Reaction Mechanism of Water Oxidation Catalyzed by Iron Tetraamido Macrocyclic Ligand Complexes – A DFT Study

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Density functional calculations are used to elucidate the reaction mechanism of water oxidation catalyzed by iron tetraamido macrocyclic ligand (TAML) complexes. The oxidation of the starting TAML–Fe³⁺–OH₂ complex by removing three electrons and two protons leads to the formation of a key intermediate, TAML·–Fe⁵⁺=O, which can undergo nucleophilic attack by either a water molecule or a nitrate ion. Both pathways involve attack on the oxo group and lead to the production of O₂. The water attack is more favorable and has a total barrier of 15.4 kcal/mol. The alternative nitrate attack pathway has a barrier of 19.5 kcal/mol. Nitrate functions as a cocatalyst by first donating an oxygen atom to the oxo group to form O₂ and a nitrite ion, which can then be re-oxidized to regenerate a nitrate ion. Three possible competing pathways result in ligand modification, namely, water and nitrate attack on the ligand, as well as ligand amide oxidation. The water attack on the ligand has a low barrier of only 10.9 kcal/mol and leads to the opening of the benzene ring, which explains the observation of fast catalyst degradation. The lack of activity or lower activity of other catalysts with different substituents is also rationalized.

Introduction

The conversion of water into molecular oxygen and hydrogen by using sunlight is a very promising process to supply a clean and renewable source of energy. The oxidation of water by the liberation of four protons and four electrons is the bottleneck in this task. The reaction is not thermodynamically favourable and is associated with a relatively large energy penalty (E₀ = 1.23 V, standard reduction potential at pH 0). In addition, an efficient catalyst with high stability and turnover number (TON) is needed to promote the O–O bond formation. Extraordinary efforts have been devoted to the development of both heterogeneous and homogeneous water oxidation catalysts (WOCs), but most are based on expensive heavy transition metals such as ruthenium and iridium. Therefore, it is of high interest to develop a WOC based on abundant and inexpensive first-row transition metals. Recently, Ellis et al. synthesized five Fe³⁺ complexes based on tetraamido macrocyclic ligands (Fe³⁺–TAMLs, Scheme 1); four of them (WOCₐ–WOCₐ) catalyze water oxidation in the presence of excess ceric ammonium nitrate (CAN) at pH 0.7. WOCₐ gave the highest activity and showed a turnover frequency larger than 1.3 s⁻¹, whereas only a small activity was observed for WOCₐ. However, for WOCₐ, a rapid release of O₂ could only be observed in the first 20 s, which suggests a quite fast catalyst degradation. Kinetic studies also suggest that the formation of O₂ catalyzed by WOCₐ is first order and, therefore, exclude the possibility of a cooperative metal–oxo coupling mechanism, which has been found for mononuclear Ru-based catalysts.

Scheme 1. Five Fe³⁺–TAMLs used for water oxidation.

Recently, Cramer and co-workers performed density functional and multireference second-order perturbation calculations to understand the reaction mechanism of water oxidation enabled by the WOCₐ catalyst. They suggested that the reaction starts from two sequential proton-coupled electron transfer (PCET) steps from the TAML–Fe³⁺–OH₂ complex to form a TAML–Fe⁵⁺=O species, followed by a one-electron oxidation of the ligand to generate a
TAML$^+\text{–Fe}^{5+}=\text{O}$ intermediate (Scheme 2). Therefore, the key oxidizing species is formally Fe$^{6+}$, but this high-valent oxidation state is delocalized over two redox-active centres, namely, the metal centre and the TAML ligand. A water molecule then performs a nucleophilic attack on the oxo group facilitated by a microsolvation shell of water molecules. This type of water attack mechanism has also been suggested for a number of mononuclear Co-, Ru-, and Ir-based catalysts$^{[25–31]}$. This step was calculated to be rate-limiting with a total barrier of ca. 30 kcal/mol. This is much too high compared with the experimental rate constant (1.3 s$^{-1}$) at room temperature, which can be converted to a barrier of 17.3 kcal/mol. This is much too high compared with the experimental rate constant (1.3 s$^{-1}$) at room temperature, which can be converted to a barrier of 17.3 kcal/mol by using classical transition-state theory. Once the O–O bond is formed, a proton can easily be released into solution to form a TAML–Fe$^{4+}$–$\text{OOH}$ intermediate. Subsequently, proton-coupled electron transfer occurs, followed by O$_2$ release and water binding, which regenerates the TAML–Fe$^{3+}$–$\text{OH}_2$ species. As a technical note, the computed barrier was very sensitive to the density functional used; for example, B3LYP gives a barrier of 14.6 kcal/mol.$^{[24]}$

