Influences of pH and Ionic Strength on Aqueous Vanadate Equilibria

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^{51}V NMR spectroscopy is used to investigate the thermodynamics of the reaction $HVO_4^{2-} + H^+ \rightleftharpoons H_2VO_4^-$. The enthalpy and entropy of this reaction are found to be very close to those of analogous reactions with phosphate and arsenate. This provides firm evidence that incorporation of water into the vanadate ion does not accompany the protonation of the dianion. Therefore, the tri-, di-, and monoanionic vanadates are all four-coordinate. The oligomerization reactions of vanadate are studied as a function of ionic strength and of pH and the results displayed graphically. The formation of the vanadate trimer and pentamer is examined in some detail, the identities of these materials are confirmed, and the apparent disappearance of the trimer at near-neutral pH is discussed.

Introduction

The aqueous chemistry of vanadium(V) oxoanions has been a topic of continuing interest for a number of years. To a large extent, this interest has been stimulated by the evidence which suggests that vanadium is an essential element. Furthermore, vanadate is an efficient inhibitor of the function of a number of enzymes and an activator of others. These, and a variety of other important biochemical properties of vanadium, have been reviewed in depth by a number of authors.[1,2]

Proper interpretation of many studies of vanadate interactions depend on the presence of reliable information concerning the derivatives of vanadate which are present in solution and on knowledge of their coordination. Such species include the monomer, dimer, tetramer, and other oligomers. It is well-known that the formation constants for the various products are dependent on the pH and ionic strength of the medium. There does not, however, appear to be a tabulation of these values for a range of ionic strengths.

In addition to vanadate itself, most of the oligomers appear to exhibit biochemical activity. For instance, the dimer activates the phosphatase activity of phosphoglycerate mutase[3] but inhibits the function of prostatic acid phosphatase.[4] The tetramer is an inhibitor of a number of 6-phosphogluconate dehydrogenases[5] and apparently is responsible for the vanadate-catalyzed photocleavage in myosin subfragment 1.[6] The enzymatic function of vanadate and various of its oligomers has been examined in some detail.[2,7]

The oligomerization of vanadate and the effects of pH on the protonation state of the various oligomers have been extensively studied by ^{51}V nuclear magnetic resonance (NMR) spectroscopy,[8] by a combination of ^{51}V NMR spectroscopy and potentiometry,[9,10] and by spectrophotometry.[11] Under the conditions of the individual studies, the various products have, in general, been well characterized. There is some concern about the coordination about vanadium in the monoanionic species. It has generally been accepted that the monoanionic, dianionic, and trianionic vanadates are all tetrahedrally coordinated. Recently, however, on the basis of the characteristics of the UV/visible and magnetic circular dichroism spectra, it was argued that protonation of the dianion is accompanied by incorporation of water and that monoanionic vanadate has trigonal bipyramidal coordination.[12]

It is important that the coordination of the vanadate ions is known because our understanding of the aqueous chemistry of vanadate relies to a large extent on knowing the properties of the aqueous oxoanions. In this communication, the temperature dependence of the protonation of HVO_4^- is studied and the thermodynamic parameters associated with this reaction are obtained. These parameters are directly relevant to any changes in coordination that may accompany the protonation step. In addition to this, the vanadate oligomerization reactions, as a function of both pH and anionic strength, are determined so that the various formation constants are immediately accessible for different reaction conditions. There is some disagreement in the literature regarding the identification of the vanadate pentamer. The signal in the NMR spectrum that corresponds to the product in question has been assigned both to a cyclic pentameric oligomer[9] and to a hexameric[6,13] oligomer. There seems little reason to doubt the assignment to a pentameric product, and it should be noted that an NMR signal at −586 ppm has been assigned to a hexamer.[9] However, the assignment of the −583 ppm signal is not unequivocal, so the formation of this product is examined in detail here, as are the other oligomerization reactions.

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Experimental Section

Materials. Vanadium pentoxide (99.99%) and KCl from Aldrich Chemical Co. and *N*-(2-hydroxyethyl)piperazine-*N'*-ethanesulfonic acid (HEPES) buffer from Boehringer Mannheim GmbH were used as provided.

The procedures previously described for the preparation of vanadate stock and final solutions were followed here.[14] Stock solutions containing 1.0 M HEPES and 2.2 M KCl were prepared in distilled water, as were vanadate stock solutions at 0.1 M. The final solutions all contained 20 mM HEPES buffer but varying amounts of KCl to give ionic strengths ranging from approximately 0 to 2 M.

