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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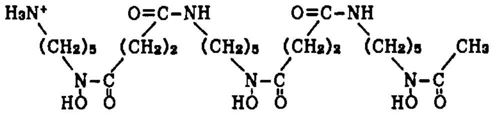
The activation and reaction volumes for the formation and aquation of (acethydroxamato)iron(III) complexes, as well as the activation volumes for the formation of the (desferrioxamine B)iron(III) complex, have been obtained by high-pressure stopped-flow and UV-vis spectral measurements. The data indicate 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.

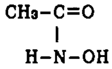
Introduction

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]



$$\begin{array}{c} CH_3-C=O \\ | \\ H-N-OH \end{array}$$

HA

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-

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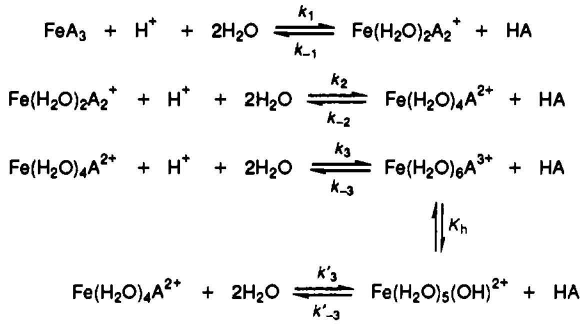
Scheme I



hydroxamato)iron(III), however, indicated that the pathway including $Fe(H_2O)_6^{3+}$ follows an I_a mechanism, whereas the pathway including $Fe(H_2O)_5OH^{2+}$ proceeds via an I_d mechanism.[7]

In this work we report the results of a high-pressure study on the formation of the tetraaqua(desferrioxamine B)iron(III) complex and the three-step hydrolysis of tris(acethydroxamato)iron(III) in acidic aqueous medium. The results throw more light on the mechanism of ligand substitution at the iron(III) metal center.

Experimental Section

Iron(III) perchlorate (Aldrich) was dissolved in 0.2 M $HClO_4$, and its concentration was determined spectrophotometrically using a molar absorbance coefficient of $4.16 \times 10^3\ M^{-1}\ cm^{-1}$ at 240 nm.[8] Sodium perchlorate solution was prepared by dissolving the solid salt (Merck) in deionized water and was standardized against sodium hydroxide after passing through a cation-exchange resin in the H^+ form. Acethydroxamic acid was obtained from Aldrich whereas desferrioxamine B was kindly granted by Ciba-Geigy. Through all the experiments the ionic strength was kept at 2.0 M by addition of $NaClO_4$.

Kinetic experiments were performed on a high-pressure stopped-flow instrument described in detail elsewhere.[9] In a typical experiment two reagents were thermostated for approximately 20 min in the instrument and were mixed in the observation cell within ca. 30 ms. The absorbance change was then monitored at an optimal wavelength as already described.[4,10] The solutions of the tris(acethydroxamato)iron(III) complex used in the hydrolysis experiments were prepared by neutralization of a solution containing 10-fold molar excess of acethydroxamic acid over iron perchlorate.