In this paper, we revisit the reaction mechanism of this catalytic reaction by density functional calculations. An alternative mechanism involving a nitrate cocatalyst is proposed. A full energy diagram for the whole catalytic cycle is constructed, similarly to our previous studies on photosystem II and two Ru-based catalysts.$^{[32–38]}$ Possible competing catalyst degradation pathways, which have not been considered before, have also been explored. The lower activity and lack of activity of WOCA and the relatively lower activity of WOCB–WOCD will be rationalized. Finally, the computed energy profiles derived from the two different functionals B3LYP*-2D and M06L will be compared.

**A. O$_2$ Formation by Direct Water Attack**

As mentioned in the Introduction, Cramer and co-workers have suggested all intermediates and transition states for the O$_2$ formation by a direct water attack on the high-valent iron–oxo group.$^{[24]}$ In the present study, we construct the full energy diagram by using the experimental driving force, which was not done before. This will be helpful for the understanding of the rate-limiting step and the total barrier.

The resting state is a pentacordinate ferric complex (labelled as 1, or Fe$^{3+}$–$\text{OH}_2$, Figure 1) with a water molecule bound to the metal. The complex has a quartet ground state, and the sextet and doublet are 14.0 and 30.9 kcal/mol higher in energy, respectively. The first oxidation step is a one-electron oxidation to form the triplet species Fe$^{4+}$–$\text{OH}_2$ (2). This step is calculated to be exothermic by 15.1 kcal/mol (Figure 2), and, thus, the redox potential for the 2/1 pair is 1.07 V (Table 1). From 2, a PCET oxidation takes place to form a doublet TAML–Fe$^{4+}$–$\text{OH}$ complex (4), which is best described as an intermediate-spin Fe$^{4+}$ ($S_{\text{Fe}} = 1$) centre antiferromagnetically coupled to the ligand radical cation ($S = 1/2$). The quartet and sextet states are 1.6 and 19.4 kcal/mol higher in energy, respectively. Thus, during the oxidation, one electron is released from the ligand, rather than from the metal centre. The redox potential for this step is calculated to be 1.75 V. Subsequently, another PCET oxidation of 4 (redox potential 1.75 V) leads to the formation of TAML–Fe$^{5+}=\text{O}$ (6), which is the proposed oxidant for the following O–O bond formation. The ground
The broken-symmetry singlet state with the two radicals antiferromagnetically coupled is +3.0 kcal/mol higher in energy than the triplet state. In contrast to B3LYP*-2D, the state of 6 is a triplet at the B3LYP*-2D level and has a low-spin iron centre \( (S_{\text{Fe}} = 1/2) \) that interacts with the TAML ligand radical cation \( (S = 1/2) \) in a ferromagnetic fashion.

Figure 1. Selected optimized structures along the reaction pathway of direct water attack. Distances are given in angstroms. Spin densities for Fe and other important atoms are indicated in italics. For all structures, the spin state with the lowest energy is shown. Superscripts indicate the multiplicity of the structure.
M06L functional favours the singlet by 0.4 kcal/mol. Previous CASPT2 calculations showed that the singlet–triplet gap is 3.3 kcal/mol.\[24\] However, this gap might be overestimated as entropy corrections could favour the triplet by 1–2 kcal/mol. This is quite similar to compound I in P450 enzymes, in which the porphyrin radical cation can interact with the iron centre in both an antiferromagnetic and a ferromagnetic fashion. The electronic structure of 6, equivalent to TAML–Fe^{4+}–O and 8.3 kcal/mol higher in energy than the triplet, is best described as an intermediate-spin iron centre ($S_{Fe} = 1$) ferromagnetically coupled to the oxyl radical ($S = 1/2$) and to the TAML ligand radical cation ($S = 1/2$).