The pH meter was calibrated immediately prior to sample preparation using pH 10.0 and pH 4.0 standard buffer solutions. The stock solutions were all prepared at pH values sufficiently low so that when they were combined during sample preparation, the pH was below the desired value. The pH was then adjusted upward with NaOH. This procedure was followed in order to prevent formation of decavanadate, which rapidly forms under locally acidic conditions but which hydrolyzes only slowly at higher pH. Small adjustments with distilled water were made in order to achieve the final volumes. In an effort to minimize pipetting errors during sample preparation, all additions were cross-checked by weighing.

Thermodynamic Measurements. For all thermodynamic measurements, the distilled water used for sample preparation was boiled immediately prior to use in order to remove any dissolved CO_2 and all samples were prepared under an argon atmosphere. The temperature of all samples used for the thermodynamic measurements was maintained using the temperature regulator of the NMR spectrometer ($T \pm 0.1$ K). NMR spectra were obtained as a function of pH at various temperatures within the range 270–320 K. The complete temperature study was repeated, and no discrepancies outside the experimental errors of either experiment were found. pK_a values were determined at each temperature using the dependence of the ^{51}V chemical shift of the vanadate ion on the pH of the medium.[8,15]

Spectroscopy. All NMR spectra were obtained at 105.4 MHz using a Bruker AMX-400 NMR spectrometer. Except for the thermodynamic measurements, all spectra were obtained at ambient temperature (21 ± 1 °C). ^{51}V chemical shifts are referenced to an external $VOCl_3$ reference assigned to 0.0 ppm. A polynomial baseline correction was applied to all spectra before integrals were obtained. Spectral widths of 80 kHz, 60° pulse widths, and 0.05 s acquisition times were used for all spectra.

Methods. The appropriate equations were put into a linear form as outlined under Results. The experimental quantities were then analyzed using a standard least-squares procedure for obtaining the slopes and, if non-zero, the intercepts of the lines. The errors are quoted at the 95% confidence level.

Results

The protonation of HVO_4^{2-} to give the monoanionic vanadate is accompanied by a change in vanadium chemical shift of about 22 ppm. The protonation/deprotonation reaction is rapid, so there is a continuous variation in chemical shift as the pH is varied throughout the range of values used. If δ_l and δ_h represent the chemical shifts of the monoanionic and dianionic species, obtained at low and high pH, respectively, and δ_{obs} is the chemical shift actually observed, then the pK_a of the monoanion is given by eq 1.[15] The pK_a is then given simply

$$pH = pK_a + \log\{(\delta_l - \delta_{obs})/(\delta_{obs} - \delta_h)\} \qquad (1)$$

from the *y*-intercept of the plot of pH vs the term in logarithms. The enthalpy (ΔH) and entropy (ΔS) of the protonation reaction are related to the pK_a in a simple manner as expressed in eq 2 where *R* is the gas constant and *T* is the absolute temperature.

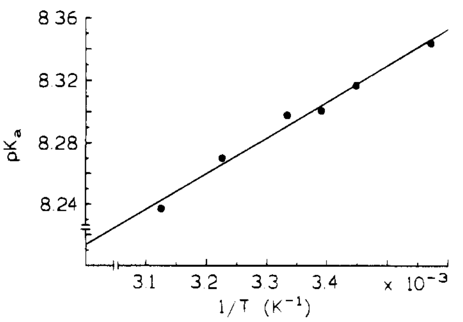

Figure 1. Dependence of the second pK_a of vanadate on the inverse of the absolute temperature. Conditions of the experiments: 0.2 mM vanadate; 0.1 M NaCl; 20 mM HEPES buffer; variable temperature; variable pH, pH 6.0–10.0 for each temperature.