UV–vis measurements at ambient conditions were performed on a Shimadzu UV-250 spectrophotometer, whereas spectra under high pressure were measured in a pillbox cell on a Zeiss DMR 10 spectrophotometer equipped with a high-pressure cell previously described in the literature.[11] The reaction volume for the formation of bis(acethydroxamato)iron(III) from mono(acethydroxamato)iron(III) and acethydroxamic acid was determined by measuring the spectral change of a solution containing 0.25 mM $Fe(ClO_4)_3$, 3.25 mM acethydroxamic acid, and 2.25 mM $HClO_4$ as a function of pressure within the range 5–125 MPa. Under these experimental conditions, the concentrations of the tris complex and the free metal ion and ligand are negligible. The measured absorbance data points were fitted to the equation $A = l[Fe(III)]\{\epsilon_b[HA]K \exp(-P\Delta\bar{V}/RT) + \epsilon_m[H^+]\}/\{[H^+] + [HA]K \exp(-P\Delta\bar{V}/RT)\}$, where A, l, ϵ_m, ϵ_b, K, and $\Delta\bar{V}$ are the measured absorbance, light path length in the pillbox cell at ambient pressure, molar absorbance coefficient of the mono- and bis-complex species, formation constant, and reaction volume, respectively. The value of K (=1.16) was determined under the same experimental conditions at ambient pressure before[10] and was not varied during the iterative procedure. An analogous procedure was employed for the determination of the reaction volume for the formation of mono(acethydroxamato)iron(III) from acethydroxamic acid and Fe(III) by measuring the spectral change of a solution containing 1.5 mM $Fe(ClO_4)_3$, 0.5 mM acethydroxamic acid, and 51.5 mM $HClO_4$. However, in this experiment iron(III) could not be kept in a large molar excess over acethydroxamic acid in order to have ca. 50% uncomplexed acethydroxamic acid in the solution (at higher acidities slow decomposition of acethydroxamic acid was observed), and it was therefore necessary to calculate the concentration of each species present in the solution for each absorbance measurement as a function of pressure. This was done by a Fortran iterative procedure based on the Newton–Raphson method[14] in which the pressure dependence of the stability constant was incorporated. The absorbance data points were fitted to the equation $A = l\epsilon_m[Fe(III)][HA][H^+]^{-1}K \exp(-P\Delta\bar{V}/RT)$, where the stability constant of $Fe(H_2O)_4A^{2+}$ was reported in the literature.[10] The observed pressure dependence of the absorbance related to the formation of tris(acethydroxamato)iron(III) was too small to give reliable values for the reaction volume for the formation of this species.

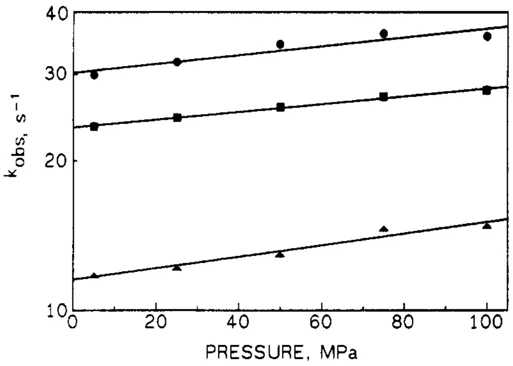


Figure 1. Pressure dependence of the first hydrolysis step of 0.1 mM FeA_3 at −0.5 °C and I = 2.0 M (H/$NaClO_4$). Conditions: triangles, [HA] = 1.0 mM, [H^+] = 1.0 mM; squares, [HA] = 51 mM, [H^+] = 1.0 mM; circles, [HA] = 2.5 mM, [H^+] = 2.5 mM.

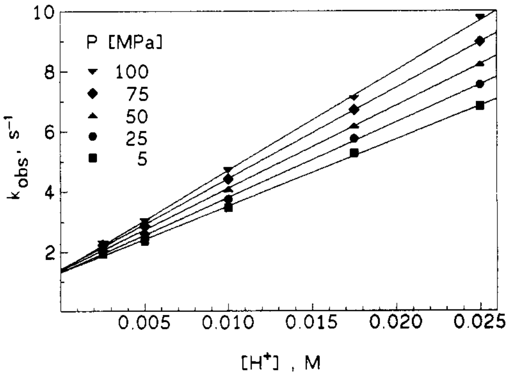


Figure 2. Proton dependence of the second hydrolysis step of 0.25 mM FeA_3 as a function of pressure at 3.0 °C, I = 2.0 M (H/$NaClO_4$), and [HA] = 2.5 mM.

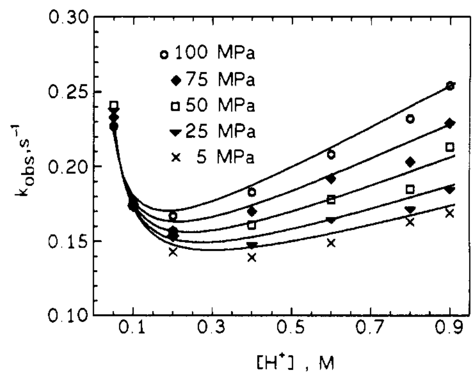


Figure 3. Proton dependence of the third hydrolysis step of 0.1 mM FeA_3 as a function of pressure at 25.0 °C, I = 2.0 M (H/$NaClO_4$), and [HA] = 1.1 mM.