In the previous study it was shown that 6 is the active species for O–O bond formation by water attack.\[24\] The authors suggested that a proper description of this process requires four water molecules. The main reason for the addition of more water molecules is that a proton is released into solution during the attack, and two additional water molecules are needed to explicitly solvate the newly formed hydronium ion. They also tried with only three water molecules, and the barrier is slightly higher. Following the previous calculations, we added four water molecules into 6 to form complex 7, from which one water molecule performs a nucleophilic attack on the oxo group. During the O–O bond formation, a proton is transferred to the nearby water molecule. The optimized transition state in the triplet state $3^{TS_{OO}}$ is shown in Figure 1. The triplet barrier is calculated to be 12.9 kcal/mol relative to 7, whereas the quintet barrier is 10.3 kcal/mol higher than the triplet one. This step is calculated to be almost isoergonic, and the resulting interme-

diate 8 is only 0.5 kcal/mol higher than 7. At $3^{TS_{OO}}$, the critical O–O bond is 1.73 Å, and the Fe–O bond is elongated to 1.70 Å (1.58 Å in 7). It should be pointed out that the conformation of $3^{TS_{OO}}$ is different from the previously reported one. Owing to the presence of a hydrogen bond between a water molecule and the fluoro group (hydrogen bonding distance 1.93 Å), the new transition state is 1.5 kcal/mol lower in energy than the previous one. During the O–O bond formation, one electron with β spin is transferred from a water molecule to the ligand radical cation.

<table>
<thead>
<tr>
<th>Redox Couple</th>
<th>Redox potential [V]</th>
<th>B3LYP*-2D</th>
<th>M06L[a]</th>
<th>M06L[b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Fe^{4+}–OH$_2$ (2) + e$^-$ → Fe^{3+}–OH$_2$ (1)</td>
<td>1.07</td>
<td>1.02</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>II Fe^{4+}–OH (3) + (e$,H^+$) → Fe^{3+}–OH$_2$ (1)</td>
<td>1.46</td>
<td>1.16</td>
<td>1.04</td>
<td></td>
</tr>
<tr>
<td>III Fe^{4+}–OH (4) + e$^-$ → Fe^{4+}–OH (3)</td>
<td>1.36</td>
<td>1.44</td>
<td>1.02</td>
<td></td>
</tr>
<tr>
<td>IV TAML–Fe^{4+}–OH (4) + (e$,H^+$) → Fe^{4+}–OH$_2$ (2)</td>
<td>1.75</td>
<td>1.58</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>V Fe$^{3+}=$O (5) + (e$,H^+$) → Fe^{4+}–OH (3)</td>
<td>1.68</td>
<td>1.49</td>
<td>1.33</td>
<td></td>
</tr>
<tr>
<td>VI TAML–Fe$^{3+}=$O (6) + e$^-$ → Fe$^{3+}=$O (5)</td>
<td>1.43</td>
<td>1.65</td>
<td>1.09</td>
<td></td>
</tr>
<tr>
<td>VII TAML–Fe$^{3+}=$O (6) + (e$,H^+$) → TAML–Fe$^{4+}–$OH (4)</td>
<td>1.75</td>
<td>1.70</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>VIII TAML–Fe$^{4+}–$OOH (10) + e$^-$ → Fe$^{3+}–$OOH (9)</td>
<td>1.29</td>
<td>1.46</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Mean absolute deviation (MAD)</td>
<td>0.14</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

\[a\] Present calculations with fitting. \[b\] Previous calculations.\[24\]

Figure 2. Energy diagram (in kcal/mol at the B3LYP*-2D level) for the two possible catalytic cycles of O$_2$ formation enabled by WOCFe. The black curve shows O–O bond formation by a water attack, whereas the red curve shows the nitrate attack.
and the other electron with α spin is transferred from the oxo ligand to the metal centre, which leads to the formation of an intermediate-spin Fe⁴⁺ complex (S_{Fe} = 1). In the following step, a PCET oxidation takes place with the formation of TAML·Fe⁴⁺–OOH (10), which is a doublet with the quartet and sextet 5.5 and 7.2 kcal/mol higher in energy, respectively. Further deprotonation of 10 leads to Fe³⁺–OO (11), in which an intermediate-spin iron centre (S_{Fe} = 3/2) is antiferromagnetically coupled to the triplet oxygen molecule (S_{O₂} = 1). Partial electron transfer can be seen from the iron atom to the O₂ molecule. The liberation of O₂ and coordination of H₂O can regenerate 1 and start the next catalytic cycle.

From Figure 2, we can see that the oxidative formation of 6 from 2 is endothermic by 1.5 kcal/mol. The O–O bond formation step is rate-limiting and has a total barrier of 15.4 kcal/mol (TS_{OO} relative to 2). The experimental turnover frequency is larger than 1.3 s⁻¹ at room temperature and can be converted to a barrier of ca. 17 kcal/mol by using transition-state theory. The calculated barrier is slightly underestimated compared to the experimental one. It should be pointed out that previous CASPT2 calculations showed that the singlet–triplet gap is 3.3 kcal/mol in favour of the singlet state. The present B3LYP*-2D calculations suggest that the triplet is the ground state. If the CASPT2 correction is taken into account, the total barrier becomes 17.2 kcal/mol, which is in excellent agreement with the experimental kinetic results.

