J. Am. Chem. Soc. 1990, 112, 2627-2632

Synthesis and Characterization of a Series of Vanadium–Tunichrome B 1 Analogues. Crystal Structure of a Tris(catecholamide) Complex of Vanadium

A. Ray Bulls, C. Greg Pippin, F. Ekkehardt Hahn, and Kenneth N. Raymond*

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. Received May 8, 1989

Abstract: Two isomeric tris(pyrogallol) derivatives, 2,3,4-TRENPAM and 3,4,5-TRENPAM, have been synthesized with the use of β,β',β''-triaminotriethylamine (TREN) as the molecular skeleton and the 2,3,4 or 3,4,5 isomers of trihydroxybenzoic acid ligand groups. Vanadium(IV) complexes of these ligands have been prepared in 25 and 66% yields, respectively. The water-soluble 2,3,4-TRENPAM complex of vanadium(IV) has been characterized by spectrophotometric and voltammetric methods; the (3,4,5-TRENPAM)V^{IV} complex is an insoluble polymer. The reduction potential for the vanadium(IV/III) couple of $[V(2,3,4\text{-TRENPAM})]^{2-}$ is pH dependent, varying from −0.41 V (vs NHE in H_2O, pH 7) to −0.67 V (vs NHE in H_2O, pH 11.7). Complexes of the previously described macrocyclic tris(catecholate) ligand (TRENCAM) with vanadium(III) and vanadium(IV) are reported. The vanadium(III)–TRENCAM salt $K_3[V(\text{TRENCAM})]$ crystallizes in cubic space group $P2_13$ with $Z = 4$. The vanadium ion is ligated by the six catechol oxygens in a distorted octahedral environment (crystallographic C_3 symmetry) with V–0 distances of 1.985 (5) and 2.007 (5) Å and a trigonal twist angle of 40.8 (6)°. The reduction potential for the vanadium(IV/III) couple of [V(TRENCAM)] is −0.37 V (vs NHE in H_2O, pH 11.7) and is essentially pH independent. The reduction potential of the vanadium(V/IV) couple is +0.53 V (vs NHE in dimethylformamide). The implications of these results for the in vivo stabilization of vanadium(III) by tunichrome B 1 are discussed.

The ability of marine organisms such as the tunicates to accumulate vanadium from sea water has attracted considerable recent attention.[1-4] Several authors[5-7] have suggested that low molecular weight pigments known as tunichromes serve as complexing agents for the accumulation and storage of the intracellular vanadium. The tris(trihydroxyphenyl) derivative, tunichrome B 1 (Figure 1), has been isolated from the blood of *Ascidia nigra* and has been suggested to be such a vanadium complexing agent.[5-7] The biological role of the intracellular vanadium and the vanadium oxidation state and coordination environment remain matters of controversy. Data obtained by magnetic susceptibility measurements suggest that the vanadium is present within the blood cells of *A. nigra* in predominately the III state,[8] but other reports suggest the vanadium is predominately in the IV oxidation state.[9]

While the binding of tunichrome B 1 to vanadium has not been structurally characterized, the presence of three pyrogallol moieties suggests the possibility of a tris-"catechol" mode of bonding. This type of bonding has been suggested in a recent communication that describes the synthesis of vanadium complexes of N,N',N''-tris(2,3,4-trihydroxybenzoyl)-1,5,10-triazadecane.[10] However, the first structure of a vanadium–pyrogallol complex determined by X-ray diffraction shows it to be a pyrogallol-bridged dimer.[11]

This paper reports the synthesis of two isomeric tris(trihydroxyphenyl) derivatives containing the β,β',β''-triaminotriethylamine (TREN) backbone (Figure 1). The preparation and characterization of the vanadium(IV) complexes of these new ligands are presented. The synthesis, characterization, and crystal structure of a vanadium(III) complex ligated by the analogous tricatecholate ligand TRENCAM[12] (Figure 1) are presented for comparison. Since the vanadium may be coordinated by three catechol (or pyrogallol) groups for each of these ligands, their complexes provide models for the possible hexadentate binding of tunichrome B 1 to vanadium in the polymeric solid complex. [In the following paper, when the degree of ligand protonation needs to be explicit, it will be denoted by putting the number of protons at the end of the ligand name. Thus, the TREN catechol derivative, with six dissociable protons, as the neutral molecule is tRENCAMH_6. For the pyrogallol derivative, with nine dissociable protons, the neutral ligand is TRENPAMH_9, and the tris(catechol)vanadium(IV) complex is $[V(\text{TRENPAMH}_3)]^{2-}$.]

Experimental Section

Synthesis. All manipulations were performed under an argon atmosphere with standard Schlenk line techniques. All solvents were reagent grade and were used as received. The reagents 2,3-dimethoxybenzoic acid, 2,3,4-trimethoxybenzoic acid, and 3,4,5-trimethoxybenzoic acid were obtained from Aldrich Chemical Co.; TREN (98%) was a generous gift from W. R. Grace Co. The ^1H NMR spectra were recorded on 200- or 400-MHz spectrometers with Me_4Si as an internal standard. Thin-layer chromatography was performed on precoated Analtech GHLF silica get sheets and visualized by UV light. Microanalysis and positive FAB mass spectra (thioglycerol matrix) were performed by the Analytical Services Laboratory at the College of Chemistry, University of California, Berkeley.

Physical Measurements. Visible spectra were measured in a quartz cuvette fitted with a Kontes needle valve on a Hewlett-Packard 8450A diode array spectrophotometer. Electrochemical experiments were performed with a Princeton Applied Research 174A polarographic analyzer. All potentials are relative to the saturated sodium calomel electrode (SSCE) or the Ag/AgCl electrode and are uncorrected for junction potentials. A platinum disk or hanging-drop mercury electrode was used for cyclic voltammetric experiments. Aqueous solutions were 0.4 M in sodium perchlorate ($NaClO_4$) and pH 11.7; distilled, anhydrous dimethylformamide (DMF) solutions were 0.1 M in tetrabutylammonium perchlorate (TBAP).

---

* To whom correspondence should be addressed.

(1) Bayer, E.; Koch, E.; Anderegg, G. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, no. 6, and references therein.

(2) Oltz, E. M.; Bruening, R. C.; Smith, M. J.; Kustin, K.; Nakanishi, K. *J. Am. Chem. Soc.* **1988**, *110*, 6162–6172, and references therein.

(3) Bonadies, J. A.; Pecoraro, V. L.; and Carrano, C. J. *J. Chem. Soc., Chem. Commun.* **1986**, 1218.

(4) Hawkins, C. J. *Pure Appl. Chem.* **1988**, *60*, 1267–1270.

(5) Bruening, R. C.; Oltz, E. M.; Furukawa, J.; Nakanishi, K.; Kustin, K. *J. Am. Chem. Soc.* **1985**, *107*, 5298–5300.

(6) Bruening, R. C.; Oltz, E. M.; Furukawa, J.; Nakanishi, K.; Kustin, K. *J. Nat. Prod.* **1986**, *49*, 193–204.

