Formation, stability, and reactivity of a mononuclear nonheme oxoiron(IV) complex in aqueous solution†

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A mononuclear nonheme oxoiron(IV) complex bearing a pentadentate N5 ligand was prepared in aqueous solution; the pH dependence of its stability and reactivities was reported along with the mechanistic details of sulfide oxidation by the oxoiron(IV) species.

Mononuclear nonheme iron enzymes are involved in many oxidative metabolic pathways in nature.[1] Our understanding of the catalytic transformations of the enzymes, especially the nature of active oxidizing species, has increased dramatically with the intensive mechanistic studies of the enzymes and their model compounds.[2] For example, a high-valent iron(IV)-oxo intermediate has been characterized as an active oxidizing species in *Escherichia coli* taurine: α-ketoglutarate-dependent dioxygenase (TauD).[3] In biomimetic studies, Münck, Nam, Que, and their co-workers have reported the generation and isolation of mononuclear nonheme oxoiron(IV) complexes bearing tetradentate N4 and pentadentate N5 ligands.[4] A high-resolution X-ray structure of a nonheme oxoiron(IV) intermediate, $[Fe(IV)(O)(TMC)(NCCH_3)]^{2+}$ (TMC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane), has been obtained for the first time,[4a] and other nonheme oxoiron(IV) complexes have been well characterized with various spectroscopic techniques.[4,5] In addition, it has been demonstrated that nonheme oxoiron(IV) complexes are capable of oxygenating various organic substrates such as PPh_3, thioanisole, olefins, and alkanes.[4,5] Since nonheme oxoiron(IV) complexes reported so far have been prepared only in organic solvents (*e.g.*, CH_3CN), we decided to explore the chemistry of nonheme oxoiron(IV) species in aqueous solution.[6] In this communication, we report the first example of a mononuclear nonheme oxoiron(IV) complex bearing a pentadentate N5 ligand, $[(N4Py)Fe^{IV}{=}O]^{2+}$ (**1**) (N4Py = *N*,*N*-bis(2-pyridylmethyl)-bis(2-pyridyl)methylamine),‡ in aqueous solutions.

The reaction of $[Fe^{II}(N4Py)(ClO_4)_2]$ with oxidants such as peracetic acid (CH_3CO_3H), potassium monopersulfate ($KHSO_5$), iodosylbenzene (PhIO), and H_2O_2 at 25 °C in H_2O–CH_3CN mixture (v/v = 3 : 1) produces a pale green intermediate **1** with a maximum absorption wavelength λ_{max} at 680 nm (Fig. 1a, bold red color).§[4c] The electrospray ionization mass spectrum (ESI MS) of **1** exhibits a prominent ion at a mass-to-charge ratio (*m*/*z*) of 538.1, whose mass and isotope distribution pattern corresponds to $[Fe(IV)(O)(N4Py)(ClO_4)]^+$ (calculated *m*/*z* of 538.1) (Fig. 1b). When the identical reaction was carried out in isotopically labeled water, $H_2{}^{18}O$ (95% ^{18}O-enriched), a mass peak corresponding to $[Fe(IV)(^{18}O)(N4Py)(ClO_4)]^+$ appeared at *m*/*z* of 540.1 (Fig. 1b, inset), indicating that **1** exchanges its oxygen with $H_2{}^{18}O$.[7] Further, although **1** was stable for several days ($t_{1/2} \approx 48$ h) at 25 °C, the intermediate reacted with thioanisole and reverted back to the starting $[Fe^{II}(N4Py)]^{2+}$ complex with a clear isosbestic point at 520 nm (Fig. 1a). Product analysis of the reaction mixture revealed that methyl phenyl sulfoxide was yielded quantitatively.

We then investigated the dependence of the formation and stability of **1** on the pH of reaction solutions, by carrying out reactions of $[Fe^{II}(N4Py)]^{2+}$ and $KHSO_5$ at different pH values in buffered H_2O–CH_3CN mixture (*v*/*v* = 3 : 1) at 5 °C. The formation of **1** was observed in the pH range 5–9,¶ and the UV-vis spectra of **1** in buffered solutions were identical to that observed in

