

Original Article

KINETICS AND MECHANISM OF OXIDATION OF AN ANTIARRHYTHMIC DRUG
PROCAINAMIDE HYDROCHLORIDE BY Mn (VII) IN AQUEOUS SULPHURIC ACID MEDIUM: A
STOPPED FLOW TECHNIQUE

MANJANATH B. PATGAR, MANJUNATH D. METI, SHARANAPPA T. NANDIBEWOOR AND SHIVAMURTI A. CHIMATADAR*

P. G. Department of Studies in Chemistry, Karnatak University, Pavate Nagar, Dharwad 580003, India.
Email: schimatadar@gmail.com

Received: 05 Aug 2014 Revised and Accepted: 10 Sep 2014

ABSTRACT

Objective: To understand the kinetics and mechanism of oxidation of procainamide hydrochloride by Mn(VII) in aqueous sulfuric acid medium at 298K and at constant ionic strength, $I = 3.0 \times 10^{-3} \text{ mol dm}^{-3}$ and to identify its oxidation products.

Methods: Kinetic measurements were performed on a Varian CARRY 50 Bio UV- visible spectrophotometer connected to a rapid kinetic accessory (HI-TECHSFA-12 unit). The products are characterized by FT-IR, GC-MS and NMR studies.

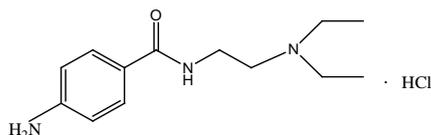
Results: The reaction stoichiometry was determined and the results indicate that five moles of procainamide require four moles of Mn(VII). The oxidation products were identified as Mn(II), p-aminobenzoic acid and N,N-diethyl-2-nitrasoethanamine. The reaction shows first-order kinetics with respect to MnO_4^- and fractional order with respect to procainamide. Increase in sulphuric acid concentration increased the rate of reaction with fractional order dependence on H^+ ion concentration. The effect of added products, ionic strength, and dielectric constant of the medium were studied on the rate of reaction.

Conclusion: A suitable mechanism is proposed on the basis of experimental results. The activation parameters with respect to the slow step of the mechanism were evaluated and the thermodynamic parameters are also determined and discussed.

Keywords: Oxidation, Kinetics, Mechanism, Procainamide, Permanganate.

INTRODUCTION

Procainamide (PAH) is a pharmaceutical antiarrhythmic agent used for the medical treatment of cardiac arrhythmias and used for both supraventricular and ventricular arrhythmias indicated in the treatment of premature ventricular contractions, ventricular tachycardia, atrial fibrillation and paroxysmal atrial tachycardia [1]. Procainamide's major active metabolite is N-acetylprocainamide (NAPA), which is approximately equipotent with the parent drug as an antiarrhythmic agent [2]. NAPA has an elimination half-life about twice that of procainamide, and it can reach somewhat higher plasma levels during chronic procainamide administration [3]. PAH measurement in plasma is advocated as a useful, if not mandatory, guide to therapy. The accepted therapeutic concentration range for PAH is 4-8 mg/liter, but its major metabolite, N-acetylprocainamide, which also has an antiarrhythmic effect in humans, is found in similar concentrations in the plasma of patients who are undergoing therapy with procainamide. Therefore, therapy can be optimal only if both procainamide and N-acetylprocainamide are considered [4]. The structure of procainamide hydrochloride is shown below.



In the present investigation, the authors have obtained the evidence for the reactive species for permanganate in acid medium. A literature survey reveals that there are no reports on the kinetics of oxidation of PAH by Mn(VII). Hence, in order to understand the active species of oxidant and to propose a suitable mechanism based on experimental results, the title reaction is investigated.

Mn(VII) is widely used as an oxidizing, disinfectant and also as an analytical reagent. These reactions are governed by the pH of the medium. Among six oxidation states of manganese, from +2 to +7, Mn(VII), is the most potent oxidation state in acid medium with

reduction potentials [5] 1.69 V of Mn(VII)/Mn(IV) couple and 1.51 V of Mn(VII)/Mn(II) couple. Chemical oxidation using Mn(VII) has been widely used for treatment of pollutants in drinking water and wastewater applications for over 50 years. The oxidation by Mn(VII) ion finds extensive applications in organic syntheses [6]. During oxidation by Mn(VII), it is evident that Mn(VII) is reduced to various oxidation states in acidic, alkaline and neutral media. According to Insauti et al. [7], it has several advantages as an analytical reagent e. g. it is strong vividly colored serving as its own indicator. In acidic medium active species of Mn(VII) exists in different forms as HMnO_4 , H_2MnO_4^+ , HMnO_3 , and Mn_2O_7 depending on the nature of the reductant, the oxidant has been assigned both inner sphere and outer sphere pathway in their redox reactions [8, 9]. In earlier report on oxidation by Mn(VII) in acidic media, it has been observed that some investigators have found the induction period [10] and some have noticed autocatalytic nature either by Mn(II) or by one of the products obtained by substrates [11]. Hence it is worthwhile to investigate the Mn(VII) oxidation of procainamide hydrochloride in acid medium to see such ambiguity.

