independent determinations were made for a given photooxygenation temperature and solvent; the reproducibility among independent runs was ±3%. For photooxygenation of **9** in CS_2 solution, the mixture was combined with 0.50 mL of acetone-d_6 before analysis to dissolve the precipitated **10**.

The yield of the [2 + 2] cycloaddition product **12** was determined by NMR spectroscopy from the integral of the methoxy resonance (δ 3.61) of the mono methyl ester of **13**, with *p*-dichlorobenzene as the internal standard. For photooxygenation in MeOH, the reaction mixture was kept at room temperature for 2 h, the resulting solution was concentrated under vacuum, and the residue was dissolved in acetone-d_6 for analysis. For photooxygenation in CS_2, the reaction mixture was dissolved in 0.50 mL of ether and then added to 3 mL of MeOH, after which, the above procedure for photooxygenation in MeOH was followed. For photooxygenation in acetone-d_6 at −78 °C, the reaction mixture was immediately poured into 5 mL of MeOH and the above analysis procedure performed. For photooxygenation at 0 °C in acetone-d_6, the enol lactone was photooxygenated for 5 min and then immediately poured into 5 mL of MeOH, after which the analysis procedure was performed.

Determination of k_r by Competitive Photooxygenation. The relative rate constants (k_A/k_B) of two $^1O_2$ substrates (A and B), when photooxygenated competitively, were determined by using the relationship $k_A/k_B = \ln([A]_0/[A]_t)/\ln([B]_0/[B]_t)$.[10] Enol acetate **1** was photooxygenated in competition with 2-methyl-2-pentene (2M2P). The relative rate of disappearance of **1** and 2M2P was determined by integration of the vinyl hydrogens in the NMR spectrum of these compounds with *p*-dichlorobenzene as an internal standard. The value of k_r for **1** was calculated by using the value of k_r for 2M2P reported by Manring and Foote.[10a] The value of k_r for **7** was determined in the same manner by competition with **1**.

The value of k_r for **9** was determined by its competitive photooxygenation with 2M2P. After photooxygenation, the mixture was reduced with an excess of Ph_3P and analyzed by GC (injector = 220 °C; oven = 3 min at 40 °C and then 15 °C/min to 200 °C; He = 30 mL/min), using tridecane as an internal standard. In this way, the disappearance of **9** and the appearance of the two photooxygenation products of 2M2P (P_1 and P_2) were followed. Using the relationship $\ln([2M2P]_0/[2M2P]_t) = \ln\{[P_1 + P_2]_f/([P_1 + P_2]_f - [P_1 + P_2]_t)\}$ (where $[P_1 + P_2]_f$ = concentration of the sum of the products after complete conversion of 2M2P), the relative rate constants were determined by plotting $\ln\{[P_1 + P_2]_f/([P_1 + P_2]_f - [P_1 + P_2]_t)\}$ vs. $\ln([\mathbf{9}]_0/[\mathbf{9}]_t)$. The response factors of P_1 and P_2 were determined by taking 2M2P to complete conversion and using the values reported by Manring and Foote for P_2/P_1.[10a] The value of k_r for **9** was then calculated from the reported value of k_r or 2M2P.[10a]

Acknowledgment. This work was supported by grants from the National Science Foundation and from the Office of Naval Research. We thank Dr. John Hurst, formerly of this Department, for his assistance with the measurement of the rate constants.

Registry No. **4**, 101470-98-8; **5**, 101470-99-9; **7**, 91056-64-3; **8**, 6553-64-6; **9**, 700-82-3; **10**, 101471-00-5; **11**, 101471-01-6; **13**, 71759-57-4; **13** (monomethyl ester), 101403-81-0; 2-adamantyl methyl ketone, 22635-58-1; 2,2-dimethylcyclohexanone, 1193-47-1; 2-oxocyclohexanepropanoic acid, 2275-26-5.

Kinetics of the Oxidation of Isoquinolinium Cations by Ferricyanide Ion

John W. Bunting* and Dimitrios Stefanidis

Department of Chemistry, University of Toronto, Toronto, Ontario M5S 1A1, Canada

Received April 19, 1985

The rates of the ferricyanide oxidation of a number of isoquinolinium cations have been investigated in the range pH 11–14 in 20% CH_3CN–80% H_2O at 25 °C (ionic strength 1.0). The oxidation of the 2-methylisoquinolinium cation is kinetically first order in each of ferricyanide ion and isoquinolinium cation but is subject to pronounced inhibition by the ferrocyanide ion reaction product. Second-order rate constants evaluated from initial reaction rates display a pH dependence which is consistent with rate-determining ferricyanide attack on the pseudobase alkoxide ion derived from the isoquinolinium cation. Ferrocyanide ion inhibition is shown to be consistent with this initial electron transfer being a reversible process. Similar observations are made for a number of substituted isoquinolinium cations. Substituent effects are shown to be consistent with electron abstraction from the endocyclic nitrogen atom rather than the exocyclic oxyanion of these pseudobase alkoxide ions. The initially formed radical then undergoes a base-catalyzed deprotonation from C-1, and this is confirmed by deuterium kinetic isotope effects when a deuterium label is present at C-1. The combination of these pH effects leads to ferrocyanide ion inhibition becoming less pronounced with increasing pH. These observations have prompted us to reinvestigate the ferricyanide ion oxidation of some of the 5-nitroisoquinolinium cations that we have previously studied.[1] We find that ferrocyanide ion inhibition is observable when the initial rates of these reactions are examined in the stopped-flow spectrophotometer. Detailed kinetic analysis of these oxidations is shown to be consistent with the reaction scheme detailed above for the 2-methylisoquinolinium cation. In the light of this work, we must now withdraw our earlier claim for rate-determining hydride abstraction in these reactions. Substituent effects on the oxidation of these isoquinolinium cations allow the development of a relationship which can be used to predict the pH–rate profile for the ferricyanide ion oxidation of any isoquinolinium cation for which pK_{R^+} for pseudobase formation is available, provided that steric hindrance from the N substituent is not significant.

There have been recent reports from our laboratory on the kinetics of oxidation of 5-nitroisoquinolinium[1] and acridinium[2] cations by ferricyanide ion in aqueous base. Both of these reactions were characterized by rate laws which appeared cleanly first order in each of ferricyanide ion and heterocyclic cation. Unlike many other ferricyanide ion oxidations,[3-5] these reactions gave no indication

---

(1) Bunting, J. W.; Lee-Young, P. A.; Norris, D. J. *J. Org. Chem.* **1978**, *43*, 1132.

(2) Bunting, J. W.; Kauffman, G. M. *Can. J. Chem.* **1984**, *62*, 729.

(3) Thyagarajan, B. S. *Chem. Rev.* **1958**, *58*, 439.

(4) Wilson, I. R. *Rev. Pure Appl. Chem.* **1966**, *16*, 103.

0022-3263/86/1951-2060$01.50/0

of being susceptible to inhibition by the ferrocyanide ion reaction product.

We have recently been extending these kinetic studies of ferricyanide ion oxidation to other heterocyclic cations. In the course of these studies, we have found that inhibition by ferrocyanide is observable during the oxidation of some heterocyclic cations. We report, herein, a detailed analysis of this phenomenon for the ferricyanide oxidation of the 2-methylisoquinolinium cation. These observations have lead us to reexamine the kinetics of the oxidation of 5-nitroisoquinolinium cations by ferricyanide ion. We find that the initial rates of these reactions are extremely sensitive to inhibition by ferrocyanide ion but that this inhibition is only observable when the initial rates of reaction are examined in the stopped-flow spectrophotometer.

