Mendeleev Commun., 2003, 13(4), 175–177

Stability of low-spin ferric hydroperoxo and alkylperoxo complexes with tris(2-pyridylmethyl)amine

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10.1070/MC2003v013n04ABEH001727

Quantitative data on the stability and reactivity of the peroxidic intermediates [Fe^{III}(TPA)(OOH)L](ClO_4)$_2$ and [Fe^{III}(TPA)(OOBu^t)L](ClO_4)$_2$ [TPA = tris(2-pyridylmethyl)amine; L = MeCN, H_2O, MeOH and Py] were obtained for the first time.

In the past decade, many groups have made efforts to model the reactivities of mononuclear nonheme iron enzymes.[1–24] The [Fe^{II}(TPA)(MeCN)$_2$](ClO_4)$_2$/H_2O_2 [TPA is tris(2-pyridylmethyl)amine] catalytic system in MeCN is the first example of a nonheme iron catalyst/H_2O_2 combination capable of stereospecific alkane hydroxylation[15] and olefin *cis*-dihydroxylation.[18–20] Low-spin ferric hydroperoxo intermediate [Fe^{III}(TPA)(OOH)L](ClO_4)$_2$ **1**, where L is H_2O or MeCN, has been identified in the [Fe^{II}(TPA)(MeCN)$_2$](ClO_4)$_2$/H_2O_2 system in MeCN at –40 °C by EPR, UV-VIS and resonance Raman spectroscopy and electrospray mass spectrometry.[15,16] It is assumed that either **1** or a Fe^V=O intermediate derived therefrom is the active species of selective hydrocarbon oxidation by the [Fe^{II}(TPA)(MeCN)$_2$](ClO_4)$_2$/H_2O_2 catalytic system.[3] However, direct kinetic measurements of the stability and reactivity of **1** were not performed to elucidate its actual role in selective oxidation. A high excess of H_2O_2 with respect to [Fe^{II}(TPA)(MeCN)$_2$](ClO_4)$_2$ (about 10–20) normally used for the detection of **1** hampers such studies since the observed concentration of **1** reflects competition between the rates of its formation and decay. The addition of small H_2O_2 amounts (1.5–2 equiv. with respect to Fe^{II}) also allowed us to detect the EPR spectra of **1**. Thus, it is possible to reliably measure the kinetics of its self-decay and the effects of various substrates on this process.

We report here a quantitative study of the stability of **1** and an attempt to probe the reactivity of **1** towards cyclohexane and cyclohexene (L = MeCN, MeOH and Py) in comparison with the corresponding data for alkylperoxo intermediate [Fe(TPA)(OOBu^t)L](ClO_4)$_2$ **2** (L = MeCN, MeOH, Py). The nature of L in the coordination sphere of complexes **1** and **2** can be determined by EPR spectroscopy.

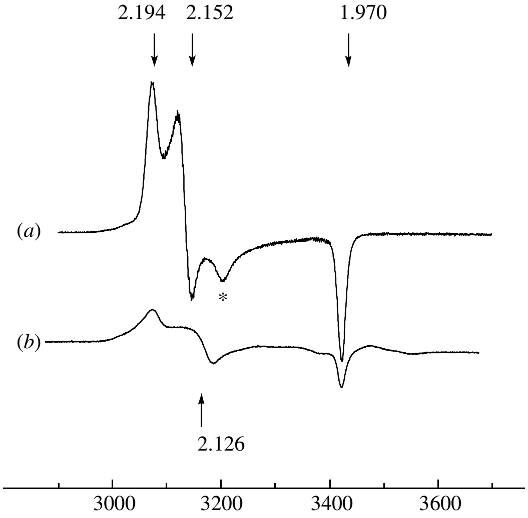

Figure 1 X-band EPR spectra of complexes **1**·MeCN and **1**·MeOH formed in the reaction of [Fe^{II}(TPA)(MeCN)$_2$](ClO_4)$_2$ with 4 equiv. of H_2O_2 at –50 °C: in (*a*) MeCN–CH_2Cl_2 (1:1) and (*b*) MeCN–CH_2Cl_2–MeOH (2:2:1). The spectra were recorded at –196 °C. The signal marked with an asterisk probably belongs to the **1**·H_2O adduct.

