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OSMIUM(VIII)-CATALYZED OXIDATION OF SOME CYCLIC AMINES BY POTASSIUM HEXACYANOFERRATE(III) IN ALKALINE MEDIA: A KINETICS AND MECHANISTIC STUDY

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Reactions of morpholine, piperidine, and piperazine with Os(VIII)-catalyzed hexacyanoferrate(III) in alkaline media to produce the corresponding lactam have been studied at constant temperature and ionic strength. The reactions followed first-order kinetics with respect to [amine] and [Os(VIII)] but were independent of [$Fe(CN)_6^{3-}$] and [OH^-]. The effects of introduced electrolytes, potassium hexacyanoferrate(II), relative permitivity, and temperature have also been studied. A mechanism accounting for these results has been proposed.

Keywords: morpholine, piperidine, piperazine, Os(VIII), hexacyanoferrate(III), lactam, kinetics, oxidation.

The use of oxidizing agents in attacking particular groups in simple and large organic molecules has received great attention [1, 2]. Among these is potassium hexacyanoferrate(III) [3-7], a one-electron oxidant with a redox potential of 0.36 V. Although hexacyanoferrate(III) has some advantages that make it suitable for the oxidation of several organic substrates [8, 9], in particular its stability over the entire pH scale and its being a moderate oxidant, its reactions with some nitrogen-containing compounds are not facile and require the presence of a catalyst [10, 11]. The present work aimed to investigate the suitability of employing Os(VIII) as a catalyst in the oxidation of some six-membered cyclic amines by alkaline $Fe(CN)_6^{3-}$. Furthermore, the effect of the atom occupying position 4 in the cyclic amine molecule will be explored.

MATERIALS AND METHODS

Reagents. Potassium hexacyanoferrate(III), piperidine, and metal halides (Riedel-deHaen), morpholine, piperazine, and $K_4Fe(CN)_6$ (Merck), and OsO_4 (Sigma) were used in the purest form available without further purification. Deionized distilled water was used for the preparation and dilution of all solutions. The desired hydroxide ion concentration was achieved using prestandardized NaOH solution. The required ionic strength was achieved by adding NaCl. The reactions were initiated by simultaneous addition of the required volume of $K_3Fe(CN)_6$ and the amine solutions to keep the total volume constant in all runs.

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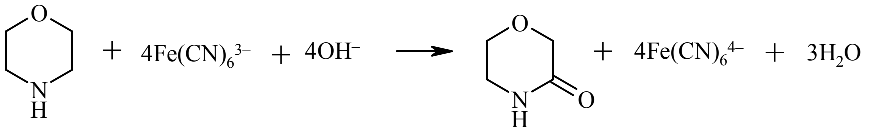
Kinetics Studies. The kinetics were studied by measuring the absorbance of the unreacted $K_3Fe(CN)_6$, at 414 nm, by transferring some of the reaction mixture, within 20-25 s, into the thermostated cell of the spectrophotometer. The absorbance was recorded at appropriate intervals for more than four half-lives.

Stoichiometry. The stoichiometry of the reactions was determined by reacting the corresponding amine (1.0×10^{-4} mol·dm^{-3}) with $Fe(CN)_6^{3-}$ (1.00×10^{-3} mol·dm^{-3}) for 96 h to ensure complete reaction as indicated by the constant absorbance of $Fe(CN)_6^{3-}$. The [OH^-] was kept constant at 0.100 mol·dm^{-3} and the temperature at 308 K; the concentration of OsO_4 was also kept constant at 1.0×10^{-5} mol·dm^{-3}. The consumed $Fe(CN)_6^{3-}$ was found to be $(4.0 \text{ to } 4.2) \times 10^{-4}$ mol·dm^{-3} for the case of morpholine and piperidine, and about 2.0×10^{-4} mol·dm^{-3} for the case of piperazine. The presence or absence of OsO_4 has no effect on the total consumption of $Fe(CN)_6^{3-}$.

