Regioselectivity of aliphatic versus aromatic hydroxylation by a nonheme iron(II)-superoxo complex†

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Many enzymes in nature utilize molecular oxygen on an iron center for the catalysis of substrate hydroxylation. In recent years, great progress has been made in understanding the function and properties of iron(IV)-oxo complexes; however, little is known about the reactivity of iron(II)-superoxo intermediates in substrate activation. It has been proposed recently that iron(II)-superoxo intermediates take part as hydrogen abstraction species in the catalytic cycles of nonheme iron enzymes. To gain insight into oxygen atom transfer reactions by the nonheme iron(II)-superoxo species, we performed a density functional theory study on the aliphatic and aromatic hydroxylation reactions using a biomimetic model complex. The calculations show that nonheme iron(II)-superoxo complexes can be considered as effective oxidants in hydrogen atom abstraction reactions, for which we find a low barrier of 14.7 kcal mol\(^{-1}\) on the sextet spin state surface. On the other hand, electrophilic reactions, such as aromatic hydroxylation, encounter much higher (>20 kcal mol\(^{-1}\)) barrier heights and therefore are unlikely to proceed. A thermodynamic analysis puts our barrier heights into a larger context of previous studies using nonheme iron(IV)-oxo oxidants and predicts the activity of enzymatic iron(II)-superoxo intermediates.

Introduction

Nature has established a large group of oxygen activating enzymes for the catalysis of substrate hydroxylation reactions, which are important biotransformations with functions ranging from biosynthesis to biodegradation of compounds. One of the large classes of oxygen activating enzymes includes monooxygenases, such as the cytochromes P450 (P450s),\(^1\) which contain a heme active site. The P450s are versatile oxidants that catalyze not only substrate hydroxylation of aliphatic as well as aromatic substrates, but also olefin epoxidation, heteroatom oxidation (e.g., sulfoxidation) and desaturation reactions.\(^2\) They are very common in biosystems and, for instance, catalyze vital reactions in the human body, including detoxification processes in the liver,\(^1\) the biosynthesis of the neurotransmitter NO,\(^3,c\) and drug metabolism.\(^1,c\) The P450s undergo a catalytic cycle that starts from a resting state structure, where water is bound to the sixth ligand site of the heme, while a cysteinate residue occupies the fifth ligand site opposite to it (see Scheme 1). Upon substrate (SubH) binding, the water molecule is released, the heme is reduced and binds molecular oxygen to form an iron(II)-superoxo species that picks up another electron to form an iron(III)-peroxo/iron(II)-superoxo complex. The latter is doubly protonated to form a high-valent iron(IV)-oxo heme cation radical

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Scheme 1 Extract of the catalytic cycle of P450 enzymes.
complex, which is also known as Compound I (Cpd I), and is the active species of P450 enzymes that abstracts a hydrogen atom from the substrate and then rebounds the OH radical to form alcohol products. Recent computational studies ruled out the iron(III)-superoxo complex as a possible oxidant in hydroxylation reactions in P450s. This contrasts recent studies of a nonheme iron(II)-superoxo complex that was found to be able to activate aliphatic substrates at least with weak C–H bonds.

By contrast to heme enzymes, metal-peroxo and/or metal-superoxo complexes have been identified as active oxidants in hydrogen atom abstraction or heteroatom addition reactions in several nonheme iron enzymes. For example, the nonheme iron enzyme cysteine dioxygenase catalyzes the detoxification of toxic cysteine in the body through an oxygen atom transfer from an iron(II)-superoxo complex. Despite the fact that nonheme iron(II)-superoxo complexes appear to be efficient oxidants in oxygen atom transfer reactions, very little knowledge on their catalytic ability in biomimetic complexes has been obtained; therefore, we have done a computational study on aliphatic and aromatic hydroxylation of a model substrate (e.g., ethylbenzene, EB) by a nonheme iron(II)-superoxo complex.

