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Mads Sørensen Vad,*,† Anders Lennartson,*,† Anne Nielsen,*,† Jeffrey Harmer,§ John E. McGrady,§ Cathrine Frandsen, Anne Nielsen, Steen Mørup and Christine J. McKenzie**

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The Fe(IV)oxo complex of a coordinatively flexible multidentate monocoxybutyloxy 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 monooanionic and providing a weak ligand field.1–5 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.4 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)-ethylenediimine-N’-acetato, tpena †)[FeIV(O)(tpenaH)]2+ (1),

![Diagram](image_url)

Fig. 1 (a) Diagram of [FeIV(O)(tpenaH)]2+ (1) and (b) crystal structure of isostructural [VIV(O)(tpenaH)]2+ (4). Thermal ellipsoids drawn at 50% probability.

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, [VIV(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 Npy•••H•••OscCO 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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![Fig. 2(a). The second minor species in this spectrum (Fe(III) centers 11 (see Fig. S5, ESI)](image)

...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)(tpena)]^{2+} or [Fe(O)(tpena)]^{+} as candidates for 1 but the pK_{a} value of pyridinium ion (pK_{a} ~ 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 FeIVO group. Similarly we note that the VIVO moiety in 4 is not involved in 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(II) 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), 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 realizes its full potential as a hexadentate ligand. This structural assignment is supported by the structural characterization of [Fe^{IV}(tpena)(OIPh)]^{2+} \text{ and } [Fe^{IV}(tpena)(H2O)]^{2+} \text{ which likewise has a N}_{5}O_{2} 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+},

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

<table>
<thead>
<tr>
<th>Complex</th>
<th>(\delta) (mm s(^{-1}))</th>
<th>(\Delta E_Q) (mm s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>[FeO(tpenaH)]^{2+}</td>
<td>0.004</td>
<td>0.82</td>
</tr>
<tr>
<td>[FeOH(tpenaH)]^{2+}</td>
<td>-0.032</td>
<td>2.25</td>
</tr>
<tr>
<td>[FeO(tpena-H)]^{2+}</td>
<td>-0.006</td>
<td>1.19</td>
</tr>
<tr>
<td>[FeOH(tpena)]^{2+}</td>
<td>-0.035</td>
<td>2.41</td>
</tr>
<tr>
<td>[FeO(tpena)]^{+}</td>
<td>-0.003</td>
<td>0.91</td>
</tr>
</tbody>
</table>

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

![Fig. 3](image)
in which tpena− is six coordinated, or its “hydrate” [Fe(OH)−(tpenaH)2]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(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)(bztppen)]2+.15

The EPR spectrum of the starting material, 3(CIO4)2(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(m) species 2, 3 and 5 can be found in the solvent-dependent ESI mass spectra of 3(CIO4)2(H2O)2. The base peak in the spectrum from water, Fig. 3(b), at m/z 463.13 is due to 5 (C22H22N2O4Fe expected at m/z 463.13). The minor ion peak at m/z 446.13 is assigned to [Fe(tpena)]− (C22H22N2O4Fe 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 expected to be EPR silent) is cleaved, at least partially, on dissolution. Noteworthy is the fact that no signal for this equivalent of base is added per iron. Under the latter conditions the signal for 5 is evident (Fig. S6, ESI†). δ = 0.46 mm s−1 and ΔE = 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(m) 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 [FeIVO]+ 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.

Notes and references