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Note

Siderophore Chemistry of Vanadium. Interaction Between Vanadium(V) and Desferrioxamine B in Aqueous Acidic Perchlorate Solution

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Complexation of vanadium(V) at 25 °C in 2 M $NaClO_4/HClO_4$ by desferrioxamine B chelator results in the formation of 1 : 1 complex when concentration of $HClO_4$ in the reaction mixture is higher than 0.1 M. The apparent equilibrium constant and the second order rate formation constant in 0.5 M $HClO_4$ are: $K_{app} = (6 \pm 2) \times 10^6$ M^{-1}, $k = (2.3 \pm 0.2) \times 10^5$ M^{-1} s^{-1}, respectively.

INTRODUCTION

Essentiality of vanadium was long suspected[1] and in the early 1970's it was confirmed with experiments employing laboratory animals that vanadium is an essential element.[2,3] Over the past decade many physiological effects of vanadium have been recognized suggesting a prominent place of vanadium in biology. An overview of vanadium in biology and biochemistry including the results of exogenous additions of vanadium and their relation to the basic inorganic chemistry of vanadium are presented in two recent reviews.[4,5] Recently, vanadium phenolates have been proposed as models for vanadium in biological systems.[6]

In spite of the large volume of the published material dealing with biochemical effects of vanadium, which has grown enormously in recent years, our knowledge of vanadium in biology is presently very much in a state of flux.[5] For example, a possible link between vanadium and iron metabolism has been suggested.[5,7] It has been hypothesised that the transferrin is the carrier protein for VO^{2+} in blood, since the experiments *in vitro* show that VO^{2+} binds stoichiometrically to two specific Fe^{3+} binding sites of various transferrins.[9–11]

However, correlation of vanadium and iron biochemistry is not generally understood. One obvious difference is that there is relatively little vanadium in the body and it is not needed in large amounts and therefore, a storage protein per se would not seem to be a necessary component of its biochemistry,[7] which is an important feature of iron biochemistry. In addition, the

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concentration of vanadium in biological fluids is of the order of ppm-ppb which is considerably lower value than iron concentration. This fact may indicate that the formation constants of vanadium biocomplexes are significantly larger than those of iron complexes.

The iron carriers in microbes are well known siderophores which currently constitute a fast developing area of research in bioinorganic chemistry.[12–14] To the best of our knowledge the possibility that vanadium binds to siderophore such as naturally occuring hydroxamate molecules have not been investigated.

Here we present the first results on the vanadium siderophore chemistry describing the complex of vanadium(V) with desferrioxamine B, which is a linear trihydroxamic acid with molecular formula $NH_2(CH_2)_5[N(OH)C(O)(CH_2)_2$-$C(O)NH(CH_2)_5]_2 \cdot N(OH)C(O)CH_3$ (H_3 DFB).

EXPERIMENTAL

Water used throughout the experiments was doubly distilled from an all in glass apparatus over alkaline permanganate. Desferrioxamine B (Desferal® CIBA) was recrystallized from methanol (m. p. 151 °C, uncorrected).

All other chemicals were of highest purity. The spectrophotometric measurements were performed on a Pye Unicam SP 8—100 and a Perkin Elmer Lambda 3 instruments equipped with thermostated cell compartment. The absorbance measurements of equilibrated solutions were taken at 25 ± 0.1 °C. In all the experiments 2.0 M ionic strength was held by $NaClO_4$.

Equilibrium constants and molar absorptivities were calculated on a UNIVAC 1100 computer at the University Computer Centre, Zagreb, using a published program[15] that essentially fits the experimental data to a function of form $A = \sum_{i=1}^{n} c_i \varepsilon_i$. Parameters A, c_i, ε_i and n have a meaning of measured absorbance, molarity, molar absorptivity and number of proposed species present in equilibrated solution, respectively. Here c_i is a function of the total concentration of vanadium, H_4DFB^+, and H^+ ions as well as of the values of the respective equilibrium constants.

All kinetic experiments were measured on a stopped-flow Durrum D-110 Spectrophotometer at 25 °C and I = 2 M ($HClO_4/NaClO_4$). In a typical run solutions of vanadium(V) ions, initially added as an V_2O_5, were flown together with the solutions of desferrioxamine B. The increase in absorbance was followed at 485 nm. Solutions of vanadium and desferrioxamine B to be mixed were of the same acidity.

RESULTS AND DISCUSSION

Mixing of acidic solution of V_2O_5 and H_4DFB^+ is followed by an immediate formation of color which fades slowly due to ligand decomposition[16] in highly acidic solutions. On the other hand at lower acidities reduction of vanadium(V) is solely responsible for the color disappearance. The latter was confirmed by measured spectra which entirely resembled the spectra formed in the reaction of desferrioxamine B with vanadyl sulphate. The formation of collor is rapid relative to the times of its dissappearance in both strong and weak acid solutions.

