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Autocatalysed oxidation of etophylline by permanganate in aqueous sulphuric acid medium- kinetics and mechanistic study

H. V. Rajeshwari, K. S. Byadagi, S. T. Nandibewoor and S. A. Chimatadar*

Department of Studies in Chemistry, Karnatak University, Pavate Nagar, Dharwad 580003, India.

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The reaction kinetics of oxidation of etophylline by permanganate ions has been investigated in sulphuric acid medium using spectrophotometric techniques at 25°C and at constant ionic strength, 1.60 mol dm⁻³, under pseudo-first order conditions. An autocatalysis reaction is observed due to the formation of one of the products, Mn^{II}. The order with respect to etophylline and Mn^{VII} concentrations are found to be unity in each, whereas fractional order with respect to autocatalyst, Mn^{II}. As the concentration of acid increases the rate of the reaction increases. The order with respect to acid concentration is less than unity. Based on the experimental results a suitable mechanism is proposed. The influence of temperature on the rate of reaction is studied. The activation parameters and thermodynamic quantities have been determined with respect to slow step of the mechanism.

Key words: Autocatalysis, oxidation, etophylline, permanganate.

INTRODUCTION

Permanganate is a unique oxidizing agent in neutral, alkaline and acid medium. In general reduction of the permanganate, in acid medium goes to either Mn^{IV} or Mn^{II} having the reduction potential of the couple Mn^{VII}/ Mn^{IV}: 1.695 V and Mn^{VII}/ Mn^{II}: 1.51 V (Day and Selbin, 1985). During the oxidation by permanganate, it is evident that permanganate is reduced to various oxidation states in acidic, alkaline and neutral media. The manganese chemistry involved in these multistep redox reactions is an important source of information as the manganese intermediates are relatively easy to identify when they have a sufficiently long lifetimes, and the oxidation states of the intermediate permit useful conclusion as to the possible reaction mechanisms, including the nature of the intermediates. In acid medium it exists in different forms

such as HMnO₄, H₂MnO₄⁺, HMnO₃, Mn₂O₇ and depending on the nature of reductant, the oxidant has been assigned both inner sphere and outer sphere mechanism path ways in their redox reactions (Joaquin and Perenz-Benito, 2009; Babatunde, 2008). Etophylline, (3, 7-dihydro-7-(2-hydroxyethyl)-1, 3-dimethyl-1H-purine-2, 6-Dione) (ETO) is a bronchodilator and is normally applied in combination with theophylline. Etophylline also acts as a proconvulsant (Girish et al., 1996). Although the pharmacological actions of the etophylline are generally considered like those of theophylline, Merkus and Zuidema pointed out different aspects of the two drugs (Merkus and Zuidema, 1980). In view of potential pharmaceutical importance of etophylline and lack of literature on the oxidation of this drug by any oxidant and the complexity of the reaction, a detailed study of the reaction becomes important.

In autocatalytic pathways in which Mn^{II} ions have been determined responsible for the effect, a mechanism with

*Corresponding author. E-mail: schimatadar@gmail.com.

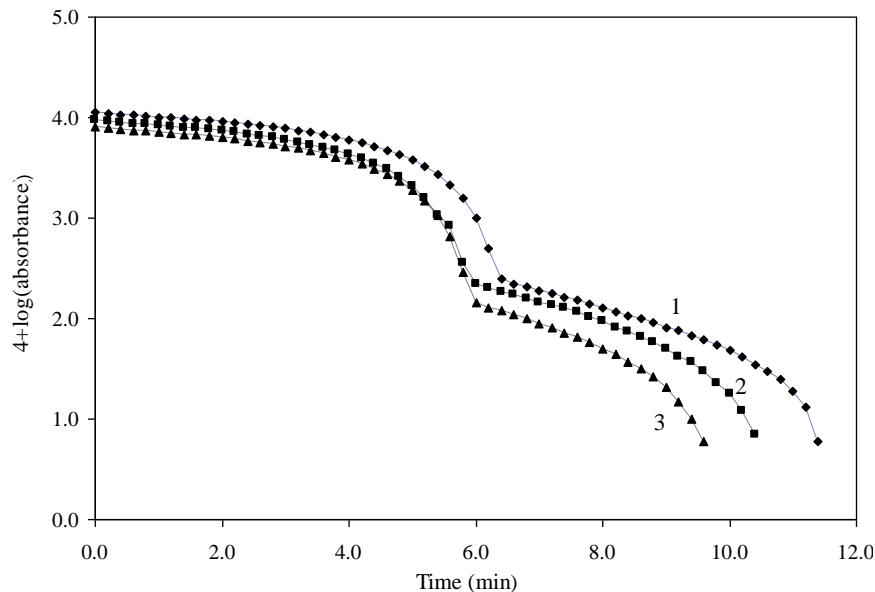


Figure 1. Plot of $\log [\text{MnO}_4^-]$ versus time $[\text{ETO}] = 2.0 \times 10^{-3}$; $[\text{H}_2\text{SO}_4] = 0.50$; $[\text{MnO}_4^-] \times 10^4 \text{ mol dm}^{-3} = (1) 3.0, (2) 4.0, (3) 5.0$.

