Comparative Kinetic Study of Palladium(II) Catalyzed and Uncatalyzed Oxidation of Ambroxol Hydrochloride with Potassium Permanganate in an Aqueous Alkaline Medium: A Mechanistic Approach

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   The comparative kinetic study of the oxidation process of ambroxol hydrochloride (AMH) by potassium permanganate ($KMnO_4$) in an alkaline aqueous environment in the presence and absence of palladium(II) catalyst has been analyzed at 25 °C. The reaction shows the dependence of the first order on $KMnO_4$ and fractional order with respect to AMH, sodium hydroxide medium. The addition of the salt component has no effect on the reaction. Dependence of temperature, dielectric constant, and intervention of free radicals had been also studied. The reaction stoichiometry was found to be 1:1 relative to the substrate and oxidant respectively. The obtained oxidation products are identified as 2-amino-3,5-dibromobenzaldehyde hydrochloride and 4-aminocyclohexanone by liquid chromatography-mass spectra. Thermodynamic parameters such as change in entropy, enthalpy, and free energy, and activation energy regarding the slow step of the mechanism are calculated and included in the table. Moreover, a suitable mechanism for the reaction is proposed and rate laws are derived and verified.

Keywords: Kinetics, Oxidation, Ambroxol hydrochloride, Potassium permanganate, Sodium hydroxide

INTRODUCTION

   Ambroxol hydrochloride (AMH) with molecular formula $C_{13}H_{19}Br_2ClN_2O$ is an active *N*-desmethyl metabolite of the mucolytic bromhexine [1]. It is an expectoration improver that facilitates the mucolytic agent used in the production of viscid or mucous membranes and is used to treat respiratory diseases [2]. It eases cough to ensure deep breathing and promotes mucus clearance. AMH drug is remedies for pain killer in severe viral sore throat and also acts as an anti-inflammatory agent. AMH reduces bronchial hyperactivity, stimulates cellular surfactant production, and increases the amount of antibiotic penetration [3]. AMH is a well-established secretolytic and seteromotoric agent. Earlier, in the development of AMH, a strong local anesthetic effect was observed in pre-clinical studies. Ambroxol influences the transport of transepithelial Na^+ in the tracheal wall (thus incorporating hyperpolarization into the upper respiratory tract mucosal surface of the trachea). Has bio-directional effects on trans-membrane Na^+ transport, elevating agonistic features partially at the level of membrane receptors later ambroxol was shown to block hyper-polarized cloned neuronal voltage-regulated sodium channels invitro, binding was dependent on back-to-back and it depends on its use [4]. The chemical structure of AMH is provided in Fig. 1:

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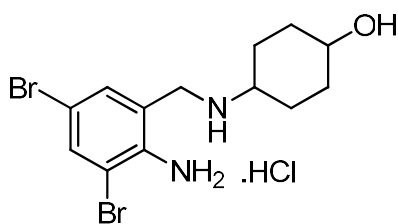
Fig. 1. Chemical structure of Ambroxol hydrochloride.

Permanganate is a unique oxidizing agent in both alkaline, as well as in acidic mediums [5] and oxidizes a variety of substances and has found expensive use in the synthesis of organic substances. In the oxidation process, Mn(VII) in permanganate is reduced to various oxidation numbers depending on the applied media [6]. The typical reduction power of Mn(VI)/Mn(VII) in alkaline and acidic medium is 1.69 V and 1.51 V [7]. In the presence of weak and strong acidic solutions the permanganate changes to Mn(IV) and Mn(II), and in strong alkaline media, it forms stable reduction product manganate ion (MnO_4^{2-}) [8].

Clearly, the role of palladium(II) chloride catalyst has been widely recognized in the oxidation and reduction reactions, especially in the higher pH state, however, little devotion has been given to utilizing Pd(II) as an auto catalyst in the oxidation of the drug. This makes us the impetus to study the current redox system in the alkaline state in the presence of palladium(II) catalyst to determine the pathways and interaction of Pd(II), AMH, and MnO_4^{2-}. Palladium(II) generally forms a more activated complex with a molecule that is used as a substrate previously to the final products [9]. The main goal of the present work is to clarify the oxidation mechanism of AMH in the uncatalyzed and Pd(II) catalyzed reactions and to obtain a standard rate law corresponding to the results found in experiments.

EXPERIMENTAL

Reagents and Apparatus

Potassium permanganate, NaOH, and KCl were purchased from NICE chemicals and Ambroxol hydrochloride from (Sigma Aldrich, India). Palladium(II) chloride from Reach Lab Chem Pvt. Ltd.

Absorbance was recorded using a smart double-beam UV-Vis spectrophotometer at wavelength 525 nm, performed on model 2203 (Systronics Instruments). The LC-MS spectrum was recorded at Acquity Lab. A 1 cm quartz cell was used in the thermostatic cell compartment of the UV-Vis spectrophotometer. Corning glassware was used for all tests. All tests are performed at room temperature (RT).

