Preparation of VO^{3+} and VO_2^+ Complexes Using Hydrolytically Stable, Asymmetric Ligands Derived from Schiff Base Precursors

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The synthesis and characterization of the first water-stable monomeric monooxovanadium(V) complexes are reported. These complexes are chelated by novel multidentate N/O donor ligands. The ligands were synthesized by reduction of the Schiff base precursors H_2sal_2en, *N,N'*-bis(salicylidene)ethylenediamine, and H_2shed, *N*-salicylidene-*N'*-(2-hydroxyethyl)ethylenediamine, using sodium borohydride to produce H_2sal_2enr, *N,N'*-bis-((*o*-hydroxyphenyl)methyl)ethylenediamine, and H_2shedr, *N*-((*o*-hydroxyphenyl)methyl)-*N'*-(2-hydroxyethyl)-ethylenediamine, which are stable to hydrolysis at the imine linkage. Alkylation of H_2shed followed by reduction leads to the higher denticity, hydrolytically stable ligands $H_3heshedr$, *N*-((*o*-hydroxyphenyl)methyl)-*N'*-bis(2-hydroxyethyl)ethylenediamine, and $H_3salshedr$, *N*-(2-hydroxyethyl)-*N,N'*-bis((*o*-hydroxyphenyl)methyl)ethylene-diamine. Similarly, alkylation of H_2sal_2enr with 2-(bromomethyl)phenyl acetate produces H_3sal_3enr, *N,N,N'*-tris((*o*-hydroxyphenyl)methyl)ethylenediamine. These ligands have been developed in order to solve the problem of imine hydrolysis that is often associated with vanadium Schiff base complexes. Reaction with sodium vanadate or triethyl vanadate gives a series of dioxo- and monooxovanadium(V) complexes. The compound $[VO_2(Hshedr)]_2$, **2**, is a water-soluble and water-stable analogue of $[VO_2(Hshed)]_2$, **1**, whose X-ray structure reveals that it is isostructural with **1**. Complexation of vanadium by the higher denticity ligands leads to monooxovanadium(V) compounds with the general composition seen in the X-ray structure of VO(salshedr), **4**. The complexes VO-(sal_3enr), **5**, and **4** are stable in mixed organic/aqueous solution and in the presence of hydrogen peroxide. In contrast, VO(heshedr), **3**, will convert to $VO_2(H_2heshedr)$, **6**, with trace water. The application of ^{13}C and ^{51}V NMR spectroscopies allows evaluation of the solution complexation behavior of both the VO_2^+ and VO^{3+} compounds. These data show that the molecules retain their integrity in solution and allow us to specify which ligand heteroatoms dissociate on metal hydrolysis or reaction with peroxide. X-ray parameters for **2**: triclinic, space group $P\bar{1}$ (No. 2), $a = 7.112(1)$ Å, $b = 8.407(2)$ Å, $c = 11.280(3)$ Å, $\alpha = 92.66(2)°$, $\beta = 95.57(2)°$, $\gamma = 97.31(2)°$, $V = 664.7(2)$ Å^3, and $Z = 1$. The final *R* indices were $R = 0.0350$ and $R_w = 0.0376$. The complex forms a dimer in the solid state with a vanadium–vanadium separation of 3.1 Å. The hydroxyl remains unbound and is hydrogen-bonded to a water molecule. The complex [VO(salshedr)], **4**, has the following crystallographic parameters: monoclinic, space group $P2_1/c$ (No. 14), $a = 6.825(2)$ Å, $b = 19.23(1)$ Å, $c = 12.901(5)$ Å, $\alpha = 90.000°$, $\beta = 92.49(3)°$, $\gamma = 90.000°$, $V = 1692(1)$ Å^3, and $Z = 4$. The final *R* indices were $R = 0.0756$ and $R_w = 0.0658$.

Introduction

The characterization of a new class of haloperoxidase enzymes requiring vanadium for activity[1,2] has led to increased interest in the coordination chemistry of oxovanadium(IV) and -(V) with biologically relevant ligand donors.[3,4] The active site of vanadium haloperoxidase has been shown to consist of an oxovanadium(V) coordinated by oxygen and nitrogen donors.[5,6] The mononuclear vanadium(V) is likely found as either a monooxovanadium(V) (VO^{3+}) or a vanadate ester ($VO(OR)^{2+}$). It is unlikely that tyrosine is bound to a VO^{3+} core since strong phenolate to metal charge transfer excitations are associated with this structure type.[7] Imidazole coordination to vanadium(V) has been inferred on the basis of ESEEM measurements of the reduced, catalytically inactive enzyme.[8] The unprecedented high-field ^{51}V NMR chemical shift, −1250 ppm vs $VOCl_3$, has led to the proposal of a carboxylate-rich coordination sphere.[9]

The haloperoxidases catalyze the production of a large variety of halogenated organics *in vivo*.[10] Although often referred to in the literature as vanadium bromoperoxidase, some vanadium haloperoxidases have been shown to utilize chloride as well as bromide and iodide.[11] While mechanistic studies on the native enzyme are consistent with an ordered mechanism employing hydrogen peroxide and then halide ion,[12] the exact compositions of the active oxidant and active halogenating intermediate are unknown.[13] Most intriguingly, the vanadium center does not appear to undergo redox cycling during turnover. This is in marked contrast to the more widely distributed heme enzymes that appear to form ferryl heme intermediates during catalysis.[14]

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The potential of vanadium to act as a clinical alternative to insulin for the treatment of diabetes has recently been recognized.[15,16] Vanadate has been known to be an insulin mimic for many years, and when administered orally to hyperglycemic rats, vanadate has been shown to lower blood glucose to normal levels. In addition, the development of insulin resistance does not inhibit the action of vanadate which bypasses the early receptors of the hormone. The mechanism of action of vanadate is not clear and is currently under investigation as is the optimal chemical composition for administration to a patient.

The aqueous solution chemistry of vanadium primarily involves the interrelationships of the oxovanadium(IV) and -(V) species.[17] In the presence of suitable ligand donors, the relevant forms become dioxovanadium(V), monooxovanadium(IV) and -(V), and occasionally "bare" vanadium(IV) and -(V). The oxovanadium cations are often carried through a reaction intact. Due to the synthetic simplicity of the organic ligands that are used in these reactions, vanadium complexes with highly symmetric ligand donor sets are isolated. Furthermore, the Schiff base ligands that are often utilized are sensitive to hydrolysis in aqueous media, under highly acidic or basic conditions or in the presence of peroxide. We felt that it was necessary to use a convenient synthetic methodology to prepare hydrolytically stable ligands that allow for the presentation of mixed functional groups to vanadium. In particular, we desired high-denticity ligands that would leave at most one coordination site vacant in the metal coordination sphere. Such new vanadium complexes might serve both as better models for vanadium haloperoxidase and as alternative forms of water-soluble precursors for vanadates in a clinical setting.

