

Chapter 21

Non-Organometallic Mechanisms for C–H Bond Oxidation: Hydrogen Atom versus Electron versus Hydride Transfer

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Oxidations of C–H bonds in alkylaromatic substrates can occur by initial electron, hydrogen atom, or hydride transfer. Presented here are oxidations by $[(\text{phen})_2\text{Mn}(\mu\text{-O})_2\text{Mn}(\text{phen})_2]^{n+}$ ($n = 3, 4$) and $[(\text{bpy})_2(\text{py})\text{Ru}(\text{O})]^{2+}$. All three pathways are observed; which mechanism is preferred depends on the thermochemistry and the intrinsic barriers.

The activation of C–H bonds by metal complexes via organometallic mechanisms has been a major focus of research for some time, and is the dominant theme of this volume. Organometallic mechanisms for C–H activation include oxidative addition, formation of σ -complexes, σ -bond metathesis, and [2+2] additions to metal-ligand multiple bonds. These hold great promise for the functionalization of alkanes because all of these processes are selective for the least hindered C–H bond, such as the terminal methyl group of a chain. The promise of organometallic C–H activation has, however, been slowed by the difficulty in functionalizing the carbon after the activation step.

The organometallic approach should be contrasted with non-organometallic metal-mediated oxidations of hydrocarbons. In these mechanisms, the

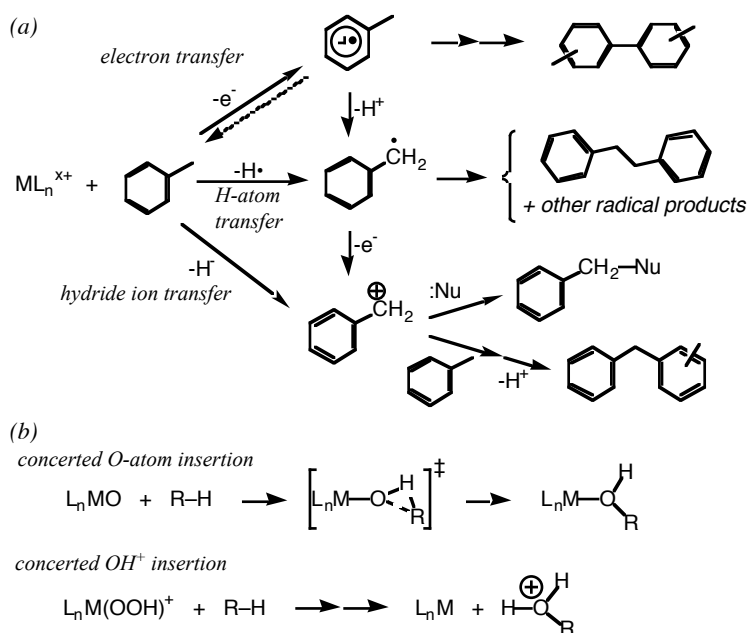
hydrocarbon substrate does not bind to the metal. Instead, bond cleavage and bond formation occur at a metal-bound ligand, such as an oxo group. Such mechanisms are in general selective for the weakest bond in the molecule, typically activating tertiary or benzylic C–H bonds. Because of this selectivity, reactions that follow these mechanisms are unlikely to solve the challenge (the “holy grail” (1)) of selectively converting methane to methanol or linear hydrocarbons to terminally functionalized products. Still, it should be emphasized that essentially all commercial metal-mediated C–H bond oxidations proceed by non-organometallic pathways (including metal-mediated radical processes in which the metal is not involved in C–H activation) (2). This includes both homogeneous oxidations, such as *para*-xylene to terephthalic acid (for polyethylene terephthalate [polyester]) and heterogeneous processes over metal oxides such as butane to maleic anhydride (for THF).

It is interesting to compare the terminology of the two approaches. The organometallic approach is termed “activation and functionalization” because these are separate processes. This distinction is not made in the non-organometallic processes, typically called “selective oxidations,” because in these processes functionalization almost inevitably follows C–H bond cleavage. The difference in large part follows from the properties of the metal complexes involved. The active species or reagents in the non-organometallic approaches are oxidants, and often strong ones. In the organometallic reactions, however, the metal center that activates the C–H bond is typically reducing (as required for C–H bond oxidative addition) or redox-neutral (as in the formation of σ -complexes, σ -bond metatheses, and [2+2] additions). Since the “functionalization” desired is typically oxidative, it is not surprising that the organometallic compounds that activate C–H bonds do not functionalize them. In general, functionalization of the metal-bound C–H activated species requires a subsequent oxidation step. It is interesting that an exception to this pattern, the catalytic alkane borylation developed by Hartwig *et al.*, is formally not an oxidation of carbon ($C^{\delta-}-H^{\delta+} \rightarrow C^{\delta-}-B^{\delta+}$) (3).

