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Nonheme Iron Mediated Oxidation of Light Alkanes with Oxone: Characterization of Reactive Oxoiron(IV) Ligand Cation Radical Intermediates by Spectroscopic Studies and DFT Calculations**

*Chun-Wai Tse, Toby Wai-Shan Chow, Zhen Guo, Hung Kay Lee, Jie-Sheng Huang, and Chi-Ming Che**

Abstract: *The oxidation of light alkanes that is catalyzed by heme and nonheme iron enzymes is widely proposed to involve highly reactive* {Fe^V=O} *species or* {Fe^{IV}=O} *ligand cation radicals. The identification of these high-valent iron species and the development of an iron-catalyzed oxidation of light alkanes under mild conditions are of vital importance. Herein, a combination of tridentate and bidentate ligands was used for the generation of highly reactive nonheme* {Fe=O} *species. A method that employs* $[Fe^{III}(Me_3tacn)(Cl\text{-}acac)Cl]^+$ *as a catalyst in the presence of oxone was developed for the oxidation of hydrocarbons, including cyclohexane, propane, and ethane* (Me_3tacn *= 1,4,7-trimethyl-1,4,7-triazacyclononane; Cl-acac = 3-chloro-acetylacetonate). The complex* $[Fe^{III}(Tp)_2]^+$ *and oxone enabled stoichiometric oxidation of propane and ethane. ESI-MS, EPR and UV/Vis spectroscopy,* ^{18}O *labeling experiments, and DFT studies point to* $[Fe^{IV}(Me_3tacn)(\{Cl\text{-}acac\}^{\bullet+})(O)]^{2+}$ *as the catalytically active species.*

Reactive high-valent iron–mono(oxo) intermediates beyond {Fe^{IV}=O}, such as {Fe^V=O} or {$Fe^{IV}(L^{\bullet+})$=O} ($L^{\bullet+}$ = ligand cation radical), are among the species that are proposed to be directly responsible for the oxidation of hydrocarbons in processes that are catalyzed by heme and nonheme iron enzymes and in biomimetic alkane hydroxylations that are catalyzed by synthetic nonheme iron complexes.[1–3] These reactive {Fe=O} species are usually generated from an Fe^{III} complex and an oxygen-donor ligand[4a] or by two-electron oxidative deprotonation of {Fe^{III}–OH} or {Fe^{III}–OH_2} species. Although a considerable number of nonheme {Fe^{IV}=O} complexes have recently been characterized,[3] there are only a few studies on nonheme {Fe^V=O} species[3] and heme[4] or heme-like[5] {Fe^{IV}=O} π-cation radicals. Notable recent examples include *cis*-{X-Fe^V=O} (**I**; X = solvent[2i] or OH[6]) and {Fe^V=O} (**II**,[7] **III**[2k]) complexes that are supported by polydentate ligands, or the cationic radical $[Fe^{IV}(salen^{\bullet+})(O)(X)]$ (**IV**; X = Cl), where salen is a tetradentate Schiff base ligand[8] (Figure 1). In the literature, experimental evidence can be found that supports participation of {Fe^V=O} or {$Fe^{IV}(L^{\bullet+})$=O} species in the iron-catalyzed oxidation of strong C–H bonds of light alkanes (≤ C4).[9,10]

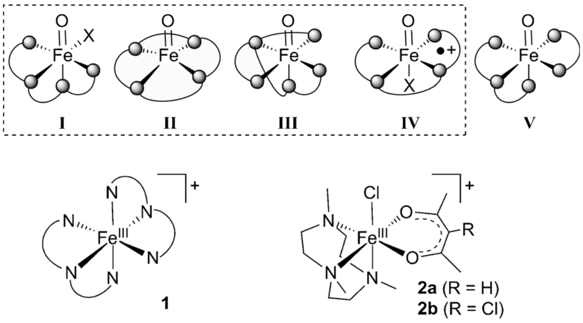

Figure 1. Chelating ligand systems that were either previously reported (**I–IV**) or used in this work (**V**) for supporting nonheme {Fe=O} species with oxidation states beyond Fe^{IV} (charges of complexes, if any, are omitted), along with schematic representations of the catalysts $[Fe^{III}(Tp)_2]^+$ (**1**) and $[Fe^{III}(Me_3tacn)(R\text{-}acac)Cl]^+$ (**2**).