Partial molar volumes were calculated from density measurements performed on a Paar (Wien) digital densitometer at 25.000 ± 0.008 °C in solutions of 2.0 M ionic strength (Na/$HClO_4$).

Results

Kinetics of Hydrolysis of Tris(acethydroxamato)iron(III) Complexes. The hydrolysis of tris(acethydroxamato)iron(III) has already been described in the literature,[10] and essentially the same

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Table I. Kinetic Parameters for Complex Formation and Aquation of Hydroxamic Acids with Fe(III) Ion at 25 °C and 2.0 M Ionic Strength (H/NaClO$_4$)

reacn	k/M^{-1} s^{-1}	$\Delta V^{\ddagger}$/cm^3 mol^{-1}
$FeA_3 + H^+ + 2H_2O \rightarrow Fe(H_2O)_2A_2^+ + HA$	$9.3 \times 10^{4\,a}$	$-5.4\ (0.5)^b$
$Fe(H_2O)_2A_2^+ + H^+ + 2H_2O \rightarrow Fe(H_2O)_4A^{2+} + HA$	$1.3 \times 10^{3\,a}$	$-9.1\ (0.6)^c$
$Fe(H_2O)_4A^{2+} + H^+ + 2H_2O \rightarrow Fe(H_2O)_6^{3+} + HA$	$7.2 \times 10^{-2\,a}$	$-15.6\ (1.5)$
$Fe(H_2O)_4A^{2+} + 2H_2O \rightarrow Fe(H_2O)_5(OH)^{2+} + HA$	$7.8 \times 10^{-2\,a,d}$	$-3.3\ (0.6)$
$Fe(H_2O)_5(OH)^{2+} + HA \rightarrow Fe(H_2O)_4A^{2+} + 2H_2O$	5.7×10^3	$+5.2\ (0.5)$
	$4.9 \times 10^{3\,e}$	$+7.7\ (0.6)^e$
	$4.1 \times 10^{3\,f}$	
	$2.0 \times 10^{3\,g}$	
$Fe(H_2O)_6^{3+} + HA \rightarrow Fe(H_2O)_4A^{2+} + H^+ + 2H_2O$	4.8	$-6.3\ (1.4)$
	6.4^e	$-10.0\ (1.4)^e$
	4.8^f	
	1.2^g	
$Fe(H_2O)_4A^{2+} + HA \rightarrow Fe(H_2O)_2A_2^+ + H^+ + 2H_2O$	$2.4 \times 10^{3\,a}$	$-2.2\ (0.5)^b$
$Fe(H_2O)_2A_2^+ + HA \rightarrow FeA_3 + H^+ + 2H_2O$	$1.6 \times 10^{3\,a}$	$-2.2\ (0.9)^c$
$Fe(H_2O)_5(OH)^{2+} + H_4dfb^+ \rightarrow Fe(H_2O)_4(H_3dfb)^{3+} + 2H_2O$	3.0×10^3	$+4.3\ (0.5)$
	$3.6 \times 10^{3\,h}$	
$Fe(H_2O)_6^{3+} + H_4dfb^+ \rightarrow Fe(H_2O)_4(H_3dfb)^{3+} + H^+ + 2H_2O$	3.8	$-4.7\ (1.6)$
	2.0^h	
$Fe(H_2O)_6^{3+} + H_2O^* \rightarrow Fe(H_2O)_5(H_2O^*)^{3+} + H_2O$	$1.6 \times 10^{2\,d,i}$	$-5.4\ (0.4)^i$
$Fe(H_2O)_5(OH)^{2+} + H_2O^* \rightarrow Fe(H_2O)_4(H_2O^*)(OH)^{2+} + H_2O$	$1.2 \times 10^{5\,d,i}$	$+7.0\ (0.5)^i$

[a] Data cited from ref 10. [b] Determined at −0.5 °C. [c] Determined at 3 °C. [d] Rate constant expressed in s^{-1}. [e] Data at 1 M ionic strength cited from ref 7. [f] Data at 1 M ionic strength cited from ref 15. [g] Data cited from ref 6. [h] Data cited from ref 4. [i] Data at 6 m ionic strength cited from ref 13.

