

Research Article

Kinetics and Mechanistic Approach to the Permanganate Oxidation of L-Glutamine in Alkaline Medium

Fawzy A^{1,2*} and Altass HM¹¹Associate Professor, Chemistry Department, Faculty of Applied Science, Umm Al-Qura University, Makkah, Saudi Arabia²Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt***Corresponding author:** Fawzy A, Associate Professor, Chemistry Department, Faculty of Applied Science, Umm Al-Qura University, 21955 Makkah, Saudi Arabia, Assiut University, 71516 Assiut, Egypt**Received:** May 12, 2016; **Accepted:** May 31, 2016;**Published:** June 02, 2016**Abstract**

The kinetics of oxidation of L-glutamine (Gln) by permanganate ion has been investigated in alkaline medium at a constant ionic strength of 0.2 mol dm⁻³ and at 25°C using spectrophotometric technique. A first order kinetics with respect to [permanganate] and less than unit order dependences on [Gln] and [OH⁻] were revealed. No pronounced effect on the reaction rate by increasing either ionic strength or solvent polarity of the medium was recorded. Intervention of free radicals was observed in the reaction. The reaction mechanism describing the kinetic results was suggested. The final oxidation products of L-glutamine were identified as formyl propanamide, ammonia and carbon dioxide. The rate-law expression for the oxidation reaction was deduced and the reaction constants have been evaluated. The activation parameters associated with the rate-limiting step of the reaction, along with the thermodynamic quantities of the equilibrium constants have been calculated and discussed.

Keywords: L-Glutamine; Permanganate; Oxidation; Kinetics; Mechanism

Introduction

Amino acids are biologically important organic compounds composed of both amine and carboxylate functional groups, along with a side-chain specific to each amino acid. Due to the biological importance of amino acids, the kinetics and mechanistic studies of their oxidation by a variety of oxidants have received considerable attention [1-20]. L-Glutamine is a α -amino acid that is used in the biosynthesis of proteins. It is non-essential and conditionally essential in humans who are synthesized by the enzyme glutamine synthetase from glutamate and ammonia. Glutamine plays a role in a variety of biochemical functions [21-23]. In human blood, glutamine is the most abundant free amino acid. The demand for glutamine increases with physical and mental stress. Production of this important amino acid, which takes place in the body, often slows down with age and does not generate sufficient amounts. Glutamine plays a decisive role in keeping a balanced acid-base ratio. The most relevant glutamine-producing tissue is the muscle mass. If not enough glutamine is available, the body takes the necessary protein from muscle mass and converts it to glutamine and energy. This leads to muscle proteins being lost, muscle strands becoming thinner and the skin becoming generally saggy. Although the liver is capable of relevant glutamine synthesis, its role in glutamine metabolism is more regulatory than producing, since the liver takes up large amounts of glutamine derived from the gut. Glutamine can be converted to glucose in the kidneys, without effecting glucagon or insulin levels. There are also indications that glutamine can reduce the demand for sugar and alcohol [22,23].

Potassium permanganate is extensively used as an oxidizing agent for numerous organic molecules in various media [24-34]. The oxidation reaction mechanisms by permanganate are governed by pH of the medium [33]. Among six oxidation states of Mn(II) to Mn(VII), permanganate, Mn(VII) is found to be the most powerful oxidation state in both acid or alkaline media. By using permanganate

as oxidizing agent, it is understandable that, the Mn(VII) in permanganate is reduced to a variety of oxidation states in acidic, alkaline and neutral media.

There are no reports on the kinetics and mechanism of oxidation of L-glutamine by permanganate ion. This motivates us to investigate the title reaction. The objectives of the present study aimed to shed more light and establish the most favorable conditions affecting oxidation of such amino acid and to elucidate a plausible oxidation reaction mechanism.

Experimental

Materials

All reagents were from Merck or Sigma. A stock solution of L-glutamine was prepared afresh by dissolving the appropriate amount of the sample (E. Merck) in the required volume of bidistilled water. Solution of potassium permanganate was prepared and standardized as reported earlier [35]. Other chemicals were of analytical grade and their solutions were prepared by dissolving requisite amounts of the samples in bidistilled water. Sodium hydroxide solution was used to provide the required alkalinity. Sodium per chlorate and t-butyl alcohol were used to study the effects of ionic strength and dielectric constant of reaction medium, respectively.

