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Ligand Effect on Oxidation Rates of Cysteine by Iron (III) Complexes

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Kinetics of oxidation of cysteine by iron(III). complexes of urea, $C_2O_4^{-2}$, H_2O,–NCS⁻, CN⁻, acac, phen, and EDTA were studied by stopped-flow spectrophotometry. Kinetic measurements were done at constant ionic strength in aqueous solutions at 25°C. Reaction rates were measured spectrophotometrically by following the change in the oxidizing agent concentration under pseudo-first order conditions in which the concentration of cysteine was between one and two orders of magnitudes greater than that of the iron (III) complex. The results showed that the observed rate of the redox reaction depended inversely on both the strength of the ligand in the iron (III) complex and its size.

Key words: Cysteine, Iron (III), Oxidation

Introduction

Oxidation-reduction or electron transfer reactions of complexes are important in coordination chemistry. These reactions have been widely studied by different methods, including stopped-flow spectrophotometry, chemical analysis of products and the use of radioactive and stable isotopes tracers. The methods involved alongwith much of the data produced in this field have been discussed elsewher (Meyer and Taube 1987). Of great interest, are the oxidation reactions of amino acids which have a particular importance both chemically and biologically. The kinetics of their oxidation with several oxidizing agents have been extensively studied (Kudesia and Sharma 1981; Hogale *et al* 1986; Narayanan and Srinivasam 1986; Gowda and Vijayalakshmi 1988; Gowda and Rao 1988; Rama chanadram *et al.* 1988; Yaamuna *et al.* 1988; Laloo *et al* 1990; Reddy *et al* 1990; Sharma and Bielski 1991; Abdel-Halim and Al-Lawatia 1994; Karim and Mahanti 1994). A recent publication (Basolo and Person 1967) from this laboratory dealt with the oxidation of some amino acids by transition metal complexes. The kinetics of amino acids oxidation by quinolinium dichromate was studied by (Gowda and Vijayalakshmi 1988) while a free radical mechanism for the oxidation of some amino acids was reported (Karim and Mahanti 1992). However, the effect of the nature of the ligand in a transition metal complex on the rate of oxidation of amino acids has not been studied before.

In the present work, iron (III) complexes of several lignds were prepared. Ligands of various sizes and various electron donating/accepting abilities were chosen: urea, $C_2O_4^{2-}$, H_2O, -NCS⁻,CN⁻, acac, phen, and EDTA. The kinetics of oxidation of cysteine by these complexes in aqueous solutions at 25°C have been studied using stopped-flow spectrophotometry. The effect of the nature of the ligand in the complex on the rate of cysteine oxidation is presented.

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Experimental

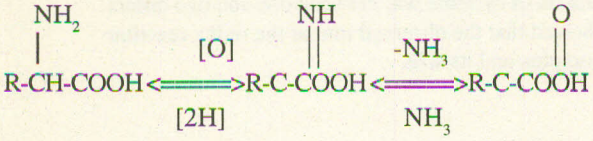
Preparation and Characterization of Iron(III) Complexes: Cysteine and potassium hexacynoferrate were both BDH (minimum assay 99%) and used without further purification. The other iron(III) complexes used in the study (Table 1), were prepared as described in the literature (Nicholls *et al* 1975) and purified by double recrystallization. The complexes were characterized by different physical and spectroscopic methods. Elemental analysis for the complexes, were performed (Butterwoth Laboratories, UK). The percentage of iron was determined by atomic absorption using (Spex Model Alpha 4) and the existence of Fe(III) was confirmed by Mossbaur room temperature measurements using a Co^{57} source with a spectrometer driven in the constant acceleration mode, interfaced to a PC- based multichannel analyzer.

