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Aromatic Hydroxylation by Fenton Reagents {Reactive Intermediate[$L_x^+Fe^{III}OOH(BH^+)$], not Free Hydroxyl Radical (HO·)}

John P. Hage, Antoni Llobet and Donald T. Sawyer*

Department of Chemistry, Texas A&M University, College Station, TX 77843-3255, U.S.A.

Abstract—Several iron complexes [$Fe^{II}(bpy)_2^{2+}$, $Fe^{II}(OPPh_3)_4^{2+}$, and $Fe^{II}(PA)_2$] in combination with hydrogen peroxide (HOOH) catalytically hydroxylate aromatic substrates (ArH). The base-induced nucleophilic addition of HOOH to the electrophilic iron center yields the reactive intermediate of Fenton reagents [$Fe^{II}L_x^{2+}$ + HOOH $\overset{B}{\rightleftharpoons}$ $L_x^+Fe^{II}OOH(BH^+)$(**1**)]. The latter includes a 'stabilized' hydroxyl radical that is able to replace an aromatic hydrogen (H) with a hydroxyl group (HO) via an initial addition reaction. With $PhCH_3$ and $PhCH_2CH_3$ as substrates free HO· (from the radiolysis of H_2O) reacts via aryl addition (97 and 85%, respectively) to give Ar–Ar as the predominant product, whereas **1** favors H-atom abstraction from the alkyl group (50 and 80%, respectively) and the only detectable products from aryl addition are the respective substituted phenols (*o*:*p*-ArOH). Other substituted benzenes (PhX) undergo addition by free HO· at the *ortho* and *para* aryl carbons (*o*:*p* ratio, 2), followed by dimerization and elimination of two H_2O molecules to yield substituted biphenyls. In contrast, **1** reacts with PhX to yield substituted phenol (ArOH; *o*:*p* ratio, 0.5–1.1). With phenol (PhOH) as the substrate, reaction with **1** yields mainly catechol (*o*-$Ar(OH)_2$; *o*:*p* ratio, 20). In a solvent matrix of MeCN:H_2O (3:1 mol:mol ratio) the reaction efficiencies with $Fe^{II}(bpy)_2^{2+}$ and $Fe^{II}(OPPh_3)_4^{2+}$ for the hydroxylation of benzene to phenol are 36 and 42%, respectively (product per HOOH).

Introduction

Because most regard Fenton chemistry to be synonymous with the *in situ* production of hydroxyl radical (HO·),[1–5] there has been a belief that the reaction of aromatic substrates with free HO· (from radiolysis) and Fenton reagents is identical. However, free HO· reacts with toluene ($PhCH_3$) via aryl addition (97%) to give [$HOPhCH_3$],[6] which dimerizes and eliminates H_2O to yield aryl dimer $CH_3C_6H_4$–$C_6H_4CH_3$.[7] In contrast, the dominant products from the reaction of Fenton reagents with $PhCH_3$ are cresols, $PhCH_2OH$, PhCH(O), and PhC(O)OH.[8,9]

A recent study[10] of the reactivity of Fenton reagents with aliphatic hydrocarbons has demonstrated that the reactive intermediate is a nucleophilic adduct (rather than free HO·); [$L_x^+Fe^{II}OOH(BH^+)$] (**1**). Species **1** hydroxylates hydrocarbons, and in the presence of O_2 ketonizes methylenic carbons [e.g. *c*-C_6H_{12} → *c*-C_6H_{10}(O)] via oxygenated Fenton chemistry.[9]

Although numerous investigations have shown that Fenton reagents hydroxylate aromatic substrates,[11] the interpretations have assumed free HO· to be the reactive intermediate. When this is coupled with the recognition that the hydroxylation of aromatic molecules is a fundamental process in biology (e.g. phenylalanine hydroxylase and tyrosine hydroxylase)[12] and the chemical industry (e.g. autoxidation of cumene),[13] there is a clear need for a better understanding of iron(II)/HOOH chemistry. These considerations have prompted a systematic study of HOOH activation by several iron(II) complexes (Fenton reagents) for the hydroxylation of aromatic substrates via species **1**.