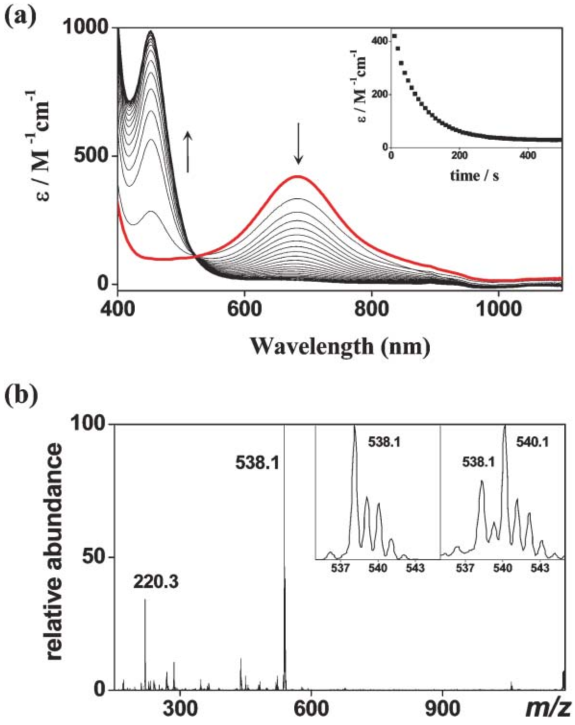

Fig. 1 (a) UV-vis spectral change of **1** (2 mM) upon addition of 10 equiv. thioanisole at 25 °C. Scan interval: 10 s (first scan was 10 s after the addition of thioanisole). Inset shows time course of the decay of **1** monitored at 680 nm. (b) Electrospray ionization mass spectrum of **1** prepared in the reaction of $Fe^{II}(N4Py)(ClO_4)_2$ (2 mM) and CH_3CO_3H (4 mM) at 25 °C. The mass peak at *m*/*z* of 220.3 corresponds to $[Fe(III)(OH)(N4Py)]^{2+}$. Insets show observed isotope distribution patterns for $[Fe(IV)(O)(N4Py)(ClO_4)]^+$ (left panel) and $[Fe(IV)(^{18}O)(N4Py)(ClO_4)]^+$ (right panel).

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† Electronic supplementary information (ESI) available: Experimental details, Tables S1–S2, and Figs. S1–S3. See http://www.rsc.org/suppdata/cc/b4/b415507f/

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the H_2O–CH_3CN mixture (Fig. 1a). Interestingly, the stability of **1** was found to depend significantly on the pH of reaction solutions (Fig. 2a), in which **1** was stable at low pH (*i.e.*, pH 5–6) but decayed at a fast rate with increasing pH of the reaction solutions. To the best of our knowledge, this study provides the first direct observation that the stability of high-valent iron-oxo complex is controlled by the pH of reaction solutions. Although it may be suggested that the increased stability of **1** at low pH results from the protonation of the iron(IV)-oxo group,[8] more detailed investigations are needed to understand the effect of pH on the stability of **1**.

The pH dependence of the reactivity of **1** in oxygen atom transfer reactions was also examined in the pH range 5–7,|| by carrying out thioanisole oxidation by **1** in buffered H_2O–CH_3CN mixture (v/v = 3 : 1) at 10 °C. Upon addition of 10 equiv. thioanisole to the solution of **1**, the intermediate reverted back to the starting $[Fe^{II}(N4Py)]^{2+}$ complex with a clear isosbestic point at 520 nm (Fig. 1a), yielding the corresponding sulfoxide product quantitatively. Pseudo-first-order fitting of the kinetic data allowed us to determine k_{obs} values to be $4.6(2) \times 10^{-3}$ s^{-1}, $6.2(3) \times 10^{-3}$ s^{-1}, and $7.3(3) \times 10^{-3}$ s^{-1} at pH 5, 6, and 7, respectively, showing very little dependence on the pH of reaction solutions in the oxo transfer from **1** to sulfide. When pseudo-first-order rate constants determined in the reactions of **1** and various *para*-substituted thioanisoles at pH 5 were plotted against σ_p, a good correlation was observed with Hammett ρ value of −1.0(2) (Fig. 2b; See ESI†, Table S1 for k_{obs} values). The negative ρ value indicates the electrophilic character of the oxo group of **1** in oxygen atom transfer reactions.[9] Further, the pseudo-first-order rate constants increased proportionally with the thioanisole concentration, leading us to determine second-order rate constants for the *para*-substituted thioanisoles (See ESI†, Fig. S1 and Table S2). By plotting the second-order rate constants against the one-electron oxidation potentials (E^{o}_{ox}) of the sulfides, a linear line with the slope of –2.0(3) was obtained (See ESI†, Fig. S2 and Table S2). Such a small number indicates that the oxidation of sulfides by **1** occurs *via* direct oxygen atom transfer mechanism rather than involving an electron-transfer process.[10] Finally, by determining the rate constants for the oxidation of thioanisole by **1** from 283 to 308 K at pH 5, we were able to calculate activation parameters of $\Delta H^{\ddagger}$ = 13(2) kcal mol^{-1} and $\Delta S^{\ddagger}$ = −25(2) cal mol^{-1} K^{-1} (See ESI†, Fig. S3).