Preparation

All chemicals and reagents used in this work are in the grade of analytical grade and utilized without any more purification. Double distilled water (DDW) without dissolved oxygen was used for the preparation of all the solutions. Standard solutions of Mn(VII) (1×10^{-4} M) were prepared using water; this was measured in proportion against oxalic acid [9]. 1×10^{-3}, 1×10^{-2} and 0.5×10^{-3} M of AMH, sodium hydroxide, and potassium chloride were prepared respectively and used as standard solutions. Palladium(II) chloride (0.5×10^{-5} M) is prepared using HCl, and concentration was tested by EDTA titration [10].

RESULTS AND DISCUSSION

Kinetic Study

First-order conditions were considered for the reaction kinetics, where the concentration of the AMH substrate was 10 times higher than the oxidant Mn(VII) concentration, and the ionic strength of KCl is 1.0×10^{-3} M at 298 K. In the nonexistence and existence of Pd(II) catalyst, the reaction was started by combining the MnO_4^- and AMH in addition to the known concentration of ionic and alkaline respectively. The evolution of Pd(II) catalyzed and uncatalyzed reactions were tracked to monitor the drop in absorption of MnO_4^- at 525 nm and 30 s. The molar extinction coefficient was determined at 525 nm with various Mn(VII) concentrations under experimental conditions it was found to be $\epsilon = 2390 \pm 20$ dm^3 mol^{-1} cm^{-1} [11]. The first-order rate constants k_U for uncatalyzed and k_C for catalyzed reactions were found from the slope of $\log_{10}$ (Abs) to the time plot which is linear up to 85% completion. The obtained values are reproducible within $\pm$ 5% error. The rate constants for catalyzed and uncatalyzed reactions are shown in Tables 1 and 2.

Stoichiometry and Product Analysis

The reaction mixture enclosing various stoichiometric ratios of excess potassium permanganate over AMH

Table 1. Concentration Variation of MnO_4^- ($0.5\text{-}2.5 \times 10^{-4}$), AMH ($0.5\text{-}2.5 \times 10^{-3}$), NaOH ($0.5\text{-}2.0 \times 10^{-2}$), and KCl ($0.5\text{-}2.5 \times 10^{-3}$) in M on Oxidation of AMH by $KMnO_4$ in the Basic Medium at 298 K

$MnO_4^- \times 10^4$ (M)	$AMH \times 10^3$ (M)	$OH^- \times 10^2$ (M)	$KCl \times 10^3$ (M)	$k_{U\,obs} \times 10^3$ (s^{-1})
0.5	1.5	1	1.5	2.3
1	1.5	1	1.5	2.35
1.5	1.5	1	1.5	2.4
2	1.5	1	1.5	2.45
2.5	1.5	1	1.5	2.4
1.5	0.5	1	1.5	1.41
1.5	1	1	1.5	1.94
1.5	1.5	1	1.5	2.4
1.5	2	1	1.5	2.66
1.5	2.5	1	1.5	2.9
1.5	1.5	0.5	1.5	1.66
1.5	1.5	0.75	1.5	1.92
1.5	1.5	1	1.5	2.4
1.5	1.5	1.5	1.5	2.66
1.5	1.5	2	1.5	2.79
1.5	1.5	1	0.5	2.4
1.5	1.5	1	1	2.4
1.5	1.5	1	1.5	2.4
1.5	1.5	1	2	2.4
1.5	1.5	1	2.5	2.4

containing a significant amount of Pd(II) and KCl, in the presence of NaOH medium was allowed to be stored for 24 h at 298 K under stirred conditions. After the reaction was completed the unresponsive permanganate concentration was measured at 525 nm absorption using a UV-Vis spectrophotometer for both catalyzed and uncatalyzed reactions, stoichiometry obtained was 1:1 (AMH:$KMnO_4$) in both cases (Eq. (1)). As in Eq. (1), the reaction products were extracted with ether, and the product of oxidation was found to be 2-amino-3,5-dibromo benzaldehyde hydrochloride and 4-aminocyclohexanone which were recognized by liquid chromatography-mass spectra (LC-MS) analysis and gives molecular ion peak at m/z 316 and 114 (Fig. 2).

Reaction Orders

The reaction order relating to catalyst, substrate, and alkali was found on the slope of log10 (k_U/k_C) *vs*. log10 (concentration) by changing each concentration at constant temperature and keeping other parameters constant (Tables 1 and 2).

Effect of Mn(VII) Concentration

In the Pd(II) catalyzed and uncatalyzed reaction, the effect of permanganate concentration on the oxidation rate of AMH was examined by changing the concentration of Mn(VII) ($0.5\text{-}2.5 \times 10^{-4}$ M) at RT with other reactants concentration unchanged. In permanganate concentrations, approximately statistical values of k_U and k_C were obtained (Table 1) indicating unit order with respect to permanganate concentration. Pseudo-first order plots, log10 (absorbance) *versus* time are linear over 85% completion of the reaction also confirms the first-order dependence on Mn(VII).