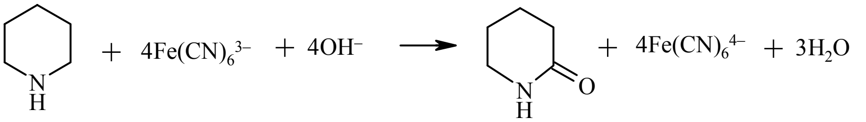
Product Analysis. A known amount of the amine was placed in a flask, and a tenfold excess of $Fe(CN)_6^{3-}$ and the required amount of OH^- were added. The resulting solution was shaken and kept for 96 h to ensure completion of the reaction. The precipitate was filtered off and the organic material was extracted from the mixture by chloroform (4 × 60 ml). The chloroform solution was evaporated to a small volume, until the organic material precipitated. The products, 2-morpholinone, 2-piperidinone, and 2,5-piperazinedione, were identified by comparison of their IR spectra, obtained by a Pye Unicam Sp200 spectrometer, and the mass spectra, obtained at the Midwest Center for Mass Spectroscopy at the University of Nebraska-Lincoln, with those of authentic samples.

RESULTS AND DISCUSSION

The stoichiometric analysis showed that 1 mol of the amine consumes 4 mol of $Fe(CN)_6^{3-}$ regardless of the presence of OsO_4. This indicates that OsO_4 has no effect on the final outcome. Furthermore, product analysis showed that the products of the catalyzed and uncatalyzed reactions of $Fe(CN)_6^{3-}$ with morpholine, piperidine, and piperazine were 2-morpholinone, 2-piperidinone, and 2,5-piperazinedione, respectively. Accordingly, the overall balanced equations can be written as



(1)



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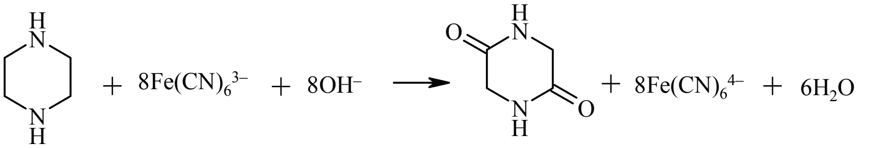

(3)

The relative reactivity of the amines toward hexacyanoferrate(III), as indicated by the initial rate values, followed the order piperidine > piperazine >> morpholine.

The effect of [OsO_4] on the reaction rate of the amines with $Fe(CN)_6^{3-}$ is shown in Table 1. Plots of -log[initial rate] *versus* -log[OsO_4] indicate that the reaction order with respect to [OsO_4] is 1.0 ± 0.1 in all cases.

Species such as OsO_4, $[OsO_4(H_2O)_2]$, $[OsO_4(H_2O)(OH)]^-$, and $[OsO_4(OH)_2]^{2-}$ coexist in fast equilibria with each other, as different forms of Os(VIII), in basic medium [12]. Since the present reaction medium is strongly basic, the total [Os(VIII)] can be assumed to be $[OsO_4(OH)_2]^{2-}$ [4].

TABLE 1. Dependence of Initial Rate on Initial [Os(VIII)]

10^5 [Os(VIII)], mol·dm^{-3}	10^3[initial rate], mol·dm^{-3}·s^{-1}		
	morpholine	piperidine	piperazine
1.00	1.73	2.77	2.05
2.00	3.50	5.33	4.00
3.00	5.15	8.31	5.98
4.00	6.90	10.45	7.90
5.00	8.60	13.10	9.98
6.00	9.95	15.98	12.04

10^3 [Fe(CN)$_6^{3-}$] = 1.00, 10 [amine] = 1.00, 10 [OH$^-$] = 1.00 mol·dm^{-3}, temp. 35°C, and 10μ = 1.5 mol·dm^{-3}.

The orders with respect to [amine] (Table 2) and [Fe(CN)$_6^{3-}$] (Table 3) were 1.0 ± 0.15 and 0.0 ± 0.1 respectively. Similar results were reported for the oxidation of carbonyl compounds with Fe(CN)$_6^{3-}$ catalyzed by Os(VIII) [3, 4]. The nearly zero-order effect of the hydroxyl ion (Table 4) is acceptable as a result of its relatively high concentration (0.10 mol dm^{-3}) relative to [Os(VIII)] (1.0×10^{-5} mol dm^{-3}). Moreover, the hydroxyl ion may not act as free OH$^-$ but as a part of the [Os(VIII)] complex. Addition of Fe(CN)$_6^{4-}$ retarded the

TABLE 2. Dependence of Initial Rate on Initial [Amine]