Kinetics Measurements: A stopped-flow spectrophotometer (Hi-Tech Scientific Model SF-16) was used for kinetics measurements. The reaction was maintained by following the decrease in absorbance of the iron (III) Complex with time at a predetermined wavelength. The absorption spectral curves for each iron (III) complex and for its mixture with cysteine after the completion of the reaction were recorded on the Diode-Array UV/VIS spectrophotometer (HP Model 8453). The reaction progress was monitored at the wavelength of maximum absorbance difference between the absorption of the complex and the mixture. The monochromator of the stopped-flow apparatus was tuned to this wavelength and the reaction rate was measured. The wavelengths chosen for the

various reactions are shown in (Table 1). All oxidation reactions were studied under pseudo-first order conditions. The concentration of the amino acid was chosen to be 1-2 orders of magnitude larger than that of the iron (III) complex. The ionic strength of the solution was kept constant at 0.50 mol dm^{-3} using $NaC1O_4$. The temperature of the solution was maintained at 25±0.1°C.

Results and Discussion

Oxidation of amino acids leads to formation of keto acid, as shown below:



The stoichiometry for the oxidation reaction of the amino acid (A.A.) by the iron (III) complex (TMC) is as follows

A.A. + 2 TMC——> Products (2)

The rate of the reaction, R, is given by

$R=k[A.A.]^a[TMC]^b$ (3)

where 'k' is the reaction rate constant and a,b are the orders of the reaction with respect to the concentration of A. A. and TMC, respectively. For this kind of reactions, the rate is dependent on the first power of the concentrations of substrate and oxidant (Hogale *et al.* 1986; Laloo *et al.* 1990; Abdel Halim and Al-Lawatia 1994; Karim and Mahanti 1994), i.e., a=b=1. At pseudo-first order conditions, in which [A.A.]>> [TMC], the concentration of the amino acid is essentially constant throughout the reaction. The reaction rate is then given by

$$R \approx \frac{d[TMC]}{dt} = k_{obs}[TMC] \quad (4)$$

where 'k'_{obs} is the observed rate constant for the reaction given by

$k_{obs}=k[A.A.]$ (5)

For a first-order dependence of the reaction of [TMC], the experimental absorbance-time data pairs were fit to the exponential function

$A_t=(A_o-A_\infty)\exp(-k_{obs}t)+A_\infty$ (6)

Where A_t i∞s the absorbance of the iron (III) complex at time through the reaction, A_o and A_∞ are the initial and the final absorbance of the complex. For most of the reactions, $A_\infty \approx O$, and the experimental results fit the simple equation.

$A_t=A_o \exp(-k_{obs}t)$ (7)

The value of 'K'_{obs} can be obtained from a plot of 1n A_t versus time. A plot of 'K'_{obs} versus [A.A.] gives the value of the rate constant, k. Kinetics results for the oxidation of cysteine by various iron (III) complexes are shown in Table 1.

Table 1also shows that the rate constant for the oxidation of cysteine varies widely with the type of the ligand in the iron (III) complex. For outer-sphere reactions, like those studied in the present work, the rate of electron transfer in complex should depend on the nature of the ligand in addition to many other factors (such as the nature of the metal ion and its oxidation state, the rate of substitution in the coordination sphere of the reactants, the match of energy levels of the two reactants, and the solvation of the two reactants). The nature of the ligand determines the ability of the electron(s) to tunnel through it to reduce the metal ion. Ligands with electrons (donors or acceptors) provide better pathways for tunneling, and hence faster redox rates than ligands with no extra lone pairs and no low - lying antibonding orbitals are expected. The rate of electron transfer through ligands with strong acceptor effect, like CN, is slower than the transfer rate through weaker π acceptor ligands or π donor ligands. The presence of vacant π* in strong π acceptor ligands makes electron transfer harder due to the possiblity of the electron getting "trapped"or"captured", momentarily, in the vacant π* of the ligand, which is unlikely to occur in electrons "rich" π or δ, donor ligands. This explains the drop in the reaction rate constant for the first five complexes in (Table 1). Since strong acceptors are strong

Table 1
Rates of oxidation of cysteine by various iron(III) complexes in aqueous medium at 25°C and ionic strength=0.50 mol dm^{-3}

Complex	Ligand	λ (nm)	k ($dm^3\ mol^{-1}\ s^{-1}$)
$[Fe(urea)_6]C1_3$	urea	490	3100
$K_3[Fe(C_2O_4)_3].3H_2O$	$C_2O_4^{2-}$	518	2300
$[Fe(H_2O)_6]C1_3$	H_2O	550	450
$K_3[Fe(SCN)_6]$	—NCS–	459	250
$K_3[Fe(CN)_6]$	CN–	420	250
$Fe(acac)_3$	acac	462	10
$[Fe(phen)_3](ClO_4)_3.H_2O$	phen	510	4.0×10^{-3}
$Na[Fe(EDTA)].3H_2O$	EDTA	380	very slow

ligands, due to the possiblity of back bonding, the strength-order for ligands shown in Table 1 is as follows:

urea < $C_2O_4^{2-}$ < - NCS^- < acac < EDTA < phen < CN^-.