Table 2. Concentration Variation of MnO_4^- (0.5-2.5×10^{-4}), AMH (0.5-2.5×10^{-3}), NaOH (0.5-2.0×10^{-2}), KCl (0.5-2.5×10^{-3}), and Pd(II) (0.1-1.25×10^{-5}) in mol/dm^3 on Oxidation of AMH by $KMnO_4$ in Alkaline Medium at 298 K

$MnO_4^- \times 10^4$ (M)	$AMH \times 10^3$ (M)	$OH^- \times 10^2$ (M)	$Pd(II) \times 10^5$ (M)	$KCl \times 10^3$ (M)	$k_T \times 10^2$ (s^{-1})	$k_{U\,obs} \times 10^3$ (s^{-1})	$k_{C\,obs} \times 10^1$ (s^{-1})
0.5	1.5	1	0.5	1.5	5.23	2.3	0.5
1	1.5	1	0.5	1.5	5.74	2.35	0.55
1.5	1.5	1	0.5	1.5	6.44	2.4	0.62
2	1.5	1	0.5	1.5	5.45	2.45	0.52
2.5	1.5	1	0.5	1.5	4.74	2.4	0.45
1.5	0.5	1	0.5	1.5	4.14	1.41	0.4
1.5	1	1	0.5	1.5	5.29	1.94	0.51
1.5	1.5	1	0.5	1.5	6.44	2.4	0.62
1.5	2	1	0.5	1.5	7.17	2.66	0.69
1.5	2.5	1	0.5	1.5	7.79	2.9	0.75
1.5	1.5	0.5	0.5	1.5	4.27	1.66	0.41
1.5	1.5	0.75	0.5	1.5	5.59	1.92	0.54
1.5	1.5	1	0.5	1.5	6.44	2.4	0.62
1.5	1.5	1.5	0.5	1.5	7.47	2.66	0.72
1.5	1.5	2	0.5	1.5	8.28	2.79	0.8
1.5	1.5	1	0.1	1.5	1.84	2.4	0.16
1.5	1.5	1	0.25	1.5	5.04	2.4	0.48
1.5	1.5	1	0.5	1.5	6.44	2.4	0.62
1.5	1.5	1	1	1.5	13.04	2.4	1.28
1.5	1.5	1	1.25	1.5	19.44	2.4	1.92
1.5	1.5	1	0.5	0.5	4.74	2.4	0.45
1.5	1.5	1	0.5	1	5.54	2.4	0.53
1.5	1.5	1	0.5	1.5	6.44	2.4	0.62
1.5	1.5	1	0.5	2	5.34	2.4	0.51
1.5	1.5	1	0.5	2.5	4.44	2.4	0.42

Effect of AMH concentration

The effect of the concentration of AMH on the reaction rate has been studied with a variation of AMH from (0.5-2.5×10^{-3} M) at 298 K and all other reagent concentrations were unchanged. AMH concentration increases with the linear rise in the k_U and k_C values (Tables 1 and Table 2). The obvious dependence, which is less than the unit order in the concentration of AMH is found in the slope of the log10 k_U *vs.* log10 (concentration) and is 0.56 for the uncatalyzed reaction and 0.43 for catalyzed reaction.