MATERIALS AND METHODS

Chemicals and solutions

All reagents were of analytical reagent grade and millipore water was used throughout the work. A solution of PAH (Sigma Aldrich) was prepared by dissolving an appropriate amount of procainamide in millipore water. The stock solution of Mn(VII) was prepared by dissolving potassium permanganate (s. d. fine Chem. Ltd) in water and concentrations were ascertained by titrating against oxalic acid [12]. Manganese (II) solution was prepared by dissolving manganese sulfate (s. d. fine Chem. Ltd) in water. While Na_2SO_4 (s. d. fine Chem. Ltd) and H_2SO_4 (Fisher scientific) were used to maintain the required ionic strength and acidity of the reaction mixture respectively.

Instruments used

For kinetic measurements, a Peltier accessory (temperature-controlled) attached to a Varian CARY 50 Bio- UV vis

spectrophotometer (Varian, Victoria-1370 Australia) connected to a rapid kinetic accessory (HI-TECHSFA-12) was used. For product analysis, Shimadzu 17A gas chromatograph with a Shimadzu QP-5050A mass spectrometer with electron impact (EI) ionization technique, a Nicolet 5700 FT-IR spectrometer (Thermo Electron Corporation, Madison, WI), and a 300 MHz ^1H NMR spectrometer (Bruker, Switzerland) were used.

Kinetic measurements

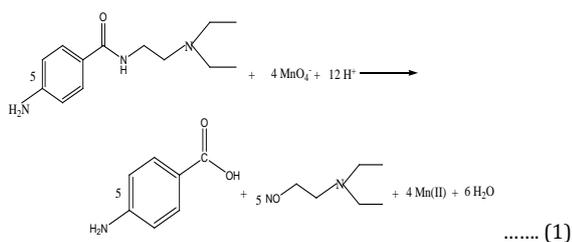
Since the reaction was too fast to be monitored by the usual method, kinetic measurements were performed on a Varian CARRY 50 Bio UV- visible spectrophotometer connected to a rapid kinetic accessory (HI-TECHSFA-12 unit). All kinetic measurements were followed under pseudo-first-order conditions at 298K where the substrate (PAH) concentration was used in excess over oxidant (Mn(VII)) concentration at a constant ionic strength of $3.0 \times 10^{-3} \text{ mol dm}^{-3}$. The reaction was initiated by adding thermally equilibrated ($25 \pm 0.1^\circ\text{C}$) solutions of Mn(VII) , PAH, in addition to that required quantities of H_2SO_4 , Na_2SO_4 are added to provide required acidity and ionic strength of reaction. The application of Beer's law at 525 nm for Mn(VII) in the concentration range, $0.10 \times 10^{-4} \text{ mol dm}^{-3}$ to $8.0 \times 10^{-4} \text{ mol dm}^{-3}$ was made and extinction coefficient was found to be $\epsilon = 2200 \pm 50 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$. The kinetic runs were followed more than 80% completion of the reaction and good first order kinetics was observed. The pseudo-first order rate constants, k_{obs} were calculated from the plots of $\log [\text{MnO}_4^-]$ versus time, which are linear over 70% completion of the reaction (Fig.1). The k_{obs} values were reproducible within $\pm 5\%$ and are the average of at least three independent kinetic runs (Table 1).

Fig. 1: First order plot of oxidation of procainamide by MnO_4^- in acid media at 298K, $[\text{PAH}] = 2.0 \times 10^{-3} \text{ mol dm}^{-3}$, $[\text{H}^+] = 2.0 \times 10^{-4} \text{ mol dm}^{-3}$; $I = 3.0 \times 10^{-3} \text{ mol dm}^{-3}$, $[\text{MnO}_4^-] \times 10^4 \text{ mol dm}^{-3} =$ (1) 0.25 (2) 0.50 (3) 1.0 (4) 2.0 and (5) 3.0.

RESULTS

Stoichiometry and product analysis

Different sets of reaction mixtures containing excess of Mn(VII) to $[\text{PAH}]$ in the presence of constant amount of acid and at constant ionic strength, $3.0 \times 10^{-3} \text{ mol dm}^{-3}$, were allowed to react for about 5 h at 298K. After completion of the reaction, part of the reaction mixture was used to analyze the remaining concentration of Mn(VII) and was determined by measuring the absorbance at 525 nm. The result indicates that, five moles of procainamide requires four moles of Mn(VII) as shown in Eq. (1).



The remaining reaction mixture was acidified, concentrated and extracted with ether. The reaction products were identified as Mn(II) , p-aminobenzoic acid and N,N-diethyl-2-nitrosoethanamine.

