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Is the Oxidation of L-Ascorbic Acid by Aquated Iron(III) Ions in Acidic Aqueous Solution Substitution- or Electron-Transfer-Controlled? A Combined Chloride, pH, Temperature, and Pressure Dependence Study

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The oxidation of L-ascorbic acid by aquated Fe(III) ions was studied as a function of $[Cl^-]$, $[H^+]$, temperature, and pressure. The reaction is significantly accelerated by the presence of chloride ions, which is ascribed to the higher redox reactivity of $Fe(H_2O)_5Cl^{2+}$ and $Fe(H_2O)_4(OH)Cl^+$ as compared to the corresponding aqua complexes. The inverse $[H^+]$ dependence of the redox reaction is ascribed to the deprotonation of $Fe(H_2O)_6^{3+}$ to produce the more labile $Fe(H_2O)_5OH^{2+}$ species. From a comparison of the measured activation parameters for the redox reaction ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta V^{\ddagger}$) with those for solvent exchange on $Fe(H_2O)_6^{3+}$ and $Fe(H_2O)_5OH^{2+}$, it is concluded that the oxidation of L-ascorbic acid by these two Fe(III) species occurs according to different mechanisms. The reaction follows an outer-sphere mechanism for the oxidation by the more inert $Fe(H_2O)_6^{3+}$ species but an inner-sphere mechanism for the more labile $Fe(H_2O)_5OH^{2+}$ species. A comparison of the experimental rate constants with those calculated from the Marcus cross relationship confirms the interpretation.

Introduction

We have a long-standing interest in the oxidation of L-ascorbic acid by transition-metal ions and complexes in aqueous solution.[2-4] In many of such studies, the electron-transfer reactions are forced to follow an outer-sphere mechanism since the oxidant is an inert metal complex and does not possess vacant coordination sites, viz. $Fe(CN)_6^{3-}$, $Co(C_2O_4)_3^{3-}$, etc. However, in other systems such as aquated Mn(III), Co(III), and Fe(III), labile coordination sites may induce an inner-sphere mechanism, in which case it is not a trivial matter to pinpoint the rate-determining step, i.e. ligand substitution or electron transfer.

Some of us recently investigated the oxidation of L-ascorbic acid by Fe(III) in acidic aqueous solution[5] and interpreted the acid dependence of the reaction in terms of the reaction scheme outlined in (1), where H_2A and A represent L-ascorbic acid and

$$H_2A \overset{K_1}{\rightleftharpoons} HA^- + H^+$$

$$Fe(H_2O)_6^{3+} + H_2A \xrightarrow{k_1} Fe(H_2O)_6^{2+} + HA^{\bullet} + H^+$$

$$Fe(H_2O)_6^{3+} + HA^- \xrightarrow{k_2} Fe(H_2O)_6^{2+} + HA^{\bullet}$$

$$Fe(H_2O)_6^{3+} + HA^{\bullet} \xrightarrow{\text{fast}} Fe(H_2O)_6^{2+} + A + H^+ \quad (1)$$

L-dehydroascorbic acid, respectively. The inverse $[H^+]$ dependence was ascribed to the fact that $k_2 \gg k_1$. It was later pointed out[6] that an error was made in this study in using $FeCl_3$ as source of Fe(III), since the presence of Cl^- causes the formation of $Fe(H_2O)_5Cl^{2+}$, which reacts significantly faster with H_2A than $Fe(H_2O)_6^{3+}$. Although it is in general believed that the oxidation of ascorbic acid takes place by an outer-sphere mechanism,[6] the higher reactivity of $Fe(H_2O)_5Cl^{2+}$ and $Fe(H_2O)_5OH^{2+}$ may suggest the operation of an inner-sphere mechanism. The inverse acid dependence mentioned above[5] could be related to the deprotonation of $Fe(H_2O)_6^{3+}$ as indicated in (2). This would mean

$$Fe(H_2O)_6^{3+} \overset{K_a}{\rightleftharpoons} Fe(H_2O)_5OH^{2+} + H^+$$

$$Fe(H_2O)_6^{3+} + H_2A \xrightarrow{k_1} Fe(H_2O)_6^{2+} + HA^{\bullet} + H^+$$

$$Fe(H_2O)_5OH^{2+} + H_2A \xrightarrow{k_3} Fe(H_2O)_6^{2+} + HA^{\bullet} \quad (2)$$

