a $[L(tmpa)CrOCr(tmpa)L]^{2+}$ complex. If this is looked at from another perspective, a CrOCr dimer with strong π-bonding will resist protonation, leading to a bent hydroxo-bridged product in which such π-bonding is much weaker or is totally absent.

Figure 8 displays correlations of Cr(OH)Cr dimer acid ionization constants and $[L(tmpa)CrOCr(tmpa)L]^{2+/3+}$ oxidation half-wave potentials with $10Dq$, estimated as the energy of the Cr(OH)Cr dimer ${}^4T_{2g} \leftarrow {}^4A_{2g}$ (O_h) transition. Consistent with expectations from the π molecular orbital model, pK_a values fall off sharply with increasing $10Dq$ while $E_{1/2}$ generally follows an increasing trend as the L^- substituent moves from weaker to stronger field within the spectrochemical series. The latter observation follows from the expected enhancement of $E_{1/2}$ with decreasing energy of the redox electron,[38] which is ionized from the b_{2g} (essentially nonbonding d_{xy} (t_{2g})) molecular orbital according to our model. Thus, the relationship of electrochemical potentials to t_{2g} orbital and valence state ionization energies is well established for monomeric transition-metal redox couples.[38] From this perspective, $E_{1/2}$ values of the $[L(tmpa)CrOCr(tmpa)L]^{2+}$ complexes are not expected to correlate with the π-bonding energy of the CrOCr unit but rather more simply with $10Dq$, which may be expressed in crystal field terms as the energy difference between $d_{x^2-y^2}$ and d_{xy} orbitals (in point group D_{4h}).[32]

It should be noted that the least-squares lines in Figure 8 are not intended to imply that linear relationships between pK_a or $E_{1/2}$ values and $10Dq$ are anticipated on theoretical grounds. Rather, we are content to establish that quantitative dependences of the dimer physical parameters on $10Dq$ do in fact exist and are reasonable on the basis of a molecular orbital description of the CrOCr bonding. In order to better understand the physical properties of oxo-bridged Cr(III) dimers, it will be necessary to introduce systematic perturbations into the energies of the e_g, b_{2g}, and b_{1u} molecular orbitals, which are not actually nonbonding but may interact with the low-lying π^* levels of phen and bpy aromatic amine ligands, both of which are far better π-acids than the nonconjugated tmpa pyridyl groups. Toward this end, we report here the syntheses of the first two members of the $[L(bpy)_2CrOCr(bpy)_2L]^{2+}$ family but will reserve comment on their characteristics until continuing work on this system has progressed further.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Robert A. Welch Foundation (Grant D-735) for their generous support of this research. We also thank Professor John Kenney of Eastern New Mexico University for helpful discussions of the spectroscopic data.

Supplementary Material Available: A listing of the magnetic susceptibilities of dimer 7 as a function of temperature (1 page). Ordering information is given on any current masthead page.

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^{51}V NMR Investigation of the Interactions of Vanadate with Hydroxypyridines and Pyridinecarboxylates in Aqueous Solution

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The condensation of vanadate with salicylate, with pyridine, and with a variety of hydroxypyridines and pyridinecarboxylates in aqueous solution has been studied by using ^{51}V nuclear magnetic resonance spectroscopy. Vanadium atom, ligand, and hydrogen ion concentration studies have been carried out. Compared with the other ligands, pyridine and 3-hydroxypyridine undergo comparatively weak interactions with vanadate. 2-Hydroxybenzoate (salicylate) and 2-hydroxy-3-pyridinecarboxylate (2-hydroxynicotinate) react only weakly as chelating ligands to give products that appear to have octahedral symmetry. No evidence for condensation of vanadate between the hydroxyl and the nitrogen of 2-hydroxynicotinate was obtained. 2-Pyridinecarboxylate (picolinate) proved to be a good chelating agent to form a mixture of mono- and bis(ligand) species of apparent octahedral coordination. A further mono(ligand) product that was tentatively assigned a pentacoordinate coordination was also formed. 3-Hydroxy-2-pyridinecarboxylate (3-hydroxypicolinate) formed a complex mixture of products, with condensation of vanadate between the nitrogen and carboxylate and possibly between the carboxylate and the hydroxyl group occurring. pH studies allowed the proton stoichiometry for the various condensations to be obtained. Formation constants for the various condensation products from specified reactants have been obtained and are reported in this study.

Introduction

The aqueous chemistry of vanadium oxyanions has, over the past few years, become an area of expanding interest. There is a considerable amount of work which indicates that vanadium is an essential element.[1,2] Vanadium is extracted from seawater and concentrated to molar concentrations by ascidians, which store it as a V(III) derivative.[3] Vanadium-containing enzymes are found in various seaweeds where they are utilized for the formation of halogenated products.[2,4,5] Vanadium is also found in the enzymes of some nitrogen-fixing bacteria.[6] Furthermore, vanadate is a potent inhibitor of various enzymes and, similarly, a strong activator of a variety of others. Apparently, some of this function derives from the ability of vanadate (V(V)) (and perhaps vanadyl (V(IV))) to act as a phosphate analogue and, as such, vanadate provides a convenient probe for the investigation of mechanisms of enzyme action.

When in water, but dependent on pH, vanadate undergoes condensation reactions to form a variety of oligonuclear products including the dimer, tetramer, and decamer.[7] In the presence of aliphatic alcohols a rapid and reversible condensation occurs to provide tetrahedrally coordinated esters.[8] From water and

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ligand requirements for product formation, it was shown that pentacoordinate products are formed with 1,2-diols.[9] ^{51}V NMR studies of vanadate coordination with 2-hydroxy carboxylates suggested that both pentacoordinated and hexacoordinate products are formed.[10] Interestingly enough the 1,2-diols provide pentacoordinated products only as binuclear species whereas the 2-hydroxy carboxylate ligands form mononuclear pentacoordinate and binuclear octahedral products. These aspects of vanadate chemistry are of continuing interest, and we have made an effort to broaden our understanding of the vanadate system by investigating the condensation of vanadate with a variety of aromatic hydroxy acids, including several picolinate, nicotinate, and hydroxypyridine derivatives.

Although the interactions of vanadate with hydroxylic compounds are becoming better understood, still little is known about the interaction of vanadate with amino groups. Recent work has shown that there are strong interactions between vanadate and peptides[11,12] and between vanadate and a variety of amino buffers.[13,14]

Studies such as these are of considerable importance, since they provide the background knowledge necessary for obtaining a proper understanding of the interactions of vanadate in enzymatic systems. Recent work has suggested that, in the stimulation of the 2,3-diphosphoglycerate phosphatase activity of phosphoglycerate mutase by vanadate, vanadate is bound at the catalytic site of the enzyme through a histidine nitrogen[15] similar to vanadate in ribonuclease.[16] Histidine is a ubiquitous component of the active site of many enzymes, and as a result, the interactions between aromatic nitrogens and vanadate are of intrinsic interest.

Further impetus for the study of aromatic amines has its basis in observations that, to an extent, the metabolism of chromium involves complexes of nicotinic acid, as in the glucose tolerance factor. This chromium-containing complex is involved in glucose metabolism and, in insufficient quantities, seems to promote the symptoms of diabetes.[17,18] Vanadium is well-known to act as an insulin mimetic,[1] even in live animals,[19] and the metabolism of these to metals, to an extent, may be related.

Experimental Section

Materials. Pyridine was distilled under reduced pressure before use. All the other reagent grade materials were used without further purification. Salicylic acid and nicotinic acid were purchased from BDH Chemicals Ltd., isonicotinic acid, picolinic acid, 2-hydroxynicotinic acid, and 3-hydroxypicolinic acid, from Aldrich Chemical Co. Inc. The carboxylic acid derivatives were used as sodium salts by making neutral solutions with appropriate amounts of sodium hydroxide. The preparations of aqueous vanadate solutions for the ^{51}V NMR spectroscopy were made at constant ionic strength for each study: 3 M for nicotinate and isonicotinate, 1 M for salicylate, 0.5 M for 2-hydroxynicotinate, and 0.01 M for picolinate and 3-hydroxypicolinate, by using appropriate amounts of KCl. The general procedure has been previously described.[20]

Spectroscopy. All ^{51}V NMR spectra were obtained at ambient temperature at 105.2 MHz with a Bruker 400-MHz NMR spectrometer. Spectral widths of 20 kHz, 0.05 s acquisition times, and 50° pulse widths were used throughout. A line-broadening factor of 20 Hz was applied to all spectra. Before Fourier transforming to the frequency domain, the 2K data sets were zero-filled to 8K. Chemical shifts reported are relative to the external reference standard, $VOCl_3$, which has been assigned to zero ppm.

