Solution Characterization of Vanadium(V) and -(IV) *N*-(Phosphonomethyl)iminodiacetate Complexes: Direct Observation of One Enantiomer Converting to the Other in an Equilibrium Mixture[1]

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The vanadium(V) and -(IV) complexes formed with *N*-(phosphonomethyl)iminodiacetate (pida^{4-}) complexes in water and in aqueous mixed-solvent systems were characterized by employing potentiometry, multinuclear NMR, EPR, and visible spectroscopy. The vanadium(V) complexes in water had a 1:1 metal to ligand stoichiometry. The diprotonated vanadium(V)−pida complex with a charge of −1 existed below pH 2. After the first deprotonation, the dianionic species was stable from pH 1 to 6. The trianionic species was stable at neutral pH. Observations are most consistent with the protonation sites of these complexes on the organic ligand. Intra- and intermolecular exchange processes were identified using ^{13}C homonuclear EXSY spectroscopy. Given the asymmetric vanadium atom in the VO_2pida^{3-} complex, one of the exchange processes observed was the conversion of one enantiomer to the other in an equilibrium mixture. Studies of the corresponding vanadium(IV)−pida system in dioxane−water mixtures showed the presence of not only mononuclear species but also a dinuclear species (which was recently characterized by X-ray crystallography). In 80:20 (v/v) dioxane−water mixtures, the dinuclear species became the major species in solution, as evidenced by absorption spectroscopy and EPR spectroscopy. Potentiometric measurements in mixed solvents failed to conclusively favor any stoichiometry. In conclusion, the mononuclear vanadium(IV) and -(V) complexes with the H_4pida ligand appear to be structurally related and could readily be distinguished from the dinuclear vanadium(IV)−pida complex that was characterized both in the solid state and in mixed-solvent solutions.

Introduction

Recently, interest in multidentate O and N donor ligand complexes of vanadium(IV) and -(V) has increased because of their insulin-mimetic properties, model chemistry of haloperoxidases, and catalytic chemistry with potential practical applications.[2−9] Studies generally have characterized the solid-state structural properties of complexes with vanadium in either oxidation state IV or V,[10−17] even though increasingly structural details for species in both oxidation states in solution are being investigated. Redox-active complexes are anticipated to cycle between oxidation states, and a full understanding of these systems requires both solid-state and solution-state structural and reactivity considerations of the complexes involved. A recent study by Pecoraro's group demonstrated ambiguities and structural isomerism of vanadium(IV) complexes of *N*-iminodiacetic acid-based ligands,[2,3] and these results raise questions regarding the expectation, in general, that structural integrity of vanadium(IV) complexes exists. Furthermore, it was clearly demonstrated that EPR spectroscopy can provide detailed structural information[10,11,17−22] even on closely related isomeric forms.[2,3] In this work, studies will be described exploring the

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(1) Abbreviations: bmida, *N*-(benzimidazol-2-ylmethyl)iminodiacetate; DMF, dimethylformamide; edda, ethylenediamine-*N*,*N*-diacetate; H_4pida, H_3pida^-, H_2pida^{2-}, $Hpida^{3-}$, and $pida^{4-}$, various protonation states of *N*-(phosphonomethyl)iminodiacetic acid; hida^{3-}, hydroxyethyliminodiacetate; NMR, nuclear magnetic resonance; pmida^{-2}, *N*-(2-pyridylmethyl)iminodiacetate; pmide^{-2}, *N*-(2-pyridylmethyl)iminodiethanoxide); tea$^-$, triethanolaminate; tricine, *N*-[tris(hydroxymethyl)-methyl]glycine.

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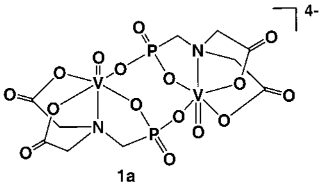
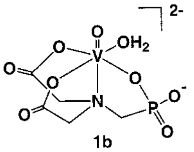
solution properties of both vanadium(IV) and -(V) complexes with one O and N donor ligands which also contain the phosphonic acid group.

Vanadium complexes with phosphoric acid ligands are of interest with respect to their properties in biological systems as well as to their applications as catalysts and sorbents.[23−25] In addition, the use of a vanadium oxide mixture as a catalyst in the production of commodity chemicals[26,27] documents the importance of the detailed coordination chemistry as well as the chemical properties of complexes existing in solution. Although the phosphonic acid group is a relatively common functionality, little information is available on the properties of vanadium complexes of ligands with multiple functionalities, including the phosphonate group. The phosphonic acid group could act as an analogue of the carboxylate group or the phosphoric acid groups. Characterization of new complexes of a variety of ligand functionalities with respect to structural preferences and lability will show how the phosphonic acid group compares to other functionalities, specifically the carboxylate and phosphate groups.

The complex that forms between vanadium(IV) and *N*-(phosphonomethyl)iminodiacetic acid (H_4pida) has been characterized.[26,27] The complex is redox active in mildly acidic aqueous solutions and in the presence of appropriate oxidants, including oxygen. Recently, we were able to crystallize two complexes from aqueous solution of this vanadium(IV)−pida system.[28] However, the structural characterizations revealed a dinuclear $(VO)_2(pida)_2^{4-}$ species (**1a**) for both crystals, in contrast to the anticipated mononuclear solution structure of this complex (**1b**). No information is currently available on the corresponding vanadium(V)−H_4pida system. The detailed structural, stability, and lability properties of the vanadium(V)−pida complex are of fundamental interest with regard to understanding this system and the affinity of the phosphonate group for vanadium. Furthermore, characterization is necessary to evaluate correctly the potential for redox cycling between the vanadium(IV)− and vanadium(V)−pida systems.[28] The existence of several mono- and dinuclear complexes for the vanadium(IV)−pida system documents the versatility of this complex and begs the analysis and comparison with the corresponding vanadium(V)−pida complexes.



1a



1b

Experimental Section

Materials. Reagent grade sodium metavanadate, vanadium sulfate, and *N*-(phosphonomethyl)iminodiacetic acid (H_4pida) were purchased from Aldrich and used without further purification. In the potentiometric studies, CO_2 was removed from the solutions whereas, in the other spectroscopic studies, no attempts were made to prevent the presence of dissolved CO_2 in solutions. Distilled and deionized water was used for the synthesis of the crystalline complexes and preparation of the stock solutions.

