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Proton-Coupled Electron-Transfer Oxidation of Phenols by Hexachloroiridate(IV)

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One-electron oxidation of phenol, 2,4,6-trimethylphenol, and 2,6-dimethylphenol by $[IrCl_6]^{2-}$ in aqueous solution has a simple pH dependence, indicating slow bimolecular oxidation of ArOH and faster oxidation of ArO^-. H/D kinetic isotope effects as large as 3.5 for oxidation of ArOH support concerted proton-coupled electron transfer with water as the proton acceptor.

One-electron oxidation of phenols in aqueous media is currently of intense interest, in part because of the proton-coupled electron transfer (PCET) reactions relating to the tyrosinyl radical in several central biochemical systems.[1] Structural constraints in these systems impose long-distance electron transfer, and so the outer-sphere mechanism of PCET (OS-PCET) from phenols is highly relevant. After some initial disagreements, there now seems to be a consensus that these reactions are subject to general base catalysis.[2,3] However, the pH dependence when water is the proton acceptor remains enigmatic: there is general agreement that the reactions are pH-independent at high acidity, increase in rate with increasing pH, and reach a limiting rate at high pH, but some reports indicate an approximate inverse half-order dependence on $[H^+]$ in the intermediate pH region,[4,5] while others support an inverse first-order dependence;[6,7] the half-order dependence has led to the controversial proposal of a pH-dependent driving force.[4,5] The question of whether the reactions in acidic media (pH 1−3) have a sequential or concerted PCET mechanism is unresolved. Here, we present kinetic data on the oxidation of a series of three phenols by $[IrCl_6]^{2-}$ (Ir^{IV}), obtained under conditions where buffer catalysis is insignificant, that support an inverse first-order dependence on $[H^+]$ near neutral pH and a concerted PCET mechanism at low pH.

The oxidation of phenol and xylenol (2,6-dimethylphenol) by Ir^{IV} was the subject of a classic study by Cecil and Littler 40 years ago.[6] That paper showed that the two reactions yield $[IrCl_6]^{3-}$ (Ir^{III}) and a variety of phenolic oxidation products and that they have a simple two-term rate law when the effects of Ir^{III} can be neglected:

$$-\frac{d[Ir^{IV}]}{dt}=\frac{(k_{ArOH}+k_{ArO-}K_a/[H^+])[Ir^{IV}][ArOH]_{tot}}{1+K_a/[H^+]} \quad (1)$$

Here, K_a is the acid dissociation constant of the phenol, ArOH. The occurrence of kinetic inhibition by Ir^{III} and other supporting results were used to infer an outer-sphere electron-transfer mechanism for both terms in the rate law.

$$Ir^{IV}+ArOH \rightleftharpoons Ir^{III}+ArO^{\bullet}+H^+ \quad k_{ArOH},\ k_{-ArOH} \quad (2)$$

$$Ir^{IV}+ArO^- \rightarrow Ir^{III}+ArO^{\bullet} \quad k_{ArO-} \quad (3)$$

$$2ArO^{\bullet} \rightarrow \text{products} \quad k_{dim}\ (\text{fast}) \quad (4)$$

This mechanism leads to non-pseudo-first-order behavior at low pH, and as the pH increases, eq 2 becomes essentially irreversible and unaffected by Ir^{III}.

Limitations to the study by Cecil and Littler included the inability to exclude completely the effects of Ir^{III}, the instrumental restriction to measuring relatively slow rates, the unknown driving forces for the two rate-limiting steps, the unknown rate of self-reaction of the phenoxyl radicals (reaction 4), the unknown pK_a of $ArOH^{\bullet+}$, and uncertainty as to whether the acid pathway (k_{ArOH}) was a sequential process of electron transfer to form $ArOH^{\bullet+}$ followed by its deprotonation or whether it was a concerted PCET process as written in reaction 2. Here we use dibromonitrosobenzenesulfonate (DBNBS) as a phenoxyl radical scavenger to eliminate the kinetic effects of Ir^{III}, we use stopped-flow methods to obtain kinetic data under conditions where the rates are much faster, we use numerical modeling and the now-known properties of the phenoxyl radicals to confirm the basic mechanism, and we use kinetic isotope effects (KIEs) to probe the concertedness of the ArOH oxidation

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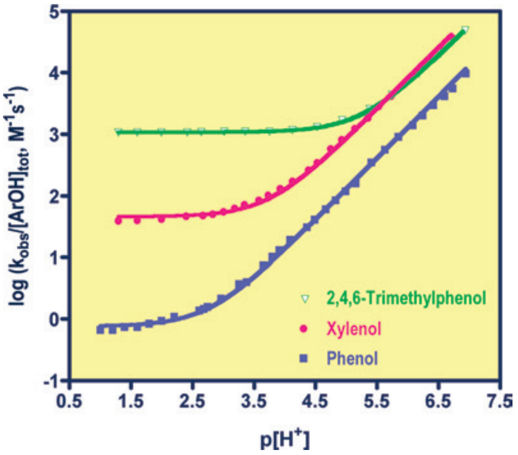

Figure 1. Plots of log(k_{obs}/[ArOH]$_{tot}$) vs p[H^+] for the Ir^{IV} oxidations of phenol in the presence of DBNBS, TMP, and xylenol. The curves are fits to eq 1. Data are from Tables S-4, S-7, and S-9 in the Supporting Information.

pathway. Moreover, we extend the range of substrates to include 2,4,6-trimethylphenol (TMP) to help define the factors controlling the various rate constants.

