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Kinetics and Mechanism of Base-Catalyzed Oxidation of 1, 4, 7, 10-Tetrazacyclododecane-1-Carbaldehyde with Hexacyanoferrate (III)

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Abstract:
1,4,7,10-tetraazacyclododecane-1-carbaldehyde, is oxidized by hexacyano ferrate (III) in alkaline media to 1,4,7,10-tetraazacyclododecane-1-formic acid. The reaction is first order with respect to to aldehyde , alkaline catalyst and hexaeyanoferrate(III). The kinetic data suggest that the oxidation involves the formation of an anion of the substrate undergoes oxidation with hexaeyanoferrate(III) via charge transfer process. The free radical thus produced is further oxidised to form the final products. The derived rate law is

$$-\frac{d[\mathrm{Fe(CN)_6}]^{3-}}{dt}=\frac{2k_1k_2[\mathrm{LC(OH)_2}][\mathrm{Fe(CN)_6}]^{3-}[\mathrm{OH^-}]}{k_{-1}[\mathrm{H_2O}]}$$

Effect of temperature was also studied for calculating different activation parameters.

Keywords: *Catalyzed oxidation, kinetics, Hexacyanoferrate, Activation parameters, Charge transfer, thermodynamic parameters.*

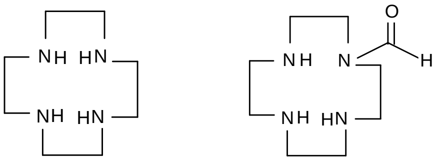
I. Introduction

N-functionalized tetraazamacrocycles such as 1,4,7,10-tetraazacyclododecane **(L)** **(Fig. 1)** and cyclam have received a great deal of attention over the last years , because of their coordination chemistry are used heavily in the fields of medical imaging, radiotherapy, antitumor drugs and anti-HIVagents.[1-3] Moreover, the magnetic properties of metals compounds of cyclens bearing carboxylic acids and alcohols pendant arms have been showed a considerable interest in magnetic interactions occurring in these systems.[4-5]

Hexacyanoferrate(III) has been extensively used to oxidize number of organic and inorganic compounds in alkaline media.[6-18] However, the oxidation of organic substrates proceeds through outer sphere mechanism, with the electron transfer occurring from the reductant to the central atom via a cyanide ligand.[18]

The alkaline hexacyanoferrate(III) ion acts as an electron-abstracting reagent in redox reactions. A free-radicals intermediate are produced from the oxidation of some substrates [19], while oxidation of others does not involve the production of such radicals.[20-21]

Herein, we report the oxidation of 1,4,7,10-tetraazacyclododecane-1-carbaldehyde (LCHO) **(Fig. 1)** with hexacyanoferrate(III) in alkaline media to investigate the redox chemistry of hexacyanoferrate(III), and to obtain additional information about the thermodynamic and reactivity of aldehyde parameter.



(L) **(LCHO)**

Figure 1: chemical structures of 1,4,7,10-tetraazacyclododecane and 1,4,7,10-tetraazacyclododecane-1-carbaldehyde.

II. Materials and Methods

1,4,7,10-tetraazacyclododecane-1-carbaldehyde was prepared and characterized as reported previously.[22] All chemicals used were of reagent grade, and doubly distilled water was used throughout the work. A solution of (LCHO) was prepared by dissolving an appropriate amount of Ligand in doubly distilled water. The required concentration of (LCHO) was prepared from its stock solution. A solution of $Fe(CN)_6^{-3}$ was prepared by dissolving $K_3Fe(CN)_6$ in H_2O and standardized iodometrically. [23] NaOH and $NaNO_3$ were employed to maintain the required alkalinity and ionic strength, respectively, in reaction solutions.

III. Kinetic measurements

All kinetic measurements were performed under pseudo first-order conditions where [LCHO] was always in large excess over $[Fe(CN)_6^{-3}]$. The reaction was initiated by mixing the thermostatted solutions of $Fe(CN)_6^{-3}$ and LCHO, which also contained the required concentration of NaOH and $NaNO_3$. The progress of the reaction was monitored by measuring the decrease in the absorbance of $Fe(CN)_6^{-3}$ in the reaction solution at 420 nm vs. time, using a Unicam UV/VIS spectrophotometer with 1.0 cm cell. The isolation method was used in this study where the concentration of the substance to be monitored is changed with the others kept constant. Aqueous solutions are prepared by making a constant total volume for all runs.