However, under the condition of Mn(VII) greater than $1.0 \times 10^{-4} \text{ mol dm}^{-3}$, the product Mn(II) was confirmed by UV-vis spectra and spot test [13]. The main reaction product p-aminobenzoic acid was identified and confirmed by TLC and further characterized by IR, GCMS and NMR spectra. IR spectrum showed C = O stretching for the carboxylic acid functional group at 1672 cm^{-1} , while $-\text{NH}_2$ stretching observed at 3366 cm^{-1} and $-\text{OH}$ stretching at 3465 cm^{-1} (Fig. 2). The presence of p-aminobenzoic acid was also confirmed by GC-MS analysis. The mass spectrum showed the base peaks at 120 amu consistent with the molecular ion of 137 amu (Fig. 3). All other peaks observed in the GC-MS can be interpreted in accordance with structure of p-aminobenzoic acid. Further p-aminobenzoic acid was characterized by $^1\text{H-NMR}$ spectra (Fig.4) (DMSO): 11.9 (s, 1H, OH), 3.5 (s, 2H, ArNH_2). Another product N, N-diethyl-2-nitrosoethanamine was confirmed by spot test [14].

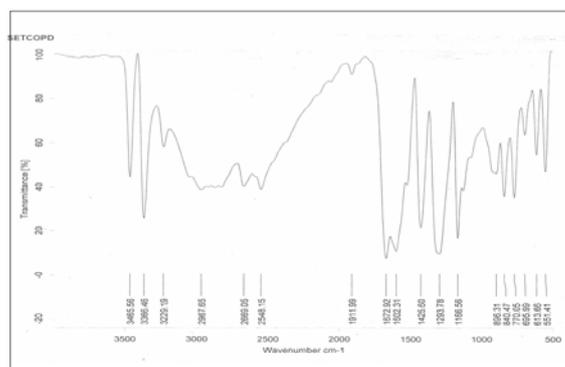


Fig. 2: FT-IR spectrum of p-aminobenzoic acid, the product obtained during the oxidation of procainamide by permanganate in acid medium.

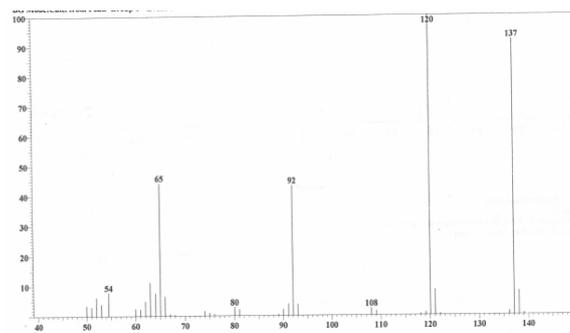


Fig. 3: GC - MS spectra of the product p-aminobenzoic acid, showed molecular ion peak at m/z 137 amu.

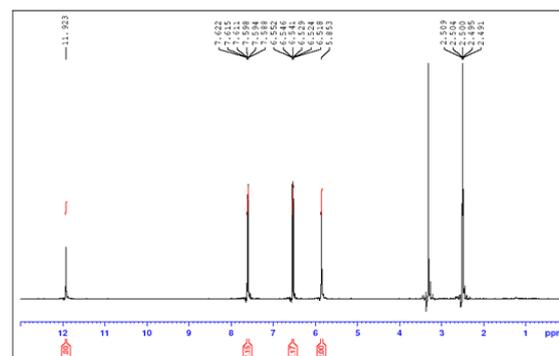


Fig. 4: ^1H NMR spectrum of p-aminobenzoic acid, the product obtained during the oxidation of procainamide by permanganate.

Reaction orders

The reaction orders were determined from the slopes of $\log k_{\text{obs}}$ versus \log (concentration) plots by varying the concentrations of PAH and acid in turn while keeping all other concentrations and conditions constant.

Effect of [Mn(VII)]

At constant concentration of PAH, acid and at constant ionic strength, $I = 3.0 \times 10^{-3} \text{ mol dm}^{-3}$, the MnO_4^- concentration was varied from $0.25 \times 10^{-4} \text{ mol dm}^{-3}$ to $3.0 \times 10^{-4} \text{ mol dm}^{-3}$. The order with respect to MnO_4^- concentration was found to be unity, since the rate constant k_{obs} , was almost constant at different MnO_4^- concentrations (Table 1). The pseudo-first order plots under these conditions were almost parallel and linear over 80% completion of the reaction (Fig. 1) also indicates first order with respect to MnO_4^- .

Effect of [Procainamide]

The PAH concentration was varied in the concentration range of $0.25 \times 10^{-3} \text{ mol dm}^{-3}$ to $4.0 \times 10^{-3} \text{ mol dm}^{-3}$ at 298K, keeping all other conditions constant. The rate constant, k_{obs} increased with increase in the concentration of PAH (Table 1). From the slope of the plot of $\log k_{\text{obs}}$ versus \log [PAH], the order with respect to PAH concentration was found to be less than unity (0.63).

