A Unique Coordination Mode for Citrate and a Transition Metal: $K_2[V(O)_2(C_6H_6O_7)]_2 \cdot 4H_2O$

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Received November 30, 1994[⊗]

Investigation of the aqueous coordination chemistry for citrate and vanadium(V) resulted in the isolation and characterization of $K_2[V(O)_2(C_6H_6O_7)]_2 \cdot 4H_2O$ (**1**). Complex **1** represents the first model of the tricarboxylic acid coordinated to the heteroatom found in the cofactor of nitrogenase and may be relevant to other physiological forms of metabolized vanadium(V). **1** was characterized by elemental analysis, IR, UV−vis, and ^{51}V NMR spectroscopy, and X-ray crystallography. Complex **1** crystallizes in the space group $P2_1/n$ (No. 14) with a = 9.3206(8) Å, b = 11.739(1) Å, c = 11.913(1) Å, β = 111.65(1)°, V = 1211.4(4) Å^3, and Z = 4. Full-matrix least-squares refinement resulted in residuals of R = 0.041 and R_w = 0.049. The citrate ligand displays a unique bidentate coordination to the vanadium via the bridging hydroxyl group and a unidentate carboxylate group. The structure is best described as a dimer of two five-coordinate vanadium centers doubly bridged by hydroxyl oxygen atoms.

Introduction

Tricarboxylic acids serve as important substrates in many biochemical processes.[1] Many of these reactions are catalyzed by metalloenzymes. Perhaps the best known of these enzymes is aconitase, which catalyzes the isomerization of citrate to isocitrate via the subsequent dehydration/rehydration of *cis*-aconitate.[2] Similar reactions are catalyzed by the [4Fe-4S]-containing enzyme maleic acid hydratase[3] and by the mononuclear Fe-containing enzymes mannonic[4] and altronic acid hydratases,[4] presumably by similar mechanisms. Another enzyme system in which a tricarboxylic acid plays a critical, but poorly understood, role is in the enzyme nitrogenase with its active site $MoFe_7S_9$·homocitrate cluster, FeMo-co.[5−8] The octahedral coordination sphere of the Mo within the cluster consists of three sulfides, a nitrogen atom from the imidazole group of a histidine residue, and two oxygen atoms from the hydroxyl group and one carboxyl moiety of the otherwise fully extended homocitric acid.[9−11] Given the spectroscopic evidence, homocitrate is presumed to bind to vanadium and iron in the alternative nitrogenases in an analogous fashion.[12−14] Citrate and other common polycarboxylic acids have also been postulated to play important physiological roles in the metabolism of metals such as iron and vanadium.[37] The variety of possible functions exhibited by citrate in its interactions with vanadium, a metal whose biological relevance is increasingly appreciated, prompted an investigation of the coordination chemistry of vanadium citrate complexes.

Experimental Section

NMR spectra were recorded on D_2O solutions that were 40 mM in **1** on either a Varian XL-300 or a Unity-300 spectrometer. IR spectra were recorded on KBr pellets on a Perkin Elmer 1600 FTIR spectrometer. Electronic absorption spectra were recorded on a Hewlett Packard 8452A spectrophotometer. Elemental analysis was performed by Robertson Analytical Laboratory.

Synthesis of $K_2[V(O)_2(C_6H_6O_7)]_2 \cdot 4H_2O$ (1). $K_2[V(O)_2(C_6H_6O_7)]_2 \cdot 4H_2O$ was prepared by modification of previously described methods.[15]

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⊗ Abstract published in *Advance ACS Abstracts,* July 1, 1995.

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Table 1. Crystallographic Data for $K_2[V(O)_2(C_6H_6O_7)]_2 \cdot 4H_2O$ (**1**)