The pseudo first order rate constants in each case were obtained from the plots of the $\ln(A_\infty - A_t)$ versus time t were made (where A_∞ and A_t are the absorbances at infinity and at time t respectively), which were linear to about 70% at various reactant concentrations. The temperature was kept constant at 35º ± 1ºC, $[OH^-] = 0.04$ mol dm^{-3} and the ionic strength was maintained constant at 0.5 $mol.dm^{-3}$ ($NaNO_3$). A typical pseudo-first order plot is presented in **(Fig. 2).**

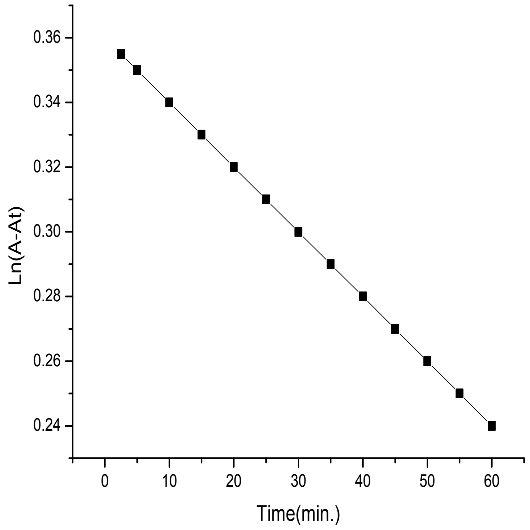
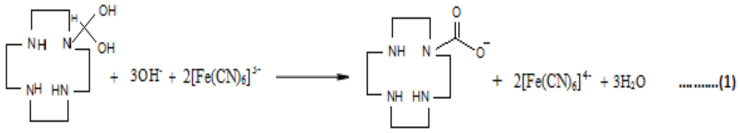


Figure (2): plot of $\ln(A_\infty - A_t)$ vs. time for the oxidation of (LCHO) at [HCF(III)] = 4 x 10^{-4} M, $[OH^-] = 0.4$M, [LCHO] = 4 x 10^{-3} M, I = 0.40 M and 35 ˚C.

IV. Results and Discussion

Determination of stoichiometric factors:

A reaction mixture, containing known excess of hexacyanoferrate(III) over 1,4,7,10-tetraazacyclododecane-1-carbaldehyde, was allowed to stand in the presence of sodium hydroxide at 30 ºC. After the completion of reaction, the result showed that one mole of ligand consumed two moles of hexacyanoferrate(III) according to the stoichiometric equation (1)



The main oxidation product 1,4,7,10-tetraazacyclododecane-1-formic acid was extracted with chloroform, the solvent was removed under reduced pressure to give a white solid. The product was dissolved in a minimum amount of methanol and precipitated with diethyl ether.

The crystalline powder was collected by filtration, washed with ether (2 × 30 ml), and dried to afford the LCOOH as a white powder. The product was characterized by elemental analysis and The recorded IR spectra of aldehyde and its oxidation product showed a decay of the band at 1725 cm−1 of aldehyde due to(C=O) . Typical bands assigned to 1,4,7,10-tetraazacyclododecane-1-formic spectra were located at 1720 cm^{-1} is due to the CO double bond, the broad band centered in the range 2900-3250 cm^{-1} is caused by the presence of the OH and a band near 1400 cm^{-1} comes from the CO single bond.

V. Reaction order

The reaction orders were determined from the slopes of log k_{obs} vs. logc plots by varying the concentrations of oxidant, reductant and alkali in turn while keeping the others constant.

