Transition-Metal Catalysts

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Amavadin and Homologues as Mediators of Water Oxidation

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Abstract: *The vanadium(IV) N-hydroxyiminodicarboxylate complexes* $[\mathrm{V(HIDPA)_2}]^{2-}$ *and* $[\mathrm{V(HIDA)_2}]^{2-}$*, close models of the amavadin (a natural product from Amanita fungi lacking the V=O group but exhibiting a rare NO-bound oxyiminate moiety), are shown to be the first recognized complexes of the early transition metals (up to periodic Group 7) that mediate the oxidation of water. The reactions were analyzed by visible spectrophotometry, mass spectrometry, and measurement of evolved dioxygen using* $\mathrm{Ce^{4+}}$ *as sacrificial oxidant. A mechanism proposed on the basis of DFT calculations involves the reversible oxidation to the mononuclear* $\mathrm{V^V}$*-{O*$\dot{\mathrm{N}}$*<} center, where the redox active oxyimino group plays a key role and metal oxidation state variation is only one unit. The more similar model of the metallobiomolecule,* $[\mathrm{V(HIDPA)_2}]^{2-}$*, displays a lower oxidation rate than* $[\mathrm{V(HIDA)_2}]^{2-}$ *but does not undergo appreciable degradation, in contrast to the latter.*

Amavadin is a natural vanadium(IV) compound bearing the $[\mathrm{V(S,S\text{-}HIDPA)_2}]^{2-}$ complex anion with two fully deprotonated (*S,S*)-*N*-hydroxyimino-(2,2′)-dipropionate ligands (Figure 1 A).[1] A few models of this metallobiomolecule have been characterized,[2–4] as well as the corresponding oxidized complexes.[5] Its biological role is yet unknown, but it exhibits peroxidase- and catalase-type activities.[6–11] It can mediate the release of O_2, using H_2O_2,[7] as other metallobiomolecules, for example, catalases[12] and photosystem II.[13]

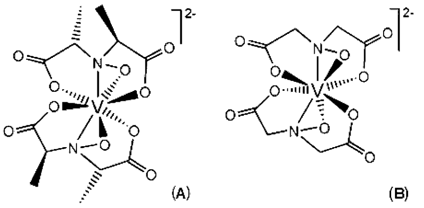

Figure 1. A) $[\mathrm{V^{IV}(S,S\text{-}HIDPA)_2}]^{2-}$; B) $[\mathrm{V^{IV}(HIDA)_2}]^{2-}$.

Progress on O_2 evolution from water oxidation is an important objective for overcoming energy challenges in the future,[13] for enhancement of aerobic in situ treatment of waters[14] or for breathing air revitalization in enclosed environments with restrictions to carry out photochemical reactions, such as manned submersibles.[15] To achieve this, several transition metal (Groups 7–11) complexes have been reported to promote water oxidation by using primary oxidants.[16–19] Alternative processes have been suggested involving electrochemical, photochemical, electrophotochemical, and thermal approaches, as well as using supercritical conditions.[20–23]

Previous studies on the reactivity of amavadin with H_2O_2 did not identify the source of gas generation.[7] Thus, an oxidant without activated oxygen or metal-oxo species, as is the case of $\mathrm{Ce^{4+}}$, could provide a useful tool to identify the origin of the dioxygen evolution and was used in this study, which shows that very similar amavadin models act as mediators of water oxidation under mild conditions without requiring light assistance.

The visible spectra of aqueous solutions of $[\mathrm{V^{IV}(HIDPA)_2}]^{2-}$ and $[\mathrm{V^{IV}(HIDA)_2}]^{2-}$ {HIDPA and HIDA = fully deprotonated forms of *N*-hydroxyimino-(2,2′)-dipropionic acid (as racemic mixture, Figure 1 A) and *N*-hydroxyiminodiacetic acid (Figure 1 B)} are shown in Figure 2 A and B, respectively (curves **1**); both complexes were prepared in situ from vanadyl sulfate as the source of metal ion). The former solution with 1 equiv $\mathrm{Ce^{4+}}$ (added as the sulfate salt) relative to the vanadium complex (which oxidizes blue $\mathrm{V^{IV}}$ to red $\mathrm{V^{V}}$) returns from red to the initial blue after 20 h (Figure 2 A, curves **2**–**6**), while for $[\mathrm{V^{IV}(HIDA)_2}]^{2-}$ the process takes less than 20 min after $\mathrm{Ce^{4+}}$ addition (Figure 2 B, curves **2**–**4**; an identical solution but covered with aluminum foil shows the same behavior, indicating that the reaction rate is independent of the presence or absence of light). Additional experiments in the presence of triflate instead of sulfate or with an excess of sulfate (ca. threefold; see the Supporting Information for the experimental details) did not result in a change of the reaction rates. The vanadium(V) complexes are unstable, as observed when using H_2O_2 as oxidant.[7] The spectrum of the final blue solution in the case of $[\mathrm{V^{IV}(HIDA)_2}]^{2-}$ displays a significantly lower absorbance than the initial one (Figure 2 B, curve **4**), which is more pronounced after further addition of $\mathrm{Ce^{4+}}$. An isosbestic point is detected in the visible spectra collected for the $[\mathrm{V^{IV}(HIDPA)_2}]^{2-}$ solution (Figure 2 A), indicating an interconversion between $\mathrm{V^{V}}$ and $\mathrm{V^{IV}}$ complexes. Moreover, evolution of gas bubbles in the solutions of both complexes was observed.