Solution Preparations for Potentiometric Studies. Dissolution of H_4pida and $NaVO_3$ in distilled water under a nitrogen atmosphere generated 0.015 and 0.100 M stock solutions. The solutions were standardized for metal concentration by permanganate titration and for hydrogen ion concentration by a pH-meter. Stock solutions were prepared in concentration ranges from 0.1 to 4.0 M for H_4pida, from 0.1 to 3.0 M for vanadate, and from 0.020 to 0.10 M for vanadyl perchlorate. KCl was used to maintain ionic strength when necessary. Samples were prepared by combining the desired amounts of ligand, vanadate, and KCl. In the case of dioxane-containing samples, the desired volume of the dioxane was also added.

Potentiometric Studies. The titrations were performed on 25.0 mL samples by the addition of KOH (ca. 0.2 M), which had been standardized and was maintained under an argon atmosphere. The pH was measured with an Orion 710A pH-meter equipped with an Orion Ross 8103BN-type combined glass electrode, calibrated for hydrogen ion concentration as described earlier.[29] The concentration of ligand ranged from 0.0060 to 0.0030 M, and the vanadate concentration series titrated was defined by the ratios of total metal ion to total ligand of 0:2, 1:2, and 2:2. The pH examined ranged from 2 to 11, and equilibrium was reached in all these solutions within 5 min. The experiments were performed in duplicate, and in all cases, the reproducibility of the curves was within 0.005 pH unit.

The stability constants calculated in this work are shown in reaction 1, where M^- refers to HVO_4^{2-} and L^{4-} refers to $pida^{4-}$.

$$pM^{2-} + qL^{4-} + rH^+ \rightleftarrows M_pL_qH_r^{(2p^- + 4q^- + r^+)} \qquad (1)$$

$$\beta(pqr) = \frac{[M_pL_qH_r^{(2p^- + 4q^- + r^+)}]}{[M^{2-}]^p[L^{4-}]^q[H^+]^r} \qquad (2)$$

The concentration stability constants $\beta(pqr)$ are defined in eq 2 and do not consider the contributions of activity coefficients. The constants were calculated using the computer program PSEQUAD.[30,31] In these calculations, the ionic product of water (pK_w) used was 13.76. The speciation of vanadate into monomeric, dimeric, tetrameric, and pentameric species was considered in calculating the overall speciation in this system.[32] When necessary, the previously reported concentration stability constants were corrected for different ionic strengths by using the Davies equation in the speciation calculations. The errors indicated in Table 1 refer to 3 SDs.

^1H, ^{13}C, ^{31}P, ^{17}O, and ^{51}V NMR Spectroscopic Studies. All NMR samples were prepared at room temperature immediately before NMR spectroscopic determinations. The samples to be analyzed by ^{51}V and ^{13}C NMR contained 20% (v/v) D_2O. Samples to be analyzed by ^1H NMR contained no H_2O; stock solutions were prepared in D_2O for the ^1H NMR studies. Vanadate and ligand concentrations were varied as needed. The ionic strength was maintained at 0.40 with 4.00 M KCl. The pH measurements were carried out at room temperature using a Corning 140 pH-meter before and after each spectroscopic measurement to ensure that no significant change (±0.05 pH unit) occurred while the spectra were recorded. The majority of the samples used in the NMR measurements were prepared and analyzed in duplicate. Selected samples were analyzed in triplicate.

^{51}V NMR spectra were recorded at 78.9 MHz (7.0 T) on a Varian Inova 300 NMR spectrometer. ^{51}V NMR chemical shifts are reported

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Table 1. Compositions, Notations, Formation Constants (β), and Acidity Constants (pK_a) for the H^+−pida,$^{4-}$ H^+−HVO_4^{2-}, and H^+−HVO_4^{2-}−pida^{4-} Systems [I = 0.20 M (KCl), 25 °C]

(r,q,p)	notation	log β ($\pm 3\sigma$)	pK_a	ref
(1,1,0)	Hpida^{3-}	10.58(1)	10.58	this work
(2,1,0)	H_2pida^{2-}	16.07(1)	5.49	this work
(3,1,0)	H_3pida^{-}	18.40(4)	2.33	this work
(4,1,0)	H_4pida	19.8(3)	1.4	this work
(5,1,1)	VO_2H_2pida^{-}	35.93(2)	~1.2	this work
(4,1,1)	VO_2Hpida^{2-}	34.77(1)	3.74	this work
(3,1,1)	VO_2pida^{3-}	31.03(1)		this work
(3,0,1)	VO_2^+	14.93		*a*
(1,0,1)	$H_2VO_4^-$	8.17	8.17	*a*
(0,0,2)	$V_2O_7^{4-}$	0.15		*a*
(1,0,2)	$HV_2O_7^{3-}$	10.49	10.34	*a*
(2,0,2)	$H_2V_2O_7^{2-}$	18.99	8.50	*a*
(2,0,4)	$V_4O_{13}^{6-}$	22.70		*a*
(3,0,4)	$HV_4O_{13}^{5-}$	32.05	9.35	*a*
(4,0,4)	$V_4O_{12}^{4-}$	41.92		*a*
(5,0,5)	$V_5O_{12}^{5-}$	52.02		*a*
(14,0,10)	$V_{10}O_{28}^{6-}$	131.98		*a*
(15,0,10)	$HV_{10}O_{28}^{5-}$	138.60	6.64	*a*
(16,0,10)	$H_2V_{10}O_{28}^{4-}$	142.77	4.17	*a*
(17,0,10)	$H_3V_{10}O_{28}^{3-}$	144.63	1.86	*a*
	no. of points		665	
	fitting parameter[b]		5.556E−03	

[a] Elvingson, K.; Gonzales, Baro A.; Petterson, L. *Inorg. Chem.* **1996**, *35*, 3388−3393. [b] Average difference between the measured and calculated titration curves expressed in mL of the titrant.