no free radicals has been suggested (Arrizbalaga et al., 1996; Arrizbalaga et al., 1997). Though, permanganate is used as an oxidant in the oxidation of several organic and inorganic substrates (Wiberg, 1965; Moghadasi et al., 2001; Surendra Rao, 1979; Ernst and Cyfert, 1987; Purohit et al., 1981; Solanki et al., 1982; Ameta et al., 1980; Tiwari et al., 1979), literature survey shows that the kinetic study of etophylline oxidation by Mn^{VII} is lacking. Hence we have investigated the oxidation of etophylline by acid permanganate. In this paper, distinct evidence of an autocatalytic influence of Mn^{II} for permanganate oxidation of etophylline in strong acid medium has been presented and free radical mechanism has been proposed.

MATERIALS AND METHODS

Throughout the work the double distilled water and reagent grade chemicals have been used. A stock solution of etophylline (AR, Arti industries) was prepared by dissolving in water. Permanganate stock solution was obtained by dissolving potassium permanganate (Glaxo, Analar) in water and standardized by titrating against oxalic acid (Vogel, 1967). The manganese (II) solution was made by dissolving manganese sulphate (AR, Analar) in water. Na_2SO_4 (AR, Rankem) and H_2SO_4 (AR, Rankem) were used to provide required ionic strength and acidity respectively.

All kinetic measurements were performed under the pseudo-first order condition with etophylline concentration greater than

permanganate concentration at constant ionic strength of 1.60 mol dm^{-3} .

The reaction was initiated by mixing thermally equilibrated ($25 \pm 0.1^\circ\text{C}$) solution of etophylline and permanganate which contained the required quantities of H_2SO_4 and Na_2SO_4 . Since the initial reaction was too fast to be monitored by usual methods, the title reaction was followed by measuring the absorbance of permanganate in the reaction mixture at 525 nm in a 1 cm cell placed in the thermostatted compartment of Varian Cary 50 Bio UV-vis spectrophotometer connected to a rapid kinetic accessory (HI-TECH SFA-12, U.K) at its absorption maximum of 525 nm as a function of time. Application of Beer's law was verified between 1.0×10^{-4} to $1.0 \times 10^{-3} \text{ mol dm}^{-3}$ of permanganate at 525 nm under the reaction conditions and the molar extinction coefficient was found to be $\epsilon = 2200 \pm 50 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ (Literature value $\epsilon = 2400 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ (Timmanagoudar et al., 1996)). The kinetic runs were followed more than 95% completion of the reaction. The pseudo first order rate constants, k_{obs} were calculated from the plots of \log (absorbance) versus time. The plots were linear over 60% completion of the reaction (Figure 1) The k_{obs} values were reproducible within $\pm 5\%$ and are the average of at least three independent kinetic runs (Tables 1 and 2).

RESULTS AND DISCUSSION

Stoichiometry and product analysis

Different sets of concentration of reactants in 0.50 mol dm^{-3} sulphuric acid at constant ionic strength, 1.60 mol

Table 1. Effect of variation of Manganese (VII) and etophylline concentrations on the oxidation of etophylline by acidic permanganate at 25°C and $I = 1.60 \text{ mol dm}^{-3}$.

$[\text{Mn}^{\text{VII}}] \times 10^4 \text{ (mol dm}^{-3}\text{)}$	$[\text{ETO}] \times 10^2 \text{ (mol dm}^{-3}\text{)}$	$[\text{H}^+] \text{ (mol dm}^{-3}\text{)}$	$k_{\text{obs}} \times 10^2 \text{ (s}^{-1}\text{)}$	$k_{\text{sec order}} = k_{\text{obs}}/[\text{ETO}] \text{ (dm}^3 \text{ mol}^{-1} \text{ s}^{-1}\text{)}$
0.5	2.0	0.50	0.43	-
1.0	2.0	0.50	0.46	-
2.0	2.0	0.50	0.45	-
3.0	2.0	0.50	0.42	-
4.0	2.0	0.50	0.41	-
5.0	2.0	0.50	0.40	-
2.0	0.5	0.50	0.11	0.21
2.0	1.0	0.50	0.21	0.21
2.0	2.0	0.50	0.42	0.21
2.0	3.0	0.50	0.63	0.21
2.0	4.0	0.50	0.84	0.21
2.0	5.0	0.50	1.05	0.21

Table 2. Effect of variation of H^+ ions concentrations on the oxidation of etophylline by acidic permanganate at 25°C and $I = 1.60 \text{ mol dm}^{-3}$.

