4
CuNTA + phen = CuNTA(phen)	$(2.2 \pm 0.3) \times 10^5$	1.3

[a] From ref 23. [b] In M^{-1} s^{-1}.

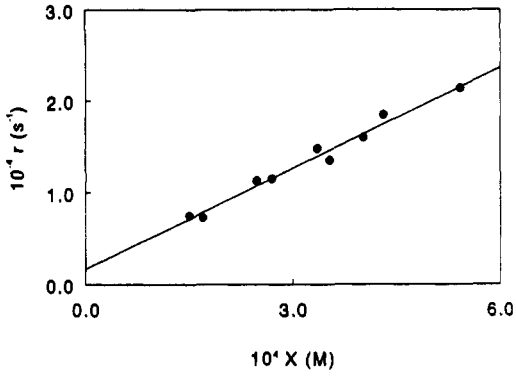

Figure 1. Plot of the experimental data for the $CuNTA^- + CH_3NH_2 = CuNTA(CH_3NH_2)^-$ reaction according to eq 7. (Experimental conditions are as given in Table I.) $X = \alpha[CuNTA^-] + [CH_3NH_2]$.

simplicity, charges are omitted when general symbols are used for the reactants.)

$$H^+ + L \rightleftharpoons HL \quad k_{1a}, k_{-1a} \tag{1a}$$

$$OH^- + HL \rightleftharpoons L + H_2O \quad k_{1b}, k_{-1b} \tag{1b}$$

$$K_p = [HL]/[H^+][L]$$

$$H^+ + In \rightleftharpoons HIn \quad k_{2a}, k_{-2a} \tag{2a}$$

$$OH^- + HIn \rightleftharpoons In + H_2O \quad k_{2b}, k_{-2b} \tag{2b}$$

$$K_{In} = [HIn]/[H^+][In]$$

$$L + HIn \rightleftharpoons In + HL \quad k_3, k_{-3} \tag{3}$$

$$K_{ex} = [In][HL]/[L][HIn]$$

Under the applied experimental conditions hydrogen and hydroxide ions were in steady state ($d[H^+]/dt \sim 0$ and $d[OH^-]/dt \sim 0$). Also, in the case of amino acids, the H_2L^+ form of the ligand was in negligible concentration. Standard derivation yields the following expression for the observed single relaxation effect:[32]

$$r = k_f([HIn] + [L]) + k_r([In] + [HL]) \tag{4}$$

where

$$k_f = k_3 + \frac{k_{1a}k_{-2a}}{k_{1a}[L] + k_{2a}[In]} + \frac{k_{-1b}k_{2b}}{k_{1b}[HL] + k_{2b}[HIn]}$$

$$k_r = k_{-3} + \frac{k_{-1a}k_{2a}}{k_{1a}[L] + k_{2a}[In]} + \frac{k_{1b}k_{-2b}}{k_{1b}[HL] + k_{2b}[HIn]}$$

Systematic analysis of the experimental data confirmed that in the CPR–NH_3 and –glycine systems the contribution of the hydrolytic pathway to the overall proton transfer reaction is negligible (pH = 5.4–6.6). In the fitting procedure, rate constants k_{-1a}, k_{-2a} and k_{-3} were replaced by k_{1a}/K_p, k_{2a}/K_{In} and k_3/K_{ex}. Thus, only the forward rate constants were fitted. The results are given in Table III.

In the BTB–methylamine and –β-alanine systems, the proton transfer reactions were studied in the neutral pH region (pH = 6.5–7.6). Under these conditions, the dominant pathway is the direct proton exchange. Thus, only rate constant k_3 could be calculated from the experimental data (Table III).

