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COMMUNICATION

An aqueous non-heme Fe(IV)oxo complex with a basic group in the second coordination sphere†

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The Fe(IV)oxo complex of a coordinatively flexible multidentate mono-carboxylato ligand is obtained by the one electron oxidation of a low spin Fe(III) precursor in water.

Coordinated aspartate, glutamate and terminal peptide carboxylato groups are ubiquitous motifs in the metal sites of dioxygen activating enzymes especially for the mononuclear non-heme iron dioxygenases for which they play a crucial role in tuning the reactivity of the enzymes by being monoanionic and providing a weak ligand field.^{1–3} Fe(IV)oxo species which can be generated at these sites from reaction with O₂, are invoked as key metal-based oxidants in the catalytic cycles where they are often proposed to react with substrates through hydrogen abstraction mechanisms.⁴ Enormous progress has been made in the understanding of the chemistry of these metalloenzymes through spectroscopic identification and reactivity studies of several synthetic models for the biological Fe(IV)oxo species in the last decade.⁵ The supporting ligands are most typically a neutral set of tetra- or pentadentate N donor (amine, pyridine) ligands and they are usually prepared using O atom transfer reagents such as iodosylarylenes, *N*-oxide amines, peroxides and hypohalides which react with precursor Fe(II) complexes in organic non-protic solvents. Conspicuous in comparisons of these synthetic Fe(IV)oxo species in terms of common features with their biological counterparts are: (i) the paucity of carboxylate donors in the first coordination sphere,⁶ (ii) that they are seldom detected in water⁷ and (iii) there are no biomimetic functionalities in the second coordination sphere.

We have identified a Fe(IV)oxo species using the carboxylato-containing hexadentate ligand (*N,N,N'*-tris(2-pyridylmethyl)-ethylenediamine-*N'*-acetato, tpena^{–8}), [Fe^{IV}(O)(tpenaH)]²⁺ (**1**),

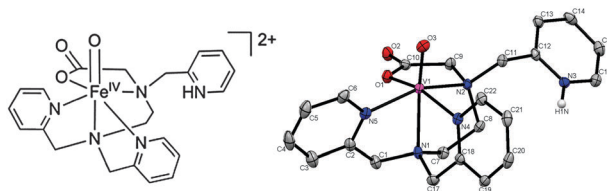
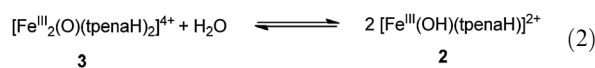
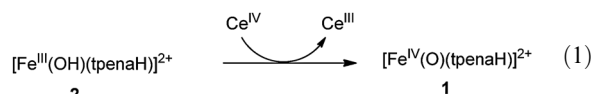


Fig. 1 (a) Diagram of [Fe^{IV}(O)(tpenaH)]²⁺ (**1**) and (b) crystal structure of isostructural [V^{IV}(O)(tpenaH)]²⁺ (**4**). Thermal ellipsoids drawn at 50% probability.

Fig. 1(a), which incorporates several biomimetic functionalities, and is observable only in water. The transient blue **1** (*t*_{1/2} = 1 h) is prepared by the one electron oxidation by (NH₄)₂[Ce(NO₃)₆] (CAN) of a mononuclear low spin Fe(III) complex, [Fe(OH)(tpenaH)]²⁺ (**2**), eqn (1). Complex **2** is generated in solution by the hydrolysis of the structurally characterised oxo-bridged diiron(III) cation in [Fe^{III}₂(μ-O)(tpenaH)₂](ClO₄)₄·(H₂O)₂ (**3**(ClO₄)₄·(H₂O)₂),⁹ eqn (2). Thus in contrast to most of the Fe(IV)oxo species reported to date, water is the source of the oxyl O atom in **1**.



Tpena[–] is a potentially hexadentate ligand, however both **1** and **2** are proposed to contain dangling uncoordinated and protonated pyridine groups. This proposal is exemplified by the X-ray crystal structure of their solid state precursor **3** and that of a stable isovalent and presumably isostructural analogue for **1**, [V^{IV}(O)(tpenaH)](ClO₄)₂·(H₂O)₂ (**4**(ClO₄)₂·(H₂O)₂), Fig. 1(b). In **4** the protonated uncoordinated pyridine group is H-bonded to the non-coordinated carbonyl O atom of the carboxylate group of an adjacent molecule (N–H⋯O, 2.662(14) Å). Adjacent cations are associated into homochiral chains by N_{py}–H⋯O_{COO} and C–H⋯O interactions extended parallel to the *b*-axis. The V=O distance is 1.595(15) Å. The carboxylate donor is located *cis* to the oxo group similarly to the arrangement for α-ketoglutarate dependent dioxygenases.⁴