Experimental Section

All isoquinolinium cations were prepared by alkylation of the appropriate isoquinoline derivative with the appropriate alkyl bromide in acetone solution in a pressure bottle at room temperature. The precipitated salts were recrystallized several times from ethanol and characterized by titration of the bromide ion with silver nitrate solution and by ^1H NMR spectroscopy with comparison with the spectra of authentic samples that were available from previous studies[6,7] in most cases.

1-Deuterioisoquinolinium cations were prepared by refluxing the salts of the corresponding protio cations in D_2O for 1 h. After evaporation of the solvent, the recovered salts were recrystallized from ethanol. ^1H NMR spectra were identical with those of the protio cations with the exception of the absence of the characteristic downfield singlet for the C(1) proton.

Kinetic Studies. All rate data were collected at 25 °C in 20% acetonitrile–80% water (v/v) at ionic strength 1.0 (KCl + KOH). Variation of pH was achieved with appropriate standard solutions of potassium hydroxide in the range pH 11–14, while 0.05 M carbonate buffers were employed in the range pH 10–11. All pH values were measured on a Radiometer PHM82 pH meter that had been standardized for use in these aqueous acetonitrile solutions by the procedure previously described.[2] Most rate data were collected by mixing a solution of the isoquinolinium bromide and potassium ferricyanide (and potassium ferrocyanide in some cases) in neutral 40% acetonitrile–60% water (v/v) with the required double strength buffer solution in the Durrum–Gibson stopped-flow spectrophotometer. All rate data refer to air-equilibrated solutions unless otherwise indicated. The influence of oxygen upon oxidation rates (Table V) was evaluated by using solutions which had been extensively deoxygenated by bubbling nitrogen for at least 1 h.

The oxidation of 5-nitroisoquinolinium cations was monitored by following the decrease in absorbance at 500 nm due to the pseudobase and/or its alkoxide ion. Other cations were monitored by following the decrease in absorbance at 420 nm upon reduction of ferricyanide ion to ferrocyanide. Absorbance vs. time curves were digitized into 118 data points. These data were then transferred to a Tektronix 4051 minicomputer for rate constant analysis. Reactions of the 4-cyano-2-methylisoquinolinium cation were sufficiently slow that they could be followed on the Cary 210 spectrophotometer.

Results

The 2-methylisoquinolinium cation is rapidly oxidized to 2-methyl-1-isoquinolinone by ferricyanide ion in aqueous base. On the basis of ^1H NMR spectral observations, this product was the only species present in chloroform extracts from basic solutions of these two reactants. The time dependence of the electronic absorption spectrum of a mixture of the 2-methylisoquinolinium cation and potassium ferricyanide in stoichiometric molar ratio (1:2) displays a clean isosbestic point at 297 nm, and the final spectrum is superimposable upon that of an authentic 1:2 mixture of 2-methyl-1-isoquinolinone and potassium ferrocyanide in this same reaction medium.

Table I. Second-Order Rate Constants Based upon the Initial Rates of Oxidation of the 2-Methylisoquinolinium Cation by Ferricyanide Ion[a]

$[IQ^+]$, mM	$[Fe(CN)_6^{3-}]$, mM	k_{2i}, M^{-1} s^{-1}
0.1	0.1	1150
0.2	0.1	1270
0.4	0.05	1400
0.4	0.1	1200
0.4	0.2	1000
		av = 1200 ± 200

[a] At pH 13.4, in 20% CH_3CN–80% H_2O, ionic strength 1.0, at 25 °C.

This reaction may be readily monitored by following the decrease in absorbance at 420 nm as ferricyanide ion is reduced to ferrocyanide ion. We have studied the time dependence of the absorbance at this wavelength for stoichiometric, and near stoichiometric, ratios of reactants and also for reactions in which the 2-methylisoquinolinium cation is in large excess over the ferricyanide oxidant over the range pH 11–14, in 20% CH_3CN–80% H_2O (v/v), ionic strength 1.0 at 25 °C. As discussed below, the observations at these quite different concentration ratios are consistent and allow the independent evaluation of rate constants which are identical within experimental error.

When the time dependence of the reaction for stoichiometric ratios of reactants is analyzed in terms of the integrated form of a rate law that assumes the reaction to be kinetically first order in each reactant, a nonlinear kinetic plot is obtained. A linear relationship is apparent at the start of the reaction; however, as the reaction progresses, the data deviate from this initial linearity in a way that suggests a decrease in second-order rate constant. The extent of the initial linear region in these second-order plots is pH-dependent. At pH 14, linearity is apparent for almost the complete reaction; the extent of the linear region decreases with decreasing pH until at pH <12.0 there is no significant linearity and initial rate constants can no longer be estimated. Attempts to fit the data to other combinations of zero-, first-, and second-order dependence on each reactant were also unsuccessful.

Second-order rate constants (k_{2i}) evaluated from the initial linear regions of these second-order plots are listed as a function of the concentration of each reactant in Table I. It is clear that these rate constants are independent of reactant concentration. Rate laws that assume kinetic orders other than first order in each reactant do not produce such concentration-independent rate constants when calculated from the initial rate data. Thus, the apparent nonlinearity in the second-order kinetic plots seems only to be consistent with a reaction which is kinetically first order in each component but which is also subject to a decrease in apparent rate constant as the reaction progresses.

One simple cause of a decrease in apparent rate constant is inhibition by a reaction product. Since there are many known cases of inhibition of ferricyanide ion oxidations by ferrocyanide ion,[3-5] we have investigated the influence of added ferrocyanide ion on the rates of this reaction. It was found that the presence of added ferrocyanide ion does dramatically reduce the rates of these oxidations. Of particular interest is the observation that the extents of the linear regions of these second-order plots are signifi-

---

[5] Powell, M. F.; Wu, J. C.; Bruice, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 3850.

[6] Bunting, J. W.; Norris, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 1189.

[7] Bunting, J. W.; Chew, V. S. F.; Sindhuatmadja, S. *Can. J. Chem.* **1981**, *59*, 3195.

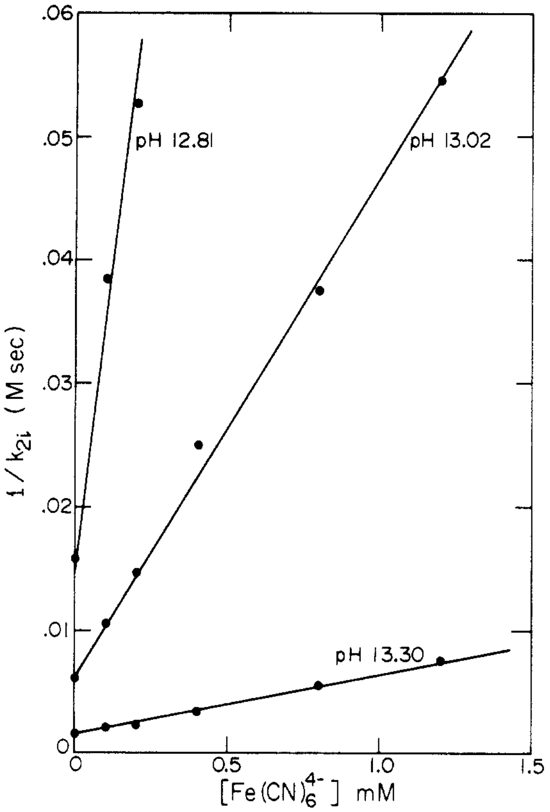


Figure 1. Influence of ferrocyanide ion upon the second-order rate constant for the ferricyanide oxidation of the 2-methylisoquinolinium cation.