According to the general theory of proton transfer reactions, a close to diffusion controlled rate constant is projected for the direct proton transfer step whenever the basicities of the reactants are substantially different.[34] In the studied systems, the difference in the pK_a of the ligand and indicator is more than 3. Nevertheless, the calculated values for k_3 are far below the expected diffusion controlled limit. Because of the small size and simple structure, the ligands are not expected to be involved in specific interactions with the indicators. Therefore, a possible interpretation of the results is that the bulky aromatic frame of CPR and BTB simple shields the leaving proton inhibiting the formation of the [L···H–In] encounter complex. Since this problem falls outside the scope of the present study, it was not further investigated. However, it needs to be emphasized, whatever the reason is for the somewhat anomalous kinetic behavior it unlikely affects the complexation kinetics. In particular because, with the exception of the $CuNTA^- + NH_3$ system, the proton transfer reactions can be treated as fast pre-equilibria.

$CuNTA^-$–NH_3 and –CH_3NH_2 Systems. The appropriate kinetic model includes the proton transfer reactions (reactions 1a, 2a, and 3) and the actual complex formation:

$$CuNTA^- + L = CuNTA(L)^- \quad k_+, k_- \tag{5}$$

$$K = [CuNTA(L)^-]/[CuNTA^-][L]$$

In the case of NH_3, the expressions for the two partially overlapping relaxation effects are given as follows:[32]

$$r_{1,2} = \frac{a_{11} + a_{22}}{2} \pm \left[\frac{(a_{11} + a_{22})^2}{4} + a_{12}a_{21} - a_{11}a_{22}\right]^{1/2} \tag{6}$$

where

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$$a_{11} = \left([\mathrm{HIn}] + [\mathrm{L}] + \frac{1}{K_{ex}}\right)\left(k_3 + \frac{1}{K_{In}}\frac{k_{1a}k_{2a}}{k_{1a}[\mathrm{L}] + k_{2a}[\mathrm{In}]}\right)$$

$$a_{12} = \left(k_3 + \frac{1}{K_{In}}\frac{k_{1a}k_{2a}}{k_{1a}[\mathrm{L}] + k_{2a}[\mathrm{In}]}\right)[\mathrm{HIn}]$$

$$a_{21} = k_+[\mathrm{CuNTA}^-] \qquad a_{22} = k_+([\mathrm{CuNTA}^-] + [\mathrm{L}] + 1/K)$$

The two relaxation times were simultaneously fitted by either using fixed values for rate constants k_{1a}, k_{2a}, and k_3 (from Table III) or by fitting these parameters together with k_+. The two fitting methods gave the same result for rate constant k_+ (Table IV).

In the case of methylamine, the pre-equilibrium model can be used. Thus, the following equation was derived for the slower relaxation process:

$$r = k_+(\alpha[\mathrm{CuNTA}^-] + [\mathrm{L}]) + k_- \qquad (7)$$

where

$$\alpha = \left(1 + \frac{K_p[\mathrm{H}^+](K_{In}[\mathrm{In}] + K_{In}[\mathrm{H}^+] + 1)}{1 + K_{In}([\mathrm{H}^+] + [\mathrm{In}]) + K_p[\mathrm{L}](1 + K_{In}[\mathrm{H}^+])}\right)^{-1}$$

The plot according to eq 7 is shown in Figure 1. The experimental data were evaluated by fitting both k_+ and k_- (Table IV). The ratio of the forward and reverse rate constants yields $\log K = 4.34$. This value is in good agreement with the equilibrium constant in Table II.

CuNTA-Glycine, -α-Alanine, and -β-Alanine Systems. The following kinetic model was considered:

$$\mathrm{H}^+ + \mathrm{In} = \mathrm{HIn} \quad \text{fast} \qquad (8)$$

$$K_{In} = [\mathrm{HIn}]/[\mathrm{H}^+][\mathrm{In}]$$

$$\mathrm{H}^+ + \mathrm{L}^- = \mathrm{HL}^\pm \quad \text{fast} \qquad (9)$$

$$K_{p1} = [\mathrm{HL}^\pm]/[\mathrm{H}^+][\mathrm{L}^-]$$

$$\mathrm{H}^+ + \mathrm{HL}^\pm = \mathrm{H_2L}^+ \quad \text{fast} \qquad (10)$$