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† Electronic supplementary information available: Mössbauer, ESI mass UV-vis, ENDOR and HYSOCORE spectra. Details for DFT calculations and crystal structure determination. CCDC 879468. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc35746a

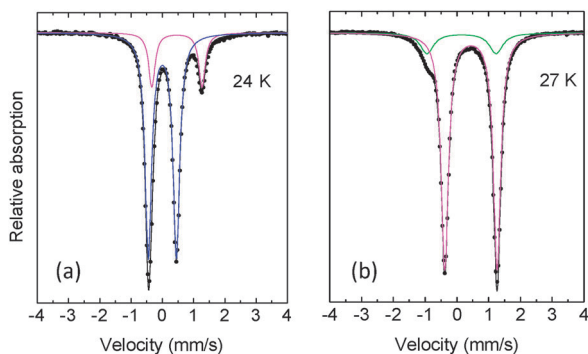


Fig. 2 Mössbauer spectrum of aqueous solutions of ^{57}Fe labeled **3** at approx. 25 K in the presence and absence of CAN. (a) [^{57}Fe -**3**](ClO_4)₄ (2.5 mg, 1.9 μmol) dissolved in 700 μl water with CAN (7.2 mg, 13.3 μmol). The mixture was frozen within approx. 30 seconds. The signal for ^{57}Fe -**1** (blue) amounts to 81% of the total Fe content. (b) The spectrum of ^{57}Fe -**3** (3.6 mM) dissolved in water and frozen within approx. 30 seconds. The absorptions for ^{57}Fe -**3** (magenta) and ^{57}Fe -**2** (green) account for 86% and 14% of the signal respectively.

The UV-visible spectrum of **1** shows an absorption maximum at 730 nm (Fig. S1, ESI †). This value is similar to the λ_{max} of known Fe(IV)oxo species.¹⁰ **1** decays over the course of 2 hours at room temperature. This process is accelerated at room temperature by the addition of “substrates” to the aqueous solutions with rates according to the following order methanol \sim ethanol $>$ cyclohexane \sim CH_2Cl_2 . One electron processes in unspecific C–H oxidations seems a likely scenario since the starting Fe(III) species are regenerated and no ligand/complex decomposition is detected by Electrospray Ionization (ESI) Mass Spectrometry after the treatment of solutions of **3** with CAN (Fig. S2, ESI †).

Mössbauer spectra show that blue aqueous solutions of **1** produce a dominant signal (81%) with an isomer shift and quadrupole splitting of $\delta = 0.00 \text{ mm s}^{-1}$ and $\Delta E_Q = 0.90 \text{ mm s}^{-1}$, Fig. 2(a). The second minor species in this spectrum ($\delta = 0.47 \text{ mm s}^{-1}$ and $\Delta E_Q = 1.60 \text{ mm s}^{-1}$) can be assigned to the starting oxo bridged diiron(III) complex, **3**. Confirmation of this assignment is found in the solid state Mössbauer spectrum of **3**(ClO_4)₄(H_2O)₂. This contains a single Fe species with similar isomer shift and quadrupole splitting of $\delta = 0.44 \text{ mm s}^{-1}$ and $\Delta E_Q = 1.57 \text{ mm s}^{-1}$ (24 K, 100% of signal) as expected for a dimer containing antiferromagnetically coupled $S = 5/2$ Fe(III) centers¹¹ (see Fig. S5, ESI †). Uncertainties in ΔE_Q are about $\pm 0.02 \text{ mm s}^{-1}$.