Effect of [acid]

The effect of acid concentration on the reaction rate was studied in the range $0.50 \times 10^{-4} \text{ mol dm}^{-3}$ to $5.0 \times 10^{-4} \text{ mol dm}^{-3}$ at constant concentrations of PAH, MnO_4^- and at constant ionic strength of $3.0 \times 10^{-3} \text{ mol dm}^{-3}$ at 298K. The rate constant increased with the increase in the acid concentration (Table 1). The order with respect to acid concentration was found to be less than unity (0.70). The experimental rate law is

$$\text{Rate} = k_{\text{obs}} [\text{MnO}_4^-] [\text{PAH}]^{0.63} [\text{H}^+]^{0.70}$$

Effect of ionic strength (I) and dielectric constant (D)

The effect of ionic strength was studied by varying the sodium sulphate concentration from $1.0 \times 10^{-3} \text{ mol dm}^{-3}$ to $5.0 \times 10^{-3} \text{ mol dm}^{-3}$ at constant concentrations of Mn(VII), PAH and H^+ . It was found that, as the ionic strength increases, the rate of reaction also increases. The plot of $\log k_{\text{obs}}$ versus \sqrt{I} is linear (Fig.5). The dielectric constant of the medium was varied by varying acetic acid - water (v/v) content in the reaction mixture from 0 to 35% with all other conditions being maintained constant. As the acetic acid concentration increased in the reaction medium, the rate of reaction also increases. The plot of $\log k_{\text{obs}}$ versus $1/D$ is linear (Fig.5).

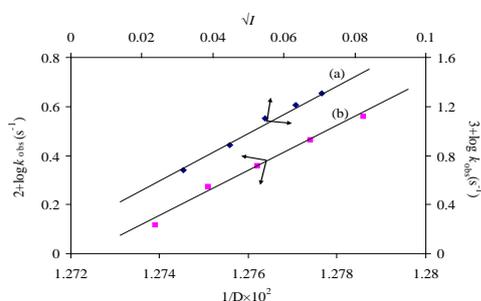


Fig. 5: Effect of (a) ionic strength and (b) dielectric constant on the oxidation of PAH by acidic MnO_4^- at 298K

Effect of added products

The effect of initially added products, p-aminobenzoic acid and Mn(II) did not have any significant effect on the rate of reaction.

Test for free radicals (polymerization study)

The intervention of free radicals was examined as follows: The reaction mixture, to which a known quantity of acrylonitrile

scavenger had been added initially, was kept in an inert atmosphere for two hours at room temperature and diluting the reaction mixture with methanol, precipitate was formed in the reaction mixture, which indicates the participation of free radicals in the reaction. Blank experiment with either procainamide or Mn(VII) alone with acrylonitrile did not induce polymerization under the present experimental conditions. The added acrylonitrile to the reaction mixture decrease the rate of reaction also indicates the involvement of free radicals in the reaction.

Table 1: Effect of MnO_4^- , PAH and H^+ concentrations on the Mn(VII) oxidation of PAH in acidic medium at 298K, $I = 3.0 \times 10^{-3} \text{ mol dm}^{-3}$.

$[\text{MnO}_4^-] \times 10^4$ (mol dm ⁻³)	$[\text{PAH}] \times 10^3$ (mol dm ⁻³)	$[\text{H}^+] \times 10^4$ (mol dm ⁻³)	$k_{\text{obs}} \times 10^2$ (s ⁻¹)
0.25	2.00	2.00	1.35
0.50	2.00	2.00	1.38
1.00	2.00	2.00	1.31
2.00	2.00	2.00	1.28
3.00	2.00	2.00	1.28
1.00	0.25	2.00	0.27
1.00	0.50	2.00	0.60
1.00	1.00	2.00	1.10
1.00	2.00	2.00	1.31
1.00	3.00	2.00	1.54
1.00	4.00	2.00	1.78
1.00	2.00	0.50	0.45
1.00	2.00	1.00	0.73
1.00	2.00	2.00	1.30
1.00	2.00	3.00	1.65
1.00	2.00	4.00	1.92
1.00	2.00	5.00	2.30

Effect of temperature

The rate of reaction was measured at four different temperatures 288, 298, 308 and 318K under varying acid and PAH concentrations. The rate was found to increase with increasing temperature. The rate constants of the slow step of the Scheme 1 were obtained from the intercepts and slopes of the plots of $1/k_{\text{obs}}$ versus $1/[\text{PAH}]$ and $1/k_{\text{obs}}$ versus $1/[\text{H}^+]$ at the four different temperature (Fig. 7). The energy of activation, E_a was evaluated from the slope of the plot of $\log k$ versus $1/T$. The enthalpy of activation, ΔH^\ddagger , the entropy of activation, ΔS^\ddagger and the free energy of activation, ΔG^\ddagger , were obtained by the Eyring equation [15] and the values are given in (Table 2).

