A New Biomimetic Model for the Active Site of Oxovanadium(IV)-Transferrins – [OV\textsuperscript{IV} (tf)]

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Reportamos neste trabalho, a síntese, a estrutura cristalina e propriedades espectroscópicas do novo complexo [OV\textsuperscript{IV} (HBIMETEN)], [H\textsubscript{3}BIMETEN = N, N\textsuperscript{},'-(2-hidroxibenzil)-N-(1-metilimidazol-2-il-metil)-N\textsuperscript{'-hidroxietil-etilenodiamina] como um exemplo de complexo V\textsuperscript{IV}O\textsuperscript{2+} o qual contém grupos 1-metilimidazol e fenolato coordenados simultaneamente ao centro metálico. Este composto apresenta propriedades espectrais (EPR e UV-Vis) similares àquelas observadas na [OV\textsuperscript{IV}(tf)].

The synthesis, X-ray crystal structure, and spectroscopic properties of the new coordination compound [OV\textsuperscript{IV} (HBIMETEN)], [H\textsubscript{3}BIMETEN = N, N\textsuperscript{},'-(2-hydroxybenzil)–N-(1-methylimidazole–2–yl-methyl)-N\textsuperscript{'}-hydroxyethyl-ethylenediamine] are reported as V\textsuperscript{IV}O\textsuperscript{2+} complex example containing phenolate and 1-methylimidazole coordinated simultaneously to the metal center. The EPR and UV-Vis properties of the title compound are similar to those observed in [OV\textsuperscript{IV}(tf)].

Keywords: VO\textsuperscript{2+} complex, crystal structure, EPR, vanadium transferrin

Introduction

Vanadium has an important role in many biological processes. Particularly it has been proposed that delivery of vanadium in higher organisms is performed by transferrin\textsuperscript{1}. Transferrins are glycoproteins whose primary function is to bind and transport iron, but they also coordinate a wide variety of other metals including vanadium. They are a single polypeptide chain with two homologous lobes, denominated C- and N-terminal, each of which binds one metal ion\textsuperscript{2,3}. Despite the binding of iron(III)-transferrin has been established through crystallographic studies (NO\textsubscript{3} coordination and CO\textsubscript{3} as synergistic anion)\textsuperscript{3}, the coordination environment around the vanadium centre in transferrins is not yet entirely known. It is well known that in the +3, +4, and +5 oxidation states, vanadium binds tightly to transferrin\textsuperscript{4,5}. In an attempt to gain insight into the biological roles of vanadium, many recent studies have focussed on the coordination chemistry of this metal, in the oxidation states +3, +4 and +5, with biologically relevant ligands\textsuperscript{6,7}. In the +4 oxidation state, a vanadyl complex structure with octahedral geometry having an NO\textsubscript{3} equatorial coordination (one tyrosinate, one aspartate, one histidine and one monodentate carbonate) has been proposed recently for vanadium human lactoferrin\textsuperscript{5}. The coordination of histidine trans to the V=O bond has also been proposed\textsuperscript{6}. This work is a continuation of a wide research program for the preparation and characterization of vanadium complexes of bioinorganic interest\textsuperscript{7}.

Experimental

Abbreviations

H\textsubscript{2}BIMETEN, N,N\textsuperscript{'}-bis-(2-hydroxybenzyl)-N-(2-methylimidazole)-N\textsuperscript{'}- (2-hydroxyethyl)ethylenediamine; H\textsubscript{2}BBIMEN, N,N\textsuperscript{'}-bis-(2-hydroxybenzyl)-N, N\textsuperscript{'}- (2-me-
thylimidazole(ethylenediamine), H2BBPEN, N,N’-bis(hydroxybenzyl)-N,N’-bis(pyridyl-methyl)ethylenediamine; HIMETEN, N-(2-thylimidazole)-N’-(2-hydroxyethyl) ethylenediamine; [OV IV(tf)], vanadium(IV)-transferrin.

Synthesis

The ligand H3BIMETEN was prepared in good yield (91.36%) by the condensation reaction of 1-methyl-2-imidazolecarboxyaldehyde with N,N’-bis(2-hydroxyethyl)ethylenediamine, followed by reduction with NaBH4 and by alkylation of the diamine (HIMETEN) with 2-bromo-methylphenyl acetate, by the route in Scheme 1. The complex [OV IV(HBBIMEN)](I) was prepared by refluxing a methanolic solution of VOSO4‧H2O (0.163 g, 1 mmol) and H3BIMETEN (0.410 g, 1 mmol) with stirring for 1 h. To the reaction was added Et3N (1 mL, 7.18 mmol), to yield a violet precipitate (0.32 g - 67.37%). Anal. Calc. for C23H30N4O4V: C, 55.98; H, 6.08; N, 11.35. Found: C, 55.63; H, 5.95; N, 10.96%. The precipitate was recrystallized in an acetonitrile-ethanol (1:1) solution at room temperature. After a few days crystals suitable for X-ray crystallography were filtered off, washed with 2-propanol and dried with ether.

