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Hydroxyl Transfer to Carbon Radicals by Mn(OH) vs Fe(OH) Corrole Complexes

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Abstract

The transfer of OH• from metal-hydroxo species to carbon radicals (R•) to give hydroxylated products (ROH) is a fundamental process in metal-mediated heme and nonheme C–H bond oxidations. This step, often referred to as the hydroxyl “rebound” step, is typically very fast, making direct study of this process challenging if not impossible. In this report, we describe the reactions of the synthetic models M(OH)(tppc) (M = Fe (**1**), Mn (**3**); tppc = 5,10,15-tris(2,4,6-

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Supporting Information

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Kinetics data, additional spectro-electrochemical data, DFT optimized structures, calculation of C–O bond energies from DFT calculations, computational tables with group spin densities, charges and absolute and relative energies of all structures, Cartesian coordinates of all optimized geometries (PDF)

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triphenyl)phenyl corrolato³⁻) with a series of triphenylmethyl carbon radical ($R^\bullet$) derivatives ((4-X-C₆H₄)₃C $^\bullet$; X = OMe, tBu, Ph, Cl, CN) to give the one-electron reduced M^{III}(tppc) complexes and ROH products. Rate constants for **3** for the different radicals ranged from 11.4(1) to 58.4(2) M⁻¹ s⁻¹, as compared to those for **1**, which fall between 0.74(2) and 357(4) M⁻¹ s⁻¹. Linear correlations for Hammett and Marcus plots for both Mn and Fe were observed, and the small magnitudes of the slopes for both correlations imply a concerted OH $^\bullet$ transfer reaction for both metals. Eyring analyses of reactions for **1** and **3** with (4-X-C₆H₄)₃C $^\bullet$ (X = tBu, CN) also give good linear correlations, and a comparison of the resulting activation parameters highlight the importance of entropy in these OH $^\bullet$ transfer reactions. Density functional theory calculations of the reaction profiles show a concerted process with one transition state for all radicals investigated and help to explain the electronic features of the OH rebound process.

Graphical Abstract

INTRODUCTION

Many biological catalysts that perform oxidation reactions utilize a heme ligand scaffold. One notable example is the enzyme Cytochrome P450 (CYP), which is a heme monooxygenase that can activate inert C–H bonds for hydroxylation with a high-valent iron oxo intermediate (Compound I) (Scheme 1).^{1–6} The rate-determining step in this process is the hydrogen atom transfer (HAT)⁷ from the C–H substrate to Compound I, forming an iron hydroxide species (protonated Compound II). Characterization of protonated Compound II was recently accomplished in the absence of substrate,⁸ but observation of this species during catalysis is essentially nonviable because of the rapid transfer of the OH group to the nascent carbon radical and the corresponding transient nature of the Fe(OH) intermediate. Computational studies on this OH “rebound” step are consistent with small reaction barriers to form alcohol products.^{9–12} However, direct experimental examination of the OH group transfer step has not been possible in an enzymatic setting. Our group has recently focused on examining synthetic model reactions of these rebound processes in order to obtain mechanistic information on this critical product-determining pathway.^{13,14} Our first success in this area came with the synthesis and structural characterization of

a protonated Compound II model complex, Fe(OH)(tppc) (**1**) (tppc = 5,10,15-tris(2,4,6-triphenyl)-phenylcorrolato³⁻), which was stabilized by the use of a sterically encumbered corrole ligand. Reaction of this complex with substituted triphenylmethyl carbon radicals (R•) led to OH transfer to give hydroxylated product (ROH) and the one-electron reduced Fe^{III}(tppc) (**2**). Kinetic analyses of these reactions pointed to a concerted transfer of OH• from the metal to R•, as opposed to a stepwise process such as electron-transfer followed by cation-transfer (ET/CT).¹⁵ Related studies in nonheme chemistry have been carried out recently by us and others for Fe, Cu, and Ni.^{16–23}

Synthetic, heme-based catalysts are also known to proceed through a mechanism similar to that shown in Scheme 1. In the synthetic systems, metals other than iron can be employed, and manganese porphyrins were employed successfully to carry out challenging C–H hydroxylation and halogenation reactions.^{24–30} There has been some effort to examine the mechanisms of these reactions, including a study with an Mn^V(O) porphyrin complex that examined the kinetics of rebound versus radical cage escape, which are divergent pathways following initial HAT. Because the putative Mn^{IV}(OH) intermediate could not be isolated, product distributions were employed to assess relative rates of cage escape and rebound reaction pathways.³⁰ Divergent pathways for the rebound step in CYP enzymes may also occur, such as hydroxylation versus alkane desaturation in olefin fatty acid decarboxylase (OleT) and related CYP152 enzymes.^{31–35} The structural and electronic characteristics of both the active sites and substrates that may favor hydroxylation versus desaturation pathways remain subjects of significant research.^{36,37}

In this work, we report a combined experimental and computational study on the reactivity of M(OH)(tppc) (M = Fe (**1**), Mn (**3**)) toward triphenylmethyl radical derivatives. These complexes are formally in the +4 oxidation state, although corroles are well-known to behave as noninnocent ligands, making metal oxidation state assignments ambiguous. However, the overall oxidation level for both the Mn and Fe complexes is the same as that of the protonated Compound II intermediate in heme enzymes. The synthesis and structure of complex **3** was reported previously,³⁸ and it is essentially isostructural with iron-containing **1**. Together with expanded, new studies on **1**, we provide a direct comparison of OH• transfer reactivity for Mn(OH) and Fe(OH) complexes. This comparative analysis has led to significant progress in our goal of understanding the structural, thermodynamic, and kinetic factors that contribute to OH• transfer, and related “rebound” processes, in heme enzymes and catalysts.