Kinetic measurements

The kinetic measurements were followed under pseudo-first order conditions where L-glutamine substrate (Gln) was exist in a large excess over that of permanganate. Initiation of the reaction was done by mixing the formerly thermostatted solutions of permanganate and substrate that also contained the required amounts of NaOH and NaClO₄. The course of the reaction was followed up to not less than two half-lives by monitoring the absorbance of permanganate as a function of time at its absorption maximum ($\lambda = 525\text{nm}$), whereas the other constituents of the reaction mixture did not absorb considerably

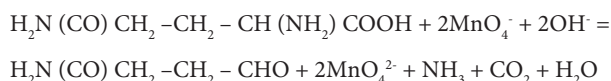
at the determined wavelength. The absorption measurements were done in a temperature-controlled Shimadzu UV-VIS-NIR-3600 double-beam spectrophotometer. The reactions temperature was controlled to $\pm 0.1^\circ\text{C}$.

First order plots of $\ln(\text{absorbance})$ versus time were recorded to be straight lines up to at least two-half lives of the reaction completion and the observed first order rate constants (k_{obs}) were calculated as the gradients of such plots. Ordinary values of at least two independent determinations of the rate constants were taken for the analysis. The rate constants were reproducible to 2-3%. The orders of the reaction with admiration to the reactants were calculated from the slopes of the $\log k_{\text{obs}}$ versus $\log(\text{concentration})$ plots by varying the concentrations of both substrate and alkali, in turn, while keeping other conditions constant.

Results

Stoichiometry and product analysis

Reaction mixtures containing different initial concentrations of the reactants with an excess of permanganate ion concentration at $[\text{OH}^-] = 0.05 \text{ mol dm}^{-3}$ and at 0.2 mol dm^{-3} ionic strength, were equilibrated for about 24h at room temperature. The unconsumed permanganate was estimated periodically until it reached a constant value, i.e. completion of the reaction. Estimation of unconsumed $[\text{MnO}_4^-]$ revealed that approximately 2.0mol of permanganate consumed 1.0 mol of L-glutamine. This result confirms to the following stoichiometric equation,



The above stoichiometric equation is consistent with the results of product analysis. The products were identified as the corresponding aldehyde (formyl propanamide) by spot test [36], intermediate manganate(VI) by its visible spectrum, ammonia by Nessler's reagent [37] and carbon dioxide by lime water. The product, formyl propanamide was also estimated quantitatively as its 2,4-DNP derivative [37].

Spectral changes

Spectral changes throughout the oxidation of L-glutamine by alkaline permanganate are represented in Figure 1. The main characteristic feature manifested in the figure is the gradual decay of permanganate band at its absorption maximum ($\lambda = 525\text{nm}$) as a result of its reduction of permanganate by the amino acid.

Effect of permanganate concentration

Permanganate oxidant was diverse in the concentration range of 1.0×10^{-4} to $8.0 \times 10^{-4} \text{ mol dm}^{-3}$ while the other reactant concentrations, pH and temperature were kept constant. It has been found that, plots of $\ln(\text{absorbance})$ versus time were linear up to about two-half lives of the reaction achievement. Furthermore, the increase in the oxidant concentration did not change the oxidation rate as listed in Table 1. These results confirm the first order dependence with respect to the oxidant.

Effect of L-glutamine concentration

The observed first order rate constant (k_{obs}) was measured at different concentrations of the L-glutamine keeping others constant.

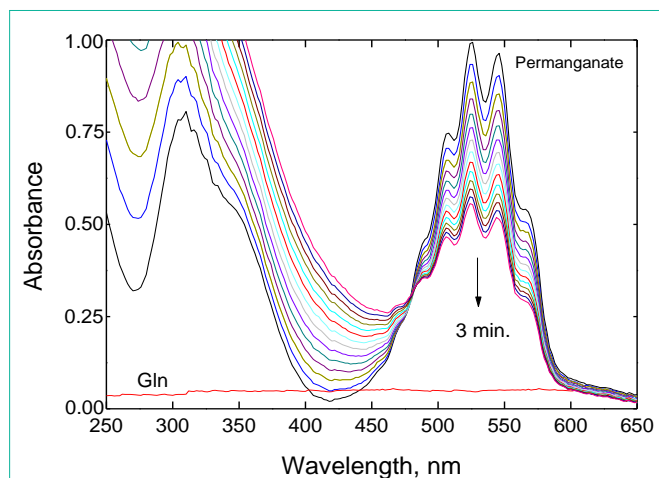


Figure 1: Spectral changes throughout the oxidation of L-glutamine by alkaline permanganate. $[\text{MnO}_4^-] = 4.0 \times 10^{-4}$, $[\text{Gln}] = 0.01$, $[\text{OH}^-] = 0.05$ and $I = 0.2 \text{ mol dm}^{-3}$ at 25°C .