against external neat $VOCl_3$ (0 ppm). A spectral window of 150 ppm, a 90°-pulse angle, and an acquisition time of 0.25 s with no relaxation delay were used. A 15 Hz exponential line broadening was applied before Fourier transformation. ^1H and ^{13}C NMR spectra were recorded on the Varian Inova 300 spectrometer at 300 and 76 MHz, respectively. The ^1H NMR spectra were acquired using standard parameters, and the chemical shifts are reported with respect to the external standard DSS (sodium 3-(trimethylsilyl)-1-propanesulfonate). The ^{13}C NMR spectra were acquired with a 200 ppm spectral window, a 90° pulse, and a relaxation delay of 0.7 s. A 2 Hz exponential line broadening was applied to the FID before subjecting the FID to Fourier transformation. The chemical shifts were recorded against the instrument frequency that was calibrated against the external standard TMS (and DSS) at 0 ppm. The ^{31}P NMR spectra were recorded at 121 MHz, using an external lock with spectral windows of 40−50 ppm. The ^{31}P chemical shifts were referenced to an external standard (0 ppm), 85% H_3PO_4. A 90°-pulse angle and an acquisition time of approximately 0.8 s were used. The number of scans acquired was 500−1500. ^{17}O NMR spectra were acquired on the Varian Inova 300 spectrometer at 41 MHz. Samples were enriched to 3.5% with ^{17}O-labeled water. A spectral window of 2000 ppm, a 90°-pulse angle, a 0.017 s acquisition time, and a 0.07 s relaxation delay were employed. No line broadening was applied before Fourier transformation, and water was used as an internal reference at 0 ppm.

2D EXSY Spectroscopy. The phase-sensitive ^{13}C homonuclear 2D EXSY experiments were done at 76 MHz on the Varian Inova 300 spectrometer. The standard NOESYPH pulse sequence (90°−t_1−90°−T_m−90°) supplied with the Varian software was used to define the experiment. The 2D EXSY ^{13}C NMR spectra were acquired with a 90° pulse, a mixing time of 0.1 s, and a relaxation delay of 1.2 s. Spectra were recorded with mixing times in the 0.1−0.2 s range, but best results were obtained with 0.1 s. Spectra were recorded of full (200 ppm) and partial (10−20 ppm) regions of the spectrum. The spectra were recorded at 10, 22, and 28 °C.

UV−Visible Studies. The UV−vis spectra were recorded on a Lambda 4B Perkin-Elmer spectrometer. Crystalline $Na_4(VO)_2$(pida)$_2$ was dissolved directly into the solvents under examination. Most of the work described in this paper was carried out in aqueous dioxane; however, additional studies in aqueous solution also were performed. In cases of high ratios of organic solvents (60−80%, v/v), the dissolution of 1.5−8.0 mM $Na_4(VO)_2$(pida)$_2$ required sonication.

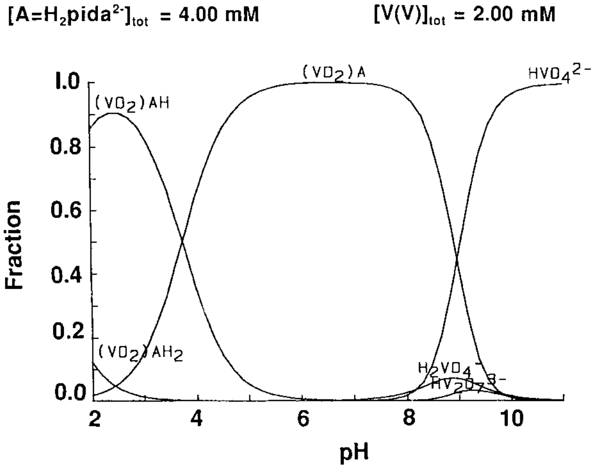

Figure 1. Speciation diagram of the HVO_4^{2-}−pida^{4-}−H^+ system in aqueous solution. The total vanadium(V) to ligand ratio is 1:2 (A = H_2pida^{2-}).

Dissolution of $Na_4(VO)_2$(pida)$_2$ in aqueous organic solvent resulted in colored solutions; at low organic solvent ratios, the solutions were blue; at high ratios, they were brown. Samples for analysis were prepared immediately before the UV studies, unless otherwise indicated. The extinction coefficients for the complexes were calculated at the respective absorbance maxima from solutions at several concentrations.

EPR Spectroscopic Studies. The aqueous and aqueous dioxane samples (1.5 mM) examined by EPR spectroscopy were prepared by dissolving the crystalline $(VO)_2$(pida)$_2^{4-}$ complex directly into the solvent mixture, which required sonication as described above. The EPR spectra were recorded using disposable 0.4 mm path length flat-cells on a Varian E-9 spectrometer. The spectrometer was operated at X-band frequency (9.17 GHz) with a microwave power of 50 mW (18 °C). The EPR spectra were recorded at 18 °C, using a modulation frequency of 100 kHz, a modulation amplitude of 5.0 G, a time constant of 128 ms, and a conversion time of 120 s (18 °C).

Results and Discussion

Potentiometric Studies of the Vanadium(V)−H_4pida System. Titrations of the H^+−HVO_4^{2-}−pida^{4-} system yield the concentration stability constants given in Table 1. The stabilities of the complexes are illustrated in the speciation diagram in Figure 1. The formation constants related to the simple binary (proton−ligand and proton−vanadate) systems are in agreement with the results found previously.[29,33]

In the ternary system, three new species were identified. The stability of the resulting complexes was so high that only a limited range of metal ion to ligand ratios was needed to describe the system: 1:2 and 2:2. The diprotonated VO_2H_2pida$^-$ species was only observed in appreciable concentrations at the 2:2 metal to ligand ratio and below pH 3.5. The monoprotonated VO_2Hpida^{2-} was observed below pH 5.5 and became the dominant species below pH 4. The VO_2pida^{3-} complex was the major species in most of the pH and concentration ranges examined, reflecting the stability of this complex. As shown in Figure 1, this complex was present from pH 2 to pH 10 and was the major species from pH 4 to pH 9. The pK_a value for the monoprotonated species is 3.74, and the pK_a value for the diprotonated species is around 1.2, consistent with the observation that VO_2H_2pida$^-$ is only a minor contributor even at pH as low as 2.