$$K_{p2} = [\mathrm{H_2L}^+]/[\mathrm{H}^+][\mathrm{HL}^\pm]$$

$$\mathrm{CuNTA}^- + \mathrm{L}^- = \mathrm{CuNTA(L)}^{2-} \quad k_+, k_- \qquad (11)$$

$$K = [\mathrm{CuNTA(L)}^{2-}]/[\mathrm{CuNTA}^-][\mathrm{L}^-]$$

$$\mathrm{CuNTA}^- + \mathrm{HL}^\pm = \mathrm{CuNTA(L)}^{2-} + \mathrm{H}^+ \quad k_+', k_-' \qquad (12)$$

$$K' = [\mathrm{CuNTA(L)}^{2-}][\mathrm{H}^+]/[\mathrm{CuNTA}^-][\mathrm{HL}^\pm]$$

Since two largely isolated relaxation effects were observed, reactions 8–10 were treated as fast pre-equilibria. In order to confirm this assumption, the shorter relaxation times were calculated according to eq 4 by using the rate constants from Table III. (In these calculations only those experimental points were included in which H_2L^+ was in negligible concentration.) As expected in the absence of kinetic coupling between the proton transfer and complex formation reactions, the calculated and measured relaxation times showed excellent agreement.

The following expression was derived for the slower relaxation process:

$$r = k_+\alpha + k_- + k_+'\beta + k_-'\gamma \qquad (13)$$

where

$$\alpha = \frac{1 + a + K_{p1}[\mathrm{L}^-] + 4K_{p1}K_{p2}[\mathrm{H}^+][\mathrm{L}^-]}{b}[\mathrm{CuNTA}^-] + [\mathrm{L}^-]$$

$$\beta = \frac{K_{p1}[\mathrm{H}^+](1 + a + 2K_{p1}K_{p2}[\mathrm{H}^+][\mathrm{L}^-])}{b}[\mathrm{CuNTA}^-] + [\mathrm{HL}^\pm]$$

$$\gamma = \frac{K_{p1}[\mathrm{H}^+] + 2K_{p1}K_{p2}[\mathrm{H}^+]^2}{b}[\mathrm{CuNTA(L)}^{2-}] + [\mathrm{H}^+]$$

and

$$a = \frac{K_{In}[\mathrm{In}]}{1 + K_{In}[\mathrm{H}^+]}$$

$$b = (1 + a)(1 + K_{p1}[\mathrm{H}^+] + K_{p1}K_{p2}[\mathrm{H}^+]^2) + K_{p1}[\mathrm{L}^-] + 4K_{p1}K_{p2}[\mathrm{H}^+][\mathrm{L}^-] + K_{p1}^2K_{p2}[\mathrm{H}^+]^2[\mathrm{L}^-]$$

After rearrangement and by replacing the reverse rate constants by k_+/K and k_+'/K', eq 13 can be rewritten in the following linearized form:

$$\frac{r}{\beta + \gamma/K'} = \frac{\alpha + 1/K}{\beta + \gamma/K'}k_+ + k_+' \qquad (14)$$

The plots according to eq 14 are shown in Figure 2.

In the final evaluation rate constants k_+, k_+', and in the case of glycine k_- were fitted according to eq 13. The results are shown in Table IV.

CuNTA-2,2′-Bipyridine and -1,10-Phenanthroline Systems. The concentrations of the free aromatic ligands were adjusted such that complexes $CuNTA^-$ and $CuNTA(L)^-$ were formed in comparable concentration ($[L] \sim 1/K$). Under the applied conditions ($[CuNTA^-], [CuNTA(L)^-], [HNTA^{2-}] \gg [H_2NTA^-], [NTA^{3-}]$ and $[CuNTA(L)^-], [L] \gg [HL^+]$) the contribution of the proton transfer reactions to the relaxation effect is negligible small. Moreover, at least 90% of the total metal ion is in complexes $CuNTA^-$ and $CuNTA(L)^-$. The rest of copper(II) is present as CuL_2^{2+} and CuL_3^{2+}. Therefore, the only side reaction to be considered is the formation of the tris complex:

$$\mathrm{CuL_2}^{2+} + \mathrm{L} = \mathrm{CuL_3}^{2+} \qquad (15)$$

$$K_3 = [\mathrm{CuL_3}^{2+}]/[\mathrm{CuL_2}^{2+}][\mathrm{L}]$$

According to our earlier report, the forward and reverse rate constants for this reaction are $8.6 \times 10^8\ M^{-1}\ s^{-1}$, $4.5 \times 10^5\ s^{-1}$ for bpy and $1.8 \times 10^9\ M^{-1}\ s^{-1}$, $1.1 \times 10^4\ s^{-1}$ for phen, respectively.[21] These kinetic data would be consistent with a relaxation rate several orders of magnitude faster than that observed. Thus, reaction 15 was treated as a fast pre-equilibrium and the relaxation effect was assigned to the formation of the ternary complex (reaction 5). The appropriate expression for r is

$$r = k_+(\delta[\mathrm{CuNTA}^-] + [\mathrm{L}]) + k_- \qquad (16)$$

where

$$\delta = \frac{1/K_3 + [\mathrm{L}]}{1/K_3 + [\mathrm{L}] + [\mathrm{CuL_2}^{2+}]}$$

The plots of the experimental data according to eq 16 are shown in Figure 3. The results of the fitting procedure are listed in Table IV.

Discussion

In order to elaborate the mechanistic details, first the structural features of the $CuNTA^-$ complex need to be clarified. Previous

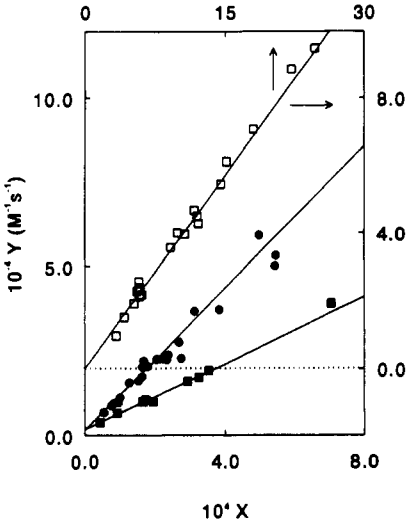

Figure 2. Experimental kinetic data for the formation of $CuNTA(L)^{2-}$ complexes according to eq 14. Key: L = gly^- (●); L = α-ala^- (■); L = β-ala^- (□). (Experimental conditions are as given in Table I.) $X = (\alpha + 1/K)/(\beta + \gamma/K)$ and $Y = r/(\beta + \gamma/K')$.

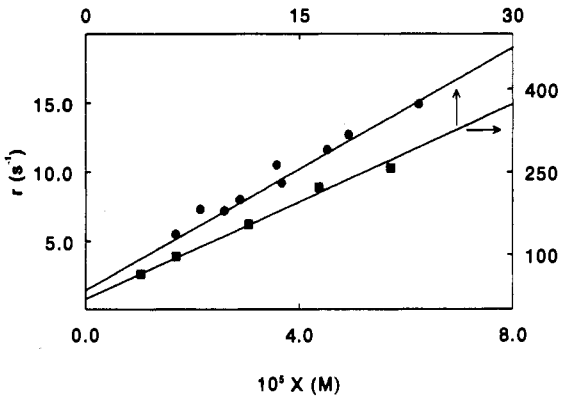

Figure 3. Kinetic data for the $CuNTA^- + L = CuNTA(L)^-$ reaction according to eq 16. Key: L = phen (●); L = bpy (■). (Experimental conditions are as given in Table I.) $X = \delta[CuNTA^-] + [L]$.

studies served indirect evidence that in aqueous solution this species exists as a distorted octahedral complex with two water molecules in cis position.[16,17] Recent ^1H NMR relaxation studies in related systems corroborate this conclusion. In the absence of ligand-assisted proton exchange reactions between the complex and the bulk water, the paramagnetic line-broadening effect of an octahedral copper(II) is proportional to the number of water molecules in the first coordination sphere.[23,35-38] In the case of the $Cu(bpy)_2^{2+}$ complex, for which a cis-octahedral geometry was verified,[39] the relaxation effect was attributed to two coordinated water molecules.[38] The almost identical molar relaxation coefficients of $CuNTA^-$ ($714\ M^{-1}s^{-1}$)[23] and $Cu(bpy)_2^{2+}$ ($680\ M^{-1}s^{-1}$)[38] strongly suggest a structural analogy between the two complexes.