empirical formula	$C_6H_{10}O_{11}KV$
fw	348.18
crystal color, habit	colorless, parallelpiped
crystal dimens	0.240 × 0.320 × 0.300 mm
crystal system	monoclinic
no. of reflns used for unit cell determn (2θ range)	23 (17.0−28.0°)
ω−scan peak width at half−height	0.33°
lattice parameters:	$a = 9.3206(8)$ Å
	$b = 11.739(1)$ Å
	$c = 11.913(1)$ Å
	$\beta = 111.65(1)°$
	$V = 1121.5(4)$ Å^3
space group	$P2_1/n$ (No. 14)
Z value	4
D_{calc}	2.063 g/cm^3
F_{000}	704
μ (Mo Kα)	11.86 cm^{-1}
diffractometer	Enraf−Nonius CAD−4
radiation	Mo Kα ($\lambda = 0.710\,69$ Å)
temperature	23 °C
attenuator	Zr foil (factor = 17.9)
takeoff angle	2.8°
detector aperture	3.0−4.0 mm horizontal
	3.0 mm vertical
crystal to detector distance	17.3 cm
scan type	$\omega-2\theta$
scan rate	1.9−16.5°/min (in ω)
scan width	$(1.10 + 0.35 \tan\theta)°$
$2\theta_{max}$	54.9°
no. of reflns measd	total: 3090
	Unique: 2920 ($R_{int} = 0.039$)

A colorless solution of potassium vanadate(V), prepared by dissolving V_2O_5 in an aqueous solution of KOH at 40 °C overnight, was cooled in an ice bath, and 1 equiv of aqueous citric acid was added dropwise. X-ray-quality crystals were obtained by cooling the solution to 4 °C for 2 days. Occasionally, when crystal growth was not forthcoming, a small quantity of cooled ethanol would be slowly added to the solution. Yield: 80%. Due to the efflorescence of crystals of complex **1**, elemental analysis was obtained for a sample exhaustively dried *in vacuo*. Anal. Calcd for $KVC_6H_6O_9$: K, 12.5; V, 16.3; C, 23.1; H, 1.9. Found: K, 12.41; V, 16.25; C, 23.04; H, 1.89. IR: ν_{as}(COO) 1688; ν_s(COO) 1396, 1332; $\nu_s(VO_2)$ 955; $\nu_{as}(VO_2)$ 889 cm^{-1}. ^{51}V NMR: a single broad peak at −545.27 ppm relative to $VOCl_3$.

Structure Determination. A colorless parallelepiped crystal of $K_2[V(O)_2(C_6H_6O_7)]_2 \cdot 4H_2O$ having approximate dimensions of 0.240 × 0.320 × 0.300 mm was mounted on a glass fiber. The intensity data were collected on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Mo Kα ($\lambda = 0.710\,69$ Å) radiation. Pertinent crystal data are given in Table 1. Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 23 carefully centered reflections in the range $17.00 < 2\theta < 28.00°$ corresponded to a monoclinic cell. On the basis of the systematic absences of $h01$, $h + 1 \neq 2n$, and $0k0$ $k \neq 2n$, and the successful solution and refinement of the structure, the space group was determined to be $P2_1/n$ (No. 14). The data were collected at a temperature of 23 ± 1 °C using the $\omega-2\theta$ scan technique to a maximum 2θ value of 54.9°. Of the 3090 reflections which were collected, 2920 were unique; equivalent reflections were merged. The intensities of three representative reflections which were measured after every 60 minutes of X-ray exposure remained constant throughout data collection, indicating crystal and electronic integrity.

The structure was solved by direct methods. The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 2365 observed reflections and 173 variable parameters. The refinement converged with $R = 0.041$ and $R_w = 0.049$. The final difference Fourier map showed residual maxima and minima of 0.73 and 0.80 e/Å^3, respectively. Neutral atom scattering factors were taken from Cromer and Waber.[16a] Anomalous dispersion effects were included in F_c;[16b] the values of $\Delta f'$ and $\Delta f''$ were those of Cromer.[16c] All calculations were performed using the TEXSAN[17] crystallographic software package of the Molecular Structure Corp.