We were interested in developing the oxidation chemistry of reactive {Fe=O} species by reacting Fe^{III} precursors with a two-electron oxygen atom donor.[11a] Herein, we used a combination of tridentate and bidentate ligands for the preparation of Fe^{III} precursors. By coordination of one neutral tridentate ligand and one monoanionic bidentate ligand to the octahedral Fe^{III} center, a single labile coordination site is obtained, so that these complexes are suitable for the formation of highly oxidizing cationic {Fe^V=O} or {$Fe^{IV}(L^{\bullet+})$=O} (**V**; Figure 1) species. The neutral tridentate ligand employed is the strongly σ-donating Me_3tacn

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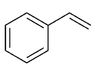
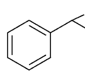
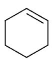
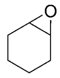
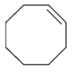
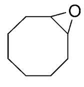
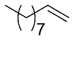
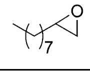
(Me_3tacn = 1,4,7-trimethyl-1,4,7-triazacyclononane), which is known to support highly oxidizing {Ru=O} complexes.[12]

In initial studies, we found that that propane and ethane could be oxidized within five minutes at room temperature in the presence of $[Fe^{III}(Tp)_2]^+$ (**1**; Tp = hydrotris(1-pyrazolyl)-borate)) and oxone (potassium peroxymonosulfate, $2\,KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$), albeit in a stoichiometric manner. We subsequently turned our attention to the $[Fe^{III}(Me_3tacn)(R\text{-}acac)Cl]^+$ system (**2**, R-acac = 3-R-acetylacetonate; R = H: **2a**, R = Cl: **2b**; Figure 1). Herein, we report the oxidation of light alkanes that was mediated or catalyzed by the iron complexes **1** and **2**. Remarkably, the oxidation of propane with oxone that was catalyzed by **2** afforded a total turnover number (TON) of approximately 14 for a five-minute reaction at room temperature.

Complexes **1**[13] and **2**[14] were prepared as their ClO_4^- salts; the structures of **1** and **2a** were determined by X-ray crystallography (Supporting Information, Figure S1 and S2).[15] The cyclic voltammograms of aqueous solutions of **1** (pH 7) and **2c** ($[Fe^{III}(Me_3tacn)(acac)(CH_3CN)]^{2+}$; pH 1) gave $Fe^{III/II}$ reduction potentials at $E_{pa}/E_{pc} = 0.27/0.17$ V (**1**) and 0.54/0.1 V (**2c**), and a large catalytic oxidation current, which is indicative of an electrochemical oxidation reaction, at approximately 1.5 V relative to the saturated calomel electrode (SCE); the latter is tentatively assigned to oxidation of the reaction medium, presumably water (Figure S3 and S4). **2c** also gave an irreversible two-electron oxidation wave at 1.46 V (vs. SCE).

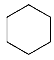
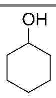
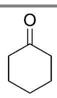
The catalytic oxidation of styrene, cyclohexene, cyclooctene, and 1-decene in the presence of **1** or **2** (4 mol %) and oxone in CH_3CN/H_2O or acetone/H_2O at room temperature yielded the corresponding epoxides in up to 96 % yield within five minutes (alkene as the limiting reagent; Table 1). Importantly, cyclohexane was oxidized to cyclohexanol and cyclohexanone within five minutes with a total TON of up to approximately 41 (Table 2; catalyst loading: 0.6 or 0.06 mol %).

Table 1: Epoxidation of alkenes with oxone catalyzed by **1** and **2**.[a]

Entry	Catalyst	Substrate	Conv.[b] [%]	Product	Yield[b,c] [%]
1	**1**		85		72[d] (85[e])
2	**1**		81		75 (93[e])
3	**1**		97		96 (99[e])
4	**2a**		99		79 (80[e])
5	**2b**		97		87 (90[e])
6	**1**		77[f]		67 (87[e])

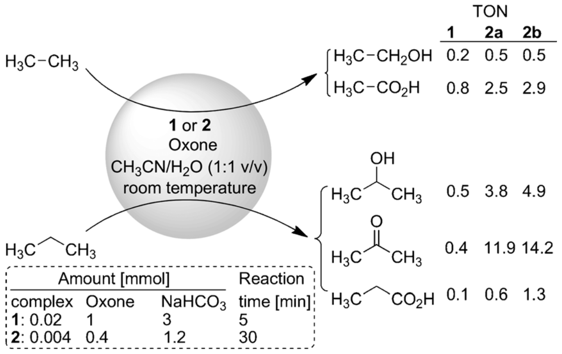
[a] Reaction conditions: substrate (0.5 mmol) in CH_3CN (3 mL) for **1** or in acetone (3 mL) for **2**, aqueous solution of oxone (0.75 mmol, 3 mL), $NaHCO_3$ (2.25 mmol), catalyst (0.02 mmol), RT, 5 min. [b] Determined by GC analysis. [c] Based on the starting substrate. [d] Benzaldehyde was also formed (9.4 % yield). [e] Selectivity (yield of epoxide product divided by substrate conversion). [f] Reaction time: 15 min.

Table 2: Oxidation of cyclohexane with oxone catalyzed by **1** and **2**.[a]

Entry	Catalyst	Substrate	Product TON[b] Alcohol		Ketone		Total TON
1	**1**			6.4		6.3	12.7
2[c]	**2a**			13.0		28.1	41.1
3[c]	**2b**			17.5		17.6	35.1

[a] Reaction conditions: cyclohexane (5 mmol), catalyst (0.03 mmol), oxone (1.5 mmol), $NaHCO_3$ (4.5 mmol), acetone (5 mL), H_2O (5 mL), RT, 5 min. [b] Number of micromoles of product (determined by GC) divided by number of micromoles of catalyst. [c] Cyclohexane (7 mmol), catalyst (0.004 mmol), oxone (0.4 mmol), $NaHCO_3$ (1.2 mmol).