PRODUCT ANALYSIS

Examination of the reactivity of the Mn(OH) complex **3** with carbon radicals was initiated with triphenylmethyl radical, as shown in Scheme 2. The stable, crystalline compound Ph₂C=C₆H₄–CPh₃ is in equilibrium with ~2% of the radical form, Ph₃C•, in toluene.^{39,40} Addition of six equivalents of Ph₂C=C₆H₄–CPh₃ to **3** in toluene at 23 °C led to a color change from brown to green over a period of 2 h. Monitoring the reaction by UV–vis spectroscopy revealed isosbestic conversion of the spectrum for **3** to a spectrum that corresponded to that of the reduced Mn^{III}(tppc) (**4**) (λ_{max} = 417, 435, 450, 660 nm).³⁸ One-electron reduction of **3** is consistent with formal OH• transfer to the triphenylmethyl radical

and production of the alcohol, Ph_3COH . The UV-vis spectrum for $\text{Mn}^{\text{III}}(\text{Et}_2\text{O})(\text{tppc})$ was reported previously ($\lambda_{\text{max}} = 413, 446, 660 \text{ nm}$)⁴¹ and was therefore used as a standard to assess the yield of the Mn^{III} complex. Addition of excess Et_2O to the final reaction mixture resulted in small changes in the UV-vis spectrum consistent with formation of the $\text{Mn}^{\text{III}}(\text{Et}_2\text{O})$ adduct. Quantitation of the absorbance at 660 nm gave a yield of $88 \pm 1\%$ (average of 3 runs) for $\text{Mn}^{\text{III}}(\text{tppc})$ (Figure S3).

Formation of the expected alcohol, (Ph_3COH) , was measured by ^1H NMR spectroscopy. Reaction of **3** and 6 equiv of $\text{Ph}_2\text{C}=\text{C}_6\text{H}_4\text{-CPh}_3$ in toluene- d_8 led to a change in the ^1H NMR spectrum. The aromatic region is complicated by overlapping peaks from the starting Gomberg's dimer, but formation of a well-separated singlet at 2.28 ppm can be assigned to the hydroxyl group of Ph_3COH based on comparison with an independent sample. The yield of alcohol was quantified by integration of the peak at 2.28 ppm and comparison against an internal standard (Figure S1), giving a yield of $90 \pm 1\%$ (average of three runs). This yield is an excellent agreement with the yield of reduced Mn^{III} complex.

Addition of the *para-tert*-butyl-substituted radical derivative $(4\text{-tBu-C}_6\text{H}_4)_3\text{C}^\bullet$ to **3** led to similar reactivity. This radical is generated in situ from treatment of the corresponding triphenyl methyl halide with Cu^0 ,⁴² giving a stable radical in solution that is blocked through the *para* substituent from the dimerization seen for $\text{Ph}_2\text{C}=\text{C}_6\text{H}_4\text{-CPh}_3$. Addition of $(4\text{-tBu-C}_6\text{H}_4)_3\text{C}^\bullet$ to **3** in toluene- d_8 led to the expected color change from brown to green. The monitoring of this reaction by ^1H NMR spectroscopy revealed production of $(4\text{-tBu-C}_6\text{H}_4)_3\text{COH}$, which exhibits a unique singlet at 1.21 ppm corresponding to the *para-tert*-butyl substituents. Integration of this peak and comparison with an internal standard afforded a yield of $90 \pm 1\%$ (Figure S2), matching that found for the unsubstituted triphenylmethyl radical.

KINETICS

Substitution of the *para*-phenyl positions leads to radical derivatives that remain monomeric in solution, providing a convenient series of radicals for kinetics measurements as shown previously for $\text{Fe}(\text{OH})(\text{tppc})$ with $(4\text{-X-C}_6\text{H}_4)_3\text{C}^\bullet$ ($\text{X} = \text{OMe, tBu, Cl, Ph}$) derivatives.¹⁵ The kinetics of the reaction of **3** with the radical derivatives $(4\text{-X-C}_6\text{H}_4)_3\text{C}^\bullet$ ($\text{X} = \text{OMe, tBu, Cl, Ph, CN}$) in toluene was monitored by UV-vis spectroscopy. Addition of excess radical (pseudo-first-order) leads to the isosbestic conversion of **3** to **4**. These changes are shown in Figure 1 for the tBu derivative. The peak for the radical at 525 nm remains unchanged because it is in large excess, while the Soret band for **3** at 420 nm disappears at the same time that the Q-band for **4** grows in at 660 nm. A plot of the absorbance at 660 nm versus time is given in the inset of Figure 1b, showing single exponential behavior that was fit to give a pseudo-first-order rate constant $k_{\text{obs}} = 6.67 \times 10^{-3} \text{ s}^{-1}$. Varying the concentration of the tBu radical derivative led to a linear plot of k_{obs} versus $[(4\text{-tBu-C}_6\text{H}_4)_3\text{C}^\bullet]$, and the slope of the best-fit line gave a second-order rate constant, $k_2 = 30.5(1) \text{ M}^{-1} \text{ s}^{-1}$, which is similar in value to the $49(1) \text{ M}^{-1} \text{ s}^{-1}$ value recorded for this reaction with the analogous Fe complex **1**.

Reactions of **3** with the other $(4\text{-X-C}_6\text{H}_4)_3\text{C}^\bullet$ derivatives were carried out similarly to the tBu derivative, as shown in the scheme in Figure 2. Reaction kinetics were monitored by

UV-vis spectroscopy, and each radical exhibited good pseudo-first-order kinetics, leading to second order rate constants from 11.4(1) to 58.4(1) M⁻¹ s⁻¹ for the different radical derivatives (Figures S6–S11, Supporting Information). The rate constants are listed in Figure 2 together with the sum of the Hammett parameters ($3\sigma^+$) for each of the *para* substituents, with lower σ^+ values corresponding to the more electron-donating substituents.⁴³ The rate constants vary by a relatively modest factor of ~5, despite a relatively large change in Hammett values. A Hammett plot, i.e., $\log(k_2)$ versus $3\sigma^+$, for **3** is shown in Figure 3, together with the same plot for the analogous Fe(OH) complex **1**.¹⁵ Both compounds exhibit a linear correlation, but the line for **3** exhibits a significantly smaller Hammett slope ($\rho = -0.15$) than for **1** ($\rho = -0.62$). These trends indicate that the rates of OH• transfer from Mn(OH)(tppc) to the radical derivatives are much less sensitive to the electron-rich nature of the carbon radical center and imply that there is less charge-transfer in the transition state for the Mn(OH) as compared to the Fe(OH) complex.^{15,44} A crossover in relative rates of reaction for Mn versus Fe is also observed because of the difference in ρ values in Figure 3, with the crossover point close to $\sigma^+ = 0$. This change in reactivity leads to the Mn complex being ~15 times more reactive toward the electron-poor *para*-CN substrate than the Fe analogue.