Intermediate **1** was prepared[15] by the addition of 1.5–2 equiv. of H_2O_2 to a 0.01 M [Fe^{II}(TPA)(MeCN)$_2$](ClO_4)$_2$ solution in MeCN–CH_2Cl_2 (1:1) at –50 to –55 °C in an argon atmosphere.[†] 95% H_2O_2 solution diluted with MeCN was used for sample preparation. The resulting concentration of **1** reached 5–10% of the concentration of the initial ferrous complex. The additives of CH_2Cl_2 were used to decrease the temperature of the reaction solution (down to –50 °C) without freezing and provided more sharp resonances in the EPR spectra of frozen solutions (–196 °C). The latter effect can be attributed to the formation of a better glass upon freezing. Intermediate **2** was prepared[22] for kinetic measurements by the addition of a stoichiometric amount of Bu^{t}OOH to a 0.01 M [Fe^{II}(TPA)(MeCN)$_2$](ClO_4)$_2$ solution in MeCN–CH_2Cl_2 (1:1) at –50 to –55 °C. For spectroscopic studies, **2** was prepared[17] by the addition of 10–20 equiv. of Bu^{t}OOH to a solution of [(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)$_2$](ClO_4)$_4$ in MeCN.

The EPR spectrum of **1** in MeCN–CH_2Cl_2 (1:1) at –196 °C displays intense peaks at $g_1 = 2.194$, $g_2 = 2.152$ and $g_3 = 1.970$ denoted by arrows and an additional weak peak at $g = 2.12$ marked with an asterisk [Figure 1(*a*)]. The EPR spectrum ($g_1 = 2.194$, $g_2 = 2.152$ and $g_3 = 1.970$) belongs to the **1**·MeCN adduct with MeCN molecule at the sixth coordination site of **1**, while the signal at $g = 2.12$, probably, originates from the **1**·H_2O adduct exhibiting an EPR spectrum with $g_1 = 2.19$, $g_2 = 2.12$ and $g_3 = 1.97$. Indeed, the EPR spectrum of the **1**·MeOH adduct prepared by the addition of MeOH to a solution of **1** in a MeCN–CH_2Cl_2 mixture at –45 °C exhibits an EPR spectrum with $g_1 = 2.194$, $g_2 = 2.126$ and $g_3 = 1.972$ [Figure 1(*b*), Table 1]. It is reasonable to expect that the EPR spectra of **1**·MeOH and **1**·H_2O are similar, since the EPR spectra of the related complexes **2**·MeOH and **2**·H_2O coincide and noticeably differ from that of **2**·MeCN [Figures 2(*a*),(*b*), Table 1]. Direct preparation of **1**·H_2O was complicated by the low solubility of H_2O in MeCN at low temperatures and by rapid decomposition. The results show that the EPR spectrum of **1** ($g_1 = 2.19$, $g_2 = 2.15$ and $g_3 = 1.97$) reported by Que *et al.*[6] belongs to the **1**·MeCN adduct. The EPR parameters previously reported for complex **2** ($g_1 = 2.19$, $g_2 = 2.14$, $g_3 = 1.98$)[22] correspond to the adduct **2**·H_2O or **2**·ROH.

Based on the above results, it is possible to determine the amounts of intermediates **1** and **2** with different L at the sixth

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[†] *General experimental details.* Intermediates **1** and **2** were prepared as described elsewhere.[15,17,22] Their identity was confirmed by EPR spectra. For kinetic studies, solutions containing complexes **1** or **2** were placed in a thermostat at an appropriate temperature directly in glass EPR tubes (d = 5 mm). To stop the reaction, the EPR tube was immersed in liquid nitrogen, followed by the measurement of the EPR spectrum at –196 °C. If necessary, the appropriate amounts of cyclohexene and cyclohexane were added to solutions containing **1** or **2**. The EPR signals were quantified by double integration with copper(II) chloride as a standard at –196 °C. The EPR spectra (–196 °C) were recorded at 9.2–9.3 GHz on a Bruker ER-200 D spectrometer. The ^{2}H NMR spectra were recorded at 61.425 MHz in 10 mm tubes on a Bruker MSL-400 NMR spectrometer. The yields of reaction products were measured using a Saturn 2000 GC-MS instrument (Varian). Magnetic resonance parameters of frozen solutions were obtained using the EPR1 spectra simulation program.[25]