To this end, we report the synthesis and characterization of a series of dioxo- and monooxovanadium(V) complexes using ligands that are derived from the previously employed Schiff base ligands *N,N'*-bis(salicylidene)ethylenediamine (H_2sal_2en)[18] and *N*-salicylidene-*N'*-(2-hydroxyethyl)ethylenediamine (H_2shed).[19] The new ligands are modified either through reductive amination or by alkylation with subsequent reduction to form potentially tetradentate and pentadentate donor sets. These higher denticity, hydrolytically stable ligands, illustrated in Figure 1, are excellent precursors to highly stable monooxovanadium(V) and dioxovanadium(V) complexes.

Experimental Section

The following abbreviations are used throughout the text: H_2sal_2en = *N,N'*-bis(salicylidene)ethylenediamine; H_2sal_2enr = *N,N'*-bis((*o*-hydroxyphenyl)methyl)ethylenediamine; H_2shed = *N*-salicylidene-*N'*-(2-hydroxyethyl)ethylenediamine; H_2shedr = *N*-((*o*-hydroxyphenyl)-methyl)-*N'*-(2-hydroxyethyl)ethylenediamine; H_3salshedr = *N*-(2-hydroxyethyl)-*N,N'*-bis((*o*-hydroxyphenyl)methyl)ethylenediamine; H_3heshedr = *N*-((*o*-hydroxyphenyl)methyl)-*N'*-bis(2-hydroxyethyl)-ethylenediamine; H_3sal_3enr = *N,N,N'*-tris((*o*-hydroxyphenyl)methyl)-ethylenediamine.

Salicylaldehyde, ethylenediamine, *N*-(2-hydroxyethyl)ethylenediamine, *o*-cresol, vanadium oxide, 2-bromoethanol, and sodium borohydride were purchased from the Aldrich Chemical Co. All other chemicals and solvents were reagent grade.

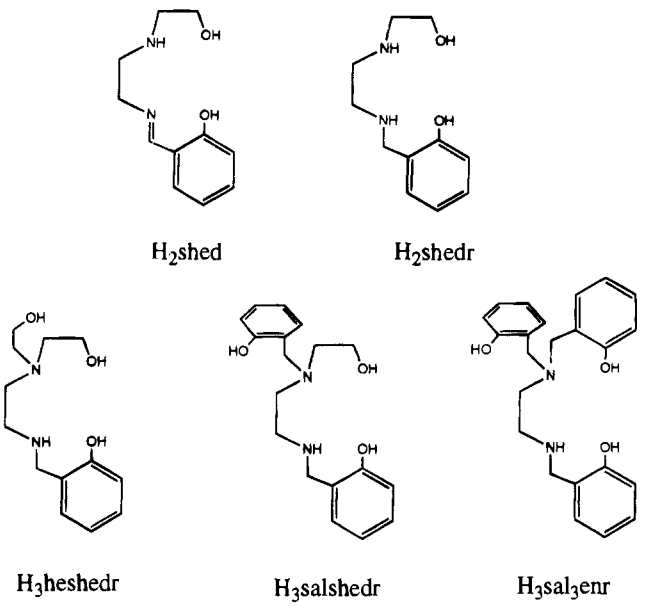

Figure 1. Reduced Schiff base ligands used in this study. The key to abbreviations is given in the text.

Preparation of Compounds. The synthesis of 2-(bromomethyl)-phenyl acetate[20] and H_2sal_2enr[21] was similar to previous preparations. The synthesis of H_2shed and $[VO_2(Hshed)]_2$ (**1**) was as described previously.[19] Reactions were performed in air, and solvents were used as received. Triethyl vanadate was generated by refluxing V_2O_5 in ethanol overnight and filtering, with the concentration determined by measurement of the visible extinction coefficient at 477 nm (ϵ = 4430 M^{-1} cm^{-1}) in the presence of excess H_3salshedr. Sodium vanadate was generated by reaction of V_2O_5 with 2 equiv of NaOH in aqueous solution. These ligands were used as synthesized to form vanadium-(V) complexes which were purified by crystallization. ^{13}C NMR data reported for complexes are for the major isomer in solution.

H_2shedr. H_2shed (2.1 g, 10 mmol) was dissolved in 50 mL of methanol. Sodium borohydride (152 mg, 4 mmol) was added slowly over 2 h, and the pale yellow solution was stirred overnight. The resulting solution was acidified with concentrated HCl, followed by evaporation to dryness, extraction with anhydrous methanol/ethanol, and filtration. The filtrate was dried to give the product as an HCl salt. Yield = 2.51 g (89%). ^{13}C NMR (dmso-d_6): 156.0, 131.4, 130.3, 118.9, 117.7, 115.5, 56.3, 49.2, 45.2, 42.9, 42.6 ppm.

H_3heshedr. H_2shed (2.1 g, 10 mmol) was dissolved in 50 mL of methanol. 2-Bromoethanol (0.71 mL, 10 mmol) and 1 equiv of sodium methoxide in methanol were added, and the solution was stirred overnight. The product (H_3heshed) was purified on a silica gel column using methanol, and the first major fraction was collected and concentrated. Sodium borohydride (152 mg, 4 mmol) was added slowly over 2 h to H_3heshed in methanol, and the pale yellow solution was stirred overnight. The resulting solution acidified with concentrated HCl was evaporated to dryness, and the residue was extracted with acetonitrile. The acetonitrile was then evaporated, leaving the product as a viscous yellow oil. Yield = 1.47 g (58%). ^{13}C NMR (MeOH-d_4): 157.6, 132.8, 132.7, 121.2, 118.4, 116.6, 57.6, 57.0, 51.2, 48.8, 42.8 ppm.

H_3salshedr. Salicylaldehyde (2.1 mL, 10 mmol) and *N*-(2-hydroxyethyl)ethylenediamine (1.0 mL, 10 mmol) were dissolved in 50 mL of methanol. Sodium borohydride (380 mg, 10 mmol) was added slowly over 4 h, and the pale yellow solution was stirred overnight. The resulting solution acidified with concentrated HCl was evaporated to dryness, followed by extraction with dry methanol and filtration. The filtrate was cooled to induce precipitation as an HCl salt. Yield = 1.75 g (47%). ^{13}C NMR (dmso-d_6): 157.0, 156.3, 133.5, 131.8, 131.6,

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130.9, 119.8, 119.5, 118.0, 117.9, 116.3, 115.9, 55.6, 55.1, 53.0, 49.0, 46.1, 41.8 ppm.