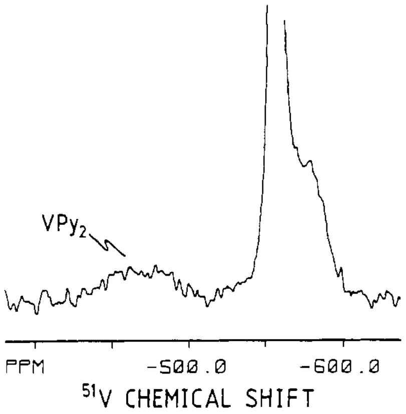

Figure 1. ^{51}V NMR spectrum demonstrating that the reaction of pyridine with vanadate forms a product giving a broad NMR signal with a ^{51}V chemical shift at −477 ppm. A further reaction that could not be properly characterized leads to the signal at −572 ppm, which derives from a pyridine/divanadate interaction. Conditions of the experiment were as follows: 0.5 mM vanadate; 5.0 M pyridine; 20 mM HEPES buffer; pH 7.0.

Data Analysis. Base-line roll was removed from all spectra before signal intensities were measured. The signal intensities were obtained by using the integration routine of the instrument manufacturer's software.

The results were analyzed by writing the equilibria in the appropriate linear form as outlined in the text. The graphs were then plotted and the slopes and intercepts obtained by least-squares analysis.

Results and Discussion

The inorganic vanadate ions $H_2VO_4^-$ and HVO_4^{2-} react spontaneously and reversibly with each other to produce a variety of oligomeric products.[7] The formation of those of predominent importance in this study is summarized in eq 1 and 2, where the

$$4T_i \xrightleftharpoons{K_0} T_4 \qquad [T_i]^4K_0 = [T_4] \tag{1}$$

$$2T_i \xrightleftharpoons{K_1} T_2 \qquad [T_i]^2K_1 = [T_2] \tag{2}$$

abbreviation T refers to the presumed tetrahedral nature of the vanadate species and $[T_i]$ to the concentration $[H_2VO_4^-]$ + $[HVO_4^{2-}]$. When vanadate species are in the presence of ligands, further reactions may occur to give a variety of products of which some characteristics can be deduced from ^{51}V NMR experiments.

Condensation of vanadate with a number of pyridine derivatives occurs spontaneously in aqueous solution to provide a limited variety of products, the formation of which have been characterized by hydrogen ion, vanadate, and ligand concentration studies.

Pyridine plus Vanadate. The study of the condensation of pyridine with vanadate is complicated by two factors that mitigate against a detailed analysis of this system. At pH 7.0 the product of the reaction of pyridine with vanadate gives rise to a rather broad NMR signal centered at about −467 ppm. In addition to this, there apparently is a specific reaction with divanadate that leads to a broadened NMR signal at about −570 ppm that overlaps the signals from T_4 and T_i. It was not possible to alleviate the problem of the broad signals by working at low concentrations of vanadate, since the signal intensity then became comparable to the artifacts in the base line. Figure 1 depicts a ^{51}V NMR spectrum obtained at 0.5 mM vanadate that shows the signal from the vanadate/pyridine complex at −467 ppm and the broadened signal at −572 ppm arising from the pyridine/divanadate interaction. At a concentration of 0.1 mM total vanadate this latter signal was almost unobservable in the spectrum, which showed that this signal does not arise from a monovanadate/pyridine complex.

Because of the relative sharpness of the T_i and T_4 signals compared to the broad signal at −572 ppm, it did prove possible to make a reasonable separation of the contribution to T_i.

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The vanadate concentration study did show that the product giving rise to the −467 ppm signal was mononuclear in vanadium, while the results of the pyridine concentration study were consistent with incorporation of two pyridine moieties into the product. The formation of the product can then be written as eq 3, where the

$$T_i + 2py \overset{K_2}{\rightleftharpoons} -467 \qquad (3)$$

chemical shift is used to identify the product. This chemical equilibrium can be rewritten as the equilibrium expression eq 4.

$$[T_i]K_2 = [-467]/[py]^2 \qquad (4)$$

When the results of the vanadate concentration study were plotted according to eq 4, a value for K_2 of (8.1 ± 0.9) × 10^{-3} M^{-2} was obtained for 5.0 M pyridine solutions at pH 7.0. This formation constant is comparable to those measured for the formation of vanadate diesters from vanadate and two alkyl alcohol ligands.[21]

Recently, ^{51}V NMR studies have been carried out for the anhydrous $VOCl_3$/pyridine system. In this study a major product was observed that was characterized as $[VOCl(py)_2]Cl_2$ and had a chemical shift of −403 ppm.[22] Replacement of the coordinating Cl by OH can be expected to shift the chemical shift to a considerably more negative position,[11,23] and this may indicate that the −467 ppm shift observed here for the bis(pyridine) complex corresponds to a tetrahedral product. However, it is expected that the change from a nonaqueous to an aqueous medium will also significantly affect chemical shifts. In this study the formation of the pyridine complex was not favored at higher pH, indicating that condensation occurred with $H_2VO_4^-$, not HVO_4^{2-}. Because of complications resulting from decavanadate formation and the uncertainty in determining K_2, it did not prove possible to determine whether uptake of protons was required for the formation of the pyridine product from $H_2VO_4^-$.

None of the reactions between the nitrogen of the pyridine ring and vanadate are favored to an extent comparable to condensations with the other pyridine derivatives of this study, and since consideration of their formation will have a minimal effect on any conclusions obtained, they are generally ignored.

Hydroxypyridines plus Vanadate. The 2-hydroxy- and 4-hydroxypyridines exist in solution almost completely in their tautomeric keto forms.[24] The vanadium NMR spectrum of vanadate in the presence of up to 3.0 M concentrations of either ligand did not indicate any significant interaction with vanadate. An interesting facet of this study was the observation that at the highest 2-hydroxypyridine concentration the signal from T_4 showed a substantial line broadening. This broadening was specific to T_4, and the signals from T_2 and T_i did not appear to be perturbed. The signal broadening indicated the presence of an exchange process. That it was restricted to T_4 was surprising, particularly in view of our previous observations that this oligomer is generally quite unreactive.[9,25] Interestingly enough, no such broadening was observed with 4-hydroxypyridine at similar concentrations.

At concentrations of less than 10% of the ligand concentrations of the above study, reaction of vanadate with the 3-hydroxypyridine (ℓ) can be observed. The product formed can be expected to result from condensation of the hydroxyl group of the aromatic ring with vanadate to give the pyridol ester, $T\ell$, a product similar to that formed from vanadate in the presence of phenols.[26,27] In aqueous solution the ester signal is not separated from that of T_i at −560 ppm; however, it can be observed in a 40% acetone/water solution. The reaction to form the ester proceeds as indicated in eq 5, but since the NMR signals from T_i and $T\ell$ overlap, a

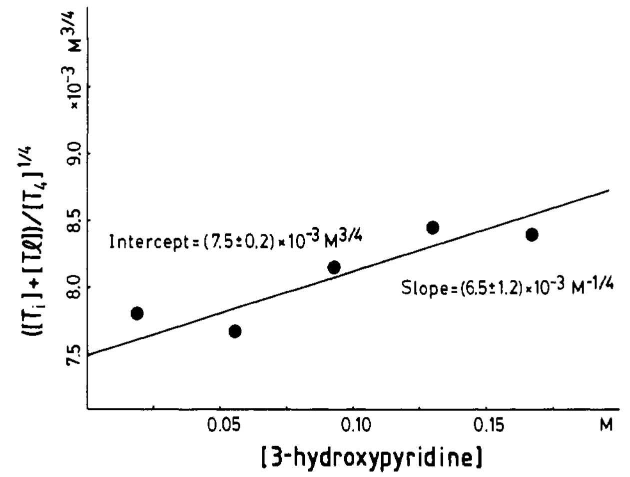

Figure 2. Graph demonstrating by its positive slope the reaction of vanadate with 3-hydroxypyridine to give the vanadate ester. The conditions of the experiments were as follows: 3.0 mM total vanadate; 20 mM HEPES buffer; pH 7.0; indicated amounts of 3-hydroxypyridine.

$$T_i + \ell \overset{K_3}{\rightleftharpoons} T\ell \qquad [T_i][\ell]K_3 = [T\ell] \qquad (5)$$

reference is needed. This is provided by T_4, as indicated by eq 1. Combination of eq 1 with eq 5 leads to eq 6. A plot of the

$$\frac{[T_i] + [T\ell]}{[T_4]^{1/4}} = K_0^{-1/4} + K_0^{-1/4}K_3[\ell] \qquad (6)$$

relevant parameters in eq 6 is shown in Figure 2. The *y* intercept of this plot gave $K_0^{-1/4}$ = (7.5 ± 0.2) × 10^{-3} $M^{3/4}$, from which K_0 = (3.2 ± 0.5) × 10^8 M^{-3}. The slope of this plot ($K_0^{-1/4}K_3$ = (6.5 ± 1.2) × 10^{-3} $M^{-1/4}$) then gave K_3 = 0.9 ± 0.2 M^{-1}. This formation constant is a factor of 100 larger than that determined for the formation of the vanadate/pyridine complex of eq 3 but is close to that for the formation of phenyl vanadate (K = 0.97 ± 0.02 M^{-1}).[26] The dipyridol vanadate probably is also formed, but this could not be established under the conditions of this experiment. It would be a minor product, as would the product from the condensation of vanadate at the nitrogen of 3-pyridol.