Table II. Pseudo-First- and Second-Order Rate Constants Based upon the Initial Rates of Oxidation of the 2-Methylisoquinolinium Cation by Ferricyanide Ion[a]

$[IQ^+]$, mM	$[Fe(CN)_6^{3-}]$, mM	k_{1i}, s^{-1}	k_{2i}, M^{-1} s^{-1}
3.0	0.2	1.16	193
6.0	0.1	1.80	150
	0.2	1.95	163
	0.4	2.05	171
	0.5	2.13	177
12.0	0.2	3.90	163
			av = 170 ± 20

[a] At pH 13.0, in 20% CH_3CN–80% H_2O, ionic strength 1.0, at 25 °C.

cantly increased by added ferrocyanide ion. At high ferrocyanide ion concentrations, clean second-order kinetic behavior is observed for essentially the complete reaction. Apparent second-order rate constants as a function of initial ferrocyanide ion concentration are shown in Figure 1. Addition of the other reaction product, 2-methyl-1-isoquinolinone, had no influence on the reaction kinetics at concentrations similar to those used in the ferrocyanide ion inhibition experiments.

Further kinetic studies were also carried out for reactions in which the 2-methylisoquinolinium cation was in 10- to 30-fold excess over the ferricyanide ion. Under such conditions, a reaction which is formally first order in each reactant should approximate pseudo-first-order behavior in the limiting reactant. Pseudo-first-order kinetic plots for these reaction conditions are also curved, implying a decrease in apparent first-order rate constant as the reaction progresses but also seem to approach linearity again late in the reaction. Again the initial linear region extends over more of the reaction at high pH than in less basic solutions, and the pseudo-first-order rate constants (k_{1i}) evaluated from the initial rates are independent of ferricyanide ion concentration at constant 2-methylisoquinolinium cation concentration (Table II). Such pseudo-first-order rate constants are proportional to the concentration of 2-methylisoquinolinium cation and allow the evaluation of second-order rate constants (Table II).

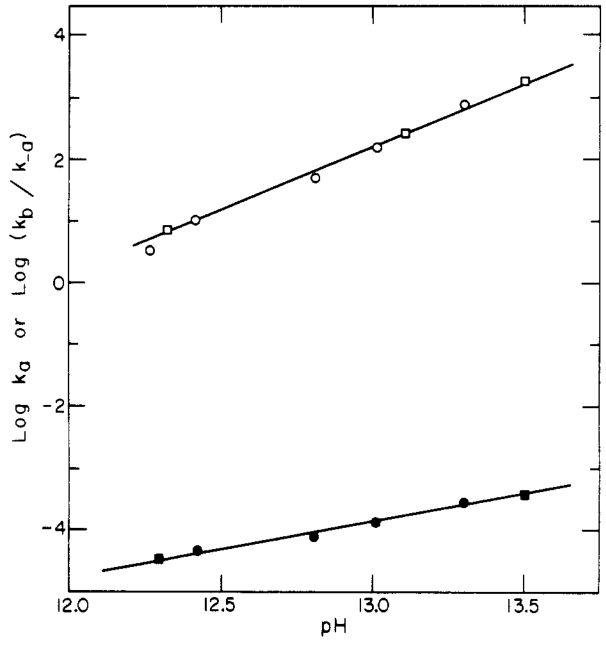


Figure 2. The pH dependence of log k_a (= log k_{2i}) (○ and □: slope 2.0) and log (k_b/k_{-a}) (● and ■: slope 1.0) for the ferricyanide oxidation of the 2-methylisoquinolinium cation at 0.1 mM (□ and ■) or 3 mM (○ and ●).

Scheme I

$$IQ^+ + Fe^{III} \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} X + Fe^{II}$$

$$X \xrightarrow{k_b} Y$$

$$Y + Fe^{III} \xrightarrow{\text{fast}} Fe^{II} + \text{2-methyl-1-isoquinolinone}$$

The influence of added ferrocyanide ion on these pseudo-first-order kinetic studies is similar to that shown in Figure 1 for an analogous study under second-order conditions. The extent of the initial linear regions increases in the presence of added ferrocyanide ion, with the complete reaction approaching pseudo-first-order behavior at high concentrations of this species. Some second-order rate constants estimated for these inhibited reactions from data obtained under pseudo-first-order conditions are included in Figure 1 and are found to be in agreement with values obtained directly from second-order kinetic studies.

The pH dependence of k_{2i} is shown in Figure 2. This figure includes data determined directly under second-order kinetic conditions (e.g., Table I) as well as data from pseudo-first-order kinetic experiments (e.g., Table II). Data from these two types of experiment fit the same linear plot of slope 2.0 within experimental error.

A kinetic scheme that is consistent with the observed first-order dependence upon 2-methylisoquinolinium cation (IQ^+) and ferricyanide ion (Fe^{III}) and also includes inhibition by ferrocyanide ion (Fe^{II}) is shown in Scheme I.

If it is assumed that the intermediate species X is a steady-state intermediate, then Scheme I generates rate eq 1, where $[IQ^+]_0$, $[Fe^{III}]_0$, and $[Fe^{II}]_0$ represent the initial concentrations of these species.

$$\frac{-d[Fe^{III}]}{dt} = [k_a k_b([IQ^+]_0 - 0.5([Fe^{III}]_0 - [Fe^{III}])) \times [Fe^{III}]]/[k_b + k_{-a}([Fe^{II}]_0 + [Fe^{III}]_0 - [Fe^{III}])] \quad (1)$$

Table III. Proportionality Constants for Equations 6 and 7 for N-Substituted Isoquinolinium Cations

N substituent	a (L·mol^{-1} s^{-1})	b (mol·L^{-1})
methyl	$1.6(\pm 0.3) \times 10^4$	$1.4(\pm 0.2) \times 10^{-3}$
isopropyl	$1.7(\pm 0.1) \times 10^3$	*a*
benzyl	$3.6(\pm 0.1) \times 10^4$	$3.2(\pm 0.4) \times 10^{-4}$
3-cyanobenzyl	$7.5(\pm 0.2) \times 10^4$	6.2×10^{-4} [b]

[a] Not determined. [b] Calculated from one observation at pH 12.7.

Table IV. Rate Data for the Ferricyanide Ion Oxidation of the 2-Methylisoquinolinium Cation and Its 1-Deuterio Derivative[a]

pH	k_a (M^{-1} s^{-1})	(k_b/k_{-a}) (M)	$(k_b/k_{-a})^H/(k_b/k_{-a})^D$
		1-H-2-CH_3	
12.31	7.0	3.14×10^{-5}	
13.10	160	3.22×10^{-4}	
13.50	2110	3.78×10^{-4}	
		1-D-2-CH_3	
12.31	7.0	1.57×10^{-5}	2.0
13.10	160	1.57×10^{-4}	2.0
13.50	2080	1.60×10^{-4}	2.3

[a] In 20% CH_3CN–80% H_2O, ionic strength 1.0, at 25 °C.