Solution Structures of the Complexes in the Vanadium(V)−H_4pida System. Three lines of evidence were obtained

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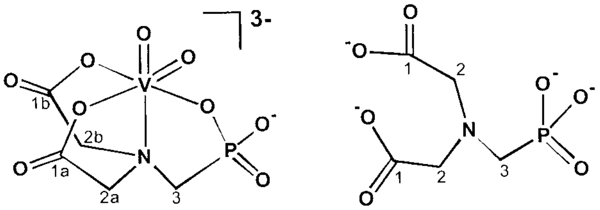
Table 2. ^{13}C NMR Chemical Shifts for the Vanadium(V)−pida Complexes and Free Ligands at pH 6.50 (±0.05) and 2.39 (±0.05)[a]

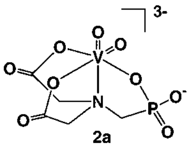


complex	C_{1a}	C_{1b}	C_{2a}	C_{2b}	C_3	pH	^{51}V NMR δ (ppm)	^{31}P NMR δ (ppm)
VO_2pida^{3-}	182.0	183.1	66.3	70.7	62.1 ($J = 138$ Hz)	6.50	−526	26
H_2pida^{2-}	174.5	174.5	61.1	61.1	56.1 ($J = 126$ Hz)	6.50		
VO_2Hpida^{2-}	181.7	183.0	65.9	70.4	61.4 ($J = 140$ Hz)	2.39	−521	29
H_2pida^{2-}/H_3pida^{-}	173.3	173.3	61.1	61.1	54.9 ($J = 135$ Hz)	2.50		

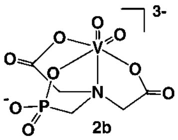
[a] The data were obtained in a solution with an ionic strength of 0.40 M at 4 °C.

using NMR spectroscopy to characterize the solution structures of these complexes.[34] First, ^{1}H, ^{13}C, and ^{17}O NMR studies were used to determine ligand connectivity of the major VO_2pida^{3-} species. Second, these studies were expanded to determine symmetry and geometry of the complex in solution. Third, ^{51}V and ^{31}P NMR studies, in combination with ^{1}H and ^{13}C NMR studies, were used to explore geometries of the monoprotonated complex.

Both ^{1}H and ^{13}C NMR studies were pursued to determine ligand connectivity. As the ^{13}C NMR shifts shown in Table 2 indicate, all the carbon atoms adjacent to the carboxylate groups, the phosphonic acid, and the tertiary amine functionalities show significant shifts from the free ligand. These CIS (coordination-induced shift) values are consistent with a complex in which the ligand is tetradentate. Given the precedence for *cis*-dioxo complexes with coordination number 6 or 5, the most likely structure possibilities are shown (**2a**−**e**). A five-coordinate monooxovanadium(V) complex when the ligand is coordinated to VO(V) through four functionalities (**2c**) is less likely in aqueous solution than the corresponding six-coordinate **2a** and **2b**. Alternative structures with a tridentate ligand and five-coordinate vanadium (**2d**, **2e**) are less consistent with the observed CIS values.



2a



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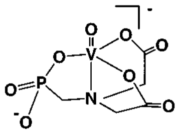
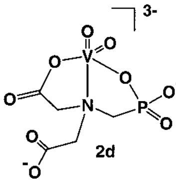


2c



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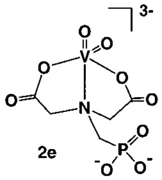
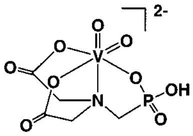
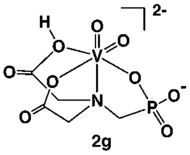


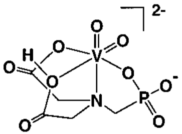
2e



2f



2g



2h

The type of geometry with six-coordinate vanadium and two carboxylate functionalities coordinated cis to each other in **2a** is that reported for VO_2peida^{-},[13] $VO_2Hpmide$,[14] VO_2pmida^{-},[12] and VO_2bmida^{-}.[14] Most of these complexes were examined both in the solid state and in the solution state. The alternative trans coordination mode was recently reported for the VO_2Hhida^{-} complex[11] and is shown in **2b**. The ^{13}C and ^{1}H NMR spectra for the VO_2pida^{3-} complex can distinguish between these complexes, because **2b** should give a symmetric spectrum with the two functionalities having the same chemical shifts. However, at ambient temperature, the signals in the ^{13}C NMR spectra for these complexes were very broad and were indicative of a significant degree of dynamic processes in the complex (data shown in Figure S1, Supporting Information). Accordingly, when these spectra were recorded at 4 °C, these signals sharpened, and two signals emerged for each of these signals (Figure S1). Coordination of one of the carboxylates trans to the phosphonic acid would allow observation of coupling to the phosphorus in **2a**, whereas the coupling constant would be much smaller and not observed for **2b**. Indeed, one of the two CH_2 groups of the carboxylates does show a 12.2 Hz splitting. This fact is only consistent with the geometry shown in **2a**. Corresponding patterns can be obtained using ^{1}H NMR spectroscopy, however, these spectra are more complex and are not shown here. On the basis of these deductions, we conclude that the VO_2pida^{3-} species has the structure shown in **2a**.

Finally, NMR spectroscopy was used to characterize the protonated species. Given the structure for **2a**, the most likely possibilities for protonation of **2a** involve the O^{-} on the phosphonic acid group (**2f**) or the carbonyl oxygen atoms in the carboxylate groups (**2g** or **2h**), all formulated as VO_2Hpida^{2-}. Solutions containing mainly VO_2pida^{3-} and its protonated counterpart gave ^{51}V NMR chemical shifts of −526 (pH 6.50) and −521 ppm (pH 2.39). An intermediate cis value of 5 ppm is most consistent with structures **2f**−**h** (the site of protonation is less likely to be at the oxo group). Solutions containing the VO_2pida^{3-} and VO_2Hpida^{2-} species give ^{31}P NMR chemical shifts of 26 and 29 ppm, respectively. The change in the ^{31}P NMR chemical shift is most consistent with the interpretation that, at low pH, the proton is located on the phosphonic acid group in the protonated VO_2pida^{3-} species (described as VO_2Hpida^{2-}) (**2f**). This interpretation is supported by ^{13}C NMR spectroscopic data (Table 2), where the CIS value for the carbon adjacent to the phosphonic acid group is most different compared to the values for the corresponding carbons in the VO_2Hpida^{2-}species.