that the lability of the Fe(III) center[7] controls the rate of the electron-transfer process such that $k_3 \gg k_1$. In such a case the rate and activation parameters should correlate with those for typical substitution reactions of such species. It is important to note that $K_a = 2 \times 10^{-3}$ M (at 25 °C and 1 M ionic strength[8]) is significantly larger than $K_1 = 8 \times 10^{-5}$ M,[2,4] with the result that under such conditions the deprotonation of $Fe(H_2O)_6^{3+}$ will occur to a significantly larger extent than that of H_2A as a function of decreasing $[H^+]$. Furthermore, evidence has been reported in the literature for the formation of a complex intermediate in the oxidation of ascorbic acid by Fe(III) ions.[9,10] In this respect, it is important to note that very recently, following completion of the work described in this report, Xu and Jordan[11] reported a detailed kinetic study of both the formation and subsequent redox decomposition reactions of the Fe(III)–ascorbic acid intermediate species. They studied the reactions under conditions of an excess Fe(III), which differs totally from the present study, and reported evidence for the formation of $Fe(AH)^{2+}$ and $Fe(AH_2)^{3+}$, followed by outer-sphere electron transfer with $Fe(H_2O)_6^{3+}$ and $Fe(H_2O)_5OH^{2+}$ that is inhibited by Fe(II).[11]

It can be concluded from the above-outlined information that both outer-sphere and inner-sphere electron-transfer mechanisms are quite feasible to account for the observed behavior. In this respect, it is interesting to note that Swaddle and co-workers recently reported significantly different volumes of activation for the inner-sphere and outer-sphere self-exchange reactions of aquated Fe(II) and Fe(III).[12] We have therefore performed a combined $[H^+]$, temperature, and pressure dependence study of the oxidation of L-ascorbic acid by aquated Fe(III) in acidic aqueous solution ($0.2 \leq [H^+] \leq 1.0$ M) in an effort to throw more light on the intimate nature of the redox process.

Experimental Section

All chemicals were of analytical reagent grade and used without further purification. Solutions were prepared with deionized (Millipore) water and used immediately after preparation. Iron(III) perchlorate was used as source of Fe(III) ions. Perchloric acid was used to adjust the acidity of the test solutions, whereas $NaClO_4$ was used to adjust the ionic strength. Reactions were studied on Durrum D110 and Dasar stopped-flow instruments at ambient pressure and on a homemade high-pressure stopped-flow unit[13] at pressures up to 100 MPa. The chloride dependence

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Table I. Observed First-Order Rate Constants for the Oxidation of L-Ascorbic Acid as a Function of $[Cl^-]$ at Various $[H^+]$[a]

		k_{obs},[b] s^{-1}						
$[H^+]$, M	ionic strength, M	$10^2[Cl^-]$ = 1.0 M	$10^2[Cl^-]$ = 1.25 M	$10^2[Cl^-]$ = 1.5 M	$10^2[Cl^-]$ = 1.75 M	$10^2[Cl^-]$ = 2.0 M	10^3K_a,[c] M	K_2,[d] M^{-1}
0.3	1.0	0.431	0.465	0.494	0.523	0.549	2.0	5.2
0.5	1.0	0.295	0.317	0.337	0.363	0.381	2.0	5.2
0.8	1.0	0.185	0.205	0.227	0.234	0.247	2.0	5.2
1.0	1.0	0.163	0.180	0.196	0.206	0.222	2.0	5.2
1.3	1.3	0.129	0.140	0.152	0.164	0.172	1.95	5.7
1.8	1.8	0.134	0.140	0.162	0.175	0.192	1.85	6.6

[a] $[Fe(III)] = 1 \times 10^{-3}$ M; [total H_2A] $= 1 \times 10^{-2}$ M; $T = 25.0$ °C. [b] Mean value of at least four kinetic runs. [c] Taken from ref 8. [d] Taken from ref 15.

study was performed in Madrid, whereas the temperature and pressure dependence work was performed in Witten, Germany. In the former case chloride was added to both solutions prior to mixing in the stopped-flow in order to prevent dilution effects to influence the observed kinetic traces. The stopped-flow instruments were thermostated to ± 0.1 °C, and the kinetic traces were stored directly on a data acquisition and analysis system.[14] The redox reactions were followed at 300 nm under pseudo-first-order conditions, i.e. at least a 10-fold excess of ascorbic acid. The corresponding first-order plots were linear for at least three half-lives of the reaction. No kinetic evidence for the formation of intermediate complex species could be found under the selected experimental conditions.

