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Kinetics of Ligand-exchange of $Cu(dien)^{2+}$ with EDTA

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The ligand-exchange of $Cu(dien)^{2+}$ *with EDTA has been studied between pH = 3.5–4.9 by stopped-flow spectrophotometry. The reaction is first order with respect both to* $Cu(dien)^{2+}$ *and EDTA. Both* H_2EDTA^{2-} *and* $HEDTA^{3-}$ *contribute to the observed rate. The reactivity of* $HEDTA^{3-}$ *is about 100 times greater than that of* H_2EDTA^{2-}*. The mechanism of the exchange reaction is discussed within the framework of other Cu(II) ligand exchange reactions.*

Introduction

Ligand exchange reactions of copper(II) complexes have received considerable attention during the last decade. It is now known that distinctly different mechanisms can operate in different cases as shown by some recent studies.

In the cases of several Cu(II)–peptide complexes, the displacement of the peptide by EDTA [1] or by trien** [2] implies, at least in part, acid catalysis. The attack of an acid on the deprotonated peptide is required to assist in the breaking of a Cu(II)–peptide bond. This type of mechanism operates also in the substitution of Cu(II)–8-hydroxyquinoline and Cu(II)–biuret complexes by EDTA [3].

A fundamentally different mechanism is proposed for the exchange between $Cu(dien)^{2+}$ and tetren. It implies the rate determining loss of an axially bound water molecule from $Cu(dien)^{2+}$, and the rate constants decrease with increasing acidity due to the protonation of the incoming ligand [4]; this excludes, of course, any kind of acid catalysis.

We now wish to report the results of an investigation of the reaction of $Cu(dien)^{2+}$ with EDTA between pH 3.5 and 4.9, and discuss the mechanism in the framework of other Cu(II) ligand exchange reactions.

Experimental

The solutions were prepared from distilled water and reagent grade materials. The stock solution of Cu(II) perchlorate was obtained by dissolving CuO in perchloric acid. Dien (J. T. Baker) was purified by recristallization of its salt. The concentrations used were $[Cu^{2+}] = 2.0 \times 10^{-3}$ *M*, [dien] = 2.0×10^{-3} *M* to 8.0×10^{-2} *M*, EDTA = 1.0×10^{-2} *M* to 8.0×10^{-2} *M*.

The kinetics have been studied by stopped-flow spectrophotometry using a Durrum–Gibson instrument. The temperature of the drive syringes and of the cell-block was maintained at 25 ± 0.1 C. One of the syringes contained $Cu(dien)^{2+}$ and the other EDTA. The pH of the two solutions was different in some cases. In each case the pH of the experiment is that obtained after mixing. When changing the concentration of EDTA, preliminary experiments were needed to insure that the right pH was obtained. The contribution of EDTA to the ionic strength at each pH has been calculated using the acidity constants of the literature [6]; the ionic strength was brought to 0.5 *M* by means of $LiClO_4$.

The reactions were followed by the decrease in absorbance at $\lambda = 595$ nm. The signal of the photomultiplier is introduced in a data-acquisition system of our own conception [5] and the pseudo-first-order rate constants are obtained directly by means of a least-squares program using a Tektronix 31 calculator. The observed rate constants are the average of at least five experiments.

Results

Copper(II) and dien form two complexes in aqueous solution: $Cu(dien)^{2+}$ and $Cu(dien)_2^{2+}$. The stability of these complexes is known ($\log\beta_1 = 15.9$; $\log\beta_2 = 20.9$ [7]).

The kinetics of ligand exchange with EDTA have been investigated in the pH range 3.5–4.9. At lower pH the solubility of EDTA is the limiting factor while at higher pH the rates become too high to be studied by stopped-flow methods.

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**As usual: dien = diethylenetriamine, trien = triethylenetetramine, tetren = tetraethylenepentamine.