VI. Effect of alkali

To study the effect of alkali concentration on the rate of reaction, $[OH^-]$ was varied in the range of 0.10 to 0.50 $mol.dm^{-3}$ at constant concentrations of HCF(III) and Ligand at a ionic strength of 0.6 $mol.dm^{-3}$. The rate constants of the reaction were found to increase with increase in $[OH^-]$ (Table **1**). Plot of log k_{obs} versus log $[OH^-]$ was linear with a slope of 0.89 (r = 0.998), suggesting the reaction to be first order with respect to $[OH^-]$ **(Fig. 3).**

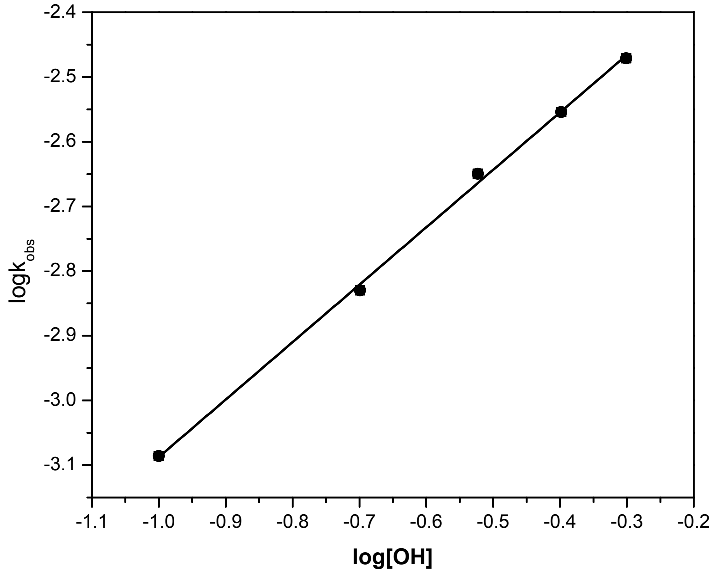


Figure 3: Plot of log k_{obs} vs. log [OH$^-$] for the oxidation of (LCHO) by alkaline HCF(III)

VII. Effect of 1,4,7,10-tetraazacyclododecane-1-carbaldehyde (LCHO)

Reaction was carried out keeping all experimental conditions constant and by varying initial concentration of aldayde from 1.0×10^{-3} to 5.0×10^{-3} mol.dm^{-3}. It was found that the rate of reaction increases with increasing [LCHO]. (Table 1). The plot of log k_{obs} versus log [LCHO] was linear with a slope of 1.06 (r = 0.995), suggesting the reaction to be first order with respect to [LCHO] **(Fig. 4).**

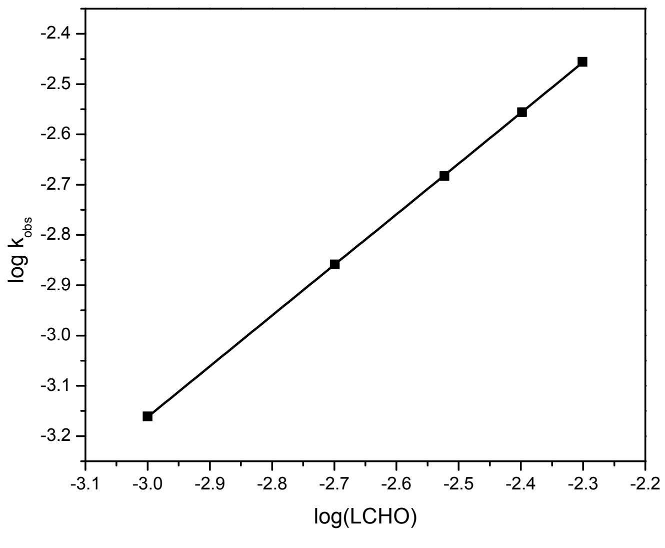


Figure 4: Plot of log k_{obs} *vs.* log [LCHO] for the oxidation of (LCHO) by alkaline HCF(III).

VIII. Effect of hexacyanoferrate (III) HCF(III).

The $[Fe(CN)_6^{-3}]$ was varied in the range, 2.0×10^{-4}–10.0×10^{-4} mol.dm^{-3} and keeping all other reactant concentrations as constant and the rate were measured (Table 1). The rate of oxidation increases with increase in hexacyanoferrate (III) concentration. The plot of log k_{obs} versus log [HCF(III)] gave the slope of 0.99 (r = 0.998), **(Fig. 5)** shows that this oxidation reaction was first order with respect to [HCF(III)]