Results

Hydroxylation of benzene

Table 1 summarizes the yields of phenol and the reaction efficiencies from the combination of an iron(II) complex, HOOH, and benzene in three solvent matrices. The $Fe^{II}(bpy)_2^{2+}$ and $Fe^{II}(OPPh_3)_4^{2+}$ complexes in MeCN:H_2O (3:1 mol:mol) are the most efficient catalysts for the production of phenol at room temperature; 5 mM $Fe^{II}(OPPh_3)_4^{2+}$/50 mM HOOH yields 21 mM PhOH (42% efficient) and 5 mM $Fe^{II}(bpy)_2^{2+}$/50 mM HOOH yields 18 mM PhOH (36%). The $Fe^{II}(OPPh_3)_4^{2+}$ and $Fe^{II}(bpy)_2^{2+}$ complexes in MeCN:H_2O are 3–4 times more efficient toward aromatic hydroxylation than when the solvent matrix is pure MeCN (Table 1).

The $Fe^{II}(PA)_2$ complex in py:HOAc (2:1 mol:mol) also activates HOOH to produce phenol; 5 mM $Fe^{II}(PA)_2$/50 mM HOOH yields 10 mM PhOH (20% efficient relative to HOOH). When the same ratio of $Fe^{II}(PA)_2$/HOOH is used in a 1:1 py:HOAc solvent matrix, 14 mM PhOH is produced (29%).

Table 1. $Fe^{II}L_x$/HOOH induced hydroxylation of benzene in various solvent systems

$Fe^{II}L_x$/HOOH	phenol product (mM, ± 5%)[a] [reactn effn, %][b]				
	$Fe^{II}(bpy)_2^{2+}$		$Fe^{II}(OPPh_3)_4^{2+}$		$Fe^{II}(PA)_2$
(mM/mM)	MeCN	MeCN/H_2O[c]	MeCN	MeCN/H_2O[c]	py/HOAc[d]
5/10	1.3 [13]	4.0 [40]	0	3.9 [39]	1.8 [18]
5/20	2.6 [13]	7.1 [36]	1.4 [7]	7.9 [40]	4.2 [21]
5/50	5.6 [11]	18 [36]	5.3 [11]	21 [42]	10 [20][e]
10/10	1.4 [14]	3.8 [38]	0	2.8 [28]	1.7 [17]
10/20	2.4 [12]	7.7 [39]	0.9 [4]	5.9 [30]	3.9 [19]
10/50	5.3 [11]	18 [36]	3.4 [7]	17 [34]	9.9 [20]

[a]Benzene (1 M), $Fe^{II}L_x$, and HOOH combined in designated solvent to give indicated initial concentrations in a total volume of 5.0 mL. Product solutions were analyzed by capillary-column gas chromatography and GC–MS after a reaction time of 3 h at 24 ± 2 °C.
[b]Per cent reaction efficiency; mmol of PhOH per mmol of HOOH.
[c]90% MeCN:10% H_2O by volume (3:1 MeCN:H_2O mol:mol).
[d]2:1 pyridine:HOAc mol:mol.
[e]5 mM $Fe(PA)_2$:50mM HOOH in pyHOAc (1:1 mol:mol) yields 14 mM PhOH (efficiency, 28%).

Hydroxylation of substituted benzenes

Table 2 summarizes the product profiles for benzene and substituted benzenes when iron complexes activate HOOH under two sets of reaction conditions. The results in section A are for the combination of 5 mM $Fe^{II}L_x$ [$Fe^{II}(bpy)_2^{2+}$) or $Fe^{II}(OPPh_3)_4^{2+}$] and 50 mM HOOH with 1 M substrate (PhX) in a MeCN:H_2O solvent matrix, and those in section B are for the combination of 5 mM $Fe^{II}(PA)_2$ and 200 mM HOOH with 2 M substrate (PhX) in either a $(py)_{1.4}$HOAc or $(py)_2$HOAc solvent matrix.