$[\text{H}_2\text{SO}_4] \text{ (mol dm}^{-3}\text{)}$	$[\text{HSO}_4^-] \text{ (mol dm}^{-3}\text{)}$	$[\text{SO}_4^{2-}] \text{ (mol dm}^{-3}\text{)}$	$[\text{H}^+] \text{ (mol dm}^{-3}\text{)}$	$k_{\text{obs}} \times 10^2 \text{ (s}^{-1}\text{)}$
0.1	0.175	0.857	0.0247	0.04
0.3	0.490	0.542	0.109	0.18
0.5	0.721	0.311	0.278	0.42
0.7	0.847	0.185	0.552	2.73
0.9	0.905	0.127	0.894	1.03
1.0	0.928	0.104	1.071	1.15

dm^{-3} , were kept for over 5 h at 25°C in a closed container. When $[\text{permanganate}] > [\text{etophylline}]$, the remaining permanganate concentration was assayed by measuring the absorbance at 526 nm. The reaction products were identified as Mn^{II} and 1, 3-dimethyl-2, 6-dioxo-1, 2, 3, 6, tetrahydro-purin-7yl)-acetaldehyde. The results indicate that 5 moles of etophylline consumes two moles of permanganate according to Appendix 1.

The stoichiometric ratio of oxidation of etophylline by permanganate suggests that the main product as 1, 3-dimethyl-2, 6-dioxo-1, 2, 3, 6, tetrahydro-purin-7yl)-acetaldehyde (A). The product was extracted with ether and recrystallized from aqueous alcohol. The obtained product was further purified by column chromatography (Harihar et al., 2000) using the mixture of benzene (65%) and ethyl acetate (35%) as mobile phase and fractions are subjected to spectral investigations. From the spot test (Hosahalli et al., 2010), IR (Figure 2), GCMS (Figure

3) spectra, the main oxidation product was identified as A. The IR spectroscopy showed an aldehydic, C=O stretching at 1707 cm^{-1} indicating the presence of aldehydic C=O functional group. C=O stretching at 1657 and 1604 cm^{-1} indicating the presence of two amide group in the product. The presence of A was also confirmed by GC-MS analysis (Figure 3), obtained on a Shimadzu 17A gas chromatograph with a Shimadzu XP-5000A mass spectrometer using EI ionization technique. The mass spectrum showed the molecular ion peak at 224 amu consistent with the molecular mass of 224 amu. All other peaks are observed in the GC-MS can be interpreted in accordance with the structure of A.

