Palladium(II)-Catalyzed Oxidation of Pyrimidine Derivative by Hexacyanoferrate(III) in Aqueous Alkaline Medium: A Kinetic Study

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Abstract: The of kinetics of oxidation of a pyrimidine derivative, *N,N*-dimethyl-*N'*-(pyrimidin-2-yl) formamidine (Pym-F), by hexacyanoferrate(III) (HCF) was studied in aqueous alkaline medium in the presence of palladium(II) catalyst. The reaction did not proceed in the absence of Pd(II) catalyst. The progress of the catalyzed reaction was followed spectrophotometrically. The reaction showed a first order kinetics in both [HCF] and [Pd(II)], and less than unit orders with respect to both [Pym-F] and [OH⁻]. Increasing ionic strength and dielectric constant of the medium increased the reaction rate. A mechanistic scheme for the catalyzed oxidation reaction has been proposed. The final oxidation products are identified as 2-aminopyrimidine, dimethylamine and carbon dioxide. The rate law expression associated with the reaction mechanism is derived and the reaction constants involved in the different steps of the mechanism are calculated. The activation parameters with respect to the rate-determining step have been computed and discussed.

Keywords: Pyrimidine Derivative, Oxidation, Kinetics, Mechanism, Palladium(III), Hexacyanoferrate(III)

1. Introduction

Pyrimidine is a six-membered heterocyclic organic compound with two nitrogen atoms at positions 1 and 3 in the ring. The pyrimidine ring system has a wide occurrence in nature as substituted, ring fused compounds and derivatives, including the nucleotides, thiamine (vitamin B1) and alloxan [1]. It is also found in many synthetic compounds such as barbiturates and the HIV drug, zidovudine. Pyrimidine also photolytically decomposes into uracil under UV light [2]. Among the significant pyrimidine derivatives is *N,N*-dimethyl-*N'*-(pyrimidin-2-yl) formamidine (Pym-F) where formamidines have attracted increasing interest in recent decades, because of their very broad spectrum of biological activities [3, 4]. The *N,N*-dialkyl derivatives of formamidines are highly effective acaricides

and the most rewarding of these studies resulted in discovery of the acaricide insecticide chlordimeform [5, 6]. The oxidative cleavage of formamidines is quite important, since the *N,N*-dialkyl formamidine group is one of the most versatile protecting groups, especially in biosynthetic applications.

On the other hand, formamidines form complexes with transition metal ions [7, 8] and such complexes exhibit remarkable biological activity against certain microbes, viruses and tumors [9, 10]. The presence of heteroatom in such ligands plays a key role when coordinated with these metal ions such as pyrimidine derivatives. Furthermore, transition metal ions are used as catalysts in various oxidation-reduction reactions because they have various oxidation states [11-14].

Hexacyanoferrate(III) is an efficient one-electron oxidant for oxidation of various organic compounds especially in

alkaline media [7, 8, 15-26]. The usefulness of HCF may be due to its high stability, water solubility and its moderate reduction potential of 0.45 V, leading to its reduction to HCF(II), a stable product [27]. In addition, it adds less error to the experimental results, and data can be analyzed meticulously to establish the reaction path.

Although, the kinetics of the oxidation of Pym-F by permanganate ions have been studied in both alkaline [28] and acid [29] media, there are no reports describing its oxidation kinetics when other oxidants are used. This observation prompted us to investigate the title reaction. The aims of the present study are to establish the optimum conditions affecting oxidation of Pym-F by HCF in aqueous alkaline medium, to understand the active species of the reactants in such medium, to examine the catalytic activity of Pd(II) catalyst and finally to elucidate a plausible oxidation reaction mechanism.
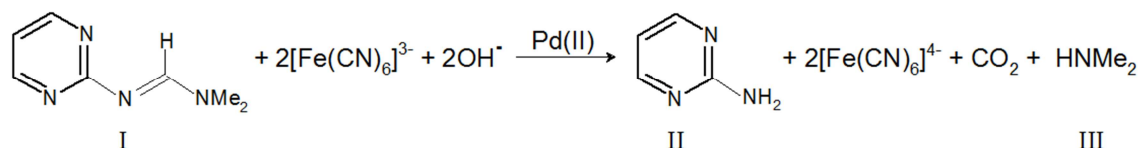
2. Experimental

2.1. Materials

All chemicals used throughout the present work were of reagent grade and doubly distilled water was used in all preparations. The solution of Pym-F was freshly prepared by dissolving the sample in doubly distilled water. A solution of hexacyanoferrate(III) was prepared by dissolving potassium hexacyanoferrate(III) (BDH) in water and its concentration was ascertained spectrophotometrically. Hexacyanoferrate(II) solution was obtained by dissolving potassium hexacyanoferrate(II) (S.D fine Chem.) in water and standardizing with cerium(IV) solution [30]. The Palladium(II) chloride solution was prepared by dissolving a known weight of the sample (S.D fine Chem.) in hydrochloric acid and stored in a black coated bottle to prevent any photochemical deterioration. Sodium hydroxide, sodium perchlorate and *t*-butyl alcohol were used to vary the alkalinity, ionic strength and dielectric constant in the reaction medium, respectively.

