excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow-orange filtrate was evaporated in vacuo (rotary evaporator), and the yellow-orange residue was dissolved in methylene chloride (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow-orange solid. The solid was washed with ether (5 mL) and dried in vacuo to yield a bright yellow-orange solid: 0.045 g, 82% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.99 (s, 3 H), 7.39 (dd, J = 8.3, 1.9 Hz, 1 H), 7.48 (m, 1 H), 7.75 (t, J = 8.0 Hz, 1 H), 7.90 (dd, J = 8.4, 1.4 Hz, 1 H), 8.26 (dt, J = 8.7, 1.9 Hz, 1 H), 8.84 (dd, J = 4.9, 2.2 Hz, 1 H), 9.10 (d, J = 1.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 56.55, 117.83, 118.44, 118.75, 121.28, 123.99, 129.15, 131.71, 135.78, 136.28, 150.90, 154.46, 155.13, 160.44, 178.11, 178.92, 191.55; IR (KBr) 2999, 2950, 2930, 2842, 1676, 1668, 1654, 1644, 1602, 1583, 1577, 1474, 1274, 1242, 1194, 1154, 1052, 1038, 988, 795, 787, 761, 736, 700 cm^{-1}; mp 180-185 °C (decomposed); high-resolution mass spectrum (EI) M^+ for $C_{17}H_{10}INO_4$, calcd 418.9655, found 418.9654 (±0.0006).

2-Iodo-5-methoxy-3-(thien-2-ylcarbonyl)-1,4-naphthoquinone (Table III, Entry 8). To a solution of 2-iodo-1-[(2-methoxyethoxy)methoxy)-5-methoxy-3-(thien-2-ylcarbonyl)naphthalene (Table II, entry 14) (0.1004 g, 0.2 mmol) in acetone (20 mL) was added Jones's reagent[8] (3 mL), and the solution was allowed to stir at room temperature for 40 min, during which time blue-green Cr(III) salts precipitated. Isopropyl alcohol (ca. 3 mL) was added dropwise to destroy excess chromic acid followed by sodium bicarbonate (ca. 4 g), and the suspension was allowed to stir 5 min. The suspension was filtered and the filter cake washed with acetone (2 × 20 mL). The bright yellow-orange filtrate was evaporated in vacuo (rotary evaporator), and the yellow-orange residue was dissolved in methylene chloride (200 mL), washed with water, saturated $NaHCO_3$, and brine, and dried over $MgSO_4$. The solvent was removed (rotary evaporator) to yield a bright yellow solid. The solid was washed with diethyl ether (5 mL) and dried in vacuo to yield a bright yellow-orange solid (recrystallized from ether to yield bright orange crystals): 0.075 g, 89% isolated yield; ^1H NMR (300 MHz, $CDCl_3$) δ 3.99 (s, 3 H), 7.15 (dd, J = 5.4, 3.5 Hz, 1 H), 7.37 (m, 1 H), 7.64 (dd, J = 4.0, 0.8 Hz, 1 H), 7.73 (t, J = 8.1 Hz, 1 H), 7.80 (dd, J = 5.4, 1.2 Hz, 1 H), 7.89 (dd, J = 8.4, 1.4 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$) δ 56.56, 117.72, 118.58, 118.73, 121.18, 128.62, 131.80, 135.15, 135.58, 136.10, 140.40, 155.68, 160.41, 178.45, 178.59, 184.47; IR (KBr) 3111, 3090, 2975, 2839, 1664, 1643, 1617, 1599, 1578, 1473, 1432, 1411, 1358, 1306, 1267, 1236, 1189, 1152, 1043, 829, 775, 737, 726 cm^{-1}; mp 237.5-238.6 °C. Anal. Calcd for $C_{16}H_9IO_4S$: C, 45.30; H, 2.14. Found: C, 45.32; H, 1.97.