Table 1: Effect of variation of $[\text{MnO}_4^-]$, $[\text{Gln}]$, $[\text{OH}^-]$ and I on the observed first order rate constants (k_{obs}) in the oxidation of L-glutamine by alkaline permanganate at 25°C .

$10^4 [\text{MnO}_4^-]$ (mol dm^{-3})	$10^2 [\text{Gln}]$ (mol dm^{-3})	$10^2 [\text{OH}^-]$ (mol dm^{-3})	I (mol dm^{-3})	$10^5 k_{\text{obs}}$ (s^{-1})
1.0	1.0	5.0	0.2	39.8
2.0	1.0	5.0	0.2	36.0
3.0	1.0	5.0	0.2	37.4
4.0	1.0	5.0	0.2	39.4
6.0	1.0	5.0	0.2	39.7
8.0	1.0	5.0	0.2	40.1
4.0	0.4	5.0	0.2	19.9
4.0	0.7	5.0	0.2	31.1
4.0	1.0	5.0	0.2	39.4
4.0	1.3	5.0	0.2	50.3
4.0	1.6	5.0	0.2	58.1
4.0	2.0	5.0	0.2	67.8
4.0	1.0	3.0	0.2	32.1
4.0	1.0	5.0	0.2	39.4
4.0	1.0	7.0	0.2	47.6
4.0	1.0	9.0	0.2	54.2
4.0	1.0	12.0	0.2	59.3
4.0	1.0	15.0	0.2	66.6
4.0	1.0	5.0	0.2	39.4
4.0	1.0	5.0	0.3	43.7
4.0	1.0	5.0	0.4	48.2
4.0	1.0	5.0	0.5	51.3
4.0	1.0	5.0	0.6	53.6
4.0	1.0	5.0	0.8	57.1

Experimental error $\pm 3\%$.

A plot of k_{obs} versus $[\text{Gln}]$ was found to be linear with a positive intercept on the k_{obs} axis (Figure 2) confirming fractional-first order dependence with respect to the amino acid concentration.

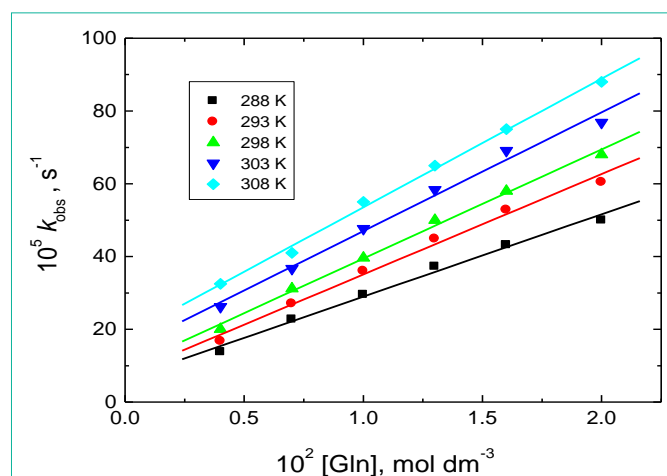


Figure 2: Plots of the observed first order rate constant (k_{obs}) versus $[\text{Gln}]$, at different temperatures, in the oxidation of L-glutamine by alkaline permanganate. $[\text{MnO}_4^-] = 4.0 \times 10^{-4}$, $[\text{OH}^-] = 0.05$ and $I = 0.2 \text{ mol dm}^{-3}$.