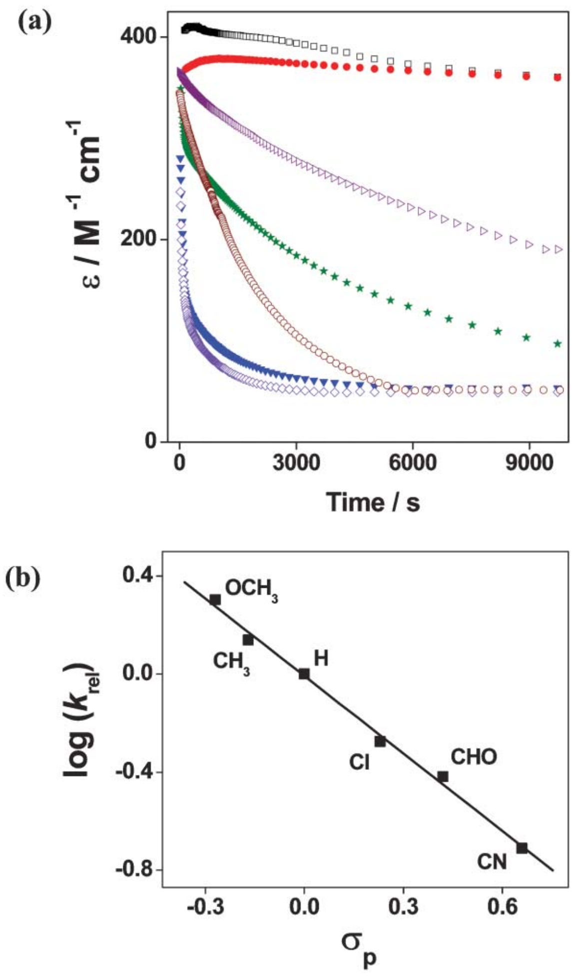

Fig. 2 (a) Time course of the natural decay of **1** monitored at 681 nm at different pH values; pH 5.0 (□, black), pH 6.0 (●, red), pH 6.5 (▷, cerise), pH 7.0 (★, green), pH 7.5 (○, wine), pH 8.0 (▼, blue), pH 9.0 (◇, lilac). Reactions were performed at pH 5–6 in acetate buffer (0.1 M) and at pH 7–9 in TRIS buffer (0.1 M). (b) Hammett plot of log k_{rel} against σ_p of thioanisoles in the reactions of **1** (2 mM) and *para*-X-substituted thioanisoles (20 equiv. to **1**) at 10 °C.

In summary, we have reported the generation and reactivities of a synthetic mononuclear nonheme oxoiron(IV) complex at different pH values in aqueous solution. By using the *in-situ* generated oxoiron(IV) intermediate directly in oxygen atom transfer reactions, we were able to provide mechanistic details of sulfide oxidation in a nonheme iron model system.

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Notes and references

‡ Although other nonheme oxoiron(IV) complexes such as $[(TMC)Fe^{IV}{=}O]^{2+}$ were generated in aqueous solutions, reactivity studies were performed only with an oxoiron(IV) complex bearing a pentadentate N5 ligand, to avoid a possible involvement of buffers as a ligand that may change chemical properties of oxoiron(IV) species in different buffer solutions.

§ It is worth noting that the formation of **1** was faster in aqueous solution than in acetonitrile solution. For example, the formation of **1** in the reaction of $[Fe^{II}(N4Py)]^{2+}$ and CH_3CO_3H took ∼30 s and ∼25 min in aqueous and acetonitrile solutions, respectively.

¶ Since the reaction solution became turbid below pH 5 and above pH 9 upon addition of oxidants to the solution of $Fe^{II}(N4Py)(ClO_4)_2$, the reactivity studies were performed only in the pH range of 5–9.

|| Due to the fast natural decay of **1** at high pH, we were unable to examine its reactivity with substrate at pH 8 and 9 (see Fig. 2a).

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