H_3sal$_3$enr. 2-(Bromomethyl)phenyl acetate (2.17 g, 10 mmol) was slowly added to H_2sal$_2$enr (2.72 g, 10 mmol) dissolved in 100 mL of acetonitrile. Anhydrous potassium carbonate (1.38 g, 10 mmol) was added and the solution was stirred overnight. The resulting solution was filtered, acidified with concentrated HCl, and cooled to induce precipitation as an HCl salt. Yield = 1.15 g (31%). ^{13}C NMR (dmso-d_6): 156.5, 156.0, 131.6, 130.7, 129.8, 127.5, 119.2, 118.8, 117.8, 117.3, 115.6, 114.8, 53.0, 47.9, 45.7, 42.7 ppm.

[VO_2(Hshedr)]$_2$ (2). A solution of sodium vanadate (1 mmol) in H_2O (pH = 9) was added slowly with stirring to the ligand (1 mmol) in water. The dark yellow solution was adjusted to pH = 8 with dilute HCl and stirred for 2 h. The yellow precipitate was filtered off and air-dried. The filtrate formed additional yellow crystals upon standing overnight. The crystals were filtered off and air-dried. Yield = 201 mg (65%). The compound can be recrystallized from H_2O solution (pH = 9). Anal. Calcd (found) for $C_{11}H_{17}N_2O_4V$ (MW 292.21): C, 45.21 (44.83); H, 5.86 (5.87); N, 9.59 (9.34). ^{51}V NMR (dmso) −529 ppm. ^{13}C NMR (dmso-d_6) 164.3, 128.6, 125.5, 118.5, 117.5, 116.6, 58.3, 57.1, 52.2, 49.3, 48.9 ppm.

[VO(heshedr)] (3). The ligand (1 mmol) was dissolved in dmf, and a solution of triethyl vanadate (1 mmol) in ethanol was added slowly with stirring to the ligand solution. The dark red-brown solution was stirred for 2 h, concentrated, and filtered. All attempts to isolate and characterize the compound as a pure solid were unsuccessful due to its hydrolytic instability. ^{51}V NMR (dmf): −445 ppm. ^{13}C NMR (dmf-d_7): 161.1, 129.9, 129.0, 119.7, 117.6, 116.8, 81.2, 77.8, 57.4, 56.8, 54.5, 53.6, 48.5 ppm.

[VO(salshedr)] (4). The ligand (1 mmol) was dissolved in methanol, and the solution was neutralized with 2 equiv of sodium methoxide. A solution of sodium vanadate (1 mmol) in H_2O was added slowly with stirring to the ligand (1 mmol) in methanol. The dark red solution was stirred for 2 h and filtered. The dark red crystals that formed upon standing for a few days were filtered off and air-dried. Yield = 320 mg (84%). Anal. Calcd (found) for $C_{18}H_{21}N_2O_4V$ (MW 380.32): C, 56.84 (56.07); H, 5.57 (5.62); N, 7.36 (7.37). ^{51}V NMR (dmso): −449, −481 ppm. ^{13}C NMR (dmso-d_6) 162.7, 161.8, 129.5, 128.7, 127.6, 127.4, 124.9, 120.4, 119.8, 117.4, 116.8, 116.6, 72.4, 58.7, 55.5, 55.3, 53.2, 47.8 ppm.

[VO(sal$_3$enr)] (5). The ligand (1 mmol) was dissolved in methanol, and the solution was neutralized with 2 equiv of sodium methoxide. A solution of sodium vanadate (1 mmol) in H_2O was added slowly with stirring to the ligand solution (1 mmol) in methanol. The dark blue solution was stirred for 2 h and filtered. The dark blue crystals that formed upon standing for a few days were filtered off and air-dried. Yield = 304 mg (71%). Anal. Calcd (found) for $C_{23}H_{23}N_2O_4V$ (MW 442.39): C, 62.44 (61.70); H, 5.24 (5.61); N, 6.33 (6.11). ^{51}V NMR (dmf) −470, −498 ppm. ^{13}C NMR (dmso) 165.0, 164.6, 164.2, 130.5, 130.2, 129.3, 128.6, 128.3, 127.9, 122.8, 121.9, 121.5, 121.2, 119.7, 119.2, 118.6, 117.5, 116.6, 61.1, 58.0, 56.8, 53.2, 48.2 ppm.

Physical and Spectroscopic Studies. Infrared spectra were recorded as KBr pellets on a Nicolet 60 SX Fourier transform spectrometer. UV/vis spectra were recorded on a Perkin-Elmer Lambda 9 spectrophotometer. NMR spectra were produced using a Bruker 360 or 200 MHz instrument. Electrochemical measurements were performed at room temperature on a BAS-100 electrochemical analyzer using a platinum button working electrode, a platinum wire auxiliary electrode, and a saturated calomel reference electrode. Elemental analyses were performed by the University of Michigan Microanalysis Laboratory.

Collection and Reduction of X-ray Data. Suitable crystals of [VO_2(Hshedr)]$_2$ (**2**) and [VO(salshedr)] (**4**) were obtained as described above and mounted in glass capillaries. Intensity data were obtained on a Siemens R3m/v or Syntex P2$_1$m/v diffractometer using Mo Kα radiation (0.7107 Å) monochromatized from a graphite crystal whose diffraction vector was parallel to the diffraction vector of the sample. Three standard reflections were measured every 97 reflections. Modified crystal and data parameters are given in Table 1. Intensity data were collected using Θ/2Θ scans. The data were reduced, the structure solved, and the model refined using the SHELXTL PLUS program package. Computations were carried out on a VAX Station 3500. In the subsequent refinement, the function $\sum w(|F_o| - |F_c|)^2$ was minimized where $|F_o|$ and $|F_c|$ are the observed and calculated structure factor amplitudes. The agreement indices $R = \sum(||F_o| - |F_c||/|F_o|)$ and $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$ were used to evaluate the results. Atomic scattering factors are from *The International Tables for X-Ray Crystallography*. Hydrogen atoms were located on a difference Fourier map and allowed to refine isotropically. Unique data and final R indices are reported in Table 1. Fractional atomic coordinates for **2** and **4** are given in Tables 2 and 3. Selected bond distances and angles for these compounds are provided in Table 4.

