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## Kinetics of the Formation and Hydrolysis of (Desferrioxamine B) Aluminium(III) and Gallium(III) Complexes in Acidic Aqueous Perchlorate Solutions

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The kinetics of complexation of desferrioxamine B with M (M = Al(III) and Ga(III) in acidic aqueous perchlorate solutions at 25 °C and 2 M ionic strength are reported. The pseudo-first order complex formation and hydrolysis reactions were followed spectrophotometrically in the UV region. For both metals, a parallel-path mechanism, in which the  $M(H_2O)_6^{3+}$  and  $M(H_2O)_5(OH)^{2+}$  ions react with the fully protonated ligand ( $H_4dfb^+$ ) to form  $M(H_2O)_4(H_3dfb)^{3+}$  complexes, is operative. The calculated formation rate constants for unhydrolyzed and hydrolyzed Al(III) ions are  $0.0211(17) s^{-1} M^{-1}$  and  $189(3) s^{-1} M^{-1}$ , whereas for Ga(III) are  $5.45(77) s^{-1} M^{-1}$  and  $2.15(3) \cdot 10^4 s^{-1} M^{-1}$ , respectively. For the reaction of  $H_4dfb^+$  with the unhydrolyzed Al(III) and Ga(III) ions, enthalpies and entropies of activation are:  $97.6 \pm 8.2 kJ mol^{-1}$ ,  $52.5 \pm 2.9 J K^{-1} mol^{-1}$ , and  $87.2 \pm 7.2 kJ mol^{-1}$ ,  $71.3 \pm 2.9 J K^{-1} mol^{-1}$ , respectively. The results are discussed in terms of a model in which the loss of the first water molecule coordinated to the metal ions is the rate determining step. The obtained *ca.*  $10^4$  times higher reactivities of the hydrolyzed than the unhydrolyzed metal ions are consistent with the dissociative (Eigen) mechanism.

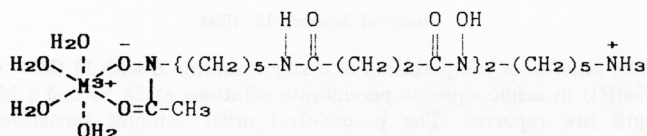
### INTRODUCTION

There has been considerable interest in the mechanism of the substitution reactions of aluminum, gallium and other readily hydrolyzed ions because both associative<sup>1,2</sup> and dissociative<sup>3,4</sup> activations have been proposed for the complexations of these ions in aqueous solutions. Controversial interpretations of the kinetic results are due to »proton ambiguity« raised by the deprotonation of both the metal-ions and the

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weakly acidic ligands in aqueous solutions. Therefore, of particular importance are the data related to the metal-ion reactivity of ligands for which »proton ambiguity« does not occur. Such ligands are hydroxamic acids since their relatively high  $pK_a$  ( $\sim 9$ ) eliminates deprotonated species as potential reactants at  $pH \leq 3$ . On the other hand, these acids are constituents of many siderophores and the results could be important in view of their relevance to the understanding of microbial iron transport.<sup>5,6</sup> One of the most extensively studied hydroxamic acids is the siderophore desferrioxamine B (the abbreviation  $H_4dfb^+$  is used for the fully protonated ligand,  $^+NH_3(CH_2)_5[N(OH)C(O)(CH_2)_2C(O)NH(CH_2)_5]_2N(OH)C(O)CH_3$ ,<sup>7</sup> owing to its ready availability since it is a drug used in the treatment of transfusion induced iron overload associated with  $\beta$ -thalassemia or Cooley's anaemia,<sup>8</sup> and as a aluminum chelator for removal of aluminum from the patient suffering from dialysis encephalopathy<sup>9</sup> or Alzheimer's disease.<sup>10,11</sup>

Recently, a comparison of the aqueous coordination chemistry of aluminum(III) and iron(III) was reported.<sup>12,13,14</sup> In this paper, we report kinetic data for the hydrolysis and the formation of bidentate Ga(III)- and Al(III)- $(H_3dfb)^{3+}$  complexes, (I), extending the possible comparison to Ga(III) and augmenting the kinetic results on the Al(III)-system.



Formula I.

## EXPERIMENTAL

### Materials

Reagents were chemically pure. The methanesulfonate salt of desferrioxamine B (Desferal<sup>R</sup>) was kindly supplied by Ciba Geigy Corp. The salt, recrystallized from hot methanol, was stored in a vacuum desiccator over  $P_4O_{10}$  (m.p. 149–151 °C, uncorrected).