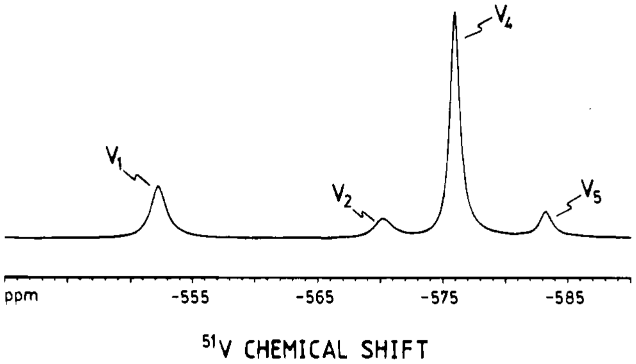

Figure 2. ^{51}V NMR spectrum showing monomeric vanadate and its predominant oligomers. Experimental conditions: 3.0 mM total vanadate; pH 8.0; 20 mM HEPES buffer; 0.75 M KCl; 298 K.

$$pK_a = -\Delta H/2.303RT + \Delta S/2.303R \qquad (2)$$

Figure 1 shows the results obtained from a temperature-dependence study of the pK_a of $H_2VO_4^-$ plotted as a function of the inverse temperature for the reaction $HVO_4^{2-} + H^+ \rightleftharpoons H_2VO_4^-$. From this graph, the values $\Delta H = -4.4 \pm 1.0$ kJ/mol and $\Delta S = 144 \pm 3$ J/(mol K) were obtained. A repetition of the complete temperature study provided values for the entropy and enthalpy that agreed well with those from the initial study, $\Delta H = -4.0 \pm 1.8$ kJ/mol and $\Delta S = 145 \pm 6$ J/(mol K). For these measurements, CO_2 was removed from the distilled water immediately prior to use by boiling the water. Carboxylic acids such as acetic acid are known to undergo a rapid complexation/decomplexation reaction with vanadate,[16] and it is highly likely that the hydrogen carbonate anion will also do so and thus provide a source of error for the thermodynamic measurements.

Under near-neutral pH conditions, the predominant oligomers of vanadate are the dimer, cyclic tetramer, and cyclic pentamer. A ^{51}V NMR spectrum of an equilibrium solution of 3.0 mM total vanadate was obtained at pH 8.0 and is displayed in Figure 2. The trimer and the hexamer are minor products under the conditions of this study and are not observable in the above spectrum, although at this concentration (3.0 mM), the trimer is observed at a pH of about 9. These and other minor oligomeric products have been characterized.[8-10]

The formation of the oligomers can be represented as in eqs 3–5. The concentrations of the various reactants can be readily

$$2V_1 \overset{K_{12}}{\rightleftharpoons} V_2 \qquad [V_1]^2K_{12} = [V_2] \qquad (3)$$

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$$4V_1 \overset{K_{14}}{\rightleftharpoons} V_4 \qquad [V_1]^4K_{14} = [V_4] \qquad (4)$$

$$5V_1 \overset{K_{15}}{\rightleftharpoons} V_5 \qquad [V_1]^5K_{15} = [V_5] \qquad (5)$$

obtained from integration of the ^{51}V NMR spectra so that the appropriate ratio from the desired equation gives the required parameter.

The pentameric product is of some interest here. The assignment of the signal (−583 ppm) in Figure 2 to a cyclic pentamer is based on reasonably firm evidence.[9,10] However, it has also been assigned to a V_6 product.[6,13] This problem can be resolved in a straightforward manner by writing the formation of this product from V_4 as in eq 6. Since n is not known, this

$$nV_4 \rightleftharpoons 4V_n \qquad (6)$$

equation can be rewritten in terms of the vanadium atom concentration of the product, $n[V_n]$, to give eq 7, which directly gives the logarithmic expression eq 8.

$$[V_4]^{n/4}K_{4n}' = n[V_n](1/n) \qquad (7)$$

$$(n/4) \log [V_4] + \log K_{4n}' = \log(n[V_n]) - \log n \qquad (8)$$

A plot of log $(n[V_n])$ vs log $[V_4]$ will then give a straight line of slope $n/4$. The overall result is shown in Figure 3 for concentration studies carried out at pH 7.0, 7.5, 8.0, and 9.1. The slopes for the individual studies were 1.28, 1.28, 1.22, and 1.26, respectively, for the above pH values. The average of these values, 1.26 ± 0.03, gives $n/4$. It is clear that n is equal to 5 and this product is a pentamer not a hexamer.

In addition to this study of the formation of the vanadate pentamer, the pH-dependent formation constants for the predominant oligomers have been obtained as a function of both ionic strength and pH. These formation constants are plotted in Figures 4−6. Within the range of these graphs, any formation constant can be directly obtained for specific reaction conditions. If the concentration of one derivative is known, that of the others can easily be calculated. The conservation equation can also be used in conjunction with the known total concentration of vanadate and the appropriate constants from the graphs to calculate the concentrations of all species.