Table II. Reaction Volumes and Partial Molar Volumes at 25 °C and 2.0 M Ionic Strength (H/NaClO$_4$)

reacn	$\Delta \bar{V}$/cm^3 mol^{-1}
$FeA_3 + H^+ + 2H_2O \rightleftharpoons Fe(H_2O)_2A_2^+ + HA$	$-3.2\ (0.7)^{a,b}$
$Fe(H_2O)_2A_2^+ + H^+ + 2H_2O \rightleftharpoons Fe(H_2O)_4A^{2+} + HA$	$-6.9\ (0.5)^{a,c}$
	$-6.7\ (0.2)^d$
$Fe(H_2O)_4A^{2+} + H^+ + 2H_2O \rightleftharpoons Fe(H_2O)_6^{3+} + HA$	$-9.3\ (0.1)^d$
$Fe(H_2O)_6^{3+} \rightleftharpoons Fe(H_2O)_5(OH)^{2+} + H^+$	$+0.8^e$
$CH_3C({=}O)N(-H)OH \rightleftharpoons CH_3C(=O)N(-H)O^- + H^+$	$-16.1\ (1.0)^f$
substance	**$\bar{V}$/cm^3 mol$^{-1\,f}$**
$CH_3C(=O)N(-H)OH$	$+58.8\ (0.5)$
$CH_3C(=O)N(-H)O^-$	$+47.7\ (0.5)^g$

[a] Calculated from the kinetic data ($\Delta \bar{V}_n = \Delta V_n^{\ddagger} - \Delta V_{-n}^{\ddagger}$). [b] Determined at −0.5 °C. [c] Determined at 3 °C. [d] Determined by measuring the pressure dependence of the absorbance of the equilibrated solution as described in the Experimental Section. [e] Data at 6 m ionic strength cited from ref 13. [f] Determined by density measurements. [g] Calculated on the basis that the partial molar volume of $H^+ = -5$ cm^3 mol^{-1}.[18]

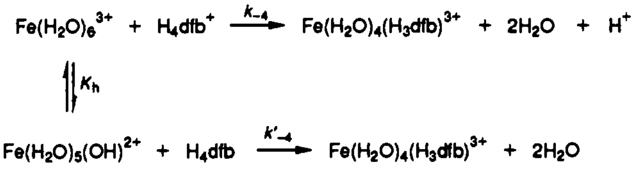
procedure was repeated in this work except that the reactions were followed at various pressures. The three hydrolysis steps, outlined in Scheme I, can be nicely separated kinetically and were treated independently.

The first and second hydrolysis steps are too fast at room temperature to be monitored on the high-pressure stopped-flow instrument and were therefore measured at −0.5 and 3 °C, respectively. Even at these low temperatures the measured rate constants for the first step are subjected to large uncertainties, since only the third half-life of the reaction could be measured. The results of these measurements are shown in Figures 1–3. From the data of Figure 1 it is obvious that an increase in pressure results in an increase in the observed rate constant. The slope of ln k_{obs} versus pressure in 1 mM HClO$_4$ is smaller at the higher concentration of acethydroxamic acid. This indicates that in this step the activation volume for hydrolysis, which contributes more at the lower ligand concentration, is more negative than the one for the formation reaction. This is even more clearly seen for the second step in Figure 2, where the intercepts, which correspond to the formation rate constant, show almost no pressure dependence. The observed rate constants of the first and second steps were fitted to eq 1, where n = 1 and 2 for the first and second

$$k_{obs} = k_n[H^+] \exp(-P\Delta V_n^{\ddagger}/RT) + k_{-n}[HA] \exp(-P\Delta V_{-n}^{\ddagger}/RT) \quad (1)$$

steps, P is pressure, and $\Delta V^{\ddagger}$ is the activation volume, respectively. The nonlinear fit to this equation gives the activation volumes listed in Table I. The calculated reaction volume for the second step ($\Delta V_2^{\ddagger} - \Delta V_{-2}^{\ddagger}$) is in an excellent agreement with the one obtained from the spectrophotometric measurements at various pressures, as reported in Table II.