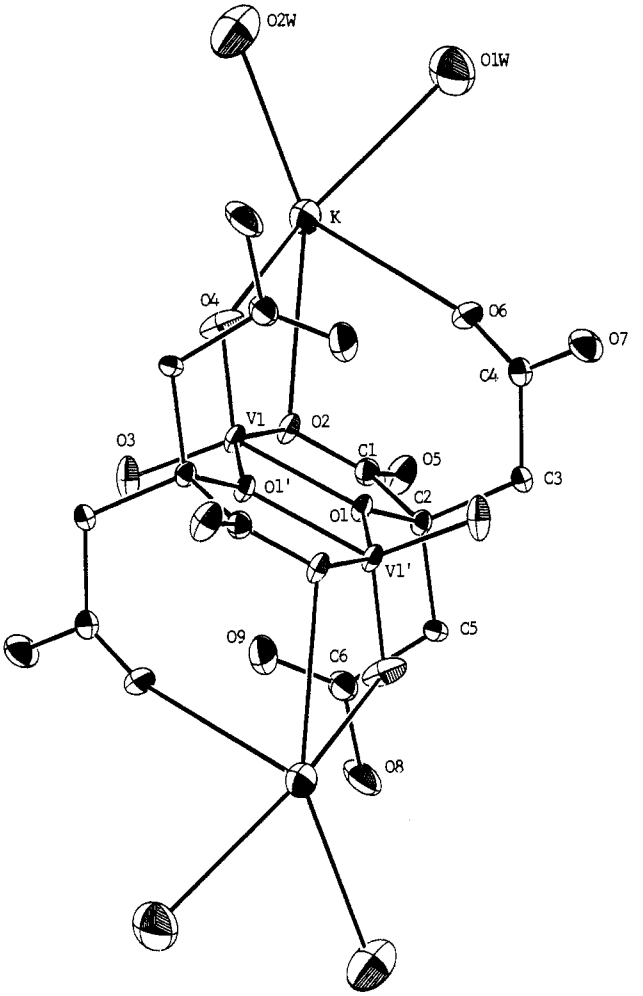

Figure 1. ORTEP drawing of $K_2[VO_2C_6H_6O_7]_2 \cdot 4H_2O$ (**1**). Distances (Å) and angles (deg): V−V′ = 3.211(2), V−O(1) = 2.013(2), V−O(1′) = 1.957(2), V−O(2) = 1.980(2), V−O(3) = 1.623(2), V−O(4) = 1.611(2); O(1)−V−(O1′) 72.00(8), O(1)−V−O(2) = 77.29(7), O(1)−V−O(3) = 130.5(1), O(1)−V−O(4) = 123.0(1), O(1′)−V−O(2) = 149.20(7), O(1′)−V−O(3) = 100.07(9), O(1′)−V−O(4) = 101.55(9), O(2)−V−O(3) = 97.92(9), O(2)−V−O(4) = 97.02(9), O(3)−V−O(4) = 106.4(1).

Results and Discussion

The structure of **1** (Figure 1) is best described as a dimer of two five-coordinate vanadium centers doubly bridged by hydroxyl oxygen atoms. The coordination sphere of the vanadium consists of the O(1′) and O(1) hydroxyl groups and an oxygen atom, O(2), from the C(1) carboxylate group of citrate as well as two oxo ligands, O(3) and O(4) (Table 2). The bidentate citrate ligand itself is fully extended, leaving the two terminal COOH groups uncoordinated. The vanadium atoms are related by an inversion center in the V_2O_2 core and are separated by a V−V′ distance of 3.211(2) Å. The core is further defined by the O(1′)−V−O(1) angle of 72(8)° and the V−O(1)−V′ angle of 108(8)° (Table 3).

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Table 2. Selected Atomic Coordinates and Thermal Parameters[a,b] for Compound **1**

atom	*x*	*y*	*z*	B_{eq}, Å^2
V(1)	0.12520(5)	0.09114(4)	0.07872(4)	1.49(2)
K	0.04308(8)	0.38934(6)	0.17346(7)	3.12(3)
O(1W)	−0.1999(4)	0.5510(3)	0.0920(3)	6.00(2)
O(1)	−0.0693(2)	0.0072(1)	0.0637(2)	1.42(6)
O(2)	0.0857(2)	0.1436(2)	0.2227(2)	1.78(7)
O(2W)	0.1166(4)	0.5871(3)	0.0781(3)	5.50(1)
O(3)	0.3050(2)	0.0557(2)	0.1463(2)	2.77(8)
O(4)	0.1248(3)	0.2149(2)	0.0203(2)	3.09(9)
O(5)	−0.0467(2)	0.1215(2)	0.3420(2)	2.61(8)
O(6)	−0.2248(2)	0.2513(2)	0.0823(2)	3.47(9)
O(7)	−0.4413(3)	0.1817(2)	−0.0519(2)	2.97(8)
O(8)	0.0064(4)	−0.2554(3)	0.3124(4)	8.10(2)
O(9)	0.1400(3)	−0.1228(2)	0.2647(3)	4.60(1)
C(1)	−0.0241(3)	0.1002(2)	0.2491(2)	1.65(9)
C(2)	−0.1306(3)	0.0158(2)	0.1568(2)	1.32(8)
C(3)	−0.2970(3)	0.0595(2)	0.1035(2)	1.67(9)
C(4)	−0.3143(3)	0.1742(2)	0.0444(3)	2.00(1)
C(5)	−0.1316(3)	−0.0992(2)	0.2162(2)	1.68(9)
C(6)	0.0212(4)	−0.1573(3)	0.2669(3)	2.70(1)
H(1)	−0.443	0.251	−0.072	5.0
H(1W)	−0.293	0.569	0.091	13.0
H(2W)	−0.210	0.592	0.047	13.0
H(2)	−0.360	0.006	0.048	2.3
H(3W)	0.095	0.651	0.118	6.7
H(3)	−0.338	0.064	0.166	2.3
H(4)	−0.176	−0.089	0.278	2.6
H(4W)	0.226	0.586	0.094	6.7
H(5)	−0.192	−0.152	0.164	2.2
H(6)	0.013	−0.300	0.285	6.2