Pyridinecarboxylates plus Vanadate. The reaction of vanadate with each of the three pyridinecarboxylates has been investigated. Neither the 3- (nicotinate) nor 4- (isonicotinate) substituted derivative undergoes a significant reaction with vanadate except at concentrations above 2 M. At such concentrations the interactions between vanadate and the nitrogen of the pyridine ring become observable. In addition to this, there is a marked broadening of the signal from T_i. Vanadate reacts readily with carboxylic acids[28] so it seems likely that the line broadening of the T_i signal derives from interactions with the carboxyl function of the nicotinic and isonicotinic acids. The study of this interaction has not been pursued in this work.

In contrast with the above two pyridinecarboxylates, vanadate undergoes an exceptionally favorable interaction with 2-pyridinecarboxylate (picolinate). Picolinate has frequently been utilized, in combination with other ligands, to form crystalline vanadate complexes. X-ray structure analysis of such derivatives typically shows bonding of the vanadium to the ring nitrogen and to one of the carboxylate oxygens.[29,30] In aqueous solution, even at low concentrations of the picolinate, several vanadate products could be observed in the NMR spectrum, as can be seen in Figure 3, for which the ligand concentration was 8.0 mM, the total

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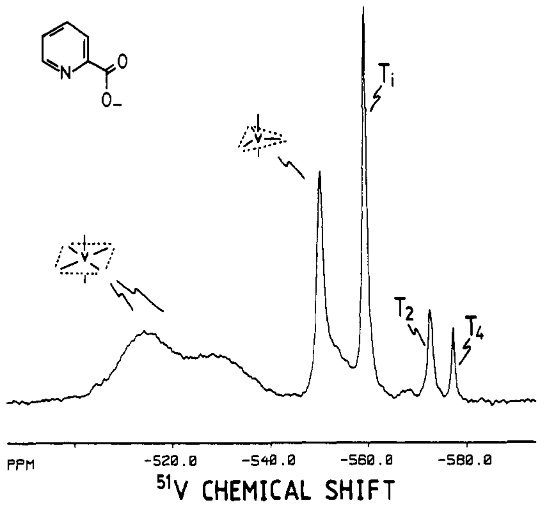


Figure 3. ^{51}V NMR spectrum showing the products of the equilibration of vanadate with picolinate. The products giving rise to the signals at −515 and −529 ppm have been tentatively assigned to isomers with octahedral coordination, while the product providing the −550 ppm signal has been assigned a pentacoordinate geometry. The conditions of the experiment were as follows: 3.0 mM total vanadate; 8.0 mM total picolinate; 20 mM HEPES; pH 7.0; 0.01 M ionic strength maintained with KCl.

vanadate concentration was 3.0 mM, and pH was 7.0. In addition to vanadate and its oligomers (T_i, −559.4 ppm; T_2, −572.7 ppm; T_4, −577.2 ppm), four major products can be observed. These products give rise to vanadium NMR signals at −513, −529, −550, and −552 ppm. A minor product was observed to give rise to a signal at −568 ppm; this product was not further characterized.

It was possible to determine the number of picolinate ligands and the number of protons required for the formation of each product. It was also possible to determine the number of vanadium nuclei in each complex. However, this study did not provide water stoichiometry, a knowledge of which would aid in the assignment of coordination geometry. This system was investigated by varying the total vanadate and total ligand concentration. The analysis of the results was straightforward although, because the formation of products was so highly favored, it was necessary to apply the conservation equation, eq 7, to determine the free ligand concentration.

$$[\text{pic}]_t = [\text{pic}]_f + \sum n[\text{V}_i\ell_n] \qquad (7)$$

In this equation $[\text{pic}]_t$ is the total picolinate concentration, $[\text{pic}]_f$ is the concentration of ligand free in solution, and $[\text{V}_i\ell_n]$ corresponds to the reaction products. Since it is necessary to employ eq 7, an iterative process was utilized when attempts were made to determine the vanadium and ligand numbers for the complexes studied.

A vanadium concentration study (1.0–3.5 mM V_i) was done at a fixed total picolinate concentration of 5.0 mM. The NMR spectra indicated that the products giving rise to the −513, −529, and −552 ppm signals did not significantly change their relative concentrations in solution. This indicated that these three products had the same number of vanadium nuclei and probably the same number of ligands. Furthermore, the proportions of these products increased with decrease in total vanadium atom concentration relative to T_i and the −550 ppm product. This relative increase in proportions results from an increase in free ligand concentration with decrease in total vanadium atom concentration as less ligand is incorporated into products. The result then is fully consistent with one vanadium nucleus per product and indicated that the above three derivatives contained two or more ligands, while the fourth product (corresponding to the −550 ppm signal) contained only one. This conclusion was supported by a ligand concentration study (1.0–8 mM picolinate) at a constant 3 mM total vanadate concentration. The change in proportions of the products giving rise to the −513, −529, and −552 ppm signals strongly supported the conclusion that each was formed from two ligands while the −550 ppm product was formed from only one ligand.

On the basis of the vanadium atom and ligand concentration studies, eq 8–11 were written where the product was identified by its chemical shift. These equations in combination with eq

$$\text{T}_i + 2\text{pic} \overset{K_4}{\rightleftharpoons} -513 \qquad [\text{T}_i][\text{pic}]^2K_4 = [-513] \qquad (8)$$

$$\text{T}_i + 2\text{pic} \overset{K_5}{\rightleftharpoons} -529 \qquad [\text{T}_i][\text{pic}]^2K_5 = [-529] \qquad (9)$$

$$\text{T}_i + 2\text{pic} \overset{K_6}{\rightleftharpoons} -552 \qquad [\text{T}_i][\text{pic}]^2K_6 = [-552] \qquad (10)$$

$$\text{T}_i + \text{pic} \overset{K_7}{\rightleftharpoons} -550 \qquad [\text{T}_i][\text{pic}]K_7 = [-550] \qquad (11)$$

7 then fully characterize the system. Application of the appropriate equation to the results of the concentration studies gave excellent linear correlations such as for the plot of $[-513]/[\text{T}_i]$ vs $[\text{pic}]^2$ as required for application of eq 8. From the slope of the straight line in that graph a value for K_4 equal to $(8.4 \pm 0.4) \times 10^4\ \text{M}^{-2}$ was obtained. Similar correlations gave the values $K_5 = (4.0 \pm 0.4) \times 10^4\ \text{M}^{-2}$, $K_6 = (1.5 \pm 0.3) \times 10^4\ \text{M}^{-2}$, and $K_7 = (2.0 \pm 0.2) \times 10^2\ \text{M}^{-1}$. These formation constants are very large, indicating the almost stoichiometric nature of these condensations. It is interesting to note in this regard that the mono(picolinate) complex (−550 ppm) has a formation constant 15 times larger than that determined for a mono(oxalate) complex[10] and 20 times larger than for a mono(lactate) complex,[10] both determined under similar conditions. Since the three types of ligands can all form five-membered-ring cyclic products, it may be that the enhanced stability of the product derives in part from aromatic π-interactions with available d orbitals of the vanadate nucleus.[27] Alkyl amino acids, which are somewhat similar in structure to picolinic acid, undergo only very weak interactions with vanadate.[11,28]

The effect of pH on the formation of the picolinate products is remarkable. At pH 8.0 (1 pH unit above that used in the experiments of Figure 3) all of the bis(picolinate) species have become unobservable and only a small fraction of the mono(picolinate) product remains. It proved possible to determine proton stoichiometry by using the vanadate species VO_4H_2^- (T_i^-) as a reference. VO_4H_2^- is in rapid equilibrium with its deprotonated analogue VO_4H^{2-} (T_i^{2-}). If δ_l is the ^{51}V chemical shift for T_i^- and δ_h the shift for T_i^{2-}, then the observed chemical shift for T_i is related to the pK_a of T_i^- by eq 12, and a plot of pH vs the logarithm

$$\text{pH} = \text{p}K_{a2} + \log \frac{\delta_l - \delta}{\delta - \delta_h} \qquad (12)$$

term will give a line of slope 1 and y intercept equal to the pK_a. From the observed chemical shifts obtained as a function of pH and with the use of the values −560.3 and −536.1 ppm for δ_l and δ_h, respectively, in eq 12, a value for the pK_{a2} of T_i^- of 8.44 ± 0.02 was obtained from the graph. The measured slope of the line was 0.99. The pK_a or indeed the observed chemical shift of T_i can be used to provide the concentrations of VO_4H_2^- and VO_4H^{2-}.