Scheme II



It is shown in Figure 3 that the third hydrolysis step exhibits a nonlinear dependence of k_{obs} on the proton concentration at different pressures, in agreement with the results obtained at ambient pressure.[6] Therefore the data points were first fitted to the full rate expression given by eq 2 using a nonlinear fitting

$$k_{obs} = \{k_3[H^+] \exp(-P\Delta V_3^{\ddagger}/RT) + k'_3 \exp(-P\Delta V'^{\ddagger}_3/RT)\}f_m + \{k_{-3} \exp(-P\Delta V_{-3}^{\ddagger}/RT) + k_{-3}K_h[H^+]^{-1} \exp[-(\Delta \bar{V}_h + \Delta V'^{\ddagger}_{-3})P/RT]\}[HL] \quad (2)$$

procedure. In this equation f_m, K_h, and $\Delta \bar{V}_h$ represent the fraction of the total complex in the form of $Fe(H_2O)_4A^{2+}$, the hydrolysis constant of $Fe(H_2O)_6^{3+}$, and the reaction volume for the hydrolysis of $Fe(H_2O)_6^{3+}$, respectively. It should be noted that the calculated value of f_m was under our experimental conditions larger than 0.97, whereas K_h = 1.1 mM and $\Delta \bar{V}_h$ = 0.8 cm^3/mol were taken from the literature.[12,13] However, such a fitting procedure resulted in a refinement of the parameters with extremely large standard deviations, and it was therefore necessary to reduce the number of parameters to be varied during the fitting procedure. On substitution of $k_3 \exp(-P\Delta V_3^{\ddagger}/RT)$ and $k'_3 \exp(-P\Delta V'^{\ddagger}_3/RT)$ in eq 2 by $k_{-3}K_3 \exp\{-P(\Delta V_{-3}^{\ddagger} + \Delta \bar{V}_3)/RT\}$ and $k'_{-3}K_3K_h \exp\{-P(\Delta V'^{\ddagger}_{-3} + \Delta \bar{V}_3 + \Delta \bar{V}_h)/RT\}$, respectively, the number of parameters to be varied was reduced from eight to only four. The dissociation constant of $Fe(H_2O)_4A^{2+}$, K_3, determined under the same experimental conditions but at ambient pressure is available from the literature,[10] whereas $\Delta \bar{V}_3$ was determined independently

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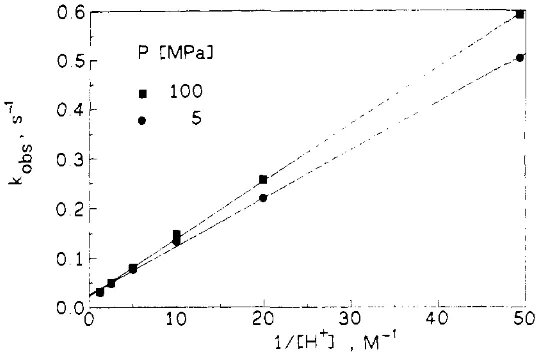

Figure 4. Proton dependence of the formation of bidentate ferrioxamine B as a function of pressure at 25.0 °C. Conditions: $[H_4dfb^+]$ = 4.0 mM; $[Fe(ClO_4)_3]$ = 0.3 mM.

from the spectrophotometric measurements at different pressures as described in the Experimental Section. When the values of $K_3 = 0.15$ and $\Delta\bar{V}_3 = -9.3$ cm^3/mol were kept constant, the fitting procedure resulted in the activation volumes and rate constants for the third step given in Table I. The formation rate constants agree favorably with the hitherto reported values at ambient pressure,[6,7,15] and a similar agreement exists for the activation volumes.[7]