Table 1. Summary of Crystallographic Data for [VO_2(shedr)]$_2$, **2**, and VO(salshedr), **4**

	2	**4**
formula	$C_{22}H_{38}N_4O_{10}V_2$	$C_{18}H_{21}N_2O_4V$
MW	650.52	380.32
cryst syst	triclinic	monoclinic
space group	$P\bar{1}$ (No. 2)	$P2_1/c$ (No. 14)
a, Å	7.112(1)	6.825(2)
b, Å	8.407(2)	19.23(1)
c, Å	11.280(3)	12.901(5)
α, deg	92.66(2)	90
β, deg	95.57(2)	92.49(3)
γ, deg	97.31(2)	90
V, Å^3	664.7(2)	1692(1)
Z	1	4
abs coeff (μ), cm^{-1}	7.38	5.91
cryst size, mm^3	0.10 × 0.20 × 0.32	0.20 × 0.22 × 0.42
2θ scan range, deg	5−52	5−55
temp, °C	−122	25
no. of unique data	2632	3892
no. of refined data	2308	2828
R^a	0.0350	0.0756
R_w^b	0.0376	0.0658
residual density, e/Å^3	+0.35/−0.38	+0.41/−0.37

^{a} $R = \sum(||F_o| - |F_c||/|F_o|)$. ^{b} $R_w = [\sum(w|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$.

Table 2. Fractional Atomic Coordinates for [VO_2(shedr)]$_2$, **2**

atom	x	y	z	U_{eq},^{a} Å^2
V1	0.03371(6)	0.18471(4)	0.01286(3)	0.0100(1)
O1	0.1663(2)	0.35772(2)	0.0127(1)	0.0151(5)
O2	0.1801(2)	0.0429(2)	0.0237(1)	0.0115(5)
O3	−0.387(2)	0.1841(2)	0.1711(1)	0.0138(5)
O4	0.3570(3)	0.1333(3)	−0.4014(2)	0.0322(7)
O5	0.6374(3)	−0.0637(3)	−0.3583(2)	0.0323(7)
N1	−0.2336(3)	0.2859(2)	−0.0331(2)	0.0116(6)
N2	0.0039(3)	0.1600(2)	−0.1807(2)	0.0117(6)
C1	−0.1546(3)	0.2698(3)	0.2271(2)	0.0137(7)
C2	−0.1044(4)	0.3248(3)	0.3468(2)	0.0178(7)
C3	−0.2249(4)	0.4078(3)	0.4080(2)	0.0219(8)
C4	−0.3973(4)	0.4394(3)	0.3516(2)	0.0222(8)
C5	−0.4480(4)	0.3860(3)	0.2334(2)	0.0182(8)
C6	−0.3300(3)	0.3012(3)	0.1702(2)	0.0139(7)
C7	−0.3888(3)	0.2413(3)	0.0431(2)	0.0144(7)
C8	−0.3004(3)	0.2494(3)	−0.1608(2)	0.0144(7)
C9	−0.1286(4)	0.2679(3)	−0.2304(2)	0.0158(7)
C10	0.1901(3)	0.1773(3)	−0.2314(2)	0.0160(7)
C11	0.1707(4)	0.1297(3)	−0.3639(2)	0.0211(8)

^{a} $U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i\cdot\mathbf{a}_j$.

Results

Description of the Structure of [VO_2(Hshedr)]$_2$, 2, and Comparison with [VO_2(Hshed)]$_2$, 1. Reduction of the imine function of H_2shed leads to the new ligand H_2shedr. This ligand forms a complex, [VO_2(Hshedr)]$_2$, **2**, that is isostructural with the previously described [VO_2(Hshed)]$_2$, **1**.[19] The latter compounds were the first examples of two pervanadyl units forming a bis(μ-oxo)-bridged V(V) Schiff base dimer. The subtle modifications in bond lengths and angles that result from reduction of the imine are provided in Table 4. The ORTEP diagram of **2**, given as Figure 2, demonstrates that each V(V) ion is six-coordinate with two distinct oxo groups being

Table 3. Fractional Atomic Coordinates for VO(salshedr), **4**

atom	*x*	*y*	*z*	U_{eq},[a] Å^2
V1	0.17345(9)	0.04645(4)	0.15685(5)	0.0527(2)
O1	0.2925(4)	0.0335(2)	0.0545(2)	0.071(1)
O2	0.3305(4)	−0.0040(1)	0.2572(2)	0.058(1)
O3	−0.0421(4)	0.0831(1)	0.0866(2)	0.060(1)
O4	0.2778(4)	0.1282(1)	0.2085(2)	0.059(1)
N1	0.0148(4)	−0.0502(2)	0.1397(3)	0.058(1)
N2	−0.0486(4)	0.0558(2)	0.2864(2)	0.049(1)
C1	0.3205(5)	−0.0658(2)	0.3041(3)	0.057(1)
C2	0.4015(5)	−0.0745(3)	0.4042(3)	0.061(2)
C3	0.3913(6)	−0.1377(3)	0.4542(4)	0.073(2)
C4	0.2979(7)	−0.1925(3)	0.4069(4)	0.079(2)
C5	0.2145(6)	−0.1846(2)	0.3088(4)	0.074(2)
C6	0.2277(6)	−0.1222(2)	0.2557(3)	0.060(2)
C7	0.1424(6)	−0.1133(2)	0.1488(3)	0.070(2)
C8	−0.1599(6)	−0.0546(2)	0.2047(4)	0.067(2)
C9	−0.1301(6)	−0.0141(2)	0.3031(4)	0.065(2)
C10	−0.1995(5)	0.1055(2)	0.2459(3)	0.061(1)
C11	−0.2244(6)	0.1001(3)	0.1300(4)	0.075(2)
C12	0.0461(5)	0.0815(2)	0.3840(3)	0.054(1)
C13	0.1502(5)	0.1499(2)	0.3766(3)	0.050(1)
C14	0.1450(6)	0.1963(2)	0.4593(3)	0.064(2)
C15	0.2461(7)	0.2580(3)	0.4609(4)	0.076(2)
C16	0.3566(6)	0.2754(2)	0.3778(4)	0.071(2)
C17	0.3623(6)	0.2315(2)	0.2938(3)	0.060(1)
C18	0.2609(5)	0.1684(2)	0.2924(3)	0.049(1)

[a] $U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i\cdot\mathbf{a}_j$.