Work in the Mayer labs has focused on non-organometallic oxidations, and hydrogen atom transfer reactions in particular. Rates of H-atom transfer to a transition metal oxidant depend not on the radical character of the oxidant, but on the thermochemical affinity of the oxidant for H^{\bullet} (4) and its intrinsic barrier toward hydrogen atom transfer (5). In this chapter we discuss the factors that influence the choice of non-organometallic mechanism for C–H bond activation, between initial H-atom transfer, electron transfer, and hydride transfer.

Mechanistic overview

Common pathways in non-organometallic metal-mediated oxidations of hydrocarbons are summarized in Scheme 1a, using toluene as a typical substrate. Electron transfer oxidation of alkanes is quite difficult because of their high ionization energies, but electron transfer from aromatic compounds is frequently

Scheme 1. (Adapted in part from reference (6) with permission.)

observed and often leads to biaryl products. Hydrogen atom transfer yields carbon radicals, which are sometimes indicated by radical coupling or rearrangement products. Hydride transfer gives carbocations which can be trapped by nucleophiles, including the aromatic substrate itself. Carbon radicals can also be formed by deprotonation of organic radical cations (which are often quite acidic) and similarly, carbocations can be formed by oxidation of radicals.

Concerted oxygen atom insertion into C–H bonds has also been discussed (Scheme 1b), for instance by the oxo complexes $[(bpy)_2(py)Ru(O)]^{2+}$ (7) and $[(TPA)Fe^V=O]$ (TPA = tris(2-pyridylmethyl)amine and its derivatives (8)). Newcomb and co-workers have also suggested a mechanism of concerted OH⁺ insertion into a C–H bond (9). This mechanism (with subsequent water loss) is used to explain the observed carbocation intermediates in C–H bond oxidations by cytochrome P450 and methane monooxygenase enzymes. These direct insertions in C–H bonds are analogous to the proposed reactivity of singlet methylene (¹CH₂) (10a). Concertedness is usually indicated by observing only the products of direct insertion, without any rearrangement, racemization, or inversion of an intermediate radical or carbocation. It should be noted, however, that there is a mechanistic continuum between concerted insertion and hydrogen removal (as H[•] or H⁻). Computational studies suggest that O–H bond formation is typically more advanced than C–O bond formation (11), as indicated in Scheme 1b. If C–O bond formation is sufficiently rapid or if the C–O bond is

formed to only a small extent, then reactions may appear concerted while the transition state closely resembles a hydrogen atom or hydride transfer.

Thermochemistry and its connection to kinetic barriers

The thermodynamic properties of the reactants and products are very valuable in understanding a chemical reaction and the pathway(s) it follows. For each of the mechanisms in Scheme 1, the thermochemistry varies significantly with the nature of the C–H bond being oxidized. For instance, oxygen atom insertion into the tertiary C–H bond of isobutane is 12 kcal mol⁻¹ more favorable than the analogous conversion of methane to methanol. Such values can be calculated from standard Tables (and are given in reference (12)). If C–H bond strengths are needed, the most current values (13) should be used if possible as the “accepted” values have risen 1–4 kcal mol⁻¹ over the last few decades (13). A valuable advance in this area was the development by Bordwell and coworkers (based on precedents) of a simple thermochemical cycle to determine X–H homolytic bond strengths from redox potentials (E°) and acidities (pK_a values) (14). A similar approach to hydride affinities in MeCN has been described by Parker (15).

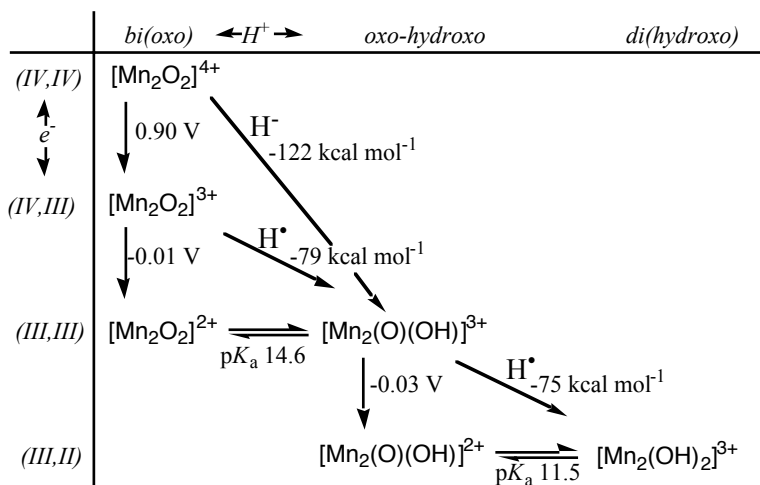
This chapter describes oxidations by two metal-containing oxidants, manganese-oxo-phenanthroline dimers [(phen)₂Mn(μ-O)₂Mn(phen)₂]ⁿ⁺ (n = 3, 4) and the ruthenium-oxo-polypyridyl complex [(bpy)₂(py)Ru(O)]²⁺. The abbreviations used here omit the pyridyl ligands, **Mn₂O₂ⁿ⁺** and **RuO²⁺**. In both cases, addition of electrons and protons generates reduced hydroxo (or aquo) species. Measured redox potentials and pK_a values are presented in Schemes 2 and 3, which are organized such that one row differs from the next by one electron, and one column differs from the next by one proton. The affinities of the oxidants for H[•] or H⁻ are calculated using thermochemical cycles (12,15).