Therefore, one can conclude that the redox rate decreases as the ligand strength in the spectrochemical series increases.

Table 1 also shows another important factor that affects the rates of the redox reaction. Among donor or acceptor ligands, the rate of reaction decreases as the size of the ligand increases. The large size of a bulky ligand, such as phen and EDTA, makes electron tunneling through it hard and slow. Thus the rate is slower. The transition probability of an electron between two gas molecules as calculated from time- dependent perturbation theory, is given (Zemer 1951; Allyn and Bacon 1992).

$$P(t) = \sin^2 (2\pi H_{12} t/h) \quad (8)$$

Where 't' is time,'h' is Planck's constant and 'H'_{12} is the exchange integral, or the interaction energy, between the initial state orbital described by the wave function ϕ_1 and the final state orbital described by the wave function ϕ_2. It is given by

$$H_{12} = \pi \int \phi_1 H \phi_2 \, dt \quad (9)$$

Where *'H'* is the Hamiltonian of the transferring electron. The interaction energy depends on the extent to which the orbitals centered on the two interacting particles overlap each other. In solutions, electronic transfer between two particles will be hindered by the presence of solvent molecules because such molecules prevent the extension into space of the orbitals on the exchanging particles. Also, the ligands of a complex ion will act as good insulating groups for electrons and orbitals of the central metal ion. Considerable insight into the electron transfer process in solution is given by the electron tunneling theory developed by (Weiss 1954; Marcus *et al.* 1954).The result is that the tunneling of the electron in solution is related to the extension in space of the electronic orbitals in connection with gas-phase transfer process. The probability of transfer for an electron leaking through a potential energy barrier across the ligand around the central metal ion is given by the Gamow equation (Mott and Sneddon 1948).

$$k = \exp\{-(8\pi d/3h)[2m(U-W]^{1/2}\} \quad (10)$$

where 'k' is known as the transmission coefficient, 'U' is the height of the potential barrier, 'W' is the kinetic energy of the electron, 'm' is the mass of the electron, 'd' is the width of the barrier at the height of the penetration. As an approximation one may consider U to represent the potential of an electron moving in the coulomb field of two ions. Therefore, U is given by the coulomb equation

$$U = \frac{q_1 q_2}{Dd} - \frac{eq_1}{Dx} - \frac{eq_2}{D(d-x)} \quad (11)$$

where 'q'_1 and 'q'_2 are the charges of each of the ions (the iron(III) complex and cysteine respectively), 'D' is the dielectric constant of the solvent, and 'x' is the distance of the electron from the cation of charge q_1, which depends on the size of the ligand around the central metal ion. The net charge on the amino acid q_2 is zero. Therefore, equation (10) reduces to the simple form

$$U = -\frac{eq_1}{Dx} \quad (12)$$

The rate constant,'k' (T), for electron transfer is given by the transition state theory (Gardiner 1969) as

$$k(T) = k \frac{kT}{h} e^{-\Delta G^*/kt} \quad (13)$$

where 'T' is the reaction temperature, 'k' is the Boltzmann's constant, and 'G*' is the free energy change at the activated complex.

Equations (10), (12) and (13) show that as the size of the ligand in the complex (i.e. the distance from the electron donor (cysteine) to the center of the electron acceptor (iron (III), increases, the transmisson coefficient and hence the rate constant decreases. This is in agreement with the results shown in (Table 1).

In conclusion, the rate of oxidation of cysteine by various iron(III) complexes was found to depend inversely on both the strength of the ligand in the complex and its size. The effect of the size was found to be predominant.

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