Figure S1 (Supporting Information) shows a typical kinetic trace for the consumption of Ir^{IV} in its reaction with 0.44 M phenol in 0.05 M $HClO_4$; such kinetic traces do not give good fits with either first- or second-order rate laws. The figure also shows the same reaction when performed in the presence of a 5-fold excess of Ir^{III}, which illustrates the strong kinetic inhibition by Ir^{III}. DBNBS is a well-known radical spin trap,[8,9] and it has been shown to be effective with phenoxyl radicals.[10] In the presence of 10 mM DBNBS, the reaction of Ir^{IV} with phenol in 0.05 M $HClO_4$ is considerably faster, is unaffected by the presence of Ir^{III}, and obeys pseudo-first-order kinetics (Figure S-2 in the Supporting Information). With DBNBS in 0.05 M $HClO_4$, the rate law is first-order in [phenol] from 0.022 to 0.44 M phenol; it is also first-order in [phenol] at p[H^+] = 5.1 (0.02 M acetate buffer) ([phenol] = 1.8−44 mM). (We use p[H^+] = −log [H^+], as described in the Supporting Information). The p[H^+] dependence (Figure 1) at p[H^+] = 1−7 at 25 °C and μ (=ionic strength) = 0.1 M ($LiClO_4$) shows that the rates conform to eq 1 with $k_{ArOH} = 0.75 \pm 0.03$ M^{-1} s^{-1} and $k_{ArO^-} = (7.8 \pm 0.2) \times 10^6$ M^{-1} s^{-1} (pK_a = 9.79 at μ = 0.1 M).[11]

At higher p[H^+], the reaction of phenol with Ir^{IV} is less sensitive to Ir^{III}, and good-quality pseudo-first-order fits could be obtained at and above p[H^+] = 2.5 without the addition of DBNBS as long as no Ir^{III} was added to the reactants. Under these conditions, rate law 2 was also obeyed, although the rate constants were only about half as large with $k_{ArOH} = 0.54 \pm 0.02$ M^{-1} s^{-1} and $k_{ArO^-} = (5.01 \pm 0.08) \times 10^6$ M^{-1} s^{-1}. The doubling of the rate constants caused by DBNBS can be explained if the DBNBS/phenoxyl adduct undergoes rapid oxidation by Ir^{IV} as in

$$ArO^{\bullet} + DBNBS \rightarrow adduct^{\bullet} \tag{5}$$

$$adduct^{\bullet} + Ir^{IV} \rightarrow adduct^{+} + Ir^{III} \tag{6}$$

In the absence of DBNBS, the rates may still be somewhat affected by Ir^{III}, and thus the most accurate values for k_{ArOH} and k_{ArO^-} are half of the values obtained in the presence of DBNBS, i.e., $2k_{ArOH} = 0.75 \pm 0.03$ M^{-1} s^{-1} and $2k_{ArO^-} = (7.8 \pm 0.2) \times 10^6$ M^{-1} s^{-1}. These results are in good agreement with those reported previously.[6] The p[H^+] dependence near p[H^+] = 7 is clearly incompatible with the weaker dependence reported for the oxidation of phenol by $[Ru(bpy)_3]^{3+}$;[5] studies with other oxidants, to be published, may reveal the origins of this behavior.

A test of the mechanism proposed in reactions 2−4 is provided by numerical simulation of the effects of Ir^{III} in 0.05 M H^+ in the absence of DBNBS. At this pH, the phenolate path can be neglected, the effects of Ir^{III} are quite strong, and a suitable mechanism consists simply of reaction 2 treated reversibly (k_{ArOH} and k_{-ArOH}) plus the irreversible dimerization of the phenoxyl radical (k_{dim}). A value of 2.3×10^9 M^{-1} s^{-1} has been reported for $2k_{dim}$ from direct pulse-radiolytic measurement.[12] The results of the numerical simulations were quite sensitive to the value of k_{-ArOH} used, and an optimal (excellent) fit to the two kinetic traces in Figure S-1 in the Supporting Information was achieved manually by adjusting k_{-ArOH} to 2.9×10^7 M^{-2} s^{-1}. The ratio k_{ArOH}/k_{-ArOH} was obtained with these rate constants of 1.3×10^{-8} M, which is the equilibrium constant for that step in the mechanism. A value of 5.8×10^{-9} M for this equilibrium constant can be calculated completely independently by combining the formal reduction potential of the Ir^{IV}/Ir^{III} couple (=0.893 V vs NHE at μ = 0.1 M)[13] and the standard reduction potential of the $ArO^{\bullet},H^+/ArOH$ couple (=1.38 V); the latter is derived from $E°(C_6H_5O^{\bullet}/C_6H_5O^-)$ (=0.79 ± 0.01 V)[14] and the pK_a of phenol. In view of the approximations made by mixing standard and formal potentials, the agreement between these two calculations of the equilibrium constant provides strong support for the proposed mechanism and rate constants.