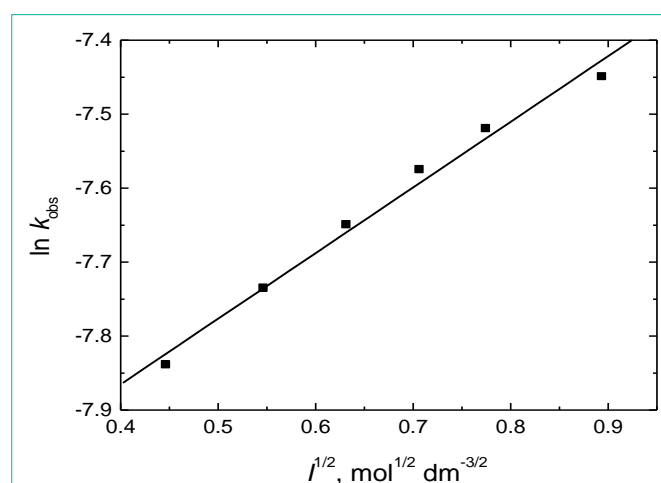


Figure 4: Debye-Huckel plot in the oxidation of L-glutamine by alkaline permanganate. $[\text{MnO}_4^-] = 4.0 \times 10^{-4}$, $[\text{Gln}] = 0.01 \text{ mol dm}^{-3}$ at 25°C .

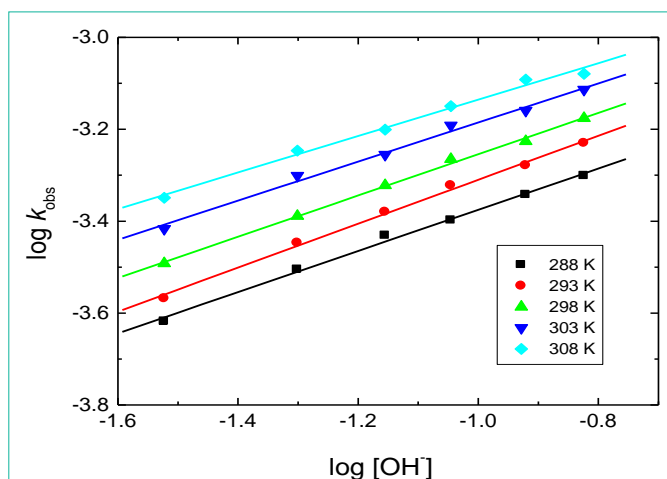


Figure 3: Plots of $\log k_{\text{obs}}$ versus $\log [\text{OH}^-]$, at different temperatures, in the oxidation of L-glutamine by alkaline permanganate. $[\text{MnO}_4^-] = 4.0 \times 10^{-4}$, $[\text{Gln}] = 0.01$ and $I = 0.2 \text{ mol dm}^{-3}$.

Effect of alkali concentration

The influence of alkali on the reaction rate was deliberated at various $[\text{OH}^-]$, keeping all other reactant concentrations constant. An increase in the rate constant with increasing alkali concentration was achieved (Table 1). A plot of $\log k_{\text{obs}}$ versus $\log [\text{OH}^-]$ was found to be linear with a slope of less than unity as shown in Figure 3, suggesting that the reaction order with respect to $[\text{OH}^-]$ was fractional-first.

Effect of ionic strength and solvent polarity

The effect of the ionic strength was studied by varying the concentration of NaClO_4 in the reaction medium at constant concentrations of permanganate, L-glutamine and alkali. It was found that increasing the ionic strength increased the oxidation rate as observed from the data listed in Table 1. The Debye-Hückel plot ($\ln k_{\text{obs}}$ vs. $I^{1/2}$) was found to straight with a positive slope as shown in Figure 4.

The solvent polarity of the reactions media, ϵ , was varied by varying the t-butyl alcohol–water content (0–40%) in the reaction

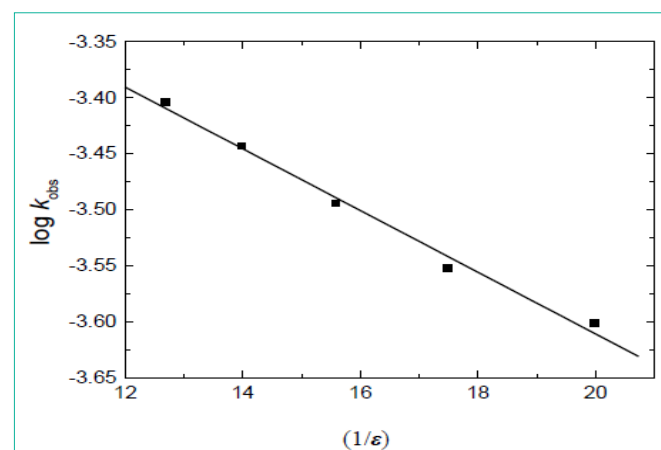


Figure 5: Plot of $\log k_{\text{obs}}$ versus $1/\epsilon$ in the oxidation of L-glutamine by alkaline permanganate. $[\text{MnO}_4^-] = 4.0 \times 10^{-4}$, $[\text{Gln}] = 0.01$ and $I = 0.2 \text{ mol dm}^{-3}$ at 25°C .