An excess of $\mathrm{Ce^{4+}}$ relative to $[\mathrm{V^{IV}(HIDPA)_2}]^{2-}$ (up to 5 equiv) was also used for the water oxidation (Supporting Information), but degradation of the complex was then

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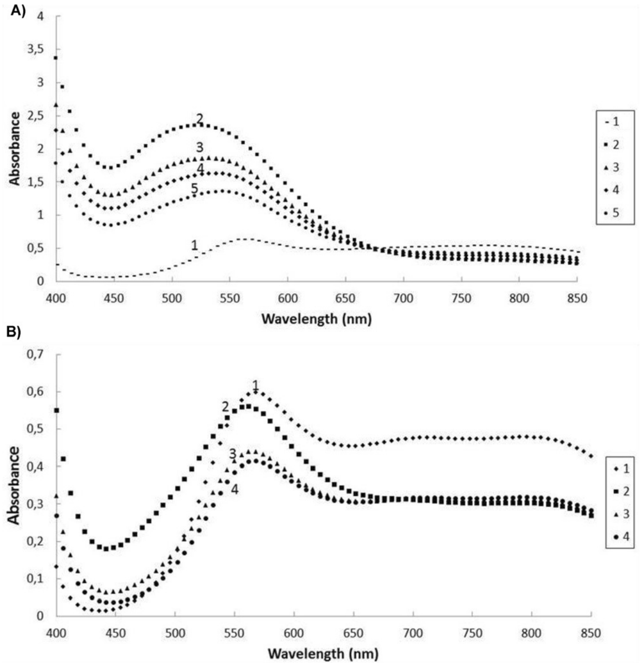


Figure 2. Solutions of $[V^{IV}(HIDPA)_2]^{2-}$ (A) or $[V^{IV}(HIDA)_2]^{2-}$ (B, concentrations 0.02 M), before and after treatment with Ce^{4+} (pH ca. 1). A) **1**, before addition of Ce^{4+}; **2**, 5 min after addition of ca. 1 equiv Ce^{4+} relative to the vanadium complex; **3**, 2 h 30 min; **4,** 4 h; **5**, 6 h; **6**, 20 h (identical to **1**). B) **1**, before addition of Ce^{4+}; **2**, 7 min after addition of ca. 1 equiv Ce^{4+} relative to the complex; **3**, 9 min; **4**, 12 min.

detected by visible spectrophotometry when Ce^{4+} is taken in excess.

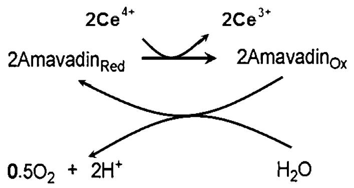
Analysis of the gaseous atmosphere of a $[V^{IV}(HIDA)_2]^{2-}$ solution with 1 equiv Ce^{4+} by electron ionization Fourier transform ion cyclotron resonance mass spectrometry shows the presence of O_2 and CO_2. This, together with the lower absorbance of the final spectrum of Figure 2B, suggests O_2 release and a partial decomposition of the complex, although some of the liberated CO_2 could be due to degradation of a slight excess of the pro-ligand.

Deoxygenated aqueous solutions of $[V^{IV}(HIDA)_2]^{2-}$ and $[V^{IV}(HIDPA)_2]^{2-}$ were monitored at room temperature with O_2 measuring systems, which showed the liberation of O_2 upon the addition of 1 equiv Ce^{4+} under a N_2 atmosphere. For example, an eightfold increase of dissolved O_2 occurred after 12 min in the case of $[V^{V}(HIDA)_2]^{-}$ (from 0.58 $mg\,L^{-1}$ to 4.60 $mg\,L^{-1}$), whereas a comparable enhancement was observed after 24 h in the case of $[V^{V}(HIDPA)_2]^{-}$ (Supporting Information).

The methyl groups at carbon 2 and 2′ in HIDPA conceivably reduce the reaction rate and the ligand decomposition on account of steric effects.

As the Ce^{4+} counterion (sulfate) cannot be a source of oxygen (even the exchange rate with the oxygen atom of water is very slow),[24] one can conclude that the amavadin models are able to mediate water oxidation.