For the substituted benzenes, hydroxylation occurs at the *para* (favored) and *ortho* positions. Toluene is distinctive because the alkyl substituent is preferentially oxygenated to $PhCH_2OH$, PhCH(O), and PhC(O)OH (up to 50% of the HOOH is utilized for side-chain oxygenation).

The $Fe^{II}(PA)_2$/$(py)_{1.4}$HOAc system gives larger product yields than the $Fe^{II}(PA)_2$/$(py)_2$HOAc system. When pyridine is a component of the solvent, these $Fe^{II}L_x$/HOOH systems yield significant amounts of 3-hydroxypyridine (3-HOpy) via hydroxylation of an aryl carbon center. In the absence of substrate, the $Fe^{II}(PA)_2$/$(py)_{1.4}$HOAc system (about 8.5 M pyridine) yields mainly 3-HOpy with some 2- and 4-hydroxy isomers (product ratios for 3-HOpy:2-HOpy:4-HOpy; 7.4:3.0:1.0). Small amounts of pyridine coupling products (2,2'-, 4,4'-, and 2,4'-bpy) are also formed.

The predominant product from the hydroxylation of substituted-benzene substrates is the *p*-isomer, with the exception of anisole (MeOPh) and phenol. Hydroxylation of MeOPh with the $Fe^{II}(PA)_2$/$(py)_{1.4}$HOAc and $Fe^{II}(PA)_2$/$(py)_2$HOAc systems yields *o*:*p* product ratios of 2.4 and 2.7, respectively (Table 2). For $Fe(bpy)_2^{2+}$ or $Fe^{II}(OPPh_3)_4^{2+}$ in MeCN:H_2O, the *o*:*p* ratio is 1.0. When phenol (PhOH) is the substrate, the *ortho* dihydroxy isomer (catechol) is the major or sole product.

Reaction dynamics

The rate of formation of phenol from benzene (1–2 M) by the $Fe^{II}(PA)_2$ (2.5–5.0 mM)/HOOH (100–200 mM)/$(py)_{1.4}$HOAc system conforms to a rate law that is first-order each in the concentration of $Fe^{II}(PA)_2$, HOOH, and benzene. On the basis of initial rates of reaction, the apparent rate constant, k_{ox}, is 7.8×10^{-3} M^{-2} s^{-1} at 25 °C {$d[PhOH]/dt = k_{ox}[Fe^{II}(PA)_2][HOOH][PhH]$}. The apparent rate constants ($k_{ox} \times 10^3$) for the other substrates are: $PhCH_3 \rightarrow$ *o*-ArOH, 4.3 and *p*-ArOH, 3.8; PhCl → *o*-ArOH, 1.9 and *p*-ArOH, 1.7; PhOMe → *o*-ArOH, 9.5 and *p*-ArOH, 3.3; and py → 3-HOpy, 0.23.

The normalized active-site rate constants ($k' \times 10^3$) [$k' = k(ortho)/2 + k(para)$] for the substrates are: PhOMe, 4.3; PhMe, 2.7; PhH ($k/3$), 2.6; PhBu-*t*, 2.2; PhCl, 1.2; and pyridine, 0.2. Electron donating groups activate the aromatic ring for hydroxylation reactions, whereas electron withdrawing groups produce the opposite effect.

Discussion and Conclusions

The results of Tables 1 and 2 demonstrate that the $Fe^{II}(OPPh_3)_4^{2+}$, $Fe^{II}(bpy)_2^{2+}$, and $Fe^{II}(PA)_2$ complexes activate hydrogen peroxide for the efficient hydroxylation of aromatic substrates. The $Fe^{II}(OPPh_3)_4^{2+}$ and $Fe^{II}(bpy)_2^{2+}$ complex systems in MeCN:H_2O are superior, with efficiencies of 42 and 36% for the conversion of benzene to phenol. The 5 mM $Fe^{II}(PA)_2$:200 mM HOOH:2 M benzene system in $(py)_{1.4}$HOAc is also effective with an efficiency of 29% and nearly 12 catalytic cycles with respect to $Fe^{II}(PA)_2$.