The comparison of the rate constants presented here with those for ligand substitution reactions of $CuTREN^{2+}$ (TREN = 2,2′,2″-triaminotriethylamine)[40-42] provide further kinetic evidence for the octahedral structure. The five-coordinated $CuTREN^{2+}$ has a relatively rigid trigonal-bipyramidal geometry which brings about dramatic kinetic effects. In sharp contrast with other copper(II) complexes, ligand substitution reactions of $CuTREN^{2+}$ proceed through an associative interchange mechanism. Also, these reactions are slower by 3–4 orders of magnitude than similar reactions of the octahedral complexes.[40-42] The structural similarity between NTA^{3-} and TREN, i.e. the ability to form three fused five-membered chelate rings with the tertiary amine group in central position, would suggest analogous structural and kinetic behavior of the corresponding complexes. However, the reactions between $CuNTA^-$ and the aliphatic ligands are too fast to be consistent with the trigonal bipyramidal structure. Moreover, no correlation was found between the rate constants and the pK_a's of the ligand which would support an I_a mechanism. These findings indicate that $CuNTA^-$ and $CuTREN^{2+}$ are characterized with different geometries. It is interesting to note that the extrapolation of the solid phase structure to solution is generally regarded as unreliable. Apparently it is not the case with these complexes. Both of them retain the main characteristic of the solid phase structure in aqueous solution.

While the octahedral geometry for aqueous $CuNTA^-$ seems to be evident, there is still some uncertainty about the actual configuration. The main concern is whether each of the three carboxylic groups of the ligand is coordinated to the metal ion. The comparison of the stability constants[24] for $Cu(gly)^+$ ($\log\beta = 8.20$), CuIDA ($\log\beta = 10.56$; IDA^{2-} = iminodiacetate ion) and $CuNTA^-$ ($\log\beta = 13.00$) reveals that the addition of a carboxylic arm to gly^- and IDA^- increases the stability of the corresponding complexes by about the same magnitude. This, coupled with the earlier discussed NMR arguments, strongly suggest that all donor groups of the NTA^{3-} ligand are coordinated to copper(II). If a partially coordinated $CuNTA^-$ complex exists, it is very likely present at extremely low concentration levels. Therefore, its kinetic role in the ternary complex formation must be negligible.

In the case of a bidentate ligand (A–B), the generally accepted mechanism for ligand substitution reactions of copper(II) includes the following steps:

outer-sphere complex formation:

$$Cu(H_2O)_6^{2+} + A\text{–}B = \{Cu(H_2O)_6A\text{–}B\}^{2+} \quad K_{os}, \text{ fast} \quad (17)$$

axial coordination:

$$\{Cu(H_2O)_6A\text{–}B\}^{2+} = Cu(H_2O)_5(A\text{–}B)_{ax}^{2+} + H_2O \quad k_{ex}, \text{ rate det.} \quad (18)$$

Jahn–Teller inversion:

$$Cu(H_2O)_5(A\text{–}B)_{ax}^{2+} = Cu(A\text{–}B)(H_2O)_5^{2+} \quad k_{JT}, \text{ fast} \quad (19)$$

ring closure:

$$Cu(A\text{–}B)(H_2O)_5^{2+} = Cu(A\text{–}B)(H_2O)_4^{2+} + H_2O \quad k_{rc}, \text{ fast} \quad (20)$$

Special properties of the ligand, such as the presence of bulky substituents, relatively rigid structure, increased distance between the donor groups, etc., may shift the rate determining step in the mechanism. In the absence of such complications, the observed

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rate constant, k_+, is given by

$$k_+ = {}^3/_4 K_{os} k_{ex} \quad (21)$$

The $^3/_4$ factor was introduced by Neely and Connick[43] in order to take into account that there are eight outer-sphere species, centered over the octahedral triangles, which compete for the six inner-sphere positions.