Results and Discussion

In some preliminary experiments the effect of $[Cl^-]$ on the oxidation of L-ascorbic acid by aquated Fe(III) was studied at various $[H^+]$. The results in Table I clearly demonstrate that k_{obs} increases significantly with increasing $[Cl^-]$, which can be ascribed to the formation of the stronger oxidant $Fe(H_2O)_5Cl^{2+}$ under these conditions.[6] A general reaction scheme to account for the combined $[Cl^-]$ and $[H^+]$ dependences is given in (3), in which it was

$$Fe(H_2O)_6^{3+} \overset{K_a}{\rightleftharpoons} Fe(H_2O)_5OH^{2+} + H^+$$

$$Fe(H_2O)_6^{3+} + Cl^- \overset{K_2}{\rightleftharpoons} Fe(H_2O)_5Cl^{2+} + H_2O$$

$$Fe(H_2O)_5Cl^{2+} \overset{K_3}{\rightleftharpoons} Fe(H_2O)_4(OH)Cl^+ + H^+$$

$$Fe(H_2O)_6^{3+} + H_2A \xrightarrow{k_1} Fe(H_2O)_6^{2+} + HA^\bullet + H^+$$

$$Fe(H_2O)_5OH^{2+} + H_2A \xrightarrow{k_3} Fe(H_2O)_6^{2+} + HA^\bullet$$

$$Fe(H_2O)_5Cl^{2+} + H_2A \xrightarrow{k_4} Fe(H_2O)_5Cl^+ + HA^\bullet + H^+$$

$$Fe(H_2O)_4(OH)Cl^+ + H_2A \xrightarrow{k_5} Fe(H_2O)_5Cl^+ + HA^\bullet$$

$$Fe(III) + HA^\bullet \xrightarrow{fast} Fe(II) + A + H^+ \qquad (3)$$

assumed that protonation and deprotonation of L-ascorbic acid do not play a significant role under the selected experimental conditions; viz. $0.3 \le [H^+] \le 1.8$ M.[15,16]

Under pseudo-first-order conditions, the rate law for the oxidation of H_2A is given by (4). K_3 is unknown in this expression,

$$k_{obs} = 2\left(\frac{k_1[H^+] + k_3K_a + k_4K_2[H^+][Cl^-] + k_5K_2K_3[Cl^-]}{[H^+] + K_a + K_2[H^+][Cl^-] + K_2K_3[Cl^-]}\right) \times [\text{total } H_2A] \qquad (4)$$

but cannot be larger than K_a. Under the selected experimental conditions, $[H^+] + K_2[H^+][Cl^-] \gg K_a + K_2K_3[Cl^-]$ such that eq 4 can be simplified to (5) and rewritten as shown in (6). The

$$k_{obs} = 2\left(\frac{k_1 + k_3K_a/[H^+] + k_4K_2[Cl^-] + k_5K_2K_3[Cl^-]/[H^+]}{1 + K_2[Cl^-]}\right) \times [\text{total } H_2A] \qquad (5)$$

$$\frac{k_{obs}(1 + K_2[Cl^-])}{2[\text{total } H_2A]} = (k_1 + k_3K_a/[H^+]) + (k_4 + k_5K_3/[H^+])K_2[Cl^-] = k_a + k_bK_2[Cl^-] \qquad (6)$$

data in Table I at constant $[H^+]$ were plotted according to eq 6, from which k_a and k_b were obtained as a function of $[H^+]$. Subsequently, the inverse $[H^+]$ dependence of k_a and k_b can be seen from the plots in Figure 1, from which it follows that $k_1 = 0.80 \pm 0.07$, $k_3 = (2.15 \pm 0.02) \times 10^3$, $k_4 = 33 \pm 5$ M^{-1} s^{-1} and $k_5K_3 = 35 \pm 3$ s^{-1} at 25 °C. The values of K_a and K_2 employed in these calculations are given in Table I. The results in Figure 1 demonstrate that the experimental data are reasonably well described by eq 4, i.e. the mechanism in (3). In principle the reported value of k_1 is rather inaccurate since it was obtained as an intercept of a plot of intercepts, from the $[Cl^-]$ dependence measurements, versus $[H^+]^{-1}$. This may account for the fact that our value is significantly smaller than the value of 7.3 s^{-1} reported

