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Model Investigations for Vanadium–Protein Interactions: Synthesis and X-ray Structures of *mer*-[$VOCl_3$(Hpycan)] and [$VOCl_2$(CH_3CN)(Hpycan)] {Hpycan = *N*-(2-Nitrophenyl)pyridine-2-carboxamide}

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Current interest in vanadium biochemistry has been stimulated by the discovery of vanadium in biomolecules such as marine algal bromoperoxidase[1] and nitrogenase from *Azobacter vinelandii*[2] as well as by its ability to produce significant physiological effects,[3] in particular its insulin-like properties.[4] The elucidation of the biological role of vanadium requires the exploration of its basic coordination chemistry.

A good starting point is the investigation of vanadium–protein interactions. Potential metal–ion binding sites on proteins are principally the polar side chains which are separated by many amino/acid residues and the –NHCO– groups of the peptide chain backbone. A literature survey revealed surprisingly little information concerning the ligation of the amide(peptide) functionality to vanadium.[5–7] It is worth noting that the very few structurally characterized vanadium(III)[5c] and oxovanadium(IV)[5,6]–amidate species contain a vanadium-deprotonated amide nitrogen bond (V–N_{amide}). We now wish to report here the synthesis and structural characterization of V^V and V^{IV} complexes [$VOCl_3$(Hpycan)] (**1**) and [$VOCl_2$(CH_3CN)(Hpycan)] (**2**). The structure of **1** is the first example of an oxovanadium(V) complex containing a vanadium–amide bond to be structurally characterized. Furthermore, the structures of **1** and **2** are the first examples of oxovanadium(IV/V) species with a V–O_{amide} mode of coordination. The synthesis of the vanadium(III) analogue is also reported.

The mononuclear brick-red complex *mer*-[$VOCl_3$(Hpycan)] (**1**) was prepared by slow addition of Hpycan (4.1 mmol) in dry CH_2Cl_2 (20 mL) under magnetic stirring to a solution of oxovanadium(V) chloride (4.0 mmol) in dry CH_2Cl_2 (10 mL), under argon (eq 1). The resulting brick-red precipitate[8] was filtered off, washed with CH_2Cl_2 (2 × 5 mL), and dried in vacuo over P_4O_{10} (yield 70%).

The compounds [$VOCl_2$(CH_3CN)(Hpycan)][9] (**2**) and [VCl_3(CH_3CN)(Hpycan)] (**3**) were synthesized by addition of Hpycan

$$\mathrm{VOCl_3 + Hpycan \rightarrow \mathit{mer}\text{-}[VOCl_3(Hpycan)]} \qquad (1)$$

in dry CH_3CN to acetonitrile solutions of $VOCl_2$ and VCl_3, respectively, under argon. Compound **2** was also prepared by reduction of **1** with ferrocene (eq 2) in acetonitrile. The CH_3CN ligand of complexes **2** and **3** can be metathesized readily with imidazole (im) in nitromethane to provide the complexes [$VOCl_2$(im)(Hpycan)] **4** and [VCl_3(im)(Hpycan)] (**5**).

$$\mathrm{\mathit{mer}\text{-}[VOCl_3(Hpycan)] + cp_2Fe \rightarrow [VOCl_2(CH_3CN)(Hpycan)] + [cp_2Fe]Cl} \qquad (2)$$

All the complexes are air sensitive in the solid state and solution as well and hydrolyzed to Hpycan and various vanadium species. Although air sensitive, they are indefinitely stable in the solid state and quite stable in solution under an inert atmosphere. Thus compound **1** constitutes an excellent entry for vanadium(V) chemistry in organic solvents. Crystals of **1** suitable for X-ray diffraction studies were obtained by vapor diffusion of a dichloromethane solution of $VOCl_3$ into a dichloromethane solution of Hpycan, while crystals of **2** were formed by slow diffusion of an acetonitrile solution of $VOCl_2$ into acetonitrile solution of Hpycan, and their crystal and molecular structures were determined.[10,11]

The molecular structure and atomic numbering scheme of **1** are shown in Figure 1. The vanadium atom has distorted octahedral coordination, with the oxo ligand trans to the amide oxygen and the three chlorine atoms occupying meridional positions. The V=O distance [1.572(1) Å] is consistent with values found in other octahedral oxovanadium(V) complexes.[12] A strong trans effect observed in most oxovanadium(IV/V) species suggests that the weakest donor atom of the variable ligand should be trans to the oxo group. This expectation is fulfilled in compound **1**, which adopts the predicted structure with a long V–O_{amide} bond [2.214(1) Å] oriented trans to O^{2-}. The amide group C(6)-C(13)O(1)N(2) is planar within the limits of precision. The deviation of the vanadium atom from the amide group plane is 0.06 Å. **2** has a similar gross structure (Figure 2) except that a nitrogen atom (from a coordinated acetonitrile molecule) has been substituted for a chlorine (3) atom at the vanadium center. A comparison of the structures of complexes **1** and **2** reveals that the molecules are very similar, the main differences between them being the V=O and V—Cl bond distances which are reduced in complex **1**. It is worth noting that the V–O and V–N bond lengths are almost identical in both complexes.