Effect of Pd(II) Catalyst

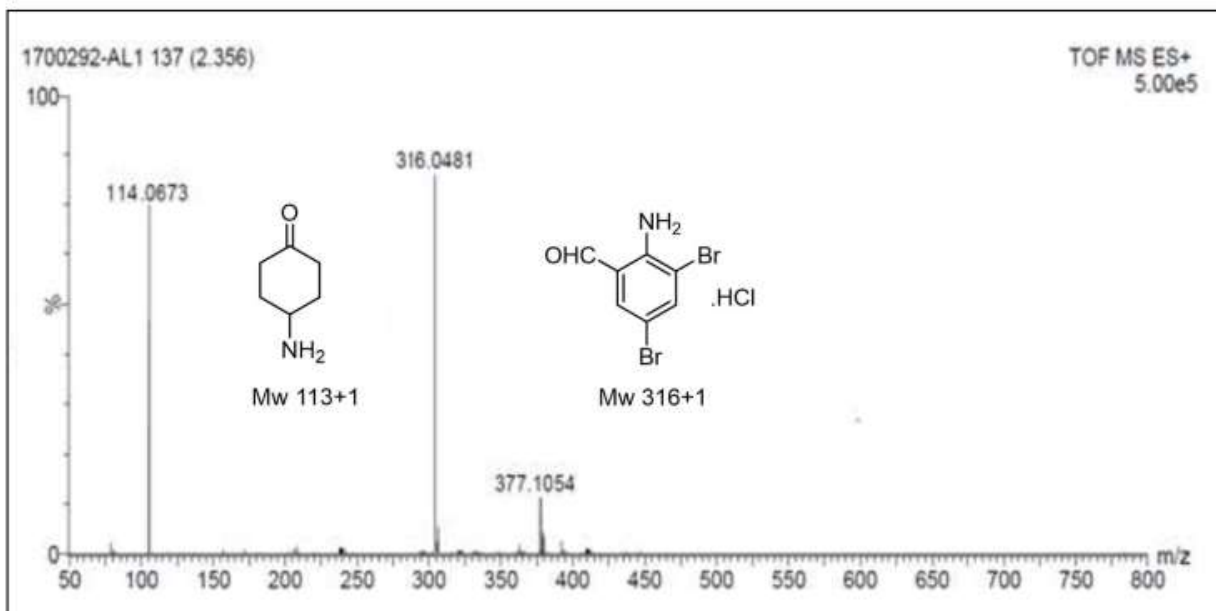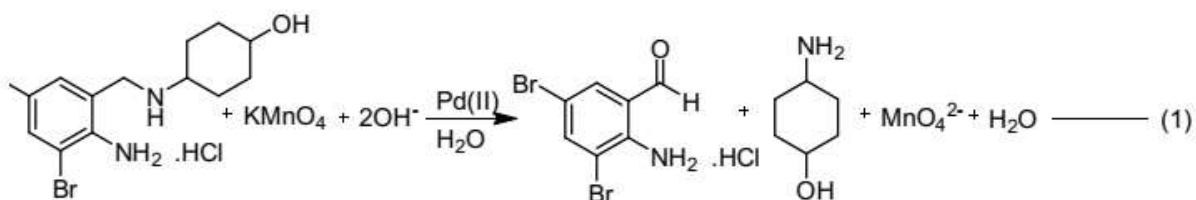The order of Pd(II) in the reaction was calculated by

Fig. 2. LC-MS spectrum of 2-amino-3,5-dibromo-benzaldehyde hydrochloride and 4-aminocyclohexanone.

varying the Pd(II) over a range (0.5-1.25 × 10⁻³ M) at 298 K with all the other reactant concentration constants. The reaction rate increases with the concentration of the catalyst (Table 2). The Pd(II) shows unit order dependence on reaction rate [12].

Effect of NaOH Concentration

The effect of alkali concentration on reaction rate has been studied with a variation of NaOH from (0.5-2.5 × 10⁻³ M) at 298 K with all other reagent concentrations unchanged. The alkaline concentration increases with the linear increase in k_U and k_C observed (Table 1 and Table 2). The obvious dependence, which is less than the unit order in the NaOH concentration was found in the slope of the log10 k_U against log10 (concentration) (0.39) and the log10 k_C with log10 (concentration) (0.46).

The Effect of Ionic (I) Strength and Dielectric Constant (D) Medium on Reaction Rate

The concentration of KCl (0.5-2.5 × 10⁻³ mol dm⁻³) was varied with all other reactants unchanged. In Pd(II), the catalyzed and uncatalyzed reaction, and KCl concentration has no significant effect [13]. The Dielectric effect was studied with different percentages of water and t-butyl alcohol (0-25% v/v) in the reaction solution. It was found that the dielectric constant (D) has not shown any effect on the rate [14].

From the above reaction orders

• For uncatalyzed reaction the rate law is:

$$Rate = k_U \, [Mn(VII)]^{1.0} \, [AMH]^{0.56} \, [OH^-]^{0.39}$$

• For catalyzed reaction the rate law is:

$$Rate = k_C [Mn(VII)]^{1.0} \, [Pd(II)]^{1.0} \, [AMH]^{0.43} \, [OH^-]^{0.46}$$

Polymerization Study

The oxidation of AMH by KMnO₄ was monitored with the addition of acrylonitrile (monomer) to uncatalyzed and Pd(II) catalyzed reactions, and 2 h stored in an inert condition [15]. After two hours methanol was used to dilute the reaction mixtures and there is no formation of precipitation indicating the absence of free-radical species which concludes reaction follows an ionic mechanism.

Effect of Temperature

The reaction rate of uncatalyzed and catalyzed reactions was studied at five different temperatures (298, 303, 308, 313, and 318 K) and the concentration of AMH, alkali, and all other reaction conditions were maintained constant. The reaction rate increases with increasing temperature [16] (Table 3, Fig. 3). The values of k1 and k2 of the slower step for Schemes 1 and 2 were found from intercepts of the plots of $1/k_U$ *vs.* $1/AMH$ and $1/k_C$ *vs.* $1/AMH$ respectively. The activation energy associated with these statistical values has been calculated from Arrhenius plot $\log_{10}$ (k_U and k_C) *vs.* $1/T$ plot from which thermodynamic parameters were calculated [17] and tabulated (Table 4).