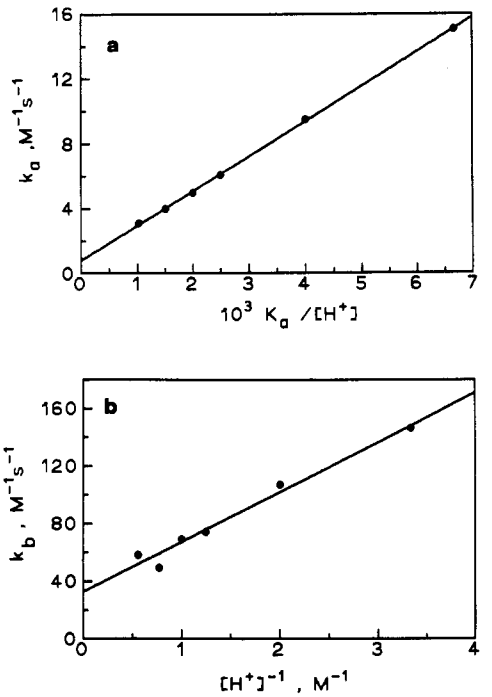

Figure 1. (a) Plot of k_a versus $K_a/[H^+]$ for the data in Table I according to eq 6. (b) Plot of k_b versus $[H^+]^{-1}$ for the data in Table I according to eq 6.

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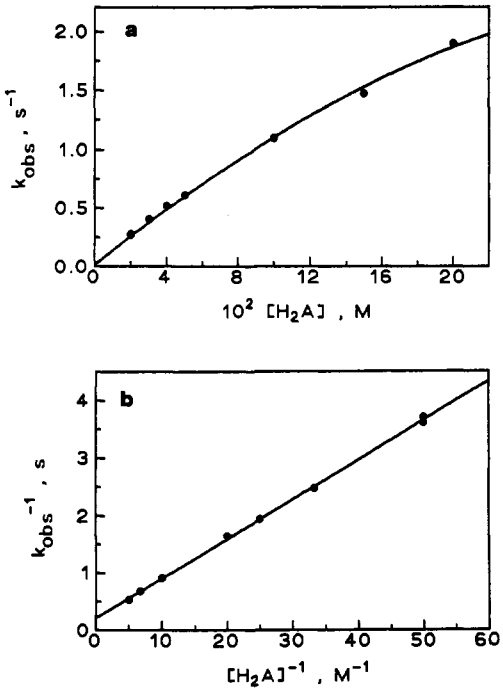

Figure 2. (a) Plot of k_{obs} versus [H_2A] for the oxidation of L-ascorbic acid by Fe(III) in acidic aqueous solution. (b) Plot of k_{obs}^{-1} versus [H_2A]$^{-1}$ for the data in plot a. Experimental conditions: [total Fe(III)] = 2.0×10^{-3} M; [H^+] = 1.0 M; ionic strength = 1.0 M; T = 25.0 °C; pressure = 0.1 MPa.

by Hynes and Kelly,[6] although the exact experimental conditions were not quoted by these authors.

From the above experiments it can be concluded that the reaction of $Fe(H_2O)_5OH^{2+}$ with H_2A is significantly faster than the reaction of $Fe(H_2O)_6^{3+}$. This same ratio exists for the chloro complexes, i.e. k_4 and k_5, if we assume that $K_3 \leq K_a$. The chloro complexes react significantly faster with H_2A than the corresponding aqua complexes, based on the difference between k_4 and k_1. Possible reasons for this effect could be a significantly higher redox potential for the chloro complex, i.e. a higher driving force, which is not the case,[17,18] or an increased lability of the chloro complex, i.e. labilization of coordinated water and a more rapid inner-sphere electron-transfer process. The details of the electron-transfer mechanism itself will be discussed in the following section.

For this purpose, the oxidation of L-ascorbic acid by Fe(III) was studied in a direct way (i.e. in the absence of Cl^-) as a function of [H^+], temperature, and pressure. Experimental conditions were selected in such a way as to simplify the overall system,[6,11] i.e. a relatively high acidity range to ensure the presence of mainly H_2A, $Fe(H_2O)_6^{3+}$, and $Fe(H_2O)_5OH^{2+}$. It is usually reported that the pseudo-first-order rate constant depends linearly on the [total H_2A].[2-5] We investigated this aspect in more detail in an effort to find kinetic evidence for the formation of precursor complexes. Such evidence usually comes from nonlinear concentration dependences, i.e. saturation kinetics at high [total H_2A]. Indeed, plots of k_{obs} versus [total H_2A] started to deviate from linearity at [total H_2A] $\geq$ 0.1 M at [H^+] = 0.2 and 1.0 M. A typical example is shown in Figure 2 along with the double reciprocal plot procedure usually adopted to linearize such relationships. For the simplified reaction scheme in (7), $k_{obs} = kK[H_2A]/\{1 +$

$$Fe(III) + H_2A \overset{K}{\rightleftharpoons} [Fe(III)\cdot H_2A]$$

$$[Fe(III)\cdot H_2A] \xrightarrow{k} Fe(II) + H_2A^+ \qquad (7)$$

$K[H_2A]\}$, i.e. $k_{obs}^{-1} = k^{-1} + (kK[H_2A])^{-1}$, such that K and k can be separated kinetically.[4,19,20] Our results indicate K values of