2.2. Kinetic Measurements

Kinetic measurements were performed under pseudo-first order conditions where Pym-F was present in a large excess over over hexacyanoferrate(III) concentration at a constant ionic strength of 1.0 mol dm^{-3} and at a constant temperature of $(25 \pm 0.1)°C$ unless otherwise stated. The progress of HCF reduction was followed by measuring the decay of its absorption spectrophotometrically at λ_{max} = 420 nm, its absorption maximum, where it absorbs to a considerably greater extent than any of the other reactants and products. It was also verified that there is no interference from other reagents at this wavelength. The spectrophotometer was Shimadzu UV-VIS-NIR-3600 double-beam. Solutions of the oxidant and the mixture containing Pym-F substrate, alkali and palladium(II) chloride catalyst were separately thermostated for nearly 30 min. The oxidant was then added to the mixture, the overall reaction mixture was transferred to the cell of path length 1 cm, and 3-4 experimental readings were taken in each run. It was observed that the oxidation reaction do not proceed in the absence of palladium(II) catalyst. Good straight lines for ln(absorbance) versus time plots were obtained for about two half-lives of the reaction completion. The pseudo-first order rate constants of the catalyzed reaction (k_C) were calculated as the gradients of such plots. The rate constants were reproducible to within 4%. The order of reaction with respect to the reactants were determined from the slopes of log k_C versus log(concentration) plots by varying the concentrations of substrate, alkali and catalyst, in turn, while keeping other conditions constant. A few kinetic runs were carried out after bubbling purified nitrogen and compared with those taken under air, and the results were found to be the same. Thus the dissolved oxygen did not have any effect on the oxidation rate.

3. Results

3.1. Stoichiometry and Product Identification

Reaction mixtures containing varying ratios of hexacyanoferrate(III) to Pym-F at a constant ionic strength of 1.0 mol dm^{-3} were kept for over 24 h at 25°C in a closed vessel for completion of the reaction. The unreacted [HCF] was analyzed spectrophotometrically by measuring its absorption at 420 nm. The results indicated that two moles of HCF are consumed by one mole of Pym-F to yield the oxidation products as shown in the following stoichiometric equation:

where compound I, II and III refer to Pym-F, 2-aminopyrimidine and dimethylamine, respectively. The above stoichiometric equation is consistent with the results of product identification which carried out by spectral and elemental analysis as described elsewhere [28-32].

3.2. Spectral Changes

The spectral changes during the palladium(II)-catalyzed oxidation of Pym-F by HCF in aqueous alkaline medium are shown in Figure 1. The scanned spectra indicate gradual disappearance of HCF band with time at its absorption maximum, λ = 420 nm, as a result of its reduction HCF(II).
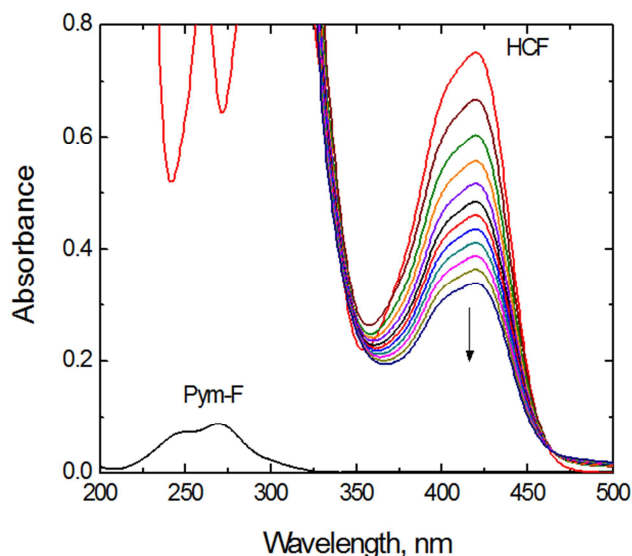
Figure 1. Spectral changes for Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [Pym-F] = 1.2 x 10⁻², [HCF] = 7.0 x 10⁻⁴, [OH⁻] = 0.5, [Pd(II)] = 6.0 x 10⁻⁵ and I = 1.0 mol dm⁻³ at 25°C. Scanning time intervals = 4.0 min.