Of some interest in this work is the vanadate trimer. At pH 9.1, a single broad signal at −569.7 ppm is observed. Other workers have assigned signals in this region to a linear tetramer[9,10] and to a combination of linear trimer and linear tetramer.[8] The present work is consistent with the trimer being the product, but a superposition of NMR signals cannot be ruled out. It is possible to show that this signal corresponds predominantly to a trimeric product by using a procedure similar to that used for identification of the pentamer. When the appropriate quantities were plotted according to the requirements of eq 8, a line of slope 0.72 ± 0.24 was obtained. This corresponds to a value of 3 for the number of vanadium nuclei in this product; $n/4$ = 0.72, but certainly does not rule out a contribution from a tetramer. Observation of the signal position of this product revealed that it undergoes a change in position with pH, from −569.7 ppm at pH 9.06 to −572.1 ppm at pH 8.50.

A detailed examination of the formation of the trimer and also of the other oligomers was carried out for conditions of 1.0 M KCl, 20 mM HEPES buffer, and various pH values. The results are summarized in Table 1.

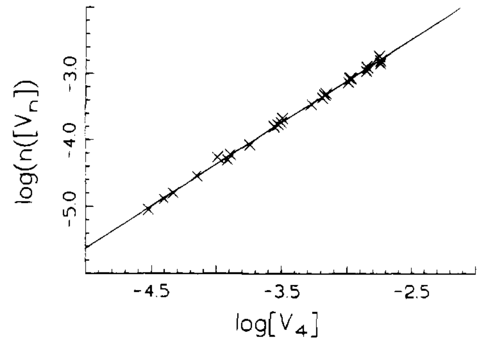


Figure 3. Logarithm of the vanadium atom concentration of the −583 ppm product shown as a function of the logarithm of the concentration of tetrameric vanadate. Conditions for the experiments: HEPES buffer, 20 mM; ionic strength, 1.0 M with KCl; vanadate concentration variable for each of pH 7.0, 7.5, 8.0 and 9.1.

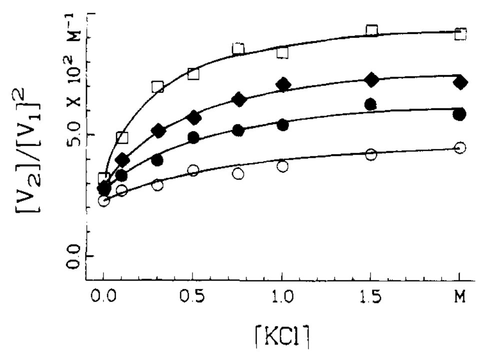


Figure 4. pH-dependent formation constant for divanadate as a function of ionic strength: ○, pH 8.0; ●, pH 7.5; ◆, pH 7.0; □, pH 6.5. Experimental conditions: 3.0 mM total vanadate; 20 mM HEPES buffer; KCl and pH as indicated; ambient temperature (294 ± 1 K). The solid lines are included as an aid in following the curves.

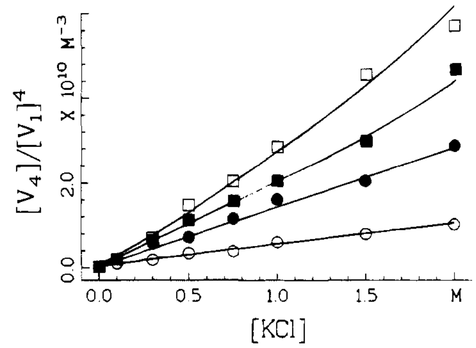
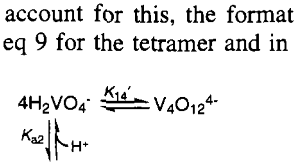
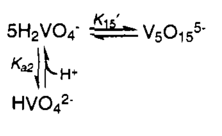


Figure 5. Formation constant for the vanadate tetramer as a function of ionic strength: ○, pH 8.0; ●, pH 7.5; ◆, pH 7.0; □, pH 6.5. Experimental conditions: 3.0 mM total vanadate; 20 mM HEPES buffer; KCl and pH as indicated; ambient temperature (294 ± 1 K). The solid lines are included as an aid in following the curves.