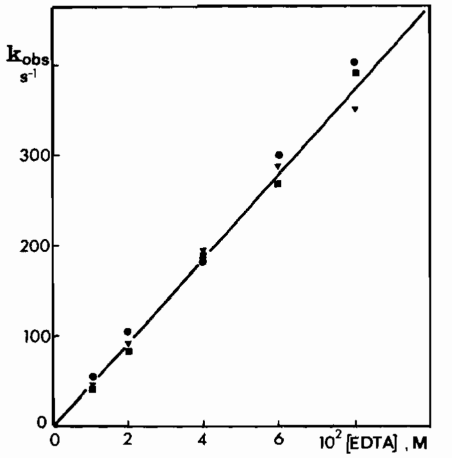

Figure 1. Pseudo-first order rate constants, k_{obs}, at different EDTA concentrations. T = 25 °C; pH = 4.0; μ = 0.5; $[Cu^{2+}]$ = 2.0 × 10^{-3} *M*. ● [dien] = 2.0 × 10^{-3} *M*; ■ [dien] = 4.0 × 10^{-3} *M*; ▲ [dien] = 8.0 × 10^{-3} *M*.

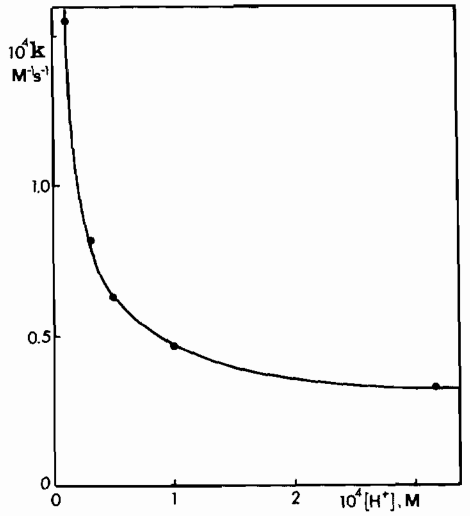

Figure 2. Influence of the acidity on the second order rate constant, k. T = 25 °C; μ = 0.5; $[Cu(dien^{2+})]$ = 2.0 × 10^{-3} *M*.

It can be shown, taking into account the protonation of dien, that between pH = 3.5 and 4.9 and at the concentrations of dien used ($\leqslant 8.0 \times 10^{-3}$ *M*), only $Cu(dien)^{2+}$ exists in significant concentrations. Furthermore the exchange reaction 1 is complete under these conditions due to the higher stability of $CuEDTA^{2-}$ ($\log\beta = 18.7$ [6])*.

$$Cu(dien)^{2+} + EDTA^{4-} \longrightarrow CuEDTA^{2-} + dien \qquad 1)$$

The rate of exchange has been studied at different concentrations of EDTA and different ratios of $[Cu^{2+}]/[dien]$. Typical results are shown in Figure 1. They indicate that excess dien has no effect on the rate constants. This is contrary to the case of the exchange between $Ni(dien)^{2+}$ and EDTA, where excess dien caused the rate to decrease [8]. However, as pointed out above, under our conditions there is no $Cu(dien)_2^{2+}$ formed. The pseudo first-order rate constant, k_{obs}, is proportional to the concentration of EDTA at a constant pH. This leads to a second-order rate law:

$$\frac{-d[Cu(dien)^{2+}]}{dt} = k[Cu(dien)^{2+}][EDTA]_{total} \qquad (2)$$

In equation 2, the second-order rate constant, k, represents the slope of the straight line in Figure 1. Its value increases with pH as shown in Figure 2.

These results have been interpreted taking into account the acid–base equilibria of EDTA. Between pH = 3.5 and 4.9 the major species in solution is H_2EDTA^{2-} having a contribution of more than 80% based on the pK_a's of the literature [6]. The increase of k with the pH is thus attributed to an increase in the concentration of $HEDTA^{3-}$, the latter having a higher rate of exchange than H_2EDTA^{2-}. At pH = 5 the contribution of hydroxylated species, such as $Cu(dien)OH^{+}$, can be safely excluded.

The interpretation of the data is therefore based on equation 3:

$$k_{obs} = k_{H_2EDTA}[H_2EDTA^{2-}] + k_{HEDTA}[HEDTA^{3-}] \qquad (3)$$

The calculation of the resolved rate constants has been achieved by weighted regression analysis using a Tektronix 31 calculator. The following rate constants have been obtained at 25 °C:

$$k_{H_2EDTA} = 3.3 \times 10^3\ M^{-1}\ sec^{-1};$$
$$k_{HEDTA} = 2.6 \times 10^5\ M^{-1}\ sec^{-1}$$

The agreement between k_{obs} and that calculated by equation 3 is satisfactory as shown in Table 1.