The second-order rate constant based upon the initial reaction rate is then given by

$$k_{2i} = k_a k_b/(k_b + k_{-a}[\mathrm{Fe^{II}}]_0) \tag{2}$$

Equation 2 has the form of the two-parameter eq 3, with $z_1 = k_a k_b/k_{-a}$ and $z_2 = k_b/k_{-a}$. We have fitted data such

$$k_{2i} = z_1/(z_2 + [\mathrm{Fe^{II}}]_0) \tag{3}$$

as those shown in Figure 1 to eq 3 by an iterative curve-fitting procedure which then allows the evaluation of the parameters z_1 and z_2. This procedure in general gave close fits to the experimental data (see Figure 1), with an average deviation of only 6% between calculated and experimental rate constants. Values of $k_a = z_1/z_2$ evaluated in this way were in close agreement with $k_{2i} = k_a$ obtained from initial rate data in the absence of added ferrocyanide ion.

Equation 3 has been used to analyze the kinetics of oxidation of the 2-methylisoquinolinium cation as a function of pH over the range pH 12.3–13.5. The pH dependences of k_a and k_b/k_{-a} are shown in Figure 2. Least-squares fitting of the data in Figure 2 gives the correlation equations:

$$\log k_a = 2.1(\pm 0.1)\mathrm{pH} - 25(\pm 1) \quad \text{(corr coeff 0.994)} \tag{4}$$

$$\log (k_b/k_{-a}) = 0.9(\pm 0.1)\mathrm{pH} - 16(\pm 1) \quad \text{(corr coeff 0.965)} \tag{5}$$

Thus k_a is proportional to $[^-\mathrm{OH}]^2$ and the ratio k_b/k_{-a} is proportional to $[^-\mathrm{OH}]$ as shown by eq 6 and 7, with the parameters a and b as indicated in Table III.

$$k_a = a[^-\mathrm{OH}]^2 \tag{6}$$

$$k_b/k_{-a} = b[^-\mathrm{OH}] \tag{7}$$

Kinetic data for the ferricyanide ion oxidation of the 1-deuterio-2-methylisoquinolinium cation are summarized in Table IV. While k_a shows no kinetic isotope effect, k_b/k_{-a} does display an appreciable effect which shows little (if any) pH dependence.

We have also compared the rates of ferricyanide ion oxidation of the 2-methyl- and the 2-(trideuteriomethyl)isoquinolinium cations under a variety of conditions. No detectable differences could be detected as a result of deuterium substitution in the *N*-methyl substituent, and thus species such as the ylides described by Manring and Peters[8] cannot be of any kinetic significance in these ferricyanide oxidations.

Table V. Influence of Oxygen upon the Oxidation of the 2-Methylisoquinolinium Cation by Ferricyanide Ion[a]

		k_{2i}, M^{-1} s^{-1}	
pH	$[\mathrm{Fe(CN)_6}]^{4-}$, mM	O_2 present[b]	O_2 absent
13.72	0	5.66×10^3	1.00×10^4
13.50	0	1.94×10^3	2.84×10^3
13.31	0	7.10×10^2	1.03×10^3
13.01	0	177	222
	0.2	63	68
	0.4	41	46
	0.8	24	27
	1.6	16	15

[a] Determined from initial rates using $[\mathrm{Fe(CN)_6}]^{3-}$ = 0.2 mM and [2-methylisoquinolinium cation] = 3 mM. [b] In air-equilibrated solutions.

All of the above data refer to studies in air-equilibrated solutions. However, in view of the recently reported observations[5] of the oxygen dependence of the rates of ferricyanide ion oxidation of 1,4-dihydronicotinamide derivatives, we have also briefly investigated the current reactions in deoxygenated solutions. These data are summarized in Table V and indicate that the presence of oxygen does produce an appreciable reduction in reaction rate. However, the kinetic order, pH dependence, and susceptibility to ferrocyanide ion inhibition are similar in both aerated and deaerated solutions.

2-Isopropyl-, 2-Benzyl-, and 2-(3-Cyanobenzyl)isoquinolinium Cations. We have also briefly compared the rates of ferricyanide ion oxidation of these N-substituted isoquinolinium cations with the *N*-methyl cation that is considered in some detail above. The kinetic orders, pH dependences, and susceptibilities to ferrocyanide ion inhibition are similar for these four N-substituted cations. The pH dependences of k_a are similar to those shown for the *N*-methyl cation in Figure 2. In each case k_a is proportional to $[^-\mathrm{OH}]^2$, with the proportionality constants that are listed in Table III. Parameters for the ferrocyanide inhibition of the oxidation of the *N*-benzyl and *N*-(3-cyanobenzyl) cations are also included in Table III.

2-Methyl-5-nitroisoquinolinium Cation. The ferrocyanide ion inhibition reported above in the ferricyanide ion oxidation of the 2-methylisoquinolinium cation contrasts with the earlier report[1] from our laboratories on the insensitivity of rates of 2-benzyl-5-nitroisoquinolinium cation oxidations to the presence of ferrocyanide ion. The current results have therefore lead us to reexamine the kinetics of the ferricyanide ion oxidation of 5-nitroisoquinolinium cations. We will first present data for the 2-methyl-5-nitroisoquinolinium cation and then reexamine some of our earlier data for 2-(substituted-benzyl)-5-nitroisoquinolinium cations.

The oxidation of the 2-methyl-5-nitroisoquinolinium cation (0.1 mM) in basic solutions was monitored by observing the disappearance of its pseudobase (and/or pseudobase alkoxide anion) at 500 nm in the presence of excess ferricyanide ion (1.5 mM). Pseudo-first-order kinetic plots under these conditions proved to be nonlinear, with the curvature indicative of an apparent decrease in pseudo-first-order rate constant as the reaction proceeds. This phenomenon is analogous to the result described above for the 2-methylisoquinolinium cation and again proved to arise from inhibition of the ferricyanide oxida-

---

[8] Manring, L. E.; Peters, K. S. *J. Am. Chem. Soc.* **1983**, *105*, 5708.

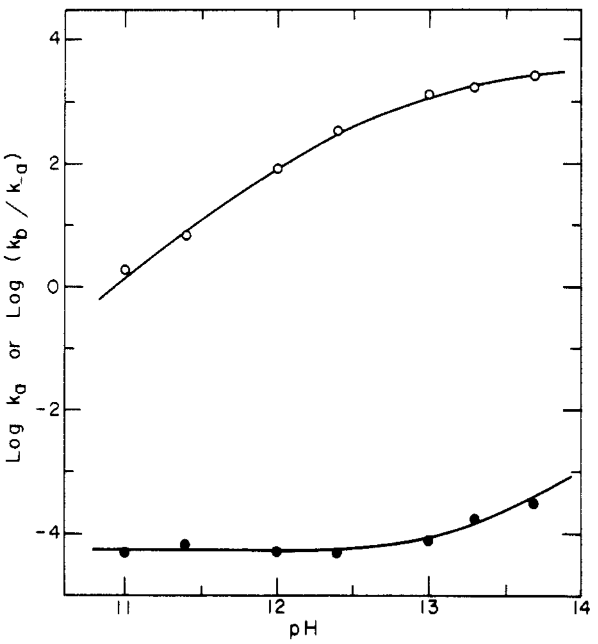


Figure 3. The pH dependence of log k_a (= log k_{2i}) (○) and log (k_b/k_{-a}) (●) for the ferricyanide oxidation of the 2-methyl-5-nitroisoquinolinium cation.