The pH-dependent oligomerization constants are, of course, pH dependent because the charge states of vanadate and possibly its oligomers vary with pH according to their respective pK_a values. In order to account for this, the formation constants can be written as in eq 9 for the tetramer and in eq 10 for the



$$4H_2VO_4^- \overset{K_{14}'}{\rightleftharpoons} V_4O_{12}^{4-} \qquad (9)$$
$$K_{a2} \updownarrow H^+ \quad HVO_4^{2-}$$



$$5H_2VO_4^- \overset{K_{15}'}{\rightleftharpoons} V_5O_{15}^{5-} \qquad (10)$$
$$K_{a2} \updownarrow H^+ \quad HVO_4^{2-}$$

pentamer. An equation similar to these (eq 11) can be written

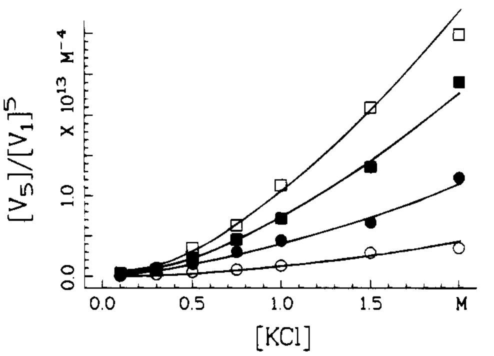
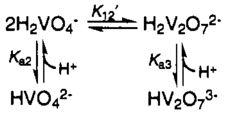


Figure 6. Formation constant for the pentameric vanadate as a function of the ionic strength: ○, pH 8.0; ●, pH 7.5; ◆, pH 7.0; □, pH 6.5. Experimental conditions: 3.0 mM total vanadate; 20 mM HEPES buffer; KCl and pH as indicated; ambient temperature (294 ± 1 K). The solid lines are included as an aid in following the curves.



$$\begin{tikzcd} 2H_2VO_4^- \arrow[r, shift left, "K_{12}'"] \arrow[d, shift left, "K_{a2}"'] & H_2V_2O_7^{2-} \arrow[l, shift left] \arrow[d, shift left, "K_{a3}"'] \\ HVO_4^{2-} \arrow[u, shift left, "H^+"'] & HV_2O_7^{3-} \arrow[u, shift left, "H^+"'] \end{tikzcd} \qquad (11)$$

for the dimer. In this equation, K_{a3} of divanadate is taken into account. For the pH values of this ionic strength study, there is little contribution from this second pK_a term, but it will be important at higher pH values. As a point of interest, the data from the more extended pH study of Table 1 affords a pK_{a3} of 8.5 for divanadate.

Both the pK_a of vanadate and the pH-independent formation constants are affected by the ionic strength of the medium as can readily be seen from Figure 7. The values for Figure 7 are taken from Table 2. The pH-independent formation constants are related to the pH-dependent constants by eqs 12–14.

$$(1 + K_{a2;V}/[H^+])^2K_{12} = K_{12}'(1 + K_{a3;V2}/[H^+]) \qquad (12)$$

$$(1 + K_{a2;V}/[H^+])^4K_{14} = K_{14}' \qquad (13)$$

$$(1 + K_{a2;V}/[H^+])^5K_{15} = K_{15}' \qquad (14)$$

Obviously, the curves of Figures 5 and 6 can be obtained from the information in Table 2. Application of eq 12 requires K_{a3}, but $K_{a3;V2}/[H^+]$ will be small for pH values lower than about 8.0 and this term can be ignored for most applications.