With xylenol and TMP as the substrates, qualitatively similar results were obtained, although the degree of kinetic inhibition by Ir^{III} was considerably weaker. The rate constants for these reactions are summarized in Table S-1 in the Supporting Information. Simulations of kinetic inhibition in the xylenol reaction were performed with the literature value for k_{dim} [=(4.2 × 10^9) M^{-1} s^{-1}],[15] and they yielded a value of 3.5×10^6 M^{-2} s^{-1} for k_{-ArOH}. The value of K_{ArOH} derived from k_{ArOH}/k_{-ArOH} is 9.1×10^{-6} M, and thus $E°(xylO^{\bullet},H^+/xylOH)$ is 1.19 V. Unfortunately, there is no independent

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report of this standard potential to be used in comparison. In the case of TMP, it may be anticipated that k_{dim} is considerably smaller than those for the other phenoxyl radicals because the C−C coupling process is hindered, but there is no literature value for this rate constant in aqueous solution. An explanation of the varying degrees of sensitivity to Ir^{III} in these three reactions is nontrivial, because it depends on the variations in k_{ArOH}, $k_{-\text{ArOH}}$, and k_{dim} in eqs 2 and 4; this question will be explored in a subsequent publication.

Tests for general base catalysis were performed as follows: for the phenol reaction at $p[H^+] = 6.5$, the cacodylate buffer concentration was varied from 2 to 20 mM, and after correction for pH fluctuations, no significant corresponding rate variation was detected. Tests were also performed where the concentration of ammonium was varied from 0.2 to 0.7 mM because the oxidant used was $(NH_4)_2[IrCl_6]$; again, no kinetic effect was detected. Third, if phenol itself were a catalyst, then a second-order dependence on [phenol] would be expected, contrary to our observations. In summary, the kinetic data in Table S-1 in the Supporting Information are free of complications arising from general base catalysis. This conclusion is in agreement with the recent report from Irebo et al. that general base catalysis in outer-sphere phenol oxidations can be insignificant under certain conditions.[3]

The half-order dependence on $[H^+]$ previously reported for the reaction of phenol with $[Ru(bpy)_3]^{3+}$ was derived by fitting of the data to eq 7, where α is the fraction of ArOH in the phenol form[5]

$$\frac{k_{\text{obs}}}{[\text{ArOH}]_{\text{tot}}} = \alpha(k_1 + k^\circ \times 10^{0.5\text{pH}}) + (1 - \alpha)k_2 \qquad (7)$$

Compared to eq 1, fits to eq 7 yielded moderately improved residuals for all three phenols, but the fitted values for k_1 and k_2 were not statistically different for the two functions. The additional k° term never contributed more than 28% to the overall rate. We suggest that the empirical improvements afforded by use of eq 7 with the present reactions are not mechanistically significant and could be a consequence of other minor effects such as small variations in activity coefficients as the medium changes from 0.1 M $HClO_4$ to mostly $LiClO_4$.

Measurements of the deuterium KIEs were performed by conducting the reactions in a D_2O solution and comparing the rates to those in normal H_2O. The experiments were limited to rather acidic solutions, where the k_{ArO^-} term in eq 1 is completely negligible, the rates are independent of pH, and equilibrium isotope effects on K_a are not an issue. The results, summarized in Table S-1 in the Supporting Information, show that the KIE is 2.0 for TMP, 2.6 for xylenol, and 3.5 ± 0.3 for phenol. KIEs of this magnitude are clearly indicating a primary KIE and imply cleavage of the O−H bond in the rate-limiting step. Although these results are taken as evidence of a concerted PCET mechanism, the measured KIEs are not extremely large, so it is conceivable that the measured k_{ArOH} values include a small contribution from a parallel sequential PCET mechanism. Focusing on the (major) concerted PCET component, the solvent (water) must be acting as the proton acceptor because Ir^{III} is not appreciably basic and no other bases appear in the rate law. A similar KIE and mechanism were recently reported for the oxidation of hydroxylamine by Ir^{IV}.[16] The measured phenol KIEs correlate with both the inverse pK_a's of the phenols and $E^\circ(\text{ArO}^\bullet,\text{H}^+/\text{ArOH})$; further studies will include phenols where these two properties vary independently.

In summary, the current results show that phenols can undergo outer-sphere oxidation through the classical rate law 1 and with only marginal evidence for the "pH-dependent" rate constant k°. At low buffer concentrations, the reactions can display kinetics that are unaffected by general base catalysis. H/D KIEs as large as 3.5 for the ArOH pathway can be obtained with $[IrCl_6]^{2-}$ as the oxidant, supporting a concerted proton−electron transfer mechanism. A multisite concerted PCET mechanism is inferred for this pathway, in which water acts as the proton acceptor.

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Supporting Information Available: Figures S-1 and S-2, Table S-1 giving kinetic data, Tables S-2−S-11 giving k_{obs} values, and experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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