SPECTROELECTROCHEMISTRY

The redox potential of **3** was measured by a combination of cyclic voltammetry (CV) and spectroelectrochemistry in order to gain further insight into the relative reactivity of **3** versus **1** for the different substrates. The CV of **3** is shown in Figure 4a together with that previously reported for **1**. The CV of **3** in PhCN exhibits two reversible waves at -0.07 and +0.60 V versus ferrocene/ferrocenium (Fc⁺/Fc) and a third, irreversible peak at -1.04 V. Comparison with the CV for **4** suggests that the reversible couple at $E_{1/2} = -0.07$ V is the formal [Mn^{IV}(OH)]⁰/[Mn^{III}(OH)]⁻ reduction potential, with the analogous couple at -0.11 V for **1** assigned previously to the formal [Fe^{IV}(OH)]⁰/[Fe^{III}(OH)]⁻ couple.¹⁵ These assignments were corroborated by spectroelectrochemical measurements. Controlled potential electrolysis (CPE) of **3** in PhCN at -0.30 V was accompanied by isosbestic changes in the UV-vis spectrum that indicated the one-electron reduction of **3** ($\lambda_{\text{max}} = 425$ nm) to [Mn^{III}(tppc)] ($\lambda_{\text{max}} = 450, 514, 675$ nm) (Figure 4c). The same solution was reoxidized by CPE at $E_{\text{appl}} = +0.10$ V, leading to the restoration of the spectrum for **3** (97% yield) (Figure S4). The CPE measurements on **1** in PhCN led to similar one-electron reversible behavior (Figure 4d) at applied potentials bracketing the -0.11 V reversible wave in Figure 4a and confirmed that this couple corresponds to the reversible one-electron reduction of the Fe(OH)(tppc) complex (Figure S5).¹⁵

The two values are similar and also indicate that electron transfer (ET) reactions with these radical substrates will be exergonic, with the exceptions of the *p*-Cl and presumably *p*-CN radicals. Thus, to determine the role that ET may play in these reactions, a Marcus plot was produced (Figure 4b) by plotting $(RT/F) \ln(k_2)$ vs the E_{ox} of the radicals used.⁴⁵ For reactions where the thermodynamic driving force ($-G_{\text{et}}^\circ$) is significantly less than the reorganization energy (λ), a Marcus plot with slope = -0.5 indicates that a simple electron transfer is involved in the rate limiting step of the reaction.⁴⁶ The Marcus plot for the reaction of the Mn complex **3** reveals a linear relationship ($R^2 = 0.957$) with a slope of

–0.05, which is close to the zero slope expected for a reaction that does not involve charge separation in the transition state.^{47,48} These data are consistent with a concerted group transfer of OH•, rather than a stepwise process involving reduction of the metallocorrole followed by the resulting *para*-substituted triphenylmethyl cation bonding with the OH[–] ligand (an electron-transfer/cation-transfer (ET/CT) mechanism).

EYRING ANALYSIS

We examined the temperature dependence of the reaction rates for the MnOH and FeOH complexes with the *para*-tBu substituted triphenylmethyl derivative (Figures S12, S13) between –5 and 35 °C for Mn and –5 and 23 °C for Fe. The resulting Eyring plots are linear and are shown in Figure 5a. The activation parameters $H^\ddagger$ and $S^\ddagger$ were obtained from the best-fit lines of the data for both the Mn and Fe complexes and are also given in Figure 5a. The results show that the activation enthalpies for MnOH and FeOH are similar (within ~2 kcal mol^{–1}), but the entropies differ by approximately a factor of 3, with the MnOH complex exhibiting the more negative $S^\ddagger$. For both complexes, the $-T S^\ddagger$ term remains smaller in magnitude than $H^\ddagger$ throughout the experimental temperature range, indicating that these reactions remain under enthalpy control. However, the significantly larger magnitude of the $S^\ddagger$ for the MnOH complex suggests a more ordered transition state (TS) for this complex. The weaker slopes in the Hammett and Marcus plots for MnOH compared to FeOH are also in good agreement with this relative ordering of activation entropies, since they suggest a more concerted reaction for MnOH and thus a more ordered TS.

These trends were even more pronounced when we examined the temperature dependence for the reactions with the *para*-CN substituted radical (Figures S14, S15). As shown in Figure 5b, the data remain linear for the relatively electron-poor *para*-CN derivative, although the temperature ranges were changed to +15 to +55 °C for Mn and +23 to +65 °C for Fe, because these reactions were relatively slow and higher temperatures were employed to obtain reasonable reaction times. Fitting of the data resulted in the activation parameters for the MnOH and FeOH complexes listed in Figure 5b. The enthalpy terms are slightly smaller than those obtained for the *para*-tBu derivative, but the most dramatic change occurs in the $S^\ddagger$ terms, which are significantly larger in magnitude than those obtained for the *para*-tBu derivative. The activation entropy for the FeOH complex is still within the expected range for a bimolecular reaction, but the activation entropy for the MnOH complex is significantly more negative. It is closer to that seen, for instance, for a Diels–Alder reaction, with a highly concerted and ordered transition state.⁴⁹ The $-T S^\ddagger$ term for the MnOH complex at 298 K is 12.0 kcal mol^{–1}, which is ~3-fold larger than the $H^\ddagger$ value for this complex, and indicates this reaction is entropy-controlled near room temperature. A graphical representation of entropic versus enthalpic control of these reactions is shown in Figure S16. The aforementioned result is consistent with a highly concerted reaction in which good orbital overlap is required between the carbon radical and the acceptor orbital on the MnOH unit in order for productive OH• transfer to occur. Such a mechanism is also in agreement with the electron-poor nature of the carbon radical in this case, which strongly inhibits the involvement of stepwise electron-transfer and instead favors a concerted radical rebound process. Entropy-controlled reactions are not common^{50–55} but do include examples of radical recombination reactions in which the radicals must enter a specific orientation

in a highly ordered TS.^{54,56} It is interesting to note the parallels between a radical–radical coupling reaction and the radical rebound reactions described here, where the MnOH unit is “coupling” with the incoming carbon radical in a specific, productive orientation to make the new C–O bond.