Kinetics of Formation of the (Desferrioxamine B)iron(III) Complex. The hydrolysis of fully coordinated (desferrioxamine B)iron(III) proceeds in four distinguishable steps,[3,4] but they are too fast or too complex to be resolved satisfactorily for the determination of activation volumes. Therefore, the experimental conditions were selected in such a way that only the formation of bidentate ferrioxamine B, shown in Scheme II, was studied by means of the high-pressure stopped-flow technique. When H_4dfb^+ is in a molar excess over $Fe(ClO_4)_3$, the dependence of the observed rate constant on pressure can be expressed by eq 3. For the case

$$k_{obs} = \{k_{-4}[H^+]\exp(-P\Delta V_{-4}^{\ddagger}/RT) + k'_{-4}K_h\exp\{-P(\Delta V'^{\ddagger}_{-4} + \Delta\bar{V}_h)/RT\}\}[H_4dfb^+]/\{[H^+] + K_h\exp(-P\Delta\bar{V}_h/RT)\} \quad (3)$$

where $[H^+] \gg K_h$, eq 3 is linearized in terms of the inverse proton concentration, as is shown in Figure 4 for pressures of 5 and 100 MPa. The intercept and slope of the straight lines in Figure 4 correspond to the values of k_{-4} and k'_{-4} at two different pressures, respectively, indicating an opposite effect of pressure on these two rate constants and in turn opposite signs for the volumes of activation for these two pathways. The pressure dependence of the observed rate constant at various $[H^+]$ values is shown in Figure 5. A nonlinear least-squares fit of eq 3 to the 36 data points results in the activation volumes and rate constants listed in Table I and the lines in Figure 5. The calculated values of k_{-4} and k'_{-4} are essentially the same as those obtained under the same experimental conditions but at ambient pressure.[4]

Discussion

The results presented in Table I show that the reactions of HA and H_4dfb^+ with $Fe(H_2O)_6^{3+}$ exhibit small negative $\Delta V^{\ddagger}$ values, whereas with $Fe(H_2O)_5(OH)^{2+}$ they exhibit small positive $\Delta V^{\ddagger}$ values. The activation volume $\Delta V^{\ddagger}$ may to a first approximation be considered to consist of an intrinsic volume change due to the formation or breakage of bonds on forming the transition state and a solvational component due to charge formation or neutralization during this process.[16] In the reactions with HA no net change in charge occurs during the formation of either the outer- or the inner-sphere complexes, since a carbonyl oxygen–iron bond is formed in the rate-determining step,[6] such that a possible contribution of solvent electrostriction to the activation volumes may be neglected.[7] The almost equal activation volumes reported for both investigated ligands indicate that the increase in charge for the binding of H_4dfb^+ in the transition state or during the formation of the outer-sphere complex may also be neglected. This may be due to a large separation between the reacting hydroxamato functionality and the charge-carrying terminal ammonium group of desferrioxamine B. The obtained activation volumes can therefore be compared to the activation volumes for water exchange on $Fe(H_2O)_6^{3+}$ and $Fe(H_2O)_5(OH)^{2+}$, as seen from Table I, which suggest the operation of an I_a and I_d mechanism, respectively.

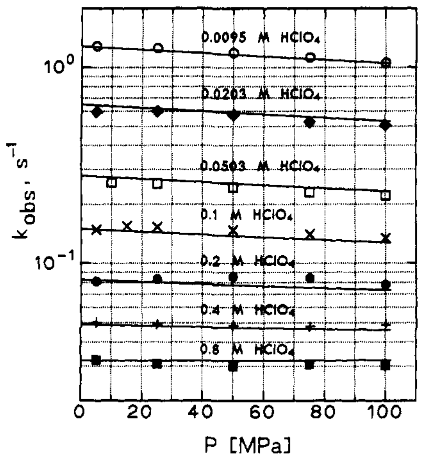

Figure 5. Pressure dependence of the formation rate of the bidentate ferrioxamine B as a function of acidity at 25.0 °C (other conditions as in Figure 4). The lines in this figure were calculated with eq 3 using the rate and activation parameters quoted in Table I.