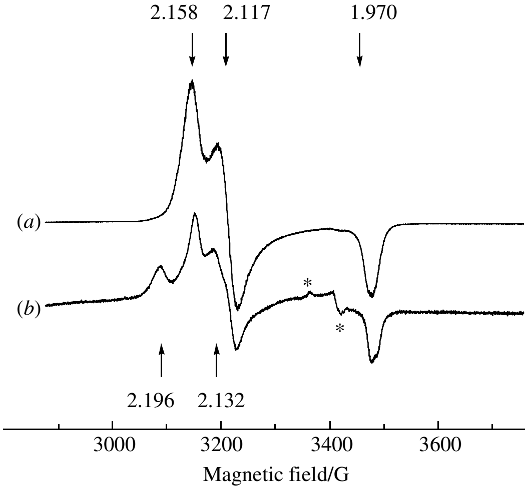

Figure 2 X-band EPR spectra of complexes **2**·MeCN and **2**·MeOH formed in the reaction of $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4$ (10^{-2} M) with 20 equiv. of Bu^tOOH at –50 °C: in (*a*) $MeCN–CH_2Cl_2$ (1:1) and (*b*) $MeCN–CH_2Cl_2–MeOH$ (2:2:1). The spectra were recorded at –196 °C. The signal marked with an asterisk belongs to the $Bu^tOO·$ radical.

coordination site by measuring the intensities of the corresponding peaks in the EPR spectra (–196 °C). The ratios between various adducts of **1** and **2** derived from the EPR spectra of frozen solutions reflect corresponding ratios at the freezing temperature of the reaction mixture (–60 to –65 °C), which is close to the temperatures used for kinetic measurements (–45 to –55 °C).

The ^2H NMR spectroscopic studies of **2** provide additional information on the structures of alkylperoxo species present in the reaction solution. When deuterated $[^2H_9]Bu^tOOH$ was added to a solution of $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4$ in a $MeCN/CH_2Cl_2$ mixture (1:1, by volume) at –52 °C, two weak resonances at –4.2 and 11.5 ppm along with an intense signal of $[^2H_9]Bu^tOOH$ and $[^2H_9]Bu^tOH$ at 1.08 ppm were observed in the ^2H NMR spectrum [Figure 3(*a*)]. The intensity of the NMR peak at –4.2 ppm correlated with the intensity of the EPR signal of **2**·MeCN. Thus, the peak at –4.2 ppm can be ascribed to the alkylperoxo moiety of **2**·MeCN. We found previously that the alkylperoxo moiety of the low-spin alkylperoxo complex $[Fe(bpy)_2(OOBu^t)MeCN](NO_3)_2$ displayed a ^2H NMR peak at –3.7 ppm.[13] The broad signal at 11.5 ppm belongs to the alkylperoxo moiety of new species, which were not reported previously. With increasing temperature, the line width of the paramagnetically broadened signal at 11.5 ppm decreased, and it appeared to be a superposition of two peaks with similar intensities [Figures 3(*a*)–(*d*)]. Probably, this new alkylperoxo complex exists in two conformations. The resonances at –4.2 and 11.5 ppm disappeared upon storage at –35 °C. The peaks at 11.5 ppm disappeared more rapidly than that at –4.2 ppm [Figures 3(*c*),(*d*)]. The addition of pyridine to a sample swown in Figure 3(*a*) ([Py] = 0.1 mol dm^{-3}, –45 °C) gave rise to the immediate disappearance of the peak at –4.2 ppm, while that at 11.5 ppm remained unaffected. In principle, the signal at 11.5 ppm can be assigned to an alkylperoxo moiety in a mononuclear high-spin ferric alkylperoxo complex or in a dinuclear antiferromagnetically coupled high-spin ferric alkylperoxo complex. The latter seems more reasonable because of a strictly different behaviour of the signals at –4.2 and 11.5 ppm towards pyridine. The binuclear complex $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4$ was used as a starting complex for sample preparation. Thus, one can expect that the peak at 11.5 ppm belongs to the alkylperoxo species $[(TPA)(OOBu^t)Fe^{III}–O–Fe^{III}(TPA)(H_2O)](ClO_4)_3$ or $[(TPA)\text{-}(OOBu^t)Fe^{III}–O–Fe^{III}(TPA)(OOBu^t)](ClO_4)_2$.