Under conditions of constant total ligand and vanadate concentrations, the proton stoichiometry of the products can readily be obtained by utilizing eq 13–16, which are analogous to eq 8–11.

$$\text{VO}_4\text{H}_2^- + 2\text{pic}^- + n\text{H}^+ \overset{K_4'}{\rightleftharpoons} -513^{n-3} \qquad (13)$$

$$\text{VO}_4\text{H}_2^- + 2\text{pic}^- + n\text{H}^+ \overset{K_5'}{\rightleftharpoons} -529^{n-3} \qquad (14)$$

$$\text{VO}_4\text{H}_2^- + 2\text{pic}^- + n\text{H}^+ \overset{K_6'}{\rightleftharpoons} -552^{n-3} \qquad (15)$$

$$\text{VO}_4\text{H}_2^- + \text{pic}^- + n\text{H}^+ \overset{K_7'}{\rightleftharpoons} -550^{n-2} \qquad (16)$$

Rewriting eq 13 as eq 17 and then rearranging and taking the

$$[\text{VO}_4\text{H}_2^-][\text{pic}^-]^2[\text{H}^+]^nK_4' = [-513^{n-3}] \qquad (17)$$

logarithms of both sides of the equation gave eq 18. Similar

$$\log \frac{[-513^{n-3}]}{[\text{VO}_4\text{H}_2^-][\text{pic}^-]^2} = -n\text{pH} + \log K_4' \qquad (18)$$

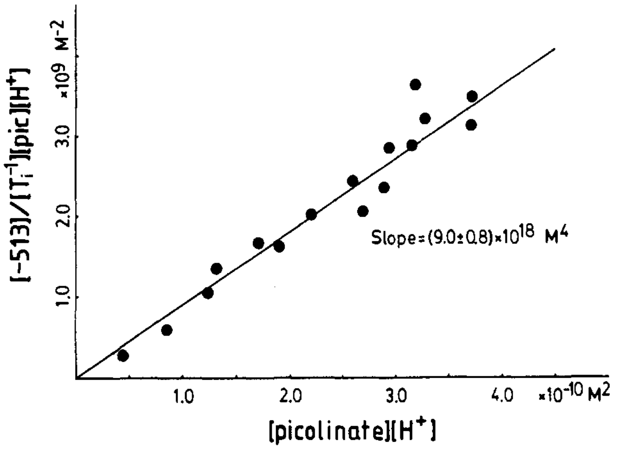


Figure 4. Graph demonstrating the incorporation of one proton for each picolinate ligand as the product giving rise to the −513 ppm ^{51}V NMR signal is formed. The zero intercept indicates that there is no product with only one ligand attached.

equations can be written for the formation of the other products. When the pH is plotted against the term in logarithms, a straight line of slope $-n$ should be obtained. When this was done, lines of slope −2 for the equilibria of eq 13–15 and −1 for that of eq 16 were obtained. These results clearly established that the formation of these picolinate/vanadate products required the uptake of one proton for each picolinate ligand incorporated into the product. When n is replaced by 2 in eq 17 and the equation is plotted as shown in Figure 4, a very good straight line was obtained, which indicated that this description of this equilibrium is correct. The zero intercept of this plot is consistent with the conclusion that no product with one ligand incorporated into it gives rise to an NMR signal at −513 ppm. Similar plots were obtained for the other products. The formation constants obtained were $K_4' = (9.0 \pm 0.5) \times 10^{18}$ M^{-4}, $K_5' = (4.7 \pm 0.6) \times 10^{18}$ M^{-4}, $K_6' = (1.6 \pm 0.4) \times 10^{18}$ M^{-4}, and $K_7' = (2.2 \pm 0.1) \times 10^9$ M^{-2}.

Without a knowledge of water requirements for the formation of these products, there is considerable ambiguity concerning possible structures. On the basis of the other ligand systems discussed above, it seems extremely unlikely that picolinate is acting as other than a bidentate ligand. It also seems probable that the protons are required for the formation of water as condensation occurs. Since only one proton is consumed as the product is formed, the product cannot be tetrahedral. If it were, OH$^-$ would be produced and a further proton would be required in order to maintain the pH. The −550 ppm product, which contains only one ligand, may then be pentacoordinate. A trigonal-bipyramidal complex of V(V) that contains a picolinate ligand has been characterized by X-ray diffraction.[30] However, the possibility of a water molecule occupying a sixth coordination site cannot be ignored.

The bis(picolinate) complexes could all be octahedral complexes. There are three possible stereoisomers for these two cis-bidentate ligands in an octahedral arrangement: the two nitrogens or the two oxygens of the ligand trans to each other in the equatorial plane or one isomer with an oxygen trans to a nitrogen in that plane. An arrangement of bidentate ligands cis to each other so as to preserve the bent rather than the linear relationship in the OVO bonds of the VO_2^+ moiety apparently is characteristic of V(V) octahedral complexes.[27] It seems likely that the −513 and −529 ppm signals derive from octahedral products. It does seem somewhat less likely that the product giving rise to the −552 ppm signal has a cis-octahedral arrangement of ligands since the chemical shift separation from the other product is quite large; however, it is difficult to assign an alternative except that perhaps the two ligands in an octahedral product are trans rather than cis to each other. Another consideration is that if the −550 ppm product is actually pentacoordinate, there is the possibility that the nitrogen or the carboxylate of a second picolinate, acting as a monodentate ligand, can coordinate to give the −552 ppm product. In view of the rather weak reaction of pyridine with vanadate the former seems unlikely, although there may be a strong synergistic reaction that accompanies the change in coordination from four to five. This type of behavior has previously been observed.[13] Scheme I depicts a possible reaction sequence for the formation of products. In this scheme the possible isomers have not been considered.

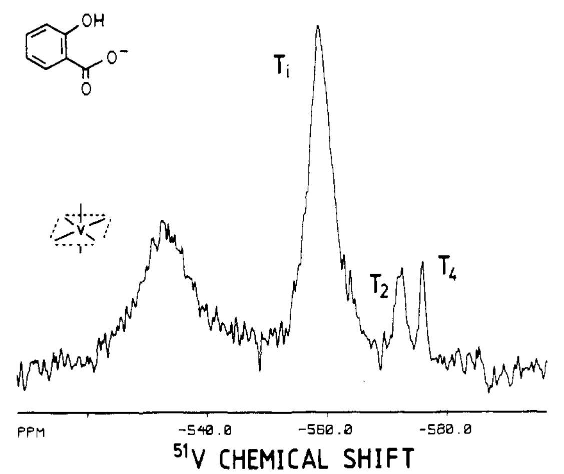
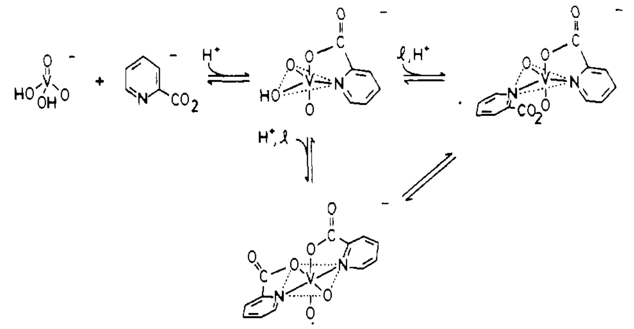


Figure 5. ^{51}V NMR spectrum of vanadate in the presence of salicylate. The occurrence of the broad signed centered at −533 ppm is consistent with the formation of an octahedral complex. The conditions of the experiment were as follows: 3.0 mM total vanadate; 0.7 M salicylate; 20 mM HEPES; pH 6.85; 1.0 M ionic strength maintained with KCl.