Table VI. Kinetic Isotope Effects upon the Ferricyanide Ion Oxidation of 5-Nitroisoquinolinium Cations and Their 1-Deuterio Derivatives

N substituent	pH	k_a^H/k_a^D	$(k_b/k_{-a})^H$	$(k_b/k_{-a})^D$	$\frac{(k_b/k_{-a})^H}{(k_b/k_{-a})^D}$
methyl	11.4	1.0	6.7×10^{-5}	2.3×10^{-5}	2.9
	12.4	1.0	4.5×10^{-5}	1.3×10^{-5}	3.4
	13.0	1.0	9.7×10^{-5}	3.6×10^{-5}	2.7
	13.7	1.0	3.4×10^{-4}	1.3×10^{-4}	2.6
4-cyanobenzyl	13.0	1.0	1.6×10^{-4}	6.4×10^{-5}	2.5
	13.7	1.0	4.1×10^{-4}	2.0×10^{-5}	2.1

tion by the ferrocyanide ion reaction product. Evaluation of pseudo-first-order rate constants from initial reaction rates in the presence of various concentrations of added ferrocyanide ion allowed the evaluation of k_a and k_b/k_{-a} as described above. The pH dependences of these parameters are displayed in Figure 3.

Analogous data were also obtained for the ferricyanide ion oxidation of the 1-deuterio-2-methyl-5-nitroisoquinolinium cation. These data, and the calculated kinetic isotope effects, are collected in Table VI.

2-Benzyl- and 2-(4-Cyanobenzyl)-5-nitroisoquinolinium Cations. The time dependence of the absorbance at 500 nm in the oxidation of the 2-benzyl-5-nitroisoquinolinium cation (0.1 mM) by ferricyanide ion (0.2 mM) in stoichiometric ratio was studied in the stopped-flow spectrophotometer. Second-order kinetic plots (first order in each reactant) are quite linear after the initial 10% of the reaction. Rate constants evaluated from this initial region are up to 50% larger (depending upon pH) than the rate constants calculated from the remaining 90% of the reaction. The current reaction conditions are identical with those used in our earlier study[1] of this oxidation, except that the previous study involved manually mixing reaction solutions prior to observing the absorbance change on a recording spectrophotometer. Such manual mixing does not allow the observation of the initial few percent of these relatively rapid reactions, and consequently the rapid initial rate region is not observable. The strictly second-order behavior observed for the majority of these reactions is identical with the report in our earlier study.[1]

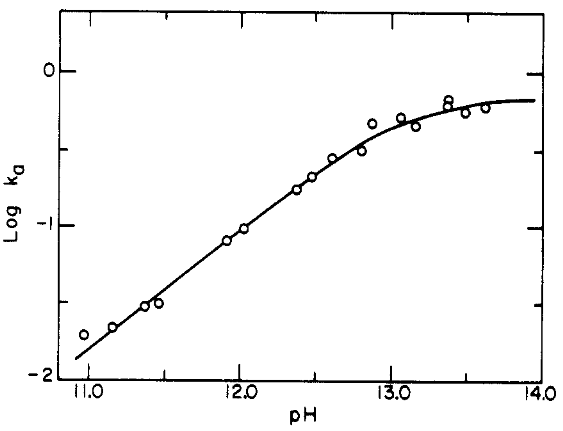


Figure 4. The pH dependence of the second-order rate constant for the ferricyanide oxidation of the 4-cyano-2-methylisoquinolinium cation.

The pH dependence of the second-order rate constants evaluated from initial rate data for the oxidation of 2-benzyl- and 2-(4-cyanobenzyl)-5-nitroisoquinolinium cations are similar to those shown in Figure 3 for the corresponding 2-methyl cation. Deuterium kinetic isotope effects from studies of the oxidation of the 2-(4-cyanobenzyl)-5-nitroisoquinolinium cation and its 1-deuterio derivative are summarized in Table VI. Although the true initial rate constant in the absence of ferrocyanide ion displays no deuterium kinetic isotope effect, the ferrocyanide ion inhibited reactions are considerably slower when deuterium is present at C-1.

4-Cyano-2-methylisoquinolinium Cation. The ferricyanide ion oxidation of this cation appears to be strictly first order in each of ferricyanide ion and total isoquinoline species over the range pH 11.0–13.8. The presence of ferrocyanide ion (up to 1.5 mM) had little discernable effect upon the rates of these reactions. The pH dependence of the observed second-order rate constants for this oxidation is shown in Figure 4.

Discussion

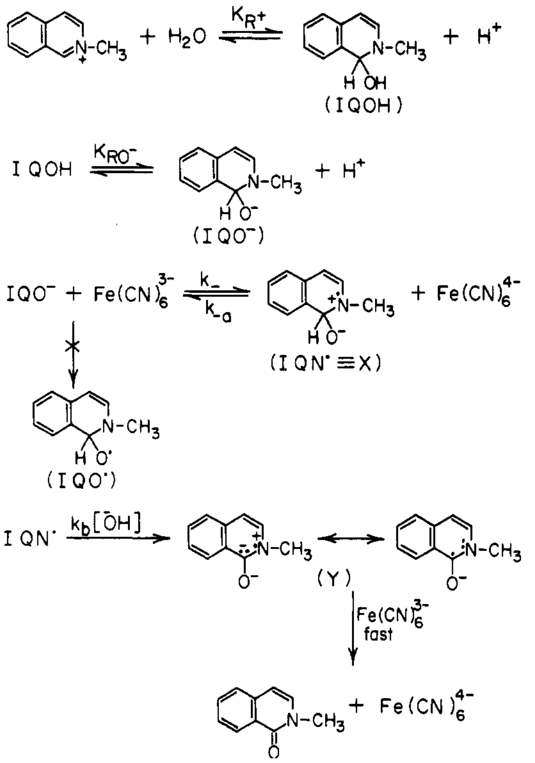
All the above observations upon the ferricyanide ion oxidation of isoquinolinium cations are consistent with the generalized reaction mechanism outlined in Scheme I. This scheme is essentially identical with that deduced for the ferricyanide ion oxidation of 1,4-dihydronicotinamides by Bruice and co-workers[5] and also for the ferricyanide ion oxidation of phenols that was investigated by McDonald and Hamilton.[9] These studies suggest that the species X in Scheme I is a radical formed upon an initial electron transfer from the isoquinoline derivative to ferricyanide ion. The susceptibility of the rate of the overall oxidation to inhibition by the ferrocyanide ion reaction product can be accounted for by assuming the reversibility of this initial electron-transfer step. Under no conditions do we find a second-order kinetic dependence upon ferricyanide ion. Thus the second ferricyanide ion required by stoichiometry can only be involved after the rate-determining step of these oxidations.