Aluminum perchlorate nonahydrate from Aldrich was used for the preparation of acidic stock solutions concentrations of which determined by standard methods. Acidic stock solutions of  $Ga(ClO_4)_3$  were prepared by dissolving weighted metal in acid. The residual excess of acid was estimated with the Dowex 50-W X-8 cation exchange resin. Perchloric acid solutions were prepared by dilution of the 70%-acid, whereas sodium perchlorate solutions were prepared from the recrystallized salt. All the solutions were prepared using doubly distilled water from alkaline  $KMnO_4$ .

### Kinetics

All the kinetics was carried out at a constant 2.0 M ionic strength held by  $H/NaClO_4$ , in Cary 16, Perkin Elmer lambda-3, and Durrum-110 stopped-flow UV-Vis spectrophotometers equipped with thermostated cell-holders.

A typical hydrolysis kinetics of  $M(Hdfb)^+$  was performed by a pH-jump (increasing the proton concentration) of the equilibrated solution containing  $M(ClO_4)_3$  in a molar excess over desferrioxamine B at an initial proton concentration lower than  $10^{-4}$  M. The reactions were fol-

lowed by measuring the absorbance change in a 225–240 nm range. At least two first order relaxation curves were observed, the slowest one separated nicely on the time scale. Only the rate of the slowest relaxation was measured since the faster one(s) should correspond to the hydrolysis of the metal-desferrioxamine B complexes of higher denticity.

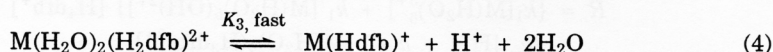
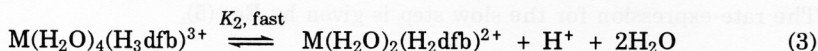
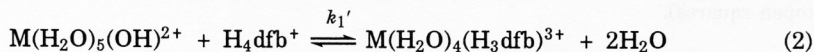
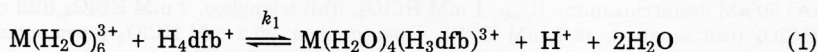
The formation kinetics were performed by mixing together the solution of metal ions with the solution of the ligand of the same acidity and ionic strength.

The observed rate constants were calculated using a commercially available Olis software, by fitting the expression  $A = A_1 \cdot e^{-kt} + A_\infty$  to the absorbance/time data. The pseudo-first order reaction conditions were assured by keeping one of the reactants in a deficiency. An already described<sup>15</sup> least-square algorithm for non-linear functions, implemented on a Compaq Deskpro 386s computer, was used for the fitting procedure.

## RESULTS

Hitherto unpublished spectral data associated with the slowest hydrolysis step of the produced Al(III)-desferrioxamine B complex are shown in Figure 1. A similar behavior is exhibited by the Ga(III)-system. A plausible explanation for the observed apparent isobestic point is that the rate determining reaction involves a slow hydrolysis of  $M(H_3dfb)^{3+}$  complex, which is in a fast equilibrium with  $M(H_2dfb)^{2+}$  and  $M(Hdfb)^+$  complexes during its hydrolysis. If all the M-desferrioxamine B complexes were not featuring a fast preequilibrium of the slowest hydrolysis step, the isobestic point would have to shift during the slowest step reaction time. The results shown in Figure 2, indicate that the rate constant of the investigated reactions, *i.e.* the hydrolysis and the formation rate contributions when system equilibrates, is linearly dependent on the metal ion concentration. The followed kinetics is that correctly assigned since only the formation of  $M(H_3dfb)^{3+}$  involves M as the reactant. All this indicates that, depending on the direction of the reaction that is followed, the rate determining step is either the hydrolysis or the formation of  $M(H_2O)_4(H_3dfb)^{3+}$  that, depending on the solution acidity, quickly equilibrates with the tetra- and hexadentate complexes. The influence of proton concentration on the values of observed rate constants obtained at constant metal ion concentrations is illustrated in Figure 3. The data can be interpreted by the empirical equation  $k_{obs} = a + b[H^+]^{-1} + c[H^+]$ . Exactly the same kinetic behavior was found to be characteristic of both the aluminum(III)<sup>14</sup> and iron(III)<sup>16,17</sup> desferrioxamine B complexes. All these facts can entirely be accommodated by the reaction model outlined in the following Scheme:

### Scheme



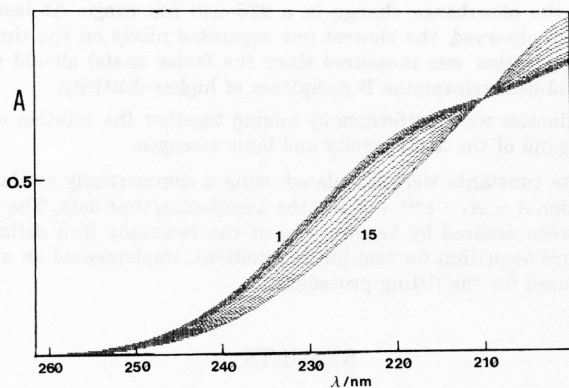


Figure 1. Spectral change accompanying the slowest hydrolysis step of  $50 \mu\text{M Al}(\text{H}_3\text{dfb})(\text{H}_2\text{O})_6^{3+}$  in  $10 \text{ mM HClO}_4$  at  $25^\circ\text{C}$ ,  $I = 2.0 \text{ M Na/HClO}_4$ . The spectra were taken at 5, 10, 15, 20, 25, 30, 45, 60, 90, 150, 180, 240 and 270 minutes.

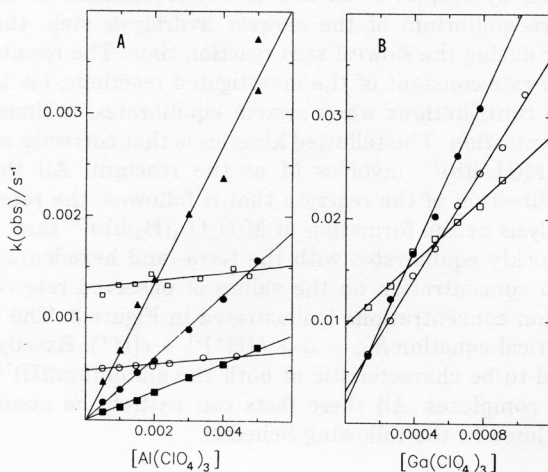


Figure 2. Dependence of the observed rate constants of the formation (full symbols) and hydrolysis (open symbols) of  $\text{M}(\text{H}_3\text{dfb})(\text{H}_2\text{O})_4^{3+}$  on the concentration of  $\text{M}(\text{ClO}_4)_3$  at  $25^\circ\text{C}$ ,  $I = 2.0 \text{ M}$ . (A)  $50 \mu\text{M}$  desferrioxamine  $\text{B}_{(\text{tot})}$ ,  $1 \text{ mM HClO}_4$  (full triangles),  $2 \text{ mM HClO}_4$  (full circles),  $5 \text{ mM HClO}_4$  (full squares),  $48.7 \text{ mM HClO}_4$  (open circles),  $95.2 \text{ mM HClO}_4$  (open squares), (B)  $9.61 \mu\text{M}$  desferrioxamine  $\text{B}_{(\text{tot})}$ ,  $0.1 \text{ M HClO}_4$  (full circles),  $0.2 \text{ M HClO}_4$  (open circles),  $0.275 \text{ M HClO}_4$  (open squares).

The rate expression for the slow step is given by Eq. (5).

$$R = \{k_1[\text{M}(\text{H}_2\text{O})_6^{3+}] + k_1'[\text{M}(\text{H}_2\text{O})_5(\text{OH})^{2+}]\} [\text{H}_4\text{dfb}^+] - (k_{-1}[\text{H}^+] + k_{-1}') [\text{M}(\text{H}_2\text{O})_4(\text{H}_3\text{dfb})^{3+}] \quad (5)$$