Scheme I



Salicylate plus Vanadate. There are several possibilities available to vanadate for reaction with salicylate (2-hydroxybenzoate) to occur. Vanadate can form the ester with the hydroxy moiety, as for other phenols[26,27] or for 3-hydroxypyridine, as described by eq 5. Reaction with the carboxylate to form the anhydride may also occur, and this may be the source of some of the line broadening observed at the higher concentrations of ligand, as discussed for the reaction of vanadate with nicotinate and isonicotinate. Salicylate may also act as a bidentate ligand to form a cyclic vanadate complex.

The vanadium NMR spectra (Figure 5) obtained for this system at pH 6.9 provided no direct evidence for formation of the vanadate ester, which indicated that the ester, if it is formed, gives rise to a signal under the T$_i$ resonance at −559 ppm. The formation of phenyl vanadates tends to be reasonably well favored with many of the formation constants, K_3, as defined by eq 5 ranging from about 2 to 10 M^{-1} in 40% v/v acetone/water.[27] Application of eq 6 to the results of this study gave a value for K_3 of $(7 \pm 3) \times 10^{-2}$ M^{-1}. This formation constant is in the order of 5 to 10% of that of phenol in water,[26] and this may indicate the presence of destabilizing electrostatic interactions resulting from the occurrence of a vanadate adjacent to the carboxylate of the aromatic ring.

Since salicylate has no nitrogen, the occurrence of a broad NMR signal at −533 ppm was taken to indicate the formation of an octahedral complex. Octahedral complexes with oxalate[10,31,32] and lactate[10] give rise to NMR signals very close to this

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[31] Scheidt, W. R.; Tsai, C.-C.; Hoard, J. L. *J. Am. Chem. Soc.* **1971**, *93*, 3867–3872.

chemical shift. During the attempt to fit the results of vanadate and salicylate concentration studies to equilibrium equations, it became evident that two products were formed, both mononuclear in vanadium but one containing one ligand and the other two ligands. The formation of these two products is described by eq 19 and 20, where ℓ refers to the ligand and Oc to the presumed

$$T_i + \ell \overset{K_8}{\rightleftharpoons} Oc\ell \qquad [T_i][\ell]K_8 = [Oc\ell] \tag{19}$$

$$Oc\ell + \ell \overset{K_9}{\rightleftharpoons} Oc\ell_2 \qquad [Oc\ell][\ell]K_9 = [Oc\ell_2] \tag{20}$$

octahedral coordination. Summation of these equations followed by rearrangement gives eq 21. The formation constants K_8 and

$$\frac{[Oc\ell] + [Oc\ell_2]}{[T_i][\ell]} = K_8 + K_8K_9[\ell] \tag{21}$$

K_9 can then be obtained by plotting the ratio on the left of this equation versus $[\ell]$. When this was done, a line of intercept $K_8 = 0.23 \pm 0.04$ M^{-1} and slope $K_8K_9 = 0.38 \pm 0.06$ M^{-2} was obtained from which $K_9 = 1.7 \pm 0.4$ M^{-1}. These formation constants are very small, about 2% of similar formation constants for lactate derivatives.[10] This may indicate that, in the absence of strong stabilizing interactions, six-membered cyclic rings are not readily formed with vanadate, possibly because of the steric strain imposed by the requirement for an OVO angle of nearly 90° within the ring. Similar behavior has been observed in 1,2-diol and 1,3-diol systems, where the products with ethylene glycol or 2,3-butanediol, for instance, are readily formed,[9] while that with 1,3-propanediol is not observed.[13] This type of behavior is of course a well-known chelate effect.

The formation of the cyclic products is pH dependent, and apparently at least one proton is required for product formation. In order to determine proton stoichiometry, it was first necessary to determine the pK_a of $VO_4H_2^-$ for the conditions of this study. The procedure described previously for the picolinate study utilizing eq 12 was used. The value obtained was p$K_{a2} = 8.12 \pm 0.03$ with $\delta_l = -559.5$ ppm and $\delta_h = -536.1$ ppm, where the conditions of this study were 0.6 M salicylate, 2 mM vanadate, 20 mM HEPES, and 1.0 M ionic strength maintained with KCl.

With this value for pK_{a2} it was possible to determine proton stoichiometry by use of a stepwise analytical procedure. The formation of products was written as in eq 22–24, where sal refers

$$VO_4H_2^- + sal^- + xH^+ \overset{K_8'}{\rightleftharpoons} Oc\ell^{x-2} \tag{22}$$

$$Oc\ell^- + sal^- + yH^+ \overset{K_9'}{\rightleftharpoons} Oc\ell_2^{x+y-3} \tag{23}$$

$$\frac{[Oc\ell] + [Oc\ell_2]}{[VO_4H_2^-][sal^-][H^+]^x} = K_8' + K_8'K_9'[sal^-][H^+]^y \tag{24}$$

to salicylate. Several general observations could be made from the results of the pH study. The first was that the ratio on the left of eq 24, when calculated by using the experimental results, was not constant with increase in pH but rather increased for all values of x. This meant that if protons were utilized for the overall formation of $Oc\ell_2$ from $VO_4H_2^-$ and salicylate, at least one more proton was required for this reaction than for the formation of $Oc\ell$ from vanadate and one salicylate. Furthermore, if the ratio on the left of eq 24 was plotted against $[sal][H^+]^y$ for assumed values of x and y equal to or greater than 1, a line of negative curvature was obtained. This is not possible chemically so $Oc\ell$ does not require a proton for its formation and the x of eq 22 is zero. Having found this, it was evident that only a single proton was required for the formation of $Oc\ell_2$, and this was confirmed by plotting the appropriate parameters of eq 24, where $x = 0$ and $y = 1$. This plot gave a straight line of intercept $K_8' = 0.25 \pm 0.05$ M^{-1}, which, since $x = 0$, should equal the value of K_8 (=0.23 ± 0.04 M^{-1}) that was previously determined (eq 19) from the concentration study. The agreement is excellent. The slope of the line obtained gave a value for $K_8'K_9'$ of $(9.7 \pm 1.0) \times 10^6$ M^{-3}, or $K_9' = (4.2 \pm 0.5) \times 10^7$ M^{-2}. Since the K_9 of eq 20 is related to K_9' ($K_9 = K_9'[H^+]$), then a value for K_9 calculated for pH 7.2 of 2.7 ± 0.7 M^{-1} is obtained, which within the error of the experiments is the same as the K_9 measured previously (1.7 ± 0.4 M^{-1}). The proton apparently is required in the second step in order to allow for the production of water as condensation occurs. This supports an octahedral structure for these products.

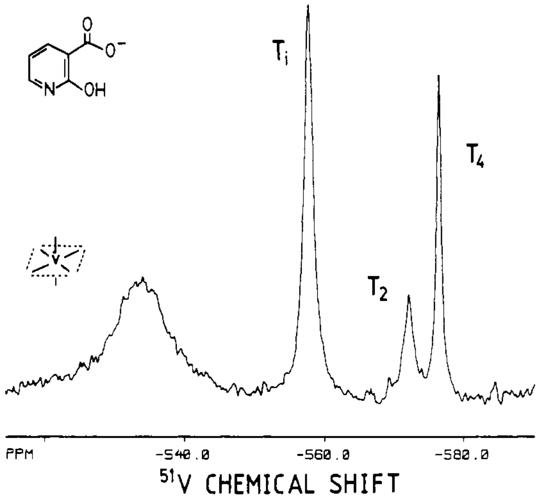
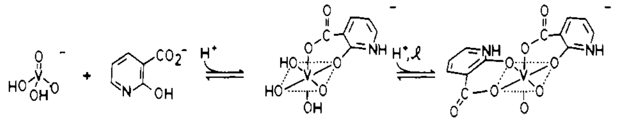


Figure 6. ^{51}V NMR spectrum of vanadate in the presence of 2-hydroxynicotinate. The signal at −534 ppm is consistent with the formation of an octahedral product, which is structurally analogous to that formed with salicylate. The conditions of the experiment were as follows: 3 mM total vanadate; 0.35 M 2-hydroxynicotinate; 20 mM HEPES buffer; pH 7.10; 0.5 M ionic strength maintained with KCl.

