Zinc(II) does not react with 3,5-di-*t*-butylpyrocatechol in mildly alkaline solution but forms soluble hydroxo complexes in the pH range 7–8 with a single, steep inflection at $m = 2$. Apparently the monoanion of the ligand is too weak and the dianion too low in concentration to compete effectively with hydroxide for the metal ion. Pyrocatechol, on the other hand, being somewhat more acidic, reacts readily and completely forming an insoluble white complex.

The original interest in using manganese(II)–3,5-di-*t*-butylpyrocatechol as a model system for the autoxidation of pyrocatechols stemmed mainly from the reported high yield of relatively stable *o*-quinone monomer at room temperature,[40] suggesting that a single reaction pathway is being followed. The fact that complexation of the model system in mixed solvent is slow may be fortuitous in the sense that experiments can be designed which allow comparison between the efficiency of the free metal ion catalyzed and metal–ligand chelate autoxidation reactions. The exceptionally high stability found for manganese(II) chelates of catechols may be quite helpful in assisting metal ion mediated oxidation of the ligand.

(40) R. R. Grinstead, *Biochemistry*, 3, 1308 (1964).

The Kinetics of the Reaction of Iron(III) Chelates of Aminopolycarboxylic Acids with Ascorbic Acid[1a]

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Abstract: The kinetics of the oxidation of ascorbic acid by the Fe(III) chelates of diethylenetriaminepentaacetic acid (DTPA), 1,2-cyclohexanediaminetetraacetic acid (CDTA), ethylenediaminetetraacetic acid (EDTA), and N-hydroxyethylethylenediaminetriacetic acid (HEDTA) have been investigated at 25 and 0.4°. In the pH range 1.8–3.45 the rates decrease in the sequence, Fe(III)–HEDTA > Fe(III)–EDTA > Fe(III)–CDTA > Fe(III)–DTPA. The differences in the rates of oxidation and the activation parameters of the oxidation reaction are discussed in terms of the charges on the oxidants.

There has been much interest recently in the study of ferric complexes as oxidants in electron-exchange reactions. The use of ferricyanide as an oxidant has been extensively reviewed by Thyagarajan.[2] The kinetics of the oxidation of Fe(II) ions by tris(1,10-phenanthroline)iron(III) ions and by a number of Fe(III) complexes of substituted 1,10-phenanthrolines, 2,2′-bipyridine, and 2,2′,2″-terpyridine have been reported by Sutin and coworkers.[3] In these previous studies, the oxidants were ferric complexes which have delocalized electrons and possess reduction potentials higher than that of the aquo ion. Ferric complexes of aminopolycarboxylic acids, which possess reduction potentials lower than that of the aquo Fe(III) ion, have been generally neglected, with the exception of the Fe(III)–ethylenediaminetetraacetic complexes used by Grinstead[4] as an oxidant in the model peroxidase system for the oxidation of the salicylate ion.

The present investigation was undertaken to study the ferric chelates of aminopolycarboxylic acids as oxidants in kinetic studies on the oxidation of ascorbic acid. The present work is part of a general study of the catalytic effects of metal ions and metal chelates in oxidation reactions.

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(2) B. S. Thyagarajan, *Chem. Rev.*, 58, 439 (1958).

(3) (a) N. Sutin and B. M. Gordon, *J. Am. Chem. Soc.*, 83, 70 (1961); (b) M. H. Ford-Smith and N. Sutin, *ibid.*, 83, 1830 (1961).

(4) R. Grinstead, *ibid.*, 82, 3472 (1960).

Experimental Section

Reagents. The L-ascorbic acid employed was Kodak White Label grade and was used without further purification. Samples of ethylenediaminetetraacetic acid (EDTA), N-hydroxyethylethylenediaminetriacetic acid (HEDTA), *trans*-1,2-diaminocyclohexanetetraacetic acid (CDTA), and diethylenetriaminepentaacetic acid (DTPA) were recrystallized from water and dried under vacuum. Purity of the various ligands was determined by potentiometric titration of dried samples, with and without the addition of excess calcium ion, with carbonate-free sodium hydroxide. Solutions of iron(III) nitrate, prepared from Fisher analytical grade materials, were standardized by titration with potassium permanganate and also by titration with EDTA,[5] with Tiron as the indicator. The results of the two methods agreed within the experimental error.