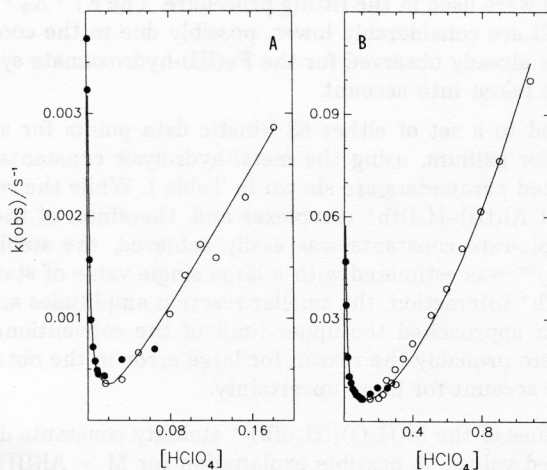


Figure 3. Dependence of the observed rate constants of the formation (full circles) and hydrolysis (open circles) of  $M(\text{H}_3\text{dfb})(\text{H}_2\text{O})_4^{3+}$  on the proton concentration at 25 °C,  $I = 2.0 \text{ M Na/HClO}_4$ . (A) 5 mM  $\text{Al(III)}_{(\text{tot})}$ , 50  $\mu\text{M}$  desferrioxamine  $\text{B}_{(\text{tot})}$ ; (B) 0.13 mM  $\text{Ga(III)}_{(\text{tot})}$ , 9.61  $\mu\text{M}$  desferrioxamine  $\text{B}_{(\text{tot})}$ .

For  $[\text{M}] \gg [\text{H}_4\text{dfb}^+]$ , and reactions (3) and (4) featuring a fast equilibrium, the observed rate constant can be described by Eq. (6),

$$k_{\text{obs}} = \left\{ \frac{k_1[\text{H}^+] + k_1'K_h}{([\text{H}^+] + K_h)} \right\} [\text{M}]_0 + f_m \cdot \left\{ \frac{k_1[\text{H}^+] + k_1'K_h}{K_1} \right\} \quad (6)$$

where  $[\text{M}]_0$  is the initial concentration of  $\text{M}(\text{ClO}_4)_3$ ,  $K_h$  is the hydrolysis constant of the aqua metal ions,  $K_1 (= k_1/k_{-1})$  is the stability constant of the  $\text{M}(\text{H}_2\text{O})_4(\text{H}_3\text{dfb})^{3+}$  complexes, and  $f_m$  is given by the quotient;  $f_m = \frac{[\text{M}(\text{H}_2\text{O})_4(\text{H}_3\text{dfb})^{3+}]}{[\text{M}(\text{H}_2\text{O})_4(\text{H}_3\text{dfb})^{3+}] + [\text{M}(\text{H}_2\text{O})_2(\text{H}_2\text{dfb})^{2+}] + [\text{M}(\text{Hdfb})^+]}$  =  $\frac{[\text{H}^+]^2}{([\text{H}^+]^2 + K_2[\text{H}^+] + K_2K_3)}$ .

An almost linear relationship of  $k_{\text{obs}}$  vs.  $[\text{H}^+]$  at the highest proton concentrations used (Figure 3), where the hydrolysis rate contributes significantly and  $[\text{H}^+] \gg K_h$ , suggests that at these acidities  $[\text{H}^+]^2 > K_2[\text{H}^+] + K_2K_3$ . Therefore,  $f_m \approx 1$  and Eq. (6) resembles the above mentioned empirical equation with  $a = k_1[\text{M}]_0 + k_1'K_hK_1^{-1}$ ,  $b = k_1'K_h$  and  $c = k_1K_1^{-1}$ . On the other hand, at the lowest proton concentrations used, where the proton concentration square term could dominate since  $K_2[\text{H}^+] + K_2K_3 \gg [\text{H}^+]^2$ , the contribution of the hydrolysis rate becomes negligible, as seen from the zero-intercepts of Figure 2A (this should also be applicable to the gallium since its stability constants with  $\text{H}_4\text{dfb}^+$  are even larger than the aluminum ones). The intermediate proton concentrations should satisfy the full kinetic expression (6) from which  $K_2$  and  $K_3$  could be calculated by a non-linear curve fitting procedure.

A knowledge of the overall stability constants for  $\text{M}(\text{Hdfb})^+$ , which are directly related to the  $K_1K_2K_3$  products, reduces the number of parameters to be refined. These stability constants were determined in 0.1 and 1.0 M aqueous  $\text{NaCl}$ .<sup>20,21</sup> The values of  $K_1 \cdot K_2 \cdot K_3 (= 2.04 \cdot 10^{-3}$  and  $21.9 \text{ M}^2$  for  $\text{M} = \text{Al(III)}$  and  $\text{Ga(III)}$ , respectively) deter-

mined in 0.1 M NaCl were used in the fitting procedure. The  $K_1 \cdot K_2 \cdot K_3$ -values determined in 1.0 M NaCl are considerably lower, possibly due to the coordination of Cl<sup>-</sup> to  $M(H_2O)_6^{3+}$  ions, as already observed for the Fe(III)-hydroxamate systems,<sup>22</sup> and for this reason were not taken into account.