Microscopic reversibility then requires that the proton-independent aquation of $Fe(H_2O)_4A^{2+}$ must also follow an I_d mechanism. Thus, the experimental $\Delta V_{-3}^{\ddagger}$ value of -3.3 cm^3/mol requires a $\Delta\bar{V}$ of ca. -8 cm^3/mol for the ring-opening step preceding the rate-determining loss of HA. This negative $\Delta\bar{V}$ may arise from the binding of a solvent molecule during the ring-opening step (which can be as large as -13 cm^3/mol on the basis of theoretical calculations for limiting A and D substitution mechanisms of octahedral complexes[17]), accompanied by a volume increase of ca. +5 cm^3/mol due to ring opening of the hydroxamato moiety. This process can be visualized in terms of either intramolecular proton transfer from a water molecule to the –NO oxygen during which $Fe(H_2O)_4({=}A)^{2+}$ (ring closed) produces $Fe(H_2O)_3(OH)({=}AH)^{2+}$ followed by ring opening as a consequence of –N(O)–Fe bond cleavage and binding of a water molecule to produce $Fe(H_2O)_4(OH)(-AH)^{2+}$ (ring opened) or ring opening and binding of a solvent molecule followed by an intramolecular neutralization step to produce the protonated ring-opened species. In the latter case ring opening will cause significant electrostriction, as large as -11 cm^3/mol on the basis of the partial molar volumes of HA and A^- reported in Table II, and the subsequent neutralization step is expected to cause a significant volume increase of ca. +16 cm^3/mol on the basis of the volume of neutralization of A^- reported in Table II. In this respect it is important to note that deprotonation of a coordinated solvent molecule is not expected to be accompanied by a significant volume change on the basis of the almost zero reaction volume found for the deprotonation of $Fe(H_2O)_6^{3+}$ (see Table II). It follows that the ring-opening process can cause a volume increase of ca. +5 cm^3/mol (i.e. $-11 + 16$; see above), which combined with the expected volume decrease of 13 cm^3/mol for the binding of a solvent molecule[17] will result in the overall volume of reaction for the ring-opening step of -8 cm^3/mol. These predictions further demonstrate that the main portion of the ligand is far enough away

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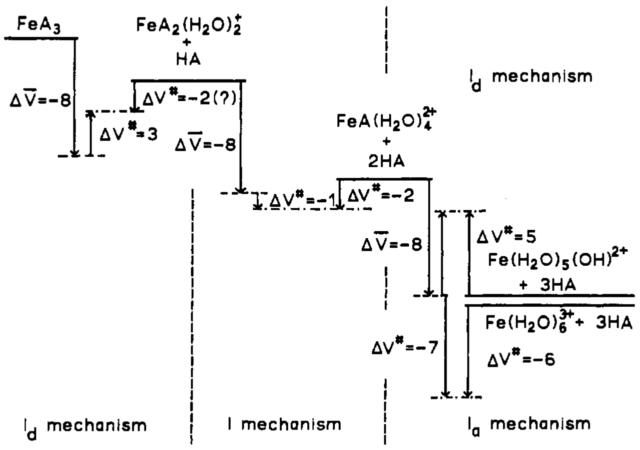

Figure 6. Overall volume profile for the stepwise aquation and formation of tris(acethydroxamato)iron(III), FeA_3: (—) reactant and product states; (- - -) ring-opened species; (- · -) transition states.

from the metal to be in direct contact with the solvent during the ring-opening process.

A similar volume collapse (ca. −8 cm^3/mol) is expected for the acid-catalyzed ring-opening reactions that occur prior to the rate-determining loss of HA during the stepwise aquation reactions. Here again protonation of coordinated A^- (ring closed) is not expected to cause a significant volume change, whereas protonation of the ring-opened species should be accompanied by a large volume increase due to the neutralization of charges. Thus in the latter case the increase in electrostriction due to the ring opening of A^- will be offset by the neutralization process and very similar volume changes are expected as for the uncatalyzed ring-opening reaction. It follows that, for all studied hydrolysis reactions, the observed ΔV^* is a composite of a reaction volume of ca. −8 cm^3/mol for the ring-opening-process and an activation volume for the subsequent rate-determining loss of the monodentate HA moiety. On the basis of these arguments it follows that ΔV^* for the loss of HA in the ring-opened $Fe(H_2O)_5AH^{3+}$ species is ca. −7 cm^3/mol (i.e. −15.6 − (−8)), which is in agreement with an I_a mechanism suggested on the basis of microscopic reversibility.