10 [amine], mol·dm^{-3}	10^3 [initial rate], mol·dm^{-3}·s^{-1}		
	morpholine	piperidine	piperazine
1.00	1.73	2.77	2.05
1.50	2.46	3.72	3.01
2.00	3.33	5.12	3.98
3.00	4.90	7.75	5.95
4.00	6.66	10.10	7.88
6.00	9.52	15.15	10.20

10^3 [Fe (CN)$_6^{3-}$] = 1.00, 10 [OH$^-$] = 1.00, 10^5 [Os(VIII)] = 1.00 mol·dm^{-3}, temp. 35°C and 10μ = 1.5 mol·dm^{-3}.

TABLE 3. Dependence of Initial Rate on Initial [Fe(CN)$_6^{3-}$]

10^3 [Fe(CN)$_6^{3-}$], mol·dm^{-3}	10^3 [initial rate], mol·dm^{-3}·s^{-1}		
	morpholine	piperidine	piperazine
0.40	1.55	2.70	1.95
0.60	1.60	2.73	1.95
0.80	1.64	2.74	1.98
1.00	1.73	2.77	2.05
1.20	1.73	2.80	2.05

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10 [amine] = 1.00, 10 [OH$^-$] = 1.00, 10^5 [Os(VIII)] = 1.00 mol·dm^{-3}, temp. 35°C and 10μ = 1.5 mol·dm^{-3}.

reaction rate (Table 5 and Fig. 1). This indicates that $Fe(CN)_6^{4-}$ is involved in a reversible step that could affect the rate-determining step. Addition of different potassium salts to maintain a constant ionic strength had no effect (within experimental error) on the reaction rates for all amines (Table 6).

TABLE 4. Dependence of Initial Rate on Initial [OH^-]

10^2 [OH^-], mol·dm^{-3}	10^3 [initial rate], mol·dm^{-3}·s^{-1}		
	morpholine	piperidine	piperazine
0.40	0.90	2.31	1.01
1.00	1.15	2.42	1.21
2.00	1.22	2.51	1.45
3.10	1.31	2.60	1.68
5.00	1.45	2.65	1.98
10.00	1.73	2.77	2.05

10^3 [$Fe(CN)_6^{3-}$] = 1.00, 10 [amine] = 1.00, 10^5 [Os(VIII)] = 1.00, 10 [OH^-] = 1.00 mol·dm^{-3}, temp. 35°C and 10μ = 1.5 mol·dm^{-3}.

TABLE 5. Dependence of Initial Rate on Added [$Fe(CN)_6^{4-}$]

10^3 [$Fe(CN)_6^{4-}$], mol·dm^{-3}	10^3 [initial rate], mol·dm^{-3} s^{-1}		
	morpholine	piperidine	piperazine
0.1	1.14	2.08	1.09
0.4	1.05	1.96	0.92
0.7	0.98	1.85	0.66
1.0	0.69	1.78	0.64
2.0	0.60	1.72	0.31
3.0	0.52	1.62	0.27

10^3 [$Fe(CN)_6^{3-}$] = 1.00, 10 [amine] = 1.00, 10^5 [Os(VIII)] = 1.00, 10 [OH^-] = 1.00 mol·dm^{-3}, temp. 35°C and 10μ = 1.5 mol·dm^{-3}.

TABLE 6. Dependence of Initial Rate on Different Electrolytic Salts

Salt	10^3 [initial rate], mol·dm^{-3}·s^{-1}		
	morpholine	piperidine	piperazine
KF	1.70	2.95	2.05
KCl	1.65	2.98	2.07
KBr	1.65	2.95	2.10
KI	1.63	2.95	2.09
KNO_3	1.64	2.97	2.10
NaCl	1.68	2.90	2.00
NH_4Cl	1.19	2.20	1.30

10^2 [salt] = 3.50, 10 [amine] = 1.00, 10^3 [$Fe(CN)_6^{3-}$] = 1.00, 10^5 [Os(VIII)] = = 1.00, 10 [OH^-] = 1.00 mol·dm^{-3}, temp. 35°C and 10μ = 1.5 mol·dm^{-3}.

