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Supporting Information

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Mechanistic Insight into Alcohol Oxidation by High-Valent Iron-Oxo Complexes of Heme and Nonheme Ligands

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Experimental Conditions

Materials and Instrumentation. All chemicals obtained from Aldrich Chemical Co. were the best available purity and used without further purification unless otherwise indicated. Solvents were dried according to published procedures [1] and distilled under Ar prior to use. $H_2{}^{18}O$ (95% ^{18}O-enriched) was purchased from ICON Services Inc. (Summit, NJ, USA). Iron(II) complexes such as Fe(TPA)$(ClO_4)_2$ and Fe(N4Py)$(ClO_4)_2$ were prepared in a glovebox by literature methods [2-3]. Fe(TMP)Cl and Fe(TDCPP)Cl were obtained from Mid-Century Chemicals (Posen, Il, USA). 4-Hydroxybutyraldehyde was prepared by a literature method [4].

Caution: Perchlorate salts are potentially explosive and should be handled with great care.

UV-vis spectra were recorded on a Hewlett Packard 8453 spectrophotometer equipped with *Optostat*^{DN} variable-temperature liquid-nitrogen cryostat (Oxford Instruments) or with a circulating water bath. Electrospray ionization mass spectra (ESI MS) were collected on a Thermo Finnigan (San Jose, CA, USA) LCQ^{TM} Advantage MAX quadrupole ion trap instrument. Product analysis for the oxidation of benzyl alcohol was performed on DIONEX Pump Series P580 equipped with a variable wavelength UV-200 detector (HPLC). Products were separated on Waters Symmetry C18 reverse phase column (4.6 x 250 mm), and detection was made at 215 and 254 nm. Product analysis for the oxidation of cyclobutanol was performed on Agilent Technologies 6890N gas chromatograph (GC) and a Hewlett-Packard 5890 II Plus gas chromatograph interfaced with Hewlett-Packard model 5989B mass spectrometer (GC-MS).

Reactions of Heme and Nonheme Oxoiron(IV) Complexes with Benzyl Alcohol. In general, reactions were run at least in triplicate, and the data represent average of these reactions. All reactions were followed by monitoring spectral changes of reaction solutions with a UV-vis spectrophotometer. Oxoiron(IV) porphyrin π-cation radicals, **1a** and **1b**, were prepared by adding 2 equiv of *m*-CPBA (4 mM, diluted in 50 μL of butyronitrile) into a 0.1-cm UV cuvette containing an iron(III) porphyrin complex (2 mM) in butyronitrile (0.5 mL). Nonheme

oxoiron(IV) complexes, **1c** and **1d**, were prepared by adding 1.2 equiv of oxidant (peracetic acid and *m*-CPBA for **1c** and **1d**, respectively) (2.4 mM, diluted in 50 μL of CH_3CN) into an 1-cm UV cuvette containing an iron(II) complex (2 mM), $Fe(TPA)(ClO_4)_2$ or $Fe(N4Py)(ClO_4)_2$, in CH_3CN (2 mL). Then, appropriate amounts of benzyl alcohol were added into the UV cuvette, and spectral changes of the oxoiron(IV) complexes were directly monitored by a UV-vis spectrophotometer. Rate constants, k_{obs}, were determined by pseudo-first-order fitting of the decrease of absorption bands at 690 nm for **1a**, 665 nm for **1b**, 720 nm for **1c**, and 695 nm for **1d**.

Product Analysis for the Oxidation of Benzyl Alcohol and Cyclobutanol. Reaction solutions containing oxoiron(IV) intermediates (2 mM) were prepared as described above. Then, 25 equiv of benzyl alcohol (50 mM) or cyclobutanol (50 mM) was added to the reaction solutions. Product analysis was performed by injecting reaction solutions directly into HPLC, GC, and/or GC-MS. Product yields were determined by comparison with standard curves of known authentic samples.