3.3. Dependence of the Reaction Rate on [HCF]

HCF concentration was varied in the range of $(1.0 - 11.0)$ x10^{-4} mol dm^{-3} at constant concentrations of other reagents and constant ionic strength and temperature. The plots of ln(absorbance) versus time were linear for about two half-lives of the reaction completion. Furthermore, the pseudo-first order rate constant, k_C, was found to be independent of the initial concentration of HCF (Table 1). These results suggest first order dependence of the reaction on [HCF].

3.4. Dependence of the Reaction Rate on [Pym-F]

The reaction rate was measured at different concentrations of the Pym-F substrate keeping other reactant concentrations constant. The plot of k_C versus [Pym-F] was found to be linear with a positive intercept (Figure 2) indicating that the reaction order with respect to [Pym-F] was found to be less than unity.

3.5. Dependence of the Reaction Rate on [OH⁻]

The effect of pH on the reaction rate was studied by varying the concentration of NaOH in the range of 0.1-1.0 mol dm^{-3} at constant [Pym-F], [HCF], [Pd(II)], ionic strength and temperature. An increase in alkali concentration was found to accelerate the oxidation rate (Table 1) indicating that the oxidation process was base-catalyzed. A plot of log k_C versus log [OH⁻] was found to be linear with a slope of 0.56 suggesting that the reaction was fractional-first order with respect to [OH⁻] as shown in Figure 3.

3.6. Dependence of the Reaction Rate on [Pd(II)]

The palladium(II) catalyst concentration was varied from 2.0 x10^{-5} to 12.0 x10^{-5} mol dm^{-3} at constant [Pym-F], [HCF], [OH⁻] and at constant ionic strength and temperature.

Reaction rate was found to increase with increasing [Pd(II)] (Table 1). The order with respect to [Pd(II)] was found to be unity as the slope of log k_C versus log[Pd(II)] plot (Figure 4).

3.7. Dependence of the Reaction Rate on Ionic Strength and Dielectric Constant

The ionic strength was varied from 1.0 to 3.0 mol dm^{-3} using sodium perchlorate at constant concentrations of Pym-F, HCF, Pd(II) and at constant pH and temperature. Increasing the ionic strength increased the reaction rate (Table 1). The Debye-Huckel plot was found to linear with a positive intercept, Figure 5.

To investigate the effect of the dielectric constant, D, of the reaction medium on the rate, the reaction was studied at different solvent compositions of t-butyl alcohol and water by varying the alcohol content from 0 to 40% (V/V) in the reaction medium at constant other variables. The results indicate that the reaction rate decreased with decreasing the dielectric constant of the medium, i.e, increasing the alcohol content and the plot of k_C versus $1/D$ was found to linear with a negative intercept as illustrated in Figure 6.

Table 1. Effect of variation of [HCF], [Pym-F], [OH⁻], [Pd(II)] and ionic strength (I) in the pseudo-first order rate constant (k_C) in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium at 25°C.

| 10^4 [HCF] (mol dm^{-3})	10^2 [Pym-F] (mol dm^{-3})	[OH⁻] (mol dm^{-3})	10^5 [Pd(II)] (mol dm^{-3})	I (mol dm^{-3})	10^3 k_C (s^{-1})
1.0	1.6	0.5	6.0	1.0	21.4
3.0	1.6	0.5	6.0	1.0	20.9
5.0	1.6	0.5	6.0	1.0	22.1
7.0	1.6	0.5	6.0	1.0	21.6
9.0	1.6	0.5	6.0	1.0	21.3
11.0	1.6	0.5	6.0	1.0	22.0
7.0	0.4	0.5	6.0	1.0	9.0
7.0	0.8	0.5	6.0	1.0	16.1
7.0	1.2	0.5	6.0	1.0	22.6
7.0	1.6	0.5	6.0	1.0	29.9
7.0	2.0	0.5	6.0	1.0	36.2
7.0	2.4	0.5	6.0	1.0	41.0
7.0	1.6	0.1	6.0	1.0	10.2
7.0	1.6	0.3	6.0	1.0	18.3
7.0	1.6	0.5	6.0	1.0	22.6
7.0	1.6	0.7	6.0	1.0	28.6
7.0	1.6	0.9	6.0	1.0	33.2
7.0	1.6	1.0	6.0	1.0	35.1
7.0	1.6	0.5	2.0	1.0	8.2
7.0	1.6	0.5	4.0	1.0	15.9
7.0	1.6	0.5	6.0	1.0	22.6
7.0	1.6	0.5	8.0	1.0	30.2
7.0	1.6	0.5	10.0	1.0	37.8
7.0	1.6	0.5	12.0	1.0	45.3
7.0	1.6	0.5	6.0	1.0	22.6
7.0	1.6	0.5	6.0	1.4	25.7
7.0	1.6	0.5	6.0	1.8	28.4
7.0	1.6	0.5	6.0	2.2	31.2
7.0	1.6	0.5	6.0	2.6	35.5
7.0	1.6	0.5	6.0	3.0	39.2