Spectra of solutions containing high concentrations of the HVO_2Hpida^{-} species were of poor quality because of the rapid redox chemistry that occurs in such solutions and because of spectral overlap of signals. However, a few results were abstracted from these studies. The second protonation significantly affects the observed ^{51}V NMR chemical shift at pH 1.5; a value of −511 ppm is observed for a solution that contains a

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(34) Crans, D. C.; Shin, P. K. *J. Am. Chem. Soc.* **1994**, *116*, 1305−1315.

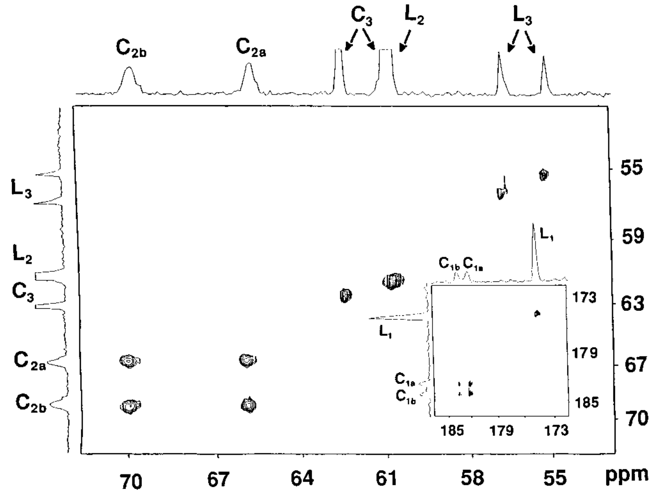


Figure 2. ^{13}C NMR EXSY spectrum of the V−pida complex formed in 1000 mM vanadate and 2000 mM H_4pida at pH 6.42 and 10 °C. The carbons assigned to the complex are labeled C_x and those of the ligand as L_x.

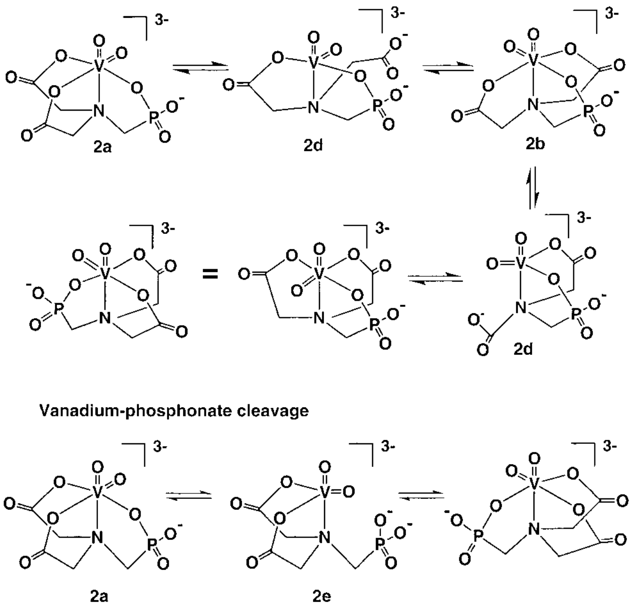
significant amount of the diprotonated species.[35] Since some ^1H and ^{13}C NMR chemical shifts are significantly affected by this pH change, it is likely that the second proton protonates one of the carboxylate groups.

An ^{17}O NMR spectrum of the VO_2pida^{3-} complex was recorded. Only the V═O oxygen atoms of the complex are subject to exchange with the ^{17}O of the enriched water. As a consequence, only these oxygen atoms will be observable. Complexes with the structures shown in **2a**−**e** should give signals of equal intensity. Interestingly, the chemical shifts for the two 1:1 signals at 1110 and 1072 ppm were very similar to those observed previously for six-coordinated *β*-*cis*-VO_2edda^- (1114 and 1087 ppm) and VO_2Hhida^- (1141 and 1085 ppm),[34] in which both have two equivalent *cis*-dioxo moieties, one oxo group trans to an amine and the other trans to a carboxylate group.

Lability of Vanadium(V)−H_4pida Complexes. The variable-temperature ^1H and ^{13}C NMR studies carried out to examine the structure of the solution complex showed that this complex is undergoing dynamic processes on the ^1H and ^{13}C NMR time scales. To examine whether the observable process(es) can be characterized as chemical exchange, a series of homonuclear ^{13}C EXSY NMR experiments were conducted to elucidate the nature of the dynamic processes observed.

The spectrum (chemical shift range from 45 to 80 ppm) recorded at 10 °C is shown in Figure 2. We also recorded full spectra for the complexes; however, the better resolution of the exchange process was observed when a limited chemical shift range was used. As shown in Figure 2, the two C_2 atoms exchange with one another, and given their connectivity, it is assumed that also the two C_1 atoms exchange. In this case, it was possible to actually observe the exchange between the C_1 atoms in another spectrum (insert). Given the functionalities and density of the ligand, the vanadium atom is in an asymmetric environment even though the solution contains a racemic mixture (see **2a** and its enantiomer, Scheme 1). Since the ligand contains two carboxylate arms, one C_1 and C_2 pair is converted to the other C_1 and C_2 pair. In the EXSY spectrum in Figure 2, we actually observe the conversion of complex **2a** into its mirror image.

Scheme 1. Possible Mechanisms for Conversion between **2a** and Its Enantiomer[a]



[a] The mechanism involving initial vanadium−carboxylate cleavage passes through species **2d** and **2b**. The mechanism involving initial vanadium−phosphonate cleavage passes through species **2e**.