In our previous studies on other systems, in which only water binding and O₂ release are involved in the catalytic cycle, the entropy effect was not considered explicitly and two empirical values were adopted, 14 kcal/mol for water binding and 12 kcal/mol for the entropy effects of releasing O₂ gas. Here, we also construct the energy diagram (Figure 3) by using this methodology for the formation of an O–O bond by water attack. The process for the binding of water molecules in the second sphere of the complex is set to be thermoneutral, which is quite a good approximation as water is the solvent. The free energy calculations also suggest that this process is endothermic by less than 1 kcal/mol (see Figure 2). For the binding of a water molecule to the metal centre, as in the final ligand exchange step from 11 to 1, the empirical 14 kcal/mol is used. In Figure 3, the black curve shows the B3LYP*-2D energies including zero-point energy (ZPE) corrections. Two sets of energies are reported. The first set uses the experimental driving force (49.1 kcal/mol) to fit the PCET steps. The second set, shown in parentheses, uses the experimental proton solvation free energy of 264.0 kcal/mol to estimate the energy gain or loss of releasing a proton, for example, from 2
to 3. The difference between the calculated and the experimental driving force then becomes 12.3 kcal/mol. In addition, the total barrier changes from 13.5 kcal/mol with fitting to 12.0 kcal/mol without fitting. The difference originates from the extra energy cost to reach oxidant 6. The comparison of the energy diagrams of the four different methodologies, namely, Gibbs free energies with and without fitting the experimental driving force and ZPE-corrected energies with and without fitting the experimental driving force, are shown in Figures S1–S4. The energy diagrams look quite similar, but the total barriers could differ by several kcal/mol depending on the energy penalty for the formation of 6.

An energy diagram (Figure 3, red curve) is also constructed by using the previously calculated redox potential for 1 to 3, 3 to 5, 5 to 6 and 9 to 11 at the M06L level. As the previous study did not report the relative energies of 9 to 6 and 1 to 11 (exchange of O2 by water), the relative energies from the present M06L calculations were used. The driving force is estimated to be 64.8 kcal/mol, which is overestimated by ca. 15 kcal/mol compared to the experimental value. The M06L energies from our calculations were also used to construct energy diagrams for comparison (Figures S5 and S6). In the previous study, the redox potentials of the four reported couples (1/3, 3/5, 5/6 and 9/11, Table 1) were calculated to be 1.04, 1.33, 1.09 and 0.38 V, respectively. Our calculations with the M06L functional give 1.00, 1.32, 1.29 and 0.44 V, respectively. The large discrepancy for the 5/6 couple is caused by the CASPT2 corrections used for the singlet–triplet gap of 6 in the previous study, in which the triplet is 3.3 kcal/mol higher in energy than the singlet at the CASPT2 level.[24]
B. \( \text{O}_2 \) Formation by Nitrate Attack

An alternative \( \text{O}–\text{O} \) bond formation pathway has been considered here, in which a nitrate ion performs the nucleophilic attack on the oxo group of 6. The involvement of nitrate ions in water oxidation has been proposed in Ru-based catalysts,[40,41] but has not yet been confirmed by theoretical calculations. As excess ceric ammonium nitrate is used as the oxidant, free nitrate ions could be available and could function as a nucleophile. The interaction of a nitrate ion and 6 to form 12 is endergonic by 4.6 kcal/mol, mainly because of the entropy lost. The optimized transition state of the nitrate attack in the triplet state (\( ^3\text{TS1} \)) is shown in Figure 4. The barrier is calculated to be 18.0 kcal/mol relative to the isolated reactants (6 and a nitrate ion). The quintet barrier is 9.4 kcal/mol higher than the triplet and is similar to that in the water attack. The attack leads to the formation of a peroxynitrate intermediate bound to the ferryl ion (13), which lies at −0.7 kcal/mol relative to 12. From 13, \( \text{N}–\text{O} \) bond cleavage via TS2 leads to the formation of \( \text{O}_2 \), which is concomitant with \( \text{O}_2 \) release and the nitrite ion binding to the metal. This step is associated with a very small barrier of 2.9 kcal/mol relative to 13 in the triplet state.