mixture with all other conditions being constant. The ϵ values were calculated from the equation: $\epsilon = \epsilon_w V_w + \epsilon_B V_B$, where ϵ_w and ϵ_B are solvent polarities of pure water and t-butyl alcohol, respectively, and V_w and V_B are the volume fractions of components water and t-butyl alcohol, respectively, in the total mixtures. The data clearly reveal that the decrease in solvent polarities of the solvent mixtures, i.e. increase the t-butyl alcohol content decreased the oxidation rate and the plot of $\log k_{\text{obs}}$ versus $1/\epsilon$ was found to be linear with a negative slope as illustrated in Figure 5.

Effect of temperature

The oxidation rate was recorded at five different temperatures, 288 - 308 K, under varying the concentrations of L-glutamine and alkali at constant ionic strength. The activation parameters of the rate constant of the slow step (kI) along with thermodynamic parameters of the equilibrium constants involved in the reaction mechanism were evaluated using Arrhenius and Eyring equations and were listed in Tables 3 and 4, respectively.

Polymerization study

To check the existence of free radicals in the reaction under investigation, the reaction mixture was mixed with identified

Table 2: Values of k_1 , K_1 and K_2 (at different temperatures) in the oxidation of L-glutamine by alkaline permanganate. $[\text{MnO}_4^-] = 4.0 \times 10^{-4}$, $[\text{Gln}] = 0.01$, $[\text{OH}^-] = 0.05$ and $I = 0.2 \text{ mol dm}^{-3}$.

Constant	Temperature (K)				
	288	293	298	303	308
$10^3 k_1 \text{ (dm}^3 \text{ mol}^{-1} \text{ s}^{-1}\text{)}$	1.43	1.56	1.67	1.75	1.82
$K_1 \text{ (dm}^3 \text{ mol}^{-1}\text{)}$	11.07	12.13	13.37	14.78	15.91
$K_2 \text{ (dm}^3 \text{ mol}^{-1}\text{)}$	71.44	82.71	92.88	104.07	117.12

Table 3: Activation parameters associated with the slow step (k_1).

ΔS^\ddagger $\text{J mol}^{-1} \text{ K}^{-1}$	ΔH^\ddagger kJ mol^{-1}	ΔG^\ddagger_{298} kJ mol^{-1}	E_a^\ddagger kJ mol^{-1}
-122.78	8.98	45.57	11.02

Table 4: Thermodynamic parameters associated with the equilibrium constants (K_1 and K_2).

Equilibrium Constant	ΔH° kJ mol^{-1}	ΔG°_{298} kJ mol^{-1}	ΔS° $\text{J mol}^{-1} \text{ K}^{-1}$
K_1	13.14	-6.44	-65.71
K_2	17.96	-11.22	-97.93

Experimental error $\pm 3\%$.

quantities of acrylonitrile monomer and stored for about 6 hours under dry nitrogen condition. On dilution with methanol, a white precipitate was formed, indicating the participation of free radicals in the oxidation reaction. The blank experiments which were carried out with either permanganate or substrate with acrylonitrile did not induce polymerization under the same experimental conditions.

Discussion

Permanganate ion is found to be a powerful oxidant in aqueous alkaline media and exhibits some of oxidation states such as Mn(VII), Mn(V) and Mn(VI). At pH > 12. The reduction product of Mn(VII) is stable Mn(VI) and no further reduction is observed [38,39]. The formation of a manganate(VI) intermediate was confirmed by the green color observed as the reactions proceeded [40] which undergoes a slow decay to give rise to the final oxidation products. The yellow color persisted after achievement of the oxidation reaction, then finally discreted brown MnO_2 sol was observed confirming that the Mn(V) species, hypomanganate(V), formed and subsequently decomposed to Mn(IV) sol [40]. The latter was coagulated by aging to give a colloidal precipitate of $\text{Mn}^{\text{IV}}\text{O}_2$.