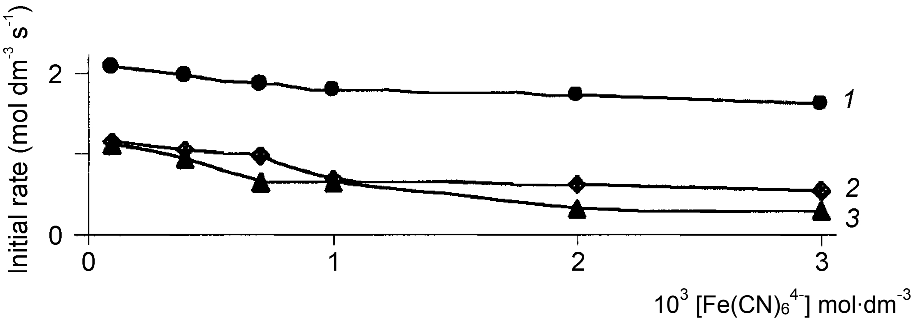

Fig. 1. Effect of potassium hexacyanoferrate(II) on the rate of oxidation of piperidine (*1*), morpholine (*2*), and piperazine (*3*) at 35°C.

Addition of chlorides showed that sodium and potassium cations have no specific effect on rate, whereas ammonium has. Being acidic, ammonium ion consumes some OH^- and thus affects the production of the assumed active form of the catalyst $[OsO_4(OH)_2]^{2-}$. The resulting ammonia could also inhibit the reaction through the formation of a complex with Os(VIII), say, $[OsO_4(NH_3)_2]$.

Added ethanol retarded the oxidation of morpholine but not that of piperazine or piperidine (Table 7). This could be due to solvation of the oxygen atom occupying position 4 in the morpholine ring.

The activation parameters were obtained by carrying out the reactions at temperatures 299, 304, 309 and 314 K. Rate constants and activation parameters were calculated (Table 8) using the rate equation (Eq. (4)) and standard relations such as Arrhenius and Gibbs free energy [13]. $\Delta S^{\neq}$ has relatively high negative values comparable to that reported for the oxidation of benzaldehyde ($\Delta S^{\neq}$ = -163.75 J·mol^{-1}·K^{-1}) by $Fe(CN)_6^{3-}$ catalyzed by Os(VIII) [4]. This indicates that the complexes formed in the present work are of the same type and the same degree of order as that reported for benzaldehyde.

TABLE 7. Dependence of Initial Rate on % Ethanol

% Ethanol (v/v)	10^3 [initial rate], mol·dm^{-3}·s^{-1}		
	morpholine	piperidine	piperazine
0.0	1.73	2.77	2.05
10.0	1.50	2.73	2.08
20.0	1.29	2.70	2.10
30.0	0.98	2.68	2.11
40.0	0.82	2.68	2.12
50.0	0.71	2.65	2.15

$10^3\,[Fe(CN)_6^{3-}] = 1.00$, $10\,[\text{amine}] = 1.00$, $10^5\,[\text{Os(VIII)}] = 1.00$, $10\,[OH^-] = 1.00$ mol·dm^{-3}, temp. 35°C and $10\mu = 1.5$ mol·dm^{-3}.

TABLE 8. Activation Parameters

Compound	*E*a, kJ·mol^{-1}	$\Delta S^{\neq}$, J·mol^{-1}·K^{-1}	$\Delta H^{\neq}$, kJ·mol^{-1}	$\Delta G^{\neq}$, kJ·mol^{-1}
Morpholine	14.80	-238.9	12.20	86.24
Piperidine	34.86	-166.4	32.27	83.64
Piperazine	23.28	-151.7	20.69	67.55

The above results suggest an experimental rate law for the initial rate, which can be written as

$$-d\,[\mathrm{Fe(CN)_6^{3-}}]\,/dt = k\,[\text{amine}]\,[\mathrm{Os(VIII)}] \qquad (4)$$

Considering the equilibria (5) and (6) for osmium tetroxide in aqueous solution, the following mechanism presented in Eq. (7)-(12) has been suggested, assuming the active form of Os(VIII) is $\mathrm{OsO_4(OH)_2^{2-}}$:

$\mathrm{OsO_4(OH)_2^{2-}}$ ($K_1 = 5.5 \times 10^{13}$ and $K_2 = 24\pm4$) and X = O, CH_2, NH.