In accord with previous work,[8–10] the present results confirm that the primary chemistry of HOOH is nucleophilic addition to the iron complex to give the reactive intermediate (**1**) of Fenton chemistry (not free HO·)

$$L_x^{2+}Fe^{II} + HOOH \underset{(B = py,\ H_2O)}{\overset{B}{\rightleftharpoons}} [L_x^{+}Fe^{II}OOH(BH^{+})]\ (\mathbf{1}) \qquad (1)$$

Species **1** reacts with aromatic rings to give their hydroxylated derivatives. Table 3 compares the primary

Table 2. $Fe^{II}L_x$/HOOH-induced hydroxylation of substituted-benzene substrates (PhX)

$Fe^{II}L_x$/ solvent	substrate	products (mM, ± 5%)[a]					
	(PhX)	*o*-ArOH	*p*-ArOH	*o*:*p* Ratio	effn,[b] %	(3-HOpy)	others (mM)
A. 5 mM $Fe^{II}L_x$/50 mM HOOH/1 M PhX							
$Fe^{II}(bpy)_2^{2+}$/ MeCN/H_2O[c]	PhH	18			36		
	PhMe	3.2	3.1	1.0	13		PhCH(O) (3.6) PhC(O)OH (1.0) $PhCH_2OH$ (0.6)
	PhBu-*t*	0.7	3.2	0.2	8		
	PhCl	7.3	6.1	1.2	27		
	PhOMe	1.2	1.2	1.0	5		
	PhOH	13	0	∞	26		
$Fe^{II}(OPPh_3)_4^{2+}$/ MeCN/H_2O[c]	PhH	21			42		
	PhMe	2.9	2.4	1.2	11		PhCH(O) (5.0) PhC(O)OH (0.7) $PhCH_2OH$ (0.4)
	PhBu-*t*	0.9	3.3	0.3	8		
	PhCl	6.2	5.3	1.2	23		
	PhOMe	0.7	0.7	1.0	3		
	PhOH	9.8	0	∞	20		
B. 5 mM $Fe^{II}L_x$/200 mM HOOH/2 M PhX							
$Fe^{II}(PA)_2$/ $(py)_{1.4}HOAc$[d]	PhH	53			27	(5)	
	PhMe	24	22	1.1	23	(3)	PhCH(O) (22) PhC(O)OH (14) $PhCH_2OH$ (8.0)
	PhBu-*t*	11	22	0.5	17	(6)	
	PhCl	20	24	0.8	22	(6)	
	PhOMe	36	11	2.4	24	(3)	
	PhOH	19	1	29	15		
$Fe^{II}(PA)_2$/ $(py)_2HOAc$[e]	PhH	27			14	(12)	
	PhMe	21	13	1.6	17	(4)	PhCH(O) (16) PhC(O)OH (16) $PhCH_2OH$ (7.0)
	PhBu-*t*	8	17	0.5	12	(11)	
	PhCl	8	12	0.7	10	(4)	
	PhOMe	48	18	2.7	33	(5)	
	PhOH	45	4	11	25	(4)	

[a] PhX substrate, $Fe^{II}L_x$, and HOOH combined in designated solvent to give the indicated initial concentrations in a total volume of 5.0 mL. Product solutions were analyzed by capillary-column gas chromatography and GC–MS after a reaction time of 3 h at 24 ± 2 °C.
[b] Per cent reaction efficiency; mmol of total ArOH products (*o* + *p*) produced per mmol of HOOH.
[c] 90% MeCN:10% H_2O by volume; (3:1 MeCN:H_2O mol:mol).
[d] 1.4:1 pyridine:HOAc mol:mol.
[e] 2:1 pyridine:HOAc mol:mol.
[f] 5 mM $Fe^{II}(PA)_2$/50 mM HOOH in py,HOAc (with 1 M PhOH) produced 11 mM *o*-Ar(OH), and 0.8 mM *p*-Ar(OH), (*o*:*p* ratio, 14; efficiency, 24%).
[g] 5 mM $Fe^{II}(PA)_2$/50 mM HOOH in (py)HOAc (with 1 M PhOH) produced 9.0 mM *o*-Ar(OH), and 0.3 mM *p*-Ar(OH), (*o*:*p* ratio, 30; efficiency, 19%).