apparent. The first of these (V1−O1) is a typical V=O distance of 1.630 Å. The second oxo group is involved in the bridge between V1 and V1a where it is strongly coordinated to V1 (V1−O2, 1.681 Å) and is weakly associated with V1′ (V1′−O2, 2.283 Å). The remaining three coordination sites are occupied by the phenolate oxygen (V1−O3, 1.905 Å), amine nitrogen (V1−N1, 2.206 Å), and amine nitrogen (V1−N2, 2.171 Å) atoms of the ligand with the hydroxyl group remaining uncoordinated. The O1−V1−O2 angle, 107.45°, again is close to that observed for **1** and many other cis-VO_2^+ (pervanadyl) units.[19] The only change in the vanadium coordination sphere that is significant between **1** and **2** is the V1−N1 distances. There is significant lengthening of the V−nitrogen distance on going from an imine (**1**: V1−N1 = 2.145 Å) to a secondary amine (**2**: V1−N1 = 2.206 Å).

Description of the Structure of VO(salshedr), 4. Complexation of vanadium by the ligand H_3salshedr leads to the monooxovanadium(V) complex VO(salshedr), **4**, shown in Figure 3. Important bond lengths and angles are provided in Table 4. The ligand acts as a pentadentate, trianionic chelating agent using one alkoxide and two phenolate oxygens and secondary and tertiary nitrogen donors. The sixth ligand to the vanadium(V) is a terminal oxo moiety. The tertiary amine nitrogen N2 is trans to the terminal oxygen O1. A phenolate oxygen O4, alkoxide oxygen O3, and secondary amine nitrogen N1 are linked to N2 in six-, five-, and five-membered chelate rings, respectively, making this portion of the molecule resemble an nta^{3-} derivative. The second phenolate oxygen participates in a six-membered chelate ring with N1. The molecule forms an isomer with the two phenolate oxygens in cis positions. In addition to having increased denticity, the salshedr ligand differs from shed, but not shedr, by having a reduced imine nitrogen. For the vanadium(V) complexes of both shed and shedr, the phenolate (O3)−imine/amine (N1)−amine (N2) atoms form a meridional chelate; however, the O2−N1−N2 atoms form a facial geometry in the VO(salshedr) complex. This causes a substantial elongation of the V−N2 distance in **4** (2.313 Å) vs **1** (2.183 Å) or **2** (2.171 Å). Additionally, the alkoxide that is protonated and uncoordinated in **1** and **2** forms a relatively long (1.835 Å) V−O bond in **4** (average V−O alkoxide bond 1.776 Å).[22] This alkoxide bond apparently weakens the trans phenolate bond (1.910 Å) to vanadium, as compared to the cis phenolate bond (1.840 Å). As noted above, the O−V−O angles for VO_2^+ or VO(OR) complexes typically are 107−110°, indicating significant double-bond character in these bonds. The most obtuse cis angle in **4** is O1−V1−O2 at 103.3°, suggesting an electronic environment for the vanadium ion in **4** that is closer to a monooxovanadium(V) rather than a dioxovanadium(V) or vanadate ester. We anticipate that complexes **3** and **5** are isostructural with **4** and differ by substituting an alkoxide at the phenolate position O4 for **3** or by substituting a phenolate at the alkoxide position O3 for **5**.

Solution Studies. While X-ray crystallography provides a detailed description of the vanadium(V) compounds in the solid state, with exchange-labile vanadium it is necessary to have a complementary technique to confirm that the complexes, when dissolved, retain the same structure in solution. The use of NMR spectroscopy nicely satisfies this requirement, as ^{1}H, ^{13}C, and ^{51}V spectra provide related and independent insight into solution structure and stability. The most useful isotopes are ^{13}C and ^{51}V, since the former can provide evidence for ligation of a particular residue while the latter is indicative of whether the metal is found as VO_2^+, VO^{3+}, $VO(OR)^{2+}$, or $VO(O_2)^+$.

The ^{13}C NMR spectra of H_2shed, [VO_2(Hshed)], H_2shedr, and [VO_2(Hshedr)] clearly show that the complexation of vanadium by the ligands remains as was shown by X-ray studies. A representation of the chemical shifts for these compounds is shown in Figure 4. Phenolate ligation is confirmed by the downfield ^{13}C shifts (ppm) on going from ligand (H_2shed, 161.2; H_2shedr, 156.0) to metal complex (VO_2(Hshed), 164.6; VO_2(Hshedr), 164.3). Similarly, the methylene carbons adjacent to the amine and imine nitrogens have downfield shifts, although this effect is less dramatic. Most important, the pendant alcohol oxygen remains unbound as is shown by the slightly upfield shift in the alcohol carbon resonance. The ^{51}V NMR data provided in Table 5 confirm the VO_2^+ formulation for the vanadium chromophore. These data, taken together with the previous solution molecular weight characterization of VO_2(Hshed), speak strongly in favor of a monomeric species with one phenolate, one imine, and one amine bound to the pervanadyl moiety for both shed and shedr.

The X-ray structure of VO(salshedr) clearly differs from that of the pervanadyl complexes of shed and shedr. The first indication that the VO(salshedr) retains its solid state structure in solution is the marked downfield shift of the ^{51}V NMR resonance of the complex into a region typical of monooxovanadium(V) compounds. The ^{51}V NMR exhibits two peaks, with one at −440 ppm and the other at −481 ppm. Both of these species are VO^{3+} complexes and represent different isomers that can form in this solution. The two most likely candidates are shown as Figure 5.

All of the VOL complexes described herein show strong ligand to metal charge transfer energies in the visible spectra. We have previously shown that ^{51}V NMR chemical shifts are extremely sensitive to the ligand to metal charge transfer energies of the complex and it is reasonable that these LMCT energies will differ between cis and trans phenolate isomers. Thus, the large difference in chemical shift for the two compounds probably is related to the different energies of charge transfer excitations between the cis and trans phenolate isomers. At this point, we have not been able to determine whether the crystalline sample that we obtained is a mixture of these two isomers (no separation was observed on silica gel plates) or if

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Table 4. Selected Bond Distances (Å) and Angles (deg) for $[VO_2(Hshed)]_2$, **1**, $[VO_2(Hshedr)]_2$, **2**, and VO(salshedr), **4**