One of the first groups to study the reactivity of biomimetic iron(II)-peroxo porphyrin complexes in oxidation reactions was Valentine and co-workers, who found that electron-rich complexes gave enhanced reactivity for substrate epoxidation over those with electron-deficient complexes. They further proposed that the axial ligand can tune the relative energies of side-on versus end-on iron(II)-peroxo complexes, whereby the latter are more reactive in olefin epoxidation reactions. Further studies on the reactivity of nonheme iron(II)-peroxo complexes were performed in several laboratories, but generally they were found to be sluggish oxidants in C–H bond activation reactions. Despite this, they were found to react via aldehyde deformylation reactions, but the origin of these reactivity differences with aldehydes and C–H bonds remains unclear.

To understand the mechanism and substrate range of catalytic oxidations by iron(II)-peroxo and its isoelectronic iron(II)-superoxo electroners and how it compares to iron(IV)-oxy chemistry, we have performed a density functional theory (DFT) study on the aliphatic and aromatic hydroxylation of ethylbenzene by a nonheme iron(II)-superoxo complex (Scheme 2) vis-à-vis that of an iron(IV)-oxy heme cation radical species. A well-studied nonheme iron biomimetic system uses a macrocyclic TMC ligand (TMC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane), the iron(IV)-oxy species using this ligand was one of the first biomimetic nonheme iron(IV)-oxy species to be fully characterized with spectroscopic methods. Reactivity studies performed with [FeXIV=O(TMC)(X)] complexes, where X is a halide or solvent axial ligand, showed efficient hydrogen abstraction reactions from substrates with weak C–H bonds as well as oxygen atom transfer to PPh3. These reactions were shown to proceed via multistate reactivity patterns on competing triplet and quintet spin state surfaces. Clearly, nonheme iron(IV)-oxy species are capable oxidants in hydrogen atom abstraction reactions, but little is known on the potential of the corresponding iron(II)-superoxo species and how it compares to the iron(IV)-oxy complexes. In order to gain insights into this, we have performed a density functional theory study on the aliphatic and aromatic hydroxylation of ethylbenzene by a nonheme iron(II)-superoxo complex bearing the TMC ligand, [Fe(II)(O2)(TMC)]+, which we describe in this work.

**Methods**

We use well tested methods and procedures that have been benchmarked in detail previously. All calculations were performed with Jaguar 7.0 and Gaussian-03 and utilize density functional theory methods. The unrestricted B3LYP hybrid density functional method was used throughout as it has been shown to correctly reproduce experimentally determined free energies of activation and kinetic isotope effects of aliphatic and aromatic hydroxylation reactions of nonheme iron oxidants as well as spectroscopic parameters. A full geometry optimization (without constraints) was followed by an analytical frequency calculation to confirm the structures as local minima or first order saddle points. These calculations use a Los Alamos-type LACVP basis set on Fe coupled to 6-31G on the rest of the atoms, basis set B2. Single point calculations with LACV3P+ on iron and 6-311+G* on the rest of the atoms were done to improve the energies; basis set B2. All energies discussed in this paper use basis set B2 and are corrected for ZPE obtained from the frequency calculations. A series of calculations obtained after a full geometry optimization at UB3LYP/B2 for a hydrogen atom abstraction reaction gave virtually identical results to UB3LYP/B2/UB3LYP/B1; therefore, we will use the latter in this work. Free energies include zero-point vibrational, thermal and entropic corrections to the enthalpy at 298 K. We also investigated the effect of the density functional method on spin state ordering and barrier heights of iron(II)-superoxo complexes and found minor changes; therefore, we will focus on the B3LYP results only.

The model studied in this work was Fe(n)-superoxo ligated with a tetradeinate TMC ligand, Scheme 2, with overall charge +1. The reaction of this oxidant with ethylbenzene was studied leading to 1-phenylethanol and para-ethylphenol products. All calculations were done on the lowest lying doublet, quartet and sextet spin state surfaces, where the spin multiplicity is identified with a superscript in the label. Although there are several isomeric forms of TMC, we used the trans conformation as displayed in Scheme 2. Previous studies on Ni(II)-superoxo complexes embedded in a TMC ligand system showed little differences in spin state ordering, electronic configuration and oxygen atom transfer reactivity between Ni(II)-superoxo complexes with isomeric TMC ligand systems. Therefore, we will focus on the trans isomer of TMC here only.