(7) Macara, I. G.; McLeod, G. C.; Kustin, K. *Biochem. J.* **1979**, *181*, 457–465.

(8) Lee, S.; Kustin, K.; Robinson, W. E.; Frankel, R. B.; Spartalian, K. *J. Inorg. Biochem.* **1988**, *33*, 183–192.

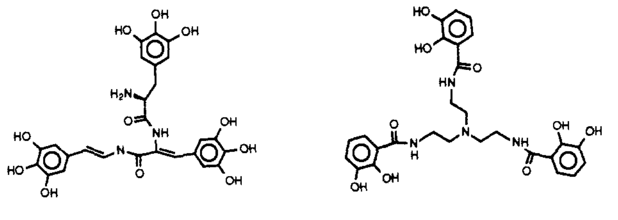
(9) Brand, S. G.; Hawkins, C. J.; Parry, D. L. *Inorg. Chem.* **1987**, *26*, 627–629.

(10) Lee, S.; Nakanishi, K.; Chiang, M. Y.; Frankel, R. B.; Spartalian, K. *J. Chem. Soc., Chem. Commun.* **1988**, 785.

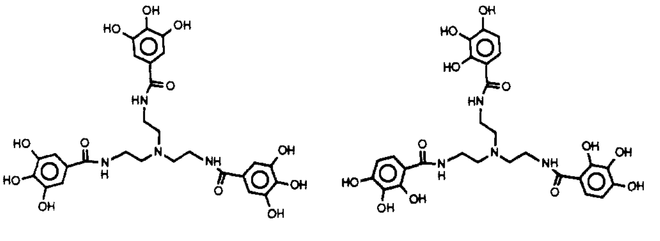
(11) Kime-Hunt, E.; Spartalian, K.; Carrano, C. J. *J. Chem. Soc., Chem. Commun.* **1988**, 1217.

(12) Rodgers, S. J.; Lee, C.; Ng, C. Y.; Raymond, K. N. *Inorg. Chem.* **1987**, *26*, 1622–1625.

0002-7863/90/1512-2627$02.50/0



Tunichrome b-1 TRENCAMH$_6$



3,4,5-TRENPAMH$_9$ (**6**) 2,3,4-TRENPAMH$_9$ (**3**)

Figure 1. Structures of tunichrome B 1 and the synthetic TRENCAMH$_6$ analogues described in this paper.

Preparation of the 2-Mercaptothiazoline Derivative of 2,3,4-Trimethoxybenzoic Acid (1). 2,3,4-Trimethoxybenzoic acid (8.1 g, 38.2 mmol), 2-mercaptothiazoline (4.55 g, 38.2 mmol), and *N,N'*-dicyclohexylcarbodiimide (8.16 g, 40 mmol) were combined in ca. 150 mL of CHCl$_3$. Upon addition of ca. 50 mg of 4-(dimethylamino)pyridine, the solution turned bright yellow and a white precipitate formed. After the solution was stirred for 12 h, the solid was removed by filtration. The filtrate was washed with 3 × 75 mL of aqueous base (pH 12), and the solvent was removed in vacuo. The crude yellow solid was recrystallized from CHCl$_3$/hexane to afford 7.79 g (65%) of bright yellow product. Anal. Calcd for C$_{13}$NO$_4$S$_2$H$_{15}$ (found): C, 49.82 (49.82); H, 4.82 (4.80); N, 4.47 (4.50).

Preparation of 2,3,4-TRENPAMMe$_9$ (2). Compound **1** (7.64 g, 24.4 mmol) and TREN (1.19 g, 8.1 mmol) were combined in 100 mL of CHCl$_3$, and the solution was stirred overnight. The CHCl$_3$ solution was washed with 3 × 100 mL of aqueous base (pH 12) to remove the 2-mercaptothiazoline byproduct, and the CHCl$_3$ was removed in vacuo. The crude solid was recrystallized from ethyl acetate/hexane to yield 5.46 g (92%) of white solid. Anal. Calcd for C$_{36}$N$_4$O$_{12}$H$_{48}$ (found): C, 59.33 (58.64); N, 7.69 (7.93); H, 6.64 (6.63). ^{1}H NMR (400 MHz, D$_2$O) δ 3.43 (br, 6 H), 3.57 (br, 6 H), 6.00 (d, 3 H, J = 7.0 Hz), 6.54 (d, 3 H, 7.0 Hz) (the hydroxyl and amide protons are unobserved due to exchange with D$_2$O).

Preparation of 2,3,4-TRENPAMH$_9$·HBr·H$_2$O·0.33C$_4$H$_{10}$O (3). Compound **2** (5.40 g, 7.4 mmol) was dissolved in ca. 100 mL of CHCl$_3$ under an argon atmosphere. BBr$_3$ (ca. 10 mL, 100 mmol) was added dropwise, and the resulting suspension was kept at reflux overnight. Methanol (ca. 50 mL) was carefully added to the reaction mixture to quench the excess BBr$_3$, and the solvents were removed in vacuo. The oily product was dissolved in ca. 75 mL of methanol, which was then removed in vacuo at 50 °C. Repeating this process (10 × 75 mL of methanol) served to remove the borate byproducts and gave an off-white solid. The solid was recrystallized from CH$_3$OH/diethyl ether to yield 3.86 g (72%) of white product. Anal. Calcd for C$_{27}$N$_4$O$_{12}$H$_{31}$Br·H$_2$O·0.33C$_4$H$_{10}$O (found): C, 46.23 (46.79); H, 4.75 (5.10); N, 7.99 (7.65); Br, 11.39 (11.97). ^{1}H NMR (400 MHz, D$_2$O) δ 3.45 (br, 6 H), 3.58 (br, 6 H), 6.51 (s, 6 H) (the hydroxyl and amide hydrogens are unobserved due to exchange with D$_2$O). Integration of the proton signals in the ^{1}H NMR showed $^1/_3$ C$_4$H$_{10}$O.

Preparation of the 2-Mercaptothiazoline Derivative of 3,4,5-Trimethoxybenzoic Acid (4). In a procedure analogous to that described for compound **1**, 9.03 g of 3,4,5-trimethoxybenzoic acid and 5.07 g of 2-mercaptothiazoline gave 7.95 g (60%) of bright yellow product. Anal. Calcd for C$_{13}$NO$_4$S$_2$H$_{15}$ (found): C, 49.82 (50.03); N, 4.47 (4.66); H, 4.82 (5.02).

Preparation of 3,4,5-TRENPAMMe$_9$ (5). In a procedure analogous to that described for compound **2**, 5.75 g of **4** and 0.89 g of TREN afforded 3.8 g (86%) of colorless, crystalline product. Anal. Calcd for C$_{36}$N$_4$O$_{12}$H$_{48}$ (found): C, 59.33 (59.51); N, 7.69 (7.98); H, 6.64 (6.85).