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Cyclic Vanadium(V) Alkoxide: An Analogue of the Ribonuclease Inhibitors

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Abstract: This article reports the preparation and structural characterization of the first cyclic vanadium alkoxide. This pinacol-vanadium(V) complex was formed from $VOCl_3$ and pinacol in methylene chloride and recrystallized from chloroform in 83% yield. The vanadium atoms in the complex were pentacoordinate in a distorted trigonal-bipyrimid geometry achieved by dimerization through bridging of one of the oxygen atoms of each of the pinacol moieties. The vanadium(V)-pinacol crystals are prismatic and possess the following crystalline properties: $P2_1/c$, Z = 2, a = 6.642 (3) Å, b = 9.834 (2) Å, c = 13.972 (7) Å, β = 99.06 (9)°, 153 K, R = 0.026. This compound is the first example of the trigonal-bipyramidal geometry of an alkyl vanadium derivative that is presumed to be a good transition-state analogue for enzymes catalyzing hydrolytic organic phosphate reactions. ^1H, ^{13}C, and ^{51}V VT-NMR studies suggest the solution structure is also dimeric in vanadium. The structural properties of the vanadium-pinacol complex are compared to the corresponding organic phosphates and the vanadate-uridine ribonuclease complex. The major structural differences between organic phosphate compounds and the vanadium-pinacol complex are the nuclearity and asymmetry in the vanadium(V)-pinacol complex. The vanadium-oxygen bond lengths to the pinacol differ by 0.19 Å, whereas the phosphate compound is symmetric. The observed asymmetry is also observed in the ribonuclease-uridine-vanadate complex and may be important for the tight binding of the vanadate-uridine complex by ribonuclease.

Introduction

Vanadium is a dietary trace element with no known function.[1] Vanadium at low concentrations is beneficial, whereas at high concentrations it is toxic. Its beneficial effects include reduction in cardiovascular degeneration; it is a known insulin mimetic agent and an epidermal growth factor.[1] Vanadium affects cAMP levels, protein kinase activity, and protein phosphatase activity.[1] Very little is currently understood about the mechanisms of action of vanadium in mammals and plants. It is very likely that the chemical and structural properties of the vanadium will dictate the biological activities of vanadium derivatives.[1-4] Vanadium(V) in the form of monomeric vanadate is a potent inhibitor for a series of enzymes including ATPases, phosphatases, and nucleases.[1,2,5] It has been suggested that vanadate coordinates so tightly to the enzyme (1000-fold tighter than subtrate) because it can easily adopt a trigonal-bipyramidal geometry and this geometry simulates a hydrolytic transition state (or a high-energy intermediate) in the enzyme reaction.[5] The initial suggestion by Linquist et al. in 1973[5] was presented without any structural precedence for such

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a pentacoordinate vanadium(V) alkyl compound. We now present chemical and the first structural evidence for such a compound.

Ribonuclease A is potently inhibited by a complex formed between vanadate and uridine or cytidine.[6] The complex between ribonuclease A (or T1), vanadate, and uridine has been characterized by biochemical methods,[6] NMR spectroscopy,[7] neutron diffraction studies,[7] and X-ray crystallography.[7,8] The last technique shows the existence of a trigonal-bipyramidal vanadium(V) alkoxide inside the protein.[8] No analogous compounds have been structurally characterized to show precedence for this type of coordination. The role of the vanadium in the vanadate–uridine complex in the inhibition of the protein is still not well defined since the chemical analogues of such compounds have not been characterized.[7,8] Ribonuclease T is potently inhibited by a complex formed between vanadate and guanosine or inosine.[9] This enzyme complex has only recently been discovered and has not been characterized to the same extent as the ribonuclease A–vanadate–uridine complex.

Aqueous mixtures of vanadate with various nucleosides have been studied by titration methods,[6] UV spectroscopy,[6] and ^{51}V NMR spectroscopy.[10] The product formed in the reaction of uridine with vanadate was characterized as a 1:1 complex by using titration and UV spectroscopy[6] and a 2:2 complex by using ^{51}V NMR spectroscopy.[10] The complex[8] inside the protein was the 1:1 complex and the authors of the NMR studies suggested that the 2:2 complex is in equilibrium with the 1:1 complex.[10] These studies therefore suggest that the inhibition of ribonuclease A is much more potent than previously anticipated because the concentration of the 1:1 complex is much lower than that of the 2:2 complex since it is not observed by NMR. The presumed cyclic product that formed between guanosine and vanadate was determined to be a 1:1 complex by using ^{51}V NMR spectroscopy.[9] The formation and hydrolysis of these derivatives in aqueous solutions is rapid,[11,12] and none of these compounds have yet yielded X-ray quality crystals from aqueous solution. Reactions between vanadate and a variety of alcohols have been characterized by ^{51}V NMR spectroscopy; however, no X-ray data are available to support the structural assignments in these studies.[13] The synthesis and structural characterization of a complex between vanadate and a vicinal diol would provide important structural information on the five-membered ring in 2,3-*O*-cyclic nucleotide vanadates. In this paper we report the first simple cyclic analogue of a vanadium 2,3-*O*-cyclic nucleotide.