COMPUTATIONAL STUDIES

We started the computational modeling with calculations of the reactant species, i.e., [Fe^{IV}(OH)(tppc)] and [Mn^{IV}(OH)-(tppc)]. Our overall computational findings are similar to those found in a previous study examining these complexes in reactions with substituted phenol substrates.⁵⁷ Geometry optimizations were performed for the iron complex in the lowest energy singlet, triplet and quintet spin state structures and for the manganese system in the doublet, quartet and sextet spin states. The calculations on the iron-hydroxo complex give a triplet spin ground state (³**1**), with the singlet and quintet states higher-lying at

$E+ZPE = 13.3$ and $5.8 \text{ kcal mol}^{-1}$, respectively. The manganese-hydroxo complex gives a quartet spin ground state (⁴**3**). The optimized geometry for ⁴**3** is shown in Figure 6, together with selected data for ³**1**. The Fe–O distance in ³**1** is 1.86 Å, while the corresponding manganese complex ⁴**3** has an Mn–O distance of 1.87 Å. The other spin state structures (coordinates given in SI) give similar distances. These distances match the experimentally determined single crystal X-ray diffraction results, with reported values of Fe–O = 1.857(3) Å and Mn–O = 1.881(2) Å.^{15,38} The triplet spin structure (³**1**) gives a calculated $\nu(\text{Fe–O}) = 548 \text{ cm}^{-1}$, which compares well with the experimental value of 576 cm^{-1} from resonance Raman spectroscopy. The computational methods give good agreement with the experimentally observed structural and vibrational features, helping to validate the overall computational results.

Group spin densities of both ³**1** and ⁴**3** give a dominant spin contribution on the metal, although a significant amount of unpaired spin density is also seen on the corrole ligand: $\rho_{\text{tppc}} = -0.7$ for Fe and -0.6 for Mn. These spin densities implicate an electronic configuration with an unpaired down-spin electron on the corrole coupled to three/four up-spin electrons in metal-type orbitals for iron/manganese. The electronic configurations indicated by the calculations are $\delta_{x^2-y^2}^1 \pi_{xz}^*{}^1 \pi_{yz}^*{}^1 \sigma_{z^2}^*{}^1 a_{2u}^1$ for ⁴**3** and $\delta_{x^2-y^2}^2 \pi_{xz}^*{}^1 \pi_{yz}^*{}^1 \sigma_{z^2}^*{}^1 a_{2u}^1$ for ³**1**. These computed configurations can be described as ⁴[Mn^{III}(OH)(tppc⁺*)] and ³[Fe^{III}(OH)(tppc⁺*)]. This type of electronic structure is different from that suggested by DFT calculations for the analogous high-valent species in porphyrins or heme enzymes, which usually converge to Fe^{IV}(OH)-(porph) structures with no spin on the macrocycle.^{58,59} However, calculations on the analogous metallocorroles commonly show spin density on the macrocycle, suggesting π -radical-cation character. Attempts were made to interchange molecular orbitals and obtain an alternative ³**1**' structure with configuration $\delta_{x^2-y^2}^2 \pi_{xz}^*{}^1 \pi_{yz}^*{}^1 \sigma_{z^2}^*{}^0 a_{2u}^2$. However, this state relaxed back to the [Fe^{III}(OH)(tppc⁺*)] state during the SCF convergence.

The mechanism of reaction between ^{1,3,5}**1** or ^{2,4,6}**3** and the triphenylmethyl substituted radical substrates (4-X-C₆H₄)₃C• (SubX, where X = H, *t*Bu, OMe, Cl, Ph, and CN) was examined by DFT. The lowest energy reaction barriers, however, are for the overall quartet spin transition state for iron and quintet spin transition state for manganese and start from

the interaction of $^3\mathbf{1}$ with $^2\text{SubX}$ or $^4\mathbf{3}$ with $^2\text{SubX}$. Note that the electronic configurations are retained in the reactant complexes with substrate and metal-hydroxo complex in close proximity, indicating that no long-range electron transfer takes place. No spin-state crossing was observed for any of the calculated reactions for $^3\mathbf{1}$ or $^4\mathbf{3}$ (calculations for the other spin states are included in the Supporting Information). The reactions start from a reactant complex composed of $\text{M}(\text{OH})(\text{ttpc})$ and SubX in close proximity (structure $\text{Re}_{\text{M,X}}$) and are followed by a single transition state ($\text{TS}_{\text{reb,M,X}}$) that separates them from alcohol product complexes ($\text{P}_{\text{M,X}}$). A concerted, one-step reaction mechanism is found for all pathways, and no long-range electron transfer is predicted.

Representative transition states $^5\text{TS}_{\text{reb,Mn,X}}$ and $^4\text{TS}_{\text{reb,Fe,X}}$ are given in Figure 7 and Figure S17, respectively, with the imaginary mode highlighted as a vector diagram. The activation enthalpies calculated at $E^\ddagger + \text{ZPE}$ level of theory (UB3LYP/BS2//UB3LYP/BS1 energies with solvent and zero-point corrections included) are given in Table 1. The $E^\ddagger + \text{ZPE}$ value for $^5\text{TS}_{\text{reb,Mn,tBu}}$ is calculated to be higher in energy by 5.9 kcal mol $^{-1}$ versus that of $^5\text{TS}_{\text{reb,Mn,CN}}$, which is close to the difference in the activation enthalpy terms ($H^\ddagger = 7.0$ kcal mol $^{-1}$) obtained from the Eyring plots for the same substrates (Figure 5). A similar trend is seen for $^5\text{TS}_{\text{reb,Fe,tBu}}$ versus $^5\text{TS}_{\text{reb,Fe,CN}}$ in which the difference in the $E^\ddagger + \text{ZPE}$ values for the two substrates give a $H^\ddagger = 5.0$ kcal mol $^{-1}$, compared to the experimental $H^\ddagger = 4.3$ kcal mol $^{-1}$. Although the calculations overestimate the absolute values for $H^\ddagger$ by 3–4 kcal mol $^{-1}$, the trends clearly indicate that the enthalpic contribution to the barrier is higher for the tBu substrate than that for the CN substrate. Previous validation studies of experimental rate constants against our computational methods showed that the correct trend in reactivity and chemoselectivity was obtained despite a systematic error.^{60,61} Given the second order rate constants for the *p*-tBu substrate reaction with $\mathbf{1}$ and $\mathbf{3}$ are faster than those for the *p*-CN (Figure 2), these calculated $E^\ddagger + \text{ZPE}$ values imply that the $S^\ddagger$ for the hydroxyl radical transfer reaction with the *p*-CN substrate must be greater in magnitude than that for the *p*-tBu substrate. This finding further supports our experimental observations of larger $S^\ddagger$ for the *p*-CN substrate (Figure 5). However, the calculated $S^\ddagger$ and their associated $G^\ddagger$ values do not match those found experimentally (Tables S11, S13). These deviations in calculated versus experimentally observed $S^\ddagger$ values may be due to the limitations of using ideal gas assumptions to estimate the translational, rotational, and vibrational entropies. In particular, the computational entropies do not take into consideration environmental effects such as solvent participation and the involvement of a solvent cage around the cluster. The large difference in dipole moment in the various transition states could be responsible for differences in local environment and the solvent cage. Recent studies on enzymatic reaction mechanisms have shown that induced dipole moment interactions in the protein can dramatically affect barrier heights and rate constants and even guide a selectivity preference.^{62–64} As such, differences in dipole moment will affect the free energies of activation through solvent reorganization and stabilization of the transition state structures.