For isotope labeling study, **1d**-^{18}O was prepared by adding a small amount of $H_2{}^{18}O$ (10 μL, 95% ^{18}O-enriched) to a reaction solution containing **1d**-^{16}O in a solvent mixture (2 mL) of CH_3CN and butyl ether (*v*/*v* = 1:1) at 25 °C. The ESI MS of **1d**-^{18}O was taken by infusing samples directly into the source at 20 μL/min using a syringe pump. The spray voltage was set at 4 kV and the capillary temperature at 70 °C. Then, 25 equiv of benzyl alcohol (50 mM, diluted in 50 μL of CH_3CN) was added and reacted with **1d**-^{18}O for 400 s. A control reaction was performed by incubating PhCH^{16}O for 400 s in the presence of $H_2{}^{18}O$ (10 μL, 95% ^{18}O-enriched) in a solvent mixture (2 mL) of CH_3CN and butyl ether (*v*/*v* = 1:1) at 25 °C. Product analysis was performed with GC and GC-MS. The ^{16}O and ^{18}O compositions in benzaldehyde were analyzed by the relative abundances of *m*/*z* = 106 for PhCH^{16}O and *m*/*z* = 108 for PhCH^{18}O.

References

[1] *Purification of Laboratory Chemicals*; Armarego, W. L. F.; Perrin, D. D., Eds.; Pergamon Press: Oxford, 1997.

[2] Zang, Y.; Kim, J.; Dong, Y.; Wilkinson, E. C.; Appelman, E. H.; Que, L., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 4197-4205.

[3] Lubben, M.; Meetsma, A.; Wilkinson, E. C.; Feringa, B.; Que, L., Jr. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1512-1514.

[4] Nakano, T.; Terada, T.; Ishii, Y.; Ogawa, M. *Synthesis* **1986**, 774-776.

Table S1. Kinetic isotope effect (KIE) values determined in the reactions of heme and nonheme oxoiron(IV) complexes and benzyl alcohols [a]

Intermediate	Temperature (^{o}C)	k_H (10^{-3} s^{-1})[b]	k_D (10^{-3} s^{-1})[c]	k_H/k_D
$[(TDCPP)^{+\cdot}Fe^{IV}=O]^{+}$ **1a**	-100	27 ± 2	1.3 ± 0.1	21
$[(TMP)^{+\cdot}Fe^{IV}=O]^{+}$ **1b**	-60	15 ± 1	0.8[d]	>20[d]
$[(TPA)Fe^{IV}=O]^{2+}$ **1c**	-40	22 ± 2	0.38 ± 0.03	58
$[(N4Py)Fe^{IV}=O]^{2+}$ **1d**	0	6.3 ± 0.3	0.13 ± 0.1	48

[a] See detailed experimental procedures in Experimental Section of this Supporting Information.

[b] Oxoiron(IV) complexes (2 mM) and 100 equiv of benzyl alcohol (200 mM) were used.

[c] Oxoiron(IV) complexes (2 mM) and 100 equiv of deuterated benzyl alcohol ($C_6D_5CD_2OH$) (200 mM) were used.

[d] The rate of the natural decay of **1b** was determined to be 0.8 x 10^{-3} s^{-1}, indicating that the k_D value should be much lower than the reported one and the k_H/k_D value should be greater than 20.