products from the reaction of several aromatic substrates with (a) Fenton reagents and (b) free hydroxyl radical (HO·). With toluene ($PhCH_3$) as a substrate, free hydroxyl radical (from pulse radiolysis) favors aryl addition over alkyl-hydrogen abstraction (30:1) and gives dimer (CH_3Ar–$ArCH_3$) as the detectable product.[6] In contrast, species **1** favors alkyl oxygenation and aryl hydroxylation.

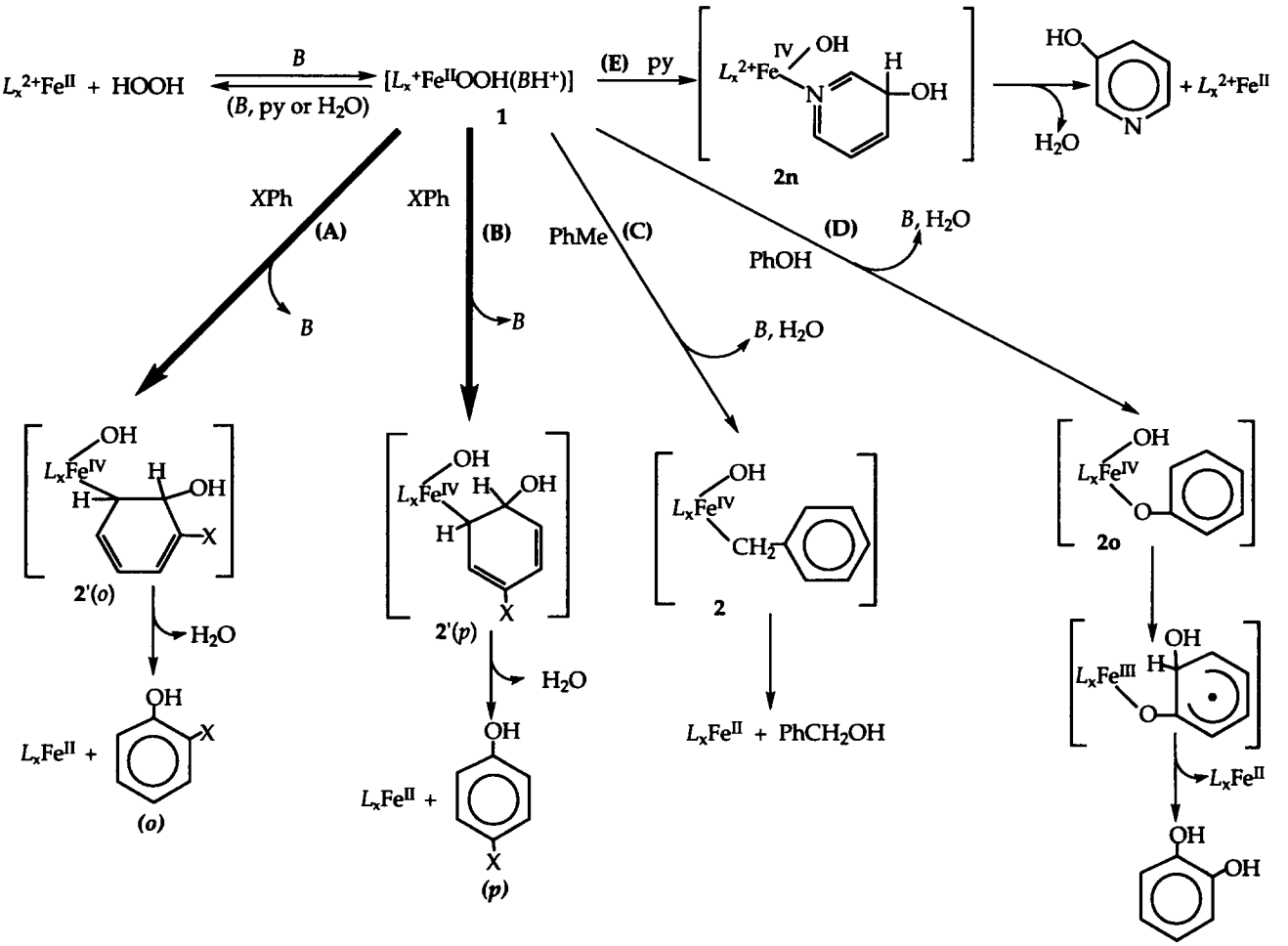
The reaction of pyridine with free HO· (from pulse radiolysis[6] or photochemical decomposition of *N*-hydroxy-2-thiopyridine[14]) yields the 2-hydroxy pyridine (2-HOpy) and 4-HOpy isomers (2:1 ratio) with only a small amount of 3-HOpy. In contrast, species **1** of the $Fe^{II}(PA)_2$/$(py)_xHOAc$ systems yields 3-HOpy as the major product (Table 2).

