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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 monoaonic 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−3), [FeIV(O)(tpenaH)]2+ (I),

Fig. 1 (a) Diagram of [FeIV(O)(tpenaH)]2+ (I) 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 carboxylato group of an adjacent molecule (N–H···O, 2.662(14) Å). Adjacent cations are associated into homochiral chains by Npy–H···Opy 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
The UV-visible spectrum of 1 shows an absorption maximum at 730 nm (Fig. S1, ESI†). This value is similar to the λmax of known Fe(IV)oxo species. 10 I 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 > ethanol > cyclohexane ~ CH2Cl2. 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 observed by ESI spectroscopies and ESI mass spectrometry (Fig. 2(b), 3 and ESI†). Confirmation of the pyH in hydrogen bonding must be intermolecular with solvent water and not intramolecular with the FeIVO group. Similarly we note that the 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 [FeIII(tpena)(PIPh)]2+ 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: [FeII(tpena)]2+,

![Fig. 2](image-url)

**Fig. 2** Mössbauer spectrum of aqueous solutions of 57Fe labeled 3 at approx. 25 K in the presence and absence of CAN. (a) [57Fe-3](ClO4)2 (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 57Fe-I (blue) amounts to 81% of the total Fe content. (b) The spectrum of 57Fe-3 (3.6 mM) dissolved in water and frozen within approx. 30 seconds. The absorptions for 57Fe-3 (magenta) and 57Fe-2 (green) account for 86% and 14% of the signal respectively.

<table>
<thead>
<tr>
<th>Complex</th>
<th>δ (mm s⁻¹)</th>
<th>ΔE_Q (mm s⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[FeO(tpena)]2+</td>
<td>0.004</td>
<td>0.82</td>
</tr>
<tr>
<td>[FeOH(tpenaH)]2+</td>
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<td>2.25</td>
</tr>
<tr>
<td>[FeO(tpena₂H)]2+a</td>
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<td>2.41</td>
</tr>
<tr>
<td>[FeO(tpena)]1−</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.*

![Table 1](image-url)

**Table 1** Calculated Mössbauer parameters for FeIVoxo/hydroxo complexes of tpena with different protonation sites.

![Fig. 3](image-url)

**Fig. 3** (a) The EPR spectrum of a solution of 3(ClO4)2(H2O)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(ClO4)2(H2O)2 complex dissolved in water. Assignments: 463.13, 5, 446.13, [FeII(tpena)]1−.
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(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)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(II) species 2, 3 and 5 can be found in the solvent-dependent ESI mass spectra of 3(ClO4)2(H2O)2. The base peak in the spectrum from water, Fig. 3(b), at m/z 463.13 is due to 5 ([C44H48N10O5Fe2 doubly-charged expected at 325.13]). The minor ion peak at m/z 467.13 is assigned to [Fe(tpena)]2− ([C54H52N10O5Fe2 doubly-charged expected at m/z 463.13]) 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 formation of [Fe(OH)(tpenaH)]2+ for 3. More favorable in high water concentrations.

Hyperfine Sublevel Correlation (HYSCORE) and Electron Double Resonance (ENDOR) spectroscopy (Fig. S8–S10, ESI†) shows 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-Ο/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 [FeIV(Ο)]+ 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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Notes and references

12 Mössbauer parameters were calculated with the program package ORCA, S. Sinnecker, L. D. Slepi, E. Bill and F. Neese, Inorg. Chem., 2005, 44, 2245–2254.