The identification of the species X and Y in Scheme I is assisted by the observed pH dependences for k_a and k_b/k_{-a}. In the oxidation of the 2-methylisoquinolinium cation k_a is observed to be proportional to $[^-OH]^2$ (eq 6). The only obvious interpretation of this dependence upon hydroxide ion concentration is in terms of the expected equilibration of the 2-methylisoquinolinium cation with

---

[9] McDonald, P. D.; Hamilton, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7752.

Scheme II



its pseudobase (IQOH) and pseudobase-derived alkoxide ion (IQO^-) in these aqueous solutions (Scheme II). Since $pK_{R^+} = 16.29$[7,10] for pseudobase formation from the 2-methylisoquinolinium cation in aqueous solution, these equilibria lie heavily in favor of the 2-methylisoquinolinium cation in the pH region covered by the current study, and thus the equilibrium concentration of the alkoxide ion IQO^- is quite small in the region pH 12–14. However, this interpretation in terms of reaction via this alkoxide ion is completely consistent with the observed pH dependences discussed below for the oxidation of the 5-nitro- and 4-cyanoisoquinolinium cations for which these equilibria favor the pseudobase and its alkoxide ion much more strongly.

For an isoquinolinium cation of $pK_{R^+} = 16.29$, the cation-pseudobase equilibrium is expected to be established much faster than the stopped-flow time scale.[6,7] Thus, the formation of IQOH and IQO^- from IQ^+ can be treated as rapid equilibria which occur prior to the rate-determining step in these ferricyanide ion oxidations. Combination of Schemes I and II in the case of the 2-methylisoquinolinium cation generates eq 8, where $K_{R^+} = [H^+][IQOH]/[IQ^+]$, $K_{RO^-} = [H^+][IQO^-]/[IQOH]$, and K_w is the ionic product of water.

$$k_a = k_- K_{R^+} K_{RO^-} [{}^-OH]^2/(K_w)^2 \qquad (8)$$

Thus for $pK_{RO^-} = 14.9$ as estimated from the linear free energy relationship of Barlin and Perrin[11] for alcohol acidities, and assuming $pK_w = 14$ as for strictly aqueous solutions at 25 °C, one can combine eq 6 and 8 to allow the evaluation of $k_- = 2 \times 10^7$ M^{-1} s^{-1} for electron transfer from IQO^- to the ferricyanide ion. This value is much larger than the second-order rate constant of 0.893 M^{-1} s^{-1} reported[5] for the analogous electron transfer from 1-benzyl-1,4-dihydronicotinamide to ferricyanide ion. This 10^7-fold rate enhancement, and the observed reaction pathway via the pseudobase alkoxide ion rather than the neutral pseudobase, could be rationalized in terms of electron transfer from the oxyanion to give the oxygen radical (IQO·) being much faster than from a neutral nitrogen atom to give a nitrogen radical cation as is required in the dihydronicotinamide oxidation. However, as discussed below, the dramatic variations in k_- observed for substituted isoquinolinium cations are only readily rationalized in terms of electron abstraction from the nitrogen atom to give the zwitterionic radicals IQN·. We therefore interpret species X of Scheme I as nitrogen radical IQN· rather than the oxygen radical IQO·.

Table VII. Rate Parameters for the Ferricyanide Ion Oxidation of Isoquinolinium Cations[a]

cation	pK_{R^+}	pK_{RO^-}	k_- (L·mol^{-1} s^{-1})
2-methyl	16.29[b]	14.9	2×10^7
2-isopropyl	17.0[c]	14.9	1×10^7
2-benzyl	15.5[d]	14.9	9×10^6
2-(3-cyanobenzyl)	14.8[e]	14.9	3×10^6
2-methyl-5-nitro	12.0	13.2	3300
2-benzyl-5-nitro	11.3[f]	13.1	150
2-(4-cyanobenzyl)-5-nitro	10.6[f]	13.1	44
4-cyano-2-methyl	7.8[g]	12.8	0.73

[a] Parameters evaluated from pH–rate profiles as described in text, unless indicated otherwise. [b] From ref 10. [c] Assuming ΔpK_{R^+}(isopropyl − methyl) = 0.7 as observed for 5-nitroisoquinolinium cations.[12] [d] Assuming ΔpK_{R^+}(benzyl − methyl) = −0.8 as observed for 5-nitroisoquinolinium cations.[12] [e] Assuming ΔpK_{R^+}(3-cyanobenzyl − benzyl) = −0.7 as observed for 5-nitroisoquinolinium cations.[6] [f] From ref 6. [g] From ref 7.

The interpretation of the pH dependence of the above reaction in terms of ferricyanide ion attack upon the pseudobase alkoxide ion is confirmed by the pH dependence observed for the oxidation of the 5-nitroisoquinolinium and 4-cyano-2-methylisoquinolinium cations (Figures 3 and 4). For each of these cases, pseudobase anion formation occurs with pK_{RO^-} within the pH range in which oxidation rates are accessible. In each of Figures 3 and 4, the value of K_a approaches pH independence above pH 13, as expected for reaction with pseudobase alkoxide ions formed with pK_{RO^-} in this vicinity.

For the 2-methyl-5-nitroisoquinolinium cation, both $pK_{R^+} = 11.7$[12] and pK_{RO^-} (expected to be about 13.0 as found for the 2-benzyl-5-nitroisoquinolinium cation[1]) fall within the experimentally accessible pH range. Under these conditions, eq 9 holds. The best fit of the data in

$$k_a = k_-/([H^+]^2/K_{R^+}K_{RO^-} + [H^+]/K_{RO^-} + 1) \qquad (9)$$

Figure 3 to eq 9 is obtained with $k_- = 3300$ L·mol^{-1} s^{-1}, $pK_{R^+} = 12.0$ and $pK_{RO^-} = 13.2$. These ionization constants in the current reaction medium are in reasonable agreement with the values quoted above for strictly aqueous solutions.

Equation 9 may be simplified to eq 10 in cases where the value of pK_{R^+} is at least 1 log unit smaller than the

$$k_a = k_-/([H^+1]/K_{RO^-} + 1) \qquad (10)$$

lowest pH that has been investigated. This condition holds in the current study for the 2-benzyl-5-nitro- ($pK_{R^+} = 11.3$[6]), 2-(4-cyanobenzyl)-5-nitro- ($pK_{R^+} = 10.5$[6]), and 4-cyano-2-methyl- ($pK_{R^+} = 7.8$[7]) isoquinolinium cations. When the experimentally observed pH–rate profiles for these three cations are fitted to eq 10, the parameters k_- and pK_{RO^-} can be evaluated and are included in Table VII.

The data collected in Table VII suggest that there is a general increase in the second-order rate constant k_- for

---

(10) Cook, M. J.; Katritzky, A. R.; Linda, P.; Tack, R. D. *Tetrahedron Lett.* **1972**, 5019.

(11) Barlin, G. B.; Perrin, D. D. *Q. Rev. Chem. Soc.* **1966**, *20*, 75.