To test the effect of the environment, we ran single point calculations as well as several geometry optimizations...
(B3LYP/B2) using the self-consistent reaction field model as implemented in either Gaussian or Jaguar using a dielectric constant of $\epsilon = 37.5$ mimicking acetonitrile with a probe radius of 2.19 Å.

Finally, we compare the substrate activation with proton abstraction from a neighbouring $\text{H}_2\text{O}^+$ ion. To this end, we created an elaborate model that includes two water molecules and a $\text{H}_2\text{O}^+$ ion in hydrogen bonding interaction with the terminal oxygen atom of the Fe(II)-superoxo group ($\text{R}_{3\text{W}}$). This model was used to investigate the proton abstraction ability of the Fe(II)-superoxo complex.

**Results and discussion**

The high-lying occupied and low-lying virtual orbitals and the optimized geometries of $^{6,4,2}\text{FeO}_2(\text{TMC})^+$ ($\text{R}$) are given in Fig. 1. Two low-lying metal 3d-orbitals are the nonbonding $\pi^*_{xz}$ and $\pi^*_{yz}$ orbitals, while the $\pi^*_{xy}$ orbital interacts with orbitals on the proximal oxygen atom. Somewhat higher in energy are two $\sigma^*$ type orbitals for the antibonding interactions of the metal with the nitrogen atoms of the TMC ligand ($\sigma^*_{x^2-y^2}$) and with the proximal oxygen atom ($\sigma^*_{z^2}$). Fig. 1 also shows two antibonding orbitals on the superoxo moiety, namely $\pi^*_{\text{OO}_{xz}}$ and $\pi^*_{\text{OO}_{yz}}$. The latter mixes somewhat with the $\sigma^*_{z^2}$ orbital. The electronic ground state of the [FeO$_2$(TMC)]$^+$ reactant has close lying quartet and sextet spin states, both with $\pi^*_{xy}^2 \pi^*_{xz}^1 \pi^*_{yz}^1 \sigma^*_{x^2-y^2}^1 \sigma^*_{z^2}^1 \sigma^*_{x^2-y^2}^1 \pi^*_{\text{OO}_{yz}}^2 \pi^*_{\text{OO}_{xz}}^1$ occupation, whereby the $\pi^*_{\text{OO}_{xz}}$ electron is either antiferromagnetically or ferromagnetically coupled to the unpaired electrons on the metal. The doublet spin state is well higher in energy (by 12.0 kcal mol$^{-1}$ above the sextet spin ground state). This spin state ordering is consistent with EPR studies on [FeO$_2$(TMC)]$^+$ that characterized it as an $S = 5/2$ spin state.$^{12}$ Solvent effects do not change the spin state ordering and relative energies dramatically and confirm the gas-phase results. The orbital occupations and group spin densities characterize all three spin states as Fe$^{III}$-peroxo complexes. Thus, the quartet and sextet spin state structures give spin densities of 3.69 on the metal, which is indicative of about four unpaired electrons on the metal. In addition, we find spin densities on the dioxygen moiety of −0.85 and 1.14, respectively, in the quartet and sextet spin states, which confirm the orbital occupation as $\pi^*_{xy}^2 \pi^*_{xz}^1 \pi^*_{yz}^1 \sigma^*_{x^2-y^2}^1 \sigma^*_{z^2}^1 \pi^*_{\text{OO}_{yz}}^2 \pi^*_{\text{OO}_{xz}}^1$, hence pointing toward an Fe$^{II}$-superoxo complex. Attempts to swap orbitals and create the alternative Fe$^{III}$-peroxo states failed and the calculations converged back to the lower lying Fe$^{II}$-superoxo intermediates; therefore, we predict the end-on Fe$^{III}$-peroxo complex to be an excited state and well higher in energy than the iron(II)-superoxo species.