Preparation of 3,4,5-TRENPAMH$_9$·HBr·1.2C$_4$H$_{10}$O·NaBr (6). In a procedure analogous to that described for compound **3**, 3.78 g of compound **5** gave 3.33 g (73%) of white product. Anal. Calcd for C$_{27}$N$_4$O$_{12}$H$_{31}$Br·1.2C$_4$H$_{10}$O·NaBr (found): C, 43.64 (44.59); H, 4.95 (5.61); N, 6.40 (6.32); Br, 18.26 (18.06). Integration of the proton signals in the ^{1}H NMR showed 1.2 C$_4$H$_{10}$O.

Preparation of [V(2,3,4-TRENPAM)](NEt$_3$H)$_2$·3H$_2$O (7). Under argon, an aqueous solution of VOSO$_4$·3H$_2$O (0.24 g, 1.1 mmol) was added to 0.81 g (1.1 mmol) of **3** dissolved in 10 mL of H$_2$O. Upon addition of 1.0 g (9.9 mmol) of NEt$_3$, the solution turned dark purple black. The solution was stirred overnight, and the H$_2$O was removed under reduced pressure. The solid was dissolved in ca. 10 mL of methanol, and diethyl ether was slowly added to induce precipitation of the deeply colored product. The solid was collected by filtration, washed with isopropyl alcohol and then diethyl ether, and dried in vacuo to yield 0.25 g (25%) of dark purple solid. Anal. Calcd for C$_{39}$N$_6$O$_{12}$H$_{56}$·3H$_2$O (found): C, 51.43 (51.61); H, 6.86 (6.83); N, 9.23 (9.36). Positive FABMS, *m/e* 650 (dianion + 3 H$^+$).

Preparation of [V(3,4,5-TRENPAM)(NEt$_3$H)$_2$]·4H$_2$O (8). Compound **6** (0.64 g, 0.73 mmol) dissolved in 10 mL of H$_2$O was added to an aqueous solution of VOSO$_4$·3H$_2$O (0.16 g, 0.74 mmol) under an argon atmosphere. Upon addition of 0.8 g (7.9 mmol) of NEt$_3$, a dark purple solid precipitated from solution. The solid was collected by filtration, washed with H$_2$O and methanol, and dried in vacuo to yield 0.45 g (66%) of product. Anal. Calcd for C$_{39}$N$_6$O$_{12}$H$_{56}$·4H$_2$O (found): C, 50.43 (50.36); H, 6.95 (6.52); N, 9.05 (9.15).

Preparation of [V(H$_3$TRENCAM)] (9). TRENCAMH$_6$·HBr (1.77 g, 2.79 mmol), prepared as described previously,[12] was dissolved in ca. 20 mL of 15% NH$_4$OH. Into this solution was syringed 0.44 g (2.8 mmol) of VCl$_3$ in ca. 20 mL of H$_2$O. Heating the resultant green suspension to 50 °C for 0.5 h gave a dark orange-brown solution. The volume of H$_2$O was reduced to ca. 10 mL, during which time a green suspension developed. The suspension was filtered, washed with 2 × 20 mL of H$_2$O, and dried in vacuo. The yield of dark green solid was 0.88 g (52%). Anal. Calcd for VC$_{27}$N$_4$O$_9$H$_{24}$ [V(H$_3$TRENCAM)] (found): C, 53.80 (52.81); N, 9.30 (10.44); H, 4.02 (5.59); V, 8.46 (7.98); Cl + Br, 0 (0.62).

Preparation of K$_3$[V(TRENCAM)]·H$_2$O·CH$_3$CH$_2$OH (10). To 0.88 g (1.5 mmol) of [V(H$_3$TRENCAM)] was added 3.5 equiv of KOH dissolved in ca. 10 mL of H$_2$O. The resultant orange-brown solution was heated to 50 °C for 1 h. The volume of H$_2$O was reduced to ca. 2 mL, and ca. 20 mL of absolute ethanol was added to the solution, resulting in an orange precipitate. This product (0.35 g, 31%) was washed with 2 × 20 mL of absolute ethanol and dried in vacuo. Anal. Calcd for K$_3$VC$_{29}$N$_4$O$_{11}$H$_{32}$ (found): C, 44.66 (44.81); N, 7.18 (7.09); H, 4.18 (4.21); V, 6.53 (6.85); K, 15.0 (14.2). Positive FABMS: *m/e* 641 (K[V(TRENCAM)]$^{2-}$ + 3 H$^+$), 679 (K$_2$[V(TRENCAM)]$^-$ + 2 H$^+$), 717 (K$_3$[V(TRENCAM)] + H$^+$).

Preparation of [NH$_4$]$_2$[V(TRENCAM)]·2H$_2$O (11). An aqueous solution of 1.0 g (5.5 mmol) of VOSO$_4$·H$_2$O in ca. 10 mL of H$_2$O was slowly syringed into 3.4 g (5.4 mmol) of TRENCAMH$_6$·HBr dissolved in ca. 30 mL of 15% aqueous ammonia. The resultant deep purple-black solution was stirred for 1 h. The volume of solvent was reduced to ca. 5 mL, resulting in the formation of a purple-black precipitate. This solid was collected by filtration, washed with ethanol, and dried in vacuo to yield 2.94 g of product (81% yield). Anal. Calcd for VC$_{27}$N$_6$O$_{11}$H$_{36}$ (found): C, 48.26 (48.60); N, 12.51 (12.30); H, 5.55 (5.40).

X-ray Crystallography. X-ray-quality crystals of K$_3$[V(TRENCAM)]·4MeOH·2H$_2$O were obtained from saturated methanol/diethyl ether solutions. Due to the extreme oxygen sensitivity of K$_3$[V(TRENCAM)], a single crystal was mounted on a glass fiber under a cold stream of N$_2$ and placed directly on an Enraf-Nonius CAD-4 diffractometer without preliminary precession photographs. Study of intense, low-angle reflections from this crystal established the space group as $P2_13$. After accurate centering of 24 high-angle reflections chosen from different regions of reciprocal space, a unique set of data was collected at 150 K. Three intensity standards were measured every 2 h of x-ray exposure time, and three orientation standards were checked every 100 reflections.

With $Z = 4$, the vanadium complex ion is constrained to lie on the 3-fold axis. The structure was solved by standard heavy-atom methods and refined by full-matrix least-squares techniques.[13] Refinement of all atoms with anisotropic thermal parameters converged to $R = 5.5\%$; refinement of the enantiomeric structure converged to 5.2%, indicating that the second choice of chirality at the metal center was correct. No hydrogen atoms were located in the final difference Fourier map and are not included in the structure model. The methanol of crystallization that sits on the 3-fold axis is severely disordered and was refined with the use of a model with three alternate positions for the oxygen and carbon atoms (O6 and C11), each with one-third occupancy. The potassium cation, K1, residing off the 3-fold axis also proved to be disordered. This disorder was successfully modeled by assuming a two-thirds potassium occupancy and a one-third water occupancy (O7) for the three potassium

---

[13] Eigenbrot, C. W., Jr.; Raymond, K. N. *Inorg. Chem.* **1982**, *21*, 2650.