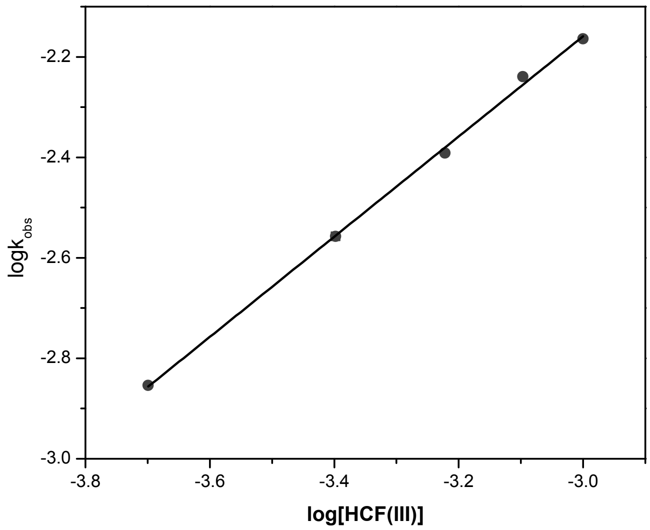


Figure 5: Plot of log k_{obs} *vs*. ionic strength for the oxidation of (LCHO) by alkaline HCF(III)

IX. Effect of ionic strength

The reactions were studied at varying ionic strength (0.02 to 0.05 $mol.dm^{-3}$) by adding potassium nitrate solution at constant concentrations of $[Fe(CN)_6^{-3}]$ $4.0x10^{-4}$ $mol.dm^{-3}$, [LCHO] 4.0 $x10^{-3}$ $mol.dm^{-3}$ and $[OH^{-}]$ 0.4 $mol.dm^{-3}$. The values of k_{obs} were found to increase with increasing the ionic strength(Table 2), suggesting that the reaction takes place between ions of similar charges.

A plot of log k_{obs} vs $\sqrt{I}/(1+\sqrt{I})$according to extended Brönsted–Debye–Hückel equation [24] was found to be linear with positive slope as shown in **(Fig. 6).**

The rate constant at infinite dilution (k_0) is 7.98×10^{-4} min^{-1} and the product of the charges ZAZB ≈3. This is the same expected value considering the proposed mechanism, which involves a collision between a monovalent $((LCO(OH))^{-}$and a trivalent anion($Fe(CN)_6^{-3}$) in the rate-determining step.

The rate was found to increase with increase in ionic strength indicating a positive salt effect **(Table 2).**

Table 1. Effect of Variations of $[Fe(CN)_6^{-3}]$, [LCHO], and $[OH^{-}]$ on the Oxidation of LCHO by $Fe(CN)_6^{3-}$ at

[HCF(III)] X 10^4 ($mol.dm^{-3}$)	**[LCHO] X10^3 ($mol.dm^{-3}$)**	**$[OH^{-}]$ ($mol.dm^{-3}$)**	**K_{obs} X 10^3** (min^{-1})
2	4	0.4	1.4
4	4	0.4	2.77
6	4	0.4	4.06
8	4	0.4	5.76
10	4	0.4	6.85
4	1	0.4	0.62
4	2	0.4	1.25
4	3	0.4	1.85
4	4	0.4	2.78
4	5	0.4	3.35
4	4	0.1	0.82
4	4	0.2	1.48
4	4	0.3	2.21
4	4	0.4	2.79
4	4	0.5	3.38

35 °C, $I = 0.40$ $mol.dm^{-3}$

Table 2: Effect of Ionic strength

[I]	**$\sqrt{I}/(1+\sqrt{I})$**	**k_{obs} x10^3**
0.02	0.1238	1.85
0.03	0.1476	2.18
0.04	0.1666	2.5
0.05	0.1827	2.77
0.06	0.1968	3.04

