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Focussed review

Aqueous vanadium ion dynamics relevant to bioinorganic chemistry: A review

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ABSTRACT

Aqueous solutions of the four highest vanadium oxidation states exhibit four diverse colors, which only hint at the diverse reactions that these ions can undergo. Cationic vanadium ions form complexes with ligands; anionic vanadium ions form complexes with ligands and self-react to form isopolyanions. All vanadium species undergo oxidation–reduction reactions. With a few exceptions, elucidation of the dynamics of these reactions awaited the development of fast reaction techniques before the kinetics of elementary ligation, condensation, reduction, and oxidation of the aqueous vanadium ions could be investigated. As the biological roles played by endogenous and therapeutic vanadium expand, it is appropriate to bring the results of the diverse kinetics studies under one umbrella. To achieve this goal this review presents a systematic examination of elementary aqueous vanadium ion dynamics.

1. Introduction

It is usual for transition metal ions to display several stable oxidation states in a given solvent but vanadium is exceptional in this regard. What is unusual about aqueous vanadium is how readily solution conditions can be manipulated to stabilize each oxidation state thereby fostering the occurrence of substitution, oxidation–reduction, and polymerization reactions for vanadium ions in each of these oxidation states. When fast reaction techniques became available, the dynamics of these elementary reactions became accessible and were intensely studied. In the last few decades, however, such studies have diminished. At the same time studies of the biological, therapeutic and catalytic properties of vanadium have increased. The occurrence of the 9th International Vanadium Symposium is an appropriate occasion to review the kinetics of the many types of reactions vanadium ions can undergo, and consider their elementary step kinetics in view of applications such as insulin enhancement for Type II diabetes therapy.

2. Substitution reactions

In solution metal ions are coordinated to solvent molecules. The formation of a metal complex is therefore considered to be a substitution reaction in which an incoming ligand substitutes for one or more coordinated solvent molecules. Prior to the advent of fast reaction techniques, the subjects of metal substitution kinetics studies were the reactions of, principally, Pt(II), Cr(III), and Co(III) [1]. The reason for this choice of ions is quite simple. Consider, for example, the substitution by thiocyanate ion of the water molecule in the complex ion $[Co(CN)_5OH_2]^{2-}$. At a thiocyanate ion concentration of 0.1 M the half-life of the substitution reaction is 3.5 h at 40 °C [2,3]. That's just the right amount of time for a "classical" kinetics study.

The advent of fast reaction techniques, particularly stopped-flow rapid mixing, chemical relaxation, and NMR line-broadening, allowed the full range of metal ion reaction times to be accessed [4]. Quite independently of a given substitution mechanism, application of these techniques to the kinetics of substitution reactions led to the useful concept of a metal ion's "characteristic rate constant (s^{-1})" that defined the fundamental time that had to be investigated, for example, to make a mechanistic determination [5,6]. As a group, the classically accessible ions have characteristic rate constants that are less than 1 (s^{-1}). The greatest characteristic rate constants, 10^8 (s^{-1}) and higher, are exhibited by the ions of main group elements such as Na^+ and transitional metal ions such as Cu^{2+} and Cr^{2+} that exhibit Jahn–Teller effects [6]. The +2 and +3 transitional elements have characteristic rate constants that lie in the broad range 10^2 to 10^8 (s^{-1}); vanadium ions fall into this category. To focus on vanadium and discuss mechanisms, it is useful to develop activated complex models.

As an incoming ligand approaches a coordinated metal ion prior to substitution, a continuum of possible transition states can be envisioned [7]. At one point in this continuum the solvated metal ion or partially substituted metal ion and the incoming ligand will be in contact. Before substitution occurs, it is possible that the metal ion and incoming ligand will separate. The species that is formed when the two reactants are in contact is referred to as an ion-pair. Formation and dissociation of the ion-pair are diffusion-controlled rate processes and, with very few exceptions, are more rapid than substitution [8]. The free metal complex and ligand are considered to be in equilibrium with the ion-pair. Let the equilibrium constant for formation of an ion-pair be K_{ip}. Now let us return to the transition-state continuum.