A visible spectrum of vanadium(V)-desferrioxamine B complex in 0.407 M $HClO_4$ is shown in Figure 1. (curve 1) and is characterised by an absorbance maximum at 485 nm, obviously of the charge-transfer origin since V(V) is of d° configuration. Spectra of equilibrated solutions (before the decomposition of the complex takes significant extent) at different acidities are also presented in Figure 1. A steady hypsochromic shift of the absorbance maximum upon a decrease of acidity is observed. This suggests presence of at least two collored complexes equilibrated by a proton.

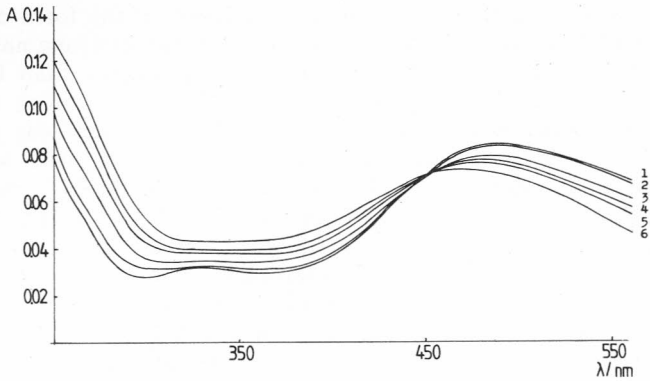

Figure 1. A proton dependence of the electronic spectra of equilibrated VO^{+}_{2} — — H_4DFB^{+} system at 25 °C, in 2.0 mol dm^{-3} (H/Na)ClO_4. Conditions: $VO^{+}_{2} = 2.42 \times \times 10^{-5}$ mol dm^{-3}; $H_4DFB^{+} = 2.49 \times 10^{-4}$ mol dm^{-3}; $H^{+} = 0.407$, 0.208, 0.048, 0.024, 0.016, and 0.006 mol dm^{-3} for the curves 1, 2, 3, 4, 5, and 6, respectively.

Job method of continuous variations shows that in high acid solution a V(V)-H_4DFB^{+} complex of 1 : 1 molar ratio is formed. (Figure 2.A). However, Figure 2.B indicates that at lower acidities the complexes of the composition other than 1 : 1 molar ratio appear. These new species have not been studied in detail and the investigations described in this paper have been done in the acid region 1.0—0.1 M $HClO_4$. At least what can be said at this stage of investigation that in 0.01 M $HClO_4$ molar ratio V(V) : H_4DFB^{+} of ~ 2 : 3 is obtained. One possible explanation is that a mixture of equal fractions of 1 : 1 and 1 : 2 complexes is formed.

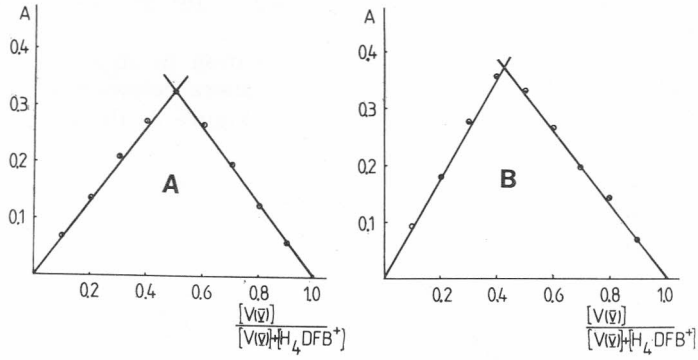

Figure 2. Job diagrams. Conditions: $[V(V)] + [H_4DFB^{+}] = 4.0 \times 10^{-4}$; A, $H^{+} = 0.4$ mol dm^{-3}; B, $H^{+} = 0.01$ mol dm^{-3}, at 25 °C, in 2.0 mol dm^{-3} (H/Na)ClO_4, at 485 nm.

Variation of H_4DFB^{+} concentration (in molar excess over V(V) in three series of experiments at constant H^{+} concentration $[H^{+}] = 1.0$, 0.5, and 0.1 M) gives almost the same value of calculated apparent equilibrium constant K_{app} (8 ± 2, 6 ± 2, and $3 \pm 1 \times 10^{6}$ M^{-1}, respectively) defined by eq. 1.

$$VO_2^{+} + H_4DFB^{+} \rightleftharpoons VO_2H_4DFB^{+2} \quad K_{app} \tag{1}$$

Under these acidities all the vanadium(V) is present in the form of VO_2^+,[4] and the ligand H_4DFB^+ is fully protonated, since all three hydroxamato groups as well as terminal amino group exhibit pK_a's values higher than 9. The small decrease in calculated K_{app} is dubious due to the large values of K_{app} that makes difficult to determine it. Therefore no proton release was proposed for this step of interaction. At lower acidity, for example in 0.01 M H^+, higher value of apparent constant was calculated $K_{app} \geq 7 \times 10^7$ M^{-1} confirming the above assumption of the formation of new species at low acidity.