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Table II. Rate Data for the Temperature Dependence of the Oxidation of L-Ascorbic Acid by Aquated Fe(III) in the Absence of Chloride[a]

	k_{obs},[b] s^{-1}			
[H^+]	T = 17.0 °C	T = 25.0 °C	T = 32.0 °C	T = 39.0 °C
0.20	0.291 ± 0.002	0.831 ± 0.006	1.89 ● 0.02	4.52 ± 0.11
0.25	0.257 ± 0.005	0.711 ± 0.011	1.60 ± 0.03	3.73 ± 0.10
0.33	0.200 ± 0.002	0.558 ± 0.003	1.28 ± 0.01	2.98 ● 0.08
0.50	0.170 ± 0.002	0.423 ± 0.002	0.929 ± 0.010	2.18 ± 0.05
1.00	0.106 ± 0.002	0.270 ± 0.005	0.607 ± 0.007	1.35 ± 0.03
k_1, M^{-1} s^{-1}	1.69 ± 0.25	3.39 ± 0.26	7.26 ± 0.54	14.6 ± 0.6
k_3K_a, s^{-1}	1.14 ± 0.07	3.52 ± 0.08	8.10 ± 0.16	19.7 ● 0.2
10^3K_a,[c] M	1.35	2.04	2.87	3.98
k_3, M^{-1} s^{-1}	846 ± 55	1728 ± 38	2824 ± 56	4959 ● 45

[a] Experimental conditions: [total H_2A] = 2.0×10^{-2} M; [total Fe(III)] = 2.0×10^{-3} M; ionic strength = 1.0 M. [b] Mean value of at least four kinetic runs. [c] Extrapolated from the literature[7,22] on the basis that ΔH° = 36.9 kJ mol^{-1} and ΔS° = 72.3 J K^{-1} mol^{-1}.

3.15 and 2.08 M^{-1} at 1.0 and 0.2 M H^+, respectively. Theoretical calculations based on the Fuoss equation[4,21] predict ion-pair formation constants of approximately 1 M^{-1}. It follows that the observed deviation of linearity in Figure 2a is realistic under the selected experimental conditions.

All subsequent measurements reported in this paper were performed at lower [total H_2A], i.e. where there is a linear dependence of k_{obs} on this concentration. The calculated second-order rate constant will then be the product of the precursor formation constant and the electron-transfer rate constant. Similarly, the reported activation parameters will also be composite quantities.

The temperature and pressure dependence of the electron-transfer process was studied as a function of [H^+] in the range 0.2–1.0 M, for which the results are summarized in Tables II and III, respectively. Under these conditions, and in the light of the arguments brought above, the reaction scheme in (3) simplifies to that shown in (2) and the final reaction in (3). The appropriate rate law for this mechanism is given in (8), from which it follows

$$k_{obs} = 2(k_1 + k_3K_a/[H^+])[\text{total } H_2A] \qquad (8)$$

that the inverse [H^+] dependence of k_{obs} can be used to determine k_1 and k_3. Such plots were linear for the data in Tables II and III, and the so-calculated values of k_1 and k_3 are included in the tables. The temperature and pressure dependence of k_1 and k_3 were used to calculate the activation parameters, $\Delta H^\ddagger$, $\Delta S^\ddagger$ and $\Delta V^\ddagger$ summarized in Table IV. By way of comparison the activation parameters for solvent exchange on $Fe(H_2O)_6^{3+}$ and $Fe(H_2O)_5OH^{2+}$ are also included in this table. It should be noted that the values of k_1 and its activation parameters are subjected to higher error limits than those for k_3, since k_1 is determined as an intercept compared to k_3 as the slope of eq 8. This can partly account for the significantly higher k_1 value reported in Table II than that obtained from the data in Table I. It should however be kept in mind that these series of measurements were performed on different instruments in different laboratories (see Experimental Section), so that the disagreement is not that unrealistic. A reviewer suggested that we fit the data in Table I as a function of [H^+]$^{-1}$ according to eq 6. If it is assumed that the intercepts of such plots do not exhibit a significant [Cl^-] dependence, i.e. $k_4K_2[Cl^-]$ is small, then k_1 = 3.9 ± 0.8 M^{-1} s^{-1}, which is indeed close to the value reported in Table II. However, the intercepts do exhibit a significant [Cl^-] dependence, which results in k_1 = 0.7 ± 0.2 and k_4 = 41 ± 4 M^{-1} s^{-1}. These values are in close agreement with our earlier analysis. We prefer to use the k_1 values quoted in Tables II–IV in the remaining discussion since these values were determined in the absence of added chloride, i.e. in a more direct way, and are in agreement with literature data.[6]