Scheme II



Vanadate plus 2-Hydroxynicotinic Acid. Vanadate in the presence of 2-hydroxynicotinic acid shows a behavior very similar to that with salicylate. The NMR spectrum (Figure 6) obtained under conditions similar to that for salicylate (Figure 5) is not significantly different. As for salicylate, a broad signal at −534 ppm was obtained. The results of the vanadium atom and 2-hydroxynicotinate concentrations studies were analyzed according to eq 19–21. When the appropriate parameters for eq 21 were plotted by using the results of the concentration studies, values of 0.58 ± 0.09 M^{-1} and 9.7 ± 0.4 M^{-2} for the slope and intercept, respectively, were obtained. This gives the formation constants $K_8 = 0.58 \pm 0.09$ M^{-1} and $K_9 = 17. \pm 3.$ M^{-1}. This value for K_9 is a factor of 10 larger than that for the formation of the corresponding salicylate product, while K_8 is only about twice as large.

The above differences in the formation constants (K_8 and K_9), compared to salicylate, are surprisingly small since the pH study showed that the formation of the hydroxynicotinate products from starting reactants required one and two protons, respectively, for the formation of the mono- and bis(ligand) species (to be compared to salicylate, zero and one proton, respectively). Analysis of the results of the pH study at fixed ligand and vanadate concentrations followed eq 22–24.

A plot of the experimental results according to eq 24 with $x = 1$ and $y = 1$ gave a good straight line from which the slope and intercept gave the values $K_8' = (6 \pm 2) \times 10^6$ M^{-2} and $K_8'K_9' = (1.6 \pm 0.3) \times 10^{15}$ M^{-4} so that $K_9' = (2.2 \pm 1.8) \times 10^8$ M^{-2}. Since $K_8'[H^+] = K_8$ and $K_9'[H^+] = K_9$, a convenient check of these values of the formation constants is provided by calculating K_8 and K_9 for pH 7.1, the pH of the ligand concentration study. The

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(32) Ehde, Per M.; Andersson, I.; Pettersson, L. *Acta Chem. Scand.* **1986**, *A40*, 489–499.

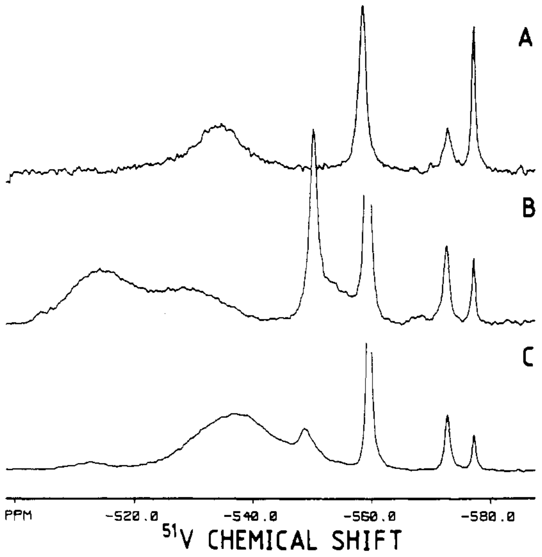


Figure 7. ^{51}V NMR spectra comparing the products of the reaction of vanadate with (A) 2-hydroxynicotinate, (B) picolinate, and (C) 3-hydroxypicolinate. The broad signals have been tentatively assigned to octahedral products, and the signal at ∼−550 ppm has been assigned to a pentacoordinate product. The remaining signals arise from vanadate and its oligomers.

values obtained were $K_8 = 0.5 \pm 0.2$ M^{-1} and $K_9 = 17 \pm 14$ M^{-1}, which agree well with the previously determined values, $K_8 = 0.58 \pm 0.09$ M^{-1} and $K_9 = 17 \pm 3$ M^{-1}.

The results of the pH study are consistent with the formation of the mono- and bis(2-hydroxynicotinate) vanadate complexes according to Scheme II. In this scheme the possible isomers are not depicted. It seems apparent that the hydroxynicotinate ligand is a net donor of electrons compared to salicylate so that the pK_a of the product complex is lower for the nicotinate than for the salicylate product. It may be possible that the nicotinate products can be formed with uptake of either zero or one proton for the mono and bis products, respectively, as for salicylate so that complex formation would be followed by a subsequent protonation step. However, no evidence for the nonprotonated product was obtained.

3-Hydroxypicolinate plus Vanadate. 3-Hydroxypicolinate offers two possibilities for complexation with vanadate. It may act similarly to 2-hydroxynicotinate (or salicylate) or may show a behavior similar to that of picolinate. Consideration of the magnitude of the formation constants for the products formed with salicylate as compared to those formed with picolinate suggests strongly that picolinate-type behavior should be predominant. However, the NMR spectrum of the products formed with this ligand (Figure 7C) as compared to the spectra of Figure 7, parts A (2-hydroxynicotinate) and B (picolinate), indicates that a mixed behavior is obtained. The NMR signals that occur at −512 and −549 ppm in this system evidently correspond to the −513 and −550 ppm signals of the picolinate system (Figure 3). Somewhat surprisingly, the major product of the reaction with 3-hydroxypicolinate gives a ^{51}V NMR signal at −536 ppm. This chemical shift is close to those observed for the octahedral products formed with salicylate (−533 ppm) and 2-hydroxynicotinate (−534 ppm), but it is also reasonably close to the −529 ppm signal of the picolinate system. It seems possible that since the −512 ppm signal of this system is of comparatively low intensity, that also a signal corresponding to the −529 ppm product of picolinate-type behavior would be of correspondingly low intensity. The major product then may be a product with a coordination analogous to that with salicylate or 2-hydroxynicotinate. If so, the pyridine nitrogen has stabilized product formation by 3 or 4 orders of magnitude. An alternative explanation may simply be that the altered substitution pattern of the pyridine ring has led to a more highly favored picolinate-type product, which gives rise to an intense −536 ppm NMR signal corresponding to a product analogous to the −529 ppm product of the picolinate ligand. It does not seem likely, though, that the signal position will be shifted −7 ppm compared to that of the picolinate product, particularly in view of the fact that the signals from other products are not shifted significantly. Even so, this latter possibility certainly cannot be ruled out.

Ligand and vanadium atom concentration studies were carried out at pH 7.0 under conditions of 0.10 M ionic strength maintained with KCl and 20 mM HEPES buffer. In order to analyze the results, it was assumed that if the minor products similar to those observed with the picolinate ligand were formed, they were present in negligible proportion.

The formation of the products corresponding to the −512 and −549 ppm signals was then examined by assuming a picolinate-type behavior as described by eq 8 and 11. The products characterized by the −536 ppm signal were analyzed according to the assumption that a 2-hydroxynicotinate-type behavior as defined in eq 19–21 described the equilibria. The occurrence of an intercept in the plot could then be taken as evidence that the assumed behavior was correct. The absence of an intercept would be indicative of a picolinate-type product complex. Because of the large formation constants involved, it was necessary to use the conservation equation equivalent to eq 7 and solve the complete system by an iterative procedure.

The results of the analysis for the −512 and −549 ppm products gave the values $K_4 = (7.6 \pm 0.8) \times 10^4$ M^{-2} and $K_7 = (1.1 \pm 0.3) \times 10^2$ M^{-1}, respectively. The values of K_4 and K_7 are very close to the values obtained for the picolinate system, $(8.4 \pm 0.4) \times 10^4$ M^{-2} and $(2.0 \pm 0.2) \times 10^2$ M^{-1}, respectively, and this results supports the assumption of picolinate-type behavior for these two products. Unfortunately, because of the broadness of the signals, values for K_5 and K_6 corresponding to the products described in eq 9 and 10 could not be obtained.

Of paramount interest in this system is the result obtained from the study of the −536 ppm signal. Both an intercept and a slope were obtained from the results of the analysis, which is consistent with this signal originating from octahedral products corresponding to those obtained with salicylate or 2-hydroxynicotinate. The mono(ligand) product has a formation constant ($K_8 = (5.7 \pm 0.6) \times 10^2$ M^{-1}) 3 orders of magnitude larger than those of the corresponding products formed with the above ligands. The addition of the second ligand ($K_9 = (4.4 \pm 0.6) \times 10^2$ M^{-1}) is favored by about 2 orders of magnitude over the previous products.

The results of the pH study were not as definitive as the concentration studies because of the broadness of the −512 and −536 ppm transitions complicated by the rather large disparity in signal intensities and an extreme sensitivity to pH. This latter source of error is exceptionally important because of the requirement that the conservation equation (eq 7) be utilized when the results are analyzed. As a consequence, proton stoichiometry is only poorly defined. Qualitatively it could be seen from the pH study that the −512 and −536 ppm signals decreased in magnitude at about the same rate as and much faster than the −549 ppm signal when the pH was increased in a stepwise fashion from 6.82 to 8.01. This clearly showed that the bis(ligand) products required more protons for their formation than did the mono(ligand) product. At pH 8.01 only the product giving rise to the −549 ppm signal was still clearly observable in the NMR spectrum.