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

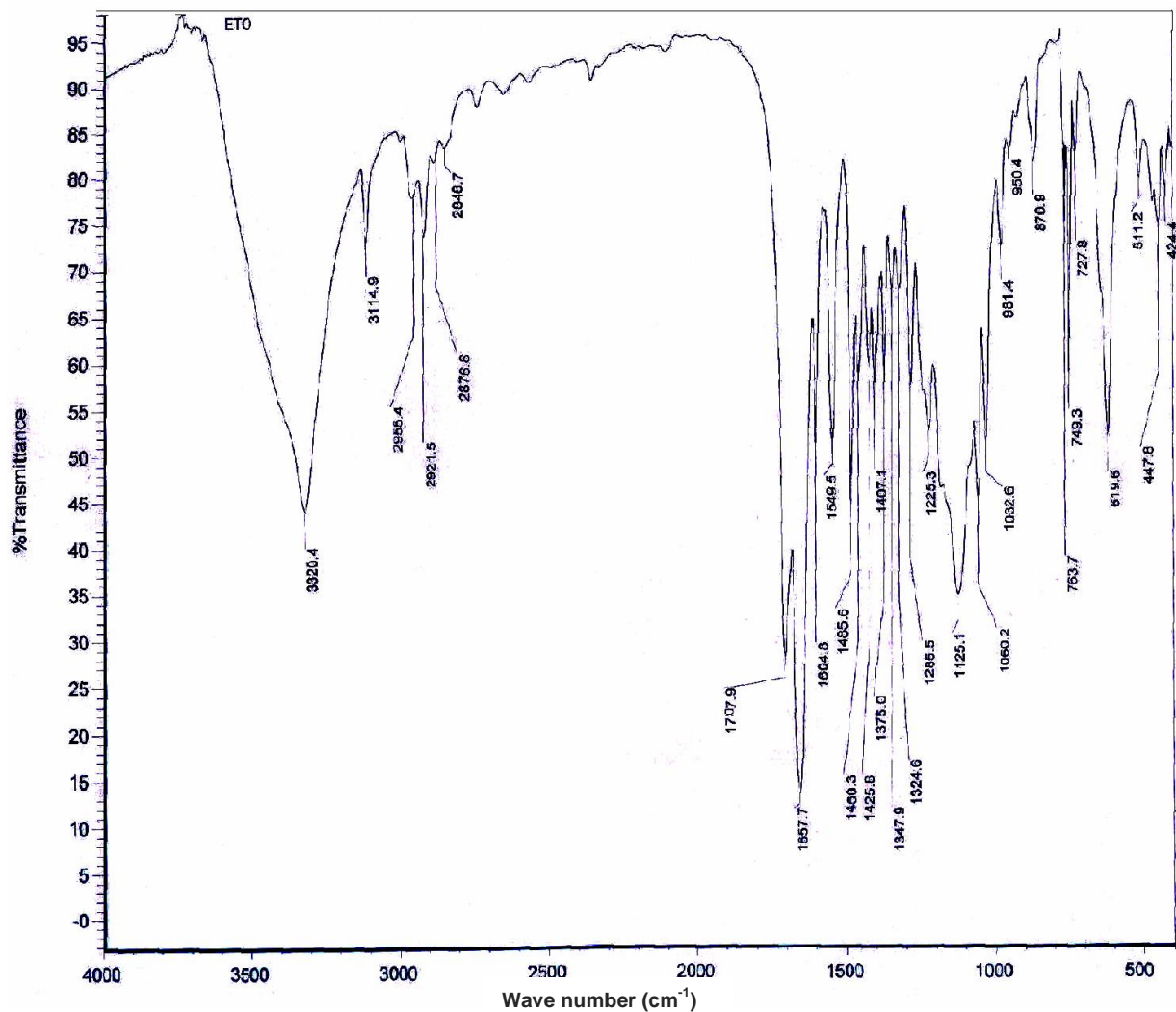


Figure 2. FT-IR spectra of the product 1, 3-dimethyl-2, 6-dioxo-1, 2, 3, 6, tetrahydro-purin-7yl)-acetaldehyde of oxidation of etophylline by permanganate.

(MnO_4^-), concentration was varied in the range 5.0×10^{-5} - 5.0×10^{-4} mol dm^{-3} . The observed pseudo-first order rate constants k_{obs} were almost constant (Table 1) indicates first order with respect to permanganate concentrations. The effect of variation of etophylline on the rate of reaction was studied in the concentration range, 5.0×10^{-3} - 5.0×10^{-2} mol dm^{-3} , at constant concentration of permanganate, acid and at constant ionic strength. It was observed that, as the etophylline concentration increases, k_{obs} also increase (Table 1). The value of the slope of the plot of $\log k_{\text{obs}}$ versus $\log [\text{etophylline}]$ was found to be unity, which indicates first order with respect to etophylline concentrations. This was

also confirmed by the plot of k_{obs} versus ETO concentration (Figure 4), which is a straight line passing through the origin. The effect of variation of sulphuric acid on the rate of reaction was studied in the concentration range, 0.1 to 1.0 mol dm^{-3} at fixed concentration of oxidant, $[\text{MnO}_4^-] = 3.0 \times 10^{-4}$ mol dm^{-3} , reductant, $[\text{etophylline}] = 3.0 \times 10^{-2}$ mol dm^{-3} and with other conditions remaining constant. The *in situ* H^+ ion concentration in the sulphuric acid – sulphate media was calculated using the known ionization constant of acid sulphate as in an earlier study (Patil et al., 2008; Ya et al., 1965). The k_{obs} was found to be increased with increase in H^+ concentration (Table 2). The order with