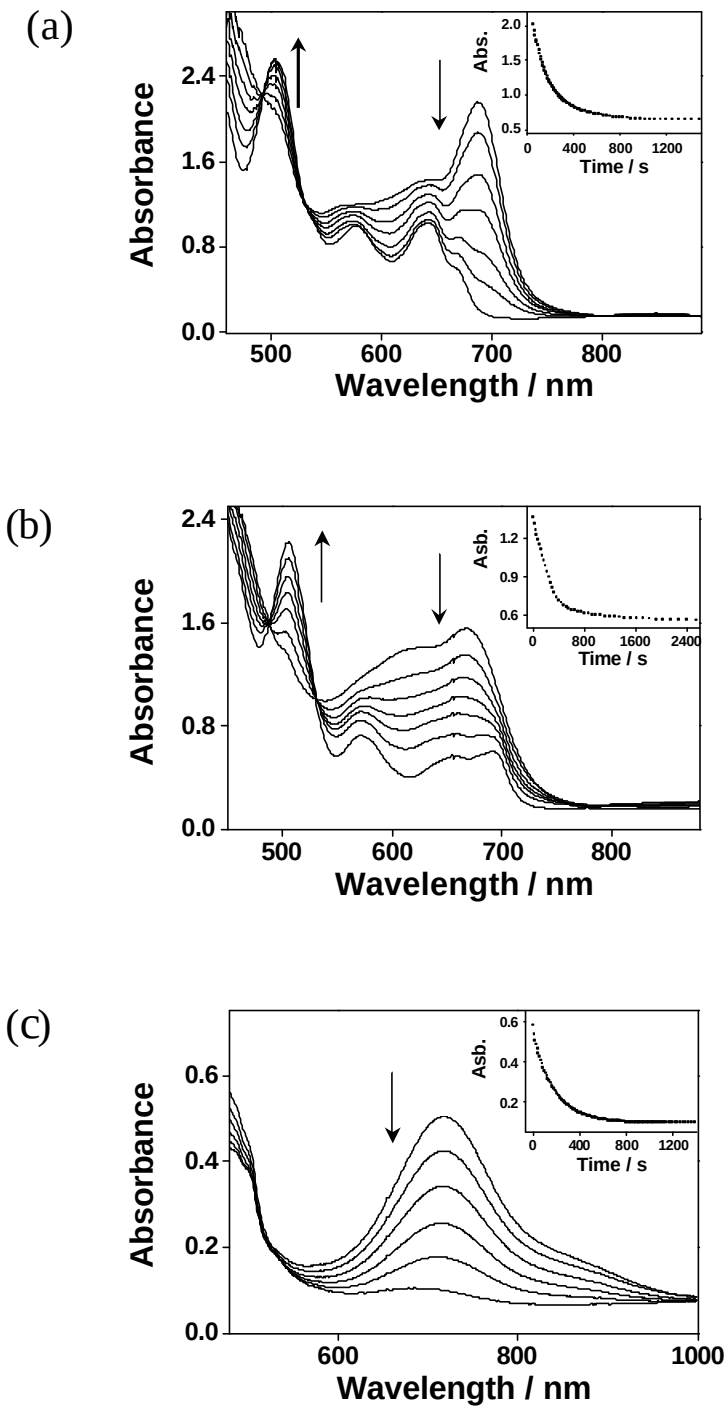
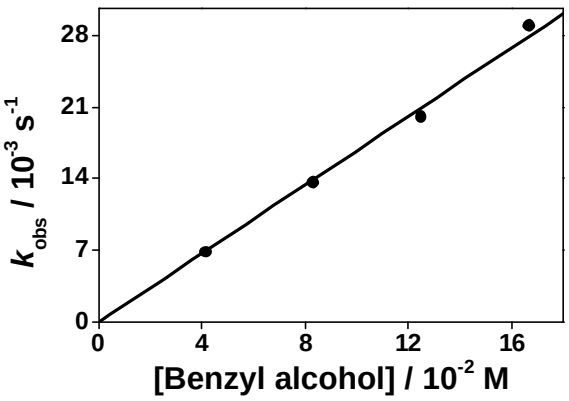
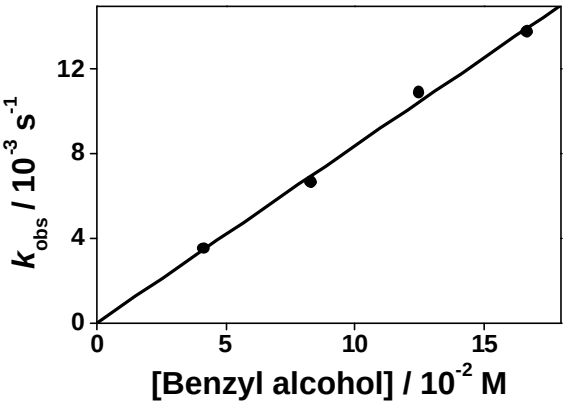


Figure S1. UV-vis spectral changes of **1a** – **1c** (2 mM) upon addition of 25 equiv benzyl alcohol (50 mM). Insets show time course of the absorption changes at 690 mm for **1a** (a), 665 mm for **1b** (b), and 720 mm for **1c** (c).