The reactivity studies of the iron(II)-superoxo complex were started with the investigation of a possible protonation mechanism to form an iron(III)-hydroperoxo complex. To this end, we set up a

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**Fig. 1** High-lying occupied and low-lying virtual orbitals of [FeO$_2$(TMC)]$^+$ ($\text{R}$) with sextet spin orbital occupation indicated with arrows. The inset gives the optimized geometries of $^{6,4,2}\text{R}$ with bond lengths in angstroms.
system containing the (TMC)FeII-superoxo complex with a hydrogen bond to a chain of two water molecules and an H2O− ion, [(TMC)FeII(OO−⋯H2O⋯H2O⋯H2O)]2+. Studies on the proton transfer mechanism in heme oxygenase showed the importance of a proton relay chain in the mechanism and kinetics of the reaction.23

Complex R3W was fully optimized in the doublet, quartet and sextet spin states and led to the structures depicted in Fig. 2. During the geometry optimization, the proton migrates from the terminal water molecule to the one that is hydrogen bonded to the distal oxygen atom of the superoxo group to give the following complex, [(TMC)FeII(OO−⋯H2O⋯H2O⋯H2O)]2+. Optimized geometries of the [(TMC)FeII(OO−)]+ entity in R3W resemble those found for the isolated complexes shown above in Fig. 1; only minor Fe–O elongations and O–O contractions are observed. The group spin densities of R3W are similar to those found for the isolated complexes and assign all lowest lying spin states as iron(II)-superoxo complexes. The hydrogen bonding water network, therefore, does not change the electronic configuration and spin state ordering of the iron(II)-superoxo complex.

We then investigated the proton transfer mechanism to form the iron(II)-hydroperoxo complex, and the obtained geometry scans are shown on the right-hand-side of Fig. 2. As follows, protonation is a high energy and dissociative process, whereby the reaction does not lead to a local minimum. That is, 2,4,6[TMC]FeII(OOH)+ is unstable molecules that will be deprotonated by a water molecule in their vicinity. Indeed, a full geometry optimization starting from 2,4,6[(TMC)FeII(OOH⋯H2O⋯H2O⋯H2O)]2+ converged back to 2,4,6R3W instead. Consequently, the iron(II)-superoxo complex cannot abstract protons from weak bases and will not react by proton abstraction during reactivity processes. This makes nonheme iron(II)-superoxo complexes fundamentally different from heme-type iron(II)-superoxo complexes, such as in the catalytic cycle of P450, where they are protonated to form an iron(II)-hydroperoxo complex. The origin of this difference stems from the relative energies of the isoelectronic iron(III)-superoxo and iron(II)-peroxo intermediates. Thus, in nonheme systems, the lowest energy state is the iron(II)-superoxo form, whereas it is an iron(III)-peroxo state in heme enzymes.24 The ligand affects the metal–dioxyn groups and orbital interactions and as a consequence, R3W is in a sextet spin ground state, while it is a double spin state in the analogous intermediate in the catalytic cycle of P450.

Subsequently, we investigated the aliphatic and aromatic hydroxylation mechanisms of ethylbenzene by [(TMC)FeII(OO−)]+ and the results are shown in Fig. 3. The aliphatic hydroxylation mechanism starts with an initial hydrogen atom abstraction via transition state TSαliph to form an iron(II)-hydroperoxo complex coupled with a substrate radical (Intαliph). Rebound of the hydroxyl group then gives 1-phenyl-ethan-1-ol and an iron(III)-oxo species. This mechanism resembles that found for the iron(IV)-oxo porphyrin cation radical species of P450 enzymes.25 The lowest hydrogen atom abstraction barrier is 14.7 kcal mol−1 on the sextet spin state surface. This is a low barrier and implies that R should be able to abstract hydrogen atoms from substrates with weak and medium strong C–H bonds. Geometrically, the hydrogen abstraction barriers are late, that is with longer C–H than O–H bond lengths in 2,4,6TSαliph. The imaginary frequencies for the hydrogen atom abstraction processes are high (>1400 cm−1), which imply that the reaction will proceed with a large kinetic isotope effect.26