[a] Estimated standard deviations in the last significant digits, as observed from the least-squares refinements, are given in parentheses. [b] *B* values for anisotropically refined atoms are given in the form of the equivalent isotropic displacement parameter defined as $B_{eq} = {}^1/_3\sum_i\sum_j B_{ij}a_ia_j$.

Table 3. Selected Bond Angles (deg) for **1**

O(1)−V−O(1′)	72.00(8)	C(3)−C(2)−C(5)	108.1(2)
O(1)−V−O(2)	77.29(7)	C(2)−C(3)−C(4)	114.4(2)
O(1)−V−O(3)	130.5(1)	O(6)−C(4)−O(7)	123.8(3)
O(1)−V−O(4)	123.0(1)	O(6)−C(4)−C(3)	124.1(3)
O(1′)−V−O(2)	149.20(7)	O(7)−C(4)−C(3)	112.1(2)
O(1′)−V−O(3)	100.07(9)	C(2)−C(5)−C(6)	115.1(2)
O(1′)−V−O(4)	101.55(9)	O(8)−C(6)−O(9)	123.6(3)
O(2)−V−O(3)	97.92(9)	O(8)−C(6)−C(5)	110.0(3)
O(2)−V−O(4)	97.02(9)	O(9)−C(6)−C(5)	126.4(3)
O(3)−V−O(4)	106.4(1)	O(1W)−K−O(2)	139.12(8)
V−O(1)−V′	108.00(8)	O(1W)−K−O(2W)	65.6(1)
V−O(1)−C(2)	120.1(1)	O(1W)−K−O(4)	126.44(9)
V′−O(1)−C(2)	131.4(1)	O(1W)−K−O(6)	76.84(9)
V−O(2)−C(1)	120.6(2)	O(2W)−K−O(4)	99.45(8)
V−O(4)−K	108.1(1)	O(2W)−K−O(6)	129.51(8)
O(2)−C(1)−O(5)	124.0(2)	O(2W)−K−O(4)	64.99(9)
O(2)−C(1)−C(2)	116.3(2)	O(2W)−K−O(6)	66.73(8)
O(5)−C(1)−C(2)	119.7(2)	O(2)−K−O(4)	53.86(6)
O(1)−C(2)−C(1)	105.3(2)	O(2)−K−O(6)	63.30(6)
O(1)−C(2)−C(3)	109.6(2)	O(2)−K−O(2W)	149.92(8)
O(1)−C(2)−C(5)	111.8(2)	O(4)−K−O(6)	76.35(7)
C(1)−C(2)−C(3)	111.6(2)	K−O(6)−C(4)	165.1(2)
C(1)−C(2)−C(5)	110.5(2)		

The carboxylate group α to the hydroxy group is clearly monodentate through O(2) with a V−O(2) bond length of 1.980(2) Å. The V=O bond lengths are 1.623(2) and 1.611(2) Å, respectively (Table 4). The structure of **1** is one of a handful of examples of a vanadium(V) species with a dioxo moiety and three other oxygen donors.[18] When compared to those of other vanadium(V) alkoxides such as $(NH_4)_2[V(OC(CH_2CH_3)_2COO)(O)_2]_2$ (**2**),[18] $K_2[VO(O_2)(C_6H_6O_7)]_2{\cdot}2H_2O$ (**3**),[15] $VO(OCH_2CH_2Cl)_3$ (**4**),[19] and $[\mu\text{-}\eta^3\text{-}C_5Me_5O_3)V(O)]_2$ (**5**),[20] the V=O bonds

