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Note

A New Di-μ-sulfate Complex as a Model of Purple Acid Phosphatase-Sulfate Complexes

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Reportamos neste trabalho, a síntese, a estrutura cristalina e as propriedades espectroscópicas e eletroquímicas do complexo $NH_4[Fe_2^{III}(bbpmp)(\mu\text{-}SO_4)_2]$ **1** onde bbpmp é o ânion do ligante 2,6-bis[(2-hidróxibenzil)(2-metilpiridil)-amino-metil]-4-metilfenol. Este representa o primeiro exemplo de um complexo contendo a unidade estrutural (μ-fenolato)$(\mu\text{-}SO_4)_2$ e um ligante N,O-doador de relevância, como um análogo sintético para os derivados sulfatos das fosfatasas ácidas púrpuras.

The synthesis, X-ray crystal structure, electrochemical and spectroscopic properties of $NH_4[Fe_2^{III}(bbpmp)(\mu\text{-}SO_4)_2]$ **1** where bbpmp is the anion of 2,6-bis[(2-hydroxy- benzyl)(2-pyridyl-methyl)-amino-methyl]-4-methylphenol, are reported; this is the first example of a (μ-phenolate)$(\mu\text{-}SO_4)_2$ complex, with a relevant N,O-donor ligand, as a synthethic analogue for the purple acid phosphatases-sulfate complexes.

Keywords: *purple acid phosphatases, oxyanion complexes, sulfate model complex, crystal structure*

Introduction

The interaction of the active site of purple acid phosphatases (PAPs) with sulfate and other perturbants has been described[1,2]. This oxyanion is known to be able to interact with the reduced enzymes, which in the presence of air form the oxidized PAP_{ox}-sulfate complexes. In a recent report, Witzel[3] has shown that the addition of SO_4^{2-} to the oxidized form (PAP_{ox}, λ_{max} = 558 nm) leads to the immediate formation of an enzyme-sulfate complex (PAP_{ox}-sulfate) with an absorption maximum at 546 nm. In order to gain more information about the binding mode of PAPs with small bridging oxyanions we describe here the synthesis, crystal structure and properties of a novel Fe_2^{III} synthetic analogue which contains the $Fe^{III}(\lambda\text{-}SO_4)_2Fe^{III}$ unit with a biologically relevant N,O-donor dinucleating ligand. This work is a continuation of a wide research program for the preparation and characterization of iron complexes with bioinorganic interest[4-8].

Experimental

Syntheses

The ligand 2,6-bis[(2-hydroxybenzyl)(2-pyridyl-methyl)-amino-methyl]-4-methylphenol (H_3bbpmp) was prepared as described elsewhere[5,7]. The $NH_4[Fe_2^{III}(bbpmp)(\mu\text{-}SO_4)_2]$ complex was prepared as follows. To a solution of $[Fe^{II}Fe^{III}(bbpmp)(OAc)_2].4H_2O$[6] (0.87 g, 1 mmol) in 20

mL of CH_3CN, was added $(NH_4)_2S_2O_8$ (0.23 g, 1 mmol) and 10 mL of water at room temperature. The clear deep blue solution was heated to 40 °C and stirred for 15 min at ambient atmosphere. After cooling the solution to room temperature, a violet microcrystalline precipitate was formed. Single crystals suitable for X-ray crystallography were obtained by recrystallization from a methanolic solution of **1**. Anal. Calc. for $C_{35}H_{37}N_5O_{11}Fe_2S_2$: C, 47.77; H, 4.24; N, 7.96%. Found: C, 47.82; H, 4.28; N,8.02%.

X-ray crystal structure determination of **1**

Crystal data for **1**. $[C_{35}H_{37}N_5S_2O_{11}Fe_2]$, M = 879.53: trigonal, $P3_1$, (No. 144), a = 19.406(4), b = 19.406(4), c = 10.759(4), V = 3509(2) Å^3 , Z = 3. D_{calc} = 1.249 g cm^{-3}. Crystal dimensions 0.10 x 0.15 x 0.35 mm, Mo-K_α (λ = 0.71073 Å); T = 293 K. Enraf-Nonius CAD-4 diffractometer. Data were reduced using the MOLEN software[9]. The structure was solved with SIR 92 and refined anisotropically for Fe and S atoms. Other non-H atoms were refined isotropically due to the low number of observed reflections ratio to refined parameters.