Oxovanadium alkoxides containing saturated alcohols are prepared from V_2O_5, NH_4VO_3, or $VOCl_3$ or by ester-exchange reactions.[14-18] Simple oxovanadium alkoxides undergo rapid ligand exchange in solution.[19] No X-ray data are currently available for a simple tetra- or pentacoordinate vanadium(V) compound as a phosphate ester analogue. We have attempted to obtain crystals suitable for single-crystal diffraction experiments from simple oxovanadium alkoxides, but even in the case of tricyclohexylvanadium alkoxide, the crystals were twinned and/or disordered. Disordered crystals were also acknowledged in the literature for both $VO(OCH_3)_3$ and $VO(OPh)_3$.[20,21] In contrast, vanadium complexes from oxygen-containing ligands, including substituted phenols or carboxylates, have been structurally characterized.[22-24] None of these compounds, however, serve as an appropriate model for vanadium 2,3-*O*-cyclic nucleotides because these molecules typically contain octahedral vanadium. When substituting a chlorine atom for an alkoxy group, we found that the rates of the rapid exchange reactions of vanadium alkoxides were significantly decreased. The chlorine atom substitution also yielded crystals suitable for the X-ray diffraction experiment. This paper describes the structural characterization and solution properties of di(μ-pinacolato)bis[oxovanadium(V) chloride] and structural comparisons that have been made with corresponding phosphorus compounds[25] and the ribonuclease–vanadate–uridine complex.[8]

Table I. Details of the Crystallographic Experiment and Computations for the Pinacol–Vanadium(V) Complex [Di(μ-pinacolato)bis[oxovanadium(V) chloride], $C_{12}H_{24}O_6Cl_2V_2$]

mol formula	$C_{12}H_{24}O_6Cl_2V_2$
formula wt	436.8
crystal system	monoclinic
space group	$P2_1/c$
lattice constants	
a, Å	6.642 (3)
b, Å	9.834 (2)
c, Å	13.972 (7)
β, deg	99.06 (4)
V, Å^3	901.1
temp, °C	−120 (153 K)
Z	2
$F(000)$	896
ρ_{calcd}, g cm^{-3}	1.61
crystal dimens, mm	0.4 × 0.5 × 0.1 mm
radiation	Mo Kα (λ = 0.7107 Å)
monochromator	graphite
μ, cm^{-1}	26.48
scan type	$\theta/2\theta$
geometry	bisecting
scan speed, deg min^{-1}	2–30 variable
2θ range, deg	$4° < 2\theta < 50°$
index restrictions	$-8 \le h \le +8$, $0 \le k \le 12$, $0 \le l \le 17$
no. of total reflcns	1737
no. of unique, obsd reflcns	1360
obsd reflcn criterion	$\lvert F_o\rvert > 2.5\sigma(\lvert F_o\rvert)$
no. of least-squares params	112
data/param ratio	12.14
R	0.026
R_w	0.040
GOF	1.84
g	0.00031 (refined)
slope, normal probability plot	1.44

Experimental Section

Preparation of Di(μ-pinacolato)bis[oxovanadium(V) chloride] (1). A 250-mL two-neck round-bottom flask containing a clear and colorless solution of 0.624 g (5.28 mmol) of pinacol in 30 mL of methylene chloride at −50 °C was stirred under slow argon flow. The round-bottom

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Table II. Bond Lengths and Bond Angles for Pinacol–Vanadium(V) Complex[a]