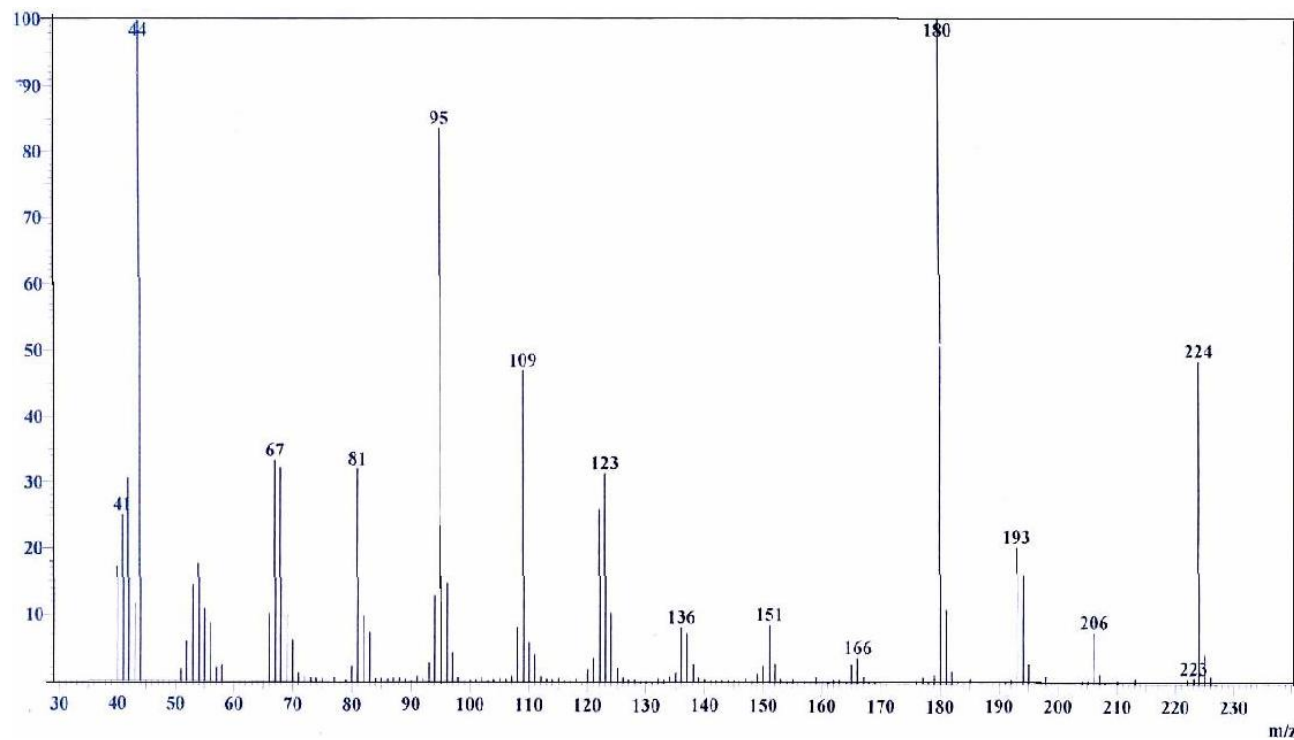


Figure 3. GC-MS spectra of the product 1, 3-dimethyl-2, 6-dioxo-1, 2, 3, 6, tetrahydro-purin-7yl)-acetaldehyde, showed molecular ion peak at m/z 224 amu.