It is informative to compare values for ΔG° for a series of related reactions with the activation free energies ΔG^\ddagger (a linear free energy relationship). The ratio of the changes in these quantities is usually referred to as α (eq 1), from the Brønsted relation for proton transfer reactions (16). For most reactions, linear

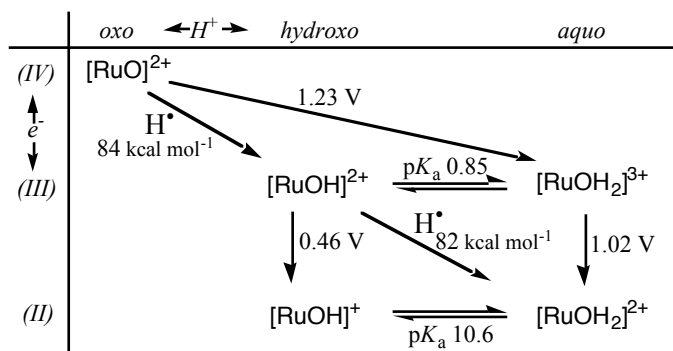
$$\alpha = \frac{\Delta\Delta G^\ddagger}{\Delta\Delta G^\circ} = \frac{\Delta\log(k)}{\Delta\log(K_{\text{eq}})} \quad (1)$$

free energy relationships hold only within a closely related series of substrates over a narrow range of driving force. For a few classes of reactions, rate constants correlate with driving force over a wider range of reactants, the most established example being electron transfer. By Marcus Theory, barriers for a series of reactions with similar intrinsic barriers will have a quadratic dependence on ΔG° – linear over a small range of ΔG° (17). Hydrogen atom transfer reactions of organic and main group radicals have long been known to have a similar correlation of barrier with driving force, typically stated as an

Scheme 2. Thermodynamic data for $[(\text{phen})_2\text{Mn}(\text{OH}_x)_2\text{Mn}(\text{phen})_2]^{n+}$ compounds (values in MeCN, potentials vs. $\text{Cp}_2\text{Fe}^{+/0}$; adapted from (6) with permission.)



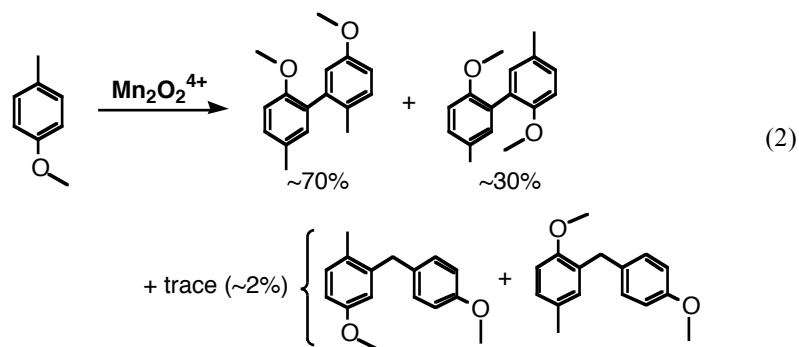
Scheme 3. Thermodynamic data for $[(\text{bpy})_2(\text{py})\text{Ru}(\text{OH}_x)]^{n+}$ compounds (in H_2O , potentials at pH 0 vs. NHE from (18); adapted from (19) with permission.)



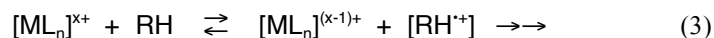
enthalpy relationship (E_a vs. bond strength) (20). This relationship holds well as long as “similar” radicals and substrates are compared. We have shown that such correlations also apply to hydrogen atom transfer reactions of transition metal complexes (4). This is one component of a more complete analysis, based on a Marcus-type approach using both driving force and intrinsic barriers (5). A Marcus treatment has also been applied to hydride transfer reactions (21).

Oxidations of alkylaromatic compounds by $[(\text{phen})_2\text{Mn}(\mu\text{-O})_2\text{Mn}(\text{phen})_2]^{n+}$.

