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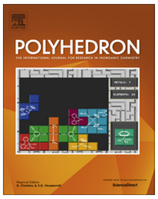

Oxidation of 2,6-di-*tert*-butylphenol by tetrapyridyl oxoiron(IV) complex

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ABSTRACT

The reactivity of the previously reported pentadentate low-spin ($S = 1$) oxoiron(IV) complex, $[Fe^{IV}(O)(asN4Py)]$ (**2**) (asN4Py = *N*,*N*-bis(2-pyridylmethyl)-1,2-di(2-pyridyl)ethylamine), has been investigated in the oxidation reaction of 2,6-di-*tert*-butylphenol derivatives. Detailed kinetic, and mechanistic studies (kinetic isotope effect (KIE) of 4.52, and Hammett correlation with $\rho = -1.83$), lead to the conclusion that the rate-determining step in this reaction involves direct hydrogen-atom transfer (HAT) from the phenol by the oxoiron(IV) species, in contrast to the heme-type horseradish peroxidase (HRP) system.

1. Introduction

Phenols, which are typical substrates for the horseradish peroxidase (HRP), are oxidized to phenoxyl radicals. Mechanistic studies suggested that the oxidation process involves a rate determining electron transfer from the phenol to the oxo–heme species [1], in contrast to the biomimic $Fe^{IV}(T2MPyP)(O)$ (T2MPyP = tetra(2-*N*-methylpyridyl)porphyrin) containing system where oxidation occurs by hydrogen atom abstraction via simultaneous removal of a proton and an electron [2]. Since phenols are one of the major water and soil pollutants, in addition to enzymatic systems, transition metal complexes [3], metalloporphyrins [4], Schiff bases [5], and metallophthalocyanines have also been investigated as catalysts for phenol oxidations or degradations [6]. On the other hand, the 2,6-di-*tert*-butylphenols are widely used as antioxidants and models of vitamin E in medicine. Despite the widespread interest in metalloporphyrin-catalyzed oxidations, there is relatively little information on the mechanism of phenol oxidations by nonheme oxoiron(IV) complexes. The oxidation of phenols and hydroquinones (H_2Q) by nonheme oxoiron(IV) complex, $[Fe^{IV}(TMC)(O)]^{2+}$ (TMC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane), has been extensively studied, and a hydrogen-atom abstraction mechanism was proposed [7].

The coordination chemistry of nitrogen-rich pentadentate ligands has received much attention. These ligands have demonstrated the ability to stabilize high-valent metal centers. Oxoiron(IV) complex supported by pentadentate N4Py (N4Py = *N*,*N*′-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine) ligand [8], has been presented to oxidize various substrates by a high variety of mechanisms, including electron transfer (ET) [9a], electron transfer-proton transfer (ET-PT) [9b], hydrogen atom abstraction (HAT) [9c,d], and oxygen atom transfer (OAT) [9e,f]. We have previously reported the synthesis and structure of iron(II) precursor complex $[Fe^{II}(asN4Py)](ClO_4)_2$ (**1**) supported by pentadentate ligand asN4Py (asN4Py = *N*,*N*-bis(2-pyridylmethyl)-1,2-di(2-pyridyl)ethylamine), the spectroscopic characterization of one of the most stable high-valent complex $[Fe^{IV}(asN4Py)(O)]^{2+}$ (**2**) derived from the reaction of **1** with PhIO, and its reactivity in OAT reaction towards PhSMe derivatives [10]. In this study, we report the stoichiometric oxidation of 2,6-di-*tert*-butylphenol (DTBP) by **2** in order to get more insight into the mechanism of O–H activation process (Scheme 1).

2. Experimental

2.1. Materials and methods

All syntheses were done under an argon atmosphere unless stated otherwise. Solvents used for the synthesis and reactions were purified by standard methods and stored under argon. The starting materials for the ligand are commercially available and they were purchased from Sigma–Aldrich. $[Fe^{II}(asN4Py)(CH_3CN)](ClO_4)_2$ and asN4Py (asN4Py = *N*,*N*-bis(2-pyridylmethyl)-1,2-di(2-pyridyl)ethylamine) were prepared as previously described [10]. Microanalyses were done by the Microanalytical Service of the University of Pannonia. The UV–vis spectra were recorded on an Agilent 8453 diode-array spectrophotometer using quartz cells. GC analyses