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Table III. Rate Data for the Pressure Dependence of the Oxidation of L-Ascorbic Acid by Aquated Fe(III) in the Absence of Chloride[a]

	k_{obs},[b] s^{-1}			
$[H^+]$, M	P = 4 MPa	P = 30 MPa	P = 60 MPa	P = 90 MPa
0.20	0.827 ± 0.010	0.782 ± 0.023	0.709 ± 0.009	0.648 ± 0.004
0.25	0.714 ± 0.011	0.679 ± 0.003	0.616 ± 0.011	0.535 ± 0.013
0.33	0.588 ± 0.016	0.560 ± 0.008	0.499 ± 0.008	0.424 ± 0.004
0.50	0.417 ± 0.009	0.393 ± 0.011	0.354 ± 0.006	0.319 ± 0.011
1.00	0.271 ± 0.008	0.251 ± 0.007	0.225 ± 0.010	0.194 ± 0.004
k_1, M^{-1} s^{-1}	3.5 ± 0.5	3.2 ± 0.6	2.8 ± 0.5	2.2 ± 0.1
k_3K_a, s^{-1}	3.52 ± 0.16	3.37 ± 0.17	3.08 ± 0.14	2.81 ± 0.04
10^3 K_a,[c] M	2.04	1.99	1.94	1.90
k_3, M^{-1} s^{-1}	1730 ± 80	1690 ± 90	1590 ± 70	1480 ± 20

[a] Experimental conditions: [total H_2A] = 2.0×10^{-2} M; [total Fe(III)] = 2.0×10^{-3} M; ionic strength = 1.0 M. [b] Mean value of at least four kinetic runs. [c] Extrapolated from the literature[8] on the basis that $\Delta\bar{V} = +1.9 \pm 0.1$ cm^3 mol^{-1}.

Table IV. Comparison of Rate and Activation Parameters for the Oxidation of L-Ascorbic Acid by Aquated Fe(III) and Solvent Exchange on Aquated Fe(III)

reaction	k at 25 °C	$\Delta H^{\ddagger}$, kJ mol^{-1}	$\Delta S^{\ddagger}$, J K^{-1} mol^{-1}	$\Delta V^{\ddagger}$, cm^3 mol^{-1}	ref
$Fe(H_2O)_6^{3+} + H_2A$	3.4 ± 0.3 M^{-1} s^{-1}	72 ± 3	+7 ± 11	+14 ± 2	*a*
$Fe(H_2O)_5OH^{2+} + H_2A$	1728 ± 39 M^{-1} s^{-1}	57 ± 2	+9 ± 5	+4.6 ± 0.7	*a*
$Fe(H_2O)_6^{3+} + H_2O$	(1.6 ± 0.2) × 10^2 s^{-1}	64 ± 2	+12 ± 7	−5.4 ± 0.4	7, 22
$Fe(H_2O)_5OH^{2+} + H_2O$	(1.2 ± 0.1) × 10^5 s^{-1}	42 ± 1	+5 ± 4	+7.0 ± 0.3	7, 22

[a] This work; activation parameters were calculated from the data for k_1 and k_3 in Tables II and III.