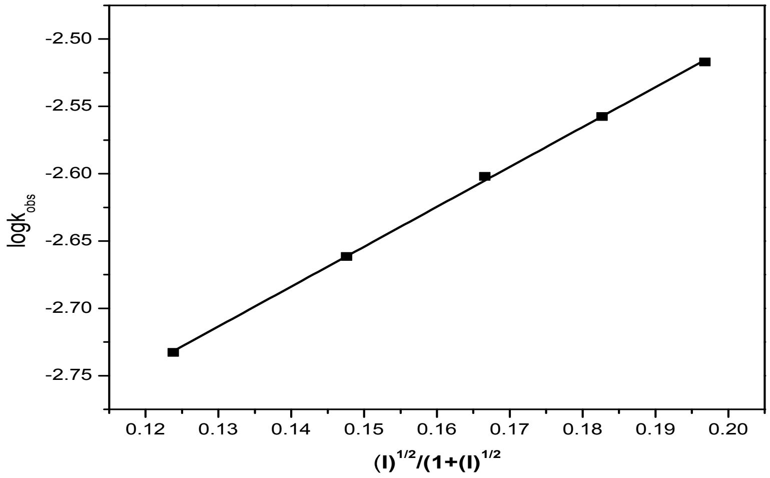


Figure 6: Plot of log k_{obs} *vs*.. ionic strength for the oxidation of (LCHO) by alkaline HCF(III).

X. Effect of Initially Added Products

The effect of initially added ($Fe(CN)_6^{-4}$) product on the rate of reaction was also studied in the range of 1.0 × 10^{-4}–5.0 × 10^{-4} mol·dm^{-3} at35 ◦C at constant [$Fe(CN)_6^{-3}$], [LCHO], [OH^-], and ionic strength. As the initial concentration of (Fe (CN) $_6{}^{-4}$) is increased, the rate of reaction progressively decreased, i.e. it retarded the oxidation process (Table 3). A similar behavior has been observed in some redox reactions involving the formation of similar intermediates. [25–26]

Table 3: Effect of Added Product, $Fe(CN)_6^{-4}$, on the Oxidation of LCHO by Hexacyanoferrate(III) in Aqueous Alkaline Medium at 35 ˚C.

[$Fe(CN)_4^{-6}$]x 10^{-5} mol.dm^{-3}	**K_{obs} X 10^{-3}**
1.0	2.47
2.0	2.21
3.0	2.05
4.0	1.88
5.0	1.78

Thermodynamic Parameters

The rate of reaction was measured at different temperatures (298 – 318 K) at constant concentrations of reactants and other conditions being constant. The rate of reaction was increased with increasing the temperature. The values of k_{obs} at different temperature were given in **Table 4.** The activation energy Ea was evaluated from the plot of lnk_{obs} *versus* 1/ T **(Fig. 7).** Eyring's plot of ln k_{obs}/T *versus* 1/T were linear (r = 0.999) **(Fig. 8)**,the activation parameters ΔH^* and ΔS^* were obtained from the slope and intercept of the Eyring's plot. Arrhenius and thermodynamic activation parameters are given in **table 5.**

Table 4: Effect of temperature on the rate of oxidation of LCHO by Hexacyanoferrate(III) in aqueous alkaline medium at different temperatures.

T(K)	**(1/T) x 10^3**	**k_{obs} x10^3**	**Ln(k_{obs})**	**Ln(k/T)**
298	3.36	18.55	-3.98729	-9.68438
303	3.30	22.24	-3.80586	-9.5196
308	3.25	27.7	-3.58632	-9.31642
313	3.19	33.36	-3.4004	-9.1466
318	3.14	39.40	-3.23399	-8.99604

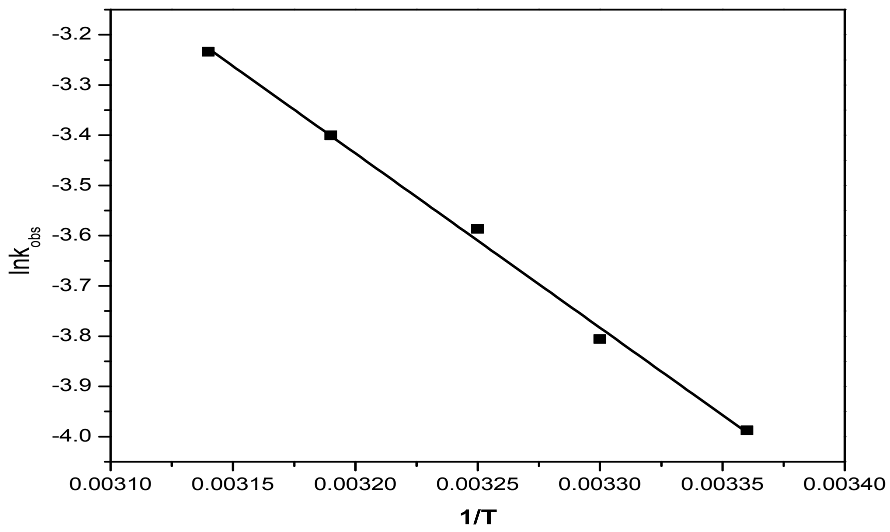


Figure 7: Plot of lnk$_{obs}$ *vs*. 1/T for the oxidation of (LCHO) by alkaline HCF(III).