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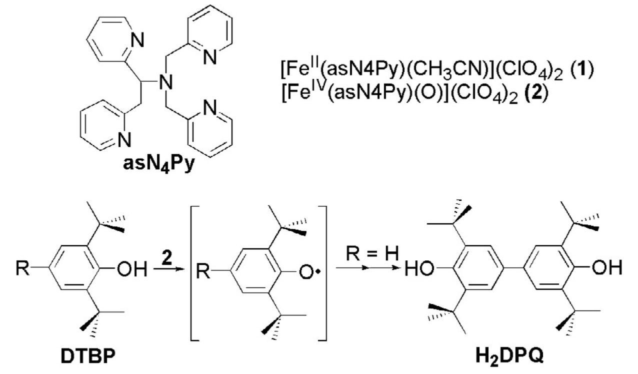

Scheme 1. Oxoiron(IV)-mediated oxidation of 2,6-di-*tert*-butylphenol derivatives.

were performed on an Agilent 6850 gas chromatograph equipped with a flame ionization detector and a 30 m CHIRASIL-L-VAL column. GC–MS analyses were carried out on Shimadzu QP2010SE equipped with a secondary electron multiplier detector with conversion dynode and a 30 m HP-5MS column.

2.2. Stoichiometric oxidations

$[Fe^{II}(asN_4Py)(CH_3CN)](ClO_4)_2$ complex (2.00×10^{-3} M) was dissolved in acetonitrile (1.5 mL), then iodosobenzene (2.4×10^{-3} M) was added to the solution. The mixture was stirred for 40 min then excess iodosobenzene was removed by filtration. Substrate (1.00×10^{-2}–4.00×10^{-2} M) was added to the solution and the reaction was monitored with UV–vis spectrophotometer at 705 nm ($\varepsilon = 400\ M^{-1}\ cm^{-1}$) (Table 1). The characterization of the product 4,4′-dihydroxy-3,3′,5,5′-tetra-*tert*-butylbiphenyl (H_2DPQ) based on previously described methods [6c].

3. Results and discussion

The reactivity of $[Fe^{IV}(asN4Py)(O)]^{2+}$ (**2**) has been studied at 25 °C in the stoichiometric oxidation reaction of DTBP and several of its 4-substituted derivatives in dry acetonitrile. Complex **2** was generated by the reaction of **1** with 1.2 equiv. of PhIO (~40 min), and the rate of its rapid decomposition at 705 nm (Fig. 1a) was measured as a function of the concentration of added DTBP. The coupled product 4,4′-dihydroxy-3,3′,5,5′-tetra-*tert*-butylbiphenyl (H_2DPQ) was characterized by GC/MS (H_2DPQ: MS, m/e: 410 (M^+), 395, 190, 162, 57.) Its yield (~90% based on [2]) was almost quantitative, indicating that the UV–vis spectral change corresponds to the oxidation process.

The rates in the presence of a large excess of DTBP obeyed pseudo-first-order kinetics, and the pseudo-first-order rate constants (k_{obs}) increased proportionally with the initial concentration of the phenol (entries 4–5, 10–12 in Table 1, and Fig. 1b). From this linear plotting, the second-order rate constant (k_2) was determined to be $1.93 \times 10^1\ M^{-1}\ s^{-1}$ at 25 °C. At constant DTBP concentration the k_{obs} values were shown to be independent of the initial concentration of the oxoiron(IV) species. The linear plot of the reaction rate values (V) against the initial concentration of **2** states that the reaction is first-order with respect to the oxoiron(IV) concentration (entries 13–18 in Table 1, and Fig. 1c). The above results establish a rate law of $-d[\mathbf{2}]/dt = k_2[\mathbf{2}][DTBP]$. Activation parameters of $\Delta H^{\neq} = 21\ kJ\ mol^{-1}$, and $\Delta S^{\neq} = -74\ J\ mol^{-1}\ K^{-1}$ (at 298 K) were calculated from plot of $\log(k_2/T)$ versus $1/T$ in CH_3CN over the temperature range 283–308 K (entries 15, 19–23 in Table 1, and Fig. 1d). The activation enthalpy of 21 $kJ\ mol^{-1}$ is relatively higher than those obtained in the oxidation of H_2Q by $[Fe^{IV}(TMC)(O)]^{2+}$ (6.9 $kJ\ mol^{-1}$) [7b] and in the oxidation of phenol by *tert*-butoxy radical (11.7 $kJ\ mol^{-1}$ in $PhCH_3$) [11], but lower than that in the oxidation of 3-CN-C_6H_4OH by $Fe^{IV}(T2MPyP)(O)$ 57.4 $kJ\ mol^{-1}$) [2]. The relatively large negative entropy is typical of associative processes. Three alternative mechanisms, namely electron

Table 1
Kinetic data for the stoichiometric oxidation of DTBP with $[Fe^{IV}(asN4Py)(O)](ClO_4)_2$.