$$k = \frac{k_B T}{h} e^{(-\Delta G^\ddagger/RT)} = \frac{k_B T}{h} e^{(-\Delta H^\ddagger + T\Delta S^\ddagger)/RT} \quad \dots\dots (2)$$

Where k is the rate constant, k_B is the Boltzmann's constant, h is the Planck's constant, R is the gas constant, T is the absolute temperature and ΔG^\ddagger is the free energy of activation. The linear form of above equation is

$$\ln \frac{k}{T} = - \frac{\Delta H^\ddagger}{RT} + \frac{\Delta S^\ddagger}{R} + \ln \frac{k_B}{h} \quad \dots\dots\dots (3)$$

The slope of the plot of $\log k/T$ versus $1/T$ gives the value of enthalpy of activation, ΔH^\ddagger . By using this value of ΔH^\ddagger , and the rate constant at a particular temperature T , the value of entropy of activation, ΔS^\ddagger was obtained by simple rearrangement of linear form of equation. Using these values of ΔH^\ddagger and ΔS^\ddagger , the free energy of activation, was obtained (Table 2).

DISCUSSION

MnO_4^- , is a powerful oxidizing agent in acid medium. The stable oxidation product of MnO_4^- in acid medium is Mn(II) and Mn(IV). The reaction between PAH and MnO_4^- has a stoichiometry 5:4 with a first-order dependence on the MnO_4^- concentration and less-than-unit order in both the PAH and H_2SO_4 concentrations. The fact that, Mn(II) is the reduced product of Mn(VII) in the present reaction

might indicate that [PAH] shows a strong reducing character in H_2SO_4 medium.

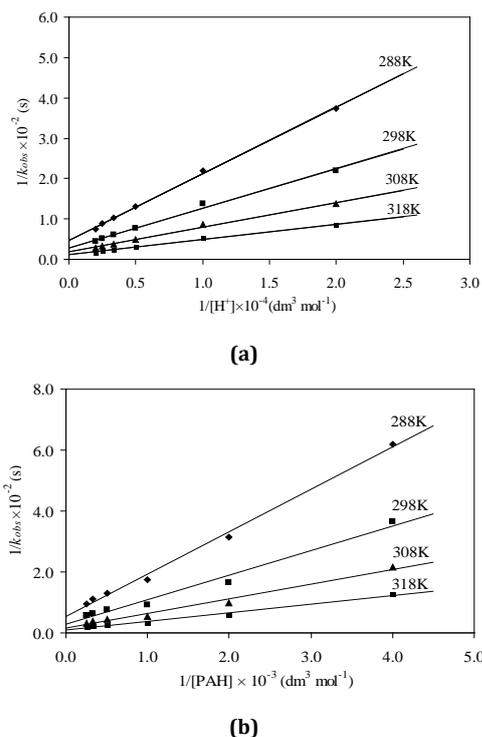


Fig. 6: Verification of rate law (9) in the form of Eq. (9) for the oxidation of procainamide by permanganate in sulphuric acid medium. Plot of $1/k_{obs}$ versus (a) $1/[H^+]$ and (b) $1/[PAH]$ at different temperature (Condition as in Table 1).

Table 2: Activation parameters and thermodynamic quantities for the oxidation of PAH by acidic Mn(VII).

(a) Effect of temperature with respect to slow step of the Scheme 1 and activation parameters

Temperature (K)	$k \times 10^2 (s^{-1})$	Parameter	Values
288	1.98	E_a (kJ mol ⁻¹)	37 ± 3
298	3.59	ΔH^\ddagger (kJ mol ⁻¹)	35 ± 3
308	7.07	ΔS^\ddagger (J K ⁻¹ mol ⁻¹)	-154 ± 4
318	8.82	ΔG^\ddagger (kJ mol ⁻¹)	81 ± 3
		log A	7 ± 0.1

(b) Equilibrium constants K_1 and K_2 at different temperatures

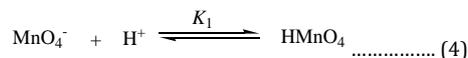
Temperature (K)	$K_1 \times 10^{-1} dm^3 mol^{-1}$	$K_2 \times 10^{-4} dm^3 mol^{-1}$
288	4.28	3.26
298	3.64	3.88
308	2.26	5.25
318	1.65	6.02

(c) Thermodynamic quantities with respect to K_1 and K_2

Quantities	Using K_1 values	Using K_2 values
ΔH (kJ mol ⁻¹)	-25	16
ΔS (J K ⁻¹ Mol ⁻¹)	-56	143
ΔG (kJ mol ⁻¹)	-8	-27