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Table 4. Selected Bond Distances (Å) for **1**

V−O(1)	2.013(2)	C(3)−C(4)	1.500(4)
V−O(1′)	1.957(2)	C(5)−C(6)	1.492(4)
V−O(2)	1.980(2)		
V−O(3)	1.623(2)	C(3)−H(2)	0.937
V−O(4)	1.611(2)	C(3)−H(3)	0.949
		C(5)−H(4)	0.971
V−V′	3.211(2)	C(5)−H(5)	0.910
O(1)−C(2)	1.426(3)	V−K	3.8407(9)
O(2)−C(1)	1.282(3)	K−O(2)	2.942(2)
O(5)−C(1)	1.227(3)	K−O(4)	3.021(2)
O(6)−C(4)	1.200(4)	K−O(6)	2.836(2)
O(7)−C(4)	1.312(4)		
O(8)−C(6)	1.301(4)	K−O(1W)	2.838(3)
O(9)−C(6)	1.189(4)	K−O(2W)	2.779(3)
		O(1W)−H(1W)	0.889
C(1)−C(2)	1.540(3)	O(1W)−H(2W)	0.701
C(2)−C(3)	1.531(3)	O(2W)−H(3W)	0.945
C(2)−C(5)	1.526(3)	O(2W)−H(4W)	0.968

of **1** (1.623 and 1.611 Å) are quite similar to those of **2** (1.617 and 1.611 Å) and **3** (1.601 Å) but longer than the same bonds in **4** (1.584 Å) and **5** (1.581 Å). Further, the bridging V−O(alkanolate) distances of **1** (2.013 and 1.957 Å) are consistent with the corresponding V−O bond lengths in **2** (1.973 and 1.984 Å), **3** (1.991 and 2.031 Å), and **5** (1.957 Å). These short V−O bonds from the hydroxyl ligands forming the O(1′)−V−O(1)−V′ core of **1** suggest that the hydroxyl oxygens are deprotonated. Such a substantial decrease in the pK_a of the citrate hydroxyl group upon coordination to vanadium has been similarly noted for a number of other transition metals.[15,21−23,26a,27]

Complex **1** represents a unique example of a structurally characterized 1:1 metal−citrate complex which exhibits bidentate coordination of the polycarboxylic acid to the metal.[24] Furthermore, the extended conformation of citrate is analogous to the unique coordination of homocitric acid to the molybdenum—and by extension the vanadium—site within the cofactor of nitrogenase.[10−12] Interestingly, the X-ray crystallographic analysis of the enzyme aconitase with both substrate and substrate inhibitors demonstrates that citrate is bound to an Fe corner of the active site [4Fe-4S] cubane in a similar bidentate fashion.[25] Nevertheless, all of the previously reported structures of biologically related metals and citrate demonstrate tridentate coordination via the hydroxyl group, the carboxylate α to the hydroxyl group, and one of the terminal carboxylates.[21,24,26 b,27,34a] Such is the case in the closely related peroxide adduct $K_2[VO(O_2)(C_6H_6O_7)]_2{\cdot}2H_2O$, prepared by Djordjevic *et al.*, in which the citrate ligand is tridentate, resulting in a crowded seven-coordinate vanadium center.[15] Additionally, the remaining free carboxylates will often coordinate to a second metal,

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forming higher nuclearity species as in the case of the iron citrate and nickel citrate complexes $[Fe^{II}(H_2O)_6][Fe^{II}(C_6H_5O_7)(H_2O)]_2 \cdot 2H_2O$ and $\{[N(CH_3)_4]_5[Ni^{II}_4(C_6H_4O_7)_3(OH)(H_2O)] \cdot 18H_2O\}$, respectively.[26] Coucouvanis *et al.* recently reported an infrared study which demonstrates that citrate can coordinate to the Mo in an $MoFe_3S_4$ cubane through two carboxylates and the deprotonated hydroxyl moiety.[27] These cubanes have been shown to be catalytically active toward the reduction of hydrazine to ammonia only if the hapticity of the tridentate citrate changes to bidentate in order to form an open coordination site for the substrate.[28]