In addition, we investigated the aromatic hydroxylation at the para-position of ethylbenzene, which starts with an electrophilic attack of the superoxo group on the para-carbon atom via a transition state TSαarom to form a radical intermediate (Intαarom) and the formation of a C–O bond. The aromatic hydroxylation mechanism obtained for iron(IV)-oxo porphyrin cation radical oxidants usually proceeds via a cationic intermediate instead.27 The corresponding radical intermediates in the Fe(IV)-porphyrin cation radical mechanism were.
found to be considerably higher in energy than these cationic species. We made attempts to swap molecular orbitals and generate a cationic intermediate; however, the wavefunction converged back to the radical intermediate instead. This suggests that the cationic intermediate in the aromatic hydroxylation mechanism for \((\text{TMC})\text{Fe}^{3+}\) is high in energy and not accessible.

As follows from Fig. 3, the lowest lying barrier is the aliphatic hydroxylation barrier on the sextet spin state, which is 14.7 kcal mol\(^{-1}\) \((\Delta E + ZPE)\) above reactants. By contrast, the corresponding doublet and quartet aliphatic hydroxylation barriers are well higher in energy and will not play a role of importance. The spin state ordering in the reactants and transition states remains the same, if enthalpies, free energies in the gas-phase or free energies in a dielectric constant are compared. The spin state ordering also implies that the reaction will take place via single-state-reactivity on the sextet spin state surface only. This contrasts the behaviour of nonheme and heme iron(IV)-oxo complexes where generally multistate reactivity patterns are obtained on competing spin state surfaces.\(^{24,28}\) On the other hand, the aromatic hydroxylation barriers are all high in energy (well over 20 kcal mol\(^{-1}\) in energy), hence \([(\text{TMC})\text{Fe}^{3+}\text{OO}^+]^+\) is expected to be a sluggish oxidant in aromatic hydroxylation reactions.

So why is \([(\text{TMC})\text{Fe}^{3+}\text{OO}^+]^+\) a possible oxidant in aliphatic hydroxylation, but not in aromatic hydroxylation? This question will be addressed in the remaining part of this manuscript.

Thermodynamically, hydrogen atom abstraction from a substrate (SubH) by \([(\text{TMC})\text{Fe}^{3+}\text{OO}^+]^+\) gives an Fe(II)-hydroperoxo complex and a radical (Sub\(^\cdot\)) (eqn (1)), with a reaction enthalpy equal to the difference in bond dissociation energy of the C–H bond of the substrate (BDE\(_{\text{CH}}\)) and the bond dissociation energy of the O–H bond of the iron(II)-hydroperoxo complex (BDE\(_{\text{OH}}\)) (eqn (2)). We calculated values for BDE\(_{\text{CH}}\) of ethylbenzene separately and found a value of 82.5 kcal mol\(^{-1}\),\(^{29}\) while the BDE\(_{\text{OH}}\) of \([(\text{TMC})\text{Fe}^{3+}\text{OOH}]^+\) is determined to be 77.2 kcal mol\(^{-1}\).

\[
\begin{align*}
[(\text{TMC})\text{Fe}^{3+}\text{OO}^+]^+ + \text{SubH} & \rightarrow [(\text{TMC})\text{Fe}^{3+}\text{OOH}]^+ + \text{Sub}^\cdot \\
\Delta H_{\text{Eq}} & = \text{BDE}_{\text{CH}} - \text{BDE}_{\text{OH}}
\end{align*}
\] (1)

\[
\begin{align*}
\Delta H_{\text{Eq}} & = \text{BDE}_{\text{CH}} - \text{BDE}_{\text{OH}}
\end{align*}
\] (2)