Eq. (6) was fitted to a set of either 63 kinetic data points for aluminum, or 74 kinetic data points for gallium, using the metal-hydrolysis constants given in literature.<sup>18,19</sup> The evaluated parameters are shown in Table I. While the refinement of the stability constants of Al(III)-H<sub>4</sub>Dfb<sup>+</sup> complexes and, therefore, of the formation and hydrolysis microscopic-rate constants was easily achieved, the stability constant of Ga(III)(H<sub>2</sub>O)<sub>4</sub>(H<sub>3</sub>dfb)<sup>3+</sup> was estimated with a large single value of standard deviation. For the Ga(III)-H<sub>4</sub>dfb<sup>+</sup> interaction, the smaller reaction amplitudes and slightly faster reaction rates, which approached the upper limit of the conventional spectrophotometric technique, were probably the reason for large error in the obtained kinetic experimental data and account for large uncertainty.

The reported values of the  $M(H_2O)_4(H_3dfb)^{3+}$  stability constants differ significantly from our calculated values. A possible explanation for M = Al(III) is given below, whereas the literature Ga(III)-constant was also reported<sup>21</sup> with large uncertainty, making any comparison meaningless. Fortunately, values of the calculated stability constants do not affect computation of the formation constants  $k_1$  and  $k_1'$  but rather affect the reliability of the corresponding hydrolysis rate constants.

The formation kinetics for the bidentate Ga(III)-desferrioxamine B complex is reported now for the first time, whereas the data obtained for aluminum can be compared to the results of Garrison and Crumbliss.<sup>14</sup> They reported both the rate and the stability constants that are about one order of magnitude higher than those calculated in this work. The observed differences could be due to the different methods employed in these two studies. They employed an NMR technique that required very high concentrations of the reactants. Though they also worked at the 2.0 M (perchlorate) ionic strength, their reaction solutions contained almost 30% of organic substance, *i.e.* desferrioxamine B. The ligand is very soluble in water, suggesting its strong solvation which may decrease water availability in the second coordination sphere of the metal ions and hence increase the ligating rate. In addition, their kinetic model does not in-

TABLE I

*Kinetic and equilibrium constants for the coordination of Al(III) and Ga(III) with desferrioxamine B at 25 °C, I = 2.0 M H/NaClO<sub>4</sub><sup>a</sup>*

Parameter	Al(III)	Ga(III)
$k_1/s^{-1} M^{-1}$	$(2.11 \pm 0.17) \cdot 10^{-2}$ 0.13 <sup>b</sup>	$5.45 \pm 0.77$
$k_1'/s^{-1} M^{-1}$	$(1.88 \pm 0.03) \cdot 10^2$ $2.10 \cdot 10^3$ <sup>b</sup>	$(2.15 \pm 0.03) \cdot 10^4$
$K_1$	$1.21 \pm 0.10$ 15 <sup>b</sup>	$7.62 \pm 6.77$ $1.87 \cdot 10^2$ <sup>c</sup>
$K_1' \cdot K_2/M$	$(6.57 \pm 0.70) \cdot 10^{-2}$	$(6.85 \pm 1.42) \cdot 10^1$

<sup>a</sup> The data for Al(III) and Ga(III) were fitted to Eq. (6) setting the values of  $K_1 \cdot K_2 \cdot K_3$  as  $2.04 \cdot 10^{-3}$  and  $21.9 M^2$ , respectively, as reported in Ref. 20. <sup>b</sup> Collected from Ref. 14. <sup>c</sup> From Ref. 21,  $I = 1.0 M NaCl$ .

clude a fast equilibrium of the bi- with tetra- and hexa-dentate complexes that eventually may affect the values of the calculated hydrolysis constants. Another significant difference between the reaction conditions used in these two studies is that in this work  $[\text{Al}(\text{ClO}_4)_3] \gg [\text{H}_4\text{dfb}^+]$ . This brings about the possibility of the formation of di-metal complex  $\text{Al}_2(\text{Hdfb})^{4+}$ . However, this was rejected on the basis of the analogous reaction of  $\text{H}_4\text{dfb}^+$  with an excess of  $\text{Fe}(\text{ClO}_4)_3$ .<sup>17</sup> The two hydroxamate groups of  $\text{H}_4\text{dfb}^+$  chelate two irons with the stability constant of the second iron being almost an order of magnitude lower than that of the first one. By analogy, Garrison and Crumbliss' value of  $K_1 = 15$  predicts under experimental conditions that not more than 5% of the total aluminum is in the form of a bimetallic complex.