(a)



(b)



(c)

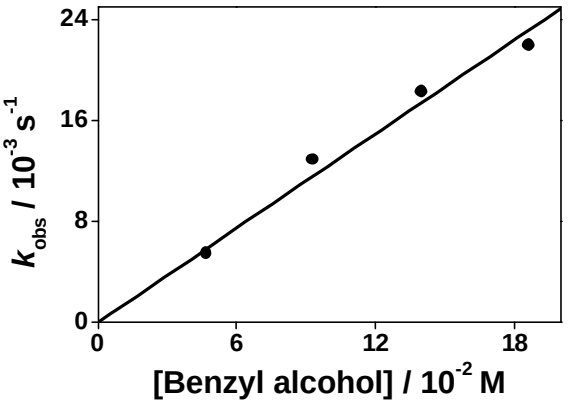
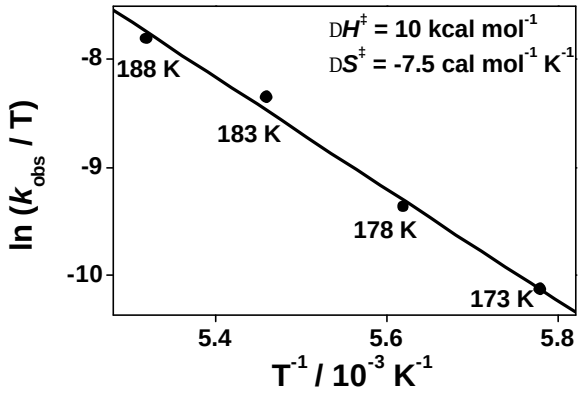
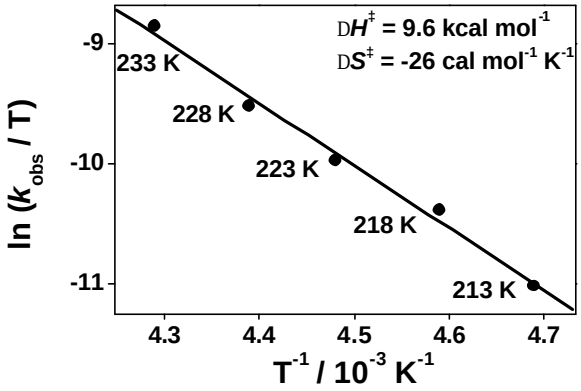


Figure S2. Plot of k_{obs} against benzyl alcohol concentration to determine second-order rate constants for the reactions of **1a** – **1c** with benzyl alcohol. Appropriate amounts of benzyl alcohol were added to the solutions of **1** (2 mM) at –100 °C for **1a** (a), –60 °C for **1b** (b), and –40 °C for **1c** (c).

(a)



(b)



(c)

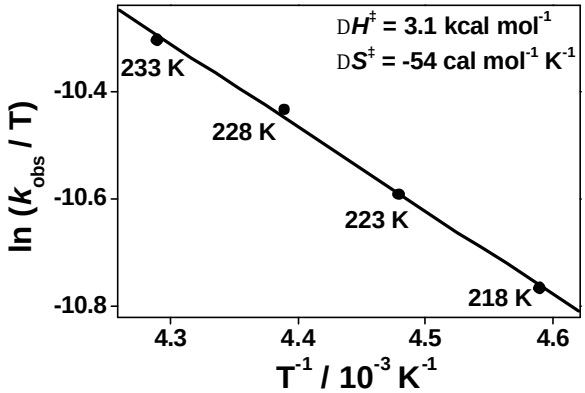
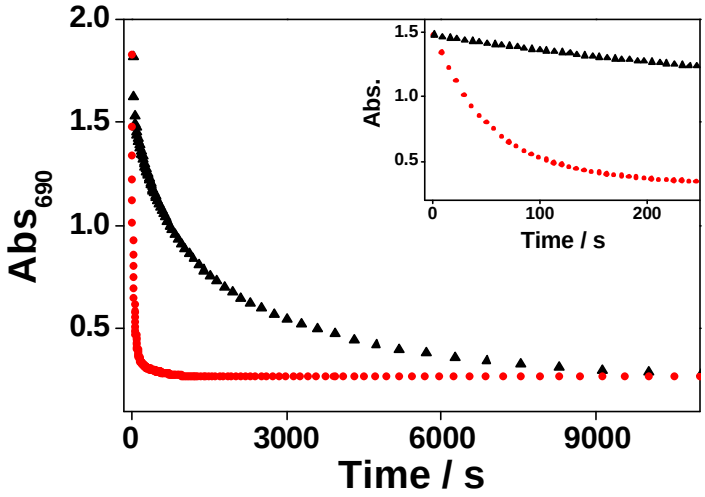


Figure S3. Determination of activation parameters by plotting first-order-rate constants of (a) **1a**, (b) **1b**, and (c) **1c** determined at different temperatures against 1/T. Reaction conditions: [**1**] = 2 mM and [benzyl alcohol] = 50 mM.