It has been suggested that a possible function of the tricarboxylic acid in the biosynthesis of the cofactor of nitrogenase is to mobilize molybdenum or vanadium from the appropriate storage enzyme.[8b] Molybdenum and vanadium are believed to be taken up by organisms as MoO_4^{2-} or VO_4^{3-},[8b,12] yet reports of the oxidation states of the heteroatom within FeMo-co and FeV-co in the resting state range from +3 to +4, thereby, requiring a one-, two-, or three-electron reduction during assembly into the final cluster.[5,13,14] It has been found that while molybdate readily undergoes electroreduction below a pH of 5, it is polarographically inactive at higher pH with common inorganic supporting electrolytes.[29] Yet, in a citrate medium at pH 7, molybdate reduction most likely proceeds from Mo(VI) to Mo(V) to Mo(III).[30,31] Potentiometric studies of the speciation of the oxomolybdenum−citrate system have shown that at neutral pH the dominant oxomolybdenum−citrate species are formulated as $[MoO_4HCit]^{4-}$ [32] and $[MoO_4H_2Cit]^{3-}$.[33] Similar studies of MoO_2(catecholate) not only demonstrate a similar reduction sequence but also reveal the binding of ligands at coordination sites made available by the reduction of the oxomolybdenum groups.[31a] Such structural changes would be essential for the assembly of the final cofactor cluster from an oxomolybdenum− or oxovanadium−citrate precursor. This redox behavior suggests that the tricarboxylic acid might be involved not only in mobilization of needed metals from their storage enzymes but also in facilitating the requisite oxidation states of the mobilized metals for subsequent processing and assembly. Therefore, complex **1** may represent an early mobilized species utilized in the assembly of FeV-co.

It is interesting to note that one of the essential features of the chemistry of high oxidation state vanadium complexes is the V(V)/V(IV) redox process. In aqueous solutions, the redox properties of V(V) can be tuned by the composition and stereochemistry of its ligand environment, resulting in reports of V(V) acting as a mild oxidant in aerobic aqueous solutions.[15,34 a,b] Such solution behavior is observed for **1**, which upon standing changes color from a pale green/yellow to an intense blue (λ_{max}= 600 nm), indicative of reduction to V(IV).[34c] Although the precise nature of this reduction has yet to be elucidated, similar chemistry occurring at a variety of rates has been reported for a number of organic acids coordinated to vanadium(V) in aqueous solution.[15,34] Such redox behavior stands in contrast to the apparent solution stability of the 2-hydroxy acid ligand complex of vanadium(V) $(NH_4)_2[V(OC(CH_2CH_3)_2COO)(O)_2]_2$.[18]

Complex **1** is also of note in light of reported interactions between vanadium(V) and the iron transport protein transferrin.[35-38] Chasteen *et al.* have demonstrated that in humans vanadium(V) is exclusively bound to transferrin.[36] Further, ultraviolet difference analysis of vanadium(V) transferrin suggests that the VO_2^+ moiety is the most likely vanadium(V) species bound to the protein.[37] Insomuch as citrate ligands within the cells and serum are known to compete for iron and aluminum ions bound to transferrin[38] and that citrate has long been proposed as a possible chelator to accelerate the release of iron within the cell's endosomal compartment,[39] citrate might, by analogy, be involved in the metabolism of vanadium transferrin proteins. Consequently, complex **1** could represent a physiologically relevant metabolized form of vanadium(V). If this is indeed the case, previously reported speciation studies using NMR and potentiometric techniques which suggest the existence of three ternary $(H^+)(H_2VO_4^-)(C_6H_5O_7)$ complexes of 1:2:1, 2:2:1, and 3:2:1 formulations in aqueous solution[40] should be reexamined.

Tricarboxylic acids interact with a number of biological metals in essential processes of metabolism.[1,5] Yet, despite the potenial for polymerization or tridentate coordination, these tricarboxylic acids appear to interact with the requisite metals solely in a bidentate fashion.[3,4,10,25] Complex **1** represents a potentially useful structural model for this type of coordination as exhibited at the heterometallic site of the cofactor of nitrogenase. The fully extended citrate is coordinated to the vanadium by the deprotonated hydroxyl group and the carboxylate α to the hydroxyl group. In addition, **1** may provide useful insights into the mobilization of vanadium, as it represents a possible early intermediate in the biosynthesis of FeV-co as well as a physiologically relevant form of metabolized vanadium(V).

Acknowledgment. We thank W. H. Armstrong and R. T. Chang for their helpful discussions. This work was supported by a grant from the National Institutes of Health, GM-283558-16.

IC9413629

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