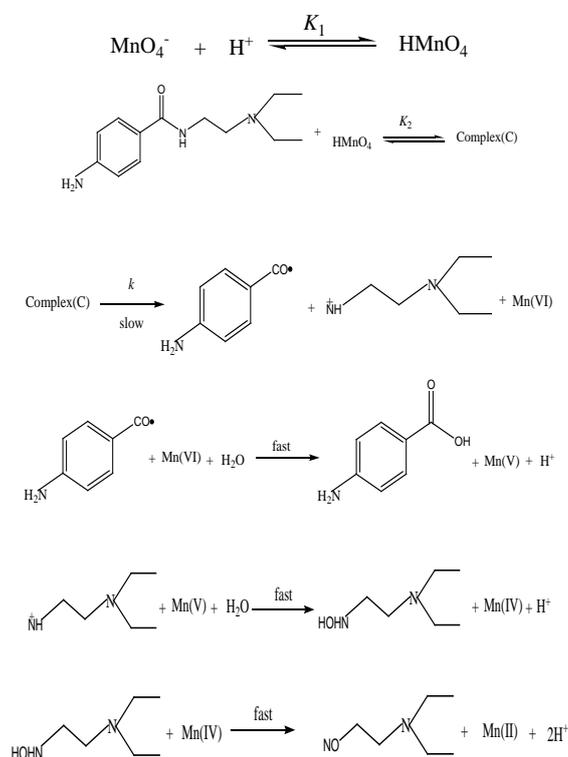
The active species of Mn(VII) in aqueous acid medium can be deduced from the dependence of the rate on the H^+ concentration in the reaction medium. The apparent order is less than unity in H_2SO_4

concentration might be an indication of Mn(VII) species as permanganic acid. In acid medium, permanganic acid ($HMnO_4$) is a more efficient oxidant species of manganese (VII) than permanganate ion [16, 17]. In addition, it was observed that the reaction rate increased with increasing H_2SO_4 concentration. The effect of ionic strength on the rate of reaction also confirms that $HMnO_4$ is the active species of MnO_4^- . Thus, in acid medium, MnO_4^- exists as $HMnO_4$.



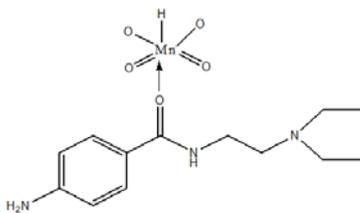
where K_1 is the formation constant of $HMnO_4$

In view of these aspects and the experimental observations, a reasonable reaction mechanism can be proposed in which all of the observed orders with respect to the concentrations of constituents, namely, MnO_4^- , PAH and H^+ can be well accommodated. The results suggest that the protonated form of Mn(VII), $HMnO_4$ is the active species of MnO_4^- in prior equilibrium, which reacts with one mol of PAH in the second equilibrium step to form a complex, then that decomposes in a slow step to give p-aminobenzaldehyde free radical and diethylethane-1, 2-diamine ion and Mn(VI). The free radical, p-aminobenzaldehyde undergoes hydrolysis in presence of Mn(VI) in a fast step to give final product, p-aminobenzoic acid and Mn(V), while diethylethane-1, 2-diamine ion undergoes hydrolysis in presence of Mn(V) in further fast step to form a product, 2-(diethylamino)-N-hydroxyethanamine and Mn(IV). In further fast step 2-(diethylamino)-N-hydroxyethanamine reacts with Mn(IV) to give a product, N,N-diethyl-2-nitrosoethanamine and Mn(II). The formed Mn(VI) and Mn(V) are unstable in acid medium [16] and could not be detected. All results may be interpreted in the form of Scheme 1.



Scheme 1

Scheme 1 is one of the proposed possible mechanisms for the reaction. The results indicate the formation of a complex between [PAH] and $HMnO_4$. The spectral evidence for a complex between the substrate and oxidant was obtained from UV-vis spectra of PAH and $PAH-MnO_4^-$ mixtures in which a hypsochromic shift of 15 nm (from 311 to 296 nm) was observed [18]. Complex formation was also confirmed by Michaelis-Menten plot. The probable structure of the complex is



Such complex formation between substrate and oxidant was also reported in the literature [19, 20]. From Scheme 1 the following rate law (9) can be derived as follows:

$$\text{Rate} = \frac{-d[\text{MnO}_4^-]}{dt} = k [\text{Complex}]$$

$$= kK_2 [\text{HMnO}_4] [\text{PAH}]$$

$$= kK_1K_2 [\text{MnO}_4^-]_f [\text{H}^+]_f [\text{PAH}]_f \quad \text{..... (5)}$$

Total concentration of MnO_4^- is given by

$$[\text{MnO}_4^-]_t = [\text{MnO}_4^-]_f + [\text{HMnO}_4] + [\text{Complex}]$$

$$= [\text{MnO}_4^-]_f + K_1 [\text{MnO}_4^-]_f [\text{H}^+]_f + K_2 [\text{HMnO}_4] [\text{PAH}]$$

$$= [\text{MnO}_4^-]_f + K_1 [\text{MnO}_4^-]_f [\text{H}^+]_f + K_1K_2 [\text{MnO}_4^-]_f [\text{H}^+]_f [\text{PAH}]$$

$$= [\text{MnO}_4^-]_f \{1 + K_1 [\text{H}^+]_f + K_1K_2 [\text{H}^+]_f [\text{PAH}]\}$$

$$[\text{MnO}_4^-]_f = \frac{[\text{MnO}_4^-]_t}{\{1 + K_1 [\text{H}^+]_f + K_1K_2 [\text{H}^+]_f [\text{PAH}]\}} \quad \text{.....(6)}$$

Therefore,

Where, $[\text{MnO}_4^-]_t$ and $[\text{MnO}_4^-]_f$ are the total and free Mn(VII) concentrations respectively.