Mechanism of the Uncatalyzed Reaction

For uncatalyzed oxidation of AMH by KMnO₄, a unit mole of base reacts with a unit mole of KMnO₄ at the initial equilibrium step to form $[MnO_4.OH]^{2-}$, as in previous literature [18]. In the second equilibrium step, a unit mole of AMH combines with $[MnO_4.OH]^{2-}$ to form a complex [19]. These complex forms intermediate (C1) on further decomposition. In successive step it consumes another mole of $[MnO_4.OH]^{2-}$ to give 2-amino-3,5-dibromobenzaldehyde hydrochloride and 4-aminocyclohexanone (Fig. 4). The mechanism matches with our test results and it is shown in Scheme 1. Spectroscopic evidence of complex formation between oxidant and substrate was found at $[OH^-] = (1 \times 10^{-2}$ M) from UV-Vis spectra of Mn(VII) (1.0×10^{-4} M), AMH (1.0×10^{-3} M) and probable structure of the complex is shown in Fig. 5.

The rate law (7) from Scheme 1 can be derived as in Fig. 4,

Table 3. Temperature Variation on the Rate of Oxidation of AMH by KMnO₄ in Aqueous Alkaline Medium at a Concentration of AMH (1.5×10^{-2} M), MnO₄⁻ (1.5×10^{-4} M), NaOH (1×10^{-2} M), Pd(II) (5×10^{-3} M) and KCl (0.5×10^{-3} M)

| Temperature (K)	$k_U \times 10^2$ (s)	$k_C \times 10^1$ (s)
298	1.56	0.35
303	2.84	1.2
308	3.98	1.4
313	4.52	1.6
318	5.46	1.9

Table 4. Thermodynamic Parameters for Oxidation of AMH by KMnO₄ in an Aqueous Alkaline Medium

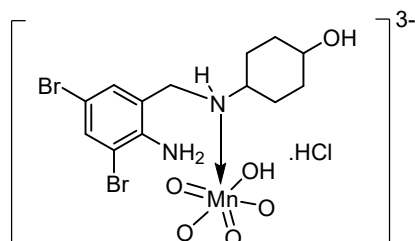| Activation parameters	Uncatalyzed	Catalyzed
Ea (kJ mol⁻¹)	52.9	31.9
ΔH# (kJ mol⁻¹)	50.4	29.4
ΔS# (J K⁻¹ mol⁻¹)	-110.16	-166.6
ΔG# (kJ K⁻¹ mol⁻¹)	17.6	20.2
logA	7.5	4.53
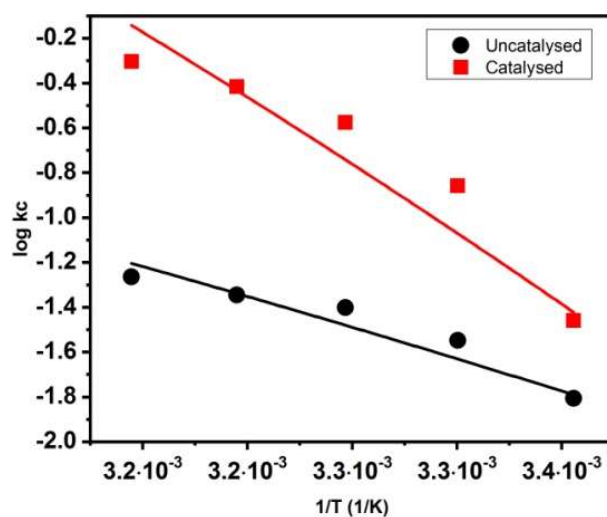
Fig. 3. Temperature dependence for uncatalyzed and catalyzed reactions.

$$\text{Rate} = \frac{-d[MnO_4^-]}{dt} = k_1 K_1 K_2 [MnO_4^-][OH^-][AMH] \quad\text{——————} \quad (2)$$

$$MnO_4^- + OH^- \underset{}{\overset{K_1}{\rightleftharpoons}} [MnO_4.OH]^{2-}$$
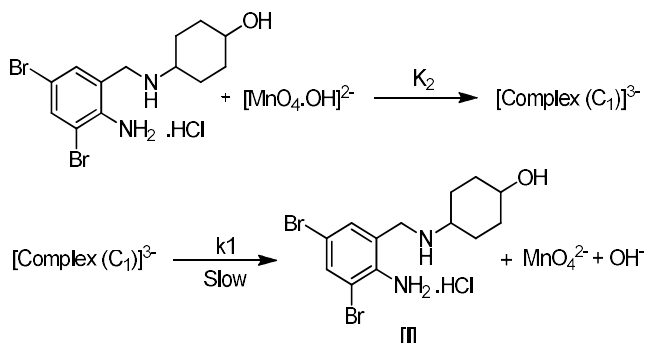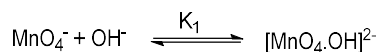
Fig. 4. Mechanism of uncatalyzed reaction with its intermediate, slow step, and fast step reactions.

