Synthesis, Structure and Properties of a New Vanadyl–Phenolate Derivative as a Model for the Vanadium(IV) Transferrins

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The synthesis, and the X-ray crystal structure, spectroeletrochemical and spectroscopic properties of [OV^{IV}(bbpen)] [H$_2$bbpen = N,N'-bis(2-hydroxybenzyl)-N,N'-bis(2-pyridylmethyl)ethylenediamime] are reported; this complex is the first VO^{2+} species that exhibits similar UV–VIS and EPR properties to those detected in VO^{2+} transferrins.

Vanadium has an important role in many biological processes.[1] It is well known that in the +3, +4, and +5 oxidation states, vanadium binds tightly to transferrins,[2–5] forming vanadium-modified transferrins, [V(tf)]. This is the probable form in which vanadium is transported in higher organisms.[6] Dietary vanadyl sulfate inhibits the development of chemically induced mammary carcinomas in rats.[7] It has been proposed that delivery of VO^{2+} to the neoplastic tissue by transferrin could be the first step in the inhibition of carcinogenesis by vanadium.[7] The coordination environment around the vanadium centre in this modified enzyme is not yet entirely known, although the presence of some ligands had been detected. A vanadyl complex structure with octahedral geometry having only oxygen donor atoms (two phenolates, one water and one carbonate/hydrogencarbonate) in the equatorial plane has been proposed for [OV^{IV}(tf)], on the

basis of extensive UV–VIS and EPR studies.[8] In the +5 oxidation state, the VO$_2$$^+$ moiety is most likely to be coordinated to transferrin.[1] The lack of charge transfer between the phenolate and the vanadium(v) eliminates the possibility of V^{5+} or VO^{3+} species.[3] Little is known about the [V^{III}(tf)] derivative, which is surprisingly stable towards atmospheric oxygen.[2] Interestingly, despite the numerous VO^{2+} complexes with nitrogen and oxygen donor atoms described in the literature,[1] neither of these species exhibit the characteristic spectral (UV–VIS and EPR) properties found in [OV(tf)].[5,8] Moreover, to understand fully the role of the vanadium in [V(Tf)], the relationships between structure, spectroscopy, electrochemistry, and reactivity of the active site must be determined. Therefore, the synthesis and complete characterization of new vanadium complexes with relevant nitrogen and oxygen donor ligands is an important
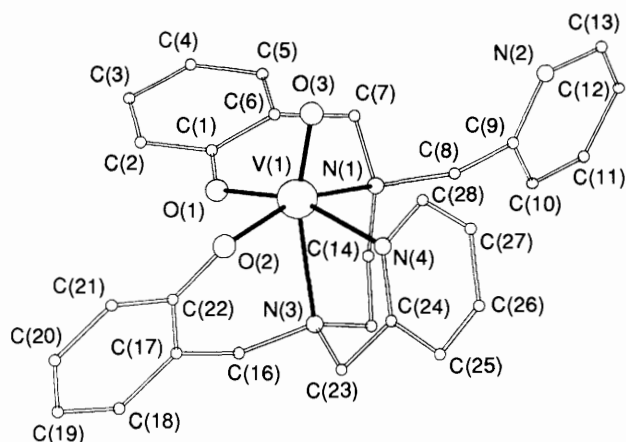
Fig. 1 X-ray structure of **2**. Selected bond lengths (Å) and angles (°) of molecules **A**: V(1)–O(1) 1.920(2), V(1)–O(2) 1.926 (3), V(1)–O(3) 1.606(2), V(1)–N(1) 2.208(3), V(1)–N(3) 2.307(2), V(1)–N(4) 2.164(2); O(1)–V(1)–O(2) 88.5(1), O(1)–V(1)–O(3) 105.9 (1), O(1)–V(1)–N(1) 85.6(1), O(1)–V(1)–N(3) 88.9(1), O(1)–V(1)–N(4) 161.8(1), O(2)–V(1)–O(3) 106.8(1), O(2)–V(1)–N(1) 159.0(1), O(2)–V(1)–N(3) 81(1), O(2)–V(1)–N(4) 85.5(1), O(3)–V(1)–N(1) 94.1(1), O(3)–V(1)–N(3) 163.2(1), O(3)–V(1)–N(4) 92.3(1), N(1)–V(1)–N(3) 78.7(1), N(1)–V(1)–N(4) 94.0(1), N(3)–V(1)–N(4) 73.3(1).

area of study. Herein, we report the preparation, structure, spectroscopic and electrochemical characterization of such a complex with bioinorganic relevance.[9,10]

The vanadium complexes were prepared by refluxing methanolic solution of $VOSO_4.5H_2O$ and H_2bbpen[9,11] [H_2bbpen = N,N'-bis(2-hydroxybenzyl)-N,N'-bis(2-pyridyl-methyl)ethylenediamine] for 1 h. After cooling the solution to room temp., a lilac precipitate of [$V_2O_2(bbpen)(SO_4)$] **1** formed immediately. Treatment of a hot suspension of **1** in water with NaOH (pH 9) afforded a clear-orange solution from which a yellow–orange microcrystalline precipitate of [OV(bbpen)] **2** was obtained after cooling to 10 °C. Single crystals of **2** were grown from a propan-2-ol–acetone–acetonitrile (2:1:1) solution of **2**. Alternatively, **2** can also be prepared by chemical oxidation of [V^{III}(bbpen)]PF_6[9] in MeOH–water (1:2) with PbO_2.