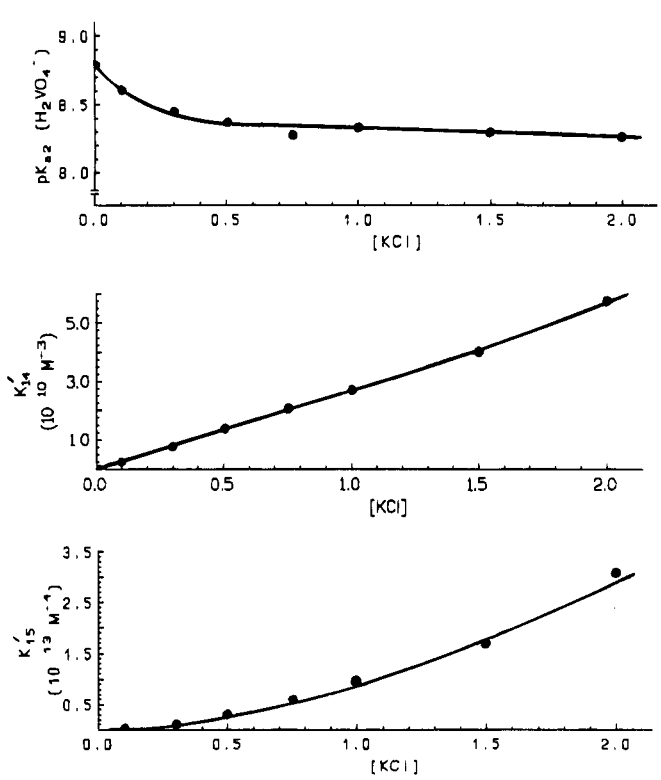


Figure 7. pK_a of vanadate and the formation constants for the cyclic tetramer ($V_4O_{12}^{4-}$) and the cyclic pentamer ($V_5O_{15}^{5-}$) from monoanionic vanadate ($H_2VO_4^-$) as a function of ionic strength. Experimental conditions: 3.0 mM total vanadate; 20 mM HEPES buffer; variable pH, pH 6.5–8.0; KCl, as indicated; ambient temperature (294 ± 1 K). The solid lines are included as an aid in following the curves.

Discussion

There is little argument about the coordination of the tri- and dianionic vanadate ions. These ions are both considered to have tetrahedral coordination. The situation changes for monoanionic vanadate, where UV/vis spectroscopic and magnetic circular dichroism studies have been used to assign a trigonal bipyramidal coordination to this anion.[12] The question then arises as to whether this is a correct assignment of coordination. The possible reactions to be compared are given in eqs 15 and 16.

Table 1. pH-Dependent Formation Constants Determined for Vanadate Oligomers as a Function of pH[a]

pH	K_{12} (M^{-1})	K_{13} (M^{-2})	K_{14} (M^{-3})	K_{15} (M^{-4})	K_{24} (M^{-1})[b]	$K_{45}^{1/4}$ ($M^{-1/4}$)
6.5	(8.6 ± 1.0) × 10^2		(2.7 ± 0.3) × 10^{10}	(9.8 ± 1.2) × 10^{12}	3.6 × 10^4	0.91 ± 0.06
7.0	(7.3 ± 0.3) × 10^2		(1.6 ± 0.2) × 10^{10}	(5.3 ± 0.8) × 10^{12}	3.0 × 10^4	0.90 ± 0.03
7.5	(5.8 ± 0.5) × 10^2		(10.5 ± 1.2) × 10^9	(3.0 ± 0.4) × 10^{12}	3.1 × 10^4	0.92 ± 0.03
8.0	(3.9 ± 0.3) × 10^2		(3.9 ± 0.5) × 10^9	(8.1 ± 0.5) × 10^{11}	2.6 × 10^4	0.84 ± 0.04
8.5	(1.4 ± 0.1) × 10^2	(1.9 ± 0.3) × 10^4	(9.1 ± 0.9) × 10^7	(7.9 ± 0.7) × 10^9	4.7 × 10^3	0.88 ± 0.04
9.1	(4.7 ± 0.2) × 10^1	(3.3 ± 0.2) × 10^3	(1.2 ± 0.1) × 10^6	(3.5 ± 0.3) × 10^7	5.4 × 10^2	0.87 ± 0.11

[a] Conditions for the measurements: variable vanadate concentrations, 0.5–10.0 mM; ionic strength, 1.0 M with KCl; buffer, 20 mM HEPES; pH, as indicated. [b] This value was calculated from $K_{12}^2K_{24} = K_{14}$.

Table 2. Formation Constants Determined for Various Vanadate Oligomers as a Function of Added KCl[a,b]

	[KCl] (M)[c]							
[KCl]	0.0	0.1	0.3	0.5	0.75	1.0	1.5	2.0
pK_a ($H_2VO_4^-$)	8.80	8.60	8.45	8.37	8.28	8.33	8.30	8.26
K_{12}' (M^{-1})[d]	3.1 × 10^2	4.1 × 10^2	5.3 × 10^2	6.5 × 10^2	7.3 × 10^2	7.7 × 10^2	8.2 × 10^2	8.9 × 10^2
K_{14}' (M^{-3})	2.8 × 10^8	2.4 × 10^9	7.5 × 10^9	1.4 × 10^{10}	2.1 × 10^{10}	2.7 × 10^{10}	4.0 × 10^{10}	5.8 × 10^{10}
K_{15}' (M^{-4})		3.2 × 10^{11}	1.1 × 10^{12}	3.1 × 10^{12}	6.2 × 10^{12}	9.8 × 10^{12}	1.7 × 10^{13}	3.1 × 10^{13}