All the H atoms were placed at geometrically calculated positions except those of the NH_4+ ion that were not found. It was assigned to them an isotropic temperature factor of 1.3 times the isotropic temperature factor of the atom to which they were attached; μ = 0.756 mm^{-1}; 14944 mesured reflections with 7942 unique reflections; 1678 with $I > 3\sigma(I)$; 241 least-square parameters; R = 0.0826 (R_w = 0.0976).

Results and Discussion

The new dinuclear complex $[Fe^{III}(bbpmp)(SO_4)_2]^-$ has been generated in CH_3CN solution (λ_{max} = 587nm/ε = 8430M^{-1}cm^{-1}/Fe$_2$) via oxidation/substitution reactions of the mixed-valence $[Fe^{II}Fe^{III}(bbpmp)(CH_3COO)_2]$[7] ($\lambda_{max}$ = 540 nm/ε = 4840 M^{-1} cm^{-1}/ Fe$_2$) by using aqueous peroxodisulfate and the spectral change is shown in Fig. 1. The maintenance of isosbestic points in successive spectra corroborates the presence of a single product throughout the course of the reactions. The bands are assigned to phenolate-to-Fe^{III} charge transfer transitions and complex **1** is blue shifted compared to $[Fe^{III}Fe^{III}(bbpmp)(CH_3COO)_2]^+$ **2** (λ_{max} = 601 nm/ ε = 7700 M^{-1} cm^{-1}/ Fe$_2$)[5,7] and red shifted compared to the enzyme PAP_{ox}-sulfate (λ_{max} = 546 nm) [3]. These observations are consistent with the stronger Fe^{III}-O interaction of the terminal phenolate groups in **2** (av. Fe^{III}-O = 1.855(8) Å), compared to 1.93(2) Å in **1**.

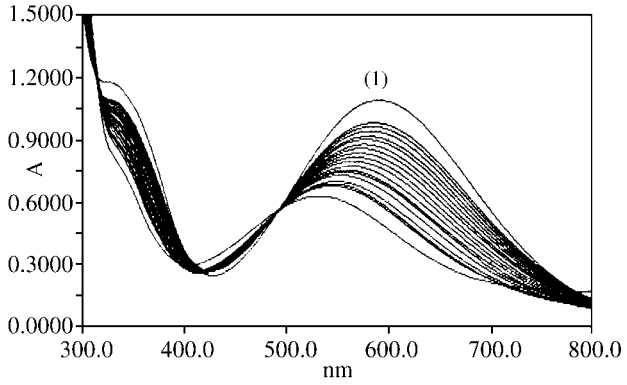

Figure 1. Spectral change during the conversion of $[Fe^{II}Fe^{III}(bbpmp)(CH_3COO)_2]$, in CH_3CN-H_2O/$(NH_4)_2S_2O_8$ solution, into $[Fe_2^{III}(bbpmp)(SO_4)_2]^-$ (**1**) with time intervals of 90 s.