Treatment of ethane (6.9 bar) with **1** and oxone in CH_3CN/H_2O at room temperature for five minutes afforded a mixture of ethanol and acetic acid; under the same conditions, propane was oxidized to a mixture of isopropanol, acetone, and propanoic acid (Scheme 1).[16] These reactions, however, each gave a total TON of 1.0 and were thus not catalytic; presumably, the Fe complex decomposed during oxidation. The oxidation was assisted by H_2O, as a control experiment for the oxidation of propane in the absence of H_2O, but in the presence of **1** and tetrabutylammonium oxone, with a reaction time of five minutes gave very little acetone (10 % yield based on **1**), and no other oxidation products were detected. Using **2a** or **2b** (1 mol %) as the catalyst, the oxidation of propane with oxone in CH_3CN/H_2O (1:1, v/v) at room temperature gave the C–H oxidized products with a total TON of 13.7 after five minutes (Table S1); the product distribution (isopropanol/acetone/propanoic acid ≈ 10:23:1) was different from that of the previously reported $FeCl_3$-catalyzed oxidation of propane with H_2O_2 (25 °C, 1 h; isopropylhydroperoxide as the major product).[9b] Overoxidation likely results in the formation of acetone and propanoic acid, as oxidation of isopropanol and propanol in the presence of **2** and oxone under similar conditions gave acetone and propanoic acid in 63 % and 52 % yield, respectively. Oxidation of ethane and propane with iron complex **2** and oxone gave the oxidized products with total TONs of up to 3.4 and 20.4, respectively after 30 min (Scheme 1).



Scheme 1. Oxidation of ethane and propane with oxone mediated by **1** or catalyzed by **2**.

The involvement of {Fe=O} intermediates **V** (Figure 1) in the hydrocarbon oxidation with oxone catalyzed by **1** or **2** is supported by the following observations: First, high-resolution ESI-MS analysis of a mixture of **1** with oxone (10 equiv) in CH_3CN/H_2O (reaction time: 15 seconds) revealed a species with *m*/*z* 498.1463, which gave an isotope pattern and a collision-induced dissociation pattern that both matched the corresponding patterns of $[Fe(Tp)_2(O)]^+$ (calcd *m*/*z* 498.1426); this species was transformed into a mixture, possibly of $[Fe(Tp)_2(OH)]^+$ and $[Fe(Tp)_2(H_2O)]^+$, within one minute (Figure S5 and S6). Second, for a mixture of **2b** with oxone (8 equiv) in CH_3CN/H_2O, high-resolution ESI-MS analysis at a reaction time of 30 seconds revealed a cluster peak at *m*/*z* 411.0787, which may be attributed to $\{[Fe(Me_3tacn)(Cl\text{-}acac)(O)]Cl\}^+$ (calcd *m*/*z* 411.0780) based on the isotope pattern and collision-induced dissociation (Figure 2). Changing the solvent to $CH_3CN/H_2{}^{18}O$ led to an ^{18}O incorporation into the $\{[Fe(Me_3tacn)(Cl\text{-}acac)(O)]Cl\}^+$ complex of approximately 60 %, which suggests that oxygen exchange between {Fe=O} and $H_2{}^{18}O$ has occurred.[1a,c] The peak at *m*/*z* 411.0787 was suppressed in the presence of cyclohexane (40 equiv). Third, neither H_2O nor O_2 served as the major oxygen source of the oxidation products. Under catalytic conditions, an ^{18}O incorporation of approximately 6 % into cyclohexanol was found for cyclohexane oxidation with **2b** and oxone in $CH_3CN/H_2{}^{18}O$ (reaction time: 5 min), and no significant change in the product yields was observed when this reaction (in CH_3CN/H_2O) was conducted under an atmosphere of argon or O_2. With **1** and oxone in $CH_3CN/H_2{}^{18}O$ or acetone/$H_2{}^{18}O$, the oxidation of styrene or cyclohexane led to no significant ^{18}O incorporation into styrene oxide or cyclohexanol. Probably, the {Fe=O} reaction intermediate underwent oxygen transfer to these two hydrocarbon substrates at higher rates than oxygen exchange with H_2O. Indeed, a stoichiometric reaction of **2b** (0.2 mmol) with oxone in $CH_3CN/H_2{}^{18}O$ at room temperature for 30 seconds to allow oxygen exchange between {Fe=O} and $H_2{}^{18}O$, followed by treatment with excess cyclohexane (3.5 mmol) for 5 min, resulted in an ^{18}O incorporation into cyclohexanol of 32 %. Fourth, the oxidation of *para*-substituted styrenes with **1** or **2b** and oxone revealed linear Hammett plots with $\rho^+ = -0.87$ (**1**), -0.63 (**2b**; Figure S7 and S8), which is in accordance with attack on the alkenes by an electrophilic {Fe=O} species. Competitive oxidation of several hydrocarbons with **2b** and oxone revealed a linear relationship between $\log k'_{\text{rel}}$ and the C–H bond dissociation energy (Figure S9), which is in agreement with rate-limiting H-atom abstraction by the {Fe=O} species.[2h] Fifth, the oxidation of cyclohexane catalyzed by **1** or **2** with oxone exhibited a primary kinetic isotope effect (KIE) of $k_H/k_D = 4.7$ (**1**), 3.6 (**2a**), or 3.8 (**2b**); these values are comparable to those reported for the cyclohexane oxidation with Fe–tpa complexes and H_2O_2 (tpa = tris(2-pyridylmethyl)amine; $k_H/k_D = 3\text{–}4$).[2a]