When an attempt was made to fit the results of the pH study to the appropriate equilibrium equations, it was found that the results were consistent with an uptake of two protons for each ligand incorporated into the product. The experimental results, however, were not sufficiently precise to resolve ambiguities concerning the possible occurrence of a pK_a near the pH range of this study. This was particularly true for the bis(ligand) complexes. The analysis is exemplified by application of eq 16 to this 3-hydroxypicolinate study. When eq 16 is rewritten as eq 25 for n corresponding to 1 or 2 protons, an equation, which when

$$[-549]/[VO_4H_2^-][\text{pic-3-OH}][H^+] = K_7'[H^+] \qquad (25)$$

plotted gives a constant value if $n = 1$, an intercept and slope if n corresponds to a mixture of 1 and 2 protons, and a slope with zero intercept if n corresponds to 2 protons, is predicted. The result

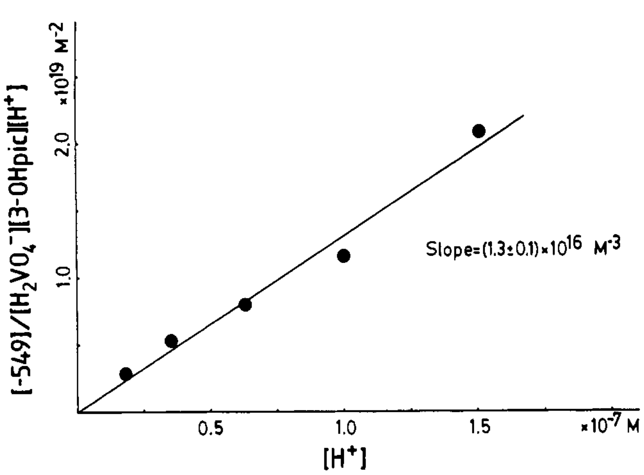
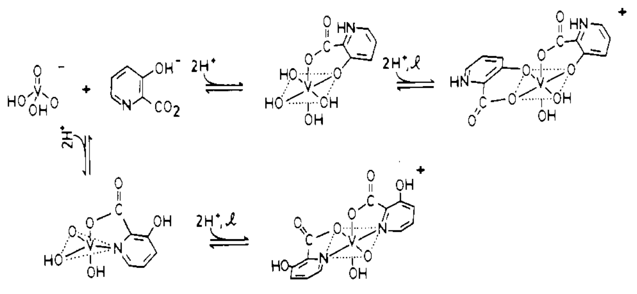


Figure 8. Plot demonstrating that formation of the product of the reaction of vanadate with 3-hydroxypicolinate giving rise to the −549 ppm NMR signals requires the consumption of two protons. The intercept, which is zero within the experimental error, indicates that this product does not have a pK_a near the pH range of this study, pH 6.84 to 7.75. The conditions of the experiments were as follows: 3.0 mM total vanadate; 20 mM HEPES buffer; 8.0 mM 3-hydroxypicolinate; 1.0 M ionic strength maintained with KCl.

Scheme III



of the plot is displayed in Figure 8. There is no clearly definable intercept for this plot, which indicates that two protons are required for product formation. The slope of the line gives the formation constant $K_7' = (1.3 \pm 0.2) \times 10^{16}$ M^{-3}, which for pH 7.0 corresponds to the formation constant $K_7 = (1.3 \pm 0.2) \times 10^2$ M^{-1}. This value is very close to that measured at pH 7.0 from the ligand concentration study, $K_7 = (1.1 \pm 0.3) \times 10^2$ M^{-1}.

Results similar to the above were obtained from analysis of the changes in intensity of the −512 ppm signal as a function of pH. Application of eq 13 to this 3-hydroxypicolinate system with $n = 4$ gave a value for K_4' of $(9.0 \pm 1.8) \times 10^{32}$ M^{-6}, which, for pH 7.0, gives $K_4 = (9.0 \pm 1.8) \times 10^4$ M^{-2}, to be compared with $K_4 = (7.6 \pm 0.8) \times 10^4$ M^{-2} from the ligand concentration study at pH 7.0, since $[H^+]^4K_4' = K_4$. It should be noted that this investigation cannot distinguish the above analysis from one in which incorporation of the two ligands is accompanied by uptake of three protons, with a fourth proton, with a pK_a of about 6.8, being subsequently incorporated.

On the tentative basis that the 3-hydroxypicolinate product giving rise to the −536 ppm signal is analogous to the products of the reaction of vanadate with salicylate, eq 22 and 23 should describe the equilibria. Application of these equations with both x and y equal to 2 gives eq 26. When the results of the pH study

$$[-536]/[VO_4H_2^-][\text{pic-3-OH}][H^+]^2 = K_8' + K_8'K_9'[\text{pic-3-OH}][H^+]^2 \quad (26)$$

are plotted according to the appropriate parameters of eq 26, a line of intercept $K_8' = (0.7 \pm 0.1) \times 10^{17}$ M^{-3} and slope $K_8'K_9' = (1.7 \pm 0.6) \times 10^{33}$ M^{-6}, from which $K_9' = (2.4 \pm 1.1) \times 10^{16}$ M^{-3}, was obtained. These values give the parameters $K_8 = (7.0 \pm 1.0) \times 10^2$ M^{-1} and $K_9 = (2.4 \pm 1.1) \times 10^2$ M^{-1}, which compare with the previously determined values $K_8 = (5.7 \pm 0.6) \times 10^2$ M^{-1} and $K_9 = (4.4 \pm 0.6) \times 10^2$ M^{-1} at pH 7.0. The agreement between the two studies is quite good, which supports this description of the various equilibria that are summarized in Scheme III.

Table I. Equilibrium Equations and Formation Constants for the Condensation of Vanadate with the Ligands Discussed in the Text[a]

equil eq	formation const
pH Fixed at pH 7	
T_i + 2py ⇌ −467	$(8.1 \pm 0.9) \times 10^{-3}$ M^{-2}
T_i + py-3-OH ⇌ −559	0.9 ± 0.2 M^{-1}
T_i + pic ⇌ −550	$(2.0 \pm 0.2) \times 10^2$ M^{-1}
T_i + 2pic ⇌ −552	$(1.5 \pm 0.3) \times 10^4$ M^{-2}
T_i + 2pic ⇌ −513	$(8.4 \pm 0.4) \times 10^4$ M^{-2}
−550 + pic ⇌ −513	$(4.2 \pm 0.4) \times 10^2$ M^{-1}
T_i + 2pic ⇌ −529	$(4.0 \pm 0.4) \times 10^4$ M^{-2}
−550 pic ⇌ −529	$(2.0 \pm 0.3) \times 10^2$ M^{-1}
T_i + sal ⇌ −559	0.07 ± 0.03 M^{-1}
T_i + sal ⇌ −533′	0.23 ± 0.04 M^{-1}
T_i + 2sal ⇌ −533″	0.38 ± 0.06 M^{-2}
−533′ + sal ⇌ −533″	1.7 ± 0.3 M^{-1}
T_i + nic-2-OH ⇌ −534′	0.58 ± 0.09 M^{-1}
T_i + 2nic-2-OH ⇌ −534″	9.7 ± 0.4 M^{-2}
−534′ + nic-2-OH ⇌ −534″	17.0 ± 2.0 M^{-1}
T_i + pic-3-OH ⇌ −549	$(1.1 \pm 0.3) \times 10^2$ M^{-1}
T_i + 2pic-3-OH ⇌ −512	$(7.6 \pm 0.8) \times 10^4$ M^{-2}
−549 + pic-3-OH ⇌ −512	$(6.9 \pm 0.8) \times 10^2$ M^{-1}
T_i + pic-3-OH ⇌ −536′	$(5.7 \pm 0.6) \times 10^2$ M^{-1}
T_i + 2pic-3-OH ⇌ −536″	$(2.5 \pm 0.3) \times 10^5$ M^{-2}
−536′ + pic-3-OH ⇌ −536″	$(4.4 \pm 0.4) \times 10^1$ M^{-1}
pH Varied	
$VO_4H_2^-$ + pic + H^+ ⇌ −550	$(2.2 \pm 0.1) \times 10^9$ M^{-2}
$VO_4H_2^-$ + 2pic$^-$ + 2H^+ ⇌ −552	$(1.6 \pm 0.4) \times 10^{18}$ M^{-4}
$VO_4H_2^-$ + 2pic$^-$ + 2H^+ ⇌ −513	$(9.0 \pm 0.5) \times 10^{18}$ M^{-4}
$VO_4H_2^-$ + 2pic$^-$ + 2H^+ ⇌ −529	$(4.7 \pm 0.6) \times 10^{18}$ M^{-4}
$VO_4H_2^-$ + sal ⇌ −533′	$(2.5 \pm 0.5) \times 10^{-1}$ M^{-1}
$VO_4H_2^-$ + 2sal$^-$ + H^+ ⇌ −533″	$(9.7 \pm 1.0) \times 10^6$ M^{-3}
$VO_4H_2^-$ + nic-2-OH + H^+ ⇌ −534′	$(6.0 \pm 2.0) \times 10^6$ M^{-2}
$VO_4H_2^-$ + 2nic-2-OH + 2H^+ ⇌ −534″	$(1.6 \pm 0.3) \times 10^{15}$ M^{-4}
$VO_4H_2^-$ + pic-3-OH + 2H^+ ⇌ −549	$(1.3 \pm 0.2) \times 10^{16}$ M^{-3}
$VO_4H_2^-$ + 2pic-3-OH + 4H^+ ⇌ −512	$(9.0 \pm 1.8) \times 10^{32}$ M^{-6}
$VO_4H_2^-$ + pic-3-OH + 2H^+ ⇌ −536′	$(0.7 \pm 0.1) \times 10^{17}$ M^{-3}
$VO_4H_2^-$ + 2pic-3-OH + 4H^+ ⇌ −536″	$(1.7 \pm 0.6) \times 10^{33}$ M^{-6}