The Fe–O bond length (Table 1) for the different SubX reactions is elongated by a similar amount ($(\text{Fe–O}) = 0.09$ Å for $^4\text{TS}_{\text{reb,Fe,tBu}}$ and $(\text{Fe–O}) = 0.17$ Å for $^4\text{TS}_{\text{reb,Fe,CN}}$, which were the smallest and largest changes, respectively). The C–O distances in the

transition states range from 2.230 Å for ${}^4\text{TS}_{\text{reb,Fe,CN}}$ to 2.550 Å for ${}^4\text{TS}_{\text{reb,Fe,tBu}}$, which are long for a C–O bond and are consistent with an early TS. The C–O bond in the TS for the *p*-CN derivative is significantly shorter than those for the other derivatives, which indicates it has a tighter transition state than the other substrates. To put these values in perspective, the C–O distances are longer than those reported for the rebound step in cycloheptatriene hydroxylation by an iron(IV)(oxo)(pentafluorophenyl-porphyrin) complex, which found doublet and quartet spin transition states with C–O distances of 1.831 and 2.053 Å.⁶⁵ Calculations for the small aliphatic substrates methane and propene and iron(IV)(oxo)(porphine) lead to much longer C–O distances of 2.556 and 2.427 Å, respectively, in the rebound transition states.¹² Long C–O distances were also found for the rebound transition states during methane hydroxylation by μ -nitrido-bridged diiron(IV)-oxo porphyrinoid complexes.⁶⁶ A large variation in geometric structure of rebound transition states is seen in the former examples, although there appears to be some dependence on the size of the substrate. The data in Table 1 show no clear trends in geometric features of the transition states for hydroxyl transfer for the different substrates.

In contrast to the structural parameters, a trend is seen in the imaginary frequencies for the transition states in Table 1, ranging for iron from $i117\text{ cm}^{-1}$ for ${}^4\text{TS}_{\text{reb,Fe,OMe}}$ to $i465\text{ cm}^{-1}$ for ${}^4\text{TS}_{\text{reb,Fe,CN}}$, and for manganese from $i69$ to $i396\text{ cm}^{-1}$. These imaginary frequencies identify a maximum along the potential energy surface for the transition state, and their magnitudes reflect the breadth of the potential energy curve around the transition state. Thus, shallow barriers have low imaginary frequencies, whereas steep barriers tend to have large imaginary frequencies. This trend means that the curvature around the barrier gets steeper as the electron-withdrawing character of the substituent increases. Stronger electron-donating substituents have broader potential energy surfaces, as seen from the smaller imaginary frequencies.

To understand the observed reactivity trends and distinguish between radical and charge-transfer pathways, a valence bond diagram was generated for the Fe complex (Scheme 3). This type of diagram give insight into the possible electron transfers and orbital reorganizations that happen during the transition state and have, for instance, been used previously to explain reactivity trends of hydrogen atom abstractions and regioselectivities.^{66,67} The differences in orbital-breaking and orbital-formation processes associated with a concerted, radical-type OH transfer versus long-range electron transfer were examined. The valence configuration of reactants and products are shown, helping to illustrate the electron transfer processes as well as the molecular orbital changes that occur during the reaction. The calculated electronic ground state for **1** has orbital occupation $\delta_{x2-y2}^2 \pi_{xz}^*{}^1 \pi_{yz}^*{}^1 \sigma_{z2}^*{}^1 a_{2u}^1$, and these valence electrons are identified with a dot in Scheme 3. A molecular orbital is depicted as a line between two dots. The δ_{x2-y2} , π_{xz}^* , and σ_{z2}^* orbitals are occupied with four electrons, have dominant contributions on the iron, and can be considered as atomic orbitals. The $\pi_{yz} \pi_{yz}^*$ pair of orbitals forms a two-center-three-electron bond along the Fe–O unit, while there is an unpaired electron on the substrate (in ϕ_{Sub}) and one on the corrole ligand (in a_{2u}).

If we consider a concerted reaction process for the OH• transfer (downward pathway in Scheme 3), then the OH• transfer to the SubX radical will form a C–O bond (σ_{CO})

by pairing up the radical on the substrate (from ϕ_{Sub}) and one electron on the hydroxo group. The latter comes from the $\pi_{yz} \pi^*_{yz}$ two-center-three-electron bond that is split back into atomic orbitals: one electron forms the σ_{CO} bond, one electron remains as $3d_{yz}$ on iron, and the third electron is promoted into the a_{2u} orbital. In valence bond theory, the product electronic configuration in the geometry of the reactants determines the height of the transition state, and therefore, for a concerted OH• transfer, the barrier should correlate with the energy to form the σ_{CO} bond ($E_{\sigma(\text{CO})}$), the energy to split the two-center-three-electron π_{yz}/π^*_{yz} orbitals back into atomic orbitals ($E_{\pi/\pi^*_{yz}}$) and the electron affinity of the corrole (EA_{cor}).