Indeed, from the difference of these BDE\(_{\text{CH}}\) and BDE\(_{\text{OH}}\) values, a \(\Delta H_{\text{Eq}}\) of 5.3 kcal mol\(^{-1}\) follows, which is close to the value \(\Delta H_{\text{Int}}\) reported in Fig. 3. Furthermore, recent studies showed that BDE\(_{\text{CH}}\) and BDE\(_{\text{OH}}\) values also correlate with barrier height of a substrate hydroxylation reaction.\(^{25}\) The BDE\(_{\text{OH}}\) value of 77.2 kcal mol\(^{-1}\) obtained for \([(\text{TMC})\text{Fe}^{3+}\text{OO}^+]^+\) is low and compares to that of an iron(IV)-oxo porphyrin (Por) cation radical model with an imidazole (ImH) axial ligand, \([\text{Fe}^{3+}\text{QO}^+\text{Por}^+\text{ImH}^+]\).\(^{30}\) As shown before, this is a relatively weak oxidant that is only able to react with substrates with weak C–H bonds like the benzyl C–H bonds of ethylbenzene.
Interestingly, the BDE$_{\text{OH}}$ value of [(TMC)Fe$^{\text{II}}$OOH]$^+$ is well
higher than that of the iron(III)-hydroperoxo intermediate in the
catalytic cycle of cytochrome P450, for which a value of
BDE$_{\text{OH}} = 63.4$ kcal mol$^{-1}$ was calculated.$^{30}$ As a consequence,
the corresponding iron(III)-superoxo intermediate in the catalytic
cycle of P450 will not be able to abstract H-atoms of substrates.

Aromatic hydroxylation proceeds via an electrophilic attack
of the terminal oxygen atom of the [(TMC)Fe$^{\text{III}}$OO$^*$]$^+$ moiety on one of the carbon atoms of the ring concomitant
with the breaking of a π-bond of the aromatic ring (Scheme 3). The
terminal oxygen atom of the superoxo group attacks a
π-bond of the aromatic ring, whereby one π-bond is broken and the
aromaticity in the phenyl group is disrupted. Energetically, the barrier
for aromatic hydroxylation is therefore proportional to the
breaking of the aromaticity of the phenyl ring and the
formation of a C–O bond. If the energy of the newly formed
C–O bond is proportional to the formation of an H–O bond,
then the barrier height for aromatic hydroxylation should correlate
with BDE$_{\text{OH}}$. Recent studies on a series of hydrogen atom abstraction reactions by iron(IV)-oxo oxidants were shown
to correlate with BDE$_{\text{OH}}$.$^{23}$ However, the BDE$_{\text{OH}}$ value of
[(TMC)Fe$^{\text{IV}}$OO$^*$]$^+$ is far too small to cover the aromaticity
loss in the substrate. Consequently, [(TMC)Fe$^{\text{III}}$OO$^*$]$^+$ is a
poor oxidant in aromatic hydroxylation reactions.

Let us in the final paragraphs of this paper make a comparison
between the aliphatic and aromatic hydroxylation reactions of
ethylbenzene with various oxidants. Recently, we reported ethyl-
benzene hydroxylation by [Fe$^{\text{IV}}$=O(Por$^+$)NCCH$_3$]$^+$ and
[Fe$^{\text{IV}}$=O(Por$^+$)Cl]$^+$. Activation energies of the aromatic and aliphatic reaction barriers calculated for ethylbenzene
using these two oxidants, as compared to [(TMC)Fe$^{\text{IV}}$OO$^*$]$^+$,
are summarized in Table 1. As can be seen in Table 1, the barrier heights obtained using [(TMC)Fe$^{\text{IV}}$OO$^*$]$^+$ as an oxidant are generally
higher than those calculated for [Fe$^{\text{IV}}$=O(Por$^+$)NCCH$_3$]$^+$
and [Fe$^{\text{IV}}$=O(Por$^+$)Cl]$^+$. The $^{\text{TS}}_{\text{aliph}}$ barrier
obtained in this work is 4.8 and 5.6 kcal mol$^{-1}$ higher in
energy than the low-spin barriers obtained for the same process
by [Fe$^{\text{IV}}$=O(Por$^+$)L] with L = NCCH$_3$ or Cl$^-$, respectively.