[a] Abbreviations used: py, pyridine; py-3-OH, 3-hydroxypyridine; pic, 2-pyridinecarboxylate; sal, 2-hydroxybenzoate; nic-2-OH, 2-hydroxy-3-pyridinecarboxylate; pic-3-OH, 3-hydroxy-2-pyridinecarboxylate.

Scheme III ignores minor products and the structural isomers that probably occur for some of the products. In Scheme III the octahedral product formed between the hydroxyl and the carboxylate groups of 3-hydroxypicolinate is firm only in the sense that its formation parallels that of the condensation of vanadate with salicylate and 2-hydroxynicotinate (Scheme II). The very large values of the formation constant compared with those of the above two compounds seem to mitigate against this interpretation, as does the proton stoichiometry. An alternative to this structure corresponding to isomers of the bottom bis(ligand) product of Scheme III has already been discussed.

Summary

In this study the condensation of vanadate with a variety of substituted pyridines has been investigated. The equilibrium equations and the formation constants describing the various products observed are summarized in Table I, where the products are identified by their ^{51}V chemical shifts. Structures proposed for the products are discussed in the text. In addition to the reactions given in the table, no appreciable reaction of vanadate with 2- or 4-hydroxypyridine (keto form) was observed, nor was there a significant reaction with the 3- and 4-pyridinecarboxylates.

Vanadate undergoes condensations with salicylate and the analogous 2-hydroxynicotinate to form mono- and bis(ligand) products. The condensation, which occurs between the carboxylate and the adjacent hydroxyl group to form a six-membered ring, is not a favored reaction, with the formation constant for the mono derivative being only 0.23 and 0.58 M^{-1} for the salicylate and 2-hydroxynicotinate ligands, respectively. Incorporation of the second ligand to form the bis(ligand) products is only slightly more favored, with the second ligand being incorporated with formation constants of 1.7 and 17 M^{-1}, respectively, for the above two systems. Apparently there is a weak synergistic effect accompanying the change in coordination geometry.

In contrast to the above reactions, vanadate condenses in an almost stoichiometric manner with the 2-pyridinecarboxylates, picolinate and 3-hydroxypicolinate. The formation of the mono(ligand) product proceeds with an equilibrium constant of approximately 150 M^{-1}. Thus, these products are favored by about 3 orders of magnitude over those formed with the hydroxy acids.

On the basis of the positions of the ^{51}V chemical shifts, there may be a change in coordination geometry upon going to the bis(ligand) derivatives from the mono products. The bis products have equilibrium constants ranging from about 200 to 700 M^{-1} for the formation of the bis products from the mono derivatives.

Of some interest in the 3-hydroxypicolinate system is the condensation of vanadate between the carboxy and hydroxy groups to form products that are analogous to those formed from salicylate and 2-hydroxynicotinate. An intense signal at a ^{51}V chemical shift of −536 ppm is observed, and this is close in frequency to the signals from the above products, i.e. approximately −534 ppm. However, the formation constant for this product is about 4 orders of magnitude larger than those observed for the salicylate and 2-hydroxynicotinate ligands. As a consequence, if this product is in fact formed with the hydroxy/carboxylate groups of the pyridine ring, then it seems that product formation is strongly promoted by protonation at the nitrogen to form a pyridinium adduct. The possibility that this derivative is simply a product of reaction at the nitrogen and carboxylate functionalities cannot be ruled out.

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Registry No. $H_2VO_4^-$, 34786-97-5; HVO_4^{2-}, 26450-38-4; 2-hydroxypyridine (keto form), 142-08-5; 4-hydroxypyridine, 626-64-2.

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Metal-Nitroxyl Interactions. 53. Effect of the Metal-Nitroxyl Linkage on the Electron-Electron Exchange Interaction in Spin-Labeled Complexes of Copper(II), Low-Spin Cobalt(II), Vanadyl, and Chromium(III)

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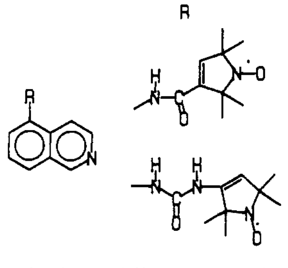
To examine the effect of several metal–nitroxyl linkages on the magnitude of the electron–electron interaction, EPR spectra were obtained for two spin-labeled isoquinolines and nine spin-labeled pyridines bound to copper(II) bis(hexafluoroacetylacetonate), cobalt(II) tetrakis(*p*-(trifluoromethyl)phenyl)porphyrin, vanadyl bis(hexafluoroacetylacetonate), and chromium(III) tetraphenylporphyrin chloride. The Cu(II) and vanadyl complexes were studied in fluid solution and frozen solution, and the Co(II) and Cr(III) complexes were studied in frozen solution. The values of the metal–nitroxyl electron–electron coupling constant, J, for the isoquinoline complexes were about a factor of 10 smaller than for complexes of spin-labeled pyridines with the same linkage between the heterocyclic ring and the nitroxyl. The differences in the value of J for isomers of the same ligand indicated that the value of J is strongly dependent on the conformation of the pyridine–nitroxyl linkage. Addition of a carbonyl group to the metal–nitroxyl linkage caused the value of J to decrease by a factor of 10–70. When the 2-isomer could not form a chelate ring, the value of J for the copper complex of the 2-isomer was about twice as large as for the 4-isomer. A saturated $(CH_2)_2$ linkage to the 2-carbon of the nitroxyl ring resulted in about the same strength of exchange interaction as an unsaturated (CH═CH) linkage to the 3-carbon. When the pyridine was attached directly to the 2-carbon of the nitroxyl ring, the exchange interaction was sufficiently large that only a lower limit on the value of J was obtained. The barrier to rotation about a single bond in four of the ligands was about 5 kcal/mol.

Introduction

Electron–electron spin–spin interaction reflects the extent of electron spin delocalization. If the strength of the interaction is of the same order of magnitude as the separation between the electron-spin energy levels, it can be measured by EPR.[1,2] These interactions frequently can be observed through as many as 8 to 12 bonds. The interaction is strongly dependent on the number of atoms in the linkage between the two paramagnetic centers, the conformation of the linkage, and the σ and π contributions to the bonding. The data currently available are not sufficient to predict the magnitude of spin–spin interaction from a knowledge of the linkage between the two paramagnetic centers. We are therefore exploring the effect of the linkage between a paramagnetic metal and a nitroxyl radical on the electron–electron spin–spin interaction.[3]

The ligands in this study were selected to examine several questions concerning electron spin delocalization. Spin-labeled isoquinolines I and II permit comparison with previously reported data on analogous spin-labeled pyridines.[3-5] Spin-labeled pyridines III–VIII permit assessment of the impact of addition of a carbonyl group to the metal–nitroxyl linkage, the impact of moving the substituent between positions on the pyridine ring, and the effect of changing the size of the nitroxyl ring. Spin-labeled pyridines IX–XI were selected because the metal–nitroxyl linkage is through the 2-carbon of the nitroxyl ring rather than the 3-carbon or 4-carbon as in III–VIII.



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II

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