The redox properties of **1** in nitromethane have been investigated by dc cyclic voltammetry. The complex displays both reversible

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[8] Anal. Calcd for **1**, $C_{12}H_9Cl_3N_3O_4V$ (fw = 416.52): C, 34.60; H, 2.18; N, 10.09; V, 12.23. Found: C, 34.57; H, 2.14; N, 10.00; V, 12.15.

[9] Anal. Calcd for **2**, $C_{15}H_{13.5}Cl_2N_{4.5}O_4V$ (fw = 442.65): C, 40.70; H, 3.07; N, 14.24; V, 11.51. Found: C, 40.65; H, 3.05; N, 14.20; V, 11.42.

[10] Brick-red crystals of **1** (MW = 416.52) are monoclinic, space group $P2_1/n$, with a = 7.827(1) Å, b = 15.740(2) Å, c = 12.854(2) Å, and β = 101.50(1)° at 298 K with Z = 4. Refinement of 2604 reflections with $F > 4.0\sigma(F_o)$ and 244 parameters gave R = 0.0268 and R_w = 0.0449.

[11] Green crystals of **2** (MW = 442.65) are monoclinic, space group $P2_1/n$, with a = 11.0322(6) Å, b = 12.0971(8) Å, c = 14.1360(9) Å, and β = 100.48(1)° at 298 K with Z = 4. Refinement of 3227 reflections with $F > 6.0\sigma(F_o)$ and 301 parameters gave R = 0.0282 and R_w = 0.0453.

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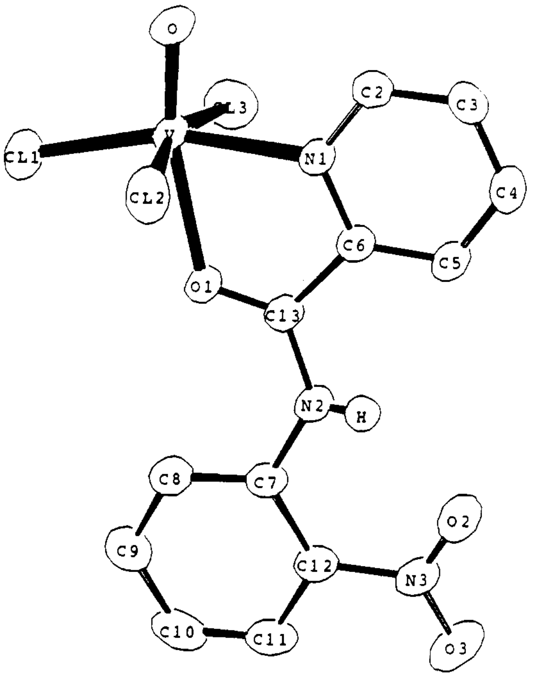

Figure 1. ORTEP drawing of *mer*-[VOCl$_3$(Hpycan)] with 50% probability ellipsoids giving atomic numbering. For clarity, hydrogen atoms are omitted. Selected interatomic distances (Å) and angles (deg) are as follows: V–Cl(1) = 2.194(1), V–Cl(2) = 2.272(1), V–Cl(3) = 2.289(1), V–O = 1.572(1), V–N(1) = 2.160(2), V–O(1) = 2.214(1), H(N2)···O(2) = 1.94(3), N(2)···O(2) = 2.608(3); Cl(1)–V–Cl(2) = 95.5(1), Cl(1)–V–Cl(3) = 95.6(1), Cl(2)–V–Cl(3) = 162.1(1), Cl(1)–V–O = 103.3(1), Cl(2)–V–O = 95.9(1), Cl(3)–V–O = 95.2(1), Cl(1)–V–N(1) = 162.9(1), Cl(2)–V–N(1) = 82.0(1), Cl(3)–V–N(1) = 83.3(1), O–V–N(1) = 93.8(1), Cl(1)–V–O(1) = 89.8(1), Cl(2)–V–O(1) = 84.3(1), Cl(3)–V–O(1) = 81.8(1), O–V–O(1) = 166.8(1), N(1)–V–O(1) = 73.1(1).

and irreversible redox processes. These processes and their potentials (V vs Ag/AgCl) are summarized in eqs 3 and 4. The electrochemistry of **2**–**4** is more complex and is under investigation.