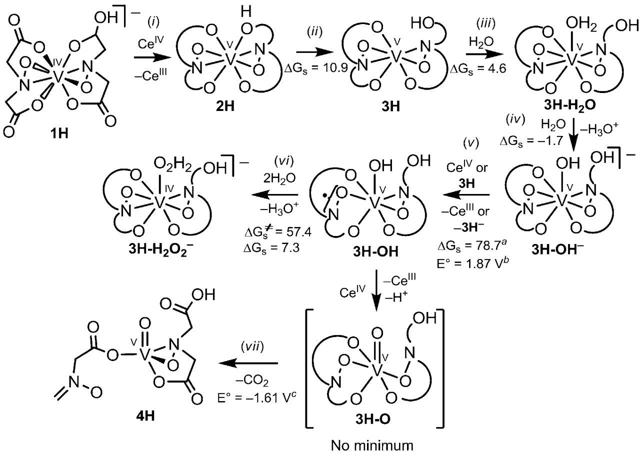
The redox reactions of Ce^{4+} do not need a supply of protons, in contrast with more common oxidants (permanganate, dichromate, and other oxyanions), although they should be carried out in acid solutions to avoid precipitation.[25] However, the solution pH decreases as the reaction proceeds when using Ce^{4+} as oxidant, and an additional experiment run at a higher initial pH led to an even more pronounced pH drop. This is consistent with the expected formation of protons, according to the overall water oxidation reaction represented in Scheme 1. The vanadium complexes display a metal oxidation state variation of only one unit.



Scheme 1. Water oxidation by amavadin using Ce^{4+} as oxidant.

The reaction was monitored by electrospray ionization quadrupole ion trap mass spectrometry (ESI-QIT/MS) studies, as well as heavy-oxygen water ($H_2{}^{18}O$) and heavy water (D_2O) (Supporting Information), which reveal the association of water to the V^V complex and $^{16}O/^{18}O$ and H/D exchanges, supporting an inner sphere mechanism for water oxidation.

A plausible mechanism of the O–O bond formation (the principal step of the whole water oxidation process) mediated by $[V(HIDA)_2]^{2-}$, accounting for the experimental results, was proposed on the basis of theoretical DFT studies (Scheme 2). Taking into account that the reaction medium is highly acidic owing to an extensive hydrolysis of the ceric aqua-complex, the monoprotonated form of $[V^{IV}(HIDA)(HIDAH)]^{-}$ (**1H**) was considered in these calculations. The mechanism includes: i) one-electron oxidation of **1H** by Ce^{4+} to the corresponding V^V species **2H**; ii) decoordination of the protonated carboxylic group to liberate one coordination site of the V atom; iii) coordination of H_2O to give the adduct **3H-H$_2$O** (a water containing species with the same *m*/*z* value was



Scheme 2. Proposed mechanism of the O–O bond formation (i–vi) and complex degradation (vii). Gibbs free energies of activation and reaction are given in $kJ\,mol^{-1}$. [a] For the oxidation with **3H.** [b] For the process **3H-H$_2$O**→**3H-OH** + H^+ + 1 e^-. [c] For the process **3H-OH**→[**4H**]CO_2 + H^+ + 1 e^-.

detected by mass spectrometry; Supporting Information, Figure S1B, panel **III**); iv) deprotonation of the highly acidic coordinated H_2O molecule (outer sphere water molecules or SO_4^{2-} anions may play the role of the base in this process); v) one-electron ligand oxidation (centered at the coordinated $^{-}\mathrm{ON}<$ moiety to form $\mathrm{O\dot{N}}<$) of the thus formed complex **3H-OH**$^{-}$ by excess of Ce^{4+} or even by another V^{V} species existing in solution (for instance, **3H** under stoichiometric reaction conditions when all Ce^{4+} is consumed for the oxidation of the initial V^{IV} complex); and vi) water addition to the OH^{-} ligand of **3H-OH** with simultaneous proton transfer to a base (solvent or the SO_4^{2-} anion) and oxidation of water and the hydroxido ligand to hydrogen peroxide upon electron-transfer to V^{V} and to the ligated $\mathrm{O\dot{N}}<$ radical moiety. As a result, the hydrogen peroxide V^{IV} adduct **3H-H$_2$O$_2$**$^{-}$ is formed. Further metal-catalyzed conversion of H_2O_2 to O_2 is a well-known process.[7,29,30]

The calculations demonstrated that the HIDA ligand plays an important role in the water oxidation process. The HIDA ligand bearing the electron rich NO group makes possible the relatively easy, ligand-centered oxidation of the V^{V} complex **3H-OH**$^{-}$ (step v), and thus the accumulation of oxidative strength of the complex toward water (step vi). Therefore, the coordinated $^{-}\mathrm{ON}<$ ligand moiety plays a key role, reversibly converting into the oxidized radical $\mathrm{O\dot{N}}<$ form.