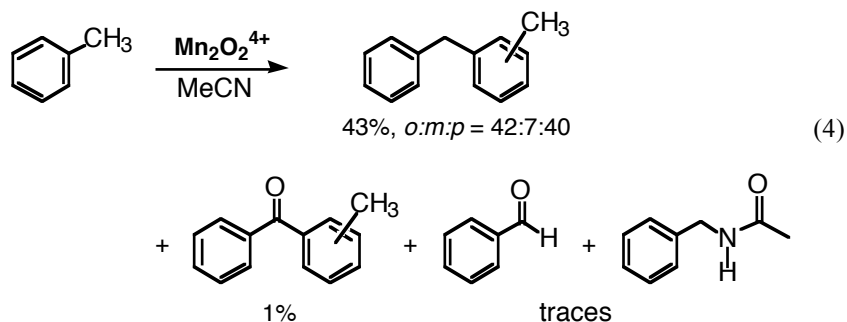
A full report of oxidations by $\text{Mn}_2\text{O}_2^{4+}$ and $\text{Mn}_2\text{O}_2^{3+}$ has appeared (6) and only the conclusions will be described here. $\text{Mn}_2\text{O}_2^{4+}$ is a quite reactive species, oxidizing all of the aromatic compounds we have examined except nitrotoluene. Organic compounds with relatively low redox potentials, such as naphthalene and *p*-methoxytoluene, are oxidized predominantly to biaryl compounds (e.g., eq 2). As shown in Scheme 1a, biaryl products indicate a



mechanism of initial electron transfer. This conclusion is supported by kinetic studies showing inhibition of the reactions by added $\text{Mn}_2\text{O}_2^{3+}$, the reduced form of the oxidant. Such inhibition is a clear marker for a pre-equilibrium electron transfer mechanism (eq 3).



The $\text{Mn}_2\text{O}_2^{4+}$ oxidation of toluene gives predominantly benzyl-toluene products from Friedel-Crafts addition of benzyl cation to toluene (along with small amount of the further oxidized products, eq 4). *p*-Methoxytoluene

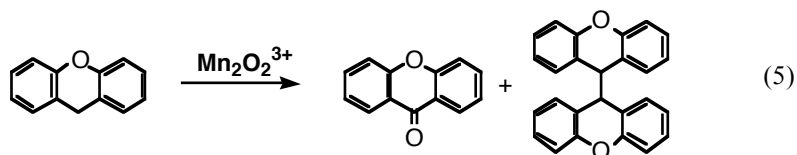


oxidation, which is 4×10^6 times faster than oxidation of toluene, also gives a trace of Friedel-Crafts products (eq 2). These products indicate the intermediacy of benzyl cations (Scheme 1a). The benzyl cations could be formed by initial electron transfer followed by deprotonation and oxidation, or by direct hydride transfer. A hydrogen atom transfer mechanism is ruled out by the very large substituent effects observed. For instance, *p*-xylene is 68 times more reactive than toluene and *p*-nitrotoluene is unreactive.

In contrast to substrates with low oxidation potentials, there are two indications that the oxidation of toluene by $\text{Mn}_2\text{O}_2^{4+}$ does not occur by electron transfer. First, addition of $\text{Mn}_2\text{O}_2^{3+}$ does not inhibit the reaction. While this could be consistent with rate-limiting (rather than preequilibrium) electron transfer, that mechanism is ruled out by the primary isotope effect of 4.3 ± 0.8 observed upon oxidation of a mixture of $\text{C}_6\text{H}_5\text{CH}_3$ and $\text{C}_6\text{H}_5\text{CD}_3$. Second, electron transfer from toluene is quite difficult because of its very high redox potential, 2.6 V vs. NHE in MeCN (0.5 V higher than naphthalene) (22). Based on this potential and the value in Scheme 2, electron transfer from toluene to $\text{Mn}_2\text{O}_2^{4+}$ is 1.2 V or 27 kcal mol⁻¹ endergonic, larger than the observed $\Delta G^\ddagger = 23.6$ kcal mol⁻¹. [ΔG^\ddagger , the corrected potential within the precursor complex (22), is even more unfavorable because of coulombic repulsion in the successor complex $\text{Mn}_2\text{O}_2^{3+}||\text{C}_7\text{H}_8^{+\cdot}$.] Thus electron transfer is not kinetically competent to account for the observed rate of oxidation, and the oxidation of toluene by $\text{Mn}_2\text{O}_2^{4+}$ occurs via initial hydride transfer.