By contrast, an initial outer-sphere electron-transfer (ET) will ionize the substrate and fill the corrole a_{2u} orbital with a second electron. A reaction starting with outer-sphere ET should have a transition state energy that correlates with the ionization energy of the substrate (IE_{SubX}) and the reduction potential or electron affinity of the metal corrole complex (EA_{cor}). The IE_{SubX} and $E_{\sigma(\text{CO})}$ values for all substrates SubX were calculated and are plotted in Figure 8 versus $3\sigma^+$ Hammett parameter. Both trends seen for IE_{SubX} and $E_{\sigma(\text{CO})}$ are consistent with the second order rate constants observed experimentally. The decreasing $E_{\text{C-O}}$ with $3\sigma^+$ should lower the overall driving force of the reaction, which is consistent with the observed slower reaction rates for the more electron-withdrawing σ^+ values. However, the changes in the calculated $E_{\text{C-O}}$ bond energies is relatively small, ranging from 26.4 kcal mol⁻¹ for the (4-OMe-C₆H₄)₃C-OH to 18.6 kcal mol⁻¹ for the (4-CN-C₆H₄)₃C-OH substrates. The differences in IE values are larger, from 105 to 132 kcal mol⁻¹ over the substrate range. This trend in substrate IE is also consistent with the degree of charge transfer calculated for the transition states of these hydroxyl transfer reactions (Table 1, Q_{CT}), which decreases as Hammett parameter increases, from 0.67 Coulombs for the OMe reagent to 0.23 Coulombs for the CN reagent. These trends, taken together with the VB analysis, support the notion that these reactions occur through a concerted •OH transfer with varying degrees of charge-transfer, and imply, more broadly, that the reaction pathway is influenced by the electronic characteristics of the substrate being modified.

CONCLUSIONS

This work provides the first study of reactions involving OH• transfer from a well-defined, Mn(OH) complex to a carbon radical. These reactions are analogous to the “rebound” step in C-H bond hydroxylation carried out by high-valent metal-oxo porphyrins, including the hydroxylation mediated by heme monooxygenases such as Cytochrome P450. The reactivity of the closely related Fe(OH) complex, which was previously described in preliminary form,¹⁵ was expanded here and provided a direct comparison between Mn(OH) and Fe(OH) species. The kinetic data obtained from a series of substituted triphenylmethyl radical derivatives show that both Mn(OH) and Fe(OH) complexes give linear Hammett and Marcus plot correlations that suggest the electronic nature of the tertiary carbon radicals plays a relatively minor role in the overall reaction rates, and point to a concerted, as opposed to stepwise (ET/CT), mechanism for OH• transfer. However, the Fe(OH) complex does have a significantly larger Hammett ρ value than the Mn(OH) complex, causing the Hammett plots for the two species to intersect near $\sigma^+ \sim 0$. Similar trends in Hammett slopes were seen for **1** and **3** in their reactions with *para*-substituted phenol HAT substrates.⁵⁷ These data hint at

a greater selectivity for Fe(OH) versus Mn(OH) rebound toward electronically differentiated substrates, which may be advantageous for controlling product distribution in the native, iron-containing biological systems. A study on porphyrin Compound-I analogs provides support for this idea in which differences in free energies of activation, resulting from the entropies of activation, for epoxidation versus hydroxylation help determine product selectivity.⁵¹

Temperature-dependent kinetic studies showed that for the tBu-substituted triphenylmethyl radical, both Fe(OH) and Mn(OH) reactions are under enthalpy control, although the Mn complex exhibits a larger entropic factor. In comparison, the entropy terms for the electron-poor CN-substituted derivative are much larger, and in the case of Mn(OH), leads to the more rare situation of an entropy-controlled reaction at 298 K ($-T \Delta S^\ddagger \gg \Delta H^\ddagger$). This finding is consistent with a concerted reaction involving a highly ordered transition state that requires good orbital overlap between reaction partners. These mechanistic features can be found in orbitally directed Diels–Alder reactions or in radical–radical coupling reactions, both of which provide other examples of entropy-controlled processes.^{49,54,56}

The DFT calculations of the reaction trajectories for these model rebound reactions provide good support for the experimentally derived mechanistic scenario: a concerted process with a single transition state is computed for both Mn(OH) and Fe(OH) with all of the substrate derivatives. The electronic structures of the transition states show relatively small amounts of charge transfer, also consistent with the experimental Hammett and Marcus plots. The overall energetics of the different calculated reaction barriers do not match the experimental kinetics, but this discrepancy in fact provides further support for the importance of the entropic factors in these reactions. Whether the major entropic contributions come from an ordering of the reaction partners in the T.S. or from environmental effects (e.g., solvent) remains an open question but suggests that entropy may play a key role in determining the ultimate outcome of the rebound step in heme enzymes.

EXPERIMENTAL SECTION

Materials.

All chemicals were purchased from commercial sources and used without further purification unless otherwise stated. Reactions involving inert atmosphere were performed under Ar using standard Schlenk techniques or in an N₂-filled drybox. Toluene and acetonitrile were purified via a Pure-Solv solvent purification system from Innovative Technologies, Inc. Benzene and benzonitrile were obtained from commercial sources. Deuterated solvents for NMR were purchased from Cambridge Isotope Laboratories, Inc. (Tewksbury, MA). The (4-*t*Bu-C₆H₄)₃CBr,⁶⁸ (4-Ph-C₆H₄)₃CBr,^{69,70} (4-Cl-C₆H₄)₃CBr,¹⁵ and (4-CN-C₆H₄)₃CBr⁷¹ were synthesized following previously reported procedures. (4-OMe-C₆H₄)₃CCl was obtained from Alfa-Aesar and used as received. All substituted triphenylmethyl radicals were generated by reduction of their corresponding halide with excess copper powder, as previously reported.^{15,16} The unsubstituted triphenylmethyl radical source, Gomberg's dimer (Ph₂C=C₆H₄-CPh₃), was synthesized following literature procedures.^{39,40} Fe(OH)(tppc), Fe^{III}(tppc), Mn(OH)-(tppc), and Mn^{III}(tppc) were

synthesized and purified as previously reported.^{15,38,41} The salt (Bu₄N)PF₆ was purchased from Sigma-Aldrich, and recrystallized from ethanol twice before use.

Instrumentation.