Fig. 5. Probable structure of AMH and KMnO$_4$ complex.

Scheme 1. Rate law derivation of uncatalyzed oxidation of AMH and KMnO$_4$

The total $[MnO_4^-]_t$ is given by

$$[MnO_4^-]_t = [MnO_4^-]_f + [MnO_4.OH]^{2-} + [Complex (C_1)]$$

$$= [MnO_4^-]_f + K_1[MnO_4^-][OH^-] + K_2[MnO_4.OH]^{2-} + [AMH]$$

$$= [MnO_4^-]_f + K_1[MnO_4^-][OH^-] + K_1K_2[MnO_4^-][OH^-][AMH]$$

$$= [MnO_4^-]_f + \left\{1 + K_1[OH^-] + K_1K_2[OH^-][AMH]\right\}$$

i.e. the subscripts 't' and 'f' are the total and free concentrations respectively. Therefore, free $[MnO_4^-]_t$ is given by

$$[MnO_4^-]_f = \frac{[MnO_4^-]_t}{1 + K_1[OH^-] + K_1K_2[OH^-][AMH]} \quad\text{——————} \quad (3)$$

Similarly, The total $[OH^-]$ can be written as

$$[OH^-]_t = [OH^-]_f + [MnO_4.OH]^{2-} + Complex (C)$$

$$= [OH^-]_f + K_1[MnO_4^-][OH^-] + K_2[MnO_4.OH]^{2-}[AMH]$$

$$= [OH^-]_f + K_1[MnO_4^-][OH^-] + K_1K_2[MnO_4^-][OH^-][AMH]$$

$$= [OH^-]_f + \left\{1 + K_1[OH^-] + K_1K_2[MnO_4^-][AMH]\right\}$$

$$[OH^-]_f = \frac{[OH^-]_t}{1 + K_1[MnO_4^-] + K_1K_2[MnO_4^-][AMH]} \quad\text{——————} \quad (4)$$

In view of the low concentrations of $[MnO_4^-]$ and $[AMH]$ used in the experiments, the denominator having the second and third terms at Eq. (4) (Scheme 1) are neglected because of their much fewer values than unity.

Therefore,

$$[OH^-]_f = [OH^-]_t \quad\text{——————} \quad (5)$$

Similarly, $$[AMH]_f = [AMH]_t \quad\text{——————} \quad (6)$$

Substituting Eqs. (3), (5), and (6) in Eq. (2) and omitting the subscripts (t and f) we get

$$\text{Rate} = \frac{d[MnO_4^-]}{dt} = \frac{k_1 K_1 K_2 [MnO_4^-][AMH][OH^-]}{1 + k_1[OH^-] + K_1K_2[AMH][OH^-]} \quad\text{——————} \quad (7)$$

OR

$$\frac{\text{Rate}}{d[MnO_4^-]} = k_U = \frac{k_1 K_1 K_2 [AMH][OH^-]}{1 + k_1[OH^-] + K_1K_2[AMH][OH^-]} \quad\text{——————} \quad (8)$$

Equation (8) confirms all the observed order with respect to different species, which can be verified by re-arranging Eq. (9).

$$\frac{1}{k_U} = \frac{1}{k_1 K_1 K_2 [AMH][OH^-]} + \frac{1}{k_1 K_2 [AMH]} + \frac{1}{k_1} \quad\text{——————} \quad (9)$$

Mechanism of Catalyzed Reaction

All other conditions are the same as that of an uncatalyzed reaction, except that in the presence of Pd(II) catalyst. In the first equilibrium step, a unit mole of MnO$_4^-$ and a unit mole of base reacts to produce $[MnO_4.OH]^{2-}$, this is in accordance with the calculated order in Mn(VII) and base concentrations [20]. This complex (C$_2$) reacts with AMH and $[Pd(OH)Cl_2]^{2-}$ which is in agreement with fractional order (0.43) in AMH and first order in $[Pd(OH)Cl_2]^{2-}$ [21]. The complex (C$_2$) in the rate-determining step reacts with $[MnO_4.OH]^{2-}$ to give a final