The hydroperoxo intermediate **1**·MeCN is very unstable and rapidly decays in accordance with a first-order kinetics even at –50 °C. The rate constants of this decay determined for the sample prepared by the addition of 2 equiv. of H_2O_2 to a solution of $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2$ in $MeCN–CH_2Cl_2$ (1:1) are $k = 0.0012$ s^{-1} (–50 °C) and $k = 0.002$ s^{-1} (–45 °C). The additives of MeOH ([MeOH] = 3–5 mol dm^{-3}) sharply increased the rate of self-decomposition of **1**. However, it is difficult to distinguish whether this effect is caused by the replacement of MeCN by MeOH as a sixth ligand or by changing the nature of a solvent. The additives of pyridine (2–10 equiv. with respect to the starting complex) gave rise to the immediate decay of **1** even at –50 °C. Thus, the adduct **1**·Py is far less stable than **1**·MeCN. The stability of the complex **1**·MeCN is dramatically lower than that of activated bleomycin $Fe^{III}(BLM)(OOH)$ (half-life time of 4 min at +4 °C in water)[21] and the hydroperoxo complex $[Fe(bpy)_2(OOH)Py](NO_3)_2$ (half-life time of 5 min at 20 °C in MeCN).[13]

The addition of substrates (cyclohexene and cyclohexane) in concentrations up to 2 M to the solution containing **1**·MeCN at –45 °C does not change the rate of self-decomposition of **1**·MeCN. The substrate oxidation products were not detected by GC-MS in the reaction solution. Thus, at a low temperature (–45 °C), **1**·MeCN rapidly converted into EPR-silent species rather than reacted with substrates. It is difficult to expect that, with an increase in the temperature, the situation would change dramatically and the intermediate **1**·MeCN would play an essential role in the selective oxidation of hydrocarbons by the $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2/H_2O_2$ catalytic system at room temperature.

Nevertheless, when 4–10 equiv. of H_2O_2 were added to a solution of $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2$ in a $MeCN–CH_2Cl_2$–substrate mixture at room temperature $\{[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2 = 0.01$ mol dm^{-3}, [substrate] = 2 mol dm$^{-3}\}$, the products of substrate oxidation were detected by GC-MS in agreement with data of Que *at al.*[18] In the case of cyclohexane, the products were cyclohexanol and cyclohexanone in a 3:1 ratio (3–5% conversion with respect to H_2O_2). In the case of cyclohexene, the major products were *cis*-cyclohexane-1,2-diol and 1,2-cyclohexane oxide in a 3:1 ratio (5–10% conversion with respect to H_2O_2). This does not mean that **1**·MeCN (or species derived therefrom) is responsible for these oxidations. Indeed, using EPR spectroscopy, Que *at al.*[15] observed the formation of

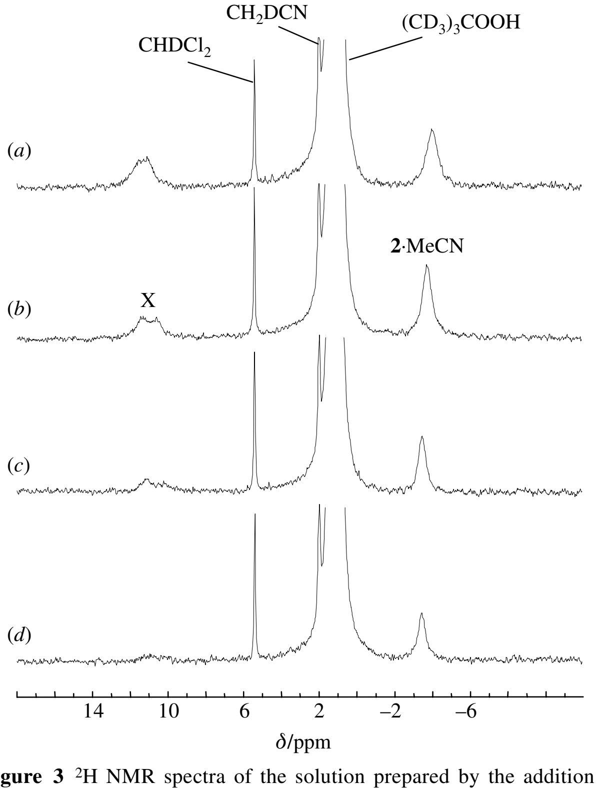

Figure 3 ^2H NMR spectra of the solution prepared by the addition of $[^2H_9]Bu^tOOH$ (20 equiv. with respect to Fe^{III}) to a solution of $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4$ in $MeCN–CH_2Cl_2$ (1:1, by volume) ([Fe] = 10^{-2} M) at (*a*) –52 °C, (*b*) –45 °C and (*c*) –35 °C. Sample in (*c*) 25 min after storage at –35 °C (*d*). The peaks at 11.5 ppm (marked with 'X') probably belong to binuclear μ-oxo bridged alkylperoxo complexes, which were not reported previously.

Table 1 EPR spectroscopic data for low-spin ferric hydroperoxo and alkylperoxo complexes with tris(2-pyridylmethyl)amine (TPA) (–196 °C).