Although $Fe^{II}(bpy)_2^{2+}$ and $Fe^{II}(OPPh_3)_4^{2+}$ are the most efficient catalysts for the hydroxylation of aromatic substrates via Fenton chemistry, their species **1** are unreactive with saturated hydrocarbons (e.g. *c*-C_6H_{12}).[10] Clearly,

Table 3. Comparison of Fenton reagents and hydroxyl radicals (HO·, from radiolysis of H_2O) in their reactivity with aromatic molecules (ArH)

	primary products	
Substrate (ArH)	Fenton Reagents (1)[a]	HO·[b]
PhH	PhOH	(HO)PhH → Ph–Ph
$PhCH_3$	ArOH (*o*:*p* = 1.0) (50%)	HOArH (*o*:*p* = 2.0)(97%) → Ar–Ar
	[$PhCH_2OH$ + PhCH(O) + PhC(O)OH] (50%)	$PhCH_2$· (3%) → $PhCH_2CH_2Ph$
$PhCH_2CH_3$	ArOH (18%)	HOArH(85%) → Ar–Ar
	$PhC(O)CH_3$ (82%)	PhCHCH$_3$(15%) → PhCH(Me)CH(Me)Ph
PhOH	$C_6H_4(OH)_2$ (*o*:*p* = 11 → ∞)	$(HO)_2C_6H_5$ (*o*:*p* = 2.0) → HOC_6H_4-C_6H_4OH
py	3-pyOH (*m*:*o*:*p* = 5/2/1)	HOpy (*o*:*p* = 2.0) → py–py

[a] $Fe^{II}(bpy)_2^{2+}$ and $Fe^{II}(OPPh_3)_4^{2+}$ in MeCN:H_2O, and $Fe^{II}(PA)_2$ in py:HOAc (Tables 1 and 2).
[b] Ref. 6.



Scheme 1. Proposed reaction pathways for the hydroxylation of aromatic molecules via Fenton chemistry.

these reactive intermediates (1) are able to transfer an HO· to aromatic substrates, but can not break a C–H bond (96 kcal mol^{-1}) of cyclohexane (in contrast to free HO· or a $Fe^{II}(PA)_2$/HOOH Fenton reagent).[9]

Scheme 1 outlines a reasonable set of reaction paths for the $Fe^{II}L_x$-induced activation of HOOH for the hydroxylation of aromatic substrates via species **1**. The 'stabilized HO·' [species **1**; estimated stabilization (bond energy), 10–15 kcal mol^{-1}] reacts with the substrate via addition to form species **2'**(*o*) or **2'**(*p*) (path A or B). Because the substituent (X) apparently blocks one of the two adjacent positions to *ortho*-addition of HO· [intermediate **2'**(*o*)], *para*-addition is favored [intermediate **2'**(*p*)] by a factor of up to 2:1 (Table 2). The resultant species **2'**(*o*) and **2'**(*p*) (stabilized by an Fe–C bond) collapse to yield the *ortho*- or *para*-hydroxylated product, water, and the initial iron complex ($Fe^{II}L_x$). Alternatively, this selectivity may be due in part to stereoelectronic or steric effects. The relative yields of the *para*-hydroxylated product [*p*-HOPhCl > *p*-HOPhBu-*t* ≈ *p*-HOPhMe > *p*-HOPhOMe, Table 2] provide a measure of the inductive