During the reaction, an oxygen atom is transferred from the nitrate ion to the oxo group, coupled with two-electron reduction to form a ferryl nitrite complex. The newly formed nitrite complex can be oxidized to regenerate a nitrate ion. The exchange of the nitrite ligand in 14 by a water molecule leads to the formation of 2, which can then be oxidized to 4. Complex 4 is able to oxidize the nitrite ion to form nitric acid, and the corresponding transition state TS3 is shown in Figure 4. This step is calculated to have a barrier of only 4.8 kcal/mol. Further ligand exchange of nitric acid by a water molecule regenerates 1.

In this mechanism, the nitrate ion acts as a cocatalyst for the formation of \( \text{O}_2 \), in which one oxygen atom in the oxygen molecule originates from a nitrate ion. The total barrier is calculated to be 19.5 kcal/mol, which is 4.1 kcal/mol higher than that for the water attack pathway. Isotope labelling by using \( \text{H}_2\text{O}^{18} \) would be helpful to verify whether nitrate is involved in the catalysis. It should be pointed out that nitric acid may oxidize 1 to form 2 and nitrogen dioxide [Equation (1)]. Calculations show that Equation 1 is endothermic by 3.5 kcal/mol. This reaction and its reverse reaction could lead to oxygen exchange between nitric acid and water. The isotope labelling with \( \text{H}_2\text{O}^{18} \) will only work if this exchange process is much slower than water oxidation. Another possible strategy is to measure the kinetic isotope effect of \( \text{N}^{15}/\text{N}^{14} \) by labelling the nitrate nitrogen atoms.

\[
\begin{align*}
\text{TMAL-Fe}^{3+}-\text{OH}_2 (1) & \rightarrow \text{NO}_2^- + 2\text{H}^+ \\
\text{TMAL-Fe}^{4+}-\text{OH}_2 (2) & \rightarrow \text{H}_2\text{O} + \text{NO}_2
\end{align*}
\]

(1)

C. Competing Pathways

A number of conceivable competing pathways have been studied to understand the experimentally observed degradation of the catalyst, which was not considered in the previous computational study.[24] The potential energy profiles are shown in Figure 5, and selected optimized structures are shown in Figures 6 and 7.

![Energy diagram (in kcal/mol at the B3LYP*-2D level) for competing pathways.](image)

As discussed above, water functions as a nucleophile to attack the oxo group and leads to \( \text{O}–\text{O} \) bond formation and reduction of the metal centre and ligand radical cation. An alternative target for the attack would be the ligand radical cation, which has been proposed for the blue dimer.[42,43] Therefore, one water molecule was added to 6 to form 17. We found that the oxo group acts as a general base and removes a proton from the water molecule, concomitant with a nucleophilic attack on one of the benzene carbon atoms by the emerging hydroxide ion. No proton is released into solution, and, therefore, no additional water molecules are needed to explicitly solvate the system. The use of the continuum solvation model should be capable of describing the solvation effect. The attack proceeds in the triplet state and is associated with a barrier of only 10.9 kcal/mol relative to 2, which is 4.5 kcal/mol lower than the desired \( \text{O}_2 \) formation pathway. This could be the origin of the observed catalyst degradation. The attack by the quintet is energetically not feasible (25.1 kcal/mol relative to 2), and the barrier is, thus, ca. 14 kcal/mol higher than the triplet one. This step was found to be exergonic by 9.7 kcal/mol (18 relative to 17), in contrast to the attack on the oxo group, which is close to isoergonic (+0.5 kcal/mol). In the subsequent step, the ferryl-bound hydroxide ion abstracts a proton from the alcohol to form alkoxide intermediate 19. Finally, the oxygen anion performs a nucleophilic attack on one of the benzene carbon atoms, which may lead to the formation of an epoxide via TS6. However, geometry relaxation results in the
epoxide C–C bond cleavage with the formation of a seven-membered ring product, complex 20, which is similar to those found in extradiol dioxygenase,[44] intradiol dioxygenase[45] and homogentisate dioxygenase.[46] The barrier for such oxygen insertion (5TS6) in the quintet state is very feasible (11.6 kcal/mol relative to 18). This side-reaction is exergonic by as much as 24.0 kcal/mol (from 6 to 20), which suggests that the catalyst degradation by this pathway would be irreversible.

The second possible pathway for ligand modification is that a nitrate ion could also perform a nucleophilic attack on the ligand benzene ring. The transition state for the attack at the CH carbon atom in the triplet state (3TS7) is shown in Figure 7, and the barrier is calculated to be 21.5 kcal/mol relative to 6. Thus, when a nitrate ion participates in the reaction, it prefers to attack the oxo group by 3.5 kcal/mol rather than the ligand. This is different from water, which prefers to attack the ligand, rather than the oxo group.