[a] Experimental conditions: 3.0 mM total vanadate; 20 mM HEPES buffer; variable pH, pH 6.5–8.0; KCl, as indicated; ambient temperature (294 ± 1 K). [b] The formation constants have an error of about ±20% at the 3σ level. [c] With no added KCl, the ionic strength of the medium will be about 0.02 M. [d] This formation constant neglects the pK_{a3} of divanadate which becomes important above pH 8.

$$HVO_4^{2-} + H^+ \rightleftharpoons H_2VO_4^- \qquad (15)$$

$$HVO_4^{2-} + H_2O + H^+ \rightleftharpoons H_4VO_5^- \qquad (16)$$

For the first example above, the thermodynamic parameters ΔH and ΔS should be comparable to those for other oxoanions such as phosphate and arsenate. A number of relevant examples are given in Table 3. If, however, the protonation reaction is accompanied by incorporation of a water molecule into the complex, as expressed by eq 10, then the reaction should be accompanied by an unfavorable entropic contribution. The reaction $MoO_4^{2-} + H^+ \rightleftharpoons HMoO_4^-$, for example, is characterized by $\Delta H = 16$ kJ/mol and $\Delta S = 123$ J/(mol K) while, for the reaction $HMoO_4^- + 2H_2O + H^+ \rightleftharpoons Mo(OH)_6$, $\Delta H = -45$ kJ/mol and $\Delta S = -76$ J/(mol K).[17]

The values determined in this study for the protonation of HVO_4^- are $\Delta H = -4.4 \pm 1.0$ kJ/mol and $\Delta S = 144 \pm 3$ J/(mol K). These quantities are very close to the relevant values tabulated in Table 3. In particular, there is a close correspondence between these measured values and those for the protonation of VO_4^{3-} to HVO_4^{2-}, $\Delta H = -24$ kJ/mol and $\Delta S = 174$ J/(mol K).[11] An even better correspondence is achieved when the protonation of HVO_4^{2-} is compared to those of HPO_4^{2-} and $HAsO_4^{2-}$, where respectively the ΔH are -3.9, -3.3 kJ/mol and ΔS are 126, 121 J/(mol K) (see Table 3). On the basis of these experiments, there seems little doubt that there is no water incorporated into the monoanionic vanadate ion as it forms from HVO_4^{2-}. Therefore, the mono-, di-, and trianionic vanadates are all tetracoordinate. It is not clear why the large change in ^{51}V chemical shift should accompany the second protonation step. It may be, in this case, that electron transfer to the proton occurs to a significant extent from the vanadium center as opposed to transfer mainly from the oxygens in the first protonation step.

The assignment of the −583 ppm NMR signal in Figure 2 has been somewhat ambiguous. However, the experimental results presented in Figure 3 confirm that the product giving rise to the −583 ppm signal arises from a pentameric product, and this resolves the problems in the literature concerning the question of whether the −583 ppm signal derives from a pentamer or hexamer. There, therefore, is little reason to doubt that the −586 ppm product (not observed in Figure 2 because of its low concentration) is a cyclic hexameric product as already assigned.[9,10]

An additional oligomer, not identified in Figure 2, also occurs and is observable at pH 8.5 and above. This latter product gives rise to a single broad NMR signal but also shows a pH dependence of its chemical shift that suggests the presence of a protonation/deprotonation reaction. The observation of only one signal for possibly two types of vanadium in a linear species raises the possibility that this product is cyclic rather than linear. However, there is no apparent reason to suspect that such a cyclic product would be more susceptible to being protonated than the cyclic tetramer or cyclic pentamer, both of which carry one negative charge per vanadium. It seems likely that the trimer is acyclic and is undergoing rapid isomerization, so that a particular vanadium is shuffled between the terminal and bridging positions. This would allow for the observation of only one signal, and also rapid protonation/deprotonation could occur and thus account for the variation of signal position with pH. Unfortunately, because of the broadness of this signal, its relatively low intensity, and its partial overlap with other signals, it is difficult to do a detailed study of this material.