The obtained results reveal the affinity of vanadium(V) for desferrioxamine B ligand as a representative of siderophore molecules and may be used for comparison with the analogous data of ferrioxamine B complex. For example, the apparent stability constants in 1.0, 0.5, 0.1, and 0.01 M $HClO_4$ of iron(III) (and those of vanadium(V)) are: 3×10^4 (8×10^6); 9×10^4 (6×10^6); 3×10^6 (3×10^6); 2×10^9 (7×10^7) M^{-1}, respectively. These approximate values of the apparent stability constants of ferrioxamine B complex are calculated from the data from reference 17.

An obvious feature of this simple comparison is that naturally occuring desferrioxamine B chelate exhibits more stable complex with vanadium in strong acid media and with iron(III) in weak acid solutions.

Preliminary kinetic results were performed by using solutions of $2.37 \times \times 10^{-5}$ M V(V), 2.5×10^{-4} M H_4DFB^+, and 0.212, 0.412, and 0.946 M $HClO_4$ giving the observed rate constants 48.4, 46.0, and 46.5 s^{-1}, respectively, where each value of k_{obs} is the average of at least three determinations. It is easy to show by using K_{app} that the reaction (1) goes to completion under our experimental conditions. Therefore, the observed rate constant is described by the expression $k_{obs} = k\,[H_4DFB^+]$. The data suggest the rate independence on the acid concentration which is also substantiated by only one straight line in Figure 3., which is obtained at two different acidities. The second order rate constant of the reaction (1) $k = (2.3 \pm 0.2) \times 10^5$ M^{-1} s^{-1} was calculated from the slope.

It is generally accepted that complex formation in aqueous solutions involves preequilibrium formation of an outer-sphere complex between metal ion and incoming ligand.[18] The straight line in Figure 3. allows only the esti-

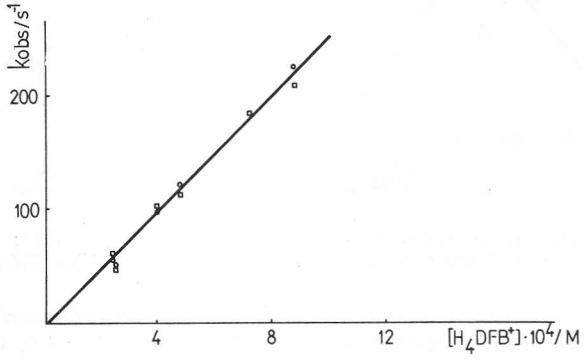

Figure 3. A dependence of the formation rate constant of $VO_2^+ - H_4DFB^+$ complex on the total concentration of H_4DFB^+ at 25 °C, in 2.0 mol dm^{-3} (H/Na)ClO_4 at 485 nm. Conditions: $VO^+_2 = 2.37 \times 10^{-5}$ mol dm^{-3}; $H^+ = 0.212$ mol dm^{-3}; $H^+ = 0.518$ mol dm^{-3}.

mation of the upper limit of the outer-sphere complex formation constant to be smaller than 100 M^{-1}. The rate constants of the analogous reaction of the same ligand H_4DFB^+ with iron(III) center are lower (k ($FeOH^{2+}$) = 4×10^3 M^{-1} s^{-1} and (Fe^{3+}) = 2 M^{-1} s^{-1} (from reference 17 and also from references therein). On the other hand, the analogous reactions of the same metal center VO_2^+ with different multidentate ligands exhibit the rate formation constants which fall in the range $\sim 1 \times 10^3 - 1 \times 10^8$ M^{-1} s^{-1} (ref. 19 and 20). These results can be interpreted in terms of I_a mechanism if one assumes the water exchange rate constant on the VO_2^+ center to be 10^4 M^{-1} s^{-1} as it has been already reported.[21] However, the same results were interpreted by the I_d mechanism based on the estimated value of water exchange rate constant on the VO_2^+ center to be as high as 10^8 M^{-1} s^{-1}.[20]

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SAŽETAK

Reakcija vanadija(V) s desferioksaminom B u kiselim vodenim otopinama perklorata

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Kompleksacijom vanadija(V) s desferioksaminom B na 25 °C u kiselim vodenim otopinama perklorata (2 M H/$NaClO_4$) nastaje 1:1 kompleks. Ravnotežni omjer koncentracija kompleksa i nekompleksiranih iona, pri kiselosti većoj od 0,1 M $HClO_4$, iznosi $K_{app} = (6 \pm 2) \times 10^6$ M^{-1}, a izračunana konstanta brzine nastajanja kompleksa $k = (2{,}3 \pm 0{,}2) \times 10^5$ M^{-1} s^{-1}.