product, 2-amino-3,5-di-bromobenzaldehyde hydrochloride and 4-aminocyclohexanone (Fig. 6). The mechanism in agreement with the obtained results is in the form of a Scheme 2. The complex between Pd(II) and AMH was confirmed from UV-Vis spectra of AMH (3.0×10^{-3} M), Pd(II) (0.5×10^{-5} M) and $[OH^-] = (1 \times 10^{-2}$ M) [22]. The probable mechanism can be given in Fig. 6.
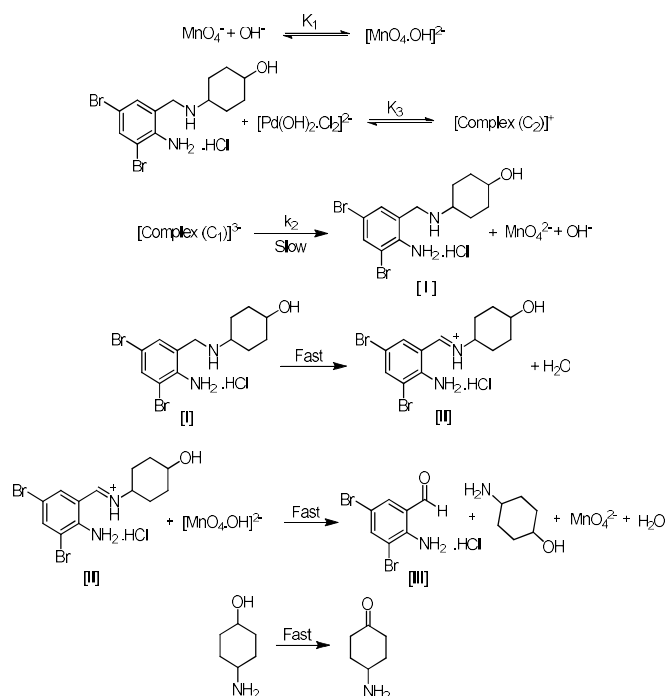
Fig. 6. Probable mechanism for Pd(II) catalyzed reaction intermediate formation, slow and fast step reactions.

Scheme 2. Rate law derivation of Pd(II) catalyzed oxidation of AMH and KMnO₄

From Scheme 2 the rate law Eqs. (10)-(17) can be derived as follows

The total $[MnO_4^-]$ is given by

$$[MnO_4^-]_t = [MnO_4^-]_f + [MnO_4.OH]^{2-}$$

$$= [MnO_4^-]_f + K_1[MnO_4^-]_f[OH^-] + K_2[MnO_4.OH]^{2-} + [AMH]$$

$$= [MnO_4^-]_f + K_1[MnO_4^-][OH^-]$$

$$= [MnO_4^-]_f \left\{ 1 + K_1[OH^-] \right\}$$

$$[MnO_4^-]_f = \frac{[MnO_4^-]_t}{1 + K_1[OH^-]} \qquad (11)$$

Similarly,

$$[OH^-]_t = [OH^-]_f + [MnO_4.OH]^{2-}$$

$$= [OH^-]_f + K_1[MnO_4^-][OH^-]_f$$

$$= [OH^-]_f + \left\{ 1 + K_1[OH^-] \right\}$$

$$[OH^-]_f = \frac{[OH^-]_t}{1 + K_1[MnO_4^-]} \qquad (12)$$

In view of the low concentration of $[MnO_4^-]$ used in the experiment $K_1[MnO_4^-]$ is negligible compared to unity and can be neglected in Eq. (12).

Therefore,

$$[OH^-]_f = [OH^-]_t \qquad (13)$$

Similarly, $\quad [AMH]_f = [AMH]_t \qquad (14)$

The free Pd(II) can be obtained as

$$[Pd(II)]_t = [Pd(II)]_f + C_2$$

$$= [Pd(II)]_f = K_3[Pd(II)][AMH]$$

$$= [Pd(II)]_f \left\{ 1 + K_3[AMH] \right\} \qquad (15)$$

Substituting Eqs. (11), (13), (14), and (15) into Eq. (10) and omitting subscripts (t and f) we get,

$$\frac{-d[MnO_4^-]}{dt} = \frac{k_2 K_1 K_3[MnO_4^-][AMH][Pd(II)][OH^-]}{\left\{ 1 + K_1[OH^-] \right\} \left\{ 1 + K_3[AMH] \right\}} \qquad (16)$$

Equation (16) confirms all the observed orders with respect to different species which can be verified by rearranging Eq. (17).

$$\frac{Pd(II)}{k_C} = \frac{1}{k_2 K_1 K_3[AMH][OH^-]} + \frac{1}{k_2 K_3[AMH]} + \frac{1}{k_2 K_1[OH^-]} + \frac{1}{k_2} \qquad (17)$$

The above rate laws derived were verified by graphs of the concentration of substrates with rate constant values.

The graph of $1/k$ *vs*. $1/[AMH]$ and $1/k$ *vs*. $1/[OH^-]$ were found to be linear line and from the intercept k_2, K_1, K_3, and slope were calculated and values are found to be 0.04 s⁻¹, 5.4×10^{-5} M⁻¹, 3475 M respectively (Figs .7 and 8).

Fig. 7. Graph of $1/k$ *vs.* $1/[AMH]$ for uncatalyzed and catalyzed reactions supporting the verification of rate law.