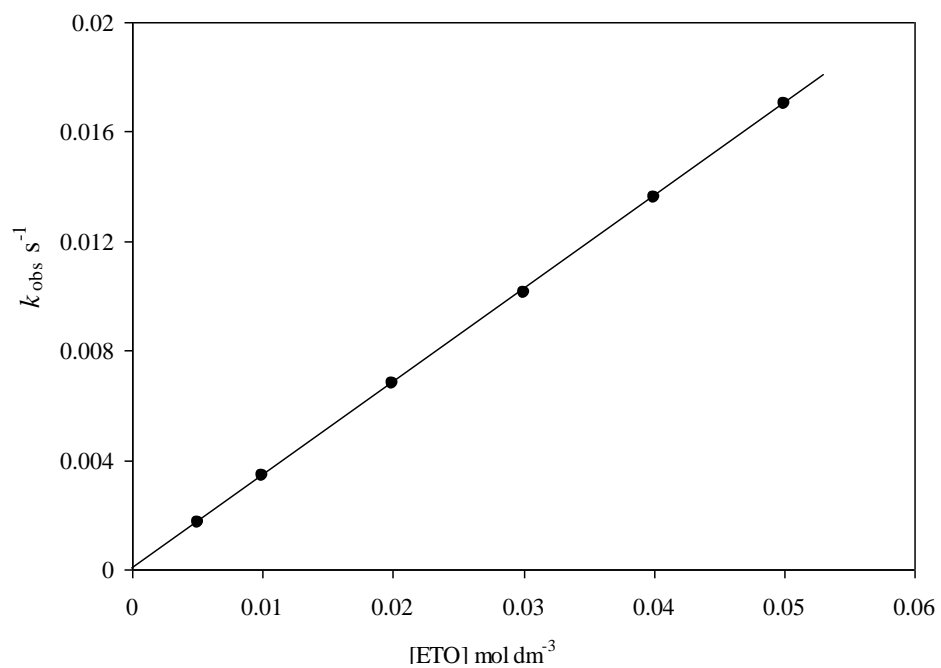
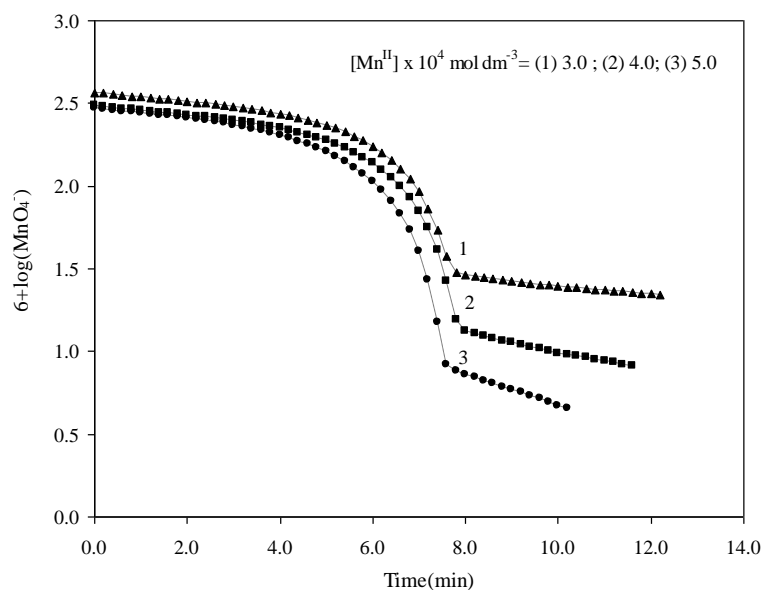


Figure 4. Plot of k_{obs} versus $[ETO]$ (conditions as in Table 1).

Table 3. Effect of added of Manganese(II) concentration on the oxidation of etophylline by aqueous acidic permanganate at 25°C.

$[\text{Mn}^{\text{II}}] \times 10^4 \text{ (mol dm}^{-3}\text{)}$	$k_{\text{autocat}} \times 10^2 \text{ (s}^{-1}\text{)}$
0.5	0.66
1.0	0.95
2.0	1.18
3.0	1.37
4.0	1.53
5.0	1.61

**Figure 5.** Effect of added product, Manganese (II) on the oxidation of etophylline by permanganate.

respect to $[\text{H}^+]$ was found to be less than unity (0.87).

The initially added products, manganese (II) were studied in the range 0.5×10^{-5} to 5.0×10^{-4} mol dm⁻³ respectively, while keeping the reactant concentrations and all other conditions constant. As the initial concentration of Mn^{II} ions increased, a notable increase in the rate (Table 3) of reaction was seen (Figure 5). In all the experiments performed, curves with the sigmoid profile (Figures 1 and 5) indicate the autocatalytic nature of the product manganese (II). The added product 1, 3-dimethyl-2, 6-dioxo-1, 2, 3, 6, tetrahydro-purin-7yl)-acetaldehyde does not change the rate appreciably.

At constant concentrations of reactants and other conditions constant, the ionic strength was varied by varying the concentration of sodium sulphate between

1.60 and 3.20 mol dm⁻³. Increasing ionic strength had negligible effect on the rate of reaction. At constant acidity and other constant conditions, as the acetic acid content increases from 0 to 50% (v/v) in the reaction mixture, change in dielectric constant had negligible effect on the rate of reaction.