$$[\mathrm{OsO_4(H_2O)_2}] + \mathrm{OH^-} \overset{K_1}{\rightleftharpoons} [\mathrm{OsO_4(OH)(H_2O)}]^- + \mathrm{H_2O} \qquad (5)$$

$$[\mathrm{OsO_4(OH)(H_2O)}]^- + \mathrm{OH^-} \overset{K_2}{\rightleftharpoons} [\mathrm{OsO_4(OH)_2}]^{2-} + \mathrm{H_2O} \qquad (6)$$

$$[\mathrm{OsO_4(OH)_2}]^{2-} + \mathrm{C_4H_9NX} \overset{\beta}{\rightleftharpoons} [\mathrm{OsO_4(OH)_2C_4H_9NX}]^{2-} \qquad (7)$$

$$[\mathrm{OsO_4(OH)_2C_4H_9NX)}]^{2-} \xrightarrow{k} \overset{\text{I}}{[\mathrm{OsO_4(H_2O)_2}]^{2-}} + \mathrm{C_4H_7NX} \qquad (8)$$

$$2[\mathrm{Fe(CN)_6}]^{3-} + [\mathrm{OsO_4(H_2O)_2}]^{2-} \rightleftharpoons 2[\mathrm{Fe(CN)_6}]^{4-} + [\mathrm{OsO_4(H_2O)_2}] \qquad (9)$$

$$[\mathrm{OsO_4(OH)_2}]^{2-} + \mathrm{C_4H_7NX} \longrightarrow [\mathrm{OsO_4(OH)_2C_4H_7NX}]^{2-} \qquad (10)$$

$$[\mathrm{OsO_4(OH)_2C_4H_7NX}]^{2-} \longrightarrow \overset{\text{II}}{[\mathrm{OsO_4(H_2O)_2}]^{2-}} + \mathrm{C_4H_7NXO} \qquad (11)$$

$$2[\mathrm{Fe(CN)_6}]^{3-} + [\mathrm{OsO_4(H_2O)_2}]^{2-} \rightleftharpoons 2[\mathrm{Fe(CN)_6}]^{4-} + [\mathrm{OsO_4(H_2O)_2}] \qquad (12)$$

The formation of a complex between Os(VIII) and benzaldehyde was proposed and supported by Michaelis–Menten type of [initial rate]$^{-1}$ *versus* [carbonyl]$^{-1}$ plots [4] and agrees well with other reported structures [14, 15]. Therefore complexes such as I and II are expected to be more stable and easier to obtain from the reaction of Os(VIII) with amines than with benzaldehyde. This is also indicated by the initial rates, obtained which are of the order of 10^{-3}, while those of benzaldehyde were of the order of 10^{-7}.

The formation and decomposition of the Os(VIII)–enamine transient complex (II) (Eqs. (10) and (11)) is expected to be faster than the formation and decomposition of the Os(VIII)–amine transient complex (I) (Eqs. (7) and (8)) as a result of the presence of the double bond in the former case. Therefore, the step desribed by Eqs. (11) is assumed to be relatively fast and has no effect on the total rate of the reaction.

The reactivity order of the amines (piperidine > piperazine > morpholine) is in reverse to the electronegativity trend of the atoms occupying positions 4 (C < N < O). Electron-withdrawing groups, through the inductive effect, are expected to destabilize the iminium cation and the subsequent carbonium ion formed as a result of the transfer of the first and second electrons, respectively, from Os(VIII) to the amine in the transient complex (I) before it splits to give the product.

The above mechanism explains also the effect of ethanol on the oxidation of morpholine. Solvation of morpholine will hinder the formation of complex (I) (Eq. (7)), and thus slow down the reaction.

The effect of potassium ferrocyanide can be seen from Eq. (9). $[\mathrm{Fe(CN)_6}]^{4-}$ is expected to retard the regeneration of Os(VIII) from Os(VI) and $[\mathrm{Fe(CN)_6}]^{3-}$, and consequently slows down the reaction.

The above mechanism enables us to derive the following rate law:

$$-d\,[\mathrm{Fe(CN)_6^{3-}}]\,/\,dt = k_0\,[\mathrm{OsO_4(OH)_2^{2-}}]\cdot[\text{amine}] \qquad (13)$$

which is in agreement with the experimental results.

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