Scheme I

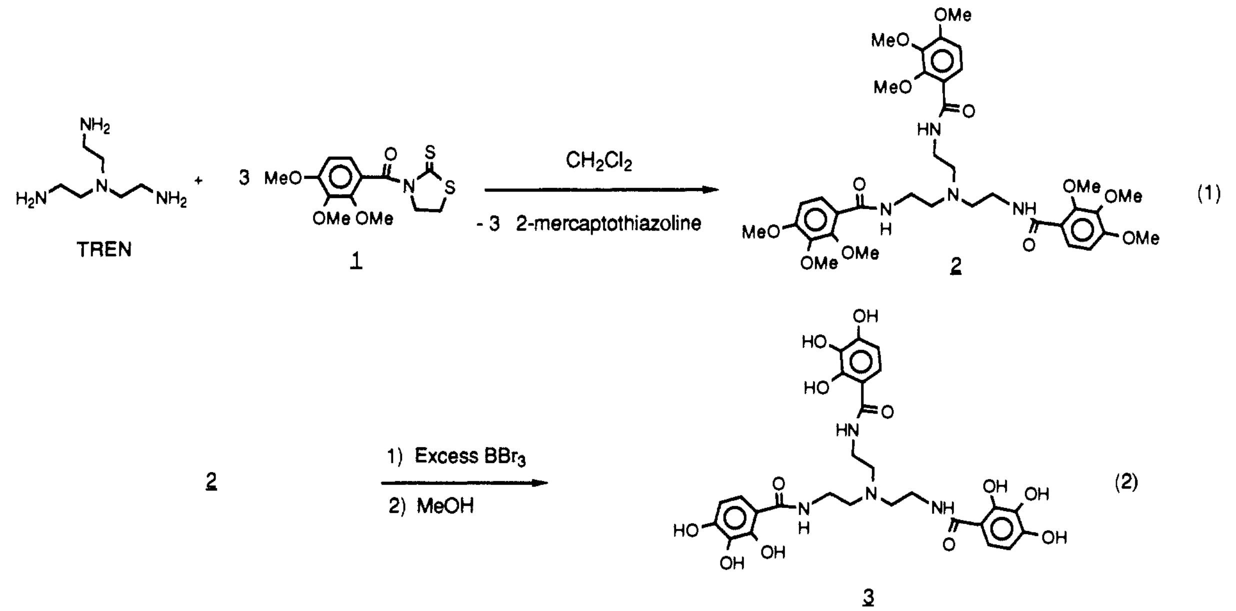


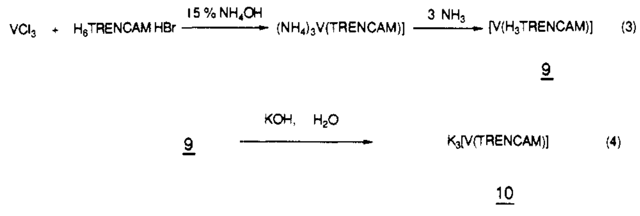
Table I. Data Collection, Solution, and Refinement Parameters for $K_3[V(TRENCAM)]\cdot 4CH_3OH\cdot 2H_2O$

empirical formula	$VK_3C_{27}N_4O_9H_{24}\cdot 4CH_3OH\cdot 2H_2O$
fw,	824.92
temp, K	150
cell param, Å	15.961
space group	$P2_13$
Z	4
calcd density, g/cm^3	1.35
radiation λ (Mo Kα), Å	0.710 73
scan type	θ–2θ
scan speed, deg/min	1.54–6.67
scan width	$0.63 + 0.35 \tan \theta$
2θ limits, deg	3.00–45.00
reflcns measd	$0 \leq h \leq 18$ $0 \leq k \leq 13$ $0 \leq l \leq 17$
no. of unique data	885
no. of obsd data, $I > 0$	1325
discrepancy indices	
R, %	5.2
R_w, %	5.9
R_{all}	12.0
goodness of fit	1.819
no. of variables	166
final diff ρ_{max}, e/Å^3	0.488

Table II. Intramolecular Bond Distances and Angles in $K_3[V(TRENCAM)]\cdot 4CH_3OH\cdot 2H_2O$

	distance, Å		angle, deg
V–O1	1.985 (5)	O1–V–O2	80.75 (18)
V–O2	2.007 (5)	V–O1–C1	113.5 (4)
O1–C1	1.327 (8)	V–O2–K2	87.24 (15)
O2–C2	1.326 (8)	V–O2–C2	113.2 (4)
O3–C7	1.230 (13)	K2–O2–C2	151.3 (4)
O4–C10	1.402 (13)	C7–N2–C8	120.4 (8)
N1–C9	1.478 (13)	O1–C1–C2	115.0 (6)
N2–C7	1.341 (13)	O1–C1–C6	125.3 (7)
N2–C8	1.449 (13)	C2–C1–C6	119.6 (7)
C1–C2	1.460 (10)	O2–C2–C1	115.1 (6)
C1–C6	1.387 (10)	O2–C2–C3	125.3 (7)
C2–C3	1.393 (10)	C1–C2–C3	119.6 (7)
C3–C4	1.404 (13)	C2–C3–C4	119.3 (8)
C4–C5	1.392 (14)	C3–C4–C5	121.2 (8)
C5–C6	1.413 (13)	C4–C5–C6	120.5 (8)
C6–C7	1.484 (13)	C1–C6–C5	119.4 (8)
C8–C9	1.554 (17)	C1–C6–C7	120.3 (8)
O6–C11	1.56 (6)	C5–C6–C7	120.3 (8)
K1–O2	2.760 (4)	O3–C7–N2	122.9 (9)
K1–O4	2.763 (7)	O3–C7–C6	118.1 (10)
K1–O5	2.762 (4)	N2–C7–C6	119.0 (8)
K2–O2	2.751 (5)	N2–C8–C9	107.6 (8)
K2–O3	2.451 (7)	N1–C9–C8	113.1 (9)

Scheme II



$$VCl_3 + H_6TRENCAM\,HBr \xrightarrow{15\%\ NH_4OH} (NH_4)_3V(TRENCAM)] \xrightarrow{3\ NH_3} \underset{\underline{9}}{[V(H_3TRENCAM)]} \quad (3)$$

$$\underline{9} \xrightarrow{KOH,\ H_2O} \underset{\underline{10}}{K_3[V(TRENCAM)]} \quad (4)$$

sites. The final least-squares cycle converged to $R = 5.2$ and $R_w = 5.9\%$ for 166 variables and 885 observations with $F_o^2 > 3\sigma(F^2)$. The largest peak in the final difference Fourier map was 0.488 e/Å^3.