Potentiometric Measurements. The dissociation constants of L-ascorbic acid at 25 and 0.4° were determined by potentiometric titration in a medium of 0.10 *M* ionic strength containing potassium nitrate, with a Beckman Model G pH meter fitted with extension glass and calomel electrodes. The pH meter was calibrated in terms of hydrogen ion concentration with acetic acid buffer, as well as with standard HCl and NaOH. The data given by Harned and Owen[6] were used to calculate the hydrogen ion concentration in the presence of the buffer. The experimental solution of ascorbic acid was prepared from air-free distilled water, and an atmosphere of purified nitrogen was maintained in the titration cell to avoid any disturbing effects resulting from oxidation by molecular oxygen.

Kinetic Measurements. The pH value of the experimental solution was maintained constant during each run by a Beckman Model K automatic titrator fitted with extension glass and calomel electrodes. It was calibrated with acetic acid buffer and by titration of standard HCl and NaOH solutions. The ionic strength of

(5) G. Schwarzenbach, "Complexometric Titrations," Interscience Publishers, Inc., New York, N. Y., 1958, p 72.

(6) H. S. Harned and B. B. Owen, "Physical Chemistry of Electrolytic Solutions," Reinhold Publishing Corp., New York, N. Y., 1950, pp 485, 578.

the experimental solution was maintained at approximately 0.10 M with KNO_3. After the pH was adjusted to the desired value, a stream of oxygen-free nitrogen was passed through the reaction cell. The nitrogen was purified by passing it successively through wash bottles containing chromous chloride and alkaline pyrogallol, and finally through water maintained at the same temperature as the reacting solution.

The rate of oxidation was measured by the amount of dehydroascorbic acid produced during the course of oxidation. The analytical procedure employed for the estimation of dehydroascorbic acid was that established by Roe.[7]

Results

Equilibrium Studies. The pK values of ascorbic acid were calculated from the titration curves at 25 and 0.4°. The dissociation constants K_1 and K_2 at 25° are respectively 9.16×10^{-5} and 4.57×10^{-12}; and at 0.4°, 3.24×10^{-5} and 1.91×10^{-13}.

Kinetic Studies. The over-all stoichiometry of the oxidation of ascorbic acid, $C_6H_8O_6$ (H_2A), by a ferric chelate, FeL^{3-n}, may be represented by

$$C_6H_8O_6 + 2Fe^{III}L^{3-n} \longrightarrow C_6H_6O_6 + 2Fe^{II}L^{2-n} + 2H^+$$

where H_nL represents the ligand combined with the metal ion.

The order of the reaction was determined by varying the concentration of the reactants. The reaction was found to be generally first order with respect to the concentrations of each of the reactants. Second-order rate constants were determined from plots of log $[b(2 - 2x)/a(b - x)]$ *vs.* time and multiplying the slopes by $2.303/(a - 2b)$, where a and b are the initial concentrations of metal chelate oxidant and ascorbic acid, respectively, and x is the concentration of the product (dehydroascorbic acid) at time t. In the case of the oxidation of ascorbic acid by Fe(III)–EDTA, typical variations with reactant concentration of the second-order rate constants were studied over a wide range of the concentrations of the reactants. These rate constants were found to be independent of the initial concentrations of Fe(III)–EDTA and ascorbic acid over a wide range. The orders of the reactions for the oxidation of ascorbic acid by Fe(III)–DTPA,Fe (III)–CDTA, and Fe(III)–HEDTA were also found to be first order with respect to each reactant. The results for these chelates conformed to the integrated second-order rate equation within ±1–2%.

In all the experiments with metal chelate compounds as oxidants, a fourfold excess of free ligand was added to the metal chelate species. Under these conditions, the only reaction which was assumed to take place is the reversible reduction of the Fe(III) chelate species to the Fe(II) chelate form. The rates of oxidation of ascorbic acid by Fe(III) chelate oxidants are given in Tables I and II at 25 and 0.4°. In the pH range 1.80–3.45, the rates decrease in the order Fe(III)–HEDTA > Fe(III)–EDTA > Fe(III)–CDTA > Fe(III)–DTPA.