The recently published value for k_{ex} is 4.4×10^9 s^{-1}.[44] Thus, for uncharged monodentate ligands the above mechanism predicts a rate constant in the range of $(3.3–9.5) \times 10^8$ M^{-1} s^{-1} (K_{os} = 0.1–0.3 M^{-1}). Literature data for the formation of binary Cu(NH$_3$)$_n^{2+}$ complexes, 2.0×10^8,[18] 2.3×10^8,[45] 3.0×10^8 M^{-1} s^{-1} (n = 1), 2.8×10^8 M^{-1} s^{-1} (n = 2), 1.7×10^8 M^{-1} s^{-1} (n = 3) and 3.5×10^8 M^{-1} s^{-1} (n = 4),[25] are consistent with this expectation. In excellent agreement with previous results,[23] a very similar rate constant was obtained for the formation of the CuNTA(NH$_3$)$^-$ complex (Table IV). This strongly suggests that the formation kinetics of this species can also be interpreted in terms of the I_d mechanism detailed above.

Statistically, the formation of the ternary complex is less favorable than the formation of the mono, bis, and tris complexes. By taking into account the available empty coordination sites, the corresponding statistical factors are $^1/_3$, $^1/_2$ and $^2/_3$, respectively. Since the entering ligand is neutral, no significant variation is anticipated in the stability of the outer-sphere complex.[46] Thus, based on eq 21, only a slightly higher water exchange rate constant is projected for the CuNTA$^-$ complex than for Cu(H$_2$O)$_6^{2+}$. The lack of significant labilization effect due to the coordinated ligands is typical for octahedral copper(II) complexes.[1] Perhaps, this is the consequence of the relatively loose coordination sites in the axial positions. Since the axial water molecules are very weakly bound, their exchange rate with the bulk is practically not affected by the basicity of the donor groups in the equatorial plane.[48]

The coordination of gly$^-$ and α-ala$^-$ to CuNTA$^-$ is slower by a factor of 40 and 26 than the formation of the corresponding mono complexes.[9,11] A great portion of this difference can be interpreted by taking into account statistical considerations. In the octahedral Cu(H$_2$O)$_6^{2+}$ ion the inversion between the equatorial and axial water molecules is very rapid,[44] $k_{JT} = 2 \times 10^{11}$ s^{-1}. Therefore, there are 12 equivalent edges for the coordination of the first bidentate ligand.[8] (Some workers consider only the eight edges which are adjacent to the axial positions.[7]) The number of the available attacking sites in the CuNTA$^-$ complex is only one. Thus, a $^1/_{12}$ (or $^1/_8$) statistical factor alone may explain about one order of magnitude drop in the rate constants.

Electrostatic differences also contribute to the variation of the rate constants. Because of the electrostatic repulsion between the reactants, the formation of the ternary complex is less favorable than that of the mono complex where a divalent metal ion reacts with a negatively charged ligand. According to previous literature, $K_{os} \sim 2$ M^{-1} for +2,–1 interactions.[7] For the formation of the ternary complex, the Fuoss equation[47] yields $K_{os} \sim 0.15$ M^{-1} (assuming 5 Å center to center distance for the reactants and at μ = 0.5 M, T = 25 °C). Since the negative charge may be shifted toward the ligand in the CuNTA$^-$ complex, this value should be considered as a rough estimate or perhaps as a lower limit. Nevertheless, a close to one order of magnitude difference in the outer-sphere stability constants for the mono and ternary complexes seems to be appropriate.