Fig. 9. Graph of Pd(II)/k_C *vs.* $1/[AMH]$ for catalyzed reaction supporting the verification of rate law.
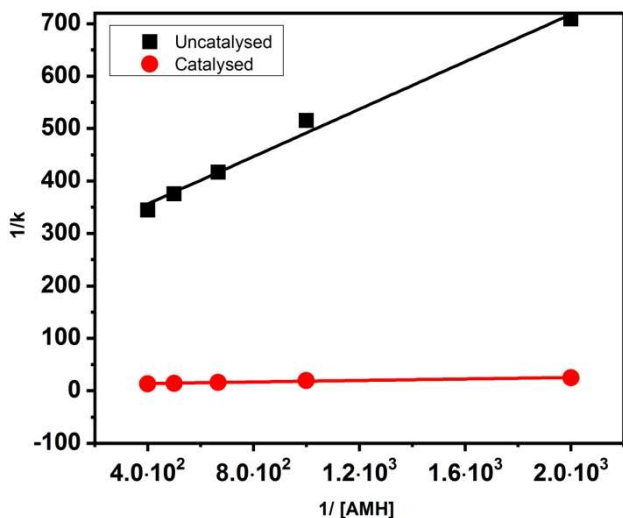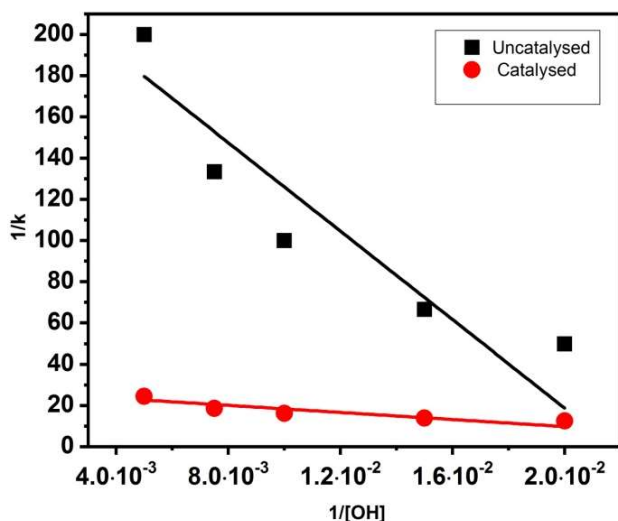

Fig. 8. A graph of $1/k$ *vs.* $1/[OH^-]$ for uncatalyzed and catalyzed reactions supporting the verification of rate law.

The graph of Pd(II)/k_C *vs.* $1/[AMH]$ Intercept and slope gives the values for $1/k_2K_3$ (Fig. 9) and values are found to be k_2K_3 = 139.6 M s^{-1} respectively.

Previously few literature have reported the utilization of potassium permanganate for the oxidation of some organic compounds. The oxid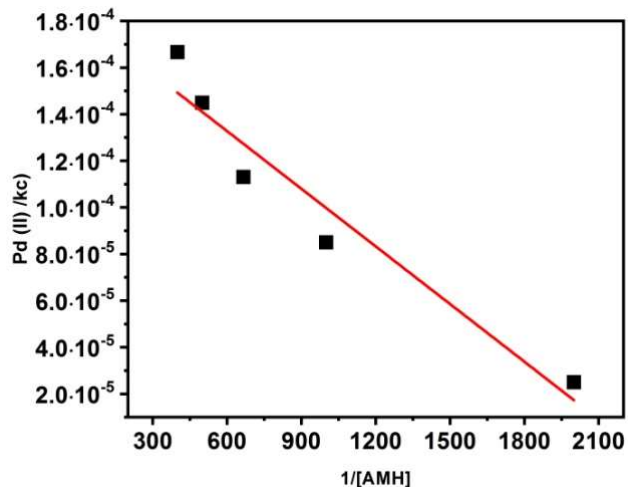ation of aspartic acid using potassium permanganate in the alkaline medium in the absence of a catalyst revealed a slow rate of reaction [23]. Moreover, the rate of the organic molecule atenolol by permanganate ion [24] has been enhanced by the addition of ruthenium(III) in the molar concentration of micro level. However, comparatively [25], in our studies, employed palladium(II) as an active catalyst has significantly improved the rate of oxidation of ambroxol hydrochloride by potassium permanganate.

CONCLUSIONS

In the present work, an uncatalyzed kinetic study and Pd(II) catalyzed oxidations of AMH by KMnO$_4$ in an alkaline aqueous region were studied spectrophotometrically at 525 nm in the temperature 298 K. Stoichiometry for both conditions 1:1, the reaction product was found to be 2-amino-3,5-di-bromobenzaldehyde hydrochloride and 4-aminocyclohexanone. Activation parameters are calculated and tabulated. Suggested suitable mechanisms and schemes were proposed.

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