Table I. Rate Constant[a] (M^{-1} sec^{-1}) for the Oxidation of Ascorbic Acid by Fe(III) Chelates

−Log [H⁺]	Fe(III)–DTPA	Fe(III)–CDTA	Fe(III)–EDTA	Fe(III)–HEDTA
1.80	0.60×10^1	0.80×10^1	0.23×10^2	1.23×10^2
2.10	1.00×10^1	1.50×10^1	0.46×10^2	2.51×10^2
2.45	2.20×10^1	3.70×10^1	1.01×10^2	5.30×10^2
3.20	7.60×10^1	9.40×10^1	3.37×10^2	18.0×10^2
3.45	13.6×10^1	20.1×10^1	6.20×10^2	...

[a] Standard deviation in $k = \pm 0.04\ M^{-1}$ sec^{-1}; 25°, $\mu = 0.10\ M$ (KNO_3).

Table II. Rate Constants[a] (M^{-1} sec^{-1}) for the Oxidation of Ascorbic Acid by Fe(III) Chelates

−Log [H⁺]	Fe(III)–DTPA	Fe(III)–CDTA	Fe(III)–EDTA	Fe(III)–HEDTA
1.80	...	...	0.40×10^1	0.19×10^2
2.10	02.0×10^1	0.30×10^1	0.80×10^1	0.37×10^2
2.45	0.40×10^1	0.60×10^1	1.60×10^1	0.90×10^2
3.00	1.40×10^1	2.10×10^1	5.80×10^1	2.20×10^2
3.45	2.60×10^1	5.20×10^1	1.56×10^1	7.60×10^2

[a] Standard deviation in $k = \pm 0.04\ M^{-1}$ sec^{-1}; 0.4°, $\mu = 0.10\ M$ (KNO_3).

Each ionic species of ascorbic acid may be considered to react independently with the metal chelate oxidant. On this basis, the rate law may be expressed in the form

$$k = \left(k_1 + k_2\frac{K_1}{[H^+]}\right)\left(\frac{[H^+]}{[H^+] + K_1}\right) \quad (1)$$

where k_1 and k_2 are the rates for the oxidation of the un-ionized and monoionic forms of ascorbic acid by the metal chelate, and K_1 is the first acid dissociation constant of ascorbic acid. In acid solution where ascorbic acid is not appreciably dissociated, H_2A may be approximately taken as the total substrate concentration.

$$k = (k_1 + k_2K_1/[H^+]) \quad (2)$$

A plot of the rate constant, k, against the reciprocal of hydrogen ion concentration gives a straight line with zero intercept ($k_1 = 0$) and slope equal to k_2k_1. The values of k_2 listed in Table III were obtained in the pH range 1.8–3.45 from the slopes of straight lines of the type illustrated in Figure 1 for 0.4°. Similar plots were obtained at 25°. The results indicate that the metal chelate oxidant is active only in the oxidation of

Table III. Specific Rate Constants[a] (M^{-1} sec^{-1}) for the Interaction of Fe(III) Chelate with the Ionic Species of Ascorbic Acid

Chelate	k_2 (25°)	k_2 (0.4°)
Fe(III)–DTPA	0.88×10^3	0.44×10^3
Fe(III)–CDTA	1.30×10^3	0.63×10^3
Fe(III)–EDTA	4.0×10^3	1.86×10^3
Fe(III)–HEDTA	21.5×10^3	9.0×10^3

[a] Standard deviation in $k = \pm 0.04\ M^{-1}$ sec^{-1}.

Table IV. Activation Parameters[a] of the Oxidation of Ascorbic Acid by Fe(III) Chelates in the Absence of Oxygen

Oxidant	$\Delta H^{\ddagger}$, kcal mole^{-1}	$\Delta S^{\ddagger}$, cal deg^{-1} mole^{-1} [b]	$\Delta F^{\ddagger}$, kcal mole^{-1} [b]
Fe(III)–HEDTA	+5.0 ± 0.2	−21 ± 1	+11.3 ± 0.2
Fe(III)–EDTA	+4.5 ± 0.2	−27 ± 1	+12.6 ± 0.2
Fe(III)–CDTA	+4.3 ± 0.2	−30 ± 1	+13.2 ± 0.2
Fe(III)–DTPA	+4.1 ± 0.2	−32 ± 1	+13.6 ± 0.2

[a] For the reaction between metal chelate and monoanion of ligand, corresponding to k_2; $\mu = 0.10\ M$ (KNO_3). [b] 25°.