	Bond Lengths, Å		
V–Cl	2.219 (1)	V–O_1	1.576 (1)
V–O_2'	1.967 (1)	V–O_3	1.773 (1)
V–O_2'	1.964 (1)	O_2–C_2	1.466 (2)
O_2–V′	1.964 (1)	O_3–C_1	1.451 (2)
C_1–C_2	1.557 (3)	C_1–C_3	1.519 (3)
C_1–C_4	1.521 (3)	C_2–C_5	1.526 (3)
C_2–C_6	1.515 (3)		
	Bond Angles, deg		
Cl–V–O_1	106.7 (1)	Cl–V–O_2	135.0
O_1–V–O_2	117.6 (1)	Cl–V–O33	99.3
O_1–V–O_3	101.4 (1)	O_2–V–O_3	79.7 (1)
Cl–V–O_2'	94.0	O_1–V–O_2'	101.1 (1)
O_2–V–O_2'	71.4 (1)	O_3–V–O_2'	149.3 (1)
V–O_2–C_2	116.3 (1)	V–O_2–V′	108.6 (1)
C_2–O_2–V′	134.5 (1)	V–O_3–C_1	119.1 (1)
O_3–C_1–C_2	102.2 (1)	O_3–C_1–C_3	108.3 (2)
C_2–C_1–C_3	113.2 (2)	O_3–C_1–C_4	108.0 (2)
C_2–C_1–C_4	113.5 (2)	C_3–C_1–C_4	110.9 (2)
O_2–C_2–C_1	102.1 (1)	O_2–C_2–C_5	110.9 (2)
C_1–C_2–C_5	112.9 (2)	O_2–C_2–C_6	106.7 (2)
C_1–C_2–C_6	112.9 (2)	C_5–C_2–C_6	110.9 (2)

[a] Estimated standard deviations in the least significant digits are given in parentheses.

flask was submerged in a Dewar containing a dry ice/acetone bath at −50 °C. $VOCl_3$ (0.50 mL, 5.2 mmol) was added dropwise with a syringe to the round-bottom flask containing the stirred pinacol solution over a period of 5 min. The clear and colorless solution turned yellow and then red as all the $VOCl_3$ was added and a white fog (HCl) formed above the solution. Fine needlelike orange-red crystals began to form at the sides of the flask. The solution was stirred for 60 min to complete the reaction, and a sample of the solution was removed by syringe and maintained at −23 °C for ^{51}V NMR analysis. The material crystallized overnight in a −20 °C freezer. The brick-red solid was filtered off with a fine glass frit filter with a vacuum side arm. The filter was connected to a receiving flask below it and an adapter with a stopcock above it. This setup proved convenient in minimizing contact with air during the filtration process. The solid was dissolved in $CHCl_3$ and recrystallized at −20 °C. The solid was dried in vacuo and yielded 0.935 g (83%) of **1**: ^{51}V NMR (CH_2Cl_2, 23 °C) −324 ppm; ^1H NMR ($CDCl_3$, 20 °C) 1.78, 1.70, 1.62, 1.43 ppm (m), ^{13}C NMR ($CDCl_3$, −13 °C), −24.5 ppm; UV λ_{max} (CH_2Cl_2, −15 °C) 400 mm. Anal. Calcd: V, 23.3; C, 33.0; H, 5.49; Cl, 16.3. Found: V, 23.9; C, 32.3; H, 5.89; Cl, 17.5.

X-ray Structure Determination of 1. Crystal data for **1**, together with details pertaining to the X-ray diffraction experiment and subsequent crystallographic calculations, are reported in Table I. Cell constants were obtained by least-squares refinement of the setting angles for 25 reflections ($2\theta_{av}$ = 22.65) on the Nicolet R3m diffractometer. All structural calculations were performed on the Data General Eclipse S/140 computer in the X-ray laboratory at Colorado State University with the SHELXTL program library written by Professor G. M. Sheldrick and supplied by Nicolet XRD Corp. Neutral-atom scattering factors[26] with anomalous scattering contributions[27] were employed for all atoms. The structure was solved by interpretation of the Patterson map. The crystallographic parameters for $[(C(CH_3)_2O)_2ClVO]_2$ are summarized in Tables I and II. Tables I–VI in the supplementary material give the bond lengths, bond angles, atomic coordinates, anisotropic thermal parameters, hydrogen coordinates, thermal parameters, and observed and calculated structure factors.

NMR Spectroscopy. ^{51}V NMR spectroscopy is a convenient and informative tool for studies of vanadium(V) compounds.[2-4,9-13,18,19] The ^{51}V NMR spectra were recorded on a ^1H 200-MHz Bruker WPSY (4.7 T) spectrometer. We typically used spectral widths of 20 000 Hz, a 90° pulse angle, an accumulation time of 0.2 s, and no relaxation delay. The chemical shifts are reported relative to the external reference standard, $VOCl_3$ (0 ppm). ^{51}V VT-NMR was carried out from 210 to 298 K.