Another possibility is the self-oxidation of the ligand amide by the Fe$^{5+}$=O group to form an N-oxide by reductive elimination. The attack can be either on the amide group that is close to the CF$_2$ group (TS8, Figure 7) or on the amide group that is connected to the benzene ring (TS9, Figure 7). The former one has a barrier of 17.6 kcal/mol relative to 6, and the reaction is exothermic by 10.7 kcal/mol. The latter one has a slightly higher barrier (18.0 kcal/mol), and the reaction is close to thermoneutral.

The calculations show that the water attack on the ligand is the main catalyst degradation pathway, and 20 is the major product. Thus, the performance of the catalyst depends on the relative barriers of the water attack on the oxo group and on the ligand. As O$_2$ formation can be observed for ca. 15 cycles, the relative barrier for the ligand modification seems to be underestimated somewhat when using both the B3LYP*2D and the M06L functionals.

It is also important to check whether 20 has water oxidation activity. If similar barriers are observed, the modified catalyst could also contribute to the TON. The electronic structure of 20 can be described as an intermediate-spin ferric ion antiferromagnetically coupled with a ligand radical. Two sequential PCET oxidations of 20 lead to the
formation of 27 (Figure 8), which is characterized as a ferryl–oxo species. During the oxidation, one electron is removed from the ligand, and the other one is removed from the metal centre. This explains the quite different redox potentials between the modified and unmodified catalyst, for example, the redox potential of the TAML3–Fe4+=O/TAML2–Fe4+=O (26 to 27) couple is 0.92 V. In 24, 25 and 27, the ligand is in the diimine form and has a total charge of –2, rather than –3 as in 6, 20 and 26.

From 27, water continues to perform a nucleophilic attack on the ligand seven-membered ring (TS10) to form an alcohol intermediate 29. During the attack, a proton is transferred to the oxo group. The barrier for this step is calculated to be only 5.0 kcal/mol (Figure 9) in the triplet state, which is even lower than that for the initial water attack (TS4). In the following step, the metal-bound hydroxide ion abstracts a proton from the alcohol intermediate, coupled with the opening of the seven-membered ring. This step is also associated with a very low barrier of 3.7 kcal/mol in the quintet state. The reaction is exothermic by more than 50 kcal/mol (from 28 to 30).

We also tried water oxidation from 27. However, owing to the relatively low oxidation state (Fe4+=O) of 27, much higher barriers of 26.0 and 27.8 kcal/mol are obtained for both the water attack and the nitrate attack, respectively. These results suggest that when the ligand is modified, water oxidation to form O2 becomes even more difficult. To increase the TON of the catalyst, one needs to modify or design a more stable ligand to prevent the destructive water attack.

It should be pointed out that further oxidation of 30 is rather difficult. Our calculations show that oxidation of 30 to form an Fe5+=O species by removing two protons and one electron is endothermic by 11.1 kcal/mol (Figure S10), which corresponds to a redox potential of ca. 2.2 V. The main reason for the high redox potential is that the π conjugation of the ligand is broken, which makes the oxidation of the ligand difficult.

Of course, we cannot rule out other possible changes from 30 that could recover some water oxidation activity. An extensive investigation on this issue is beyond the scope of the present study.

D. O2 Formation by Other Ligands

To rationalize the lack of activity of WOC_A and the relatively lower activity of other catalysts, we optimized all relevant intermediate and transition-state structures and constructed the corresponding energy diagrams, which are displayed in Figures 10–13. A summary of the total barriers is shown in Table 2.

Table 2. Summary of total barriers (in kcal/mol at the B3LYP*-2D level) for various pathways for all five catalysts.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>O2 formation Water attack</th>
<th>Nitrate attack</th>
<th>Total barrier for ligand oxidation Water attack</th>
<th>C–H activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOC_A</td>
<td>19.7</td>
<td>23.4</td>
<td>9.8</td>
<td>12.5</td>
</tr>
<tr>
<td>WOC_B</td>
<td>20.9</td>
<td>25.0</td>
<td>8.7</td>
<td></td>
</tr>
<tr>
<td>WOC_C</td>
<td>16.3</td>
<td>18.7</td>
<td>9.3</td>
<td></td>
</tr>
<tr>
<td>WOC_D</td>
<td>15.8</td>
<td>17.2</td>
<td>14.0</td>
<td></td>
</tr>
<tr>
<td>WOC_E</td>
<td>15.4</td>
<td>19.5</td>
<td>10.9</td>
<td></td>
</tr>
</tbody>
</table>