The isomer shift of **1** is lower than typical high spin ($S = 2$) iron(IV),¹⁰ and so we assign the electronic ground state of **1** as a triplet. Corroborating this, the $S = 1$ state is predicted by DFT calculations to be more stable than the $S = 2$ state by 35 kJ mol^{-1} . Ambiguity regarding the potential protonation site of a hexacoordinated Fe(IV)-tpena $^-$ species (the oxo or dangling pyridyl group) was resolved by calculating the Mössbauer parameters for each of the possible complexes through a DFT approach, Table 1.¹² Similarly Company *et al.* have used DFT to predict the Mössbauer parameters and assign structure for a Fe^{IV}O(H_2O) species *versus* that of an isomeric Fe^{IV}(OH)₂ species.¹³ The calculations support the conclusion that it is not the oxo group that is protonated under the prevailing experimental conditions. No large difference is observed in the calculated isomer shifts for ^{57}Fe , but the quadrupole splittings

Table 1 Calculated Mössbauer parameters for Fe^{IV}oxo/hydroxo complexes of tpena $^-$ with different protonation sites

Complex	δ (mm s^{-1})	ΔE_Q (mm s^{-1})
[Fe(O)(tpenaH)] ²⁺	0.004	0.82
[Fe(OH)(tpenaH)] ³⁺	-0.032	2.25
[Fe(O)(tpena $\cdot\cdot$ H)] ²⁺ ^a	-0.006	1.19
[Fe(OH)(tpena)] ²⁺	-0.035	2.41
[Fe(O)(tpena)] ⁺	-0.003	0.91

^a In this structure the protonated dangling pyridyl arm is intramolecularly hydrogen bonding to the oxo group.

differ substantially from the experimental values if the oxo group is protonated or acts as an acceptor for a H-bond from the protonated pyridyl group. It is impossible on the basis of the calculations to distinguish between [Fe(O)(tpenaH)]²⁺ or [Fe(O)(tpena)]⁺ as candidates for **1** but the $\text{p}K_a$ value of pyridinium ion ($\text{p}K_a \sim 5$) suggests that the dangling pyridine group should be protonated at pH 1. In fact the structural analogue **4** was isolated at the salient pH even higher than this (approx. 4). The calculations imply that any involvement of the pyH in hydrogen bonding must be intermolecular with solvent water and not intramolecular with the Fe^{IV}O group. Similarly we note that the V^{IV}O moiety in **4** is not involved any classic H-bonding interactions in the solid state.

In the context of reaction mechanism for the formation of **1** which we propose to be according to eqn (1), it is relevant to discuss the speciation of iron(III) when **3** is dissolved in water in the absence of CAN. When information gleaned from Mössbauer and Electron Paramagnetic Resonance (EPR) spectroscopies and ESI mass spectrometry (Fig. 2(b), 3 and ESI †) is combined, we have support, not only for the facile cleavage of **3** and formation of **2** by hydrolysis (eqn (2)), but also under more basic conditions, deprotonation of **2** and formation of its congener, a monomeric high spin Fe(III) species, formulated as [Fe(OH)(tpena)]⁺ (**5**). In accordance with its high spin state, **5** is proposed to be seven coordinate and thus tpena $^-$ realises its full potential as a hexadentate ligand. This structural assignment is supported by the structural characterization of [Fe^{III}(tpena)(OIPh)]²⁺⁹ which likewise has a N₅O₂ donor set. There are two reasonable structural proposals for the low spin species **2** which must be six coordinate with a close to regular octahedral geometry at the metal centre: [Fe^{III}(tpena)]²⁺,

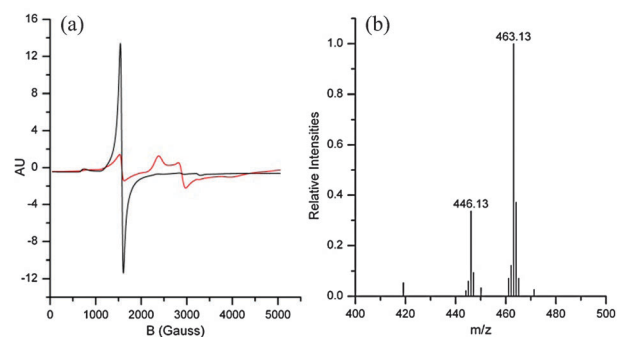


Fig. 3 (a) The EPR spectrum of a solution of **3**(ClO_4)₄(H_2O)₂ dissolved in water to generate **2** and **5** before (red) and after (black) the addition of one equivalent of NaOH per iron. (b) ESI mass spectrum of the oxo-bridged diiron(III) containing **3**(ClO_4)₄(H_2O)₂ complex dissolved in water. Assignments: 463.13, **5**; 446.13, [Fe^{II}(tpena)]⁺.