Although only one set of signals was observed for a set of enantiomers, we still were able to observe the direct exchange between enantiomers. The chiral nature of **2a** is due to the manner in which H_4pida (and its four functionalities) is chelated to the metal ion. Conversion among enantiomers occurs when the two carboxylate groups, which are not identical (pro-*R* and pro-*S* as a result of their coordination to the vanadium), interchange. Since the interchange of these two groups occurred on the time scale of a ^{13}C EXSY experiment, we were able to observe this process directly (as indicated by the off-diagonal resonance).

By which mechanism do the enantiomeric complexes interchange? A process in which the carboxylate−vanadium bond is broken could lead to enantiomer exchange when this process is coupled with cleavage of the vanadium−amine bond and hybridization at the amine nitrogen, followed by formation of the enantiomeric complex. Alternatively, cleaving the carboxylate−vanadium bond cis to the oxo group, forming **2d**, followed by formation of a new carboxylate−vanadium bond trans to the carboxylate group, results in the formation of species **2b**. This species could undergo bond cleavage and bond formation to form the enantiomer of **2a** (Scheme 1). The latter process, although involving more steps, seems more likely, given the fact that only one bond is broken in each step. A simpler mechanism involves the breakage of the vanadium−phosphonate bond and formation of the vanadium−phosphonate bond in the enantiomeric complex (Scheme 1). Additional information is needed to distinguish between these mechanisms.

Intramolecular processes have been observed for related complexes, including VO_2Htea^-,[15] VO_2edda^-,[36] VO_2Hhida^-,[11] and $VO_2H_2tricine^-$.[33] The observed intramolecular process for

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(35) The ^{51}V NMR spectra were recorded immediately after mixing 500 mM vanadate, 800 mM ligand, 0.40 M KCl, and deuterium oxide, with the pH adjusted to 1.43. The broadness of the signals from any spectrum of this solution suggests that, in addition to $[VO_2H_2pida]^-$ and $[VO_2Hpida]^{2-}$ (accounting for a total of 84% of vanadium(V)) and vanadate (16% of vanadium(V)), some significant fractions of vanadium(IV) form rapidly in these solutions.

(36) Crans, D. C.; Keramidas, A. D.; Mahroof-Tahir, M.; Anderson, O. P.; Miller, S. M. *Inorg. Chem.* **1996**, *35*, 3599−3606.

the VO_2pida^{3-} complex was found at temperatures below ambient (near 0 °C), as was also observed for VO_2Htea^- and $VO_2H_2tricine^-$. Furthermore, the intermolecular process for the VO_2Htea^- complex was observed below ambient temperature, whereas corresponding processes for $VO_2H_2tricine^{2-}$, VO_2Hhida^-, and VO_2edda^- were observed above ambient temperature. Attempts to observe the intermolecular exchange process for the VO_2pida^{3-} complex were made, but at the temperature needed to observe the intermolecular process, the two C_1 signals had coalesced and the C_2 signals had broadened so much that they were barely detectable. However, exchange was clearly observed between the merged signals for the C_1 atoms and the corresponding L_1 atoms (data not shown). In addition, exchange was observed for both C_3 signals (split by the ^{31}P) and both L_3 signals. Thus, on the basis of a comparison of lability, the VO_2pida^{3-} complex is more similar to the VO_2Hhida^-, VO_2edda^-, and $VO_2H_2tricine^-$ complexes than to the VO_2Htea^--type complex.

UV−Visible and EPR Spectroscopic Studies of the Vanadium(IV)−H$_4$pida System. Recently we completed two types of studies of the vanadium(IV)−pida system.[28] One approach used solution characterization of the aqueous vanadium(IV)−pida system using UV−vis and EPR spectroscopy. The second approach focused on isolating and structurally characterizing vanadium(IV)−pida complexes in the solid state and characterizing these species in aqueous DMF.[28] The two isolated complexes were dinuclear and contained a framework that was generated by substituting a water molecule from the mononuclear vanadium(IV)−pida complex and in its place coordinating the phosphonic acid group from an adjacent molecule (**1a**). Although the major species in aqueous solution remained a mononuclear complex, the addition of organic solvents such as DMF allowed observation of a dimer in solution, as evidenced by the emergence of one new absorption band and the disappearance of the characteristic EPR spectrum for the mononuclear complex. Although the dinuclear complex was crystallized from water, no evidence was seen by potentiometric studies for dinuclear species in water.[26,27] These observations are all consistent with the possibility that the crystal formed in the mixed-solvent layer, when diffusing in organic solvents. As a result, we were interested in carrying out the potentiometric analysis of the V(IV)−pida system in organic−water mixtures. The dioxane−water mixture was chosen for potentiometric studies because the $(VO)_2(pida)_2^{4-}$ complex is stabilized in this system and observable by various techniques. The solvent systems of DMF−water used in previous studies were not appropriate for potentiometric studies because of hydrolysis of the organic solvent, and alternative systems such as DMSO−water or methanol−water could not be used due to low solubility of the crystalline $Na_4(VO)_2(pida)_2$.

UV−visible studies were carried out for solvent mixtures ranging from 50:50 (v/v) to 80:20 (v/v) dioxane:water. The UV−visible spectra are shown in Figure 3 for the 50:50 (v/v) blue mixture, and an absorption spectrum with two maxima at 632 nm (21 M^{-1} cm^{-1}) and 878 nm (43 M^{-1} cm^{-1}) is consistent with the mononuclear $VO(H_2O)pida^{2-}$ complex. In a 60:40 (v/v) solvent mixture, a new species was formed and the solution shifted color to green. This mixture yielded an absorption spectrum containing three absorption maxima. Two maxima around 870 and 630 nm are indicative of the presence of the $VO(H_2O)pida^{2-}$ species observed in the 50:50 (v/v) solvent mixture, whereas a shoulder at about 420 nm (85 M^{-1} cm^{-1}) is indicative of the presence of the dinuclear $(VO)_2(pida)_2^{4-}$ species. We and others[37] have observed that dinuclear vanadium(IV,IV) complexes can form a brown solution, even though in our case the solution was generated from the blue crystals. To ensure that the observed color change was not simply due to oxidation of the vanadium(IV) species to the corresponding vanadium(V) mononuclear complex VO_2pida^{3-}, the UV−visible spectrum for this complex was measured. As shown in Figure 3, this vanadium(V) species does not have absorptions in the range where the dinuclear vanadium(IV) species has a maximum. However, the color of the vanadium(IV)−H$_4$pida mixture is very pH dependent; it is brown at pH 8, green at pH 4−6, and blue at pH 2. An increase in the dioxane concentration reduced the absorbance from the mononuclear species, and at 80:20 (v/v) dioxane to water, the dinuclear $(VO)_2(pida)_2^{4-}$ species was the major species in the brown solution. As expected, higher amounts of dioxane increased the stability of the $(VO)_2(pida)_2^{4-}$ species.