$$[\mathrm{V^{V}OCl_3(Hpycan)}] + e^- \rightarrow [\mathrm{V^{IV}OCl_3(Hpycan)}]^- \quad E_{1/2} = +0.85\ \mathrm{V} \tag{3}$$

$$[\mathrm{V^{IV}OCl_3(Hpycan)}]^- + e^- \rightarrow [\mathrm{V^{III}OCl_3(Hpycan)}]^{2-} \quad E_{1/2} = -0.21\ \mathrm{V} \tag{4}$$

The ^{51}V NMR (referred to VOCl$_3$) of *mer*-[VOCl$_3$(Hpycan)] in dichloromethane consists of a single resonance at −83 ppm. The upfield shift of −83 ppm, with respect to VOCl$_3$, for this octahedral d^0 complex, which is the first example of an X-ray structurally and ^{51}V NMR characterized oxovanadium(V) species with a Cl$_3$NO$_2$ coordination environment, is something expected on the basis of the so called "inverse electronegativity dependence of metal shielding",[13] which operates for d^0 metal systems. The small upfield shift may be due to the fact that the V–O$_{\mathrm{amide}}$ and V–N$_{\mathrm{pyridine}}$ bonds are not very strong. The electronic absorption spectrum of the above mentioned complex in dichloromethane [λ (nm), ε (M^{-1} cm^{-1})] consists of four bands: 442, 4850; 347, 9010; 275, 21 100; and 220, 21 700. The intense absorptions in the visible region of spectrum are assigned as ligand-to-metal charge transfer.

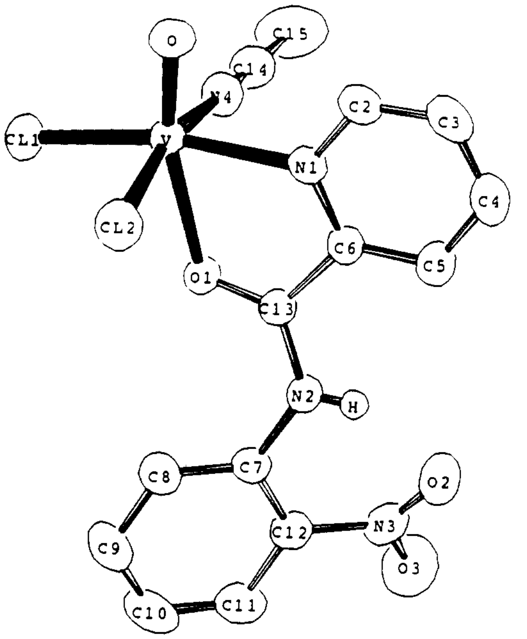

Figure 2. ORTEP drawing of [VOCl$_2$(CH$_3$CN)(Hpycan)] with 50% probability ellipsoids giving atomic numbering. For clarity, hydrogen atoms are omitted. Selected interatomic distances (Å) and angles (deg) are as follows: V–Cl(1) = 2.325(1), V–Cl(2) = 2.347(1), V–O = 1.587(1), V–O(1) = 2.206(1), V–N(1) = 2.162(2), V–N(4) = 2.110(2), H(N2)···O(2) = 2.16(2), N(2)···O(2) = 2.635(2); Cl(1)–V–Cl(2) = 94.5(1), C(1)–V–O = 102.9(1), Cl(2)–V–O = 99.9 (1), Cl(1)–V–O(1) = 92.7(1), Cl(2)–V–O(1) = 83.9(1), O–V–O(1) = 163.8(1), Cl(1)–V–N(1) = 164.3(1), Cl(2)–V–N(1) = 90.0(1), O–V–N(1) = 91.2(1), O(1)–V–N(1) = 72.8(1), Cl(1)–V–N(4) = 87.5(1), Cl(2)–V–N(4) = 164.7(1), O–V–N(4) = 95.3(1), O(1)–V–N(4) = 80.8(1), N(1)–V–N(4) = 84.3(1).

In summary, we have shown that vanadium(III) and oxovanadium(IV/V) interact with amide groups and give complexes with a vanadium–O$_{\mathrm{amide}}$ mode of coordination, which, though air sensitive, are indefinately stable in the solid state and quite stable in solution under an inert atmosphere. The chemical significance of this work lies in the fact that the X-ray structures provide the first solid-state evidence that the vanadium–O$_{\mathrm{amide}}$ binding is a possible mode of action in proteins.

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Supplementary Material Available: Tables of crystallographic data, atomic positional parameters, anisotropic thermal parameters, and complete bond distances and angles for **1** and **2** (10 pages). Ordering information is given on any current masthead page.

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