The intervention of the free radicals in the reaction was examined as follows. The reaction mixture, to which a known quantity of acrylonitrile monomer was initially added, was kept for 2 h in an inert atmosphere. On diluting the reaction mixture with methanol, a white precipitate was formed, indicating the intervention of free radicals in the reaction. The blank experiments of either etophylline or permanganate alone with acrylonitrile did not induce any polymerization under the same condition

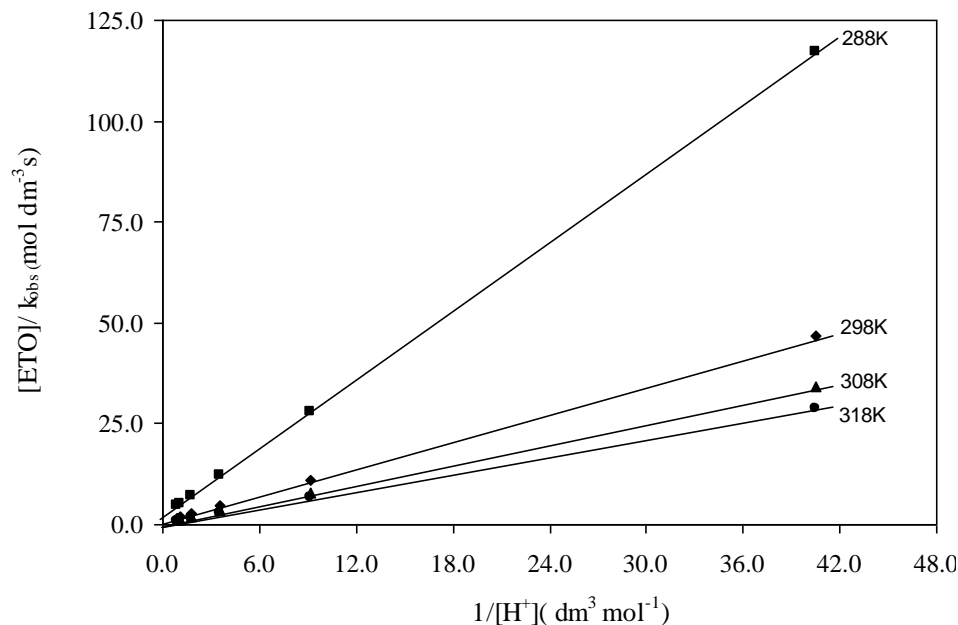


Figure 6. Verification of rate law (7) in the form of equation (8) at different temperatures. (Conditions as in Tables 1 and 2).

Table 4. Effect of temperature on the oxidation of etophylline by permanganate in sulphuric acid, $I = 1.60 \text{ mol dm}^{-3}$.

(A) Activation parameters with respect to slow step of Appendix 2		
Temp (K)	$k_1 (\text{dm}^3 \text{mol}^{-1} \text{s}^{-1})$	Activation parameters
288	0.52	$E_a = 46 \pm 3 \text{ kJ/mol}$
298	1.49	$\Delta H^\ddagger = 43 \pm 3 \text{ kJ/mol}$
308	2.38	$\Delta S^\ddagger = -94 \pm 4 \text{ J/K/mol}$
318	3.31	$\Delta G^\ddagger = 71 \pm 2 \text{ kJ/mol}$
$\log A = 8 \pm 0.4$		

(B) Thermodynamic quantities with respect to first step of Appendix 2		
Temp (K)	$K_1 (\text{dm}^3 \text{mol}^{-1})$	Thermodynamic quantities
288	0.68	$\Delta H = -11.6 \pm 0.5 \text{ kJ/mol}$
298	0.59	$\Delta S = -43.3 \pm 3 \text{ J/K/mol}$
308	0.50	$\Delta G = -2.20 \pm 0.03 \text{ kJ/mol}$
318	0.42	

as those induced for reaction mixture. Initially added acrylonitrile decreased the rate of reaction indicating free radical intervention (Farokhi and Nandibewoor, 2004).

The rate of the reaction was measured at four different temperatures 15, 25, 35 and 45°C at varying sulphuric acid concentration. The rate of the reaction increased with the increase in temperature. The rate constant, k_1 of

the slow step of Appendix 2 were obtained from the intercept of the plots $[\text{ETO}]/k_{\text{obs}}$ versus $1/[\text{H}^+]$ (Figure 6) at four different temperatures (Table 4). The energy of activation was obtained by the plot of $\log k_1$ versus $1/T$, from which the activation parameters were calculated (Table 4A). The formation constant of HMnO_4 (K_1) was evaluated from the intercept and slope of the plot $[\text{ETO}]/$