X-ray crystallography

Crystal data for C23H30N4O4V. 1/2 C2H3OH, M = 498.47, monoclinic, P21/c, (n=14), Z = 4, a = 15.304(3), b = 12.329(3), c = 12.441(3) Å, β = 94.18(3)°, V = 2341.2(9) Å3, Dc = 1.414 g cm−3, F(000) = 1048, μ = 0.465 mm−1 for Mo-Kα radiation (λ = 0.71073 Å), crystal size 0.07 x 0.20 x 0.43 mm. Nonius CAD4 diffractometer, T = 293 K. Measured reflections: 4108, with 2971 unique reflections measured in DMF in the visible region reveals the following transitions at λmax/nm (ε / dm3 mol−1 cm−1): 881 (20.08), 538 (76.28) and 441 [7c,d,e,f]. The electronic spectra of 1 measured in DMF in the visible region reveals the following transitions at λmax/nm (ε / dm3 mol−1 cm−1): 881 (20.08), 538 (76.28) and 441

Scheme 1. Synthesis of the ligand H3BIMETEN.
According to Ballhausen and Gray\textsuperscript{11}, the weak absorption at 881 nm is attributed to the d→d transition $\varepsilon_d \rightarrow d_{x^2-y^2}$ whereas those at 538 and 441 nm involve the $d_{xy}$ and $d_{xz,yz}$ orbitals in compounds of $C_{4v}$ symmetry, as in [OV\textsuperscript{IV}(HBBIMEN)]PF\textsubscript{6} for which the corresponding transitions are observed at $\lambda_{\text{max}}$nm ($\varepsilon$ mol\textsuperscript{-1} cm\textsuperscript{-1}): 826 (46), 537 (76) and 380 (462)\textsuperscript{12}. In agreement with the X-ray crystal data previously described, I is a little more distorted than [OV\textsuperscript{IV}(HBBIMEN)]PF\textsubscript{6} but not enough to split the $d_{xy} \rightarrow d_{x^2-y^2}$ transitions as in [OV\textsuperscript{IV}(tf)]\textsuperscript{2b,4b} and [OV\textsuperscript{IV}(BBPEN)]\textsuperscript{6c}.

The X-band EPR spectrum of a frozen solution of I in DMF together with the simulated spectrum is shown in Fig. 2. The Hamiltonian parameters obtained from the spectrum of I, demonstrate the low symmetry geometric structure of the molecule, as can be observed in other vanadyl complexes previously reported in the literature\textsuperscript{2b}. The pseudoaxial (because the parameters $g_x$ and $g_y$ are very similar) distortion is in agreement with X-ray diffraction data and the electronic absorption spectrum. However, this little in-plane observable anisotropy, $|g_x - g_y| = 0.001$, $|a_x - a_y| = 0.5 \times 10^{-4}$ cm\textsuperscript{-1}, demonstrates that distortions in I are somewhat little more pronounced than those observed in [OV\textsuperscript{IV}(HBBIMEN)]\textsuperscript{7}, in which the in-plane anisotropy is not observable. The smaller values of the g parameters for an $N_2O_2$ equatorial coordination are consistent with the d→d transitions with lower energy found in I, compared to the values observed in [OV\textsuperscript{IV}(HBBIMEN)]PF\textsubscript{6} ($g_x = g_y = 1.9925$, $g_z = 1.9545$) which has an $N_2O$ equatorial coordination, and consequently higher energy d→d transitions. The corresponding parameters found in the ovotransferrin\textsuperscript{2c}, a member of the family of the transferrins found in the white of eggs, are $g_x = 1.939$, $g_y = 1.978$, $g_z = 1.9436$, $A_x = 57.55$, $A_y = 57.05$, and $A_z = 164.50 \times 10^{-4}$ cm\textsuperscript{-1}.

In summary, a V\textsuperscript{IV}O\textsuperscript{2+} complex containing a novel polyfunctional ligand has been prepared and characterized structurally and spectroscopically. In spite of the numerous VO\textsuperscript{2+} complexes with nitrogen and oxygen donor atoms described in the literature\textsuperscript{6,7}, neither of these species exhibit all the characteristic spectral (UV-VIS and EPR) and structural properties found in [V(tf)]\textsuperscript{2b,4b}. Recent studies on the transferrins\textsuperscript{5}, show that the form of the bound vanadium(IV) ion is VO\textsuperscript{2+} (vanadyl). These studies also proposed that each vanadyl ion is coordinated to two tyrosine residues, one histidine residue, a monodentate carbonate ion and to an aspartic acid. The EPR and UV-Vis spectral properties of the coordination compound [O=V\textsuperscript{IV}(HBBIMEN)]\textsuperscript{7} described here, are very similar to those found in the ovotransferrin\textsuperscript{2c}, therefore we can propose that I is a very interesting model for the [OV\textsuperscript{IV}(tf)] complex.

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\textbf{References}