Total concentration of PAH is given by

$$[\text{PAH}]_t = [\text{PAH}]_f + [\text{complex}]$$

$$= [\text{PAH}]_f + K_2 [\text{PAH}]_f [\text{HMnO}_4]$$

$$= [\text{PAH}]_f \{1 + K_2 [\text{HMnO}_4]\}$$

$$[\text{PAH}]_f = \frac{[\text{PAH}]_t}{1 + K_2 [\text{HMnO}_4]}$$

$$[\text{PAH}]_f = [\text{PAH}]_t \quad \text{..... (7)}$$

Because, $K_2 [\text{HMnO}_4] \ll 1$, on account of the low concentration MnO_4^- used in the experiment.

And

$$[\text{H}^+]_t = [\text{H}^+]_f + [\text{HMnO}_4]$$

$$= [\text{H}^+]_f + K_1 [\text{H}^+]_f + [\text{MnO}_4^-]$$

$$= [\text{H}^+]_f \{1 + K_1 [\text{MnO}_4^-]\}$$

Therefore,

$$[\text{H}^+]_t = [\text{H}^+]_f \quad \text{..... (8)}$$

Substituting Eqs. (6), (7) and (8) into Eq. (5) and omitting the subscripts, we obtain

$$\text{Rate} = \frac{-d[\text{MnO}_4^-]}{dt} = \frac{k K_1 K_2 [\text{MnO}_4^-] [\text{H}^+] [\text{PAH}]}{1 + K_1 [\text{H}^+] + K_1 K_2 [\text{H}^+] [\text{PAH}]} \quad \text{..... (9)}$$

$$\frac{\text{Rate}}{[\text{MnO}_4^-]} = k_{\text{obs}} = \frac{k K_1 K_2 [\text{H}^+] [\text{PAH}]}{1 + K_1 [\text{H}^+] + K_1 K_2 [\text{H}^+] [\text{PAH}]} \quad \text{Or..... (9)}$$

The rate law (8) can be rearranged to Eq. (9) which is suitable for verification.

$$\frac{1}{k_{\text{obs}}} = \frac{1}{k K_1 K_2 [\text{H}^+] [\text{PAH}]} + \frac{1}{k K_2 [\text{PAH}]} + \frac{1}{k} \quad \text{..... (10)}$$

According to Eq. (10), plots of $1/k_{\text{obs}}$ versus $1/[\text{H}^+]$ and $1/k_{\text{obs}}$ versus $1/[\text{PAH}]$ should be linear, and this was found to be the case (Fig. 6). From the slopes and intercepts of these plots, the values of k , K_1 , and K_2 at 298K were obtained as $3.59 \times 10^{-2} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$, $36 \text{ dm}^3 \text{ mol}^{-1}$ and $3.88 \times 10^4 \text{ dm}^3 \text{ mol}^{-1}$ respectively (Table 2). The value of K_1 is in good agreement with earlier work (literature value is $40 \text{ dm}^3 \text{ mol}^{-1}$) [20]. The effect of ionic strength is consistent with reaction between ions, as in Scheme 1. The effect of solvent on the rate of reaction has been described in the literature [21, 22]. An increase in the content of acetic acid in the reaction mixture leads to an increase in the rate of reaction. The modest activation energy [23] and sizable entropy of activation support a complex transition state in the reaction.

The values of ΔH^\ddagger and ΔS^\ddagger are both favorable for electron transfer processes [24]. The negative value of ΔS^\ddagger indicates that the complex is more ordered than the reactants. The high negative entropy of activation observed in the decomposition of the intermediate complex is in accordance with the propositions suggested for oxidation reactions of an inner-sphere nature [25].

CONCLUSION

The kinetics of the oxidation of Mn(VII) by procainamide in an acid medium was investigated using a stopped flow technique. The oxidant MnO_4^- exists in acid medium as HMnO_4 , which takes part in the chemical reaction. The role of hydrogen ion is crucial to the reaction. Oxidation products were identified as Mn(II), p-aminobenzoic acid and N,N-diethyl-2-nitrosoethanamine. Rate constant of slow step and other equilibrium constants involved in the mechanism are evaluated and activation parameters with respect to slow step of reaction were computed. The proposed mechanism is consistent with all the experimental evidence.