Experimental error ± 3%
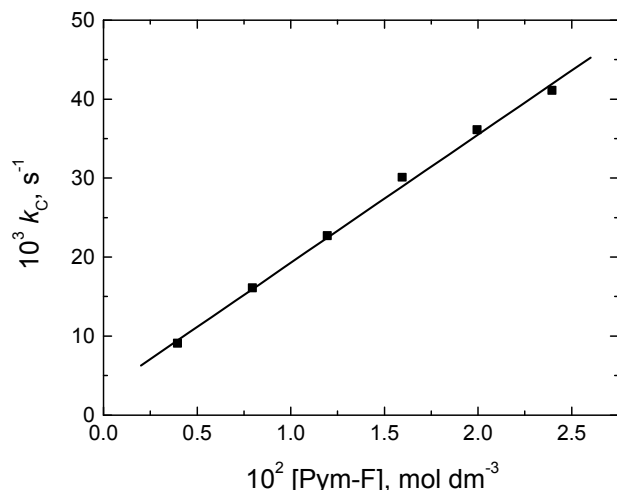
Figure 2. *Plot of k_C versus [Pym-F] in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [HCF] = 7.0 x 10^{-4}, [OH^-] = 0.5, [Pd(II)] = 6.0 x 10^{-5} and I = 1.0 mol dm^{-3} at 25°C.*
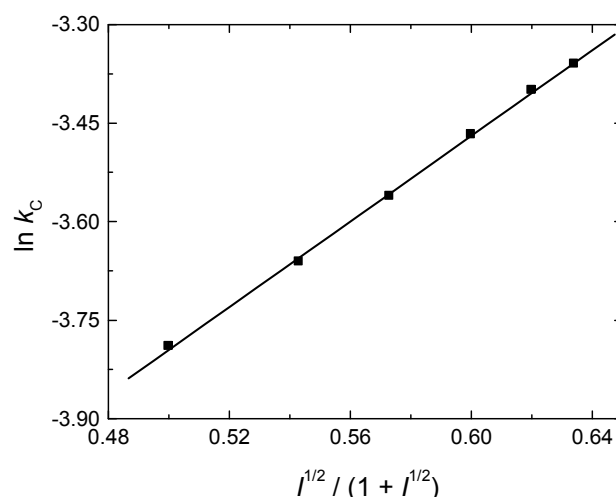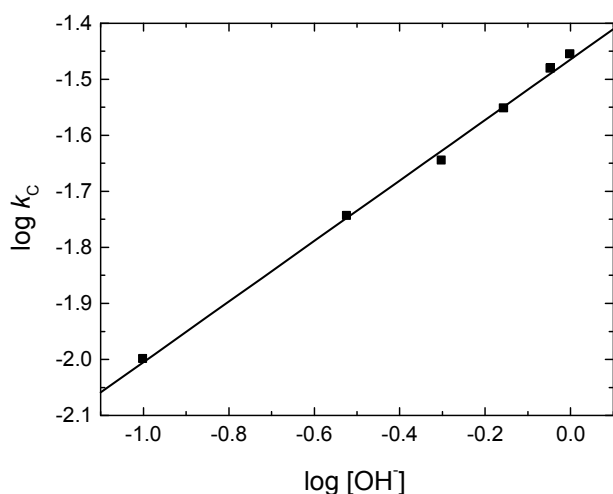

Figure 5. *Debye-Huckel plot in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [HCF] = 7.0 x 10^{-4}, [Pym-F] = 1.2 x 10^{-2}, [OH^-] = 0.5 and [Pd(II)] = 6.0 x 10^{-5} mol dm^{-3} at 25°C.*