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At one extreme activated complex configuration, a coordinated solvent molecule dissociates from the coordinated metal ion prior to substitution. Compared with the unsubstituted ion, the activated complex has a diminished coordination number. This mechanism has been termed dissociative and given the symbol **D** [1]. The **D** mechanism is distinguished by the absence of ligand property influences on the value of the observed second-order substitution rate constant, k_1. For this mechanism, $k_1 = k_d K_{ip}$, where k_d is the first-order dissociative rate constant characteristic of the parent metal ion, and which is not dependent on incoming ligand properties.

For the opposite extreme activated complex configuration of the reaction continuum, the incoming ligand bonds to the coordinated metal ion increasing its coordination number before substitution occurs. This mechanism has been termed associative and is given the symbol **A** [1]. In a subsequent, faster step a coordinated solvent molecule is released to the solvent. The rate-determining step is expansion of the coordination number and the second-order rate constant is given by $k_1 = k_a K_{ip}$ where k_a is a first-order rate constant; for a series of incoming ligands exhibiting an associative mechanism, the values of k_a would depend on incoming ligand properties.

Of the various intermediate metal–solvent–ligand separation states in the continuum, it is worthwhile to delineate a third possibility. That is a concerted path in which a distinct intermediate does not occur, because the coordination number in the activated complex is expanded, but neither the incoming ligand nor the outgoing solvent molecule are in their final, equilibrium positions. This mechanism has been termed interchange and given the symbol **I** [1]. If it can be demonstrated that properties of the incoming group exert a detectable influence on the second-order rate constant, the interchange mechanism is considered to be associative and is termed $\mathbf{I_a}$ [1]. If a sufficiently persuasive lack of such influences is observed, the interchange mechanism is considered dissociative and is termed $\mathbf{I_d}$ [1].

While fast reaction techniques such as rapid mixing and temperature-jump measure rate constants for net chemical reactions, another, powerful fast reaction technique measures rate constants for a process with no net chemical reaction. This technique is the measurement of NMR relaxation processes in which a solvent molecule is exchanged from one environment (bound to a metal ion) to another (free in solution). Let w represent a water molecule; then, in water the process can be diagrammed as, for example, $Mw_6 + w^* \rightleftarrows Mw_5w^* + w$. When M is a transitional metal ion with one or more unpaired electrons, the transverse magnetic relaxation time of the bulk solvent water molecules is perturbed. The relaxation time becomes dependent on the chemical exchange rate. By studying this phenomenon over a sufficiently wide temperature range it is possible to determine the exchange rate constant and its activation energy. Because a proton may exchange environments through hydrogen-bonding and this effect is difficult to distinguish from chemical exchange, most exchange rate studies on water have been conducted on the ^{17}O nuclear magnetic signal. Measuring this nuclear magnetic relaxation process over a wide *pressure* range allows the activation volume of the exchange rate constant, k_{ex} (s^{-1}), to be determined, and this parameter is sensitive to the composition of the activated complex and therefore to the substitution mechanism.

With sufficient sensitivity, determination of the temperature dependence of a rate constant yields the activation enthalpy $\Delta H^‡$ and entropy, $\Delta S^‡$. For discriminating among the substitution mechanism choices, the pressure dependence of a rate constant yields the activation volume, $\Delta V^‡$ and activation compressibility, $\Delta\beta^‡$ [9]. If the extreme or limiting associative mechanism prevails, the incoming ligand and outgoing water molecule will be securely bound in the activated complex and the activation volume will be negative (**A**: $\Delta V^‡ < 0$). If the extreme or limiting dissociative mechanism prevails, the activated complex comprises the reduced coordination number metal complex, the dissociated water molecule, and the incoming ligand, a loosely configured activated complex for which the activation volume will be positive (**D**: $\Delta V^‡ > 0$). The magnitude of $\Delta V^‡$ can be further used to discriminate among $\mathbf{I_a}$, **I**, and $\mathbf{I_d}$ mechanisms [7]. A similar pattern is observed for the entropy of activation (**A**: $\Delta S^‡ < 0$; **D**: $\Delta S^‡ > 0$). Primarily, the entropy of activation measures the loss of translational entropy upon binding the incoming ligand (**A**), or gain of translational entropy upon releasing a bound water molecule which becomes a freely translating bulk molecule (**D**). Activation entropies, however, cannot be measured with sufficient accuracy from the temperature-dependence of k_{ex} to make a definitive mechanistic judgment; $\Delta S^‡$ does not have the same authority as $\Delta V^‡$ [7]. With this background let us consider substitution reactions of vanadium cations.