A note of caution should be added here, that redox potentials for hard to oxidize substrates such as toluene are very difficult to measure. Highly irreversible electrochemical behavior is often observed, and the radical cations are very reactive with trace impurities in the solvent. One often finds a number of different values in the literature for the redox potential of a substrate such as toluene. Therefore arguments solely based on redox potentials – particularly relative potentials from different sources – should be viewed with caution. We have yet to find a single source that gives a consistent list for all the substrates of interest; recommended references are (22) and (23). In the case at hand, the toluene redox potential would have to be lower by more than 0.25 V lower than the value given by Ebersson (22) in order for $\Delta G(\text{Mn}_2\text{O}_2^{4+} + \text{toluene})$ to even be equal to ΔG^\ddagger . In addition, the primary kinetic isotope effect and lack of inhibition by $\text{Mn}_2\text{O}_2^{3+}$ provide a second argument against electron transfer.

$\text{Mn}_2\text{O}_2^{3+}$ is a much weaker oxidant than $\text{Mn}_2\text{O}_2^{4+}$, only oxidizing compounds with very weak C–H bonds such as xanthenone and dihydroanthracene (DHA) (6). Xanthenone is oxidized to a mixture of xanthone and bixanthenyl (eq 5). Bixanthenyl is the radical coupling product, indicating that carbon radicals



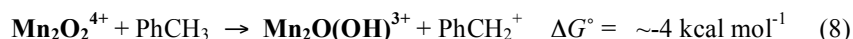
are present. The ratio of xanthone to bixanthenyl depends on the concentrations of $\text{Mn}_2\text{O}_2^{3+}$ and xanthone in a way that is consistent with the entire reaction proceeding via the xanthenyl radical, which can dimerize or be trapped by $\text{Mn}_2\text{O}_2^{3+}$ at $\sim 2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ (or by $\text{Mn}_2\text{O(OH)}^{3+}$ at $\sim 2 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$). Consistent with a radical process, the relative rates inversely correlate with the substrate C–H bond strengths ($k_{\text{xanthene}} > k_{\text{DHA}} > k_{\text{fluorene}}$).

So why does $\text{Mn}_2\text{O}_2^{3+}$ react by hydrogen atom abstraction while $\text{Mn}_2\text{O}_2^{4+}$ reacts by electron transfer and hydride transfer? The first step in answering such questions is to look at the energetics of each possible rate limiting step. $\text{Mn}_2\text{O}_2^{3+}$ is thermodynamically a reasonable hydrogen atom abstractor because it can form a 79 kcal mol^{-1} bond to H^\bullet (Scheme 2). Thus reactions with xanthene, DHA, and fluorene have $\Delta H^\circ \approx -3.5$, -1 , and $+1 \text{ kcal mol}^{-1}$ (cf., eq 6; BDE = bond dissociation energy). The affinity of $\text{Mn}_2\text{O}_2^{3+}$ for H^\bullet is due to its being a moderate outer-sphere oxidant ($E_{1/2} = -0.01 \text{ V}$ in MeCN vs. $\text{Cp}_2\text{Fe}^{+/0}$) and the

$$\Delta H^\circ(\text{Mn}_2\text{O}_2^{3+} + \text{XH} \rightarrow \text{Mn}_2\text{O(OH)}^{3+} + \text{X}^\bullet) = \text{BDE}(\text{X-H}) - \text{BDE}[\text{Mn}_2\text{O(O-H)}^{3+}] \quad (6)$$

reduced form being a good base ($\text{p}K_{\text{a}} 14.6$ in MeCN). In contrast, $\text{Mn}_2\text{O}_2^{4+}$ is not a good H-atom abstractor because its reduced form, $\text{Mn}_2\text{O}_2^{3+}$, does not have significant basicity. Thermodynamically, it is most favorable for $\text{Mn}_2\text{O}_2^{4+}$ to accept an electron or a hydride, forming stable $\text{Mn}_2\text{O}_2^{3+}$ or $\text{Mn}_2\text{O(OH)}^{3+}$.

Comparing the two possible pathways for toluene oxidation by $\text{Mn}_2\text{O}_2^{4+}$, electron transfer is uphill by $\Delta G^\circ = \sim 27 \text{ kcal mol}^{-1}$ while hydride transfer has $\Delta G^\circ = \sim -4 \text{ kcal mol}^{-1}$ (eqs 7, 8). The latter value results from the hydride affinity of $\text{Mn}_2\text{O}_2^{4+}$ being slightly larger than that of benzyl cation (122 vs. 118 kcal mol^{-1} (15)). The hydride affinities are derived with Parker's thermochemical

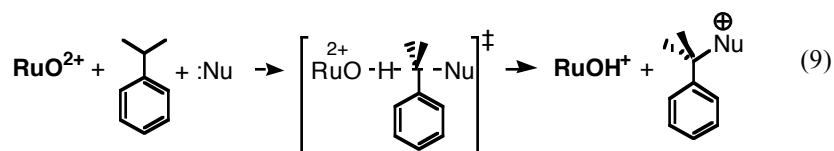


cycle and with potentials and $\text{p}K_{\text{a}}$'s in MeCN, so they should be directly comparable. There is thus a 31 kcal mol^{-1} thermodynamic bias for toluene oxidation to occur by hydride rather than electron transfer. This bias is large enough for the system to prefer the hydride transfer path.