Similar calculations for the proton-catalyzed aquation in the first and second reaction steps result in ΔV^* values of ca. +3 and −1 cm^3/mol, respectively. These suggest the operation of an I_d or I mechanism, respectively, and demonstrate the labilization effect of coordinated hydroxamate. It follows that for the proton-catalyzed aquation of the complex the calculated activation volumes indicate a mechanistic changeover from I_d to I_a depending on the number of hydroxamato ligands coordinated to the metal center.

The formation of $Fe(H_2O)_2A_2^+$ from $Fe(H_2O)_4A^{2+}$ exhibits a slightly negative ΔV^* value, which suggests an I mechanism in which bond formation and breakage participate equally. The ΔV^* value for the formation of FeA_3 is subject to large error limits, since this reaction is at the limit of the resolution of the high-pressure stopped-flow instrument, and the reported standard deviation of this parameter is just a fortunate consequence of the averaging procedure on the highly scattered individual data points. An overall volume profile for the hydrolysis of tris(acethydroxamato)iron(III) is presented in Figure 6. In this profile each hydrolysis step is presented as a volume decrease of −8 cm^3/mol for the formation of the ring-opened species (see above outlined arguments), followed by an activation volume for the rate-determining loss of HA, such that the overall values represent the volumes of activation for the hydrolysis steps reported in Table I. This volume profile clearly demonstrates a gradual changeover from I_a to I_d for the complex formation reactions of $Fe(H_2O)_6{}^{3+}$ and a changeover from I_d to I_a for the reverse acid-catalyzed aquation reactions. Furthermore, it also includes our assumption on the basis of microscopic reversibility that, in the case of the complex formation of $Fe(H_2O)_5(OH)^{2+}$ with HA, both the forward and the reverse spontaneous aquation reactions follow an I_d mechanism.

The results presented in this work reveal that the substitution behavior of the Fe(III) complexes is controlled by the presence of OH^- or A^- in the coordination sphere. This is in an agreement with the observation[15] that the formation rate of mono(acethydroxamato)iron(III), as well as its aquation rate, gradually increases by subsequent coordination of Cl^-, possibly as a consequence of a similar mechanistic changeover from I_a to I_d.

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Registry No. $Fe(H_2O)_6{}^{3+}$, 15377-81-8; acetohydroxamic acid, 546-88-3; desferrioxamine B, 70-51-9; tris(acetohydroxamato)iron(III), 14587-53-2; (desferrioxamine B)iron(III), 14836-73-8.

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Interaction of Metal Cations with Heteropolytungstate Ions $SiW_{12}O_{40}{}^{4-}$ and $P_2W_{18}O_{62}{}^{6-}$

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The stability constants for the binding of the metal cations Ca^{2+}, Eu^{3+}, Th^{4+}, and $UO_2{}^{2+}$ to two heteropolytungstates, $SiW_{12}O_{40}{}^{4-}$ and $P_2W_{18}O_{62}{}^{6-}$, have been determined by the solvent extraction technique. The stability constants increase with the positive charge of the cations, reflecting the ionic character of the interactions. The stability constants of $UO_2{}^{2+}$ provide evidence for steric effects of the linear dioxo cation in the interaction with the binding sites on the heteropolyanions.

Introduction

Solution electrochemical and solid-state structural studies[1-3] of isopoly and heteropoly oxometalates of the transition elements (e.g., Mo and W) have shown that over certain ranges of pH these species exist in solution as stable, discrete anions of the same structure as that of the solids. These heteropolyanions can bind metal cations, but quantitative data for such binding are scarce. The susceptibility of these anions to attack by base has prevented characterization of their acidity constant values by potentiometric titration although optical spectroscopy has been employed for some systems.[4-6]

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