No.	T (K)	DTBP (10^{-2} M)	$[Fe^{IV}(O)]^{2+}$ (10^{-3} M)	k_2 ($M^{-1}\ s^{-1}$)
1	298	1	2	20.8 ± 0.8
2	298	1[a]	2	7.11 ± 0.4
3	298	1[b]	2	32.1 ± 1.6
4	298	1.5	2	22.5 ± 1.1
5	298	2	2	18.4 ± 0.7
6	298	2[c]	2	27.9 ± 1.1
7	298	2[d]	2	45.2 ± 2.3
8	298	2[e]	2	0.96 ± 0.03
9	298	2[f]	2	4.35 ± 0.5
10	298	2.5	2	20.6 ± 0.5
11	298	3	2	19.5 ± 0.8
12	298	4	2	16.6 ± 0.4
13	298	2	1	17.7 ± 0.6
14	298	2	1.5	17.8 ± 0.7
15	298	2	2	18.4 ± 0.6
16	298	2	2.5	18.2 ± 0.5
17	298	2	3	16.5 ± 0.5
18	298	2	4	19.3 ± 0.7
19	283	2	2	12.1 ± 0.4
20	288	2	2	15.8 ± 0.5
21	293	2	2	17.2 ± 0.8
22	303	2	2	24.1 ± 1.2
23	308	2	2	28.9 ± 1.4

[a] $DTBP:D_2O$ = 1:100.
[b] $DTBP:H_2O$ = 1:100
[c] 4-Me-DTBP.
[d] 4-^tBu-DTBP.
[e] 4-CN-DTBP.
[f] 4-Br-DTBP.