For *p*-methoxytoluene, electron transfer has $\Delta G^\circ = 9 \text{ kcal mol}^{-1}$ and hydride transfer has $\Delta G^\circ = -15 \text{ kcal mol}^{-1}$. Again there is a large thermochemical preference for hydride transfer pathway, in this case 24 kcal mol^{-1} . *In spite of this 24 kcal mol⁻¹ bias, the oxidation of p-methoxytoluene occurs by initial electron transfer.* This is indicated by the predominant formation of biaryl products and the inhibition by added $\text{Mn}_2\text{O}_2^{3+}$. Hydride transfer is intrinsically more difficult than electron transfer in this system. If this is generally the case, hydride transfer will occur as a one step process only when it has a very large thermodynamic bias over electron transfer.

C–H bond oxidations by $[(\text{bpy})_2(\text{py})\text{Ru}(\text{O})]^{2+}$.

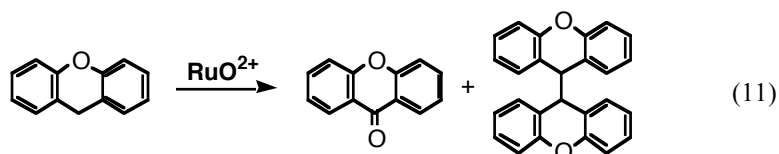
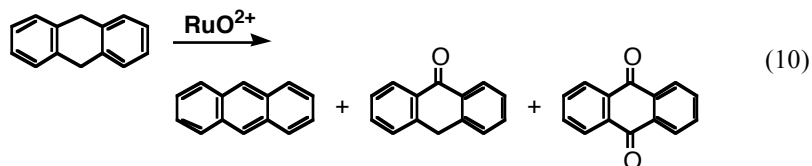
In 1982, Thompson and Meyer described oxidations of alkylaromatic compounds by RuO^{2+} in both water and acetonitrile solvents (24). They proposed a new mechanism for a C–H bond oxidation, hydride abstraction with assistance from an entering nucleophile (eq 9). The compelling evidence for this pathway was a termolecular rate law, first order each in RuO^{2+} , substrate



(cumene), and the entering nucleophile (H_2O , $t\text{BuOH}$, or Br^-). We have been particularly interested in this pathway, and we invoked it in a permanganate oxidation (25). It is a type of $\text{S}_{\text{N}}2$ reaction and therefore could show primary > secondary > tertiary selectivity. However, it is quite unusual for an $\text{S}_{\text{N}}2$ -type process to occur at a tertiary center (as in eq 9), and unusual that the relative rates, $\text{H}_2\text{O} > t\text{BuOH} > \text{Br}^-$, were opposite to typical trends in nucleophilicity (10b).

We and the Meyer group have independently re-examined the oxidation of cumene by RuO^{2+} (26). Both groups have found that the rate in MeCN is independent of the concentration of added water, contrary to the previous report. We have found no dependence on added $t\text{BuOH}$, and that RuO^{2+} is reduced by Br^- in MeCN even in the absence of substrates. Without a third-order rate law, the mechanism in eq 9 must unfortunately be put aside. We have therefore looked more broadly at oxidations of alkylaromatics by RuO^{2+} (19).

DHA is rapidly oxidized by RuO^{2+} to give a mixture of anthracene, anthrone, and anthraquinone (eq 10 (19)). Oxidation of xanthene gives predominantly xanthone, with a small amount of bixanthenyl (eq 11); the



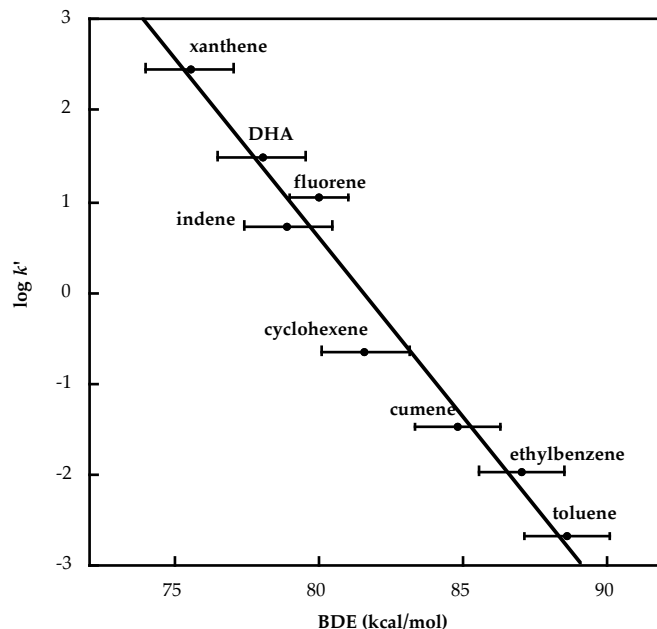
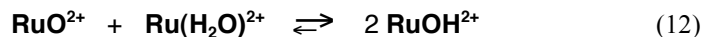