in which tpena⁻ is six coordinated, or its “hydrate” [Fe(OH)(tpenaH)]²⁺ in which tpenaH is five coordinated (like in **1**, **3** and **4**). Pertinent in the [Fe(OH)(tpenaH)]²⁺ formulation is that the coordinated water-derived ligand, requisite for a proton-coupled electron transfer reaction to form **1**, is already present. For the reasons and evidences below we favor the formulation of [Fe(OH)(tpenaH)]²⁺ for **2**, however the simpler homoleptic [Fe^{III}(tpena)]²⁺ cannot be discounted. Potential hexadentate ligands with ethylenediamine backbones often act as pentadentate ligands in order to relieve strain when the spin state of a metal ion enforces this geometry.¹⁴ DFT calculations predict a low spin state for [Fe(OH)(tpenaH)]²⁺ (see ESI[†]), reminiscent of that for the low spin [Fe(OH)(bztpen)]²⁺.¹⁵

The EPR spectrum of the starting material, **3**(ClO₄)₄·(H₂O)₂ dissolved in water, Fig. 3(a), shows that the dimeric **3** (expected to be EPR silent) is cleaved, at least partially, on dissolution. A rhombic EPR signal with $g = 2.82, 2.31, 1.7$ is consistent with a low spin **2** and the signal at around $g = 4$ with high spin **5**. The intensity of this signal increases on the addition of base and this process is reversed if an equivalent of acid is subsequently added. In corroboration, ions derivable from the Fe(III) species **2**, **3** and **5** can be found in the solvent-dependent ESI mass spectra of **3**(ClO₄)₄·(H₂O)₂. The base peak in the spectrum from water, Fig. 3(b), at m/z 463.13 is due to **5** (C₂₂H₂₅N₅O₃Fe expected at m/z 463.13). The minor ion peak at m/z 446.13 is assigned to [Fe^{II}(tpena)]⁺ (C₂₂H₂₄N₅O₂Fe expected at m/z 446.13) which can stem from **2** by concurrent dehydration and reduction which can be expected in the ESI process. Spectra obtained from acetonitrile solutions show the solid state precursor complex **3** in its deprotonated form (*i.e.*, [(tpena)₂Fe^{III}₂(μ-O)]²⁺) at m/z 454.14 (C₄₄H₄₈N₁₀O₅Fe₂ doubly-charged expected at m/z 454.13), Fig. S4 (ESI[†]), suggesting that cleavage of the dinuclear **3** is more favorable in high water concentrations.

The Mössbauer spectrum of **3**(ClO₄)₄·(H₂O)₂ in water frozen within seconds of dissolution, Fig. 2(b), shows, in contrast to the solid state spectrum of **3**(ClO₄)₄·(H₂O)₂, two Fe(III) species. The dinuclear **3** ($\delta = 0.44$ mm s⁻¹ and $\Delta E_Q = 1.65$ mm s⁻¹) accounts for 86% of the iron. The remaining 14% of the signal ($\delta = 0.16$ mm s⁻¹ and $\Delta E_Q = 2.19$ mm s⁻¹) is consistent with the low spin Fe(III) species **2**. The amount of this latter low spin signal increases if the solutions are aged before freezing. Noteworthy is the fact that no signal for this latter species is observed in the Mössbauer spectra of the blue solutions in which **1** (and CAN) is present, nor if one equivalent of base is added per iron. Under the latter conditions the signal for **5** is evident (Fig. S6, ESI[†], $\delta = 0.46$ mm s⁻¹ and $\Delta E_Q = 0.71$ mm s⁻¹) (50 K, 23% of signal, remaining 77% is due to **3**). This suggests that as depicted by eqn (1), the immediate precursor for **1** is the mononuclear low spin **2** and not the dinuclear **3** which can be observed concurrently with **1** (Fig. 2a).

Preliminary investigation of species **2** by a combination of Hyperfine Sublevel Correlation (HYSCORE) and Electron Double Resonance (ENDOR) spectroscopy (Fig. S8–S10, ESI[†]) show signals for several N atoms with strong hyperfine couplings which must correspond to the coordinated amine and py N atoms. The HYSCORE spectrum shows only one signal, consistent with a decoordinated pyN atom.

In conclusion we have delineated the aqueous Fe(III) and Fe(IV) speciation of the Fe-tpena⁻ system. This ligand favors *cis* carboxylate–O/OH coordination and is a germane biomimic for the electronic environment for mononuclear iron sites in non-heme enzymes capable of forming hypervalent metal-oxyl species with a {Fe^{IV}O}⁺ core. In water, tpena⁻ furnishes a protonated basic group in the second coordination sphere, analogous to the protonated amino acids found in enzyme active site pockets.

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