The results in Table IV demonstrate that the oxidation by $Fe(H_2O)_5OH^{2+}$ is ca. 500 times faster than by $Fe(H_2O)_6^{3+}$. A very similar ratio is observed for the solvent exchange rate constants of these complexes, and even more surprising are the very similar rate constants when those for solvent exchange are converted to second-order rate constants, viz. 2.9 and 2160 M^{-1} s^{-1} for $Fe(H_2O)_6^{3+}$ and $Fe(H_2O)_5OH^{2+}$, respectively. This similarity also shows up in the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, and suggests that the electron-transfer reaction could be substitution-controlled, i.e. determined by the lability of the coordinated solvent (water) molecules. It is important to note that no evidence for the formation of an intermediate iron(III)–ascorbate complex was observed under the selected experimental conditions, such that substitution can in principle be the rate-determining step. Other investigators have observed the formation and decay of such an intermediate complex, especially under conditions where an excess of iron(III) was employed.[9,11] Further mechanistic information comes from the values of $\Delta V^{\ddagger}$. These are very similar for oxidation of H_2A by $Fe(H_2O)_5OH^{2+}$ and for solvent exchange on the latter complex, and further support the arguments in favor of a substitution controlled (I_d mechanism[17]) electron-transfer process. The value of $\Delta V^{\ddagger}$ for oxidation by $Fe(H_2O)_6^{3+}$ is significantly more positive than that found for the oxidation by $Fe(H_2O)_5OH^{2+}$ and also differs considerably from that reported for solvent exchange on $Fe(H_2O)_6^{3+}$. This discrepancy suggests that ligand substitution cannot be the rate-controlling process during the oxidation reaction involving the $Fe(H_2O)_6^{3+}$ species. For this reason we suggest that oxidation of L-ascorbic acid by $Fe(H_2O)_6^{3+}$ follows an outer-sphere electron-transfer mechanism. In this case the positive volume of activation can be ascribed to the increase in partial molar volume during the reduction of $Fe(H_2O)_6^{3+}$ to $Fe(H_2O)_6^{2+}$ and a decrease in electrostriction due to charge dilution in going from 3+ to 2+ and 1+ species.

It follows from the above interpretation that the $[H^+]$ dependence of the electron-transfer reaction is solely ascribed to the deprotonation of $Fe(H_2O)_6^{3+}$ to produce $Fe(H_2O)_5OH^{2+}$ under the selected experimental conditions. The higher redox reactivity of $Fe(H_2O)_5OH^{2+}$ can not be due to a higher redox potential (i.e. driving force) for this species[23] (see further Discussion). The higher lability of this complex must therefore account for the higher redox reactivity, similar to that suggested for the $Fe(H_2O)_5Cl^{2+}$ species. This conclusion, as well as the changeover in electron-transfer mechanism suggested above, is also in good agreement with the rate constants that can be estimated on the basis of the simplified ($f = 1$) Marcus cross relationship (9) for

$$k_{12} = (k_{11}k_{22}K_{12})^{1/2} \quad (9)$$

outer-sphere electron-transfer processes. For this purpose the self-exchange rate constants k_{11} for Fe^{3+}/Fe^{2+} and $Fe(OH)^{2+}/Fe^{2+}$ were extrapolated from 0.1 to 1.0 M ionic strength[12,24] using the relationship in eq 10 for which $A = 0.508$ $M^{-1/2}$, $B = 32.9$ $M^{-1/2}$ pm^{-1},[25] and the mean distance of closest approach of the reacting Fe(III) cations to the perchlorate counter ions was determined to be $\dot{a} = 595$ pm. These values turn out to be 8.29 and 5158 M^{-1} s^{-1} at 25 °C and 1.0 M ionic strength, respectively. The values for the equilibrium constant K_{12} of the respective cross reactions Fe(III)/H_2A were obtained from the corresponding redox potentials of the couples Fe^{3+}/Fe^{2+}, $FeOH^{2+}/FeOH^{+}$, and $H_2A^{\bullet+}/H_2A$, which are 0.77, 0.34 (at the average $[H^+] = 0.6$ M), and 1.17 V, respectively, at 25 °C and 1.0 M ionic strength.[17,18,23,26,27] These potentials result in $K_{12} = 1.73 \times 10^{-7}$ and 9.34×10^{-15} for the quoted redox systems, respectively. In addition, $k_{22} = 7.75 \times 10^5$ ($H_2A^{\bullet+}/H_2A$) was determined[4] on the basis of the Marcus theory including all the work terms and electrolyte effects and is in good agreement with available information from the literature.[29,30]

$$\log k = \log k^{\circ} + \frac{2Z_1Z_2A\sqrt{\mu}}{1 + \dot{a}\beta\sqrt{\mu}} \quad (10)$$

Substitution of the values of k_{11}, k_{22}, and K_{12} into eq 9 results in $k_{12} = 1.1$ and 6.1×10^{-3} M^{-1} s^{-1} for the oxidation of H_2A by $Fe(H_2O)_6^{3+}$ and $Fe(H_2O)_5OH^{2+}$, respectively. These values are upper limits since on the one hand the simplified eq 9 was employed, and on the other hand the self-exchange process for $FeOH^{2+}/Fe^{2+}$ is probably an inner-sphere reaction. The calculated

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values for k_{12} must be compared to the experimental values of 3.4 and 1730 M^{-1} s^{-1}, respectively, which indicates a fairly good agreement for the reaction between Fe^{3+} and H_2A. However, the difference in the case of the $FeOH^{2+}/H_2A$ reaction is very large, and indicates that this reaction most probably does not involve an outer-sphere mechanism, in agreement with our conclusion based on the ΔV^* data.