^{13}C and ^1H NMR spectroscopy were also used as tools for characterization of the solution properties of vanadium(V) compounds. The ^{13}C and ^1H spectra were recorded on ^1H 200-, 270-, or 300-MHz Bruker spectrometers. Standard Bruker accumulation parameters were used to record the spectra and TMS was used as a reference. VT-NMR ^1H and ^{13}C was carried out from approximately 210 to 298 K.

NMR Samples. The NMR spectra were recorded in CH_2Cl_2, $CHCl_3$, $CDCl_3$, or C_6D_6 solutions depending on whether a ^{51}V, ^{13}C, or ^1H NMR spectrum was being obtained.

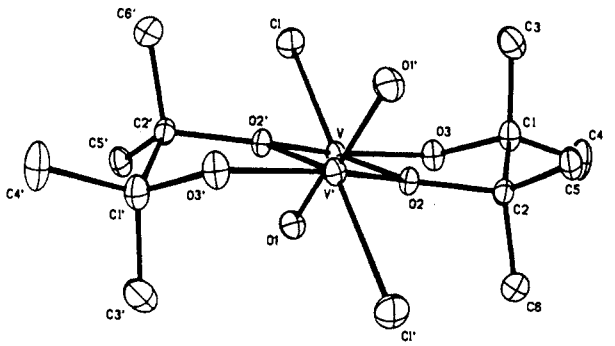
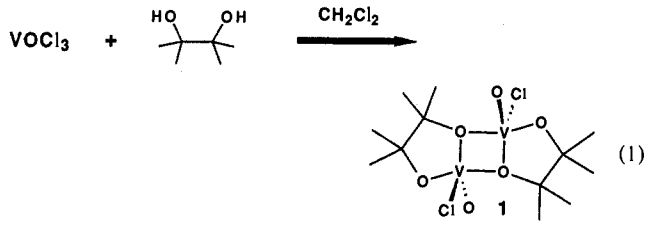


Figure 1. Pinacol–vanadate chloride complex.

Results

Di(μ-pinacolato)bis[oxovanadium(V) chloride] (1). The reaction of $VOCl_3$ with 1 equiv of pinacol in methylene chloride at −50 °C for 60 min yielded a dark-red solid according to the reaction shown in eq 1. The crystalline red solid, $[(C(CH_3)_2O)_2ClVO]_2$,



(1)

decomposed at ambient temperature both in solution or as a solid. The compound can be stored as a solid under argon at −20 °C for weeks. It dissolves in CH_2Cl_2, $CHCl_3$, CCl_4, toluene, and benzene and decomposes in water, THF, ether, CH_3CN, and DMSO. The compound has a ^{51}V NMR chemical shift of −324 ppm in CH_2Cl_2. When the compound was prepared at ambient temperatures, an unidentified impurity at −307 ppm (5%) formed and was found to coprecipitate with the compound. It is possible that this side product is responsible for the difficulty in obtaining repeatable elementary analysis. Only our best analysis result is reported here. The reaction product was either a deep-red crystalline material or orange powder. The red crystals when pulverized also formed the orange powder.

Crystallography. Structural analysis revealed the pinacol–vanadate compound to be a dimer with pentacoordinate vanadium, Figure 1. The coordination around the vanadium is distorted trigonal bipyramidal with O(3) and O(2′) in apical positions and the angle O(3)VO(2′) is 149.3°. The O(1), O(2), Cl, and V form a perfect plane, as demonstrated by the sum of the angles generated by these four atoms (359.3°). The complex is asymmetric because it contains three types of V–O bonds, the equatorial V=O bond [V—O(1), 1.576 Å], the apical V—O bond [V—O(3), 1.773 Å] and the V—O bonds in the four-membered V—O—V—O ring [V—O(2), V—O(2′), V′O(2), V′O(2′), 1.967 or 1.964 Å]. The V–O bonds in the ring are of similar length although one is axial (1.964 Å) and another equatorial (1.967 Å). It is possible these similar bond lengths are a consequence of maintaining bonding in the four-membered ring. The CH_3 groups in the pinacol are staggered and the puckering in the five-membered ring is centered on the carbon. This puckering makes the four CH_3 groups different and supports the expectation that each $[C(CH_3)_2O_2)ClVO]$ unit is asymmetric. This asymmetry is of particular interest, when one realizes that this asymmetry occurs despite the fact that pinacol is a symmetric ligand.