(7) H. Roe, "Methods of Biochemical Analysis," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1954.

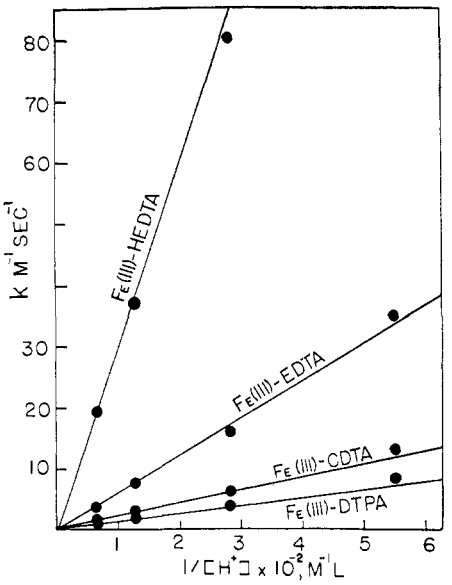

Figure 1. Dependence of rate on hydrogen ion concentration for the oxidation of ascorbic acid by Fe(III) chelate oxidants at 0.4°, ionic strength = 0.10 M (KNO_3).

the ascorbate anion, HA^-. The activation parameters of the oxidation of ascorbic acid by ferric chelate compounds are given in Table IV.

Discussion

Evidence of the Nature of the Activated Complex. The reactions of ascorbic acid with ferric chelates were found to be nicely first order with respect to the substrate and the oxidant. Since variation of the concentration of excess ligand was found to have no effect on the rate, it was concluded that the activated complex involves the metal chelate as a whole and not the free (aquo) metal ion. This conclusion is also supported by similar rate studies of ferric chelates in the presence of oxygen,[8] where it is found on the basis of the kinetic evidence that the active catalyst is the metal chelate compound.

The assignment of the metal chelate compound as the reactive species requires further consideration of the nature of these Fe(III) chelates in solution. Use of equilibrium data taken from standard compilations in the literature (*e.g.*, "Stability Constants," published by The Chemical Society) demonstrates that the free metal ion concentration is indeed insignificantly low under the conditions employed in this investigation (for all chelates the highest metal ion concentration at $-\log [H^+] = 3$ is 2×10^{-9} M). Moreover, in the pH range employed, there are no significant concentrations of protonated or hydrolyzed forms of the metal chelate compounds. Hence it seems probable that the only reasonable reactive species are the monoprotonated substrate and the normal form of the ferric chelate, FeL^{3-n}. The reaction of the monoprotonated substrate, HL^-, with the normal form of the ferric chelate is kinetically equivalent to the reaction of the undissociated species of ascorbic acid, H_2L, with the hydrolyzed form of the ferric chelate, $Fe(OH)L^{2-n}$; however, these latter two species are considered less probable as reaction intermediates.

(8) M. M. Taqui Khan and A. E. Martell, *J. Am. Chem. Soc.*, **89**, 7104 (1967).

The mechanism of the reaction therefore seems to be either a loose combination between the ascorbate anion and the oxidizing agent, with subsequent electron transfer to metal chelates, or a quantum mechanical tunneling process.[9,10] The kinetic data available in the present kinetic studies cannot distinguish, however, between the two possibilities. Evidence in favor of the former possibility seems to be the variation of rate with the reduction potential of the metal chelate oxidant. The rates decrease in the order Fe–HEDTA > Fe–EDTA > Fe–CDTA > Fe–DTPA. The reduction potentials of the metal chelate oxidants shown in Table V indicate a decrease in rate with decreasing reduction potential and increasing stability of the metal chelate compound.