Kinetics and other UV–vis spectroscopic measurements were performed on a Hewlett-Packard Agilent 8453 diode-array spectrophotometer with a 5 mL quartz cuvette (path length = 1 cm). For reactions with total reaction time of <10 s, stopped-flow experiments were carried out using a HiTech SHU-61SX2 (TgK scientific Ltd.) stopped-flow spectrophotometer with a Xenon light source and Kinetic Studio software. For all UV–vis spectroscopy measurements acquired above or below 23 °C, and for spectro-electrochemical analysis, data collections were performed on a Varian Cary 60 Bio spectrophotometer. ¹H NMR spectra were recorded on a Bruker Avance 400 MHz NMR spectrometer at 298 K, and referenced against residual solvent proton signals. Cyclic voltammetry was performed on an EG&G Princeton Applied Research potentiostat/galvanostat model 263A with a three-electrode system consisting of a glassy carbon working electrode, a Ag/AgNO₃ nonaqueous reference electrode (0.01 M AgNO₃ with 0.1 M Bu₄NPF₆ in CH₃CN), and a platinum wire counter electrode. Spectro-electrochemical cyclic voltammograms or controlled potential electrolysis measurements were collected on a 6-channel Ivium-n-Stat with a gold honeycomb card (Pine Research part AB01STC1 AU) working and counter electrode and a Ag/AgNO₃ nonaqueous reference electrode (0.01 M AgNO₃ with 0.1 M Bu₄NPF₆ in CH₃CN), with samples placed in a 1.7 mm path length cuvette under an inert Ar atmosphere. Potentials were referenced using an external ferrocene standard. Scans were run at 23 °C using Bu₄NPF₆ (0.1 M) as the supporting electrolyte.

Reaction of Mn(OH)(tppc) (**3**) with Triphenylmethyl Radical. Product Analysis.

To a solution of **3** in benzene-*d*₆ (1 mM, 1 mL) were added Ph₂C=C₆H₄-CPh₃ (1.5 mg, 6.2 μmol, 6 equiv) and the trimethylphenylsilane (TMPS) (1.0 mM) as an internal standard. The solution was stirred for 2 h and loaded into an NMR tube. A ¹H NMR spectrum was collected, and a peak at 2.28 ppm assigned to the OH proton of Ph₃COH was integrated and compared with the peak from the TMPS standard. An average yield for Ph₃COH of 90 ± 1% was found (average of 3 runs). This reaction was repeated in nondeuterated solvent by the addition of Ph₂C=C₆H₄-CPh₃ (0.15 mM, 6 equiv) to a solution of Mn(OH)-(tppc) (25 μM, λ_{max} = 420 nm) in toluene. The inorganic product, Mn^{III}(tppc) λ_{max} = 445, 660 nm) was quantified by the extinction coefficient (2.7 × 10³ M⁻¹ cm⁻¹) at 660 nm. An average yield of Mn^{III}(tppc) of 88 ± 1% was found (average of 3 runs).

Reaction of Mn(OH)(tppc) with 4-*t*Bu-C₆H₄)₃C•. Product Analysis.

To a solution of (4-*t*Bu-Ph)₃CBr (6.4 mM, 2 mL) in toluene-*d*₈ was added excess Cu powder (~200 mg), and the reaction was stirred in the dark for 4 h at 23 °C. A color change to yellow was observed, indicating formation of (4-*t*Bu-C₆H₄)₃C•. The solution was filtered through Celite to remove solid Cu, and an aliquot was obtained to determine the concentration by UV–vis spectroscopy (5.3 mM, 83% yield). The freshly prepared radical solution (500 μL) was then added to **3** in toluene-*d*₈ (500 μL) to give a final reaction mixture of **3** (2.35 mM) and (4-*t*Bu-C₆H₄)₃C• (2.65 mM, 1.1 equiv). The internal standard

trimethylphenylsilane (TMPS) (8 mM) was added, and the solution was stirred for 24 h and then loaded into an NMR tube. A ^1H NMR spectrum was collected, and a singlet at 1.21 ppm was observed corresponding to the *t*Bu groups of the alcohol $(4\text{-}t\text{Bu-C}_6\text{H}_4)_3\text{COH}$. This peak was integrated and compared to the TMPS standard, giving a yield of $90 \pm 1\%$ (average yield of 3 runs).

Kinetics.

In an N_2 -filled glovebox under low light conditions, the radical derivatives $(4\text{-X-C}_6\text{H}_4)_3\text{C}^\bullet$ ($\text{X} = \text{OMe}, t\text{Bu}, \text{Ph}, \text{Cl}, \text{or CN}$) were freshly prepared in toluene. Radical concentrations were determined by UV-vis spectroscopy. Varying amounts of radical stock solution (50–1000 μL) were immediately added to a solution of the metal complex in toluene (18 to 40 μM , 1.00 to 1.95 mL) to start the reaction. The spectral changes showed isosbestic conversion of $\text{Mn}(\text{OH})(\text{tppc})$ ($\lambda_{\text{max}} = 420 \text{ nm}$) to $\text{Mn}^{\text{III}}(\text{tppc})$ ($\lambda_{\text{max}} = 445, 660 \text{ nm}$) for the manganese system and $\text{Fe}(\text{OH})(\text{tppc})$ ($\lambda_{\text{max}} = 405 \text{ nm}$) to $\text{Fe}^{\text{III}}(\text{tppc})$ ($\lambda_{\text{max}} = 420, 575, 765 \text{ nm}$) for the Fe system. The pseudo-first-order rate constants, k_{obs} , for these reactions were obtained from plots of absorbance versus time at the wavelengths 420 or 660 nm for the Mn complex, 465 nm for the Fe complex with the *p*-CN radical derivative, and 575 nm for the Fe complex with the *p*-*t*Bu radical derivative. These plots were fit to the equation $\text{Abs}_t = \text{Abs}_f + (\text{Abs}_0 - \text{Abs}_f) \exp(-k_{\text{obs}}t)$, where Abs_t is the absorbance at time t , k_{obs} is the pseudo-first-order rate constant, and Abs_0 and Abs_f are the initial and final absorbance values, respectively. Second order rate constants (k_2) were obtained from the slope of the best-fit line from a plot of k_{obs} versus radical concentration.

Computational Modeling.

Calculations were done using density functional theory methods as implemented in Gaussian-09,⁷² and methods and procedures were followed as reported and tested previously on analogous systems.^{57,61} Calculations were carried out on the complete metallocorrole structures without any truncation of the peripheral ligand substituents. Reaction profiles were calculated for the reaction of **1** or **3** with $(4\text{-X-C}_6\text{H}_4)_3\text{C}^\bullet$ ($\text{X} = \text{H}, t\text{Bu}, \text{OMe}, \text{Cl}, \text{Ph}, \text{CN}$). The computed structures ranged in size from 191 atoms for $\text{X} = \text{H/Cl}$ to 221 atoms for $\text{X} = \text{Ph}$.