Figure 3. *Plot of log k_C versus log [OH^-] in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [HCF] = 7.0 x 10^{-4}, [Pym-F] = 1.2 x 10^{-2}, [Pd(II)] = 6.0 x 10^{-5} and I = 1.0 mol dm^{-3} at 25°C.*
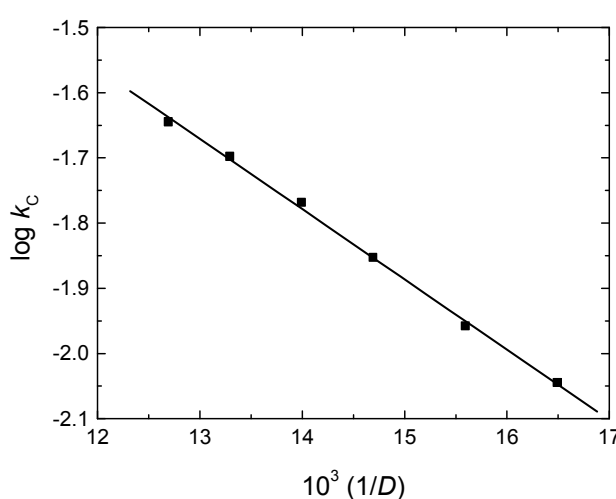

Figure 6. *Effect of dielectric constant on the oxidation rate in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [HCF] = 7.0 x 10^{-4}, [Pym-F] = 1.2 x 10^{-2}, [OH^-] = 0.5, [Pd(II)] = 6.0 x 10^{-5} and I = 1.0 mol dm^{-3} at 25°C.*

3.8. Effect of Temperature

The Pd(II)-catalyzed reaction was studied at four temperatures ranging between 288 and 318 K at constant substrate, alkali and Pd(II) concentrations. The oxidation rate was found to increase with raising temperature. The activation parameters were evaluated using Arrhenius and Eyring plots and are listed in Table 2.

Table 2. *Activation parameters associated with the slow step (k) in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [Pym-F] = 1.2 x 10^{-2}, [HCF] = 7.0 x 10^{-4}, [OH^-] = 0.5, [Pd(II)] = 6.0 x 10^{-5} and I = 1.0 mol dm^{-3}.*

$\Delta S^{\neq}$ J mol^{-1}K^{-1}	$\Delta H^{\neq}$ kJ mol^{-1}	$\Delta G^{\neq}_{298}$ kJ mol^{-1}	$E_a^{\neq}$ kJ mol^{-1}
-117.34	47.23	82.19	48.17

Experimental error ± 3%

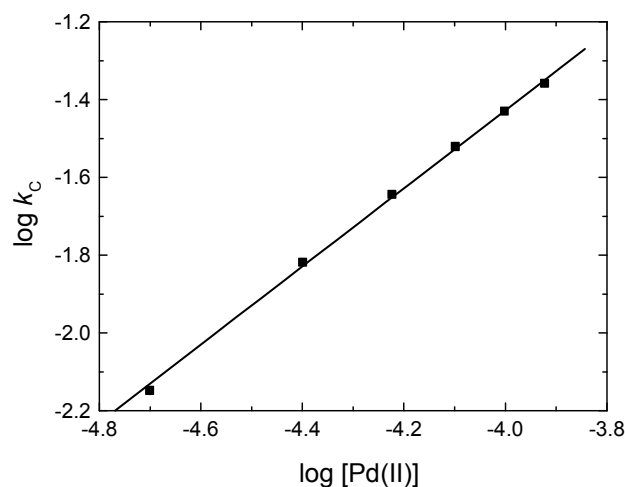**Figure 4.** *Plot of log k_C versus log [Pd(II)] in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [HCF] = 7.0 x 10^{-4}, [Pym-F] = 1.2 x 10^{-2}, [OH^-] = 0.5 and I = 1.0 mol dm^{-3} at 25°C.*

3.9. Effect of Initially Added Product

The effect of added hexacyanoferrate(II) product was studied also in the concentration range of (2.0 - 12.0) x 10^{-4} mol dm^{-3} at fixed concentrations of the oxidant, reductant, alkali and catalyst. It was found that HCF(II) did not have any significant effect on the rate of reaction.

3.10. Polymerization Test

The involvement of free radical species in the reaction was assayed by a polymerization test. A known quantity of acrylonitrile monomer was added initially to the reaction mixture in an inert atmosphere, with the result of progressive formation of a white precipitate in the whole reaction mixture indicating presence of free radical during reaction. When the experiment was repeated in the absence of Pym-F under similar conditions, the test was negative. This indicates that the reaction was routed through free radical path.

4. Discussion

Palladium(II) catalysis has been observed during various redox reactions [33-35]. In most of the studies using palladium(II) as a homogenous catalyst, it has been employed in the form of palladium(II) chloride. It is important to know the probable species of palladium(II) chloride in alkaline media which is mostly present as hydroxylated species, $[Pd(OH)_2Cl_2]^{2-}$, $[Pd(OH)_3Cl]^{2-}$ and $[Pd(OH)_4]^{2-}$ [34, 35]. The species $[Pd(OH)_3Cl]^{2-}$ and $[Pd(OH)_4]^{2-}$ are not commonly found due to their insoluble characteristic. Hence, the $[Pd(OH)_2Cl_2]^{2-}$ complex ion (written as Pd(II)* in the mechanism for brevity) has been assumed to be the reactive species in the present study.