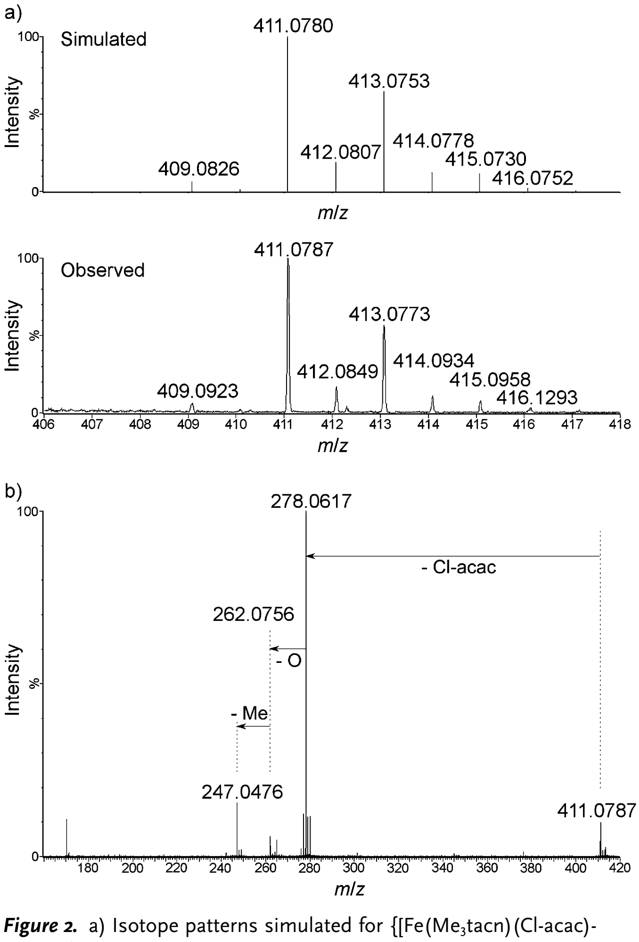
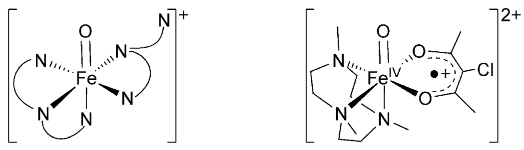


Figure 2. a) Isotope patterns simulated for $\{[Fe(Me_3tacn)(Cl\text{-}acac)(O)]Cl\}^+$ and observed for the reactive species with *m*/*z* 411.0787 in high-resolution ESI-MS analysis of the reaction mixture of **2b** with oxone (8 equiv) at 30 s. b) Collision-induced dissociation of this reactive species (collision energy: 20 eV).

The DFT-optimized structure of $[Fe(Tp)_2(O)]^+$ (**Va**, Figure S10) features a six-coordinate iron, while one of the Tp pyrazolyl groups remains uncoordinated (Figure 3), and is reminiscent of the crystal structures of $[Ti^{IV}(Tp)_2(Se)]$[17] and $[Ru^{IV}(H^+tpa)(bpy)(O)]^{3+}$[18] (Figure S11). Based on the computed frontier molecular orbitals for the ground states of **Va** (Figure S10) and **Vb** (Figure 4) and the spin distributions that were determined using B3LYP and M06L functionals (Table S2), **Va** can be described to have approximately 40 % $[Fe^V(Tp)_2(O)]^+$ character and about 60 % $[Fe^{IV}(Tp)(Tp^{\bullet+})(O)]^+$ character, whereas **Vb** has insignificant $[Fe^V(Me_3tacn)(Cl\text{-}acac)(O)]^{2+}$ character and could be described as an $\{Fe^{IV}{=}O\}$ cation radical complex $[Fe^{IV}(Me_3tacn)(\{Cl\text{-}acac\}^{\bullet+})(O)]^{2+}$ (Figure 3 and Figure S12). Changing the ligand system from two anionic Tp ligands to one neutral Me_3tacn ligand and one anionic R-acac ligand might account for the smaller amount of electronic-charge injection into the 3d shell of the iron center. Therefore, oxidation of the metal center of the latter dicationic complex is conceived to occur at



Va **Vb**

Figure 3. DFT-optimized structures of $[Fe(Tp)_2(O)]^+$ (**Va**) and $[Fe(Me_3tacn)(Cl\text{-}acac)(O)]^{2+}$ (**Vb**).