$[VO_2(Hshed)]_2$[a]		$[VO_2(Hshedr)]_2$		VO(salshedr)	
V1–O1	1.608(3)	V1–O1	1.630(1)	V1–O1	1.600(3)
V1–O2	1.680(2)	V1–O2	1.681(1)	V1–O2	1.910(7)
V1–O2a	2.376(80)[b]	V1–O2a	2.283(1)	V1–O3	1.835(3)
V1–O3	1.903(6)	V1–O3	1.905(1)	V1–O4	1.840(3)
V1–N1	2.145(4)	V1–N1	2.206(2)	V1–N1	2.160(3)
V1–N2	2.183(19)	V1–N2	2.171(2)	V1–N2	2.313(3)
V1–V1a	3.177(74)[b]	V1–V1a	3.079(2)		
O1–V1–O2	107.3(3)	O1–V1–O2	107.45(8)	O1–V1–O2	100.9(1)
O1–V1–O2a	171.2(8)	O1–V1–O2a	168.14(6)	O1–V1–O3	94.4(1)
O1–V1–O3	101.2(4)	O1–V1–O3	102.72(7)	O1–V1–O4	103.3(1)
O1–V1–N1	97.4(1.2)	O1–V1–N1	93.54(7)	O1–V1–N1	93.0(1)
O1–V1–N2	91.2(2.1)	O1–V1–N2	91.41(7)	O1–V1–N2	169.0(1)
O2–V1–O2a	78.3(4)	O2–V1–O2a	79.21(6)	O2–V1–O3	160.8(1)
O2–V1–O3	99.8(4)	O2–V1–O3	98.34(6)	O2–V1–O4	89.6(1)
O2–V1–N1	154(2)	O2–V1–N1	157.13(7)	O2–V1–N1	84.0(1)
O2–V1–N2	93.2(1.8)	O2–V1–N2	92.22(6)	O2–V1–N2	85.1(1)
O2a–V1–O3	84.3(1.4)	O2a–V1–O3	85.64(6)	O3–V1–O4	98.0(1)
O2a–V1–N1	76.3(1.2)	O2a–V1–N1	78.59(6)	O3–V1–N1	83.8(1)
O2a–V1–N2	81.6(1.1)	O2a–V1–N2	78.35(6)	O3–V1–N2	77.9(1)
O3–V1–N1	83.9(5)	O3–V1–N1	85.41(6)	O4–V1–N1	163.4(1)
O3–V1–N2	158.3(1.0)	O3–V1–N2	158.83(7)	O4–V1–N2	85.8(1)
N1–V1–N2	77.0(5)	N1–V1–N2	77.96(6)	N1–V1–N2	78.4(1)
V1–O2–V1a	101.7(4)	V1–O2–V1a	100.79(7)		
O2–V1–O2a	78.3(4)	O2–V1–O2a	79.21(6)		

[a] Average of chemically equivalent bonds for two independent structures with distinct hydrogen bonding to bridging oxygens. The numbering scheme has been converted so as to be consistent with that of $[VO_2(shedr)]_2$. [b] The two distances are markedly different due to the change in hydrogen bonding (V1–O2a = 2.455 and 2.298 Å; V1–V1a = 3.103 and 3.251 Å).

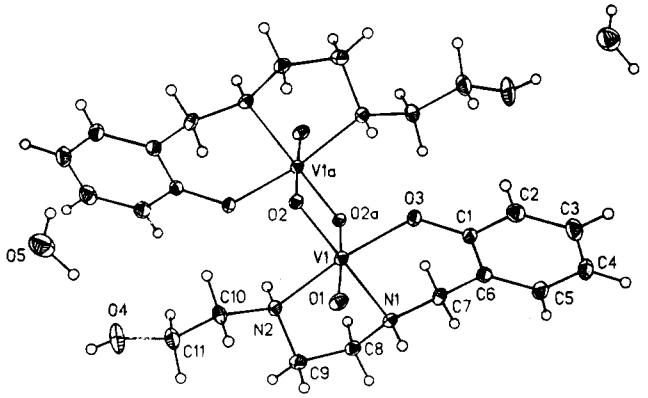


Figure 2. ORTEP diagram of $[VO_2(Hshedr)]_2$, **2**, with thermal ellipsoids at 50% probability.

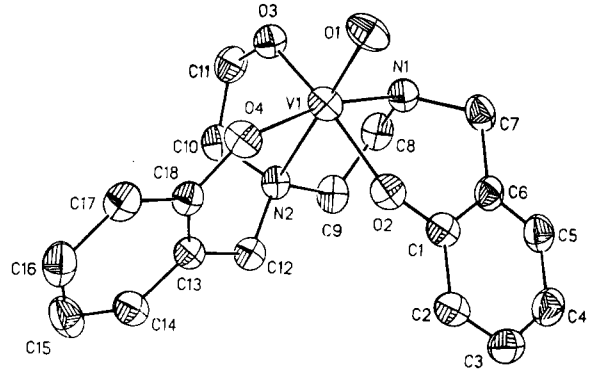


Figure 3. ORTEP diagram of [VO(salshedr)], **4**, with thermal ellipsoids at 50% probability.

we began with a pure material but the rate of interconversion to establish an equilibrium between the forms is rapid.

The ^{13}C NMR spectra strongly support a pentadentate ligand formulation for the two VO^{3+} compounds. Two sets of two phenolate resonances are observed downfield of the parent ligand phenolate carbon resonances. In addition, all of the

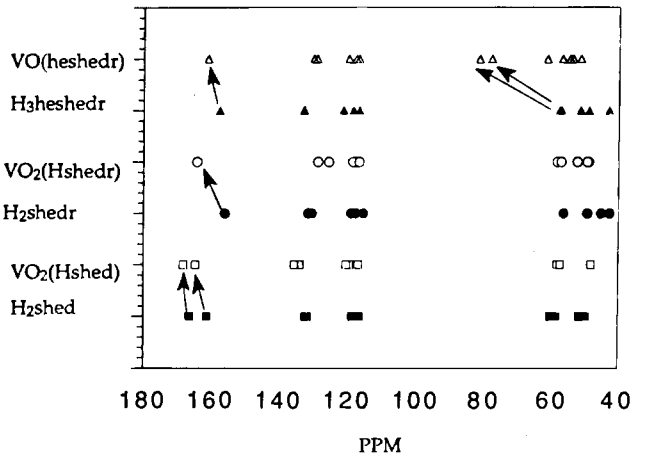


Figure 4. ^{13}C NMR shifts for H_2shed, $[VO_2(Hshed)]$, H_2shedr, $[VO_2(Hshedr)]$, H_3heshedr, and [VO(heshedr)]. The arrows connect the corresponding resonances between the ligand and metal complexes.