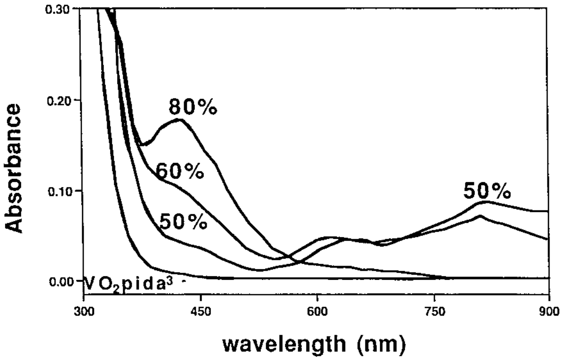

Figure 3. UV−visible spectra of $VO(H_2O)pida^{2-}$ species (2.0 mM) in 50:50 (v/v) dioxane−water, pH 5.5; $VO(H_2O)pida^{2-}$ and $(VO)_2(pida)_2^{4-}$ species in 60:40 (v/v) dioxane−water, pH 5.3; and $(VO)_2(pida)_2^{4-}$ species in 80:20 (v/v) dioxane−water, pH 4.5. The spectrum for VO_2pida^{3-}, pH 6.4 (2.0 mM), is also included.

The color of the dissolved complex in dioxane−water mixtures changed as a function of time. In solutions containing from 50:50 (v/v) to 60:40 (v/v) dioxane−water, the blue or blue-brown color of the solutions became brown over a period ranging from 24 to 72 h. The time the solutions required to change from the initial blue monomeric species to the brown dimer increased as the concentration of crystalline $Na_4(VO)_2(pida)_2$ increased (see Figure S2, Supporting Information). The color changes are evidence for the equilibrium between $VO(H_2O)pida^{2-}$ and $(VO)_2(pida)_2^{4-}$. Upon dissolution, a significant fraction of $VO(H_2O)pida^{2-}$ forms which converts to the equilibrium mixture of $VO(H_2O)pida^{2-}$ and $(VO)_2(pida)_2^{4-}$ over time. The fact that the rate of conversion decreased as the concentration of $VO(H_2O)pida^{2-}$ increased suggests that the dimerization does not simply involve combination of two $VO(H_2O)pida^{2-}$ ions. The dimerization process must be governed by a complex rate law. In pure water, this conversion was not observed; in 50:50 (v/v) DMF−water, the conversion was slower than in dioxane.

Ambient-temperature EPR spectra recorded for $(VO)_2(pida)_2^{4-}$ dissolved in 60:40, 65:35, and 80:20 (v/v) dioxane:water mixtures are shown in Figure 4. The $(VO)_2(pida)_2^{4-}$ complex dissolved in the 60:40 (v/v) system clearly shows the eight-line hyperfine splitting pattern expected for the mononuclear vanadium(IV) species. In the 65:35 (v/v) solvent system, the contribution of this species has significantly decreased, and in the 80:20 (v/v) system, none of the species is detected. However, in EPR spectra of organic solvent mixtures, it was found that

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(37) Launay, J.-P.; Jeannin, Y.; Daoudi, M. *Inorg. Chem.* **1985**, *24*, 1052−1059.

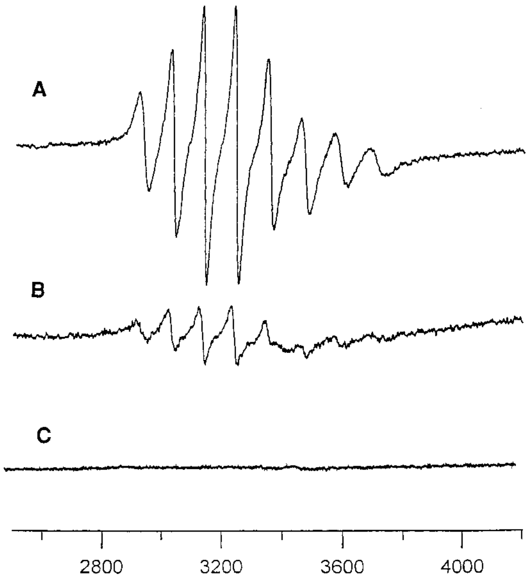
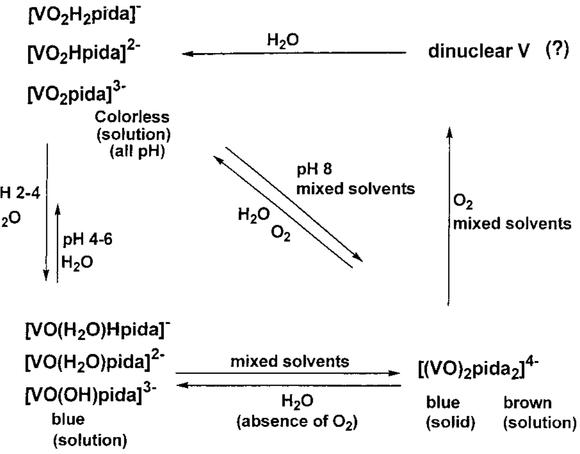


Figure 4. EPR spectra of dissolved crystalline $Na_4(VO)_2(pida)_2$ species (1.5 mM) in dioxane−water: (A) $VO(H_2O)pida^{2-}$ and $(VO)_2(pida)_2^{4-}$ species in 60:40 (v/v) dioxane−water, pH 5.3; (B) trace levels of $VO(H_2O)pida^{2-}$ and mostly $(VO)_2(pida)_2^{4-}$ species in 65:35 (v/v) dioxane−water, pH 5.2; (C) $(VO)_2(pida)_2^{4-}$ species in 80:20 (v/v) dioxane−water, pH 4.5.

the intensity of the signals in the spectra slowly decreased as a function of time when the organic solvent exceeded 60%. For other vanadium complexes, aggregation has been observed, leading to reduced signal intensities in the EPR spectrum. The observed changes in intensity may be due to a combination of dinuclear species formation and complex-spin aggregation. Recognizing these problems, we recorded all the spectra shown in Figure 4 immediately after solution preparation. Since the dinuclear species has been found to be EPR silent,[19,38,39] these spectra are consistent with the interpretation that the blue species is $VO(H_2O)pida^{2-}$ and that the brown species is $(VO)_2(pida)_2^{4-}$.