In WOC_A and WOC_B, R1 is electron-donating, which results in lower redox potentials compared to that of WOC_E. This can be confirmed from the larger exergonicity during the complex oxidation. In WOC_E, the generation of 6 from 2 is slightly endergonic by 1.5 kcal/mol. In WOC_A and WOC_B, it is exergonic by 1.5 and 3.9 kcal/mol, respectively. In WOC_C and WOC_D, R1 is electron-withdrawing, and their redox potentials are higher than those for WOC_A and WOC_B. WOC_D has a nitro group attached to its benzene ring and, thus, has the highest redox potential. Consequently, the generation of 6 is endergonic by 2.6 kcal/mol, which will contribute to the total barrier for this catalyst.

In WOC_A, R1 is a methyl group, which can undergo C–H activation to generate an alcohol. The transition state
is shown in Figure 14, and the calculated energy barrier is 12.5 kcal/mol relative to 6_A. In addition, the barrier for O_2 formation by water attack is 19.7 kcal/mol. This is 4.3 kcal/mol higher than that of WOC_E, and the difference is very similar to that found in the previous calculations.[24] These two factors could explain why only a small activity can be observed for WOC_A. The C–H activation side-reaction can be avoided by introducing –F or –CH_2 substituents, as shown in WOC_B to WOC_E.

In WOC_B, both pathways that lead to O_2 formation have significantly higher barriers than those for WOC_E, whereas the barrier for the water attack on the ligand is 2.2 kcal/mol lower than that for WOC_E. WOC_C and WOC_D have slightly higher barriers for the water attack on the oxo group, but somewhat lower barriers for the nitrate attack on the oxo group. As the water attack will be the dominant pathway for O_2 formation for all of them, the calculations reproduce quite well the trends for the relative reactivities of these catalysts.

The electronic properties of the ligand are crucial for the catalyst efficiency. Electron-donating substituents favour the thermodynamics of the oxidation but disfavour the reductive O–O bond formation. In contrast, electron-withdrawing substituents make the oxidation thermodynamically less favourable but facilitate the subsequent O–O bond formation. Therefore, the substituents need to be well-balanced to achieve the highest turnover frequency.

E. Comparison of B3LYP*-2D and M06L

The calculated redox potentials of various couples in WOC_E at the B3LYP*-2D and M06L levels are listed in Table 1. The mean absolute deviation is 0.17 V, and the largest deviation is 0.36 V for the PCET oxidation of Fe^{2+–OH}_2. In both methods, the highest redox potential is close to that of CAN (1.72 V), which suggests that the generation of oxidant 6 is possible. It should be pointed out
that the reference Ce⁴⁺/Ce³⁺ couple for M06L is shifted from 138.4 to 130 kcal/mol. Consequently, the reported one-electron redox potential is shifted by +0.36 V.

The energy diagrams at the M06L levels for all five catalysts are summarized in the Supporting Information (Figures S5–S8 and S11–S17), as are the total barriers for various pathways (Table S13).

For all catalysts, the nitrate attack becomes the preferred pathway in the O₂ formation at the M06L level. For example, the barrier for the water attack on the oxo group is calculated to be 26.0 kcal/mol in the triplet state, which is very close to the barrier reported previously (about 30 kcal/mol) when the singlet–triplet gap at the CASPT2 level (3.3 kcal/mol) is included. Instead, the nitrate attack on the oxo group has a barrier of 19.7 kcal/mol, which is ca. 6 kcal/mol lower than that for the water attack. Thus, these two functionals predict different favoured pathways for the O₂ formation. However, as the catalyst degradation by water attack on the ligand also has a lower barrier (16.6 kcal/mol) at the M06L level, both functionals suggest that the ligand modification proceeds faster than the desired O₂ formation.
Conclusions

In the present study, we have investigated the reaction mechanism of water oxidation catalyzed by iron–TAML complexes by using DFT calculations. Several possible reaction pathways were considered and full energy diagrams were constructed.

Two feasible pathways on the basis of a single metal site have been found for the O₂ formation. Catalysis involving the formation of a dimer, which has been proposed for potassium ferrate⁴⁷ and Ru-based catalysts,¹¹,²² was not considered as the water oxidation by this catalyst is first order. The key oxidant is TAML–Fe⁵⁺=O, which in agreement with the previous study,²⁴ is formed from TAML–Fe³⁺–OH₂ by the removal of three electrons and two protons.