The crystallographic data for $K_3[V(TRENCAM)]\cdot 4MeOH\cdot 2H_2O$ are summarized in Table I. Bond distances and angles are given in Table II.[14]

Results and Discussion

Ligand Syntheses. The preparation of 2,3,4-TRENPAMH$_9$ is shown in Scheme I. Acylation of TREN with 3 equiv of the 2-mercaptothiazoline derivative of 2,3,4-trimethoxybenzoic acid **1** yields the methyl-protected compound 2,3,4-TRENPAMMe$_9$ (**2**) in excellent yield. Treating **2** with excess BBr_3 removes the methyl groups and affords 2,3,4-TRENPAMH$_9$·HBr (**3**) in 72% yield. The isomeric ligand 3,4,5-TRENPAMH$_9$·HBr (**6**) is prepared by an analogous manner from 3,4,5-trimethoxybenzoic acid and TREN in a similar yield.

Preparation of Vanadium Complexes. Vanadyl sulfate reacts with 1 equiv of ligand **6** to form a deep purple solution. Within minutes, a deep purple solid precipitates from the basic aqueous solution. The solid, which was analyzed as $[V(3,4,5\text{-TRENPAMH}_3)(NEt_3H)_2]\cdot 4H_2O$ (**8**), is insoluble in water, methanol, and DMF and was not investigated further. The preparation of soluble monomeric analogues of **8** that proved to be amenable to further characterization are described below.

Vanadyl sulfate reacts with ligand **3** in the presence of triethylamine to produce dark purple $[NEt_3H]_2[V(2,3,4\text{-TRENPAM})]\cdot 3H_2O$ (**7**). Isolated samples of **7** exhibit moderate stability to oxygen in the solid state or in aqueous solution at neutral pH. Complex **7** rapidly decomposes in basic aqueous solution when exposed to oxygen, producing an intractable brown material. The positive FAB MS of **7** is dominated by the presence of a peak at

---

(14) See information regarding supplementary material at the end of the paper.

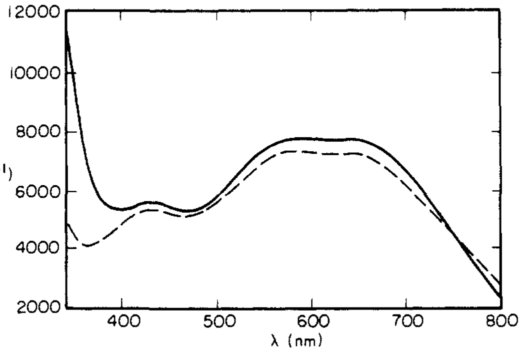


Figure 2. Visible spectra: $[V(TRENCAM)]^{2-}$ at pH 7 ($[V(TRENCAM)]^{2-}$ = 1.4×10^{-5} M), upper curve; $[V(2,3,4\text{-}TRENPAM)]^{2-}$ at pH 7 ($[V(2,3,4\text{-}TRENPAM)]$ = 1.1×10^{-5} M), lower curve.

m/e 650 (corresponding to $[V(2,3,4\text{-}TRENPAMH_3)]^{2-} + 3\ H^+$).

Vanadium trichloride reacts wwith 1 equiv of TRENCAMH$_6$·HBr in excess KOH to produce $K_3[V(TRENCAM)]$ (**10**). Complex **10** was isolated as an exceedingly oxygen-sensitive orange solid, which turns dark purple after brief exposure to air. Complex **10** typically is contaminated with varying amounts of KCl and KBr when prepared in one step from VCl$_3$ and TRENCAMH$_6$·HBr. Analytically pure **10** can be obtained in the two-step procedure shown in Scheme II. The reaction shown in eq 3 depicts the formation of orange, water-soluble $[NH_4]_3[V(TRENCAM)]$ and the subsequent loss of ammonia as the solvent is removed in vacuo.[15] The green, water-insoluble $[V(TRENCAMH_3)]$ then can be conveniently washed free of the residual NH$_4$Cl. The addition of aqueous KOH to suspensions of $[V(TRENCAMH_3)]$ (**9**) rapidly regenerates $[V(TRENCAM)]^{3-}$ as the tripotassium salt (Scheme II). The positive FABMS of $K_3[V(TRENCAM)]$ exhibits peaks at *m/e* 641 ($K[V(TRENCAM)]^{2-} + 3\ H^+$), 679 ($K_2[V(TRENCAM)]^- + 2\ H^+$), and 717 ($K_3[V(TRENCAM)] + H^+$).

The vanadium(IV) complex of TRENCAM is readily prepared from vanadyl sulfate and TRENCAMH$_6$·HBr as the diammonium salt $[NH_4]_2[V(TRENCAM)]\cdot 2H_2O$ (**11**). Complex **11** is isolated as a dark purple solid in 81% yield and is moderately air stable in the solid state; however, aqueous solutions of **11** undergo oxidation within several hours.

It is significant that tunichrome B 1, which is also a tris(3,4,5-trihydroxyphenyl) derivative, has been shown to form a network polymer with vanadium with a molecular weight of >4000.[2] This is also consistent with the suggestion that vanadium is stored within tunicates as an insoluble matrix.[16] An important difference between tunichrome B 1 (or 3,4,5-TRENPAMH$_9$) and 2,3,4-TRENPAMH$_9$ is the positioning of the hydroxyl groups. Molecular models indicate the 3,4,5-substitution of tunichrome B 1 and 3,4,5-TRENPAMH$_9$ prevents the formation of monomeric metal complexes. In contrast, the 2,3,4-substitution in 2,3,4-TRENPAMH$_9$ (or the 2,3-substitution of TRENCAM) readily accommodates the formation of monomeric metal complexes ligated by six pyrogallol (or catechol) oxygens.[17]

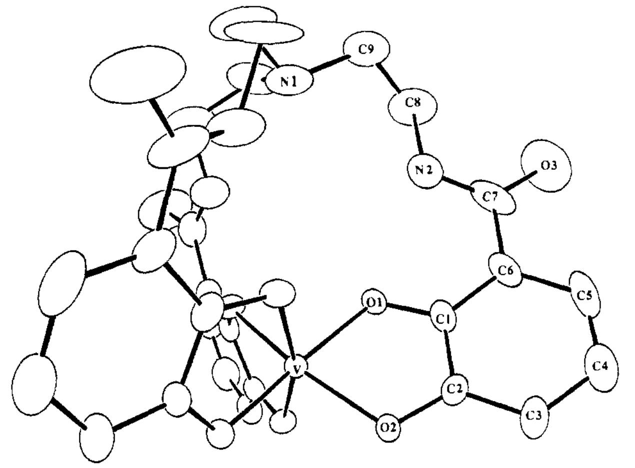


Figure 3. Molecular structure of the complex anion in $K_3[V(TRENCAM)]\cdot 4CH_3OH\cdot 2H_2O$ viewed normal to the 3-fold axis. Only the atom labels for one asymmetric unit are shown. Atoms are drawn at the 90% probability contour.