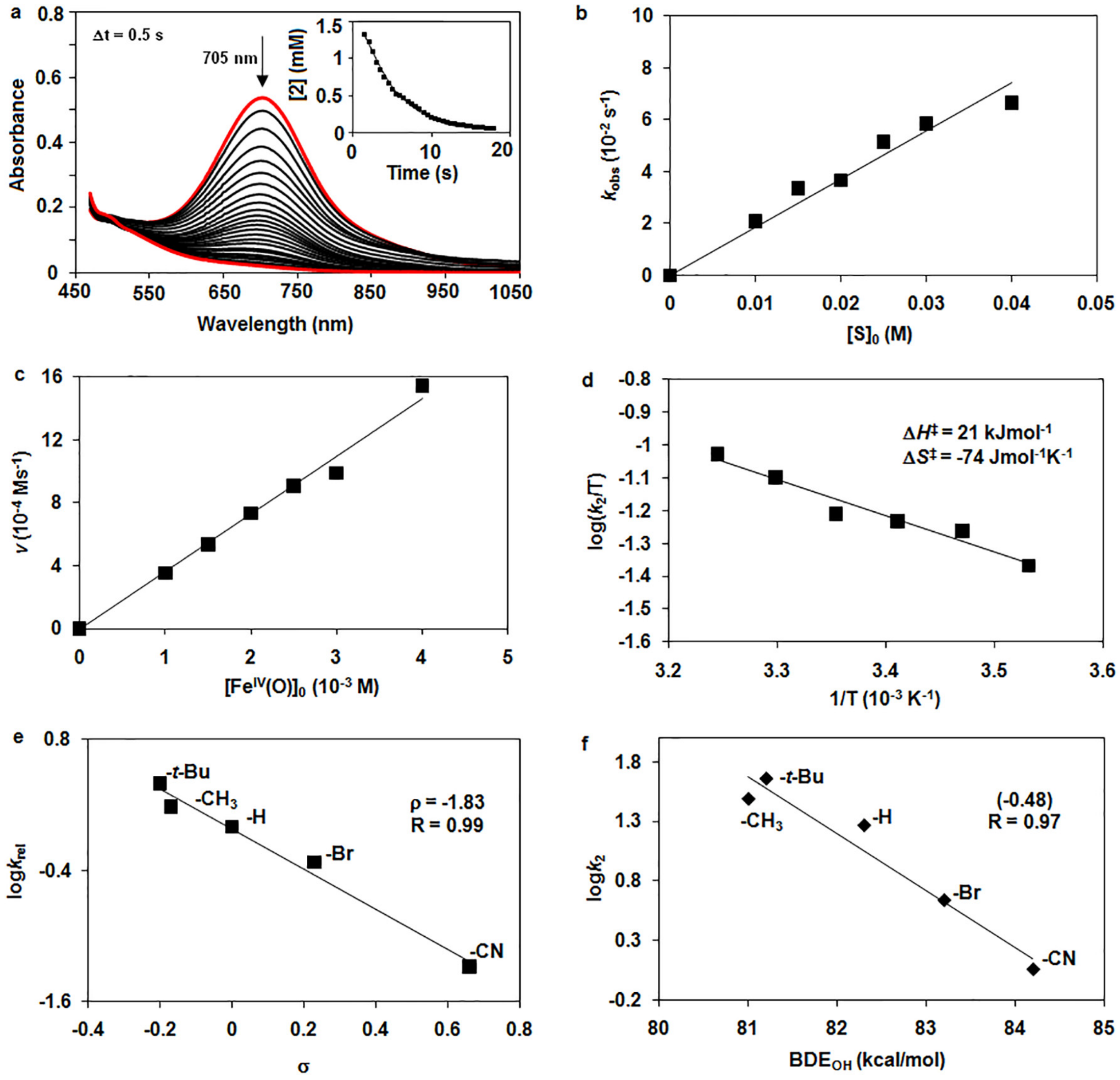

Fig. 1. Reactions of $[Fe^{IV}(asN4Py)(O)]^{2+}$ (**2**) with 2,6-di-*tert*-butyl-phenols in CH_3CN at 298 K. (a) UV–vis spectral change of **2** (1.5 mM) upon addition of 13 equiv. DTBP. Inset shows time course of the decay of **2** monitored at 705 nm. (b) Plot of k_{obs} versus [substrate] for reactions of **2** (2 mM) with DTBP. (c) Plot of reaction rate (V) versus [2] for reactions of **2** with DTBP (20 mM). (d) Eyring plot of log k/T versus $1/T$. (e) Hammett plot of log k_{rel} against σ_p of para-substituted 2,6-di-*tert*-butyl-phenols. (f) Plot of log k_2 versus homolytic bond dissociation energies ($BDE_{O\text{-}H}$) [7a].

transfer from the phenol or its phenolate ion, and hydrogen atom abstraction from the phenol can be proposed for the oxidation of phenols. The nucleophilic character of the oxoiron(IV) can be excluded since deprotonation leads to phenoxide coordination, instead of phenoxyl radical, which can lead to a 2,2′-biphenol-coupled product.

There are several lines of evidence that support a direct hydrogen-atom transfer (HAT) mechanism. Upon using *para*-substituted 2,6-di-*tert*-butylphenols with electron donating groups the rate of the decay processes were increased remarkably. When pseudo-first-order rate constants determined in the oxidation reactions of various *para*-substituted 2,6-di-*tert*-butylphenols were plotted against σ_p, a good correlation was observed with Hammett ρ value of -1.83, which suggests that the metal-based oxidant **2** is electrophilic (entries 5–9 in Table 1, Fig. 1e). This relatively small negative ρ value suggests that there is a small development of positive charge on the substrate in the transition state. If the phenolate ion is the assumed substrate, oxidation must occur by electron transfer where a more negative ρ value would be expected. Similar values, in a range -1.5 to -3.2, were reported for a concerted hydrogen abstraction mechanism in the oxidation of *para*-substituted phenols by $[Fe^{IV}(TMC)(O)(X)]^{2+}$ ($X = N_3$, CF_3COO, and CH_3CN) complexes [7a].

The involvement of the phenolic O–H bond in the rate-determining step is indicated by the magnitude of the $k_{O\text{-}H}/k_{O\text{-}D}$ kinetic (solvent) isotope effect of 4.52 in CH_3CN/H_2O and CH_3CN/D_2O (entries 1–3 in Table 1). This is in contrast to the oxidation of H_2Q by *cis*-$[Ru^{IV}(bpy)_2(py)(O)]^{2+}$ (k_{H2O}/k_{D2O} 29), where the reaction occurs by “proton-coupled electron transfer (PCET)” or “electron–proton transfer (EPT)” within a H-bonded association complex between H_2Q and $Ru^{IV}(O)$ to give semiquinone and $[Ru^{III}(OH)$ [12]. The mechanism above differs from the H-atom transfer proposed for DTBP. As shown in Fig. 1f, there is a linear correlation between log k_2 and O–H homolytic bond dissociation energies (BDEs), which suggests that the oxidant is selective in nature. The slope of -0.48 is comparable to those obtained with $[Fe^{IV}(TMC)(O)(X)]^{2+}$ (-0.36 to -0.55, $X = N_3$, CF_3COO, and CH_3CN) complexes [7a].

In summary, the reaction of $[Fe^{IV}(asN4Py)(O)]^{2+}$, generated from iron(II) and PhIO, with DTBP in MeCN shows first-order dependence on the concentration of the phenol and the oxidant. Substituent effect on the second-order rate constant was obtained from the oxidation of DTBP and four mono-substituted derivatives and these data were analyzed by Hammett and modified Hammett equations. The ρ value obtained, in conjunction with the kinetic isotope effect, suggest that the rate-determining step in these reactions involves hydrogen atom abstraction from the phenol by the oxoiron(IV) species in contrast to the heme-type horseradish peroxidase (HRP) system.

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