In the following step, a water molecule or a nitrate ion can perform a nucleophilic attack on the metal–oxo group, which leads to O–O bond formation. The water attack, here modelled by adding three additional water molecules, leads to the formation of a ferryl peroxyximate intermediate. This step is calculated to be rate-limiting and has a total barrier of 15.4 kcal/mol in the triplet state. Further oxidation by removing two protons and one electron gives a TAML–Fe⁴⁺–O₂ complex, which undergoes ligand exchange with water to regenerate the starting TAML–Fe³⁺–OH₂ complex. The alternative nitrate attack results in the formation of a ferryl peroxynitrate intermediate, from which N–O bond cleavage occurs and is coupled with O₂ release and binding of the nitrite ion to the metal centre. The attack is calculated to be rate-limiting with a barrier of 19.5 kcal/mol in the triplet state, which is only 4.1 kcal/mol higher than that for water attack. From the ferryl nitrite complex, ligand exchange with water occurs, followed by oxidation to TAML–Fe⁴⁺–OH, which can oxidize the nitrite ion to regenerate a nitrate ion. In this mechanism, the nitrate ion functions as a cocatalyst for O₂ formation, in a process in which one of the oxygen atoms in the generated O₂ molecule originates from a nitrate ion. Further isotope labelling of water and nitrate would be helpful to confirm whether nitrate ions are involved in the catalysis.

Three possible ligand modification pathways have been located to understand the low stability of this catalyst. The calculations demonstrate that water can perform nucleophilic attack on the ligand in a process that is associated with an even lower barrier (only 10.9 kcal/mol) than those for the desired O₂ formation pathways. The oxidative formation of a ligand radical opens the possibility for ligand modification and, thus, might become a drawback of the catalyst. Future ligand design for water oxidation should try to prevent this side-reaction. Further oxidation of the modified ligand leads to the second water attack, which results in the ring-opening and deactivation of the catalyst owing to the rather high redox potential for the following oxidation. Two additional pathways involving a nitrate attack on the ligand and a self-oxidation by reductive elimination to form an N-oxide have higher barriers. The ligand oxidation in this mononuclear iron catalyst should be one of the bottlenecks for electrochemical water oxidation in industrial applications. In addition, ligand oxidation should also be concerned for other homogeneous transition-metal-based catalysts⁸–¹⁶ in future studies.

An examination of the WOCA catalyst shows that the two O₂ formation pathways have higher barriers than those of WOC₆, whereas the water attack on the ligand is even lower in energy. In addition, C–H activation of the methyl substituent to form an alcohol is another possible ligand modification pathway. These two competing pathways may explain why only a small activity has been observed for WOCA. For other catalysts, we find that the barrier for the O₂ formation by water attack decreases from a ligand with more electron-donating substituents to a ligand with more electron-withdrawing substituents. However, the oxidation becomes more difficult and an extra energetic penalty needs to be added to the total barrier. Therefore, a ligand must be optimized with a balance of electron-donating and electron-withdrawing substituents.

Computational Details

The geometry optimizations presented here were accomplished with the M06L⁴⁹ functional by using the resolution-of-the-identity
(RI) approximation as implemented in the Gaussian09 program package. An automatically generated density-fitting basis set was used for all RI-M06L calculations. The SDD pseudopotential was used for Fe, and 6-31+G(d) was used for all other elements. On the basis of these optimized geometries, more accurate energies were obtained by performing single-point calculations with a larger basis set, in which all elements, except Fe, were described by 6-311+G(2d,2p) at both the M06L and the B3LYP functional (15% exact exchange) levels. Solution effects from the water solvent were taken into account by employing the SMD continuum solvation model. Therefore, the relative redox potentials of the Ce(IV)/Ce(III) couple (1.72 V) were reported in the Supporting Information. The M06L relative energies are reported in the Supporting Information.

To build the energy diagram for the full catalytic cycle, the total exergonicity derived from experiment was used. In the present case, the redox potential for the O2/H2O couple is 1.19 V at the working pH (7). The redox potential for the Ce(IV)/Ce(III) couple is 1.72 V and is pH-independent as no proton is involved in the redox reaction. Thus, the whole water oxidation reaction is exothermic by 49.1 kcal/mol. Four electrons and four protons are released during one catalytic cycle of water oxidation. As the species before and after the removal of one proton are difficult to model with quantitative accuracy, the charge of the system changes and the solvation from the environment will then play an important role. The absolute redox potentials can be derived by a fit to the above conclusion.

Supporting Information (see footnote on the first page of this article): B3LYP-2D and M06L data, structures and Cartesian coordinates of WOCF.

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