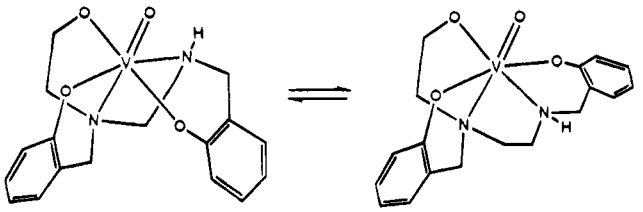
methylene carbons undergo downfield shifts. In particular, the alcohol carbons, rather than remaining in the +50 ppm range, shift to +70 to +80. This is definitive proof that the alcohol oxygen in each isomer is bound to the vanadium center. While there are formulations for isomers possible other than those shown in Figure 5, we believe that they are unlikely. Our reasoning is that the tertiary amine nitrogen is the weakest donor to the vanadium and should be oriented trans to the terminal vanadyl oxygen. Once the tertiary nitrogen is restricted to this position, there are only two sets of enantiomers possible, one from each set being shown in Figure 5.

The H_3heshedr complex of vanadium has not been crystallographically characterized; however, NMR spectroscopy allows us to deduce the structure of the predominant form of this compound. First, the ^{51}V NMR is consistent with a monooxovanadium(V) formulation (−445 ppm) as is the strong charge transfer excitation shown in Table 5. As illustrated in Figure 4, the changes in the ^{13}C NMR conclusively show that the phenolate and both alkoxides are coordinated to the vanadium.

Table 5. UV/Vis, ^{51}V NMR, and Electrochemistry for Compounds **1**–**5** in dmf

complex	UV/vis λ_{max}, nm (ϵ^a)	^{51}V NMR δ_b	E_a ($E_{1/2}$), mV (vs SCE)^c	ref
1	372 (2900)	−529		19
2	328 (2300)	−529		
3	370 sh (5900)	−431, −453	−931	
4	477 (4430)	−464, −493	−624 (−562)	
	344 (5320)			
5	544 (6400)	−470, −498	−377 (−292)	
VO_2(salimH)		−542		*d*
VO_2(Hensal)		−555		*e*

[a] Where appropriate, extinction coefficient in M^{-1} cm^{-1} per cluster. [b] In ppm vs an external $VOCl_3$ standard. [c] Electrochemistry performed in *N*,*N*′-dimethylformamide solution with tetra-*n*-butylammonium hexafluorophosphate as working electrolyte. [d] Cornman, C. R.; Kampf, J.; Pecoraro, V. L. *Inorg. Chem.* **1992**, *31*, 1981–1983. [e] Root, C. A.; Hoeschele, J. D.; Cornman, C. R.; Kampf, J. W.; Pecoraro, V. L. *Inorg. Chem.* **1993**, *32*, 3855–3861.



cis-Phenolates trans-Phenolates

Figure 5. The two most likely monooxovanadium(V) isomers that can be formed with salshedr. The isomer at the left is the crystallographically characterized species.

Thus, one predicts a structure similar to that of **4**, but with the alkoxide and phenolate positions interchanged. A similar argument can be made for **5**, giving a structure like that obtained for **4**, with a third phenolate substituted for the alkoxide.

The VO(salshedr) and VO(sal$_3$enr) complexes are stable in water and do not react with peroxide at neutral pH values. Monitoring the compounds by UV/vis spectroscopy in 4:1 dmf/H_2O or 4:1 MeOH/H_2O solution did not show any measurable decay in absorbance after 2 days. In contrast, VO(heshedr) is extremely water sensitive, decomposing, on even a humid day, to the pervanadyl complex VO_2(H_2heshedr). However, in dry dmf solution VO(heshedr) can be observed as the major species in spectroscopic studies. The solution color changes from red-brown to yellow upon this conversion, and the primary peak in the ^{51}V spectrum shifts from −445 to −538 ppm. The latter resonance is indicative of the pervanadyl complex, as commented upon above for VO_2(shed) and VO_2(shedr). The ^{13}C spectrum no longer shows the dramatically downfield-shifted alcohol carbon resonances, suggesting that VO_2(H_2heshedr) is basically similar in structure to the complexes VO_2(shed) and VO_2(shedr), with both hydroxyethyl groups pendant and uncoordinated. Another ^{51}V resonance, assigned to vanadate, is observed in the spectrum of VO_2(H_2heshedr). Thus, even with the higher denticity ligand, the tendency for vanadium to dissociate to vanadates is not completely averted. This observation has been reported for high-denticity ligands in aqueous solution.[23] Addition of hydrogen peroxide will completely displace the vanadium from the heshedr ligand.

Spectroscopic and physical properties show trends that can be attributed to the changes in ligand donor type (Table 5). The reduction potentials obtained for the monooxovanadium(V) complexes give a linear correlation with substitution by ligand donor type. The potentials (E_a) obtained are −377 mV for VO(sal$_3$enr), −624 mV for VO(salshedr), and −931 mV (vs SCE) for VO(heshedr). The triphenolate and diphenolate derivatives are pseudoreversible, but the monophenolate VO(heshedr) is not.

(23) Crans, D. C.; Ehde, P. M.; Shin, P. K.; Pettersson, L. *J. Am. Chem. Soc.* **1991**, *113*, 3728–3736.

Discussion

A major limitation of the use of the synthetically convenient Schiff base condensation for the preparation of vanadium(V) complexes that might react with hydrogen peroxide is the hydrolytic instability of the imine linkage. This hydrolytic sensitivity is particularly acute under acidic conditions, where V(V) has a high affinity for peroxides. The resulting affinity of the remaining organic fragments for vanadium is greatly diminished once the ligand has hydrolyzed, which often leads to release of the metal and formation of simple peroxovanadates. The ease, versatility, and high yields of the Schiff base condensation can still be maintained and exploited through reduction of the imine moiety to form the corresponding amine. This simple modification provides ligand stability in the presence of added acid equivalents and allows the chemistry of the complexes formed to be pursued in both aqueous and nonaqueous environments.

We have evaluated the coordination chemistry of a pair of ligands, H_2shed and H_2shedr, in order to assess the impact of reduction of the imine on the stable oxidation levels of vanadium, chelated vanadium composition, and water solubility and stability. Furthermore, we have developed a series of ligands that allow us to increase the ligand denticity and vary dramatically the functional groups that can be bound to the vanadium ion. These higher denticity reagents are prepared by the alkylation of a secondary amine prior to reduction of an imine. Thus, one may construct ligand asymmetry and control denticity in order to perturb more subtly the ligand environment while still retaining hydrolytic stability.