The oxidation of Pym-F substrate by HCF in alkaline medium did not occur in the absence of a catalyst while it proceeded in a measurable quantities in the presence of small amounts of palladium(II) catalyst. The reaction has a stoichiometry of 2:1, i.e., two moles of hexacyanoferrate(III) requires one mole of Pym-F. The order with respect to [HCF] and [Pd(II)] was found to be unity and less than unity with respect to [Pym-F] and [OH⁻]. Increasing the reaction rate with the increase in [OH⁻] suggests deprotonation of Pym-F substrate. The rate is not considerably affected by HCF(II) suggesting that the probability of any fast equilibrium with the product preceding the rate-determining step was ruled out. The rate-determining step should be irreversible as is generally the case for one electron oxidants [36] and the oxidation takes place through generation of a free radical as obtained experimentally. The effect of ionic strength and dielectric constant on the reaction rate suggests that similarly charged species are interacting in the rate-determining step [37, 38].

On the other hand, the less than unit with respect to Pym-F concentration may be due to formation of a complex (C) between Pd(II)*species and deprotonated Pym-F species in a pre-equilibrium step. Complex formation was proved kinetically by the non-zero intercept of the [Pd(II)]/k_C versus

1/[Pym-F] plot (Figure 7) in favor of possible formation of an intermediate complex between the oxidant and substrate [39]. Then, the oxidant HCF attack the formed complex in a slow (rate-determining) step to yield Pym-F free radical and HCF(II) with regeneration of the catalyst Pd(II)*. The radical intermediate reacts with another mole of the oxidant in a subsequent fast step to yield the final oxidation products. The results are accommodated in Scheme 1.

Again, it has been reported [40-42] that the entropy of activation ($\Delta S^{\neq}$) tends to be more negative for reactions of an inner-sphere nature, whereas the reactions of positive $\Delta S^{\neq}$ values proceed via an outer-sphere mechanism. The obtained large negative values of $\Delta S^{\neq}$ (Table 2) suggests that the more plausible mechanism is one-electron transfer of inner-sphere nature. Furthermore, large negative values of $\Delta S^{\neq}$ indicate that there is a decrease in the randomness during the oxidation process. This leads to the formation of compacted intermediate complex and such activated complex is more ordered than the reactants due to loss of degree of freedom. On the other hand, the positive value of $\Delta H^{\neq}$ indicates that the complex formation is endothermic. Also, the large positive value of $\Delta G^{\neq}$ suggests enhanced formation of the intermediate with raising temperature as well as to the non-spontaneity of the complex formation.
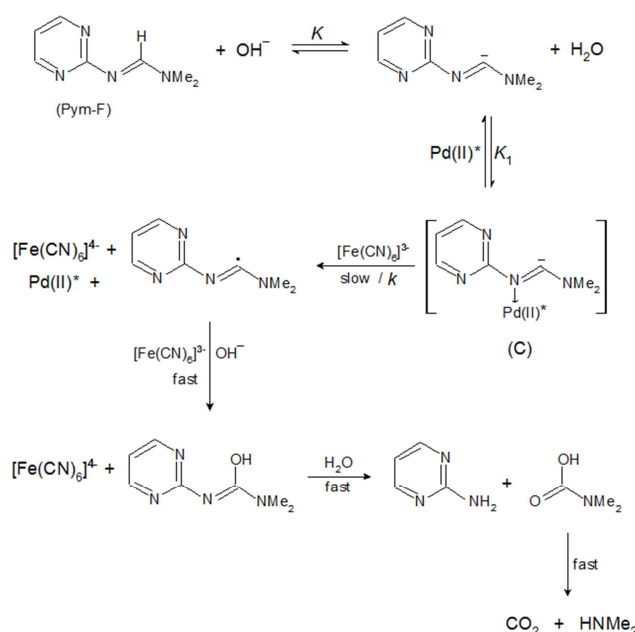
Scheme 1. Mechanism of Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium.