(12) Bunting, J. W.; Meathrel, W. G. *Can. J. Chem.* **1974**, *52*, 962.

electron abstraction from the pseudobase alkoxide ion (IQO^-) by ferricyanide ion with increasing pK_{R^+} value for pseudobase *formation* by the isoquinolinium cation. In fact, if the *N*-isopropyl cation is excluded, the remaining seven data points are closely described by the correlation line in eq 11.

$$\log k_- = 0.96(\pm 0.06)pK_{R^+} - 8.1(\pm 0.8) \quad \text{(corr coeff 0.991)} \qquad (11)$$

Two major factors have been shown to influence the susceptibility of heteroaromatic cations to pseudobase formation.[13] These are (i) the loss in resonance energy upon pseudobase formation from the cation; and (ii) substituent effects upon the neutralization of the cationic charge during pseudobase formation. To a first approximation one would expect that the loss in resonance energy upon pseudobase formation would be approximately the same for all cations in Table VII since all are isoquinolinium cations. Thus, the major influence upon the variation of pK_{R^+} for these cations is the electronic effect of the various ring substituents upon an equilibrium which formally involves charge neutralization on the ring nitrogen atom. It is clear that substituents which destabilize the heteroaromatic cation relative to the pseudobase (low pK_{R^+}) also deactivate IQO^- toward ferricyanide ion attack.

The slope of the correlation line described by eq 11 is suggestive of a significant positive charge generation upon the heterocyclic species in the transition state for electron abstraction by ferricyanide ion. In fact the close to unit slope of this correlation line suggests that the ring nitrogen atom in this transition state bears essentially the same positive charge as this nitrogen atom has in the isoquinolinium cation. This observation clearly indicates that ferricyanide ion abstracts an electron from the nitrogen atom to generate the nitrogen radical cation IQN· of Scheme II. Furthermore, the transition state for this electron abstraction is well advanced toward the radical product, as is expected for a thermodynamically unfavorable process. This generation of close to a unit positive charge on nitrogen in the rate-determining transition state was also found in a previous study of the ferricyanide ion oxidation of *N*-(substituted-benzyl) 5-nitroisoquinolinium cations.[1]

The pronounced sensitivity of k_- to substituent electronic effects also rules out the alternative electron abstraction from the oxyanion of IQO^- to give the oxygen-based radical IQO· (Scheme II). If k_- were representative of such a process, one would expect this rate constant to display a similar sensitivity to substituent effects to that observed for alkoxide ion formation from the pseudobases (i.e., pK_{RO^-}). Variations in charge on the exocyclic oxygen atom are expected to be much less influenced by substituent effects than are processes that formally involve charge neutralization (or creation) on the endocyclic nitrogen atom. This expectation is confirmed by the low sensitivity of pK_{RO^-} to substituent effects in Table VII. These substituent effects are clearly too small to account for the pronounced variation in k_- in Table VII.

The 2-isopropylisoquinolinium cation is approximately 20-fold less reactive than predicted by eq 11. This low reactivity can be readily rationalized in terms of steric hindrance to ferricyanide attack at nitrogen when this bulky substituent is present. Certainly such steric effects should be far greater in this case than for any of the *N*-methyl or *N*-benzyl cations in Table VII. This observation also indirectly confirms that ferricyanide ion attack is at nitrogen rather than on the exocyclic oxygen which is more remote from the N substituent.

The pH dependence of the k_b/k_{-a} ratio is first order in hydroxide ion (eq 7). This pH dependence can be most simply accommodated by either base catalysis of the k_b step or alternatively acid catalysis of the k_{-a} step. There is no obvious role ascribable to acid catalysis of k_{-a} as defined in Scheme II. Base catalysis of k_b can be sensibly interpreted in terms of base-catalyzed deprotonation at C-1 of IQN· to give the radical anion Y. Subsequent very rapid electron transfer from this Y species to a second ferricyanide ion then allows the formation of the observed 2-methyl-1-isoquinolinone reaction product. A similar base-catalyzed deprotonation from a saturated carbon atom has been demonstrated as the second step in the ferricyanide ion oxidation of 1,4-dihydronicotinamides[5] and 9,10-dihydroacridines.[14]

The observed isotope effects in Tables IV and VI in the presence of deuterium at C-1 of the isoquinolinium cation are also consistent with the mechanism of Scheme II. Since k_a represents electron transfer, it should display only the small isotope effects expected for K_{R^+} and K_{RO^-}; in fact k_a^H/k_a^D is experimentally indistinguishable from 1.0. In terms of Scheme II, we can attribute the isotope effect observed for k_b/k_{-a} to k_b. Our interpretation of k_b as base-catalyzed cleavage of the C(1)–H bond then predicts a significant isotope effect upon substitution of deuterium at C-1 in agreement with the experimental observation.

The magnitude of the observed oxygen inhibition of these oxidations (Table V) is similar to that reported in the ferricyanide oxidation of dihydronicotinamides[5] and is attributable to superoxide formation from reaction of oxygen with Y, followed by reaction of IQN· (= X) with superoxide in competition with ferrocyanide ion in the k_{-a} step. Thus inhibition by both ferrocyanide ion and oxygen are attributable to a net decrease in the steady-state concentration of IQN·. Consistent with this view, the magnitude of the oxygen dependence is lower in the presence of added ferrocyanide ion and increases at higher pH where the ferrocyanide ion inhibition has been demonstrated to be less effective. Thus superoxide ion is unable to compete effectively with significant concentrations of ferrocyanide, and its effect is only noticeable when ferrocyanide ion inhibition is weak.

The pH profile for k_b/k_{-a} (Figure 3) for the 2-methyl-5-nitroisoquinolinium cation is somewhat different than the pH dependence for this ratio described by eq 7 for the *N*-alkylisoquinolinium cations. In this case (Figure 3), this ratio can be described by eq 12.

$$k_b/k_{-a} = 5 \times 10^{-5} + 5 \times 10^{-4}[^-OH] \qquad (12)$$

The pH independent term in eq 12 presumably represents deprotonation of X by a water molecule while the hydroxide dependent term represents hydroxide ion catalyzed deprotonation of X as in eq 7. In fact, the value of 5×10^{-4} in eq 12 is quite similar in magnitude to the values of *b* reported in Table III for other isoquinolinium cations. To a first approximation, substituent effects upon k_b and k_{-a} are expected to be quite similar and so no clear-cut substituent effects are observed when the ratio of these two rate constants is considered. The observation of a water-catalyzed deprotonation of X in this case is consistent with the expected greater acidity of X when a 5-nitro substituent is present.

As noted earlier, ferrocyanide ion inhibition of these ferricyanide ion oxidations shows a pronounced pH de-

---

[13] Bunting, J. W. *Adv. Heterocycl. Chem.* **1979**, *25*, 1.

[14] Sinha, A.; Bruice, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 7291.

pendence, being much more obvious at lower pH than in more basic solutions. This phenomenon is consistent with Scheme II. Equation 2 may be rearranged in the form of eq 13.

$$k_{2i} = k_a/(1 + k_{-a}[\mathrm{Fe^{II}}]_0/k_b) \qquad (13)$$

It is clear that inhibition by added ferrocyanide ion will not be observed if $k_{-a}[\mathrm{Fe^{II}}]_0/k_b \ll 1$. Now, since k_b/k_{-a} is proportional to hydroxide ion concentration (eq 7), k_{-a}/k_b decreases with increasing pH, and it is clear that the above inequality will eventually hold in sufficiently basic solutions, for reasonable ferrocyanide ion concentrations.

In a similar manner, inhibition by the ferrocyanide ion product in reactions with no added ferrocyanide will become less important with increasing pH, so that these reactions will approach a kinetically simple reaction that is first order in each of heterocycle and ferricyanide ion at high pH. This is in accord with the experimental observations reported above.