Experiments analogous to those performed at 25 °C were carried out at 20 and 30 °C for Ga(III), and at 35 and 45 °C for Al(III). From the plots in Figure 4, activation parameters for the reaction (1) were calculated:  $M = \text{Al(III)}$ ;  $\Delta H^\ddagger = 97.6 \pm 8.2 \text{ kJ mol}^{-1}$ ,  $\Delta S^\ddagger = 52.5 \pm 2.9 \text{ J K}^{-1} \text{ mol}^{-1}$ , and  $M = \text{Ga(III)}$ ;  $\Delta H^\ddagger = 87.2 \pm 7.2 \text{ kJ mol}^{-1}$ ,  $\Delta S^\ddagger = 71.3 \pm 2.9 \text{ J K}^{-1} \text{ mol}^{-1}$ .

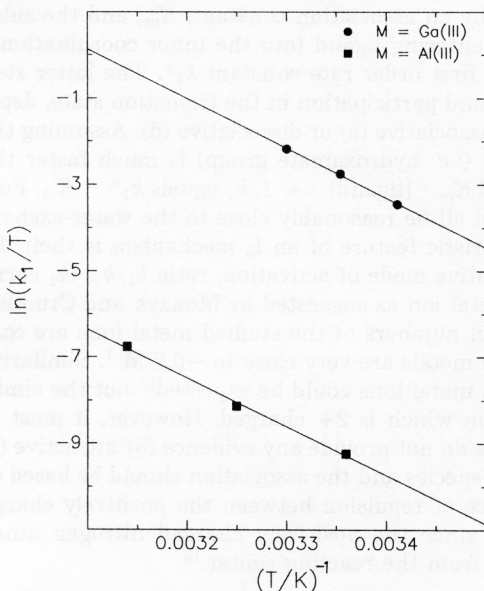


Figure 4. Eyring plot for the reaction of  $\text{H}_4\text{dfb}^+$  with  $\text{M}(\text{H}_2\text{O})_6^{3+}$ .

## DISCUSSION

In Table II, the reported first order water-exchange rate constants for the  $\text{Al}(\text{H}_2\text{O})_6^{3+}$ ,  $\text{Fe}(\text{H}_2\text{O})_6^{3+}$ ,  $\text{Ga}(\text{H}_2\text{O})_6^{3+}$  and  $\text{VO}(\text{H}_2\text{O})_6^{3+}$  ions<sup>3a,23,3b,24</sup> are compared to the second order rate constants for the formation of their bidentate complexes with  $\text{H}_4\text{dfb}^+$ . As seen from Table II, calculated ratio of the ligation and the water-exchange rate constants ( $k_1/k_{\text{ex}}$ ) for all of these metal ions is  $-0.02 \text{ M}^{-1}$ . Therefore, it can be speculated that the ratios of the second order complex formation rate constants and the first



TABLE II  
Rate constants for the water-exchange and substitution of  
coordinated water molecule with desferrioxamine B at 25 °C

Parameter	Al(H <sub>2</sub> O) <sub>6</sub> <sup>3+</sup>	Fe(H <sub>2</sub> O) <sub>6</sub> <sup>3+</sup>	Ga(H <sub>2</sub> O) <sub>6</sub> <sup>3+</sup>	VO(H <sub>2</sub> O) <sub>6</sub> <sup>3+</sup>
$k_{\text{ex}}/\text{s}^{-1}$	1.29 <sup>a</sup>	160 <sup>b</sup>	403 <sup>c</sup>	610 <sup>d</sup>
$k_1/\text{s}^{-1} \text{ M}^{-1}$	0.0211 <sup>e</sup>	2.90 <sup>f</sup>	5.45 <sup>e</sup>	16.9 <sup>g</sup>
$(k_1/k_{\text{ex}})/\text{M}^{-1}$	0.0164	0.0181	0.0135	0.0277

<sup>a</sup> From Ref. 3a. <sup>b</sup> An average value from Refs. 23a and 23b. <sup>c</sup> From Ref. 3b. <sup>d</sup> An average value from Refs. 24a, 24b and 24c. <sup>e</sup> This work. <sup>f</sup> An average value from Refs. 17 and 31. <sup>g</sup> From Ref. 29.

order water-exchange rate constants approximately equal the ratio of the ligand and water molarities ( $\sim 1/55$ ), as a consequence of the arbitrary asymmetry in the choice of standard states.

