

Understanding C–H Bond Oxidations: H· and H⁻ Transfer in the Oxidation of Toluene by Permanganate

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The oxidation of toluene by permanganate has been studied as a model for the oxidation of C–H bonds by metal reagents, metalloenzymes, and metal oxide surfaces. In water, the reaction proceeds by hydride (H⁻) transfer from toluene to a permanganate oxygen, whereas in toluene solution, permanganate abstracts a hydrogen atom (H·). The ability of permanganate to abstract a hydrogen atom is rationalized on the basis of the strong O–H bond formed on H· addition to permanganate. This approach allows understanding and prediction of the rates of hydrogen atom transfer from substrates to metal active sites.

The selective oxidation of C–H bonds by metal-oxo and related species is of fundamental and technological importance, from biological to industrial chemistry. A variety of metalloenzymes catalyze selective C–H bond oxidation reactions (1), and industrial oxidation reactions often use metal oxide surfaces as catalysts (2). Laboratory-scale syntheses of organic chemicals have utilized metal-oxo reagents such as permanganate (MnO₄⁻) for more than a century (3). Surprisingly, these areas of oxidation chemistry have developed independently, and there is little understanding of the fundamental chemical principles that must underlie them all. There is particularly little insight into the features of an oxidant that enable it to activate a C–H bond. Described here is a mechanistic study of a textbook case, the oxidation of toluene by MnO₄⁻. This reaction proceeds by different pathways in aqueous and organic solvents. The mechanism for the reaction in organic solvent is used to develop a paradigm for oxidation processes that involve hydrogen atom (H·) transfer from a substrate to a metal active site, based on the strength of the O–H bond formed at the active site and the well-known correlation of radical reaction rates with driving force. The paradigm provides qualitative and quantitative understanding of such H· transfer oxidations.

The reaction of KMnO₄ with toluene in aqueous buffer solutions forms colloidal MnO₂, as indicated by its characteristic optical spectrum [absorbance $A \propto \lambda^{-4}$ for wavelengths $\lambda > 625$ nm (4) (Fig. 1)] and by iodometric titration (average oxidation state 4.10 ± 0.09). The organic products, determined by high-performance liquid chromatography (HPLC), are benzoic acid ($42.3 \pm 2.7\%$) and benzaldehyde ($0.6 \pm 0.2\%$), in agreement with previous work (5) (yields are moles of product per mole of

MnO₄⁻). The observed products account for 85% of the oxidizing equivalents of MnO₄⁻ consumed in the reaction; the remainder are likely involved in the oxidation of the aromatic ring (5, 6). The MnO₄⁻ solutions are stable in aqueous buffer in the absence of toluene.

The kinetics of toluene oxidation have been followed by ultraviolet-visible (UV-vis) spectroscopy (Fig. 1) under pseudo-first-order conditions of excess toluene. This could be accomplished despite the limited solubility of toluene in water because of the high absorptivity of MnO₄⁻. A special cell was designed to enable anaerobic addition of a concentrated stock solution of MnO₄⁻ to an equilibrated toluene-water solution with essentially no vapor phase volume, to ensure that the toluene is in solution rather than in the gas phase (6). The disappearance of MnO₄⁻ follows first-order kinetics to greater than three half-lives with no induction period. The derived pseudo-first-order rate constant k_{obs} depends linearly on the toluene concentration and is independent of the initial permanganate concentration [MnO₄⁻], indicating the second-order rate law $d[\text{MnO}_4^-]/dt = -k_2[\text{MnO}_4^-]$

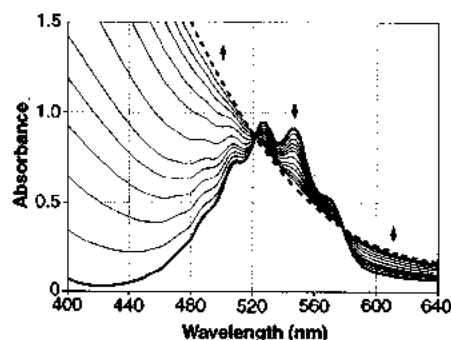


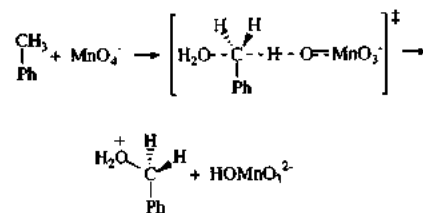
Fig. 1. Overlay of UV-vis spectra from the oxidation of toluene (6.9 mM) by potassium permanganate (0.392 mM) in pH 7.1 buffered aqueous solution at 75°C. The solid line is the initial permanganate spectrum and the dashed line is the final spectrum due to colloidal manganese dioxide.

[C₇H₈]. At 293 K, $k_2 = 7.0 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$. An Eyring plot of rate constants determined over the temperature range 293 to 368 K gives an activation enthalpy $\Delta H^\ddagger = 12.7 \pm 0.2 \text{ kcal mol}^{-1}$ and an activation entropy $\Delta S^\ddagger = -30 \pm 1 \text{ cal mol}^{-1} \text{ K}^{-1}$ (Table 1).

The second-order rate law indicates that the reaction proceeds by attack on toluene by MnO₄⁻, rather than involving intermediate species of some sort [as has been suggested (3)]. Consistent with this proposal, the rate constant is independent of ionic strength, pH (over the range 6 to 11), buffer type (phosphate and carbonate), and isotopic substitution of the solvent (H₂O versus D₂O). A substantial primary isotope effect is observed in the reaction of *d*₈-toluene: $k_{\text{C}_7\text{H}_8}/k_{\text{C}_7\text{D}_8} = 9.7$ at 293 K. The rate constant is the same for reactions performed under nitrogen and in oxygen-saturated water, under conditions where $[\text{O}_2] > [\text{MnO}_4^-]$. This finding implies that the reaction does not involve free radicals, as these would be intercepted by O₂, which traps radicals at rates near the diffusion limit (7). [MnO₄⁻ is also a highly effective radical trap (8).]

The relative rates of oxidation of the five para-substituted toluenes CH₃C₆H₄X, where X is CH₃, NO₂, COO⁻, Cl, or SO₃⁻, show a very small dependence of rate constant on substituent [a Hammett ρ value of -0.2 versus σ^+ (6, 9)]. These data rule out initial electron transfer to form a radical cation, or hydride transfer to give a free benzyl carbocation. Such intermediates would be very strongly destabilized by an electron-withdrawing substituent such as a para-nitro group, yet only a 20% decrease in rate is observed. In addition, the redox potentials for toluene [1.98 V versus Ag/Ag⁺/MeCN (10)] and MnO₄⁻ [0.56 V versus the normal hydrogen electrode (11)] indicate such an unfavorable equilibrium constant for electron transfer that the forward reaction could not occur at $7 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$.

The aqueous oxidation of toluene most likely is proceeding by hydride transfer with concurrent stabilization of the incipient carbocation by a molecule of the solvent water (Scheme 1; Ph = phenyl = C₆H₅). This pathway is analogous to that found by Meyer and Thompson for the oxidation of toluic acid by [(trpy)(bpy)RuO]²⁺ (12) (trpy, 2,2',2''-terpyridine; bpy, 2,2'-bipyri-



Scheme 1.

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