Discussion

There is a significant difference between this system and the $Ni(dien)^{2+}$–EDTA ligand exchange. In the latter case there is a fast addition of EDTA to $Ni(dien)^{2+}$ forming an intermediate mixed complex. It decomposes subsequently in $NiEDTA^{2-}$ and dien at a slower rate which is independent of the pH and of the concentration of EDTA [8].

Our results can be compared however to the $Cu(dien)^{2+}$–tetren ligand exchange [4]. In both

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*Although there is a difference in ionic strength between the literature data (0.1 *M*) and this work (0.5 *M*) its effect cannot alter these conclusions.

TABLE I. Observed and Calculated Rate Constants at Various pH and Concentrations.

T = 25 °C; [Cu(dien)$^{2+}$] = 2.0 × 10^{-3} *M*; μ = 0.5

pH	[EDTA]$_{total}$ *M*	$10^2 \times k_{obs}$ sec^{-1}	$10^2 \times k_{calc}$ sec^{-1}
3.5	1.0×10^{-2}	0.47	0.33
	2.0×10^{-2}	0.85	0.66
	3.0×10^{-2}	1.10	0.99
	4.0×10^{-2}	1.39	1.32
	5.0×10^{-2}	1.49	1.65
	6.0×10^{-2}	1.83	1.98
	8.0×10^{-2}	2.28	2.31
4.0	1.0×10^{-2}	0.54	0.46
	2.0×10^{-2}	1.13	0.92
	4.0×10^{-2}	1.83	1.84
	6.0×10^{-2}	3.06	2.76
	8.0×10^{-2}	4.03	3.68
4.3	1.0×10^{-2}	0.70	0.63
	2.0×10^{-2}	1.43	1.27
	3.0×10^{-2}	2.11	1.90
	4.0×10^{-2}	2.67	2.54
	5.0×10^{-2}	3.50	3.17
	6.0×10^{-2}	4.08	3.84
4.5	1.0×10^{-2}	0.77	0.82
	2.0×10^{-2}	1.49	1.64
	3.0×10^{-2}	2.17	2.46
	4.0×10^{-2}	3.72	3.28
4.9	1.0×10^{-2}	1.45	1.55
	2.0×10^{-2}	3.07	3.10

cases, only one reaction could be observed and it is second order. Furthermore, protonation of the incoming ligand reduces its reactivity in both cases: tetren > tetrenH$^+$ > tetrenH$_2^{2+}$ and HEDTA^{3-} > H_2EDTA^{2-}. The rate constants obtained for tetren are however higher than those for HEDTA^{3-}.

In Cu(II) ligand exchange reactions of polydentate ligands the mechanism necessarily implies a series of successive bond breaking and bond forming steps. The main question concerns then the choice and the nature of the slow step. In the case of Cu(dien)$^{2+}$ the bonds most likely to break first are the Cu(II)–H_2O bonds, the most weakly bound being the two axial H_2O molecules due to the distorted octahedral structure. In the case of the faster displacement of dien by tetren (k = 1.02 × 10^8 *M*$^{-1}$ sec^{-1} for unprotonated tetren), it was proposed that the rate determining step consists of an internal conjugate base enhanced (ICB) water loss from an axial position of Cu(dien)$^{2+}$ [4].

In our case the rate constants seem too low to be compatible with a rate determining loss of an axial water molecule. As a first approximation the rate constant for water loss, k_{-H_2O}, can be estimated, from water exchange in Cu(en)$_2^{2+}$ [9] using Eigen's mechanism to $k_{-H_2O} \geqslant 10^7$ sec^{-1}. The outer sphere complex Cu(dien)$^{2+}$–HEDTA^{3-} has a stability constant, K_{os}, higher than 1 *M*$^{-1}$ due to the strong electrostatic interaction*. These values lead to an overall rate constant: $k_{-H_2O}K_{os} \geqslant 10^7$ *M*$^{-1}$ sec^{-1} which is much larger than k_{HEDTA}.

It can therefore be assumed that the loss of the axial H_2O molecule and the formation of the first bond with an acetate group of HEDTA^{3-} is fast enough to allow this step to be at equilibrium.

The rate determining step can be the subsequent loss of the equatorial water molecule and formation of a second bond with HEDTA^{3-}. From then on the system becomes kinetically irreversible and there is unwrapping of dien and coordination by EDTA. This mechanism is shown by Scheme 1.