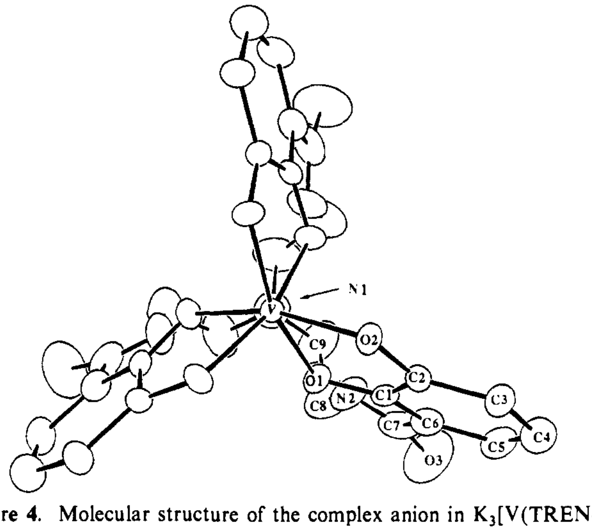


Figure 4. Molecular structure of the complex anion in $K_3[V(TRENCAM)]\cdot 4CH_3OH\cdot 2H_2O$ as observed down the 3-fold axis.

Visible Spectroscopy. The visible spectra of the vanadium(IV) complexes $[V(TRENCAM)]^{2-}$ and $[V(2,3,4\text{-}TRENPAM)]^{2-}$ in H$_2$O both contain two overlapping absorbances between 550 and 700 nm wtih ϵ s 7000, as well as a higher energy absorption near 440 nm with $\epsilon \sim 5000$ (Figure 2).[18] By analogy to $[V(cat)_3]^{2-}$ (cat = catechol dianion) these absorptions are assigned as ligand-to-metal charge-transfer bands.[19] The UV–vis spectrum of the vanadium(III) complex $[V(TRENCAM)]^{3-}$ lacks these intense ligand-to-metal charge-transfer bands, presumably due to relatively low reduction potential of the V(III) metal center, and is dominated by the ligand-based π–π^* absorption at 330 nm and d–d absorptions between 550 and 700 nm. Similarly, there is a dramatic difference between the two vanadium(IV) complexes $V(cat)_3{}^{2-}$ and $VO(cat)_2{}^{2-}$, since the latter shows only relatively weak d–d transitions.[19] In the vanadium-tunichrome preparations of Oltz et al.,[2] the EPR spectrum at 77 K was reported to have A = 162.9, A = 59.7 (10^{-4} cm^{-1}), and g = 1.990. The UV–vis spectrum showed a maximum at 647 nm. Although not noted in that paper, these results are very similar to the vanadyl–bis(catecholate) complexes (for several catechol ligands) $VO(cat)_2{}^{2-}$, for which $A_\parallel \approx 160$, $A_\perp \approx 50$ (10^{-4} cm^{-1}), $g_\parallel \approx 1.95$, $g_\perp \approx 1.99$, and $\lambda_{max} = 656$.[19] The parameters for the $V(cat)_3{}^{2-}$ complexes are very different, with (in CH$_3$CN) $A_\parallel \approx 15$, $A_\perp \approx 100$ (10^{-4} cm^{-1}), $g_\parallel \approx 1.99$, $g_\perp \approx 1.94$, and $\lambda_{max} = 552$ ($\epsilon = 9200$). This strongly indicates the predominance of a vanadyl–bis(catecholate) mode of coordination of the vanadium tunichrome[2] *for the conditions used in the preparation*, although the strong background absorbance in the UV–vis must be from another chromophore. To summarize, the bis(catechol)vanadium(IV) complexes are very strongly absorbing in EPR spectra and weakly absorbing in the

---

(15) In a similar manner, ammonia is eliminated from $[NH]_3[Cr(enterobactin)]$ to form $[Cr(H_3enterobactin)]$. Isied, S. S.; Kuo, G.; Raymond, K. N. *J. Am. Chem. Soc.* **1976**, *98*, 1763–1767.

(16) Kalk, M. *Nature* (*London*) **1963**, *198*, 1010.

(17) We thank a reviewer for pointing out that a further difference between tunichrome B 1 and **6** is the presence of double bonds in the former, which makes it more rigid. Additionally, tunichromes Mn 1 and 2 having only two polyphenolic moieties have been isolated, making the modeling of tunichrome complexation more complicated.

(18) For complex **7** these absorbances occurred at λ 444 nm ($\epsilon \simeq 5500$ M^{-1} cm^{-1}), 590 ($\epsilon \simeq 6500$), and 670 ($\epsilon \simeq 6450$); for complex **11** these absorbances occur at λ 432 nm ($\epsilon \simeq 5900$ M^{-1} cm^{-1}), 590 ($\epsilon \simeq 8100$), and 658 ($\epsilon \simeq 8000$).

(19) Cooper, S. R.; Koh, Y. B.; Raymond, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 5092–5102.

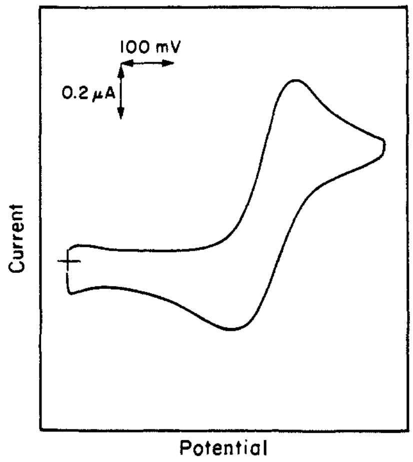


Figure 5. Cyclic voltammogram of $[V(TRENCAM)]^{2-}$ in 0.4 M $NaClO_4$ at pH 11.7. Negative potentials (V vs NHE) are plotted to the right, and reduction currents are plotted upward. Conditions: HMDE working electrode; initial potential −0.2 V; scan rate 0.2 V s^{-1}.

UV–vis. For the tris complexes just the opposite is true.

Crystallography. Two views of the trianion $[V(TRENCAM)]^{3-}$ are shown in Figures 3 and 4. As can be seen from the figures, the six catechol oxygens form a distorted octahedral environment around vanadium. The twist angle of the top trigonal face relative to the bottom is 40.8 (6)° versus 60° for an octahedron.[20] For comparison, the twist angles for the complexes $[V(cat)_3]^{3-}$, $[Cr(cat)_3]^{3-}$, and $[Fe(cat)_3]^{3-}$, are 45.6°,[19] 50.5°,[21] and 44.7°[22] (46.4° in another salt[23]), respectively. The approximately 5° decrease in the twist angle of $[V(TRENCAM)]^{3-}$ relative to $[V(cat)_3]^{3-}$ is significant and is consistent with steric constraints imposed on the catechol rings by hydrogen bonding between the catechol oxygen and the amine hydrogen of the TREN backbone. This is illustrated by the complex ferric bicapped-TRENCAM,[24] in which the two TREN ligands occupy two capping positions above and below the catechol rings and induce a twist angle of zero.

The V–O1 and V–O2 distances of 1.985 (5) and 2.007 (5) Å, respectively (Table II), are not significantly different from the V–O distances found in $K_3[V(cat)_3]$.[20] The vanadium in $[V(TRENCAM)]^{3-}$ is slightly displaced from the plane of the catechol ring; the dihedral angle between the catechol plane and the plane of the vanadium and the two ligating oxygens is 14°. As with the only other tris(catecholamide) metal complex previously crystallographically characterized, ferric bicapped-TRENCAM, the tertiary nitrogen of the TREN backbone adopts the "in" conformation. The absolute configuration of each [V(TRENCAM)] anion in the particular crystal isolated is Δ.