(a)



(b)

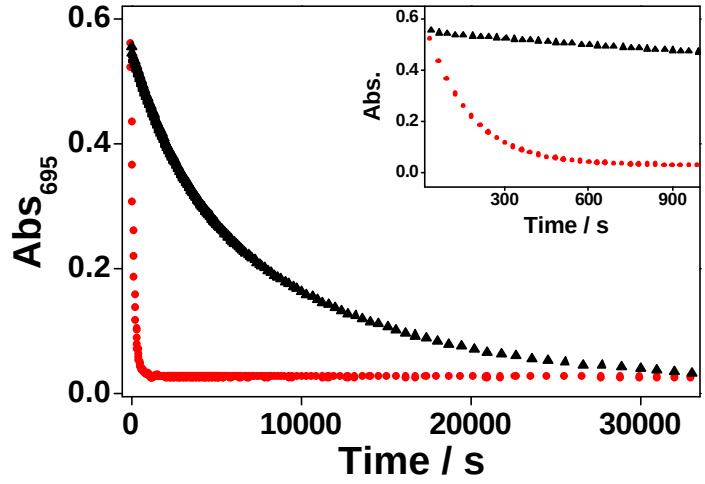


Figure S4. Time course of the absorption changes for the reactions of (a) **1a** with benzyl alcohol (?, red) and deuterated benzyl alcohol-d_7 (? , black) at –100 °C and (b) **1d** with benzyl alcohol (?, red) and deuterated benzyl alcohol-d_7 (? , black) at 0 °C. Reaction conditions: [**1**] = 2 mM and [benzyl alcohols] = 200 mM. See Table S1 of this Supporting information for the determined k_{obs} values and k_H/k_D ratios.