The direction of change in chemical shift with pH of trivanadate is such that the signal of the trimer should be shifted under that of tetravanadate at pH values of about 8 or less. It seems that the ubiquitous tendency to ignore the presence of this oligomer is ill founded. If the entries of Table 1 are examined carefully, it will be seen that the pH-dependent formation constant of the dimer increases by a factor of 3 when the pH is raised from 9.1 to 8.5. In this same pH range, the formation of the trimer increases by about a factor of 6, while that of the tetramer increases 76 times. Without further data it is difficult to extrapolate these results. However, the major driving force for the large increase in formation of the tetramer with increase in pH derives from the requirement that, unless the cyclization occurs from $H_2VO_4^-$ ions, protons are necessary for the tetramer to form. If the cyclization involves one or more HVO_4^{2-} ions, protons are utilized in order to satisfy the charge requirements of the $V_4O_{12}^{4-}$ ion. Since the pK_a of vanadate under 1 M KCl conditions is 8.3 (Table 2), the influence of pH on the formation of the tetramer is greatest near this pH. This is not true for trivanadate. In this case, product formation will more closely parallel that of divanadate. There is no reason to expect the ratio of 6 mentioned above to ever increase; rather, the formation constant for the trimer should approach a constant value with increase in acidity as the other pH-dependent formation constants, given in Table 1, do. The reason for this is evident from eqs 12−14. At lower pH, the formation of the oligomers is insensitive to the various pK_a values. It is likely that an equation, similar to eqs 12−14, also applies to formation of the trimeric product. It, therefore, seems clear that, under most circumstances below pH 8.5 when overall concentrations are high enough to observe an NMR signal at −575 ppm, the cyclic tetramer will be more abundant than the trimer. For instance, it can be estimated for pH 8.0 that, if the V_1 concentration is 0.3 mM, the trimer will have a concentration of 3 μM and the tetramer about 10 times this. The factor of 10 rises to about a factor of 25 if the V_1 concentration is 1.0 mM. Clearly, under most circumstances, the trimer can be ignored. However, in some experiments such as 2-D NMR exchange studies, observation of interactions with the −575 ppm signal should be treated with care, as the assignment of the exchange process may not be unambiguous.

Table 3. Thermodynamic Quantities That Characterize Selected Protonation Reactions

reaction	ΔH (kJ/mol)	ΔS (J/(mol K))	ref
$PO_4^{3-} + H^+ \rightleftharpoons HVO_4^{2-}$	−15	188	*a*
$AsO_4^{3-} + H^+ \rightleftharpoons HAsO_4^{2-}$	−18	158	*a*
$VO_4^{3-} + H^+ \rightleftharpoons HVO_4^{2-}$	−24	174	*b*
$HPO_4^{2-} + H^+ \rightleftharpoons H_2PO_4^-$	−3.8	126	*c*
$HAsO_4^{2-} + H^+ \rightleftharpoons H_2AsO_4^-$	−3.3	121	*c*
$HVO_4^{2-} + H^+ \rightleftharpoons H_2VO_4^-$	−4.4	144	*d*
$CrO_4^{2-} + H^+ \rightleftharpoons HCrO_4^-$	4.6	130	*c*
$HCrO_4^- + H^+ \rightleftharpoons H_2CrO_4$	38	113	*c*
$MoO_4^{2-} + H^+ \rightleftharpoons HMoO_4^-$	16	123	*e*
$HMoO_4^- + 2H_2O + H^+ \rightleftharpoons Mo(OH)_6$	−45	−76	*e*

[a] Taken from the tabulation in ref 11. [b] Taken from ref 11. [c] Taken from the tabulation in ref 17. [d] This work. [e] Taken from ref 17.

From Table 2, it can be seen that the K_a of vanadate undergoes a increase of about a factor of 3 on going from a low ionic strength aqueous solution to a 2 M KCl solution. Over the same range of ionic strength, the formation constant for the dianionic dimer similarly increases by a factor of about 3. However, the situation changes dramatically for the formation of the cyclic tetramer and cyclic pentamer, where the formation constants increase by 2−3 orders of magnitude. Evidently, the major influence of ionic strength on the oligomerization reactions is

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(17) Cruywagen, J. J.; Heyns, J. B. B. *J. Chem. Educ.* **1989**, *66*, 861−863.

at the level of the oligomerization constants, themselves. The product tetramer and pentamer have a high charge density and, presumuably, are preferentially stabilized in the more highly ionic solutions by ion-pairing interactions with the cations of the medium. This effect does not appear to be so important for divanadate, which may be a consequence of the availability of additional oxygens in divanadate for carrying the charge. This will weaken the interactions of divanadate with the cations of the medium, and consequently the influences of ionic strength will be less important for this product.

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