Table V. Comparison of the Rate Constants for the Oxidation of Ascorbic Acid and Standard Reduction Potentials of the Metal Chelates[a]

Oxidant	Rate constant, M^{-1} sec^{-1}	Std reduction potentials, V
Fe(III)–HEDTA	0.53×10^3	+0.30
Fe(III)–EDTA	1.01×10^2	+0.10
Fe(III)–CDTA	3.70×10^1	+0.08
Fe(III)–DTPA	2.20×10^1	+0.06

[a] At 25°, $-\log [H^+] = 2.45$, $\mu = 0.10$ M (KNO_3).

The standard reduction potentials shown in Table V were calculated at pH 2.45 [$\mu = 0.10$ M (KNO_3)] at 25° with the help of the equation

$$E_C^\circ = 0.059 \log K^r/K^\circ - E_S^\circ \qquad (3)$$

where Es° is the corresponding standard reduction potential for the aquo ions and where Ec° is the standard potential for the reaction

$$Fe^{III}L + e \longrightarrow Fe^{II}L$$

The equations are written with the sign convention given by Latimer.[11] The terms K^r and K° in eq 3 are the stability constants for the oxidized and reduced forms of the iron chelate, respectively.

The oxidation potential of the ascorbic acid couple (for the reaction $H_2A \rightarrow A + 2H^+ + 2e$) is 0.390 V.[12]

Cupric chelates were found to be far less active as oxidants than ferric chelates in the absence of oxygen. This may be expected on the basis of a much lower (more negative) value of the reduction potentials of the Cu(II) chelates, compared with those of the iron(III) chelates.

Activation Parameters. The slight decrease in $\Delta H^\ddagger$ that occurs with increasing stabilities of the metal chelates is unexpected and must be considered anomalous. The activation parameters listed, however, show that by far the greatest effect of constitution is on the entropy of activation.

The large negative value of the entropy of activation correlates with the interpretation that the reaction takes place *via* combination of the metal ion in the chelate

(9) R. J. Marcus, B. Zwolinski, and H. Eyring, *J. Phys. Chem.*, **58**, 432 (1954).

(10) R. A. Marcus, *J. Chem. Phys.*, **24**, 966 (1956); **26**, 872 (1957); **43**, 679 (1965); *Can. J. Chem.*, **37**, 155 (1959); *J. Phys. Chem.*, **67**, 853 (1963); *Ann. Rev. Phys. Chem.*, **15**, 7 (1964).

(11) W. M. Latimer, "Oxidation Potentials," 2nd ed, Prentice-Hall, Inc., Englewood Cliffs, N. J., 1952.

(12) E. G. Ball, *J. Biol. Chem.*, **118**, 219(1937).

compound with the negative form of the substrate. The low probability of the reaction is to be expected from the highly polar nature of the metal chelate, in which the negative carboxylate donors are concentrated near the active site of the metal ion which is available for combination with the ascorbate ion. The fact that an increase in the negative charge of the ligand attached to the Fe(III) ion correlates with a further increase in the negative value of the entropy of activation is in accord with this concept.

The slight differences in both the rates and entropies of activation for the CDTA and DTPA chelates are considered due to the characteristically different structure of CDTA. The rigidity imposed on the coordination sphere of Fe(III) by the presence of the cyclohexane ring in the CDTA ligand would be expected to make the entropy of activation for the Fe(III)–CDTA reactant somewhat more negative than that of the corresponding EDTA chelate, which occupies what is considered a more normal position in the series of chelates studied.