It was reported [41,42] that, permanganate ion in aqueous alkaline media combines with alkali to produce an alkali-permanganate species, $[\text{MnO}_4 \cdot \text{OH}]^{2-}$, in a pre-equilibrium step, as shown in Scheme 1. This is consistent with the apparent order of less than unity with respect to the alkali. The formation of $[\text{MnO}_4 \cdot \text{OH}]^{2-}$ in the present systems is further supported by the plots of $1/k_{\text{obs}}$ versus $1/[\text{OH}^-]$ shown in Figure 7, which are linear with non-zero intercepts.

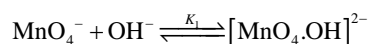
Many investigators [25-34,43-46] have suggested that, most of the permanganate ion oxidation reactions in neutral and alkaline media proceed through intermediate complexes formation between the oxidant and substrate. The kinetic evidence for such complex was established by the linearity of the plots between $1/k_{\text{obs}}$ and $1/[\text{Gln}]$ as shown in Figure 6, in favor of possible formation of a transient complex flanked by oxidant and substrate comparable with the well-known Michaelis-Menten mechanism [47] for enzyme-substrate reactions.

On the other hand, amino acid in aqueous solution is known to exist as zwitterion [48], whereas in aqueous alkaline medium it exists as anion (deprotonated species) according to the following equilibria:



The observed increase in the ionic strength and solvent polarity of the reaction medium implies association of two similarly charged ions [49,50], i.e. between negative deprotonated, anionic, amino acid (Gln^-) and negative alkali-permanganate species.

In view of the above arguments, the reaction mechanism shown in Scheme 1 may be suggested. This involves attack of the active species of permanganate, $[\text{MnO}_4 \cdot \text{OH}]^{2-}$, on the deprotonated amino acid, Gln^- , leading to the formation of a complex (C) in a pre-equilibrium step. In this complex, one electron is transferred from the substrate to permanganate. Under slow cleavage of the complex, the formation of a free radical intermediate derived from the substrate, and manganate(VI) transient species has been monitored. The intermediate radical is rapidly decarboxylated forming a new radical intermediate which attacked by another alkali-permanganate species to yield the final oxidation products.



The relationship between reaction rate and L-glutamine, hydroxyl ion and oxidant concentrations can be deduced (see Appendix) to give the following equation,

$$\text{Rate} = \frac{k_1 K_1 K_2 [\text{Gln}] [\text{OH}^-] [\text{MnO}_4^-]}{1 + K_1 [\text{OH}^-] + K_1 K_2 [\text{Gln}] [\text{OH}^-]} \quad (1)$$

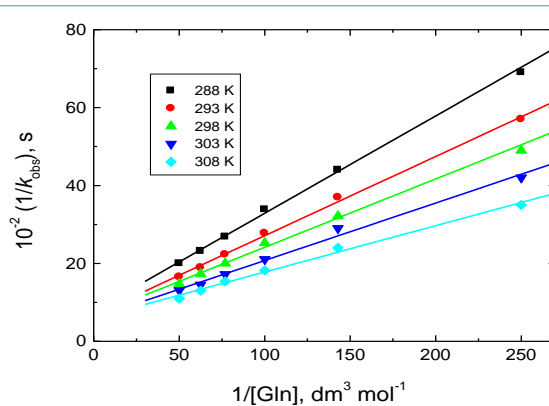
Under pseudo-first order conditions, the rate-law can be expressed as,