NMR Spectroscopy. The nature of the complex in solution was examined by VT-NMR spectroscopy. The ^{51}V NMR spectrum at 298 K showed only one signal at −324 ppm, which at lower

(26) *International Tables for X-ray Crystallography*; Kynoch: Birmingham, England, 1974; Vol. IV, p 99.
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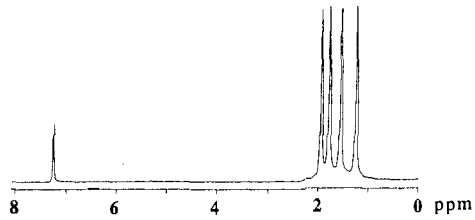
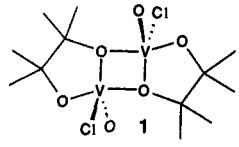


Figure 2. A 300-MHz ^{1}H NMR spectrum of the pinacol–vanadium complex in $CDCl_3$ recorded at 212 K.

temperatures showed only a small upfield change in chemical shift. The chloro substituent in the pinacol complex therefore significantly increased the stability of this complex because no evidence for oligomerization reactions, which occur with the corresponding alkoxides, was observed with ^{51}V NMR spectroscopy. Although it is possible for both the monomer and the dimer to have identical chemical shifts, it is not as likely judged by the differences in the chemical shift of the triisopropyl oxovanadium monomer (−619.4 or −624.2 ppm, depending on conditions) and the dimer (−631.0 ppm).[19] It is therefore more probable that the complex in solution is either the dimer as determined by X-ray crystallography (**1**) or a monomer (**2**). A monomer will presumably contain tetrahedral vanadium as illustrated.



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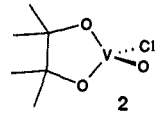

2

^{1}H and ^{13}C NMR spectroscopy was used to examine the complex in further detail. ^{1}H NMR at 293 K showed two broad peaks. As the temperature was lowered from 293 to 252 K, the spectrum changed character as if the sample was approaching coalescence. At 242 K, four distinct signals of equal intensity began to separate out, and at 212 K these signals had separated out. The ^{1}H NMR spectrum at 212 K therefore suggests that the solution structure contains *four distinct methyl groups* (Figure 2). Since the ^{51}V NMR showed no significant change in the chemical shift at low temperature, we assume that the nuclearity of the complex does not change in the examined temperature range. The ^{1}H NMR spectrum is therefore in accord with a dimeric structure of type **1** because this structure contains four different methyl groups. The monomeric structure **2** could potentially have four distinct methyl groups if the puckering in the five-membered ring is centered on a carbon, and ring-flipping processes are slow. However, if some ring-flipping processes are rapid, four different methyl groups should not be observed. The conformations of various puckered five-membered rings containing two oxygen atoms connected to a phosphorus have been shown to vary from 0.5 to 7 kcal in energy. At 212 K all possible puckering processes of this energy range are therefore not likely to have been eliminated. Alternatively, if the vanadium system has higher activation barriers than the phosphorus system, such puckering processes may have been frozen out. Our observations are, however, most consistent with the interpretation that the pinacol complex is a dimer in solution.

^{13}C VT-NMR spectra were also recorded to demonstrate that the differences in the methyl groups could also be observed in the ^{13}C NMR spectrum. Only one major signal at 24.4 ppm was observed for the complex until the sample was cooled below 245 K. At 230 K three signals at 25.5, 24.6, and 22.0 ppm were observed, supporting the observations in the ^{1}H NMR spectra that at this temperature the intramolecular movements are beginning to freeze out. At 215 K we observe six signals, 108.8, 104.1, 25.6, 24.7, 24.4, and 22.0 ppm. The two downfield signals are assigned to the quaternary carbons in the five-membered ring, whereas the four upfield signals are assigned to the four methyl groups. The chemical shift of the two carbons in the five-membered ring differed by 4.7 ppm. If indeed the complex in solution had been monomeric, the two carbons in the five-membered ring would not have given such different chemical shifts. The ^{13}C spectrum therefore further supports our assignment of a dimeric solution structure.