The structure† and atomic numbering scheme of **2** are illustrated in Fig. 1. The asymmetric unit consists of two molecules of [OV(bbpen)]. Since the bond lengths and angles and the geometry around the vanadium centre are identical in the two molecules (**A** and **B**), only the parameters of molecule **A** will be discussed here. The vanadium(IV) ion lies in a highly distorted octahedral environment, in which two phenolate oxygen, one amine, and one pyridyl nitrogen atom form the equatorial plane, where atoms of the same type occupy the *cis*-positions with respect to each other. The other amine nitrogen atom of the ethylenediamine backbone, in the *trans*-position with respect to the terminal oxo group, completes the coordination sphere. This form of coordination of the ethylenediamine group is unusual, since in most of these complexes, both the nitrogen atoms are coordinated *cis* rather than *trans* to the V=O bond.[12] This is probably due to the

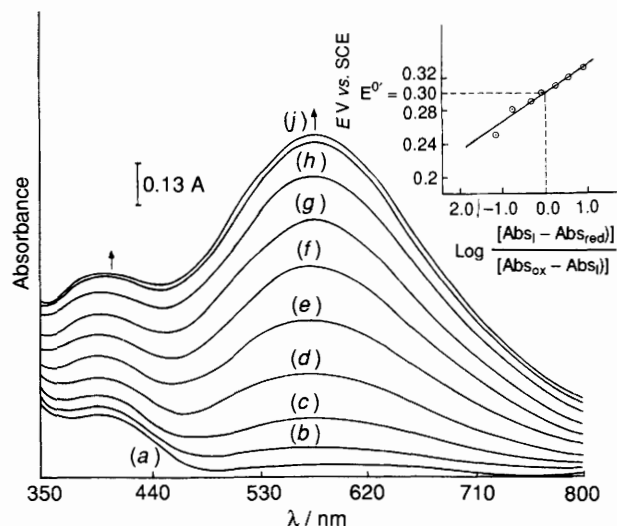**Fig. 2** Spectra recorded during spectropotentiostatic experiment on 5 × 10⁻³ mol dm⁻³ of **2** (0.1 mol dm⁻³ [Bu₄N][PF₆] in MeCN). Applied potentials in V *vs* standard calomel electrode (SCE) are: (*a*) 0.15; (*b*) 0.20; (*c*) 0.25; (*d*) 0.28; (*e*) 0.29; (*f*) 0.30; (*g*) 0.31; (*h*) 0.32; (*i*) 0.33; (*j*) 0.34.

chelate ring strain in **2**. As expected, the V–N$_{(amine)}$ bond distance of 2.307(2) Å *trans* to the V=O bond is 0.1 Å longer than the V–N$_{(amine)}$ bond in the equatorial plane and is a reflection of the strong *trans* effect of the oxo group. The V–O$_{(phenolate)}$ bond lengths in **2** (av. 1.923 Å) are identical to those found in the [OV^{IV}(salen)] complex (av. 1.923 Å) but somewhat shorter than in the [OV^{IV}(ehpg)]⁻ complex (av. 1.950 Å)[12] {ehpg = ethylenebis[(O-hydroxyphenyl)glycine]}, which has been used as a model for and [O_2V^V(thf)].

The electronic spectrum of **2** measured in CH_2Cl_2 in the visible region reveals the following transitions at λ_{max}/nm (ε/dm³ mol⁻¹ cm⁻¹): 925 (75), 870 (70), 555 (125), and 405 (940). The higher energy absorption at 405 nm is tentatively assigned as being due to a charge-transfer process and is probably a result of the pronounced distortions in **2**. The lower energy bands at 925 and 870 nm are those from d_{xy} to d_{xz} and d_{yz}, whereas that at 555 nm involves the $d_{x^2-y^2}$ orbital in low symmetry.[8] With the exception of the band at 405 nm, the spectrum of **2** is very similar to that of [OV^{IV}(tf)], which exhibits the corresponding features at 926 (25), 800 (15), and 592 (25).[5]