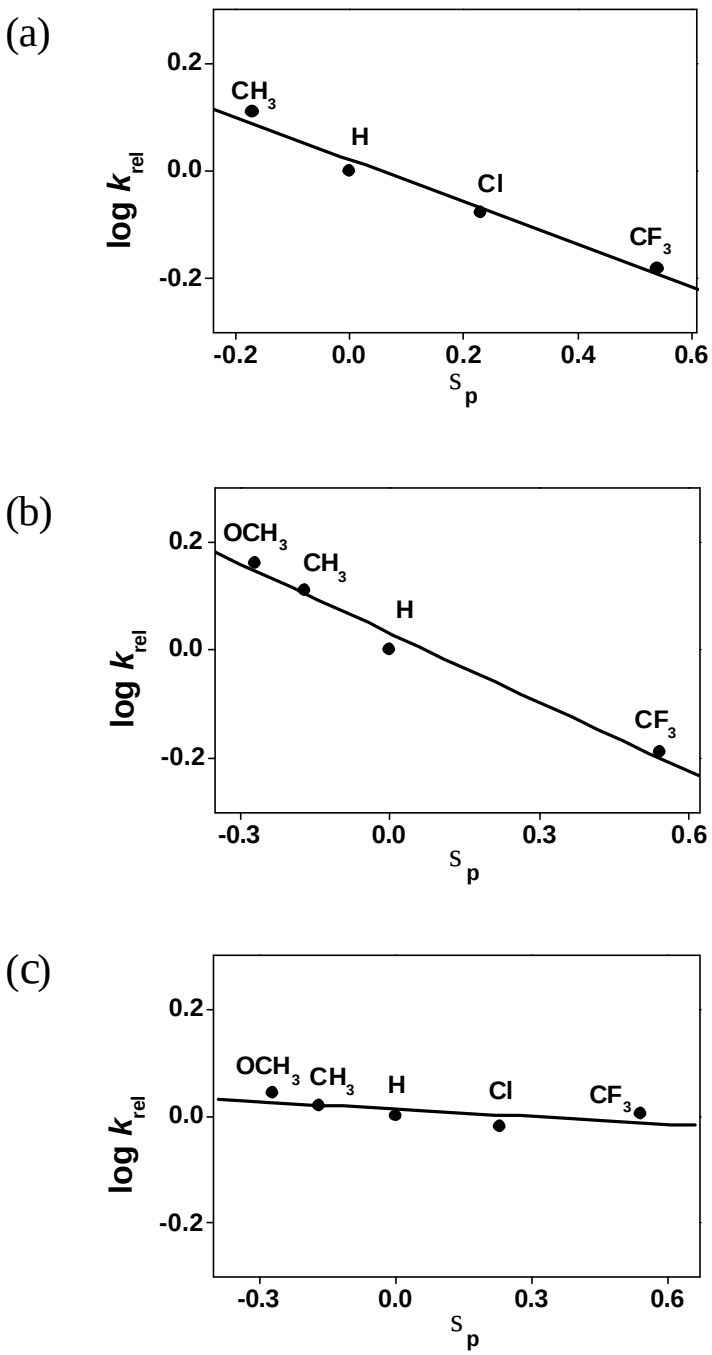


Figure S5. Plots of log k_{rel} against σ_p of *para*-X-benzyl alcohols to determine Hammett ρ values for the oxidation of *para*-substituted benzyl alcohols by (a) **1a**, (b) **1b**, and (c) **1c**. The k_{rel} values were calculated by dividing k_{obs} of *para*-X-benzyl alcohol by k_{obs} of benzyl alcohol. Reaction conditions: [**1**] = 2 mM and [*para*-X-benzyl alcohol] = 50 mM at –100 ^{o}C for **1a**, –60 ^{o}C for **1b**, and –40 ^{o}C for **1c**.

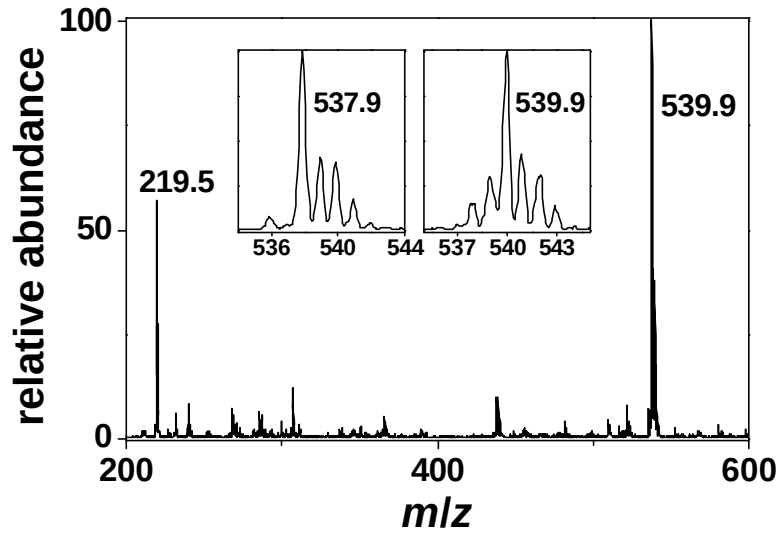


Figure S6. Electrospray ionization mass spectrum of $[(N4Py)Fe^{IV}=O]^{2+}$ prepared in the reaction of $Fe(N4Py)(ClO_4)_2$ (2 mM) and *m*-CPBA (2.4 mM) at 25 ^{o}C. The peak at *m*/*z* of 219.5 corresponds to $[Fe(IV)(O)(N4Py)]^{2+}$ (calculated *m*/*z* of 219.6). Insets show observed isotope distribution patterns for $[Fe(IV)(^{16}O)(N4Py)(ClO_4)]^{+}$ (calculated *m*/*z* of 538.1) (left panel) and $[Fe(IV)(^{18}O)(N4Py)(ClO_4)]^{+}$ (calculated *m*/*z* of 540.1) (right panel). The ^{18}O % in **1d**-^{18}O was calculated to be 80.