Table III. Bond Lengths and Bond Angles For Selected Organic Phosphates and Organic Vanadate Compounds

	methyl-pinacol phosphate[a]	chloro-pinacol-vanadate	ribonuclease-uridine-vanadate[b]	cyclic 2,3-*O*-cytidine phosphate[c]
		Bond Lengths, Å		
C_1O_5	1.49	1.45	1.63	1.47
C_1C_2	1.59	1.56	1.54	1.54
C_2O_3	1.50	1.47	1.39	1.42
O_3P/V_4	**1.59**	**1.96**	**1.89**	**1.62**
P/V_4O_5	**1.57**	**1.77**	**1.70**	**1.60**
C_1C_6	1.53	1.52	1.85 (1.52)	1.49
		Bond Angles, deg		
$O_5C_1C_2$	102	113	107	104
$C_1C_2O_3$	101	102	106	107
$C_2O_3(P/V_4)$	112	116	116	
$O_3(P/V_4)O_5$	114	79.7	86.1	96.4
$(P/V_4)O_5C_1$	112	119	115	
$O_5C_1C_6$	113	111	91.5 (116.5)	108.6
$C_6C_1C_7$	106	108		

[a] Reference 25. [b] Petsko, G.; Ringe, D., personal communication. These parameters were obtained directly from the coordinates. [c] Reference 31.

Discussion

Vanadate (VO_4^{3-}, HVO_4^{2-}, and $H_2VO_4^-$) is reported as an analogue for phosphate (PO_4^{3-}, HPO_4^{2-}, and $H_2PO_4^-$) with respect to electronic, structural, and biological properties. Vanadium in oxidation state +5 does, however, have some properties significantly different from phosphorus. Vanadate, unlike phosphate, rapidly forms oligomers or organic vanadates in aqueous solution and vanadium(V) is stable in a pentacoordinate geometry.[1] We therefore wanted to compare the structure of the pinacol–vanadium complex with pinacol phosphate derivatives.[25] The major difference between our pinacol complex and organic phosphates is the fact that the former is binuclear in vanadium and the latter will be mononuclear in phosphorus. Consequently, the vanadium is pentacoordinate in a dimeric complex whereas the phosphorus is tetracoordinate in a monomeric complex. The vanadium complex further contains a chloro substituent, which has been substituted with an alkoxy substituent in the organic phosphates. The latter is of minor importance with respect to the geometry around the pinacol moiety in analogy with a structural comparison that can be carried out between a cyclic phosphate methyl triester[28] and a cyclic phosphate diester bromide.[29] The organic phosphate has C–O bonds of 1.49 and 1.50 Å, a C–C bond in the five-membered ring of 1.59 Å, and CCO and COP angles of 102/101 and 112°. The geometry of the pinacol moiety in the pinacol–vanadium complex has C–O bonds of 1.45 and 1.47 Å, a C–C bond of 1.56 Å, and CCO and COV angles of 102/113 and 116° (Table III). Thus, the organic moieties in the chloropinacol–vanadium complex are structurally very similar to the methylpinacol phosphate despite the coordination differences around the phosphorus and the vanadium.

Ribonuclease A is believed to form a cyclic 2,3-*O*-cytidine phosphate as an intermediate when hydrolyzing RNA.[30] We therefore examined the structural properties of such a vanadate–nucleoside complex. The structure of the moiety in cyclic 2,3-*O*-cytidine phosphate containing the five-membered ring (O–C–C–O–P) has C–O bonds of 1.47 and 1.42 Å and a C–C bond of 1.54 Å, and the CCO angles are 104 and 107° (Table III).[31] This organic phosphate compound, despite the structural differences in the organic ligand, also has an organic moiety similar to the two pinacol complexes discussed above. We conclude that the organic moiety in five-membered cyclic vanadium derivatives

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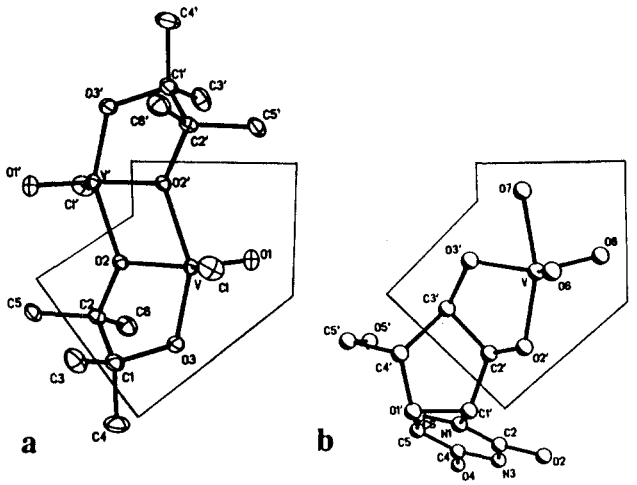

Figure 3. Comparison between the vanadium coordination in the pinacol-vanadate complex (a) and in the uridine-vanadate complex inside ribonuclease (coordinates given to us by Ringe and Petsko prior to publication) (b).

has a geometry similar to the structure of the organic moiety in organic phosphates.