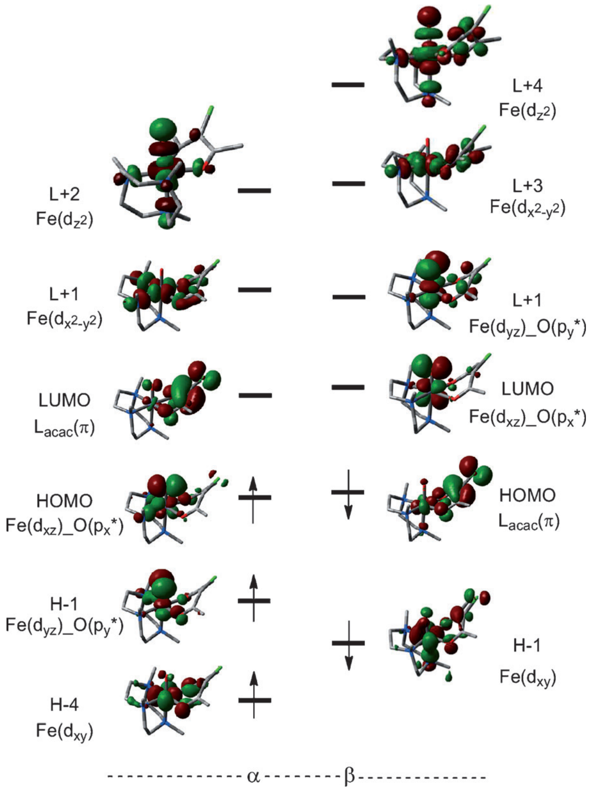


Figure 4. MO diagram for **Vb** (ground state, doublet) obtained by DFT calculations (B3LYP/def2-TZVP).

a higher potential than that of the former monocationic complex. The Fe=O distances that were computed at the B3LYP/def2-TZVP level of theory are 1.631 Å (**Va**) and 1.625 Å (**Vb**); these values are comparable to that for [Fe^{V}(taml)(O)]$^{-}$ (1.60 Å; taml = tetraamido macrocyclic ligand), which was computed with a similar method (B3LYP/6-311G).[7] Our initial calculations on the oxidation of ethane and propane by **Va** and **Va**·H$_2$O (the latter features hydrogen bonding between **Va** and H$_2$O, see Figure S10) in the gas phase with the B3LYP functional showed that these reactions involve rate-limiting H-atom abstraction by the {Fe=O} species, as was previously reported for the oxiation of light alkanes by nonheme {Fe^{IV}=O}[19a,c–e] or {Fe^{V}=O} species,[19b] which was studied by DFT calculations. The calculated reaction barriers are low (see Figure S13 and S14; the reaction barrier is lower for **Va**·H$_2$O than for **Va** because oxidation is assisted by water), which is in line with the experimentally observed oxidation of ethane and propane that occurred in the presence of **1** and oxone at room temperature within five minutes. After Wigner tunneling correction, the calculated KIE[20] for the cyclohexane oxidation by the ground state of **Va**·H$_2$O is 4.0 (Table S3), which is comparable to the experimental value of 4.7. At this stage, we cannot conclude whether the doublet state or both the doublet and quartet states are responsible for alkane oxidation. In the literature, a two-state reactivity has commonly been proposed for the hydroxylation of hydrocarbons by reactive heme or nonheme {Fe=O} species.[21] The doublet and quartet states of **Vb** are conceived to have similar reaction barriers because of the similar electron configuration/occupancy, and a two-state reactivity is thus also anticipated.

Consistent with the formulation of [Fe^{IV}(Me$_3$tacn)({Cl-acac}$^{\bullet+}$)(O)]$^{2+}$ (**Vb**, $S = 1/2$) by DFT calculations, the X-band EPR spectrum of a reaction mixture of **2b** with oxone (10 equiv) in CH$_3$CN/H$_2$O at 4 K exhibited a new signal with $g = 1.97$, 1.93, 1.91 ($g_{ave} = 1.94$) that is attributable to **Vb** (Figure 5). This new signal accounted for 35% of the total iron content in the sample (Figure S15). It resembles the signal reported for the [Fe^{IV}({TBP$_8$Cz}$^{\bullet+}$)(O)] ($S = 1/2$, $g = 2.09$, 2.05, 2.02; TBP$_8$Cz = a corrolazine ligand),[5a] but is distinct from the signal of **2b** ($S = 5/2$, $g = 7.0$, 4.8, 4.1; Figure S16) with $\mu_{eff} = 6.0\ \mu_B$ (measured by the Evans method) close to $5.9\ \mu_B$ reported for [Fe^{III}(Me$_3$tacn)(aacac)Cl]ClO$_4$ ($S = 5/2$; aacac = 3-(9-anthryl)acetylacetonate).[14] Its value of g_{ave} is similar to the g_{ave} value of 1.94 that was found for a Cytochrome P450 Compound I (CYP119-I),[22b] and is comparable to $g_{ave} = 1.90$ for [Fe^{V}(taml)(O)]$^{-}$.[7] CYP119-I and also CPO-I[22a] (another Cytochrome P450 Compound I) are {Fe^{IV}=O} porphyrin cation radicals; their $g_{ave} < 2$ values are rationalized by a spin-coupling model that exhibits substantial dependence of the g values on the J/D ratio (J: exchange coupling; D: zero-field splitting).[22] A similar rationalization could be provided for the g_{ave} value of < 2 that is attributed to **Vb** in this work. Analysis of a reaction mixture of **2b** with oxone (10 equiv) in CH$_3$CN/H$_2$O in the presence of cyclohexane (2, 5, or 12.5 equiv) by X-band EPR spectroscopy at 4 K revealed that the signal that is attributed to **Vb** had a lower intensity at higher cyclohexane concentrations and was almost completely suppressed in the presence of 12.5 equiv of cyclohexane (Figure S17); this finding corroborates the idea that **Vb** is a key reaction intermediate that is responsible for alkane oxidation in the presence of **2b** and oxone. For **1** and its reaction mixture with oxone (10 equiv) in CH$_3$CN/H$_2$O, well-defined signals could not be detected by X-band EPR at 4 K (Figure S18), which is presumably due to quick relaxation or the short lifetime of **Va**.