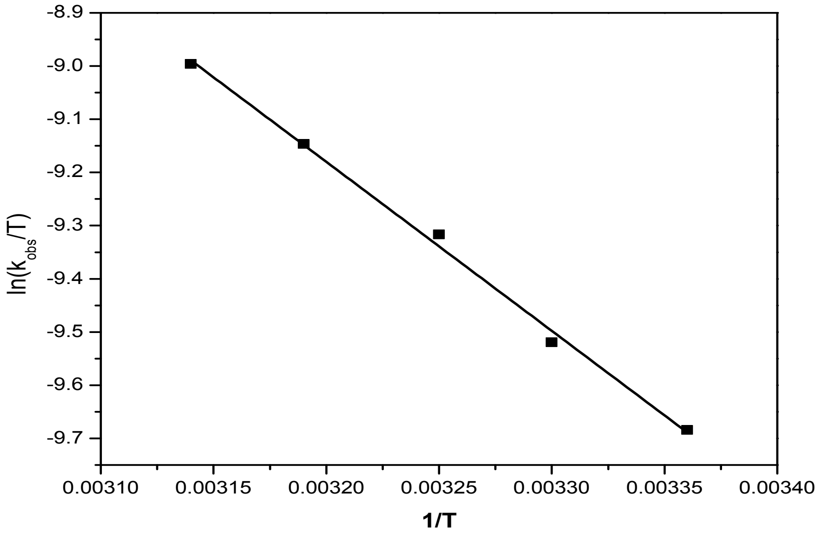


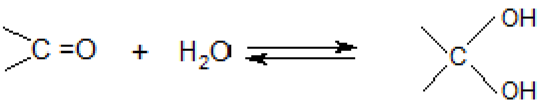
Figure 8: Plot of ln(k$_{obs}$/ T) *vs*. 1/T for the oxidation of (LCHO) by alkaline HCF(III).

Parameters	Values
Ea(k J mol^{-1})	28.88
ΔH^* k J mol^{-1})	26.41
ΔS^* (J K^{-1} mol^{-1})	-189.33
ΔG^*_8 (k J mol^{-1})	84.72
A(dm^3 mol^{-1}s^{-1})	2158.57

Table 5: Arrhenius and thermodynamic activation parameters for the oxidation of LCHO by Hexacyanoferrate(III) in aqueous alkaline medium at different temperatures.