effect for the substitituents. The aromatic hydroxylation via path **B** at the *para*-position makes these systems effective mimics of phenylalanine hydroxylase.[12]

With $PhCH_3$ as the substrate, oxygenation of the methyl side chain is favored (relative to aryl addition) via path C to form **2**, which collapses to form benzyl alcohol and $Fe^{II}L_x$. Toluene also reacts via oxygenated Fenton chemistry:[9]

$$PhCH_3 + HOOH + O_2 \xrightarrow{L_xFe^{II}} PhCH(O) + PhCH_2OH + 2\,H_2O \quad (2)$$

With MeOPh, the *ortho* positions clearly are favored for attack by the $Fe^{II}(PA)_2$/HOOH/$(py)_x$HOAc system (*o:p* ratio, 2.4–2.7). This appears to be due to an acid–base interaction of the non-bonding oxygen electron pairs of the methoxy group with the metal center of species **1**.

The almost exclusive production of catechol [*o*-$Ar(OH)_2$] from phenol (PhOH) via *ortho*-hydroxylation by species **1** is unique among the substrates and must occur via a path other than A. The favored side-chain attack of the weak C–H bond of $PhCH_3$ (H–CH_2Ph; ΔH_{DBE} = 88 kcal mol^{-1}) via path C indicates that the O–H bond of phenol (H–OPh; ΔH_{DBE} = 86.5 kcal mol^{-1})[10] should be susceptible to H-atom abstraction by species **1** to give **2o** (path D, Scheme 1). The latter rearranges via (HO)-transfer from the iron center and dissociates to *o*-$Ar(OH)_2$ and $Fe^{II}L_x$. Apparently, the three atom separation (O–C–C) of **2o** favors transfer to the *ortho* position. The hydroxylation of PhOH via path D at the *ortho*-position makes these systems effective mimics of tyrosine hydroxylase.[12]

The basicity of the nitrogen in pyridine promotes interaction with the iron center of species **1** and the subsequent intramolecular transfer of an HO· group to the 3-position [another three-atom separation (N–C–C) from the iron] to give species **2n** via path E of Scheme 1. Elimination of H_2O from **2n** yields 3-HOpy and $Fe^{II}L_x$.

The apparent rate constants for aromatic hydroxylation by the $Fe^{II}(PA)_2$/HOOH/$(py)_{1.4}$HOAc system decrease in the order MeOPh > MePh > HPh > ClPh. This is consistent with an inductive effect from the substituent group to increase the electron density of the aromatic ring and its propensity to add an electrophilic HO· group (primarily at the *para* position and secondarily at the *ortho* position).

Specific base interactions by MeOPh favor *o*-hydroxylation and by pyridine favor the production of 3-HOpy. The weak C–H bond of $PhCH_3$ and O–H bond of PhOH cause these substrates to undergo H-atom abstraction by **1** in a primary step, with subsequent transfer of an HO· to give $PhCH_2OH$ and *o*-$Ph(OH)_2$, respectively.