Figure 1. Graph of $\log k'$ (rate of abstraction by RuO^{2+} , per hydrogen) versus the bond dissociation energy for the substrate.

fluorene reaction is similar. Formation of bixanthenyl and bifluorenyl indicates the presence of xanthenyl and fluorenyl radicals in sufficient concentrations to couple. Radical coupling is competitive with trapping of the radicals by the oxidants present (RuO^{2+} and RuOH^{2+}) which leads to the oxygenated products. Consistent with this model, the yields of coupled products decrease with increasing RuO^{2+} starting concentrations. The chemistry is similar to that found for $\text{Mn}_2\text{O}_2^{3+}$ with these substrates (see above). The carbon radicals must be made by direct hydrogen atom transfer because RuO^{2+} is a very poor outer-sphere (electron transfer) oxidant (27).

The kinetics of RuO^{2+} oxidations, as shown by Meyer and co-workers (28), are complicated by the presence of multiple ruthenium species: RuO^{2+} , RuOH^{2+} , $\text{Ru}(\text{H}_2\text{O})^{2+}$, and $\text{Ru}(\text{NCMe})^{2+}$ [$\text{Ru} = \text{Ru}(\text{bpy})_2\text{py}$]. In addition, there is a comproportionation/disproportionation equilibrium among the oxygenated species (eq 12), with $K_{\text{eq}} = 50$. The DHA, xanthene and fluorene oxidations have been monitored with a stopped-flow spectrophotometer, and the optical spectra have been fit to an $\text{A} \rightarrow \text{B} \rightarrow \text{C}$ model with the SPECFITTM global analysis software. In the oxidation of 40 mM DHA by 0.2 mM RuO^{2+} , $t_{1/2}$ for the $\text{A} \rightarrow \text{B}$ phase of the reaction is 0.13 s. After this first phase, the spectra indicate most of



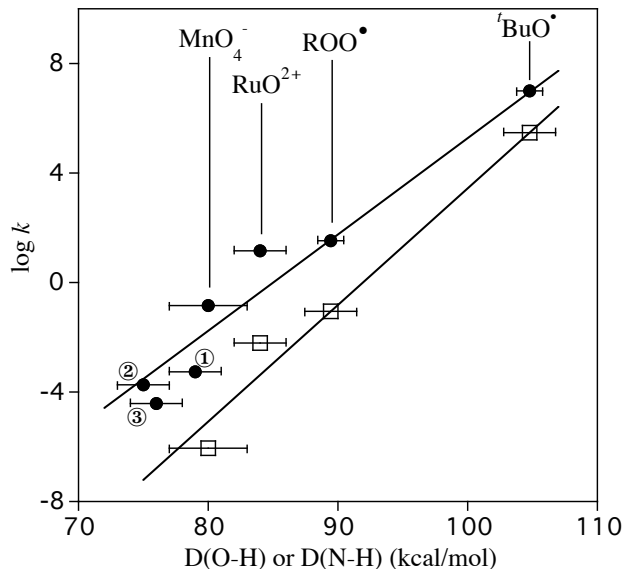


Figure 2. Plot of the log of the rate constant for H-atom abstraction for DHA (●, upper line) and toluene (□, lower line) vs. the strength of the X-H bond formed by the oxidant. In both cases, a straight line is drawn through the two oxygen radical points.

Key for numbered points: ①, $[(phen)_2Mn(O)_2Mn(phen)_2]^{3+}$; ②, $[(phen)_2Mn(O)(OH)Mn(phen)_2]^{3+}$; and ③, $[Fe(Hbim)(H_2bim)_2]^{2+}$ (6,29)

the ruthenium is $RuOH^{2+}$ or a related Ru^{III} complex. The Ru^{III} is *not* made by comproportionation (eq 12), since under these conditions the half life for $Ru(H_2O)^{2+}$ reacting to form $RuOH^{2+}$ is ≥ 0.83 s. Thus the observation of $RuOH^{2+}$ indicates that RuO^{2+} is acting as a one-electron/one-proton oxidant and supports a mechanism of initial hydrogen atom transfer.