Complex	Solvent	g_1^a	g_2	g_3	Ref.
$[Fe(TPA)(OOH)L](ClO_4)_2^b$	MeCN	2.19	2.15	1.97	15
$[Fe(TPA)(OOH)MeCN](ClO_4)_2$	MeCN/ CH_2Cl_2	2.194	2.152	1.970	this work
$[Fe(TPA)(OOH)MeOH](ClO_4)_2$	MeCN/ CH_2Cl_2	2.196	2.126	1.972	this work
$[Fe(TPA)(OOH)H_2O](ClO_4)_2$	MeCN/ CH_2Cl_2	2.19	2.12	1.97	this work
$[Fe(TPA)(OOBu^t)L](ClO_4)_2^c$	MeCN	2.19	2.14	1.98	22
$[Fe(TPA)(OOBu^t)MeCN](ClO_4)_2$	MeCN/ CH_2Cl_2	2.158	2.117	1.970	this work
$[Fe(TPA)(OOBu^t)MeOH](ClO_4)_2$	MeCN/ CH_2Cl_2	2.196	2.132	1.972	this work
$[Fe(TPA)(OOBu^t)H_2O](ClO_4)_2$	MeCN/ CH_2Cl_2	2.198	2.130	1.972	this work
$[Fe(TPA)(OOBu^t)Py](ClO_4)_2$	MeCN/ CH_2Cl_2	2.186	2.127	1.973	this work

[a] The experimental uncertainty of *g*-factor values obtained in this work was ±0.003. [b] L = MeCN or H_2O. [c] L = H_2O or ROH.

hydroperoxo intermediate **1** only *via* a reaction of H_2O_2 with the ferrous complex $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2$ rather than with the binuclear ferric complex $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4$. We found that **1** could be obtained only upon the interaction of H_2O_2 with the ferrous complex $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2$ under argon. Furthermore, the $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4/H_2O_2$ and $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2/H_2O_2$ catalytic systems had similar activities and selectivities towards the oxidation of alkanes and alkenes at room temperature.[6,18] All our attempts to restore **1** after its decay by the addition of fresh H_2O_2 portions to the reaction mixture at –50 °C were unsuccessful. This was the case even when only 1.5 equiv. of H_2O_2 were initially added; this allowed us to exclude the degradation of the TPA ligand. Thus, we found that EPR-active intermediate **1** exists only at the early stages of the interaction of $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2$ with H_2O_2 under argon atmosphere and then rapidly and irreversibly converts into another EPR-silent species. The active intermediates (or their precursors) of the $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4/H_2O_2$ and $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2/H_2O_2$ catalytic systems might be the EPR-silent binuclear species $[(TPA)(HOO)Fe^{III}–O–Fe^{III}(TPA)(H_2O)](ClO_4)_3$ or $[(TPA)(HOO)Fe^{III}–O–Fe^{III}(TPA)(OOH)](ClO_4)_2$. The formation of such species in the $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4/Bu^tOOH$ system was supported by ^2H NMR spectroscopy (Figure 3). Recently, enantioselective sulfoxidation by H_2O_2 was used as a probe for comparison of mono and binuclear iron catalysts. Whereas both systems formed peroxoiron intermediates as active species, the binuclear one proved to be more efficient and selective.[23] Further studies are needed to find actual reactive intermediates in the $[Fe^{II}(TPA)(MeCN)_2](ClO_4)_2/H_2O_2$ catalytic system.

The alkylperoxo complex **2**·MeCN is more stable than the hydroperoxo complex **1**·MeCN. It decays with a rate constant of 0.004 s^{-1} at –30 °C. The decay rate increases at least by one order of magnitude upon addition of pyridine (10 equiv. with respect to Fe) to the reaction mixture. This bears evidence in favour of lower stability of the **2**·Py adduct with respect to **2**·MeCN. As in the case of complex **1**, the addition of organic substrates (cyclohexene and cyclohexane) does not affect the rate of self-decomposition of **2**. According to Que *at al.*,[22] **2** oxidises organic substrates *via* the formation of the free radicals $Bu^tO·$. The free radicals $Bu^tOO·$ can be readily detected in the $[(TPA)Fe^{III}–O–Fe^{III}(TPA)(H_2O)_2](ClO_4)_4/Bu^tOOH$ catalytic system by EPR spectroscopy [see lines marked with asterisks in Figure 2(*b*)].

This work was supported by the Russian Foundation for Basic Research (grant no. 03-03-32009).

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Received: 17th February 2003; Com. 03/2053