Structural evidence on molecules obtained from X-ray crystallography presents precedence for the coordination geometry around vanadium. Related complexes could conceivably form in aqueous solution. We attempted to prepare and structurally characterize a complex with pinacol and various alkoxy substituents; however, we have not yet been successful in obtaining suitable crystals using this synthetic target. Chloro replacement of one alkoxy group stabilizes the vanadium complexes sufficiently so that crystals solvable by the X-ray experiment can be obtained. The replacement of the alkoxy group with a chloro substituent is not likely to effect the geometry of the diol in the vanadium complex wth respect to bond lengths and bond angles that do not directly involve the chlorine atom. The geometry observed for the chloropinacol complex therefore serves as a model for the corresponding complexes containing an alkoxide or a charged O^- as ligand.

VT-NMR studies suggest that the solution structure of the pinacol vanadium complex is a dimer. This observation is of particular interest because both 1:1 and 2:2 stoichiometries have been reported for the nucleoside–vanadate complexes in aqueous solutions. VT-NMR studies also suggest that organic solvent systems may not be all that different from aqueous solutions in terms of favoring nuclearity of complex systems.

The transition-state analogue uridine–vanadate complex binds 1000-fold better to ribonuclease A than the natural substrate.[5,6] We were particularly interested in comparing the structure of our pinacol complex with the uridine–vanadate adduct complexed to ribonuclease with respect to the geometry around the vanadium. The X-ray structure of the ribonuclease–uridine–vanadate complex has been solved independently by Petsko and Ringe and Wlodawer, but only preliminary results have been reported on this structure.[8a,b] We were, however, able to obtain the coordinates for the vanadate–uridine complex inside the protein directly from Ringe and Petsko.[8c] The structure of this uridine–vanadate complex is determined with much lower resolution than the pinacol complex, and thus the bond lengths and bond angles given in Table III are less well defined. Structural comparison between these two structures identify similarities and differences that may be important for the coordination around vanadium and the binding of the uridine–vanadate complex to ribonuclease. The chloropinacol complex differs from the uridine–vanadate complex with respect to nuclearity, a chloro substituent and the nature of the diol ligand. As seen from the insets in Figure 3, both complexes contain pentacoordinate distorted trigonal-bipyramidal vanadium with very similar geometry. In the pinacol complex the angle between apical substituents is 149° whereas the angle in the uridine–vanadate complex is 162°. The puckering in the five-membered ring in the uridine–vanadate complex is centered at the carbon atom as in the pinacol complex, although the puckering is less than observed for the pinacol complex. This difference is presumably caused by the fused organic ring in the uridine–vanadate complex. The uridine–vanadate complex also has one short (1.70 Å) and one long (1.89 Å) V–O bond in the five-membered ring. The four other V–O bonds range from 1.78 to 1.93 Å; in this complex, both the apical bonds are long (1.89 and 1.93 Å). The vanadium in the uridine–vanadate complex also contains a short and a long V–O bond in the five-membered ring, as we found in the pinacol complex. These observations suggest that vanadium will structurally favor such asymmetry with those types of ligands and consequently a uridine–vanadate complex will be asymmetric. If indeed such an asymmetric complex is similar to a complex formed along a reaction path, the complex is likely to bind tightly to the enzyme.

Conclusion. A cyclic chlorovanadium alkoxide complex was prepared and structurally characterized by X-ray crystallography to determine the coordination geometry around vanadium(V) in vanadium-containing transition-state analogues of hydrolytic enzyme reactions. We conclude that both the geometry of the organic fragment and the geometry around the vanadium are important for the tight binding of the uridine–vanadate transition-state analogue to ribonuclease. These studies suggest that vanadium complexes formed in nonaqueous media can indeed be used to obtain structural information on labile complexes formed in aqueous solutions or inside proteins.

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Registry No. 1, 130168-11-5; ribonuclease A, 9001-99-4; V, 7440-62-2.

Supplementary Material Available: Tables of bond lengths, bond angles, atomic coordinates, anisotropic thermal parameters, and calculated hydrogen atom positions (3 pages); listing of observed and calculated structure factors (8 pages). Ordering information is given on any current masthead page.