The 3–4 times difference in the forward rate constants for reactions CuL$^+$ + L$^-$ = CuL$_2$ and CuNTA$^-$ + L$^-$ = CuNTA(L)$^{2-}$ can be interpreted on the basis of analogous statistical and electrostatic arguments. The previous considerations strongly suggest again that the only kinetic consequence, if any, of replacing the inner-sphere water molecules by the NTA^{3-} ligand is a slight labilization of the axially coordinated water molecule.

The kinetic data for the formation of the CuNTA(β-ala)$^{2-}$ complex are also consistent with the mechanism given in eqs 17–21. However, the results are somewhat unexpected. The formation of CuL$^+$, CuL$_2$ binary complexes[11] and Cu(bpy)L$^+$ [14] is considerably faster with α-ala$^-$ than with β-ala$^-$. This difference was interpreted by taking into account the larger chelate ring size in the case of β-ala$^-$. According to Makinen et al., the formation of the six-membered ring is sterically hindered; therefore, the ring-closure becomes rate determining.[11]

In the CuNTA$^-$ + L$^-$ reaction, the difference between α-ala$^-$ and β-ala$^-$ vanishes. This can be attributed to the geometry of the CuNTA(L)$^{2-}$ complex, in which the second ligand most likely occupies an equatorial–axial position. Due to the elongated axial coordination, this structure is more favorable for the formation of the larger six-membered chelate ring than the equatorial–equatorial position in the binary complexes or in Cu(bpy)(L)$^+$. Consequently, the ring closure of β-ala is sterically not hindered in the formation of the CuNTA(β-ala)$^{2-}$ complex.

The reverse rate constants, which are more than an order of magnitude larger than the dissociation rate constants for the binary complexes,[9,11] lend further support to the above interpretation. In previous literature, good inverse correlation was found between the dissociation rate constants and the stability constants of Cu(II) complexes.[49] It was concluded that the rate determining step in the dissociation is the rupture of the chelate ring. If in the ternary complex the bidentate ligand occupies a weak axial position with one donor group it is expected, consistently with the results, to dissociate at a much higher rate than from the equatorial plane of the binary complexes.

As shown in Table IV, the formation of the ternary complexes with NH$_3$ and gly$^-$ is about 3–4 times faster than with CH$_3$NH$_2$ and α-ala$^-$, respectively. A very similar trend was observed in the rate constants for ternary complex formation reactions of CuIDA, CuMIDA (MIDA^{2-} = methyliminodiacetate ion) with NH$_3$ and CH$_3$NH$_2$.[50] In ligand substitution reactions of alkylamines with Ni^{2+}, the kinetic role of the alkyl substituents was investigated by Rorabacher and Melendez-Cepeda in detail.[51] It was shown that the alkyl group can significantly reduce the rate of these reactions. The results were interpreted by assuming that the donor group has to be properly oriented in the outer-sphere complex prior to the coordination. It was concluded that the orientation of the ligand becomes less favorable by increasing the bulkiness of the alkyl substituents. However, in the case of simple ligands the reorientation is very likely fast. Moreover, the outer-sphere complex is formed by electrostatic interactions between

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(46) For –1:–1 interactions the Fuoss equation[47] predicts $K_{os} \sim 0.2$ M^{-1} (μ = 2.0 M, T = 25 °C). This value is taken as a lower limit for the CuNTA + NH$_3$ reaction, in which one of the reactants is uncharged. For the reactions of a divalent metal ion with neutral ligands $K_{os} \sim 0.3$ M^{-1}.[1] Therefore, in the reactions compared here K_{os} is expected to vary within less than a factor of 1.5.
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(48) One of the reviewers suggested an alternative explanation. It assumes that the labilization effect of the NTA^{3-} ligand is not observed because it is offset by the formation of strong hydrogen bonds between the anionic carboxylate oxygens and the coordinated water molecules. While this interpretation cannot be a priory rejected, there are strong arguments against it. In the CuNTA complex the presence of a "loose" carboxylic group can be excluded (see text). Thus, the proposed model implies the formation of hydrogen bonds with oxygens which are directly coordinated to the metal ion. Even if formed, such hydrogen bonds are unlikely strong enough to efficiently immobilize the coordinated water molecules. It also needs to be emphasized that the lack of labilization effect appears to be a general feature of copper(II) complexes[1] and independent of the presence or absence of potential hydrogen bond forming donor groups.
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the metal ion and the donor group; i.e. the configuration of the outer-sphere complex is expected to be favorable for the complex formation.