The results of this investigation clearly reveal mechanistic differences between the oxidation of L-ascorbic acid by $Fe(H_2O)_6^{3+}$ and $Fe(H_2O)_5OH^{2+}$. The experimental rate and activation parameters as well as theoretical calculations clearly suggest that the oxidation by $Fe(H_2O)_6^{3+}$ follows an outer-sphere electron-transfer mechanism, whereas the oxidation by $Fe(H_2O)_5OH^{2+}$ follows a substitution-controlled inner-sphere electron-transfer mechanism. Thus the lability of the aquated Fe(III) center determines whether substitution (for the less labile $Fe(H_2O)_6^{3+}$ species) is the rate-controlling step in the oxidation of L-ascorbic acid. Under the conditions of an excess Fe(III), Xu and Jordan[11] observed the formation of the intermediate complexes $Fe(AH)^{2+}$ and $Fe(AH_2)^{3+}$ and their subsequent redox behavior. These authors reported a significantly higher reactivity for the reaction of $Fe(AH)^{2+}$ with $Fe(H_2O)_5OH^{2+}$ than with $Fe(H_2O)_6^{3+}$, which could again be due to the greater substitution lability of $Fe(H_2O)_5OH^{2+}$ to facilitate an inner-sphere electron-transfer mechanism. No activation parameters were reported[11] such that a more detailed mechanistic assignment is presently not possible. Nevertheless, the controlling effect of the aquated Fe(III) center is obvious and encourages further investigations into its intimate nature.

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Registry No. $Fe(H_2O)_6^{3+}$, 15377-81-8; $Fe(H_2O)_5OH^{2+}$, 15696-19-2; Cl^-, 16887-00-6; L-ascorbic acid, 50-81-7.

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Effect of Pressure on the Complex Formation and Aquation Kinetics of Iron(III) with Hydroxamic Acids

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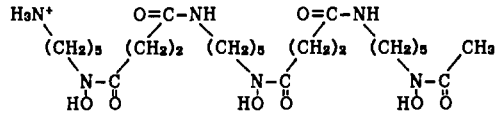
The activation and reaction volumes for the formation and aquation of (acethydroxamato)iron(III) complexes, as well as the activation volumes for the formation of the (desferrioxamine B)iron(III) complex, have been obtained by high-pressure stopped-flow and UV–vis spectral measurements. The data indicate a gradual mechanistic changeover from I_a to I_d for the stepwise proton-catalyzed hydrolysis of the tris(acethydroxamato)iron(III) complex and vice versa for the corresponding formation reactions. The activation volumes for the complexation of $Fe(H_2O)_6^{3+}$ and $Fe(H_2O)_5(OH)^{2+}$ with both acethydroxamic acid (HA) and desferrioxamine B in its fully protonated form (H_4dfb^+) exhibit opposite signs, indicating associative and dissociative modes of activation, respectively. The obtained results suggest that the substitution behavior of the Fe(III) complexes is controlled by the presence of OH^- or A^- in the coordination sphere.

Introduction

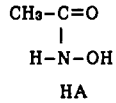
Siderophores are low molecular weight specific and strong iron(III) chelators produced by different microorganisms to mediate transport of this metal ion from the environment into the cell.[1] A hydroxamate-based siderophore desferrioxame B is currently used for removal of iron from the body in treatment of patients suffering from β-thalassemia or acute iron poisoning.[2] In order to improve the understanding of the mechanism by which siderophore-mediated iron transport occurs, the interaction of desferrioxamine B (H_4dfb^+) with iron(III) was studied in detail.[3,4]



H_4dfb^+

Although most of the studies were performed under biologically inaccessible conditions, i.e. in strongly acidic aqueous media, the mechanism postulated under these conditions was essentially the same as that found to operate at physiologically more relevant conditions.[5]

Synthetic monohydroxamic acids (such as acethydroxamic acid, HA) can serve as model ligands for the investigation of the hydroxamate-based siderophore–iron(III) interactions, which were thoroughly studied by Crumbliss and co-workers.[6] They found them to be excellent ligands for probing the intimate mechanism of substitution at the iron(III) metal ion center. The authors proposed a reaction model in which the proton dependent and independent paths for the interaction between iron(III) and hydroxamic acids were closely related and suggested for both pathways an associative mode of activation. The results of a high-pressure study on the formation of mono(acet-



HA

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