Dioxygen Activation by a Non-Heme Iron(II) Complex: Formation of an Iron(IV)–Oxo Complex via C–H Activation by a Putative Iron(III)–Superoxo Species

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Abstract: Iron(III)−superoxo intermediates are believed to play key roles in oxygenation reactions by non-heme iron enzymes. We now report that a non-heme iron(II) complex activates O2 and generates its corresponding iron(IV)−oxo complex in the presence of substrates with weak C–H bonds (e.g., olefins and alkylaromatic compounds). We propose that a putative iron(III)−superoxo intermediate initiates the O2-activation chemistry by abstracting a H atom from the substrate, with subsequent generation of a high-valent iron(IV)−oxo intermediate from the resulting iron(III)−hydroperoxo species.

The nature of metal–oxygen intermediates involved in the catalytic cycles of dioxygen activation by oxygenase enzymes has been intensively investigated over the past several decades. Among the metal–oxygen intermediates, such as metal−superoxo, −peroxo, −hydroperoxo, and −oxo, metal−superoxo species have attracted much attention recently, as iron(III)− and copper(II)−superoxo intermediates have been invoked as active oxidants in H-atom abstraction reactions by non-heme iron and copper enzymes, respectively. In biomimetic models, synthetic Cu(II)−superoxo complexes have shown reactivities in the oxidation of ligand C, H bonds of substrates, but iron(III)−superoxo species have rarely been explored in H-atom abstraction reactions. In non-heme iron models, the formation of iron(III)−hydroperoxo and iron(IV)−oxo species has recently been demonstrated in the reactions of iron(II) complexes and O2 in the presence of electron and proton donors (Scheme 1, pathway A). In accord with the cytochrome P450 paradigm, the electron and proton donors, respectively, were proposed to reduce an iron(III)−superoxo species to an iron(III)−peroxo intermediate and subsequently generate an iron(III)−hydroperoxo species by the protonation of the iron(III)−peroxo intermediate. In another case, the reaction of [FeV(TMC)]2+ (1) (TMC = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane) with O2 generated [(TMC)FeIV(O)]2+ (2) in CH3CN/alcohol or CH3CN/ether solvent mixtures, but the reaction mechanism was not well established. Herein, we report that 1 activates O2 in the presence of olefins (i.e., as an H-atom donor), thereby generating 2 via H-atom abstraction by a putative iron(III)−superoxo species (Scheme 1, pathway B).

As reported previously, 1 is air-stable in CH3CN at 25 °C (Scheme 2, pathway A). Interestingly, addition of olefins, such as cyclohexene, cycloheptene, and cyclodecane to the solution of 1 gave a green intermediate within 1 min (Scheme 2, pathway B). By UV−vis and ESI-MS analysis of the green intermediate (left panel of Figure 1a for UV−vis spectral changes; Figure S1 in the Supporting Information for ESI-MS), we confirmed the formation of 2 with a yield of >90% as determined from the absorbance at 820 nm (ε = 400 M−1 cm−1). In this reaction, the formation of 2 was observed because of the low reactivity of 2 toward olefins at 25 °C. Pseudo-first-order fitting of the kinetic data allowed us to determine kobs values (Figure 1a, right panel), and the first-order rate constants increased proportionally with the concentration of substrate (see the k2 values in the Figure 1b caption). The second-order rate constants were correlated with the C−H bond dissociation energies (BDEs) of the olefins, the formation of 2 was faster with olefins having lower BDEs (Figure 1c). In addition, through the use of deuterated cyclohexene as a substrate, a kinetic isotope effect (KIE) value of 6.3(3) in the formation of 2 was obtained (Figure 1b; compare the plots for cyclohexene (black line) and cyclohexene-d10 (red line)). The large KIE value, with the dependence of the rate constants on the allylic C−H BDE of the olefin, indicates that C−H bond activation of the olefin is the rate-determining step for the formation of 2 (see below).

Product analysis of the reaction solutions was carried out using 1H NMR spectroscopy, GC, and GC−MS after the complete formation of 2. In the reaction of 1 and O2 in the presence of...
Subsequently, discussion here is the nature of an active oxidant that activates allylic oxidation products, such as allylic oxidation and dehydrogenation products (i.e., H-atom abstraction) of the oxidized products, such as allylic oxidation and dehydrogenation products. What we can propose at this moment is that all the oxidized products, such as allylic oxidation and dehydrogenation products, might be derived from the rebound between 4 and the alkenyl radical or from the reaction of the alkenyl radical and O₂. In addition, the mechanism for the formation of dehydrogenation products is not clear at this moment, although such dehydrogenations have been observed in enzymatic reactions as well as in non-heme iron models.

In conclusion, we have shown that a non-heme iron(II) complex activates O₂ in the presence of substrates with weak C–H bonds, thereby generating an iron(IV)–oxo complex. We have proposed that an iron(III)–superoxo intermediate is the active oxidant that abstracts a H atom from the substrate. The present results are probably relevant to the chemistry of mononuclear non-heme iron enzymes such as isopenicillin N synthase and 1-aminocyclopropane-1-carboxylic acid oxidase that initiate oxidation of their substrates by putative iron(III)–superoxo species (i.e., H-atom abstraction) and then generate iron(IV)–oxo species for further oxidation reactions.

Future studies, including theoretical calculations, will focus on elucidating the chemical properties of metal–superoxo species in oxidation reactions.

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Supporting Information Available: Experimental details and Figures S1–S7. This material is available free of charge via the Internet at http://pubs.acs.org.

References

The substrates used in this study were thoroughly purified, and it was confirmed by iodometric titration that no peroxide (autoxidation initiator) was present in the olefins (<1 ppm). We thus conclude that 2 was not formed via an autoxidation process in the present case.


The rates also increased with increasing concentrations of the iron complex and O2, as expected from Scheme 2, pathway C.


The reaction rates were also dependent on the reaction temperature; linear Eyring plots between 20 and 35 °C were obtained, from which the activation parameters $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were calculated (see Figures S2 and S3).