The chemistries of **1** and **2** appear in nearly all ways to be identical. Both ligands form neutral pervanadyl dimers of composition $[VO_2L]_2$, and both react with acid reversibly to generate the oxohydroxo species $[VO(OH)L]^+$. The spectral parameters are similar, with only strong UV absorption apparent. Furthermore, derivative chemistry with catechol to give VOL(cat) or isolation of V(IV) compounds such as VOL(acac) can be achieved. Despite all of these similarities, there are two significant differences between **1** and **2**. First, **2** is hydrolytically stable even under acidic conditions. While addition of a large excess of acid will lead to loss of vanadium, the ligand remains intact. In contrast, Hshed$^-$ will, under less acidic conditions, rapidly give free vanadate, salicylaldehyde, and *N*-(2-hydroxyethyl)ethylenediamine. Second, the yellow form of $[VO_2$(Hshed)$]_2$ is light sensitive in the solid state and both yellow and orange hydrogen-bond isomers are light sensitive in dmf (both form the same monomeric species in solution: VO_2(Hshed)), giving green vanadium(IV) products. Complex **2** appears to be light stable both as a solid and in solution. We and others are investigating more fully the origins of this distinctive photochemistry and will report separately our results from these studies. Thus, the reduction of the imine satisfactorily addresses the hydrolytic instability of the previous complex **1** and suggests this as a general relatively nonperturbative approach for evaluating the aqueous chemistry of other hydrolytically unstable but potentially interesting vanadium Schiff base complexes.

Appending an additional functional moiety to the shedr framework leads to a new group of monooxovanadium(V) species. Although VO^{3+} compounds are more common today

than just 10 years ago,[24] they still represent a relatively rare group of materials for the vanadium(V) oxidation level. Previous examples included the highly reactive VO(EHPG)/VO(EHGS) series,[7] $VO(SALEN)^+$,[7] VOLL′ (where L = Hshed, salimH, and ensal and L′ = catecholate and hydroxamate derivatives),[25] vanadium metallacrowns,[26] and VO(2-OHsalpn).[27] The last molecule is of particular interest in comparison with VO(salshedr), **4**, since both molecules have a $VO(OR)_2(OR')N_2$ (R = phenyl, R′ = alkyl) chromophore. The major structural differences between the two are that VO(2-OHsalpn) has imine nitrogens rather than amine nitrogens and that the alkoxide is trans to the terminal oxo rather than an amine nitrogen.

Each of the pentadentate ligands described herein is a modification of the H_2sal_2en or H_2shedr parent compound; thus it is not surprising that one can displace the additional functional groups to form dioxovanadium(V) complexes with two pendant arms rather than one. What is most interesting about this observation is that the ease or difficulty of this hydrolysis varies significantly among the ligands. For example, complex **4**, while insoluble in pure water, is very stable to metal hydrolysis. In fact, the molecule is recrystallized from a 50:50 water:methanol solution. In contrast, **3** is rapidly hydrolyzed to $VO_2(H_2heshedr)$ even by atmospheric water.

A correlation between the reduction potentials of manganese and vanadium complexes and the donor strength of the ligands has been reported.[28,29] The trend observed in reduction potentials can be rationalized by a using a thermodynamic relationship between the potential and the ligand donor pK_a's.[30] A shift in the reduction potential for the oxovanadium(V) species of ~250−300 mV is found in substitution of a single phenolate donor for an alkoxide, or approximately 45−50 mV per pK_a unit change. This relationship can be used in the design of multidentate ligands for the stabilization of preferred oxidation states of vanadium.

In summary, one of the problems associated with the first-generation ligands that have been used to investigate vanadium reactivity with hydrogen peroxide and halides is that the ligands tended to hydrolyze at the Schiff base linkage. We solved the problem of ligand hydrolysis by reducing the Schiff base linkage using borohydride (e.g., converting H_2shed to H_2shedr). The X-ray structure of $[VO_2(Hshedr)]_2$ demonstrates that it is isostructural with $[VO_2(Hshed)]_2$. Thus, the reduced molecule forms the same structure but no longer dissociates to form salicylaldehyde and *N*-(2-hydroxyethyl)ethylenediamine when dissolved in solutions containing water. This represents a general and simple approach to solving the ligand decomposition problem for a wide variety of ligands. The second important point is the relative stability of the vanadium complexes in water, in acidic conditions, and in the presence of peroxides. The ligands $H_3heshedr$, $H_3salshedr$ and H_3sal_3enr nicely illustrate both the synthetic control and the functional group versatility available to us with our new higher denticity ligands. As an illustration, these pentadentate ligands form stable VO^{3+} species such as VO(salshedr), the first *nontetrahedral* **water-stable** monooxovanadium(V) complex. This molecule is so stable that it does not react with hydrogen peroxide in water or organic solvents and will only react with mineral acids to protonate off the coordinated alkoxide. At the other extreme is VO(heshedr), which is very water sensitive and forms a stable $VO_2(H_2heshedr)$ complex that is isostructural with $[VO_2(Hshedr)]_2$. While proton NMR provided some sense for solution integrity and ^{51}V NMR was useful in establishing broadly the coordination environment of the metal, neither technique, alone or in combination, provided data sufficient to meet our needs. However, Crans' work on vanadate interactions with buffers using ^{13}C NMR[31,32] provided a basis for the assignment of solution structure for these vanadium complexes in the presence and absence of peroxide. We can now determine whether the alkoxides begin coordinated to the vanadium (e.g.: VO(salshedr), yes; VO_2(Hshedr), no) and when complexes react, which functional groups are lost (e.g.: VO(heshedr) + $H_2O \rightarrow VO_2(H_2heshedr)$ with uncoordinated alkoxides and coordinated phenolate). This provides an opportunity for future studies to establish not only when complexes bind water, peroxides, and/or halides but also what ligand functional groups (if any) must be lost during the process.

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Supplementary Material Available: A complete crystallographic summary for **2** (Table S1), anisotropic thermal parameters, hydrogen atom fractional coordinates, and bond lengths and angles for **2** (Tables S2−S4), respectively, a complete crystallographic summary for **4** (Table S5), anisotropic thermal parameters, hydrogen atom fractional coordinates, and bond lengths and angles for **4** (Tables S6−S8), and complete numbering schemes for **2** and **4** (Figures S1 and S2) (12 pages). Ordering information is given on any current masthead page.

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