The unrestricted B3LYP hybrid density functional theory method was used for geometry optimizations, constraint geometry scans, and frequency calculations.^{73,74} Due to the size of the chemical system, all structures were optimized without constraints with an LanL2DZ basis set on iron/manganese (with core potential) and 6-31G on the rest of the atoms (H, C, N, O, Cl): basis set BS1.^{75,76} Single points using a triple- ζ quality basis set on iron/manganese (with core potential), i.e., LACV3P+, and 6-311+G* on the rest of the atoms were done to correct the energies: basis set BS2. Geometries were optimized with solvent corrections included through the conductor-like polarized continuum model (CPCM) with a dielectric constant mimicking toluene.⁷⁷ All free energy calculations were done at 298 K. Test calculations with dispersion-corrected DFT reproduced the trends well (Supporting Information); hence dispersion is not critical here.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

(a) Overlay of UV-vis spectra for **3** (red, dashed), **4** (blue, dotted), and (4-*t*Bu-C₆H₄)₃C• (green, solid). (b) UV-vis spectra for the reaction of **3** (18 μM) with (4-*t*Bu-C₆H₄)₃C• (20 equiv) in toluene-*d*₈ from 0 (red) to 400 (blue) s at 50 s intervals (gray). Inset: plot of absorbance at 660 nm versus time (open green circles) showing the growth of the Mn^{III} complex, together with the best fit line.

Figure 2. Reaction of $M(\text{OH})(\text{tppc})$ ($M = \text{Fe}, \text{Mn}$) with *para*-X-substituted triphenylmethyl radicals ($X = \text{OMe}, t\text{Bu}, \text{Ph}, \text{Cl}, \text{CN}$). Hammett parameters ($3\sigma^+$) and redox potentials (E_{ox} versus Fc/Fc^+ , MeCN) for the different radicals,^{43,45} and the corresponding second order rate constants for reactions with the $\text{Fe}(\text{OH})$ and $\text{Mn}(\text{OH})$ complexes are given below each radical structure.

Figure 3. Hammett plot for the reactions of Mn(OH)(tppc) (blue triangles) and Fe(OH)(tppc) (red diamonds) with (4-X-C₆H₄)₃C• (X = OMe, tBu, Ph, Cl, CN).

Figure 4.

(A) Cyclic voltammograms of Fe(OH)(tppc) (red) and Mn(OH)(tppc) (blue) in benzonitrile at 23 °C, with 0.1 M Bu₄NPF₆ supporting electrolyte. Electrochemical data for **1** reproduced from ref 15. (B) Marcus plots for the reactions of **3** (blue triangles) and **1** (red diamonds) with (4-X-C₆H₄)₃C• (X = OMe, tBu, Ph, Cl, CN). C–D) UV–vis spectral changes for **1** and **3**, respectively, at $E_{appl} = -0.30$ V, in benzonitrile at 23 °C.

Figure 5.

Eyring plots for the reactions of Mn(OH)(tppc) (blue triangles) and Fe(OH)(tppc) (red squares) with (A) (4-tBu-C₆H₄)₃C• and (B) (4-CN-C₆H₄)₃C•.

Figure 6.

UB3LYP/BS1 optimized geometry for **43** as obtained in Gaussian-09, together with relevant parameters for **31**. Bond lengths (Fe–O, Mn–O) are in angstroms and spin densities (ρ) in atomic units. C atoms in brown or orange, N atoms in blue, Fe atom in purple, O atom in red, H atoms in gray. Values for **31** are given in parentheses.

Figure 7. UB3LYP/BS1 optimized geometry (displayed as a vector diagram) of ${}^4\text{TS}_{\text{reb,Mn,Cl}}$ as obtained in Gaussian ian-09.

Figure 8. Ionization energy of the substrate (IE_{subX}) and energy of the sigma C–O bond formed by hydroxyl transfer ($E_{\sigma(\text{CO})}$) to $(4\text{-X-C}_6\text{H}_4)_3\text{C}^\bullet$ ($\text{X} = \text{H, OMe, tBu, Ph, Cl, CN}$).

Scheme 1.
Hydroxyl Transfer Performed by CYP Enzymes

Scheme 2. Reaction of $\text{Mn}(\text{OH})(\text{tppc})$ with $(4\text{-X-C}_6\text{H}_4)_2\text{C}\cdot$ ($\text{X} = \text{H}, t\text{Bu}$)

Scheme 3.

Concerted Radical Transfer Versus Electron Transfer Pathways for Reaction of Triphenylmethyl Radical with Fe(OH)(tppc)

Table 1.

UB3LYP/BS1 Optimized Transition State Parameters (Referring to TS_{reb,M,X}) for Both the M(OH)(tppc) (M = Mn and (Fe)) Complexes, in Their Reactions with (4-X-C₆H₄)₃C• (X = OMe, tBu, Ph, H, Cl, or CN)

M = Mn and (Fe), X:	OMe	tBu	Ph	H	Cl	CN
$E^{\ddagger}$ +ZPE (kcal mol ⁻¹) ^a	10.8 (12.7)	15.6 (17.1)	14.6 (16.2)	15.6 (17.3)	14.7 (16.6)	9.7 (12.1)
R(M-O) (Å)	2.051 (2.017)	1.980 (1.954)	1.983 (1.960)	1.978 (1.956)	1.994 (1.973)	2.066 (2.032)
R(O-C) (Å)	2.567 (2.428)	2.663 (2.550)	2.580 (2.534)	2.589 (2.484)	2.431 (2.360)	2.266 (2.230)
Imag. Freq. (cm ⁻¹)	i69 (i117)	i89 (i125)	i131 (i131)	i146 (i176)	i241 (i278)	i396 (i465)
μ_{dipole} (Debye) ^b	7.8 (6.1)	3.7 (3.3)	3.1 (4.9)	1.1 (2.3)	-3.2 (-3.2)	-2.7 (-2.0)
Q _{CT} (C) ^c	0.67 (0.65)	0.44 (0.46)	0.41 (0.50)	0.38 (0.41)	0.27 (0.30)	0.21 (0.25)

^aChange in enthalpy + zero point energy for the transition state.

^bChange in dipole moment, comparing the reactant complex and transition state complex.

^cCharge transfer in the TS, measured as the number of electrons transferred to the metallocorrole from (4-X-C₆H₄)₃C•.