The suggested mechanism leads to the following rate law expression (see Appendix A),

$$\text{Rate} = \frac{kKK_1[\text{Pym-F}][\text{HCF}][\text{Pd(II)}][\text{OH}^-]}{1 + K[\text{OH}^-] + KK_1\text{Pym-F}][\text{OH}^-]} \qquad (1)$$

Under pseudo-first order condition,

$$\text{Rate} = \frac{-d[\text{HCF}]}{dt} = k_C[\text{HCF}] \qquad (2)$$

Therefore,

$$k_C = \frac{Rate}{[HCF]} = \frac{kKK_1[Pym\text{-}F][Pd(II)][OH^-]}{1 + K[OH^-] + KK_1[Pym\text{-}F][OH^-]} \quad (3)$$

Equation (3) can be rearranged to the following forms, which is suitable for verification,

$$\frac{[Pd(II)]}{k_C} = \left(\frac{1}{kKK_1[OH^-]} + \frac{1}{kK_1}\right)\frac{1}{[Pym\text{-}F]} + \frac{1}{k} \quad (4)$$

$$\frac{[Pd(II)]}{k_C} = \left(\frac{1}{kKK_1[Pym\text{-}F]}\right)\frac{1}{[OH^-]} + \frac{1}{kK_1[Pym\text{-}F]} + \frac{1}{k} \quad (5)$$

Regarding to Eqs. (4) and (5), plots of $[Pd(II)]/k_C$ versus $1/[Pym\text{-}F]$ at constant $[OH^-]$ and $[Pd(II)]/k_C$ versus $1/[OH^-]$ at constant $[Pym\text{-}F]$ should be linear with positive intercepts. The experimental results satisfied these requirements as shown in Figures 7 and 8, respectively. The value of the rate constant of the slow step (k) obtained as reciprocal of intercept of $[Pd(II)]/k_C$ versus $1/[Pym\text{-}F]$ plot was found to be $1.68 \times 10^3 \, s^{-1}$. Also, the values of the equilibrium constants associated with the mechanistic Scheme (1) (K and K_1) are evaluated from the slope and intercept of Figures 7 and 8 and were found to be 1.32 and 71.43 $dm^3 \, mol^{-1}$, respectively.
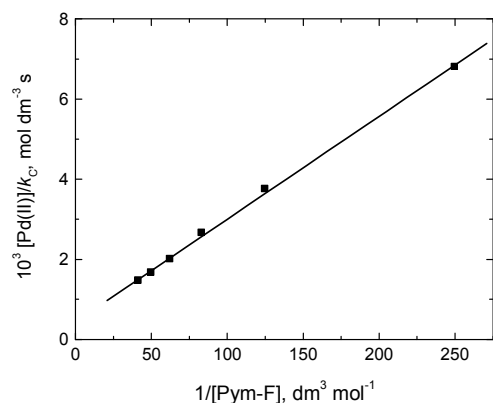

Figure 7. *Verification of equation (4) in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [HCF] = 7.0 x 10⁻⁴, [OH⁻] = 0.5 and I = 1.0 mol dm⁻³ at 25°C.*
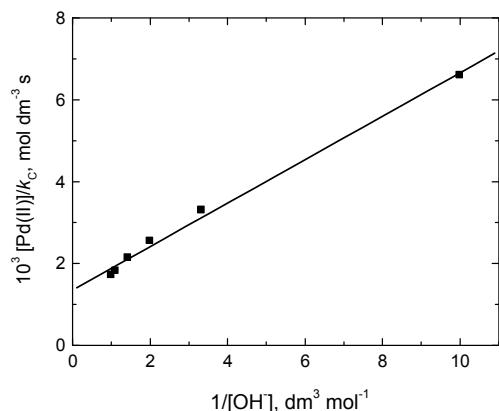

Figure 8. *Verification of equation (5) in the Pd(II)-catalyzed oxidation of Pym-F by HCF in alkaline medium. [HCF] = 7.0 x 10⁻⁴, [Pym-F] = 1.2 x 10⁻² and I = 1.0 mol dm⁻³ at 25°C.*

5. Conclusions

The catalytic effect of palladium(II) catalyst on kinetics of oxidation of *N,N*-dimethyl-*N'*-(pyrimidin-2-yl) formamidine by hexacyanoferrate(III) has been investigated in aqueous alkaline medium. The reaction did not proceed in the absence of Pd(II) catalyst. The final oxidation products are identified as 2-aminopyrimidine, dimethylamine and carbon dioxide. The rate law expression associated with the reaction mechanism is derived and the reaction constants involved in the different steps of the mechanism are calculated. The activation parameters with respect to the rate-determining step have been computed and discussed.

Appendix A.