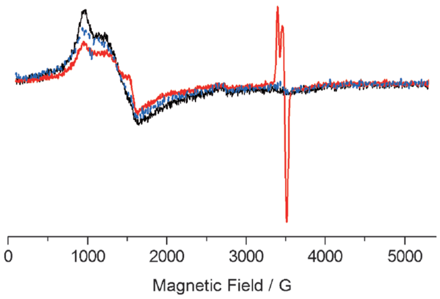


Figure 5. X-band EPR spectrum of the reaction mixture of **2b** with oxone (10 equiv) in CH$_3$CN/H$_2$O (1:1, v/v; ——) at 4 K compared with the spectrum of the reaction mixture in the presence of cyclohexane (12.5 equiv; – – –) and with the spectrum of **2b** (——).

TD-DFT calculations of the absorption spectrum of **Vb** at the B3LYP/def2-TZVP level of theory with the PCM model in water gave a simulated spectrum (Figure S19 and Table S4) that features a low-energy absorption at 737 nm. This calculated absorption band is comparable to a new absorption at approximately 750 nm that developed in the UV/Vis absorption spectrum of a reaction mixture that was obtained immediately after mixing **2b** with oxone at room temperature. The intensity of the new absorption at approximately 750 nm decreased with an increase in cyclohexane concentration (Figure S20), which is consistent with the findings by EPR spectroscopy.

To demonstrate the generality of the approach that is based on tridentate and bidentate ligands for the design of nonheme iron oxidation catalysts, we prepared **2c**, **2d**, and **3** and examined their catalytic activities (Figure 6). Complexes **2c** and **2d** catalyzed the oxidation of cyclohexane with oxone to give cyclohexanol and cyclohexanone with total TONs of 39.5 (**2c**) and 30.8 (**2d**) for a 5 min reaction at room temperature (Table S5). Under the same conditions, the oxidation of cyclooctane catalyzed by **2a**–**2d** afforded cyclooctanol and cyclooctanone with total TONs of 34.2–36.9. Replacing the catalyst for $[Fe^{III}(Me_3tacn)(aacac)Cl]^+$ (**2e**)[14] led to a slight decrease of the total TON to 29.9 and 32.2 for the oxidations of cyclohexane and cyclooctane, respectively (Tables S5 and S6). The applicability of the method that is based on the use of **2** as the catalyst and oxone was examined for the oxidation of a limiting amount of alkane substrate using adamantane as an example (Table S7); the selectivity of this process with respect to tertiary and secondary C–H bonds was also studied. The reactions that were catalyzed by **2a**–**2e** at room temperature with a reaction time of five minutes afforded adamantan-1-ol, adamantan-2-ol, and adamantan-2-one with moderate substrate conversion (43.9–52.4 %), high mass balance (73.9–85.8 %), and with a selectivity for the tertiary/secondary C–H bonds of 3.9–5.1 (per C–H bond).[11b] Complexes **2c** and **2d** effectively catalyzed propane oxidation in the presence of oxone at room temperature, although **3** exhibited a lower catalytic activity (total TON: up to 7.8) than **2** (total TON: up to 11.9; Table S8).

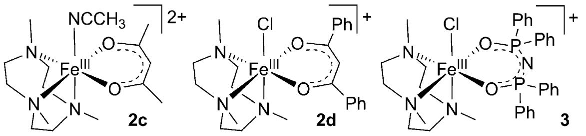


Figure 6. Nonheme iron oxidation catalysts **2c**, **2d**, and **3**.

In summary, mononuclear nonheme iron complexes **2** exhibit high catalytic activity towards the oxidation of light alkanes, including propane and ethane, by oxone at room temperature. These reactions proceed through reactive $\{Fe^{IV}{=}O\}$ ligand cation radical intermediates. It is conceived that the judicious choice of a robust neutral tripodal nitrogen-donor ligand and an anionic bidentate ligand can give nonheme iron catalysts for the oxidation of light alkanes with synthetic interest.