The redox properties of **2** have been investigated by cyclic voltammetry (CV) and spectroelectrochemistry. Between +0.60 and −2.00 V in MeCN and 0.1 mol dm⁻³ [Bu₄N][PF₆] as supporting electrolyte and scan rates of 25–600 mV s⁻¹, complex **2** exhibits a quasi-reversible one-electron-transfer wave at −0.11 V *vs*. Fc⁺/Fc, which is assigned to the [OV(bbpen)]⁺/⁰ couple. Spectroelectrochemistry in the 350–800 nm spectral region has been used to characterize the V^V analogue. The spectral change for the reaction of [OV^{IV}-(bbpen)] to [OV^V(bbpen)]⁺ is shown in Fig. 2. The $E_{1/2}$ = −0.10 V *vs*. Fc⁺/Fc and n = 1.1 ± 0.2 electrons values obtained from the Nernst plot are in very good agreement with the CV results. The spectra of the deep-purple oxidized complex has peaks at 582 nm (ε = 4900 dm³ mol⁻¹ cm⁻¹) and 400 nm (ε = 3000 dm³ mol⁻¹ cm⁻¹). The broad band at lower energy is assigned as a phenolate-to-vanadium(V) charge-transfer (CT) transition and is characteristic of monooxo-vanadium(V) phenolate complexes.[13] The higher energy transition at 400 nm is also assigned by comparison with other reported V^{V}O–phenolate complexes as being a LMCT process.[14] This fact strongly corroborates the CT assignment in complex **2** in which the absorption intensity is relatively weaker. On the other hand, reduction of **2** with dithionite results in the formation of [V^{III}(bbpen)]⁺ for which the X-ray structure has been described recently.[9] Interestingly, the
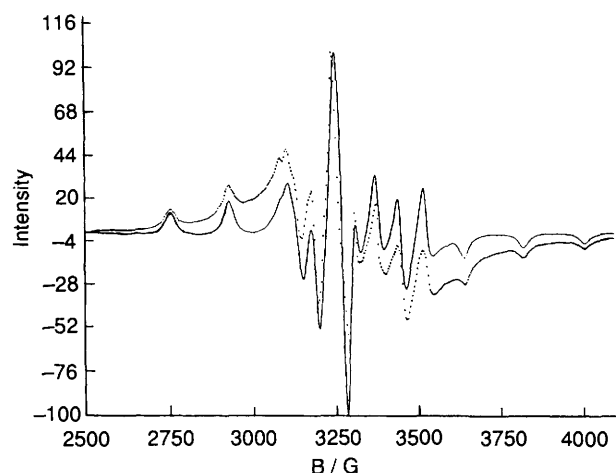
Fig. 3 X-band EPR spectrum of 2 in CH_2Cl_2 at 113 K (80 mW, gain 2 × 10^{-3}); continuous line: simulation, dot line: experimental. The Hamiltonian parameters are $g_z = 1.9375$, $g_x = 1.9705$, $g_y = 1.9765$, $A_z = 180.1$, $A_x = 61.9$, $A_y = 58.4$, 10^{-4} cm^{-1}.

UV–VIS spectral properties of this complex and [V^{III}(tf)] are also very similar.[2,9] Moreover, like [V^{III}(tf)], the [V^{III}-(bbpen)]$^+$ ion complex is totally stable towards oxidation by air, reflecting the high redox potential ($E_{1/2} = 0.27$ V vs. Fc$^+$/Fc) for the [V(bbpen)]$^{2+/+}$ couple.[9]

The X-band EPR spectrum of a frozen solution of 2 in CH_2Cl_2 together with the simulated spectrum is shown in Fig. 3. From the Hamiltonian parameters it is apparent that the spectrum of 2 exhibits in-plane observable anisotropy, $|g_x - g_y| = 0.006$, $|a_x - a_y| = 1.9$ G (1 G = 10^{-4} T), because of the different bond lengths and bond angles in the equatorial plane (Fig. 1). This is consistent with the electronic absorption spectrum of 2 which proves a highly distorted coordination site. A comparison with [OV^{IV}(tf)] shows that both species have similar spectra, with the exception of the A_z tensor value of 180.1 G which is somewhat higher for complex 2. Such a difference in A_z could be attributed to a different coordination environment in the equatorial plane {N_2O_2 for [OV^{IV}(bbpen)] and O_4 for [OV^{IV}(tf)]^8}, although chelate effects in 2 must be taken into account.

Since the UV–VIS and EPR spectral properties of $V^{IV}O$-complexes strongly indicate the presence of equatorially

coordinate functional groups[8] we conclude that the data reported in this work demonstrate that [OV^{IV}(bbpen)] is a very interesting model for the [OV^{IV}(tf)] complex. Therefore, we suggest that an alternative equatorial coordination (N_2O_2 or NO_3) in [OV^{IV}(tf)] should be taken under consideration. The iron binding site of iron(iii)-transferrin has been established through crystallographic studies (NO_3 coordination and CO_3^{2-} as synergistic anion).[15]

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