The rate constant for HEDTA^{3-} is given by equation 4:

$$k_{HEDTA} = K_1 k_2 \tag{4}$$

It does not seem reasonable to suppose that the replacement of the equatorial water molecule is also very fast and the slow step consists of the breaking of the first nitrogen–copper bond of dien. The equilibrium concentration for intermediate II, having two copper–EDTA bonds, should be high enough to be observed or at least to produce a deviation from first-order kinetics with respect to EDTA.

The loss of an equatorial water molecule in polyamine–Cu(II) complexes has a rate constant of about 2.5 × 10^5 sec^{-1} at 25 °C [10]. This value seems compatible with our results and if substituted for k_2 in equation 4 a value of $K_1 \cong 1$ *M*$^{-1}$ is obtained for HEDTA^{3-}. The smaller rate constant for H_2EDTA^{2-} can be largely accounted for by the decrease of the electrostatic contribution in the stability of intermediate I and if it is assumed that the value of k_2 does not change, $K_1 \cong 0.013$ *M*$^{-1}$ is obtained for this species.

Although in the formation of intermediate I steric effects do not play a role, it is probable that coordination by the tertiary nitrogen of EDTA will be sterically hindered.

This effect has been observed in the displacement of Cu(II)–tripeptide complexes by EDTA^{4-} which has a significantly lower rate constant than the corresponding exchange with trien [2]. Therefore, the value of k_2 used should be regarded as an upper limit and, consequently, the value of K_1 as a lower limit.

Finally, it is clear that the contribution of an acid catalysed path is negligible. This is quite significant because in this case, unlike in several other studies at higher pH values, H_2EDTA^{2-}, H_3EDTA^- and even H_3O^+ are present at reasonably high concentrations. There is however a basic difference between

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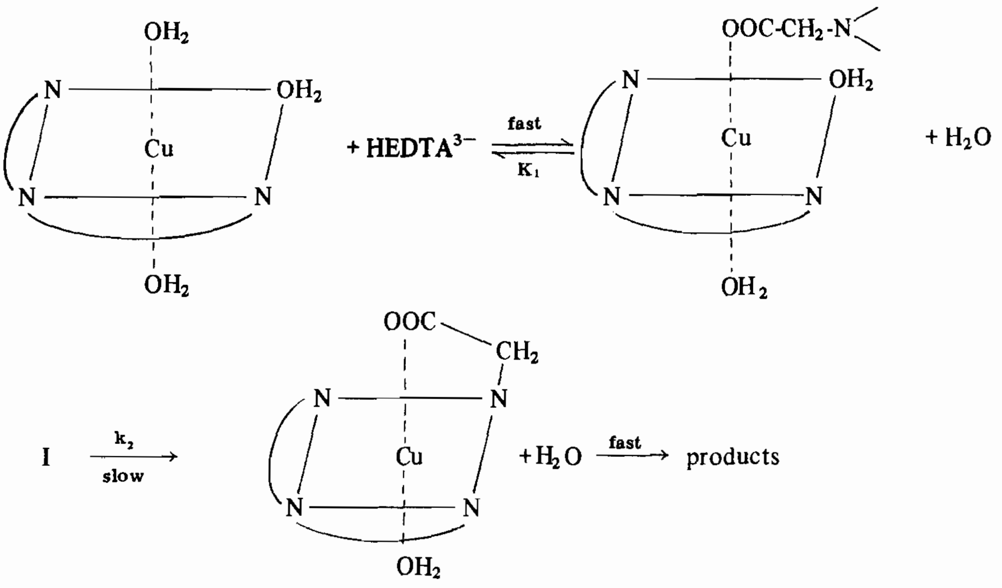
*The more exact value of K_{os} cannot be calculated at an ionic strength as high as 0.5 *M*.



(I)

(II)

Scheme 1

$Cu(dien)^{2+}$ and the Cu(II)–peptide complexes, Cu(II)–biuret, Cu(II)–oxine, 8-hydroxyquinoline where different acid catalysed mechanisms have been proposed: namely there is no available doublet in $Cu(dien)^{2+}$ to which acids could transfer a proton. This can only happen after the first copper–nitrogen bond is broken, but at that stage the rate determining step has already taken place.

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