The structure of **1** (Fig. 2) reveals discrete diiron complex anions and ammonium counterions. The iron atoms in the anion of **1** are in a pseudo-octahedral environment in which the two terminal phenolate oxygen atoms coordinate *trans* to the bridging phenolate group. This arrangement of the ligand around the Fe(3) centers is very similar to those observed in the closely related $[Fe_2^{III}(bbpmp)(CH_3COO)_2]ClO_4.H_2O$[5,7], **2** and $[Fe_2^{III}(bbpmp)(O_2P(OPh)_2)_2]ClO_4.H_2O$[10] [$OP(OPh)_2$ = diphenylphosphate] complexes, but with some significant differences in their bond lengths and angles. The Fe-O average distances within the bridging phenolate group increase from 2.055(8) Å in **2** to 2.07(2) Å in **1** to 2.13(2) Å in Krebs's complex and are significantly larger than the corresponding Fe(III)-$O_{(phenolate)}$ bond length observed in the mixed-valence $[Fe^{II}Fe^{III}(bpmp)(OPr)_2][BPh_4]_2$ complex[11] (1.943(2) Å) where bpmp is the anion of 2,6-bis[bis(2-pyridylmethyl)aminomethyl]-4-methylphenol. This is a reflection of the short terminal Fe^3-$O_{(phenolate)}$ (av. 1.93(2), 1.855(2), and 1.853(2) Å) bond lengths observed in **1**, **2**, and in the diphenylphosphate complex, respectively, which are coordinated in *trans* positions relative to the bridging phenolate group. Furthermore, it is important to note that the Fe1-O3-Fe2 bridging angle of 121.7(9)° in **1** is somewhat larger than the 118.3(4) value observed for **2,** but it is significantly smaller than the 128.2(4)° detected in $[Fe_2^{III}(bbpmp)(O_2(OPh)_2)_2]ClO_4.H_2O$[10]. Consequently, the Fe1...Fe2 distance of 3.624(6) Å for **1** is slightly longer (0.096 Å) when compared to that observed for **2**, but is significantly shorter (0.21 Å) than in the diphenylphosphate complex[10]. These facts can be correlated with the increasing O...O separation in phosphate and sulfate compared to the carboxylate bridging ligands. Similar data were reported by Wieghardt *et al.*[12] for the monophenylphosphate, sulfate and acetate diiron(III) complexes with N,N',N''-trimethyl-1,4,7-triazacyclononane as ligand. To our knowledge, **1** represents the first example of an structurally characterized Fe^{III}(μ-phenolate)(μ-$SO_4)_2$Fe^{III} unity with a biologically relevant N,O-donor dinucleating ligand.

The oxidation states of the iron centers in **1** are supported by the Mössbauer spectrum at 115 K and the following parameters: isomer shift (relative to metallic iron with the source at room temperature) δ, 0.51 mm/s and quadrupole splitting, ΔE_Q, 0.87 mm/s which indicates the presence of high-spin Fe_2^{III} centers[13].