3. Vanadium cation [V(II–V)] ligation kinetics

Vanadium forms the lightest divalent cation stable in aqueous solution for the first elemental transition series. Several complex formation rate constants for the aqueous V^{2+} ion have been determined with a wide range of values [10], due in part to problems of on-going water reduction by V(II) and air oxidation of V(II) in these solutions. The second-order substitution rate constants for V^{2+} are relatively small, which has been explained by the significant loss of crystal field stabilization energy upon substitution, which raises the activation energy [11]. An earlier ^{17}O study of the aquo V^{2+} ion [12] was superseded by a later study benefitting from more sensitive equipment and variable pressure and temperature measurements [13]. The exchange rate constants obtained by both groups were close in value; the more recent determination yielded $k_{ex} = 87$ (s^{-1}) and $\Delta V^‡ = -4.1$ ($cm^3\ mol^{-1}$) at 298 (K). It was concluded that ligation of V^{2+} follows an associative interchange ($\mathbf{I_a}$) mechanism.

There exist two studies of the kinetics of vanadium(III) ligation by the SCN^- ion; both rapid mixing and temperature-jump results essentially finding a second-order rate constant of 1.1×10^2 ($M^{-1}\ s^{-1}$) at 298 (K) [14,15]. As for the V^{2+} ion there are earlier and later ^{17}O NMR studies of water exchange on V^{3+} [16,17]. The earlier study was compromised by the presence of chloride and bromide ions which form complexes with V^{3+} that interfere with the pure aquo V^{3+} ion exchange kinetics; consequently, we rely on the later study. The NMR results are $k_{ex} = 5 \times 10^2\ s^{-1}$, $\Delta V^‡ = -4.1$ ($cm^3\ mol^{-1}$) and a small but definite compressibility component, $\Delta\beta^‡$ ($cm^3\ mol^{-1}\ MPa^{-1}$). The $\mathbf{I_a}$ interpretation by the NMR study authors is consistent with the earlier rapid-mixing and temperature-jump investigators who argued for a compatible S_N2 mechanism, following an earlier nomenclature.

A pure, aquo vanadium(IV) cation does not exist; the stable V(IV) ion is oxidovanadium(2+), VO^{2+}, ion. Oddly, no pressure-dependent NMR exchange rate study on oxidovanadium(2+) ion has been reported, although temperature-dependent NMR exchange rate studies are known [18,19]. Several chemical relaxation studies produced second-order rate constants in the same range as the NMR study and those authors concluded that substitution occurred via a **D** mechanism. Two later ligation studies disputed that conclusion. The kinetics of complexation of VO^{2+} and $VOOH^+$ ions by mandelic (*ma*), vanillylmandelic (*vma*), and thiolactic (*tl*) acid ligands (Fig. 1) was studied by temperature-jump at 298 (K) [20].

In ligands *ma* and *vma* the oxidovanadium(2+) binding sites are carboxyl and hydroxyl groups; in the ligand *tl* the carboxyl group is present, but a sulfhydryl group substitutes for the hydroxyl group. The rate constant results are collected in Table 1.

Early reports of oxidovanadium(2+) substitution rate constants exceeding those in Table 1 by an order of magnitude erred in neglecting reactions of $VOOH^+$ [e.g., [21]]. Reanalysis of this earlier work with inclusion of $VOOH^+$ led to lower second-order rate constants on the order of those shown in Table 1. The close contact between the positive vanadium(IV) center and the negative hydroxide ion decreases the effective positive charge exerted by the metal ion on the remaining bound ligands, which leads to higher substitution rate constants for $VOOH^+$ compared with VO^{2+}. Table 1 shows trends in rate constants with decreasing ligand basicity. (Basicity decreases in the order *ma* > *vma* > *tl*.) The importance of the observed trends in rate constants with ligand