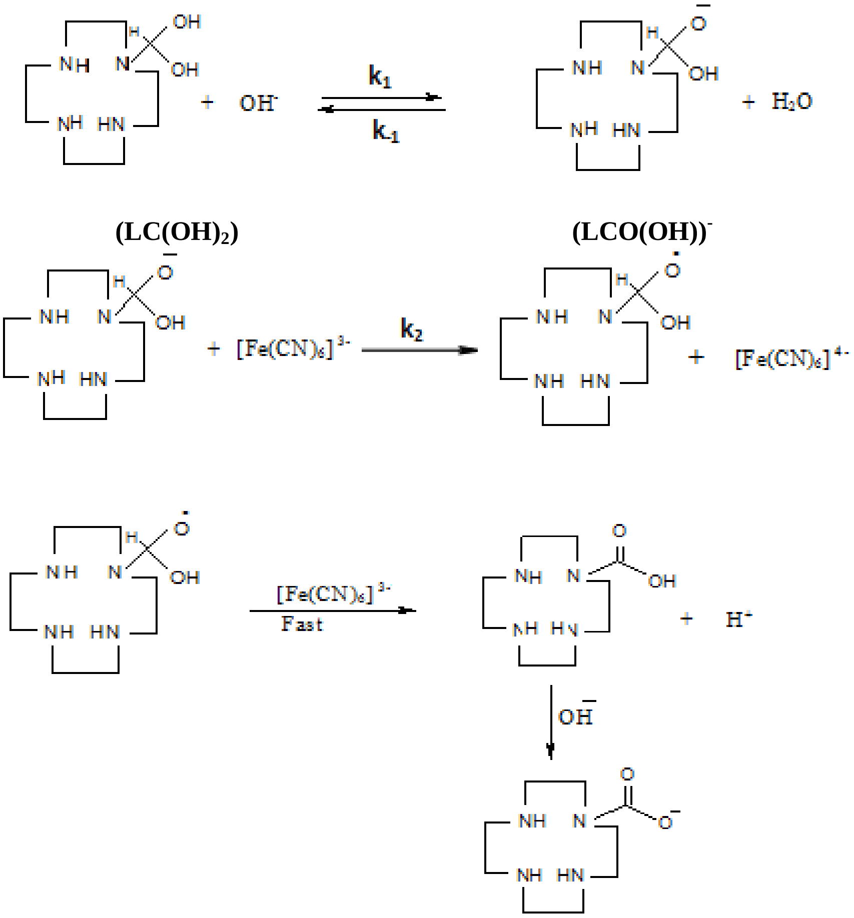
XI. Discussion

It has been reported that carbonyl compounds undergo reversible hydration in aqueous solution in the presence of acid or base catalysis.[27-28] In several ways its oxidation resembles that of aliphatic alcohols. In the present case also, one might assume that the hydrate formation occur as according to the following equilibrium:



............................(2)

On the basis of the results probable scheme of oxidation of the hydrated 1,4,7,10-tetraazacyclododecane-1-carbaldehyde**(LC(OH)$_2$)**by hexacyanoferrate(III)) ion via the formation of anion **(LCO(OH))**$^-$as an intermediate might be considered as follows be:



The formate ion is much more stable towards oxidation due to its mesomeric structure.

Now assuming steady state condition for the concentration of (LCO(OH))$^-$, the rate law might be derived as follows:

$$-\frac{d[\mathrm{LCO(OH)}]^-}{dt} = k_1[\mathrm{LC(OH)_2}][\mathrm{OH^-}] - k_{-1}\left[\left(\mathrm{LCO(OH)}\right)^-\right][H_2O] - k_2\left[\left(\mathrm{LCO(OH)}\right)^-\right][\mathrm{Fe(CN)_6}]^{3-} \quad \ldots\ldots.3$$

Now keeping the experimental conditions in mind and solving equ.(3) the final rate equation will be:

$$-\frac{d[\mathrm{Fe(CN)_6}]^{3-}}{dt}\frac{2k_1k_2[\mathrm{LC(OH)_2}][\mathrm{Fe(CN)_6}]^{3-}[\mathrm{OH^-}]}{k_{-1}[\mathrm{H_2O}] + k_2[\mathrm{Fe(CN)_6}]^{3-}} \quad \ldots\ldots 4$$

To the first approximation, if we assume that $k_{-1}[H_2O\,] \gg [Fe(CN)_6]^{3-}$, the rate law (4) reduces to (5):

$$-\frac{d[\mathrm{Fe(CN)_6}]^{3-}}{dt} = \quad \ldots\ldots\ldots\ldots 5$$

According to equation (5), the rate law clearly explains the experimental results i.e., first order kinetics with respect to hexaeyanoferrate(III), 1,4,7,10-tetraazacyclododecane-1-carbaldehyde and hydroxide ion concentration.

These results suggest that the reaction proceeds via a charge transfer process as it has already been observed in the course of the oxidation of acetone, ethylmethylketone and formaldehyde by aqueous alkaline hexacyanoferrate(III). [29-31] Furthermore, the experimental values of ΔS^* and ΔG^* were both favourable for electron transfer processes. The high negative values of ΔS^* indicates that the intermediate complex is more ordered than the reactants due to loss of degree of freedom. [32]

XII. Conclusion

The main product of the reaction were found to be 1,4,7,10-tetraazacyclododecane-1-formic acid. The reaction is first order with respect to aldahyde , alkali and hexaeyanoferrate(III).

The experimental determination of ZAZB is indicative to the enhanced formation of the charges in the rate determining step as represented by the proposed mechanism. Moreover, the negative values of $\Delta S^{\neq}$ provided support for the formation of a rigid activated complex with fewer degrees of freedom.
A mechanism in terms of active species of oxidant is proposed and the rate law is derived and
verified.

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