CONFLICT OF INTERESTS

Declared None.

ACKNOWLEDGEMENT

One of the authors (Manjanath B. Patgar) thanks Karnatak University, Dharwad for the research fellowship (KU/Sch/UGC-UPE/2013-14/1118) under the UGC-UPE programme (2013-16).

REFERENCES

1. FM Stearns, PA Trevoise. Center for laboratory medicine. Clin Chem 1981;27:2064.
2. JS Dutcher Strong, JM Lucas, SV Lee, WK Jr Atkinson. "Procainamide and N-acetylprocainamide kinetics investigated simultaneously with stable isotope methodology". Clin Pharmacol Ther 1977;22:447-50.
3. DE Drayer, MM Reidenberg, RW Sevy. "N-acetylprocainamide: an active metabolite of procainamide". Proceedings of the Society for Experimental Biology and Medicine. Soc Experimental Biol Medicine 1974;146:358-63.
4. JS Dutcher, JM Strong. Clin Chem 1977;23:1318.

5. MC Day, J Selbin. Theoretical Inorganic Chemistry, Reinhold Book Corp: New York, USA; 1964.
6. P Caron, RW Dugger, JA Ruggeri. DH brown ripin large-scale oxidations, In the pharmaceutical industry. *Chem Rev* 2006;106:2943.
7. OA Babatunde. Kinetics and mechanism of oxidation of DL- α -alanine by permanganate ion in acid perchlorate media. *World J Chem* 2008;3:27.
8. RM Hassan. Kinetics and mechanism of oxidation of DL-alanine by acid perchlorate ion mediasolution. *Can J Chem* 1991;69:2018.
9. PK Sen, A Saniyan, KS Gupta. Evidence of Protonation during oxidation of some alcohol by permanganate ions in perchloric acid medium & mechanism of the oxidation processes. *Int J Chem Kinet* 1995;27:379.
10. MM Girgis, ZH El-Shatoury, Khalil. Kinetics and mechanism of oxidation of lactic acid by KMnO_4 in H_2SO_4 medium. *Can J Chem* 1985;63:3317.
11. M Zahedi, H Bahrami. Kinetics and mechanism of the autocatalytic oxidation of l-asparagine in a moderately concentrated sulfuric acid medium. *Kinet Catal* 2004;45:351.
12. JE Knoll. Estimation of the limit of detection in chromatography. *J Chromat Sci* 1985;23:422.
13. Vogel. Vogel's Textbook of Macro and Semimicro Qualitative Inorganic Analysis, John Wiley & Sons: New York; 1967. p. 291.
14. E Wiberg, AF Holleman. Inorganic Chemistry: Elsevier; 2001.
15. KS Byadagi, DV Naik, AP Savanur, ST Nandibewoor, SA Chimatadar. Ruthenium (III) mediated oxidation of thiamine hydrochloride by cerium (IV) in perchloric acid medium: a kinetic and mechanistic approach. *React Kinet Mech Catal* 2010;99:53.
16. KB Wiberg. Oxidation in Organic Chemistry, Part A: New York; 1965. p. 657.
17. SA Chimatadar, SC Hiremath, JR Raju. Oxidation of Thallium (I) by permanganate in perchloric acid. *Indian J Chem* 1991;30A:190.
18. VC Seregar, CV Hiremath, ST Nandibewoor. Palladium(II) catalysed oxidation of l-proline by heptavalent manganese in aqueous alkaline medium: a free radical intervention and decarboxylation. *Transition Met Chem* 2006;31:541.
19. H Bahrami, M Zahedi. Evidence for delayed autocatalytic behaviour of Mn(II) ions at a critical concentration. *J Iranian Chem Soc* 2008;5:535.
20. JC Abbar, SD Lamani, ST Nandibewoor. Ruthenium-(III) catalysed oxidative degradation of amitriptyline-a tricyclic antidepressant drug by permanganate in aqueous acid medium. *J Solution Chem* 2011;40:502.
21. EA Moelwyn-Hughes, Physical Chemistry, 2nd edn, Pergamon Press: New York; 1961.
22. ES Amis. Solvent Effects on Reaction Rates and Mechanisms, Academic Press: New York; 1966. p. 183.
23. DC Bilehal, RM Kulkarni, ST Nandibewoor. Kinetics and mechanistic Study of the ruthenium (III) catalyzed oxidative deamination and decarboxylation of L-valine by alkaline permanganate. *Ca J Chem* 2001;79:1926.
24. SA Farokhi, ST Nandibewoor. The kinetics and the mechanism of oxidative decarboxylation of benzoic acid by acidic permanganate (stopped-flow technique) An Autocatalytic stud *Can J Chem* 2004;82:1372.
25. Weissberger, ES Lewis. Investigations of Rates and Mechanism of Reactions in Techniques of Chemistry: Wiley, New York; 1974;4:421.