

OXIDATION REACTIONS

A chameleon catalyst

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An Fe–
iodosylarene
complex
can act as a
chameleon
in oxidation
reactions
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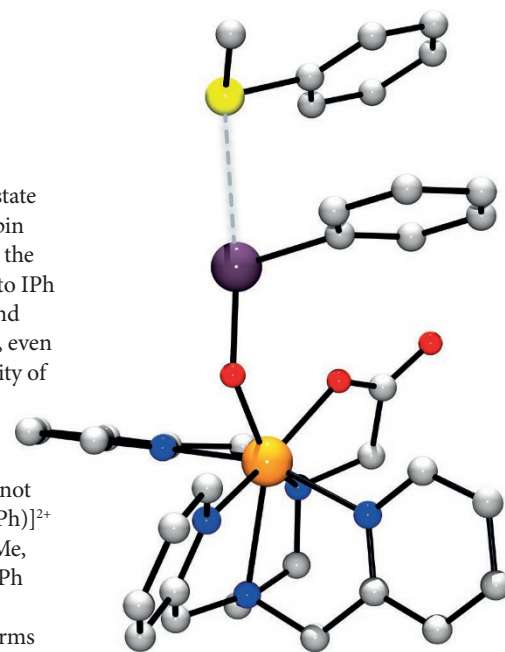
Nonhaem Fe enzymes are able to perform diverse biological roles because they can mediate many organic reactions, including ring opening and closing, halogenation and oxygenation. With respect to oxygenation, nonhaem enzymes often transfer O atoms more selectively than do haem enzymes, such that analogues based on the former may be useful oxidation catalysts. Certain Fe catalysts mediate the oxidation of organic molecules with iododisylbenzene (OIPh) through a process once thought to involve oxo intermediates. This hypothesis — dispelled by experiments showing that redox-inactive metal ions, such as Zn^{II} , also catalyse the reaction — gave way to a proposed mechanism in which the initial Fe–OIPh complex is the sole active oxidant. This has now been challenged by a team led by Yong Wang and Wonwoo Nam, who disclose in the *Journal of the American Chemical Society* a density functional theory (DFT) study that predicts that an oxo intermediate — in intimate contact with the substrate — may also take part in oxidation reactions.

The structural paradigm that is important to many nonhaem Fe enzymes is also present in the model complex $[Fe^{III}L(OIPh)]^{2+}$ ($L = N,N,N'$ -tris(2-pyridylmethyl)ethylenediamine- N' -acetate). This dication has most of its Fe coordination sites protected, in this case by a monoanionic hexadentate ligand, with one site being accessible to the substrate, namely the O atom of OIPh. Using DFT to probe the rapid transformations of the system, Wang emphasizes the importance of using a diffuse basis set to correctly reproduce the electronic structure of the heptacoordinate ferric–iodosylarene complex, which had been found to

have a high-spin $S = \frac{1}{2}$ ground state in earlier work using electron spin resonance. Wang *et al.* find that the dissociation of $[Fe^{III}L(OIPh)]^{2+}$ to IPh and $[Fe^{IV}L(O)]^{2+}$ is kinetically and thermodynamically prohibitive, even taking into account the possibility of crossing to $S = \frac{3}{2}$ or $\frac{1}{2}$ states.

Although the formation of $[Fe^{IV}L(O)]^{2+}$ in isolation is unfavourable, the oxo motif cannot be discounted. When $[Fe^{III}L(OIPh)]^{2+}$ is exposed to the thioether PhSMe, the S atom can attack ligated OIPh at either the O or I atoms. If the latter occurs, an intermediate forms in which the S, I and O atoms are almost collinear. This new soft–soft interaction between the polarizable S and I atoms induces electron transfer from S to Fe to afford a $S = \frac{1}{2}$ system that features $[Fe^{IV}L(O)]^+$; the oxido ligand interacts with the radical cation PhSMe $^+$, with the IPh product also nearby. This bond-cleavage coupled electron transfer (BCCET), with a predicted barrier of 19.4 kcal mol $^{-1}$, is followed by facile O^- transfer to afford the sulfoxide PhS(O)Me, along with the high-spin $[Fe^{III}L]^{2+}$ product. This new mechanism contrasts with the prevailing opinion that Fe–OIPh is the active species, although the calculations of Wang *et al.* suggest both to be possible. Indeed, PhSMe can also attack $[Fe^{III}L(OIPh)]^{2+}$ at the O atom of OIPh, such that formation of PhS(O)Me, IPh and the high-spin product is a concerted process with a single barrier of 18.7 kcal mol $^{-1}$. The system remains in the $S = \frac{1}{2}$ state during this direct O transfer (DOT), in which no oxo intermediates form.

So it appears that $[Fe^{IV}L(O)]^+$ can have a role in sulfoxidation, albeit under specific circumstances that allow for oxo stabilization following BCCET. Together with $[Fe^{III}L(OIPh)]^{2+}$, the active oxidant in



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the DOT scheme, we now have two distinct and equally likely mechanisms. “An Fe–iodosylarene complex can act as a chameleon in oxidation reactions, responding to trajectories of substrate attack by adapting its structure to take the form of an Fe–OIPh or a high-valent Fe–oxo species,” remarks Wang.

What remains unclear is how $[Fe^{III}L(OIPh)]^{2+}$ forms in the first instance, as OIPh typically exists as a polymer. Wang and Nam are also exploring — both through theory and experiment — the stereoelectronics of the system to ascertain if one can favour either DOT or BCCET, the latter process requiring a novel soft–soft interaction. This methodology combines a thermodynamically strong oxidant, OIPh, with a nonhaem Fe complex that is well equipped to selectively transfer O — an approach that will be warmly welcomed by synthetic chemists.

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ORIGINAL ARTICLE Kang, Y. *et al.* The mutable properties of nonheme iron(III)-iodosylarene complexes result in the elusive multiple-oxidant mechanism. *J. Am. Chem. Soc.* <http://dx.doi.org/10.1021/jacs.7b03310> (2017)