Electrochemistry. To examine the redox behavior of the $TRENCAMH_6$ and $TRENPAMH_9$ complexes of vanadium, electrochemical experiments were performed. A cyclic voltammogram of 8 mM $[V(TRENCAM)]^{2-}$ (**10**) in 0.4 M $NaClO_4$, pH 11.7, is shown in Figure 5. The reduction wave at $E_f = -0.37$ V vs NHE is quasi-reversible, with a peak separation of 125 mV (20–200 mV s^{-1}) and a ratio of cathodic to anodic peak currents of 1.2. A plot of E versus log $[(i_l - i)/i]$ from a normal pulse polarogram (Figure 6) gave a slope of 67 mV (Figure 6 inset), consistent with a quasi-reversible reduction process.[25]

Cyclic voltammetric behavior of **10** in DMF at a platinum disk electrode shows quasi-reversible waves at $E_f = -0.544$ and +0.531

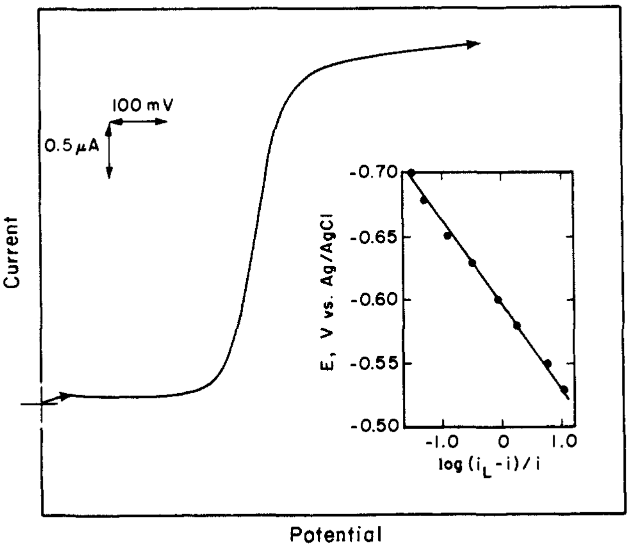


Figure 6. Normal-pulse polarogram of $[V(TRENCAM)]^{2-}$ at a dropping-mercury electrode: initial potential −0.40 V; scan rate 10 mV s^{-1}. Other conditions are the same as in Figure 5. The inset shows E vs log $[(i_l - i)/i]$ for the normal-pulse polarogram.

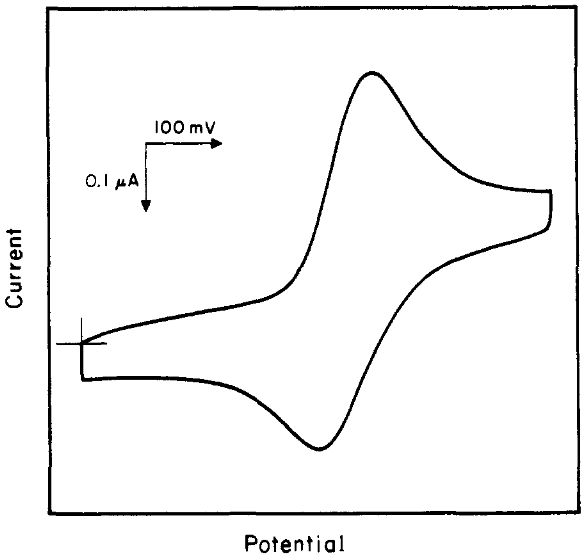


Figure 7. Cyclic voltammogram of $[V(2,3,4\text{-}TRENPAM)]^{2-}$ in 0.4 M $NaClO_4$ at pH 11.7. Negative potentials (V vs Ag/AgCl) are plotted to the right, and reduction currents are plotted upward. Conditions: HMDE working electrode; initial potential −0.2 V; scan rate 0.2 V s^{-1}.

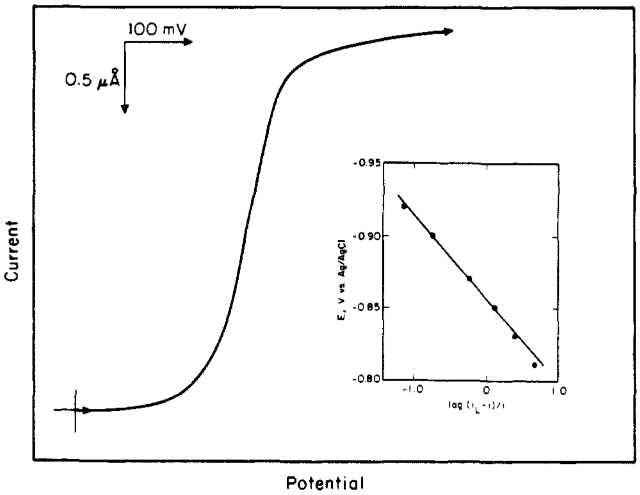


Figure 8. Normal-pulse polarogram of $[V(2,3,4\text{-}TRENPAM)]^{2-}$ at a dropping-mercury electrode: initial potential −0.40 V; scan rate 10 mV s^{-1}. Other conditions are the same as in Figure 6. The inset shows E vs log $[(i_l - i)/i]$ for the normal-pulse polarogram.

---

(20) Avdeef, A.; Fackler, J. P., Jr. *Inorg. Chem.* **1975**, *14*, 2002–2006.

(21) Sofen, S. R.; Ware, D. C.; Cooper, S. R.; Raymond, K. N. *Inorg. Chem.* **1979**, *18*, 234.

(22) Raymond, K. N.; Isied, S. S.; Brown, L. D.; Fronczek, F. R.; Nibert, J. H. *J. Am. Chem. Soc.* **1976**, *98*, 1767–1774.

(23) Anderson, B. F.; Buckingham, D. A.; Robertson, G. B.; Webb, J.; Murray, K. S. *Nature* **1976**, *262*, 722–724.

(24) McMurry, T. J.; Hosseini, M. W.; Garrett, T. M.; Hahn, F. E.; Reyes, Z. E.; Raymond, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 7196–7198.

(25) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods*; Wiley: New York, 1980; Chapters 5 and 6.