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[1] For selected reviews, see: a) X. Shan, L. Que, Jr., *J. Inorg. Biochem.* **2006**, *100*, 421; b) E. G. Kovaleva, M. B. Neibergall, S. Chakrabarty, J. D. Lipscomb, *Acc. Chem. Res.* **2007**, *40*, 475; c) P. C. A. Bruijnincx, G. van Koten, R. J. M. Klein Gebbink, *Chem. Soc. Rev.* **2008**, *37*, 2716; d) P. R. Ortiz de Montellano, *Chem. Rev.* **2010**, *110*, 932; e) K. Schröder, K. Junge, B. Bitterlich, M. Beller in *Iron Catalysis: Fundamentals and Applications* (Ed.: B. Plietker), Springer, Heidelberg, **2011**, p. 83; f) E. P. Talsi, K. P. Bryliakov, *Coord. Chem. Rev.* **2012**, *256*, 1418; g) M. Bordeaux, A. Galarneau, J. Drone, *Angew. Chem.* **2012**, *124*, 10870; *Angew. Chem. Int. Ed.* **2012**, *51*, 10712.

[2] For examples, see: a) K. Chen, L. Que, Jr., *J. Am. Chem. Soc.* **2001**, *123*, 6327; b) K. Chen, M. Costas, J. Kim, A. K. Tipton, L. Que, Jr., *J. Am. Chem. Soc.* **2002**, *124*, 3026; c) A. Bassan, M. R. A. Blomberg, P. E. M. Siegbahn, L. Que, Jr., *J. Am. Chem. Soc.* **2002**, *124*, 11056; d) A. Nielsen, F. B. Larsen, A. D. Bond, C. J. McKenzie, *Angew. Chem.* **2006**, *118*, 1632; *Angew. Chem. Int. Ed.* **2006**, *45*, 1602; e) D. Kumar, H. Hirao, S. Shaik, P. M. Kozlowski, *J. Am. Chem. Soc.* **2006**, *128*, 16148; f) S. H. Lee, J. H. Han, H. Kwak, S. J. Lee, E. Y. Lee, H. J. Kim, J. H. Lee, C. Bae, S. N. Lee, Y. Kim, C. Kim, *Chem. Eur. J.* **2007**, *13*, 9393; g) R. Mas-Ballesté, L. Que, Jr., *J. Am. Chem. Soc.* **2007**, *129*, 15964; h) J. Yoon, S. A. Wilson, Y. K. Jang, M. S. Seo, K. Nehru, B. Hedman, K. O. Hodgson, E. Bill, E. I. Solomon, W. Nam, *Angew. Chem.* **2009**, *121*, 1283; *Angew. Chem. Int. Ed.* **2009**, *48*, 1257; i) O. Y. Lyakin, K. P. Bryliakov, G. J. P. Britovsek, E. P. Talsi, *J. Am. Chem. Soc.* **2009**, *131*, 10798; j) G. Xue, R. De Hont, E. Münck, L. Que, Jr., *Nat. Chem.* **2010**, *2*, 400; k) Y. Hitomi, K. Arakawa, T. Funabiki, M. Kodera, *Angew. Chem.* **2012**, *124*, 3504; *Angew. Chem. Int. Ed.* **2012**, *51*, 3448.

[3] A. R. McDonald, L. Que, Jr., *Coord. Chem. Rev.* **2013**, *257*, 414.

[4] a) J. T. Groves, R. C. Haushalter, M. Nakamura, T. E. Nemo, B. J. Evans, *J. Am. Chem. Soc.* **1981**, *103*, 2884; b) W. Nam, *Acc. Chem. Res.* **2007**, *40*, 522; c) Z. Cong, T. Kurahashi, H. Fujii, *Angew. Chem.* **2011**, *123*, 10109; *Angew. Chem. Int. Ed.* **2011**, *50*, 9935; d) E. V. Kudrik, P. Afanasiev, L. X. Alvarez, P. Dubourdeaux, M. Clémancey, J.-M. Latour, G. Blondin, D. Bouchu, F. Albrieux, S. E. Nefedov, A. B. Sorokin, *Nat. Chem.* **2012**, *4*, 1024.

[5] a) A. J. McGown, W. D. Kerber, H. Fujii, D. P. Goldberg, *J. Am. Chem. Soc.* **2009**, *131*, 8040; b) K. Cho, P. Leeladee, A. J. McGown, S. DeBeer, D. P. Goldberg, *J. Am. Chem. Soc.* **2012**, *134*, 7392; c) P. Afanasiev, E. V. Kudrik, F. Albrieux, V. Briois, O. I. Koifman, A. B. Sorokin, *Chem. Commun.* **2012**, *48*, 6088.

[6] I. Prat, J. S. Mathieson, M. Güell, X. Ribas, J. M. Luis, L. Cronin, M. Costas, *Nat. Chem.* **2011**, *3*, 788.