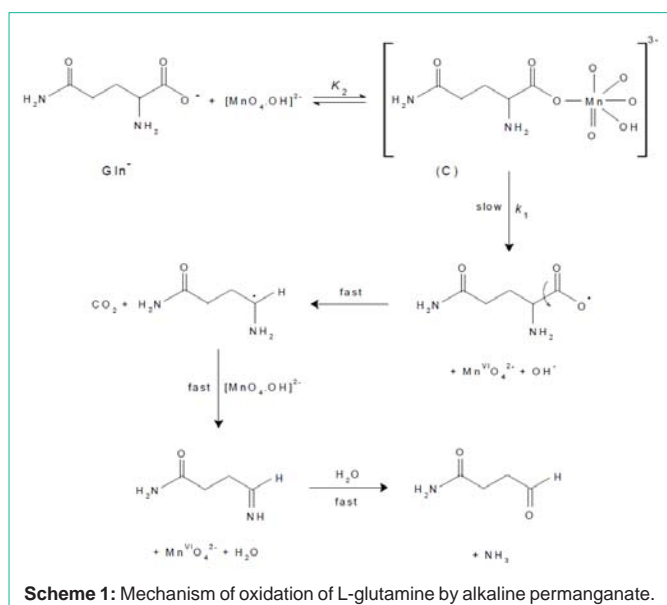
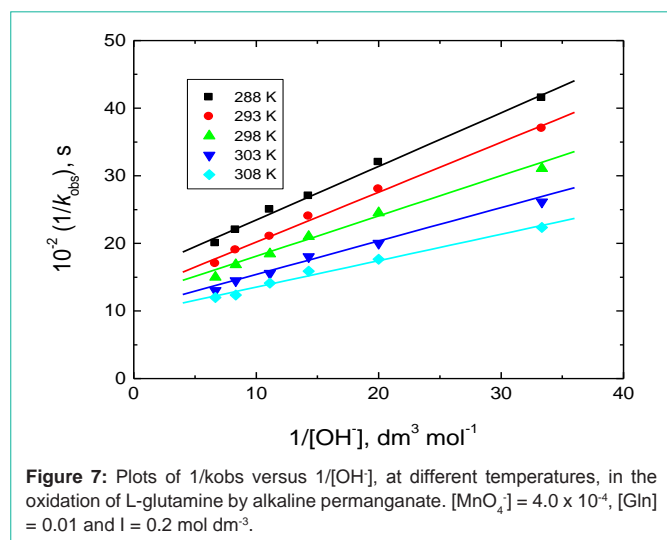
$$\text{Rate} = \frac{-d[\text{MnO}_4^-]}{dt} = k_{\text{obs}} [\text{MnO}_4^-] \quad (2)$$

Comparing equations (1) and (2) and with rearrangement we obtain the following equations,

$$\frac{1}{k_{\text{obs}}} = \left(\frac{1 + K_1 [\text{OH}^-]}{k_1 K_1 K_2 [\text{OH}^-]} \right) \frac{1}{[\text{Gln}]} + \frac{1}{k_1} \quad (3)$$

$$\frac{1}{k_{\text{obs}}} = \left(\frac{1}{k_1 K_1 K_2 [\text{Gln}]} \right) \frac{1}{[\text{OH}^-]} + \left(\frac{1}{k_1 K_2 [\text{Gln}]} + \frac{1}{k_1} \right) \quad (4)$$

**Figure 6:** Plots of $1/k_{\text{obs}}$ versus $1/[\text{Gln}]$, at different temperatures, in the oxidation of L-glutamine by alkaline permanganate. $[\text{MnO}_4^-] = 4.0 \times 10^{-4}$, $[\text{OH}^-] = 0.05$ and $I = 0.2 \text{ mol dm}^{-3}$.



According to Eqs. (3) and (4), other conditions being constant, plots of $1/k_{\text{obs}}$ versus $1/[\text{Gln}]$ at constant $[\text{OH}^-]$ and $1/k_{\text{obs}}$ versus $1/[\text{OH}^-]$ at constant $[\text{Gln}]$ should be linear with positive intercepts on the $1/k_{\text{obs}}$ axes and are certainly found to be so as shown in Figures 6 and 7, respectively. The slopes and intercepts of such plots lead to calculation of the values of k_1 , K_1 and K_2 (at different temperatures) as listed in Table 2. The obtained values of K_1 are in a good agreement with those reported in the literature [25-32]. Also, the activation parameters of k_1 along with thermodynamic parameters of K_1 and K_2 were calculated and were listed in Tables 3 and 4, respectively.

It has been previously reported [51,52] that, the entropy of activation tends to be more negative for reactions of inner-sphere nature, whereas the reactions of positive DS^\ddagger values proceed via outer-sphere mechanism. The obtained large negative values of entropy of activation (Table 3) suggest that one-electron transfer of inner-sphere nature is the more plausible mechanism for the current oxidation reaction. On the other hand, the positive values of both ΔH^\ddagger and ΔG^\ddagger specify that, the formation of the complex is

endothermic and non-spontaneous, respectively.

Conclusion

The kinetics of oxidation of L-glutamine by alkaline permanganate has been studied. The final oxidation products were identified as formyl propanamide, ammonia and carbon dioxide. The rate-law expression for the oxidation reaction was deduced and the reaction constants have been evaluated. The activation parameters along with the thermodynamic quantities have been calculated and discussed.

Acknowledgement

The Authors are highly indebted to the Chemistry Department, Umm Al-Qura University for using of all instrumentation facilities.

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