On the other hand, according to the Eigen-Wilkins mechanism,<sup>25</sup> complex formation reactions occur *via* the rapid diffusion controlled formation of an outersphere complex characterized by an association constant,  $K_{\text{os}}$ , and the subsequent rate limiting penetration of the entering ligand into the inner coordination shell of the metal ion represented by the first order rate constant  $k_1^*$ . The latter step may or may not involve the entering ligand participation in the transition state, depending on whether the activation mode is associative (a) or dissociative (d). Assuming that the ring closure of the bidentate ligand (*i.e.* hydroxamate group) is much faster than the first water molecule expulsion, and  $K_{\text{os}} \cdot [\text{ligand}] \ll 1$ ,  $k_1$  equals  $k_1^* \cdot K_{\text{os}}$ . For an I<sub>d</sub> mechanism, the values of  $k_1^*$  should all be reasonably close to the water-exchange rate constants,  $k_{\text{ex}}$ , whereas a characteristic feature of an I<sub>a</sub> mechanism is their dissimilarity.<sup>26</sup> Consequently, for a dissociative mode of activation, ratio  $k_1/k_{\text{ex}}$  ( $k_1$  corrected for solvation number of the aquo-metal ion as suggested by Monzyk and Crumbliss<sup>27</sup>) should equal  $K_{\text{out}}$ . Since the solvation numbers of the studied metal ions are *ca.* 10, the calculated values of  $K_{\text{os}}$  for all the metals are very close to  $\sim 0.2 \text{ M}^{-1}$ . Similarity of the calculated values for the trivalent metal ions could be expected<sup>12</sup> but the similarity is rather unexpected for vanadyl ion which is 2+ charged. However, it must be noted that constants of this magnitude do not provide any evidence for attractive (or repulsive) forces between the associated species and the association should be based entirely on random collisions.<sup>28</sup> The absence of repulsion between the positively charged metal ions and H<sub>4</sub>dfb<sup>+</sup> is anticipated, since the positively charged nitrogen atom of the ligand is separated by 28 atoms from the reacting center.<sup>16</sup>

Whatever is assumed as a more satisfactory alternative, the arguments presented thusfar, lead to the conclusion that the substitutions at all of these metal ions follow the same mechanism dominated by the energetics of the water exchange. Namely, either by a proper choice of the values of  $K_{\text{os}}$  and solvation numbers, or by introducing a simple correction for the asymmetry of standard states, the first-order constants of the complex formation for all the metal ions get very close to their water-exchange rate constants. However, by comparing the values of  $k_1$  with  $k_1'$ , it is seen that the effect of hydroxo ligand on the rate of the bidentate complex formation decreases in the order: vanadium, aluminum, gallium, iron (for vanadyl<sup>29</sup> and ferric ions<sup>17,30</sup> the values  $k_1'/k_1 \sim 10^5$  and  $\sim 10^3$  are reported, respectively). The decrease of the sensitivity of the substitution rate toward the labilizing effect of the hydroxo ligand on the leaving water molecule suggests a gradual changeover from a dissociative to an associative

character of the activation mode among the metal ions studied.<sup>30</sup> This is in agreement with the conclusion based on the activation volumes observed for the water exchange on the aluminum,<sup>3a</sup> gallium<sup>3b</sup> and iron<sup>23b</sup> aquo-metal ions (including the activation volume for the formation of  $\text{Fe}(\text{H}_3\text{dfb})^{3+}$  complex<sup>31</sup>). The mechanistic change for the trivalent ions could result from either the difference in ionic radii (*e.g.*  $\text{Al}^{3+}$  and  $\text{Fe}^{3+}$ ) or in electronic structure ( $\text{Ga}^{3+}$  has fully occupied d-orbitals that favour dissociative activation).<sup>7</sup> For the vanadyl ion, which has almost totally vacant d-orbitals ( $d^1$  electron structure), the dissociative activation must be a consequence of the labilization of coordinated water molecules by the oxo ligand.