[7] F. T. de Oliveira, A. Chanda, D. Banerjee, X. Shan, S. Mondal, L. Que, Jr., E. L. Bominaar, E. Münck, T. J. Collins, *Science* **2007**, *315*, 835.

[8] a) V. K. Sivasubramanian, M. Ganesan, S. Rajagopal, R. Ramaraj, *J. Org. Chem.* **2002**, *67*, 1506; b) N. S. Venkataramanan, G. Kuppuraj, S. Rajagopal, *Coord. Chem. Rev.* **2005**, *249*, 1249.

[9] A few nonheme diiron or tetrairon catalysts have been reported for the oxidation of methane, ethane, and propane with H_2O_2 at RT or 50–80 °C; for examples, see: a) G. V. Nizova, B. Krebs, G. Süss-Fink, S. Schindler, L. Westerheide, L. G. Cuervo, G. B. Shul'pin, *Tetrahedron* **2002**, *58*, 9231; b) G. B. Shul'pin, G. V. Nizova, Y. N. Kozlov, L. G. Cuervo, G. Süss-Fink, *Adv. Synth. Catal.* **2004**, *346*, 317; c) V. B. Romakh, B. Therrien, G. Süss-Fink, G. B. Shul'pin, *Inorg. Chem.* **2007**, *46*, 3166.

[10] For the involvement of heme or heme-like $\{Fe{=}O\}$ intermediates in the oxidation of methane with *meta*-ClC_6H_4COOOH or H_2O_2 catalyzed by nitrido-bridged iron porphyrin or phthalocyanine complexes, see Ref. [4d] and references therein.

[11] a) T. W.-S. Chow, E. L.-M. Wong, Z. Guo, Y. Liu, J.-S. Huang, C.-M. Che, *J. Am. Chem. Soc.* **2010**, *132*, 13229; b) P. Liu, Y. Liu, E. L.-M. Wong, S. Xiang, C.-M. Che, *Chem. Sci.* **2011**, *2*, 2187.

[12] S. L.-F. Chan, Y.-H. Kan, K.-L. Yip, J.-S. Huang, C.-M. Che, *Coord. Chem. Rev.* **2011**, *255*, 899.

[13] C.-G. Hong, A.-J. Zhou, M.-L. Tong, *Acta Crystallogr. Sect. E* **2005**, *61*, m1774.

[14] M. Müller, T. Weyhermüller, E. Bill, K. Wieghardt, *J. Biol. Inorg. Chem.* **1998**, *3*, 96.

[15] CCDC 870633 (**1**·ClO_4) and 943377 (**2a**·ClO_4) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[16] In control experiments under the same conditions, the reaction of propane with oxone in the absence of **1** gave trace amounts of acetone; neither isopropanol nor propanoic acid was detected.

[17] A. Kayal, J. Kuncheria, S. C. Lee, *Chem. Commun.* **2001**, 2482.

[18] a) T. Kojima, K. Nakayama, K. Ikemura, T. Ogura, S. Fukuzumi, *J. Am. Chem. Soc.* **2011**, *133*, 11692; b) T. Kojima, K. Nakayama, M. Sakaguchi, T. Ogura, K. Ohkubo, S. Fukuzumi, *J. Am. Chem. Soc.* **2011**, *133*, 17901.

[19] For selected examples, see: a) B. Ensing, F. Buda, M. C. M. Gribnau, E. J. Baerends, *J. Am. Chem. Soc.* **2004**, *126*, 4355; b) A. Bassan, M. R. A. Blomberg, P. E. M. Siegbahn, L. Que, Jr., *Chem. Eur. J.* **2005**, *11*, 692; c) S. P. de Visser, *Angew. Chem.* **2006**, *118*, 1822; *Angew. Chem. Int. Ed.* **2006**, *45*, 1790; d) C. Geng, S. Ye, F. Neese, *Angew. Chem.* **2010**, *122*, 5853; *Angew. Chem. Int. Ed.* **2010**, *49*, 5717; e) D. Usharani, D. Janardanan, S. Shaik, *J. Am. Chem. Soc.* **2011**, *133*, 176.

[20] KIEs are sensitive probes of spin-state reactivity: for examples, see: a) S. P. de Visser, F. Ogliaro, P. K. Sharma, S. Shaik, *J. Am. Chem. Soc.* **2002**, *124*, 11809; b) D. Kumar, S. P. de Visser, S. Shaik, *J. Am. Chem. Soc.* **2003**, *125*, 13024; c) K. Yoshizawa, Y. Shiota, *J. Am. Chem. Soc.* **2006**, *128*, 9873; d) C. Li, W. Wu, K.-B. Cho, S. Shaik, *Chem. Eur. J.* **2009**, *15*, 8492.

[21] For examples, see: S. Shaik, H. Hirao, D. Kumar, *Acc. Chem. Res.* **2007**, *40*, 532, and references therein.

[22] a) R. Rutter, L. P. Hager, H. Dhonau, M. Hendrich, M. Valentine, P. Debrunner, *Biochemistry* **1984**, *23*, 6809; b) J. Rittle, M. T. Green, *Science* **2010**, *330*, 933.