### Table 1

<table>
<thead>
<tr>
<th>[TMC]Fe$^{\text{III}}$OO$^*$]$^+$</th>
<th>[Fe$^{\text{IV}}$=O(Por$^+$)X]</th>
</tr>
</thead>
<tbody>
<tr>
<td>X = NCCH$_3$</td>
<td>9.9 (18.8)</td>
</tr>
<tr>
<td>X = Cl$^-$</td>
<td>10.9 (16.3)</td>
</tr>
</tbody>
</table>

$^a$ Energies calculated with basis set B2 and corrected for ZPE with basis set B1. $^b$ High-spin data in parentheses. $^c$ From ref. 27b.

As discussed before, this is due to the higher BDE$_{\text{OH}}$ value that makes the driving force for the reaction larger and also lowers the H-abstraction barriers. In the aromatic hydroxylation mechanism, by contrast, the differences in barrier height between iron(II)-superoxo and iron(IV)-oxo porphyrin cation radical models are much more dramatic and now the iron(II)-superoxo barriers are higher in energy by 12.1 and 10.9 kcal mol$^{-1}$, respectively. This implies that iron(II)-superoxo complexes are sluggish oxidants in aromatic hydroxylation reactions, but are able to react with substrates with weak C–H bonds via H-atom abstraction.

Recent studies by our groups on the reactivity patterns of
[(TMC)Ni$^{\text{II}}$O$_2$]$^+$ with respect to a range of substrates showed
that it is able to abstract hydrogen atoms from substrates with
weak C–H bonds, e.g. xanthene, but not from ethylbenzene.$^7$
Barriers of 20.6 kcal mol$^{-1}$ for hydrogen atom abstraction
from the benzyl position of ethylbenzene and 27.1 kcal mol$^{-1}$
for aromatic hydroxylation at the para-position were found.
These barriers are considerably higher than those found for
the [(TMC)Fe$^{\text{IV}}$OO$^*$]$^+$ complex discussed here. This implies
that the iron(II)-superoxo oxidant will be a better oxidant than
the nickel(II)-superoxo complex. However, in comparison to
iron(IV)-oxo porphyrins the iron(II)-superoxo species is not a
good oxidant, so possibly it will only be suitable for the
hydroxylation of substrates with weak C–H bonds.

### Conclusions

In summary, density functional theory calculations on
[(TMC)Fe$^{\text{IV}}$OO$^*$]$^+$ show the first example of a nonheme
iron(II)-superoxo complex that is able to activate C–H bonds
of aliphatic substrates, although only relatively weak C–H
bonds can be activated by this oxidant. A comparison with the energetics and mechanism of iron(IV)-oxo porphyrin oxidants
shows that these are superior to the [(TMC)Fe$^{\text{IV}}$OO$^*$]$^+$
complex with respect to aliphatic and aromatic hydroxylation
reactions.

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![Scheme 3](https://example.com/scheme3.png)

Scheme 3  A proposed mechanism for the aromatic hydroxylation by
a nonheme iron(II)-superoxo complex.
Although the $\text{[Fe}(\text{O}_2)\text{(TMC)}]^+$ complex was characterized structurally and spectroscopically as a mononuclear nonheme side-on iron(III)-peroxo complex, $\text{[Fe}(\text{m})(\text{TMC})\text{(OO)}]^+$ (see ref. 12), it has been shown in iron porphyrins that iron(III)-peroxo species, $\text{[Fe}(\text{III})(\text{TMC})(\text{OO})]^+$ (see ref. 12), it has been shown in iron porphyrins that iron(III)-peroxo species coexist with their isomeric iron(II)-peroxo form in solution: (a) K. Dürre, J. Ola, R. Davydov, M. Kleinmann, J. Li, N. Lang, R. Puchta, E. Hübner, T. Drellow, J. N. Harvey, N. Jux and I. Ivanovic-Burmazovic, *Dalton Trans.*, 2010, 2049; (b) K. Dürr, N. Jux, A. Zahl, R. van Eldik and I. Ivanovic-Burmazovic, *Inorg. Chem.*, 2010, 49, 11254; (c) K. Dürr, B. P. Macpherson, R. Warrat, F. Hampel, F. Tuzek, M. Helfreich, N. Jux and I. Ivanovic-Burmazovic, *J. Am. Chem. Soc.*, 2007, 129, 4217.