Isotopic Ligand-Exchange Studies on $[Re(amine)_4O_2]^+$-Type Ions

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Abstract: The rates of isotopic exchange of $[Re(amine)_4O_2]^+$ with amine are reported for amine = $^1/_2$(en), CH_3NH_2, and pyridine. With en and CH_3NH_2 the exchange follows the rate law $R = k[complex] + k_1[complex][OH^-]$. At 25° and $\mu = 0.10$, the values are $k = 8.5 \times 10^{-7}$ sec^{-1} and $k_1 = 6.9 \times 10^{-2}$ M^{-1} sec^{-1} (en), and $k = 9.4 \times 10^{-6}$ sec^{-1} and $k_1 = 4.33 \times 10^2$ M^{-1} sec^{-1} (CH_3NH_2). With pyridine the rate R is independent of $[OH^-]$ and of [py] and, at 25° and $\mu = 0.10$, $R = k$[complex], where $k = 4.17 \times 10^{-5}$ sec^{-1}. The rate of deuterium exchange on the amine hydrogens is extremely rapid. Exchange measurements have been made on the CN^-–$[Re(CN)_4O_2]^{3-}$ and Cl^-–$[ReCl_4O(OH_2)]^-$ systems. Both reactions are complete in less than 1 min under the conditions employed. A mechanism is postulated which includes two paths of exchange: (a) dissociation assisted by solvent and (b) amide formation followed by *trans* dissociation. Preliminary results are reported for the oxygen isotopic exchange $[Re(X)_4O_2]^n + H_2O$, where X = $^1/_2$(en), CN^-, and py.

Studies on the complexes of Re(III), Re(IV), and Re(V) have been expanding rapidly in recent years, but, although isotopic exchange studies are extremely valuable in the elucidation of reaction mechanisms, only a few exchange studies on these complexes have been reported.[2]

The study of the $[ReBr_6]^{2-}$–Br^- exchange[2a] was limited to high HBr concentrations because of the instability of the complex at the high temperatures required for measurable exchange. The results showed that the over-all rate increased linearly with [HBr] above 4 M and with complex concentration. With the $[ReCl_6]^{2-}$–Cl^- exchange,[2b] the observations paralleled those of the Br^- system, and a mechanism involving acid and solvent assisted Cl^- dissociation was suggested.

A study of the oxalate^{2-} exchange with $[Re_2O(OH)_2(C_2O_4)_4]^{4-}$ and $[Re_2O(OH)_6(C_2O_4)_2]^{4-}$ was reported.[2c] In the former system no exchange was observed after 200 hr at 20°, but in the latter the exchange was independent of $[C_2O_4]^{2-}$ and decreased with increasing [complex]. No pH-dependent studies were made. The author does not explain the peculiar dependence of the rate on [complex] but deduces from the ligand independence and E_a that an intermediate aquo complex is involved in the exchange. Since the structures of these ions are not known, this study is of little value in predicting the behavior of other rhenium complexes.

We have recently reported[3,4] some properties of $[Re(amine)_4O_2]^+$ ions (amine = $^1/_2$(en), CH_3NH_2, py). These complexes are of known *trans*-oxygen structure and are suitable for isotopic exchange studies since their rates are measurable over a wide range of conditions. Complexes containing the ligands en, CH_3NH_2, py, CN^-, and Cl^- were chosen so the effects of a chelate ring, an aromatic ring, π bonding, and the presence and absence of hydrogens on the coordinated nitrogens could be evaluated. The results of these studies and some oxygen exchange rates with H_2O are reported in this paper.

Experimental Section

Materials. $[Re(en)_2O_2]Cl$, $[Re(CH_3NH_2)_4O(OH_2)]Cl_3$, and $[Re(py)_4O_2]Cl$ were prepared by methods described[3,4] and had analyses as good or better than those previously reported. Their purity was also checked by ir and visible spectra measurements.

$K_3[Re(CN)_4O_2]$ was prepared by the following procedure. $[Re(en)_2O_2]Cl$ was refluxed with a tenfold excess of KCN in absolute methanol for 12 hr. The solid crude product was collected, washed repeatedly with absolute methanol, and recrystallized four times from MeOH–H_2O mixtures. The bright orange crystals were dried under vacuum for 2 days at 60°, yield 50–60%. *Anal.*

(1) National Science Foundation Postdoctoral Associate, 1964.

(2) (a) G. Schmidt and W. Herr, *Z. Naturforsch.*, **16a**, 748 (1961); (b) J. Casey and R. K. Murmann, *Inorg. Chem.*, **6**, 1053 (1967); (c) S. Wajda, "Theory and Structure of Complex Compounds," B. Jezowsha-Trzebiatowska, Ed., Pergamon Press Ltd., Oxford, England, 1964, pp 383–397.

(3) J. Beard, J. Casey, and R. K. Murmann, *Inorg. Chem.*, **4**, 797 (1965).

(4) R. K. Murmann, *Inorg. Syn.*, **8**, 173 (1966).