Other mononuclear mechanisms (such as those based on the non-oxidized ligand V^{V} complexes **3H-OH**$^{-}$ and others) and various binuclear pathways were found to be thermodynamically highly unfavorable (Supporting Information).

Complex **3H-OH** may undergo further oxidation by Ce^{4+}, resulting in the decomposition of the HIDA ligand and formation of CO_2. The calculations indicated that there is no minima on the potential energy surface corresponding to the oxidized species **3H-O**, and instead complex **4H** and CO_2 are formed upon geometry optimization (Scheme 2, vii). The estimated $E°$ value referenced to NHE for this process is negative (-1.61 V), indicating that the decomposition of **3H-OH** is spontaneous upon oxidation. Thus, the observed CO_2 formation by degradation of the complex with an excess of Ce^{4+} is accounted for by its overoxidation.

Therefore, amavadin is shown to act as a mediator of water oxidation (without requiring radiation exposure), and the second metallobiomolecule to do so after photosystem II (which requires light). Amavadin-like models are unique examples found by us wherein the water oxidation is promoted by a mononuclear center with a formal metal oxidation state variation of only one unit (V^{IV}/V^{V}). This is allowed by the ligands, whose N,O-bonded anionic hydroxyiminate group $^{-}\mathrm{ON}<$ [isoelectronic with a peroxo group[31]] is redox active (reversibly oxidizable to the bound radical $\mathrm{O\dot{N}}<$ form).

This $^{-}\mathrm{ON}<$ coordinated moiety, which makes amavadin and similar models unique vanadium complexes, is reversibly oxidizable to the bound radical $\mathrm{O\dot{N}}<$ form with a single-electron oxidation ability, allowing, in cooperation with V^{V}, the occurrence of an overall 2-electron process ($2\,O^{2-} \rightarrow O_2^{2-} + 2\,e^{-}$):

$$H_2O + HO\text{-}V^{V}\text{-}\{\mathrm{O\dot{N}}<\} \rightarrow H_2O_2\text{-}V^{IV}\text{-}\{^{-}\mathrm{ON}<\} + H^{+} \tag{1}$$

This represents an unconventional mechanism of water oxidation that requires the cooperation of a single metal and ligand as redox centers, thus increasing the oxidation ability of the system. This can inspire further studies on the design of new complexes with amavadin-related ligands and other single-electron M^{n}/M^{n+1} redox pairs toward achieving an efficient water oxidation catalysis. This promising new approach for water oxidation based on metal–ligand cooperation between a redox active ligand and a single metal ion, both undergoing single-electron redox processes, is of marked simplicity and its generality deserves to be tested for a wide variety of systems.

The capacity of the amavadin models to undergo reversible oxidation of water (which is resistant to oxidation), is consistent with the role of these complexes as catalysts for oxidation reactions, such as hydroxylation, oxygenation, peroxidative halogenation of hydrocarbons, carboxylation of alkanes, oxidation of thioanisole and alcohols, and epoxidation of allylic alcohols.[6]

Finally, these results appear to suggest amavadin is associated with the production of O_2, under suitable biological conditions. Curiously, *A. muscaria* is one of the few fungi bearing O_2-dependent enzymes in the betalain pigments synthesis.[32]

Experimental Section

Reagents were used as supplied. $VO(SO_4)\cdot 5\,H_2O$ and $Ce(SO_4)_2\cdot 4\,H_2O$ were the sources of V^{IV} and Ce^{IV}, respectively. The syntheses of H_3HIDA and H_3HIDPA (H_3L) were carried out according to known procedures.[33] The complexes were prepared in situ.[7] The aqueous solutions used for all the experiments were prepared with deoxygenated water. All reactions and operations were carried out at room temperature (20–25 °C).

Visible spectra were recorded on an UV/VIS PerkinElmer L35 spectrophotometer with the program PerkinElmer WinLab. Analyses of the gaseous atmosphere and solutions were carried out in Extrel/Finnigan FTMS 2001-DT and Bruker HCT mass spectrometers, respectively. An Inolab oxi 730 WTW equipment and a SG9-SevenGo pro^{Tm} oxygen meter were applied for O_2 measurements with $[V(HIPA)_2]^{2-}$ and $[V(HIDPA)_2]^{2-}$ in suitable flasks and using a similar procedure. The instrument readout was calibrated against air-saturated distilled water in the air-tight cell.

The full geometry optimization of all structures and transition state was carried out at the DFT/HF hybrid level of theory using the B3LYP* functional[34–37] with the help of the Gaussian-09[38] program package.

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Keywords: amavadin · ligand effects · N-hydroxyiminodicarboxylate complexes · vanadium · water oxidation

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