Potentiometric Studies of the Vanadium(IV)−H$_4$pida System. The three dioxane−water mixtures identified as containing mainly the mononuclear complex (50:50 (v/v)), mainly the dinuclear complex (80:20 (v/v)), and a mixture of both mono- and dinuclear complexes at equilibrium (60:40 (v/v)) were the chosen conditions for potentiometric studies. Since potentiometry gives the best and most accurate results when a proton is consumed or generated and the hydrolysis of $(VO)_2(pida)_2^{4-}$ to form $VO(H_2O)pida^{2-}$ does not involve any changes in protonation states, titration data for wide ranges of pHs and concentrations are needed to successfully determine formation constants and distinguish the mononuclear complex from the dinuclear complex using potentiometry.

Scheme 2. Vanadium(IV), Vanadium(V), and H$_4$pida Species in Aqueous and Mixed Solvent Systems



Titrations in the 80:20 (v/v) dioxane−water mixture were not possible because a blue product precipitated at pH 3.5, even at low concentrations. At pH 6, this precipitate had turned green and, by pH 10.3, yellowish-brown. The precipitated solids at high pH were not simply oxidation products, because upon reacidification, the solution returned to its initial blue color. Titrations in the 60:40 (v/v) dioxane−water mixture were possible at 2.0 mM ligand concentration in the presence of 1.0 and 2.0 mM metal ion. The slow complex formation was evidenced by the generation of blue and bluish-brown solution colors. The resulting titration curves are best interpreted such that, by pH 3.5, a complex of the stoichiometry $VO(H_2O)Hpida^{-}$ forms, whereas, at about pH 6.5, a complex of the stoichiometry $VO(H_2O)pida^{2-}$ forms. The extra base consumption in the neutral and slightly alkaline pH range furthermore suggests the formation of $VO(OH)pida^{3-}$. The data obtained unfortunately can be fitted by both a mononuclear and a dinuclear species within the uncertainties of the experiment. Titrations in the 50:50 (v/v) dioxane−water mixture, as expected, yielded results supporting the presence of a mononuclear species. In these solutions, the concentration of dinuclear species is low and not expected to be measurable.

The color changes in solutions of crystalline $Na_4(VO)_2(pida)_2$ from blue to brownish-green were sensitive not only to specific solvent composition but also to complex concentrations and pH. Little change in pH values was observed in the blue, high-concentration samples, but significant changes were observed in pH in the low-concentration samples; the latter changed color from blue to brownish-green. These observations suggest that the dimerization of $VO(H_2O)pida^{2-}$ is faster than the dimerization of $VO(OH)pida^{3-}$, a point which is justified by electrostatics and complex reactivity.

Summary of the Speciation of Vanadium(IV)− and Vanadium(V)−H$_4$pida Systems. In Scheme 2, we summarize the vanadium(IV) and -(V) species for which evidence was obtained in this paper. The titration studies suggest that three mononuclear vanadium(V)−pida complexes, $[VO_2H_2pida]^-$, $[VO_2Hpida]^{2-}$, and $[VO_2pida]^{3-}$, exist in aqueous solutions. Three (perhaps four) species were observed for the vanadium(IV)−pida system including two mononuclear, $[VO(H_2O)Hpida]^-$ and $[VO(H_2O)pida]^{2-}$ (perhaps also $[VO(OH)pida]^{3-}$), and one dinuclear species, $[(VO)_2(pida)_2]^{4-}$. In addition, preliminary evidence for an additional dinuclear vanadium species was obtained in mixed-solvent systems. The existence of all these species having been demonstrated, it is clear the explorations into the mechanistic studies of these complexes, as well as redox studies of these complexes, should be accompanied by speciation studies. Reduction of V(V) to V(IV) previously has been demonstrated in acidic media by the H$_4$pida ligand, leading to $HOOCCH_2NHCH_2(O)P(OH)_2$ (PMG) and other products.[27] The possibility that these reactions occurred under the more gentle conditions employed in this work was examined. Solutions of added vanadate and H$_4$pida at low pH (below 3) and high pH (~6) were monitored by ^1H NMR spectroscopy. At low pH, more than 90% of the product formed was PMG. Similar redox reactions did not occur in the solution at pH 5−6. The ^1H NMR

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(38) Castro, S. L.; Cass, M. E.; Hollander, F. J.; Bartley, S. L. *Inorg. Chem.* **1995**, *34*, 466−472.

(39) Toftlund, H.; Larsen, S.; Murray, K. S. *Inorg. Chem.* **1991**, *30*, 3964−3967.

of solutions at pH 5−6 gave, even after 2 weeks' incubation, only major signals (>98%) for the V(V)−pida complex, whereas the samples at pH <4 gave PMG and a few other oxidation products. Reduction of $[VO_2pida]^{3-}$ to $[VO(H_2O)pida]^{2-}$ may not be the mechanism of reduction and should be investigated. Indeed, it is likely that the protonation reactions are essential to the stability and observed redox chemistry of these species, and spectroscopic studies such as those presented here assist in defining the solution structures in this system.

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Supporting Information Available: Figures showing ^{13}C NMR spectra of VO_2pida^{3-} and the free ligand at pH 6.58 at 21 °C and at 4 °C and visible spectra of crystalline $Na_4(VO)_2(pida)_2$ dissolved in 50:50 (v/v) dioxane−water as a function of time. This material is available free of charge on the Internet at http://pubs.acs.org.

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