Oxidation of a number of alkylaromatic compounds by RuO^{2+} have been examined. Rate constants for the A→B step are taken as the rate of hydrogen abstraction k_H (30). These k_H values (divided by the number of reactive hydrogens in the substrate) correlate well with the C–H bond strength of the substrate (Figure 1). This linear correlation is confirmation of the hydrogen abstraction mechanism. In addition, we have often found that rate constants for hydrogen abstraction by metal-containing oxidants correlate with those for oxygen radicals (4,6). Figure 2 shows such a correlation for the oxidations of both DHA and toluene. Also included on the DHA line are rate constants for oxidations by $Mn_2O_2^{3+}$, $Mn_2O(OH)^{3+}$, and an iron(III) bi-imidazoline complex.

To further probe the hydrogen atom-transfer reactivity of RuO^{2+} , we have measured the rate of its H-atom self exchange with $RuOH^{2+}$: $k_{Ru/Ru} = 7.6 \times 10^4$ $M^{-1} s^{-1}$ (19). Rate constants were determined by 1H NMR line broadening in

MeCN solutions containing RuO^{2+} and RuOH^{2+} . The broadening was followed as a function of the concentration of RuOH^{2+} , which changes over time in these solutions because of the disproportionation of RuOH^{2+} (eq 12) and the solvolysis of the formed RuOH_2^{2+} . This self exchange rate constant can then be used in the Marcus cross relation (eq 13 (17)) to predict the rate constant of an oxidation reaction. Using the reported benzyl radical/toluene H-atom self

$$k_{\text{calc}}(\text{RuO}^{2+} + \text{PhCH}_3) = \sqrt{k_{\text{Ru/Ru}} k_{\text{C/CH}} K_{\text{Ru/CH}} f} \quad (13)$$

exchange rate constant ($k_{\text{C/CH}} = \sim 1 \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$, per hydrogen) and the equilibrium constant $K_{\text{Ru/CH}}$ (2×10^{-4} from the bond strengths assuming $\Delta S^\circ = 0$), eq 13 gives $k_{\text{calc}}(\text{RuO}^{2+} + \text{PhCH}_3) = 1.4 \times 10^{-2} \text{ M}^{-1} \text{ s}^{-1}$ (19). This is within a factor of seven of the experimental rate constant ($2.1 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$, per hydrogen). The good agreement provides another example of the applicability of the Marcus cross relation to hydrogen atom transfer reactions.

Conclusions

Many industrial and enzymatic oxidations of C–H bonds occur by non-organometallic mechanisms, without formation of M–H or M–C bonds. Mechanistic studies of two model systems are described here, to probe why a particular C–H bond oxidation follows one non-organometallic pathway versus another.

The manganese dimers $[(\text{phen})_2\text{Mn}(\mu\text{-O})_2\text{Mn}(\text{phen})_2]^{n+}$ ($\text{Mn}_2\text{O}_2^{n+}$) oxidize alkylaromatic compounds by electron transfer, hydrogen atom transfer, or hydride transfer. $\text{Mn}_2\text{O}_2^{3+}$ acts as an H-atom abstractor in large part because it can form a 79 kcal mol⁻¹ bond to a hydrogen atom (Scheme 2). $\text{Mn}_2\text{O}_2^{4+}$ is a much more potent outer-sphere electron transfer oxidant, and it oxidizes substrates by electron transfer or hydride transfer. It does not react by H-atom transfer because it does not form a strong bond to H[•], due to the low basicity of $\text{Mn}_2\text{O}_2^{3+}$. Oxidation of *p*-methoxytoluene by $\text{Mn}_2\text{O}_2^{4+}$ occurs by electron transfer, in a step that is uphill by $\Delta G^\circ = 9 \text{ kcal mol}^{-1}$. It is remarkable that electron transfer is favored over direct hydride transfer from *p*-MeOC₆H₄CH₃ to $\text{Mn}_2\text{O}_2^{4+}$, since the latter is *downhill* by $\Delta G^\circ = -15 \text{ kcal mol}^{-1}$. This shows that electron transfer is intrinsically more facile than hydride transfer.

The ruthenium-oxo-polypyridyl complex $[(\text{bpy})_2(\text{py})\text{Ru}(\text{O})]^{2+}$ (RuO^{2+}) does not oxidize cumene by the previously suggested mechanism of nucleophile-assisted hydride transfer. Instead, a common mechanism of hydrogen atom abstraction is indicated for a range of alkylaromatic compounds. One piece of evidence is the good correlation of $\log(k_{\text{H}})$ with the strength of the C–H bond being cleaved (Figure 1). RuO^{2+} is not a good outersphere oxidant, but it does have a large affinity for a hydrogen atom (84 kcal mol⁻¹). The rate constant for toluene oxidation by RuO^{2+} is predicted within a factor of 7 by the Marcus cross relation (eq 13). These results and previous studies suggest that electron transfer

and hydrogen atom transfer are the two most facile mechanisms for non-organometallic metal mediated oxidations. The choice between these pathways for a particular combination of oxidant and substrate is in large part determined by the thermochemistry of these reaction steps.

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