V vs NHE, corresponding to the V(IV/III) and V(V/IV) couples, respectively. Neither an increase in TRENCAM concentration nor the addition of excess Et_3N caused reversible reduction waves.[26]

Figure 7 shows the cyclic voltammogram of 1.5 mM [V-(2,3,4-TRENPAM)]$^{2-}$ (**7**) in 0.4 M $NaClO_4$, pH 11.7. The complex exhibits a wave at $E_f = -0.67$ V vs NHE (20–200 mV s^{-1}), with a peak separation of 65 mV and a ratio of peak cathodic to anodic currents of nearly unity. A plot of E vs log $[(i_l - i)/i]$ from a normal pulse polarogram (Figure 8) gave a slope of 60 mV (Figure 8 inset), consistent with a one-electron, Nernstian process. Above pH 7.0 the cyclic voltammograms of [V(TRENPAM)]$^{2-}$ exhibit a formal potential that becomes more negative with an increasing basicity of the solution. This may be attributed to the increasing negative charge that develops on the complex as the hydroxyl groups in the 4-position becomes fully deprotonated, thereby making reduction of [V(2,3,4-TRENPAMH$_3$)]$^{2-}$ more difficult. This behavior is in contrast to that observed for [V(TRENPAM)]$^{2-}$, for which E_f shows negligible pH dependence from pH 5 to 12. For the [V(2,3,4-TRENPAMH$_3$)]$^{2-}$ complex, the first acid dissociation constant complex is determined as $K_1 = 3.3 \times 10^{-8}$ M.

These results indicate that tunichrome B 1 complexes of vanadium(III/IV) would show similar variation in their redox couples at high pH. However, the relevant pH values for the biochemistry of vanadium tunichrome range from neutral to very acidic. At neutral pH in the presence of excess pyrogallol groups, vanadium(IV) can be expected to form the intensely colored tris(catechol) species. However, comparison of the EPR properties reported for vanadium–tunichrome preparations[2] with model vanadium(IV)–catechol complexes would indicate predominantly bis(catechol)vanadyl coordination. In any case, the vanadium(III) complexes must remain very highly reducing. The standard potential of pyrogallol is +0.79 V[27] and decreases 60 mV per pH unit (up to about pH 9) so that at pH 7 the potential is ~0.37 V. The potentials of the vanadium(IV/III) couples reported here for the tunichrome analogues are ~−0.4 V. Therefore excess pyrogallol ligand is barely able to reduce the vanadium(V)–pyrogallol complex at neutral pH (and it becomes progressively more difficult as the pH decreases) and is certainly incapable of reducing the vanadium(IV) complex, although this has been suggested.[5,6] The highly reducing vanadium(III) complex of tunichrome must be generated in some other way. If the role of the vanadium in the tunichromes is to act as a catalyst in the cross-linking of the animals' tunic, then the oxygen sensitivity of the vanadium(III)–catechol complexes may be the essential feature of these compounds.

Acknowledgment. We thank Dr. Fred Hollander of the University of California at Berkeley CHEXRAY Diffraction Facility for his assistance with various aspects of the X-ray diffraction studies and Dr. Zelideth Reyes for a preliminary electrochemical analysis. This research was supported by NIH Grant AI11744.

Supplementary Material Available: Tables III(S), IV(S), and VI(S), containing root-mean-squared amplitudes of thermal vibrations, anisotropic thermal parameters, and positional parameters for non-hydrogen atoms, respectively, and Figure 9(S) showing the pH dependence of the V$^{IV/III}$(2,3,4-TRENPAM) potential from pH 6 to 12 (5 pages); Table V(S) containing structure factor amplitudes (8 pages). Ordering information is given on any current masthead page.

---

(26) One equivalent of TRENCAMH$_6$·HBr was added to the solution.

(27) Jenny, L. *Helv. Chim. Acta* **1949**, *32*, 315–321.

Late-Transition-Metal μ-Oxo and μ-Imido Complexes. 4.[1] Preparation and Characterization of Rhodium μ-Imido/Amido A-Frame Complexes

Yuan-Wen Ge, Fei Peng, and Paul R. Sharp*

Contribution from the Department of Chemistry, University of Missouri—Columbia, Columbia, Missouri 65211. *Received June 23, 1989*

Abstract: Treating $Rh_2(CO)_2Cl_2(\mu\text{-dxpm})_2$ (dxpm = bis(diphenylphosphino)methane (dppm) or bis(dimethylphosphino)methane (dmpm)) with 2 equiv of LiNHR (R = Me, Ph, *p*-MeOPh, *p*-MePh, *o*-MePh, *o,o'*-Me$_2$Ph, *p*-FPh, *p*-BrPh, *p*-NO$_2$Ph) gives $Rh_2(\mu\text{-NR})(CO)_2(\mu\text{-dxpm})_2$ (**1**), its tautomer $Rh_2(\mu\text{-NHR})(CO)_2(\mu\text{-dxpm})(\mu\text{-dxpm-H})$ (**2**), or equilibrium mixtures of **1** and **2** (**1**/**2**) (dxpm-H = bis(diphenylphosphino)methanide or bis(dimethylphosphino)methanide). The position of the tautomeric equilibrium is determined by the electron-donating properties of R, steric effects, and the solvent. Both tautomers have been characterized by X-ray crystal structure determinations. Crystals of tautomer **1** (dppm, R = *p*-NO$_2$Ph) from CH_2Cl_2/Et_2O are monoclinic (*C*2/*c*) with $a = 11.337$ (4) Å, $b = 36.451$ (8) Å, $c = 12.821$ (3) Å, $\beta = 90.59$ (3)°, $V = 5297.7$ Å^3, and $Z = 4$. The structure is typical of A-frame complexes and contains a planar imido nitrogen at the apex. The structure of **2** (dppm, R = Me) clearly shows the presence of the dppm-H and the NHMe ligands. Crystals from toluene are triclinic ($P\bar{1}$) with $a = 10.459$ (12) Å, $b = 14.348$ (3) Å, $c = 20.867$ (6) Å, $\alpha = 104.96$ (2)°, $\beta = 101.12$ (4)°, $\gamma = 93.47$ (6)°, $V = 2948.3$ Å^3, and $Z = 2$. The solid-state structure consists of one independent A-frame molecule with a bridging NHMe group and two independent, disordered, toluene molecules of crystallization. Protonation of **1**, **2**, or **1**/**2** gives $[Rh_2(\mu\text{-NHR})(CO)_2(\mu\text{-dxpm})_2]^+$ (**3**), which can be recycled back to the starting complex(es) with LiNHR. Hydrolysis of solutions of **1**/**2** (dppm, R = Ph) gives $Rh_2(\mu\text{-O})(CO)_2(dppm)_2$ (**4**) as found by an X-ray crystal structure determination. Crystals from toluene/ether are orthorhombic (*Pccn*) with $a = 13.598$ (6) Å, $b = 17.642$ (8) Å, $c = 19.283$ (7) Å, $V = 4626.0$ Å^3, and $Z = 4$.

The majority of transition-metal oxo (O^{2-}) and imido (RN^{2-}) complexes are high oxidation state early-transition-metal (Fe triad and before) complexes. For the most part, they are known for the stability and low reactivity of the oxo or imido linkage. The reaction chemistry of these complexes rarely directly involves the oxo or imido ligand. This high stability results from the extensive multiple bonding between the electron-poor high oxidation state

---

[1] For part 3, see: Ge, Y.-W.; Sharp, P. R. *Organometallics* **1988**, *7*, 2234–2236.

0002-7863/90/1512-2632$02.50/0