Derivation of the Rate Law Expression

According to the proposed mechanistic Scheme,

$$Rate = \frac{-d[HCF]}{dt} = k[C][HCF] \quad (A1)$$

$$K = \frac{[Pym\text{-}F^-]}{[Pym\text{-}F][OH^-]} \, , \, [Pym\text{-}F^-] = K[Pym\text{-}F][OH^-] \quad (A2)$$

$$K_1 = \frac{[C]}{[Pym\text{-}F^-][Pd(II)]} \, , \, [C] = K_1[Pym\text{-}F^-][Pd(II)]$$

$$[C] = KK_1[Pym\text{-}F][OH^-][Pd(II)] \quad (A3)$$

Substituting Eq. (A3) into Eq. (A1) leads to,

$$Rate = kKK_1[Pym\text{-}F][OH^-][Pd(II)][HCF] \quad (A4)$$

The total concentration of MAPF is given by,

$$[Pym\text{-}F]_T = [Pym\text{-}F]_F + [Pym\text{-}F^-] + [C] \quad (A5)$$

where 'T' and 'F' stand for total and free concentrations.

Substituting Eqs. (A2) and (A3) into Eq. (A5) and rearrangement gives,

$$[Pym\text{-}F]_T = [Pym\text{-}F]_F + K[Pym\text{-}F][OH^-]$$
$$+ KK_1[Pym\text{-}F][OH^-][Pd(II)] \quad (A6)$$

$$[Pym\text{-}F]_T = [Pym\text{-}F]_F(1 + K[OH^-] + KK_1[OH^-][Pd(II)]) \quad (A7)$$

Therefore,

$$[Pym\text{-}F] = \frac{[Pym\text{-}F]_T}{1 + K[OH^-] + KK_1[OH^-][Pd(II)]} \quad (A8)$$

In view of low [Pd(II)], the third denominator term $KK_1[OH][Pd(II)]$ in the above equation can be neglected. Therefore, Eq. (A8) can be simplified to the following,

$$[Pym\text{-}F] = \frac{[Pym\text{-}F]_T}{1 + K[OH^-]} \quad (A9)$$

$$[Pd(II)]_T = [Pd(II)]_F + [C] \qquad (A10)$$

$$[Pd(II)]_T = [Pd(II)]_F(1 + KK_1[Pym\text{-}F][OH^-]) \qquad (A11)$$

$$[Pd(II)]_F = \frac{[Pd(II)]_T}{1 + KK_1[Pym\text{-}F][OH^-]} \qquad (A12)$$

Regarding to the concentration of OH^-,

$$[OH^-]_F = [OH^-]_T \qquad (A13)$$

Substituting Eqs. (A9), (A12) and (A13) into Eq. (A4) (and omitting 'T' and 'F' subscripts) leads to,

$$\text{Rate} = \frac{kKK_1[Pym\text{-}F][OH^-][Pd(II)][HCF]}{(1 + K[OH^-])(1 + KK_1[Pym\text{-}F][OH^-])} \qquad (A14)$$

$$\text{Rate} = \frac{kKK_1[Pym\text{-}F][OH^-][Pd(II)][HCF]}{1 + K[OH^-] + KK_1[Pym\text{-}F][OH^-] + K^2K_1[Pym\text{-}F][OH^-]^2} \qquad (A15)$$

The term $K^2K_1[Pym\text{-}F][OH^-]^2$ in the denominator of Eq. (A15) is negligibly small compared to unity in view of the low concentration of Pym-F used. Therefore Eq. (A15) can be written as,

$$\text{Rate} = \frac{kKK_1[Pym\text{-}F][OH^-][Pd(II)][HCF]}{1 + K[OH^-] + KK_1[Pym\text{-}F][OH^-]} \qquad (A16)$$

Under pseudo-first order condition, the rate-law can be expressed by Eq. (A17),

$$\text{Rate} = \frac{-d[HCF]}{dt} = k_C[HCF] \qquad (A17)$$

Therefore, comparing Eqs. (A16) and (A17), the following relationship is obtained,

$$k_C = \frac{\text{Rate}}{[HCF]} = \frac{kKK_1[Pym\text{-}F][Pd(II)][OH^-]}{1 + K[OH^-] + KK_1[Pym\text{-}F][OH^-]} \qquad (A18)$$

Equation (A16) can be rearranged to the following forms, which is suitable for verification,

$$\frac{[Pd(II)]}{k_C} = \left(\frac{1}{kKK_1[OH^-]} + \frac{1}{kK_1}\right)\frac{1}{[Pym\text{-}F]} + \frac{1}{k} \qquad (A19)$$

$$\frac{[Pd(II)]}{k_C} = \left(\frac{1}{kKK_1[Pym\text{-}F]}\right)\frac{1}{[OH^-]} + \frac{1}{kK_1[Pym\text{-}F]} + \frac{1}{k} \qquad (A20)$$

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