A possible explanation of the above contradictory conclusions drawn from the comparison of  $k_1$  with  $k_{\text{ex}}$  and  $k_1$  with  $k_1'$  is that, even though an  $\text{I}_a$  mechanism is operative for  $\text{Fe}(\text{H}_2\text{O})_6^{3+}$ , the values of  $k_{\text{ex}}$  and  $k_1^*$  can still be very similar if desferrioxamine B and water are approximately equally strong nucleophiles. Unfortunately, to the best of our knowledge, no data has been reported hitherto concerning the  $\text{H}_4\text{dfb}^+$ -standard oxidation potential for the reaction  $2\text{H}_4\text{dfb}^+ = (\text{H}_4\text{dfb})_2^{4+} + 2e^-$ . Therefore, nucleophilic constant  $E_1$ , as proposed by Edwards,<sup>31</sup> cannot be calculated. However, relative basicity of the carbonyl oxygen of the  $\text{H}_4\text{dfb}^+$ -hydroxamate moiety, whose binding to the metal ions is the rate-determining step, should be either lower than or close to the water oxygen basicity. Indeed, we observed no additional protonation of  $\text{H}_4\text{dfb}^+$  at a perchloric acid concentration as high as 1.0 M. In general, nucleophilic and basicity scales do not necessarily correlate strictly, but the linear correlation was predicted for bases of similar softness (*e.g.* for the oxygen bases:  $\text{ClCH}_2\text{COO}^-$ ,  $\text{CH}_3\text{COO}^-$ ,  $\text{C}_6\text{H}_5\text{O}^-$  and  $\text{OH}^-$ ).<sup>32</sup> Therefore, it seems reasonable to expect that the nucleophilicities of desferrioxamine B carbonyl-oxygen and water-oxygen should be quite similar.

The calculated values of activation enthalpy for aluminum and gallium (97.6 and 87.2  $\text{kJ mol}^{-1}$ ) could be compared to the values of 64.4  $\text{kJ mol}^{-1}$ , reported for the reaction of  $\text{H}_4\text{dfb}^+$  with the  $\text{Fe}(\text{H}_2\text{O})_6^{3+}$  ion.<sup>33</sup> The significantly lower value for iron can be explained by the proposed mechanistic change from a dissociative activation for the former two metal ions to an associative activation for the latter one, since the association should decrease the activation enthalpy.

Even though the errors in  $\Delta S^\ddagger$  determination allow only tentative mechanistic predictions, it is interesting to compare this activation parameter for the reaction of  $\text{H}_4\text{dfb}^+$  with  $\text{Al}(\text{H}_2\text{O})_6^{3+}$ ,  $\text{Ga}(\text{H}_2\text{O})_6^{3+}$  and  $\text{Fe}(\text{H}_2\text{O})_6^{3+}$  ions (+53, +71 and  $-17^{32}$   $\text{J K}^{-1} \text{mol}^{-1}$ , respectively). Since all three metal ions are equally charged, the approximately 80  $\text{J K}^{-1} \text{mol}^{-1}$  more negative value for iron is indicative of an associative mechanism in the case of this metal ion. A strong bond formation in the transition state between the entering ligand and central iron ion can account for the observed decrease in the entropy of activation.

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## SAŽETAK

**Kinetika stvaranja i hidrolize (desferioksamin B)-aluminij(III) i -galij(III) kompleksa u kiselim vodenim otopinama perklorata**

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Opisana je kinetika kompleksiranja desferioksamina B s Al(III) i Ga(III) u kiselim vodenim otopinama perklorata pri 25 °C i ionskoj jakosti od 2. Stvaranje i hidroliza kompleksa praćeni su spektrofotometrijski, pod uvjetima pseudo-prvog reda reakcije. Reakcije s oba metala slijede mehanizam u kojemu usporedno reagiraju hidrolizirani i nehidrolizirani akvametalni ioni s potpuno protoniranim ligandom. Izračunane konstante brzine kompleksiranja nehidroliziranih iona aluminija i galija iznose  $0.00211(17) \text{ s}^{-1} \text{ L mol}^{-1}$  i  $5.45(77) \text{ s}^{-1} \text{ L mol}^{-1}$ , odnosno  $189(3) \text{ s}^{-1} \text{ L mol}^{-1}$  i  $2.15(3) \pm 10^4 \text{ s}^{-1} \text{ L mol}^{-1}$  za hidrolizirane ione. Entalpije aktiviranja za reakcije nehidroliziranih iona aluminija i galija iznose  $97.6 + 8.2 \text{ kJ mol}^{-1}$  i  $87.2 \pm 7.2 \text{ kJ mol}^{-1}$ , a entropije aktiviranja iznose  $52.5 \pm 2.9 \text{ J K}^{-1} \text{ mol}^{-1}$  i  $71.3 \pm 2.8 \text{ J K}^{-1} \text{ mol}^{-1}$ . Rezultati su razmotreni u smislu reakcijskog modela u kojem je disocijacija prve molekule koordinirane vode odlučujući korak u reakciji.