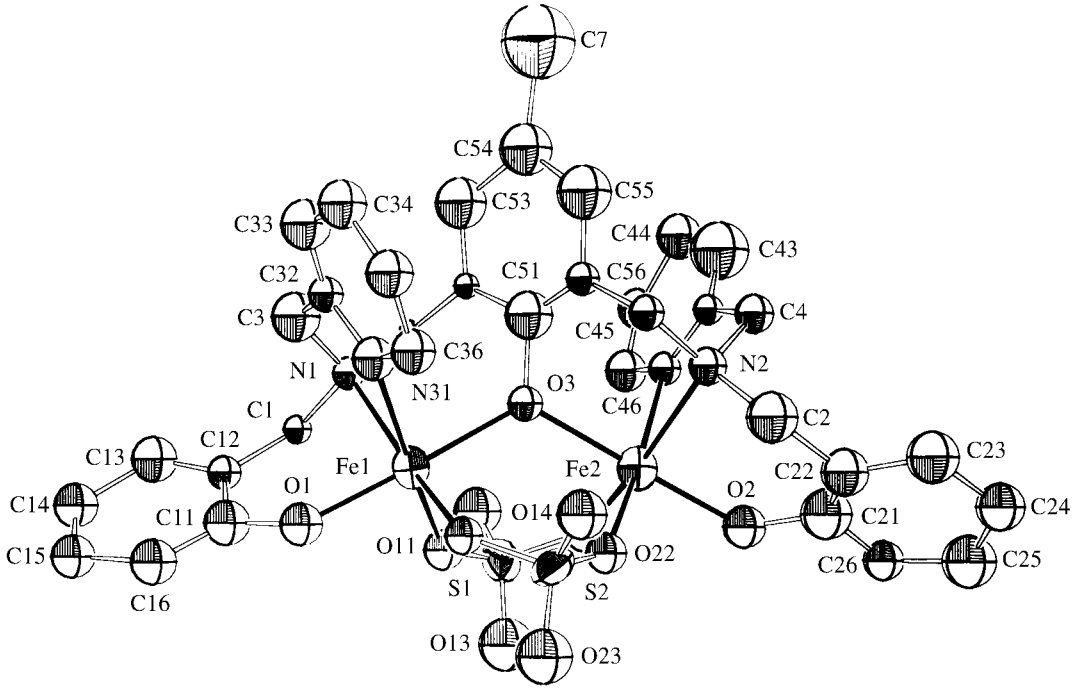

Figure 2. X-ray structure of **1**. Selected bond lenghts (Å) and angles (°). Fe1...Fe2 3.624(6), Fe1-O1 1.92(2), Fe1-O3 2.08(2), Fe1-O11 1.98(2), Fe1-O21 1.99(2), Fe1-N1 2.23(2), Fe1-N31 2.20(2), Fe2-O2 1.94(2), Fe2-O3 2.07(2), Fe2-O12 1.98(1), Fe2-O22 2.07(2), Fe2-N2 2.24(2), Fe2-N41 2.19(3), O1-Fe1-O3 175.5(8), O1-Fe1-O11 89.3(8), O1-Fe1-O21 92.7(8), O1-Fe1-N1 88.2(9), O1-Fe1-N31 93.5(9), O3-Fe1-O11 89.3(7), O3-Fe1-O21 91.7(7), O3-Fe1-N1 87.8(8), O3-Fe1-N31 87.4(9), O11-Fe1-O21 94.6(8), O11-Fe1-N1 99.1(8), O11-Fe1-N31 173(1), O21-Fe1-N1 166.3(7), O21-Fe1-N31 91.3(8), N1-Fe1-N31 75.0(8), O2-Fe2-O3 175.8(6), O2-Fe2-O12 91.9(7), O2-Fe2-O22 90.2(9), O2-Fe2-N2 89.4(8), O2-Fe2-N41 95.(1), O3-Fe2-O12 91.9(7), O3-Fe2-O22 87.6(8), O3-Fe2-N2 87.4(8), O3-Fe2-N41 86.8(9), O12-Fe2-O22 95.4(7), O12-Fe2-N2 165.4(9), O12-Fe2-N41 91.2(7), O22-Fe2-N2 99.2(8), O22-Fe2-N41 171.5(7), N2-Fe2-N41 74.2(8), Fe1-03-Fe2 121.7(9).

The magnetic data for a powder sample of **1** were collected in the temperature range of 5.1 to 300 K and indicate a weak antiferromagnetic coupling interaction for the two Fe^3 ions in the complex. The data were fitted by using the expression for the molar susceptibility *vs.* temperature from the spin-exchange Hamiltonian $H = -2JS_1S_2$ ($S_1 = S_2 = 5/2$)[14] and the following parameters: g = 2.00 (fixed); % imp = 5.5; θ = -3.5 K; $TIP = 400 \times 10^{-6}$ cm^3/ mol; $J = -6.4$ cm^{-1}. This *J* value is very similar to those detected for the complexes $[Fe_2^{III}(bbpmp)(CH_3COO)_2]ClO_4.H_2O$[5,7] and $[Fe_2^{III}(bbpmp)(O_2P(OPh)_2)_2]ClO_4.H_2O$[10], despite the structural differences detected in these complexes.

The electrochemical properties of **1** were investigated by cyclic voltammetry in acetonitrile with $[Bu_4N][PF_6]$ as the supporting electrolyte. A quasi-reversible wave is observed at -1.29 V *vs.* Fc/Fc which is ascribed to the $Fe_2^{III}/Fe^{II}Fe^{III}$ redox couple. The corresponding couple in **2**, is observed to occurs at -0.57 V *vs.* Fc^+/Fc[5,7] and, as expected, the substitution of two acetate by sulfate groups**,** shifts the redox couple to a more negative potential.

We have synthesized and characterized **1** to serve as a synthetic analogue for PAP_{ox}-sulfate complexes but, to our knowledge, there are very few informations in the literature on the corresponding PAP_{ox} complexes to make further comparisons[1,3]. On the other hand, due to the presence of two terminal phenolate groups in **1** and based on the redox potential reported for uteroferrin ($E^{o'}$ = -0.03 V *vs.* Fc/Fc at pH 5)[15] , one should expect a less negative redox potential for the PAPo-sulfate complex compared to **1**.

Finally, further preparative, structural and physicochemical studies on the XO_4^{2-} (X = Cr, Mo) complexes are in progress in our laboratory, and will be the subject of a full paper.

Supplementary Material

The following tables are available from the authors on request: complete table of crystal data, positional parameters, bond distances, bond angles, hydrogen atoms coordinates, displacement parameters (12 pages), and list of observed and calculated structure factors (79 pages).

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