In the light of the current data, it is now clear that our earlier report[1] that the ferricyanide oxidation of 5-nitroisoquinolinium cations is not susceptible to inhibition by ferrocyanide ions was erroneous. Unfortunately, our most careful checks of the influence of added ferrocyanide ion in that study were made in relatively basic solutions, in which it is now clear that such inhibition is least likely to be observable.

The most dramatic curvature occurs at relatively short times in second-order kinetic plots for reactions without added ferrocyanide ion. Well into the reaction, the concentration of ferrocyanide product, which is approaching a maximum value equal to the initial ferricyanide ion concentration, is changing much less rapidly than is the concentration of the remaining ferricyanide reactant. Under such conditions, there will exist a significant portion of the reaction which will have an apparent second-order rate constant of approximately $k_a k_b/(k_b + k_{-a}[\mathrm{Fe^{II}}]_0)$. It is apparently this function to which our k_{obsd} values refer in our earlier report.[1] The kinetic isotope effects that we report in that study appear to be contaminated by the isotope effects upon k_b that we have established in the current work. Furthermore, this observation now also enlightens our earlier difficulty in rationalizing the kinetically determined K values ($\log K = \mathrm{p}K_w - \mathrm{p}K_{\mathrm{RO^-}}$) for alkoxide ion formation with the spectrophotometrically determined values. It is now apparent that the evaluation of these ionization constants from kinetic data is influenced by the pH dependence of k_b in addition to the variation in alkoxide ion concentration with pH.

In the light of the current work, it is now clear that we must withraw our earlier claim for rate-determining hydride abstraction by ferricyanide ion in these oxidations. We are able to rationalize essentially all of the kinetic data now available for these reactions in terms of Scheme II.

One feature that we have not yet addressed is the apparent necessity for ferricyanide ion attack upon the pseudobase alkoxide ion (IQO$^-$) rather than upon the neutral pseudobase (IQOH). The substituent effects discussed above, and the relative reactivities of quinolinium and isoquinolinium cations reported in the accompanying report make it clear that electron abstraction is from nitrogen, not from O$^-$. Although a contribution from a pathway utilizing IQOH is not absolutely excluded by the current data, any reaction occurring via that route must be much slower than via the alkoxide ion in all cases that we have examined to date. It is not clear how the presence of the oxyanion can significantly stabilize the developing positive charge upon nitrogen during the formation of IQN·. In view of the fact that electrostatic repulsion of the ferricyanide ion might have been expected to lower the reactivity of IQO$^-$ relative to IQOH, it is necessary to invoke a positive role for this alkoxide ion. A possible role for the oxyanion can be postulated if electron transfer occurs intramolecularly within an IQO$^-$–ferricyanide ion complex. Thus coordination of O$^-$ to the iron or its nucleophilic addition to carbon in one of the cyanide ligands would produce such a complex. Precedents for both of these types of processes are available or have been previously postulated.[15,16]

The combination of eq 9 and 11 allows the description of the pH dependence of the second-order rate constant for ferricyanide ion oxidation of any isoquinolinium cation for which $\mathrm{p}K_{\mathrm{R^+}}$ and $\mathrm{p}K_{\mathrm{RO^-}}$ are known. The data in Table VII can also be used to derive the correlation eq 14.

$$\mathrm{p}K_{\mathrm{RO^-}} = 0.29\ (\pm\ 0.04)\mathrm{p}K_{\mathrm{R^+}} + 10.1(\pm\ 0.6) \qquad \text{(corr coeff 0.943)} \quad (14)$$

Combination of eq 9, 11, and 14 then generates eq 15.

$$k_a = (K_{\mathrm{R^+}})^{0.33}/(10^{18.2}[\mathrm{H^+}]^2 + 10^{18.2}[\mathrm{H^+}]\cdot K_{\mathrm{R^+}} + 10^{8.1}(K_{\mathrm{R^+}})^{1.29}) \qquad (15)$$

This equation allows the reactivities toward ferricyanide ion oxidation to be calculated for all isoquinolinium cations of known $\mathrm{p}K_{\mathrm{R^+}}$, provided that significant steric hindrance from the *N*-alkyl substituent is not present. The observed decrease in inhibition by the ferrocyanide product with increasing pH indicates that the greatest synthetic efficiency will be achieved by the use of the most basic aqueous solutions that are compatible with the substituents present on the isoquinolinium cation.

Acknowledgment. We appreciate the continued support of this work through an operating grant awarded by the Natural Sciences and Engineering Research Council of Canada.

Registry No. D_2, 7782-39-0; O_2, 7782-44-7; 2-methylisoquinolinium, 33718-23-9; 2-isopropylisoquinolinium, 79979-28-5; 2-benzylisoquinolinium, 38602-73-2; 2-(3-cyanobenzyl)isoquinolinium, 81246-20-0; 2-methyl-5-nitroisoquinolinium, 46271-32-3; 2-benzyl-5-nitroisoquinolinium, 52166-52-6; 2-(4-cyanobenzyl)-5-nitrosoquinolinium, 64840-42-2; 4-cyano-2-methylisoquinolinium, 46165-53-1; 2-methyl-1(2*H*)-isoquinolinone, 4594-71-2; 2-isopropyl-2(2*H*)-isoquinolinone, 101712-97-4; 2-benzyl-1(2*H*)-isoquinolinone, 59168-21-7; 2-(3-cyanobenzyl)-1-(2*H*)-isoquinolinone, 101712-98-5; 2-methyl-5-nitro-1(2*H*)-isoquinolinone, 42792-96-1; 2-benzyl-5-nitro-1(2*H*)-isoquinolinone, 64840-53-5; 2-(4-cyanobenzyl)-5-nitro-1(2*H*)-isoquinolinone, 64840-52-4; 4-cyano-2-methyl-1(2*H*)-isoquinolinone, 20334-97-8; ferricyanide, 13408-62-3.

Supplementary Material Available: Experimental rate data for the oxidation of the 2-methylisoquinolinium cation at various ferrocyanide ion concentrations (11 pages). Ordering information is given on any current masthead page.

---

(15) For seven-coordinate Fe(III) complexes: Lind, M. D.; Hamor, M. J.; Hamor, T. A.; Hoard, J. L. *Inorg. Chem.* **1964**, *3*, 34. Nelson, S. M.; Bryan, P.; Busch, D. H. *Chem. Commun.* **1966**, 641. Fleischer, E.; Hawkinson, S. *J. Am. Chem. Soc.* **1967**, *89*, 720. Nelson, S. M.; Busch, D. H. *Inorg. Chem.* **1969**, *8*, 1859. Drew, M. G. B.; bin Othman, A. H.; McIlroy, P. D. A.; Nelson, S. M. *J. Chem. Soc., Dalton Trans.* **1975**, 2507.

(16) For nucleophilic attack at a ligand carbon atom: Lancaster, J. M.; Murray, R. S. *J. Chem. Soc. A* **1971**, 2755. Casey, C. P.; Neumann, S. M. *J. Am. Chem. Soc.* **1976**, *98*, 5395. Winter, S. R.; Cornett, G. W.; Thompson, E. A. *J. Organomet. Chem.* **1977**, *133*, 339. Gladysz, J. A.; Williams, G. M.; Tam, W.; Johnson, D. L. *J. Organomet. Chem.* **1977**, *140*, C1.