Although the cost of HOOH and the reaction efficiencies for the $Fe^{II}L_x$/HOOH systems preclude their use to replace current industrial processes for the production of phenol (mainly from the autoxidation of cumene),[13] the selectivity and mild conditions of these Fenton reagents may provide unique advantages for the synthesis of fine chemicals and pharmaceuticals (e.g. L-dopa from L-tyrosine). Another consideration is that the chemistry of Scheme 1 can readily occur in a biological matrix from the combination of dysfunctional iron and HOOH. The efficient and selective reactivity of **1** with aromatic substrates makes it a more reasonable cytotoxic agent than free HO· within the oxy-radical theory of aging and heart disease.[16,17]

Experimental

Equipment

The reaction products were separated and identified with a Hewlett-Packard 5880A Series gas chromatograph equipped with a HP-1 capillary column (cross-linked methyl silicone gum phase, 12 m × 0.2 mm i.d.) and by gas chromatography–mass spectrometry (Hewlett-Packard 5790A gas chromatograph with a mass-selective detector).

Chemicals and reagents

The reagents for the investigations and syntheses were the highest purity commercially available and were used without further purification. Burdick and Jackson 'distilled in glass' grade acetonitrile (MeCN, 0.004% H_2O), pyridine (py, 0.014% H_2O), and glacial acetic acid (HOAc, ACS grade, Fisher) were used as solvents. All compounds were dried *in vacuo* over $CaSO_4$ for 24 h prior to use. Picolinic acid (PAH, 99%), 2,2'-bipyridine (bpy, 99+%), and triphenylphosphine oxide ($OPPh_3$, 98%) were obtained from Aldrich. Hydrogen peroxide (50% H_2O) was obtained from Fisher. The organic substrates obtained from Aldrich included: benzene, *t*-butylbenzene (99%), chlorobenzene (99+%), toluene (99+%, anhydrous), phenol (99%), and anisole (methoxybenzene, 99+%).

Syntheses of $(Me_4N)PA$

Tetramethylammonium picolinate [$(Me_4N)PA$] was prepared by the neutralization of picolinic acid (PAH) with tetramethylammonium hydroxide pentahydrate in aqueous solution. $(Me_4N)PA$ was recrystallized from acetonitrile. The hydroscopic products were stored under vacuum.

$[Fe^{II}(MeCN)_4](ClO_4)_2$

The $[Fe^{II}(MeCN)_4](ClO_4)_2$ complex was prepared by multiple recrystallizations of $[Fe^{II}(H_2O)_6](ClO_4)_2$ from MeCN.

Bis(picolinato)iron(II) solutions

The $Fe^{II}(PA)_2$ complex was prepared *in situ* by mixing $[Fe^{II}(MeCN)_4](ClO_4)_2$ with stoichiometric ratios of the ligand anion.

Bis(2,2'-bipyridine)iron(II) solutions

The $Fe^{II}(bpy)_2^{2+}$ complex was prepared *in situ* by mixing $[Fe^{II}(MeCN)_4](ClO_4)_2$ in MeCN with stoichiometric ratios of the bpy ligand.

Tetrakis(triphenylphosphine oxide)iron(II) solutions

The $Fe^{II}(OPPh_3)_4^{2+}$ complex was prepared *in situ* by mixing $[Fe^{II}(MeCN)_4](ClO_4)_2$ in MeCN with stoichiometric ratios of the $OPPh_3$ ligand.

Methods

The investigations of HOOH activation by the iron complexes ($Fe^{II}L_x$) used solutions that contained 1.0–3.0 M substrate (PhX), and 5–10 mM $Fe^{II}L_x$ in an appropriate solvent matrix [MeCN, MeCN:H_2O (3:1 mol:mol), py:HOAc (2:1 mol:mol)]. Total reaction solution volumes were 5.0–7.0 mL. The process was initiated by the addition of HOOH into the septum-covered glass reaction cell (volume, 21 mL; 17 mL of headspace) to give 5–200 mM HOOH. After reaction times of 3–18 h with constant stirring at room temperature (24 ± 2 °C), samples of the reaction solutions were injected into a capillary-column gas chromatograph for analysis. In some cases, the reaction was quenched with H_2O, and the product solution was extracted with Et_2O. Product species were characterized by GC–MS. Reference samples were used to confirm product identifications and to produce standard curves for quantitative assays of the product species.

The experiments were designed to be limited by HOOH in order to (a) evaluate the primary reaction efficiency with respect to oxidant and (b) minimize secondary reaction products from the primary products.

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