Perhaps, the alkyl substituents do not affect the outer-sphere to inner-sphere transition of the ligand, rather the formation of the outer-sphere complex itself. Repulsive hydrophobic interactions due to the alkyl substituents may reduce K_{os}. Whatever the underlying reason is for the observed trend of the rate constants, it is apparently determined by the properties of the entering ligands. This conclusion challenges some of the earlier reports in which kinetic steric effects were attributed exclusively to the coordinated ligand.[12]

In the formation of binary complexes, the zwitterion form of the amino acids was found to be unreactive.[9,11] The results obtained here are consistent with this finding. However, in the formation of the ternary complexes (L = gly$^-$, α-ala$^-$), the relative importance of the HL$^\pm$ path appears to be somewhat higher. This reflects that the reactions of the quasi-neutral zwitterions are less affected by electrostatic interactions than the reactions of the anionic forms.

The formation of ternary complexes with bpy and phen is relatively slow. In general, ligand substitution reactions of these ligand show specific kinetic patterns. Due to steric effects, the formation of the mono complexes with Cu^{2+} is 3–4 times slower than predicted for simple neutral ligands.[52,53] Also, an atypical, about 1.5 orders of magnitude rate enhancement was observed in the formation of the bis and tris complexes by Fábián and Diebler.[21] It was interpreted in terms of specific stacking interactions between the aromatic rings of the coordinated and entering ligands.

The sluggish ternary complex formation is most likely the consequence of steric interference between the coordinated and entering ligands. Apparently, the geometry of the CuNTA$^-$ complex is not favorable for the coordination of bulky and rigid aromatic ligands such as bpy and phen. In this context, it has to be emphasized that the formation of the other ternary complexes with CuNTA$^-$, as well as the formation of binary bpy and phen complexes, are only slightly affected by such interactions.

In principle, the steric effect may modify each individual step of the mechanism. However, while some decrease in K_{os} is anticipated, the small forward rate constants are unlikely brought about by the formation of much weaker than usual outer sphere complexes. Similarly, the coordination of the ligand in the remote axial position is not expected to be considerably inhibited by steric effects. Kinetic data for the other CuNTA(L)$^-$ complexes suggest that the Jahn–Teller inversion of the axially coordinated complex (reaction 19) is fast. These considerations lead to the conclusion that the steric interactions primarily affect the coordination of the second donor group, i.e. the ring closure, which becomes the rate determining step.

The $\sim$5 times difference in the rate constants for the coordination of bpy and phen is consistent with a mechanism in which the rate determining step is the sterically controlled ring closure. In phen the two aromatic rings are fixed in a coplanar position, while in bpy they can freely rotate around the α,α' C–C bond.[54] Due to this structural difference, the inner-sphere coordination of phen is less favorable when the access to the empty coordination sites is somewhat limited by the coordinated ligand. It should be added that in the absence of specific steric effects, as in the formation of the binary complexes, ligand substitution reactions of bpy and phen are characterized by very similar rate constants.[21,52,53]

In conclusion, the results presented here indicate that the Eigen–Wilkins mechanism, well established for the reactions of Cu$(H_2O)_6^{2+}$, can be also applied for the reactions of the CuNTA$^-$ complex. However, steric interactions may significantly modify the formation kinetics and eventually may shift the rate determining step in the mechanism. These effects are shown to be associated with bulky substituents in the entering ligand and/or steric interference between the entering and coordinated ligands. Perhaps the most interesting aspect of the results presented here is that the presence of a tetradentate ligand (NTA^{3-}) in the inner coordination sphere is not able to inhibit the Jahn–Teller inversion of the metal ion center to such an extent that it becomes rate determining in the overall ligand substitution reaction.

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