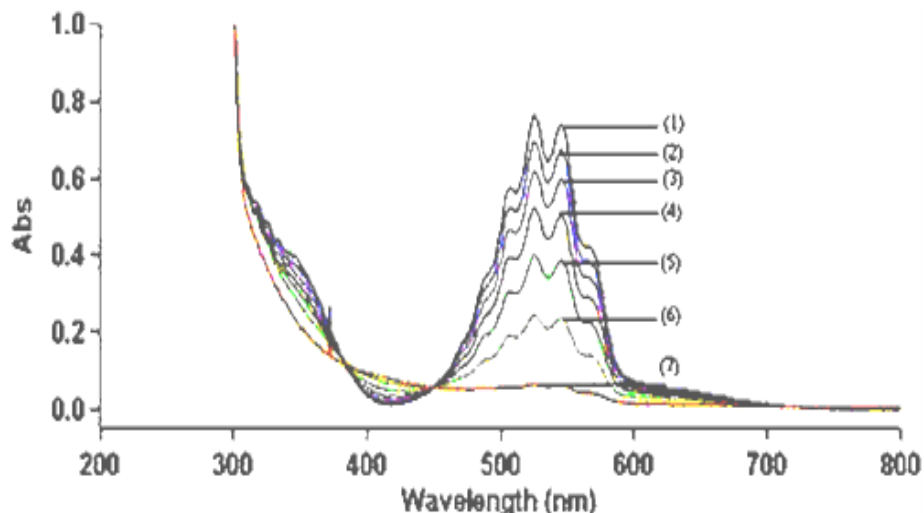


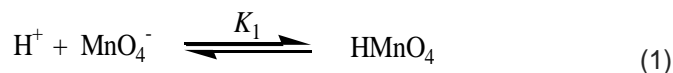
Figure 7. Spectroscopic changes occurring in the oxidation of etophylline by acidic permanganate at 25°C. $[\text{MnO}_4^-] = 3.0 \times 10^{-4}$; $[\text{ETO}] = 2.0 \times 10^{-2}$; $[\text{H}^+] = 0.5$ and $l = 1.60$ mol dm⁻³ with scanning interval of 1 min.

k_{obs} versus $1/[\text{H}^+]$ (Figure 6) at four different temperatures (Table 4B). The van't Hoff plot ($\log K_1$ versus $1/T$) was drawn and the thermodynamic quantities were calculated (Table 4B).

The expected oxidizing species of permanganate in acid media are MnO_4^- , H_2MnO_4^+ , HMnO_3 , Mn_2O_7 . Among them MnO_4^- ion is powerful oxidizing agent in aqueous alkaline as well as in acidic medium. The stable reduction product of MnO_4^- in acid medium is Mn^{II} . Figure 7 illustrates the spectroscopic changes occurring in the oxidation of etophylline by acidic permanganate at 25°C with scanning interval of 1 min. The literature survey reveals that (Joaquin and Perenz, 2009) Mn^{IV} ion absorbs in the region 400 - 650 nm. Figure 7 shows no features in this wavelength area indicating that MnO_2 is not a reaction product. The reaction between etophylline and MnO_4^- has a stoichiometry 5:2 with first order dependence on $[\text{MnO}_4^-]$ and $[\text{ETO}]$ and fractional order dependence on both $[\text{H}^+]$ and $[\text{Mn}^{\text{II}}]$ in acid medium. Mn^{II} is the reduced product of Mn^{VII} in the reaction may be that etophylline shows strong reducing character in sulphuric acid medium.

The active species of permanganate in aqueous acid medium may be deduced from the dependence of the rate on $[\text{H}^+]$ in the reaction medium. The apparent order of less than unity in $[\text{H}^+]$ may be an indication of permanganate species as permanganic acid. In acid medium, permanganic acid, HMnO_4 is more efficient oxidant species of manganese than permanganate ion

(Chimatadar et al., 1991; Wiberg, 1965). In addition it has been observed that the rate of reaction increased with increase in $[\text{H}^+]$ and was tending to attain a limiting value at high acidities (Bailar et al., 1975). The plot of k_{obs} versus $[\text{H}^+]$ is a curve of increasing slope (convex to the rate axis) (Figure 8) from which it can be inferred (Farokhi and Nandibewoor, 2004) that, a rapid equilibrium between the protonated form is involved. At higher acidities protonation is almost complete, leading to the limiting rate, this indicates that only the protonated form is active. The ionic strength on the rate of reaction also confirms that HMnO_4 as the active species of MnO_4^- . Thus the acid permanganate equilibrium is represented as:



where K_1 is the formation constant of HMnO_4 . The reaction between the permanganate and etophylline in alkaline medium has stoichiometry 5:2 ($\text{ETO}:\text{MnO}_4^-$) with first order dependence on both substrate and oxidant and apparent less than unit order with respect to acid concentration. Based on the experimental results, a mechanism is proposed for which all the observed orders in each constituent such as [oxidant], [reductant] and $[\text{H}^+]$ may be well accommodated. The results suggest the formation of protonated form of permanganate is the active species of MnO_4^- in a prior equilibrium step, which

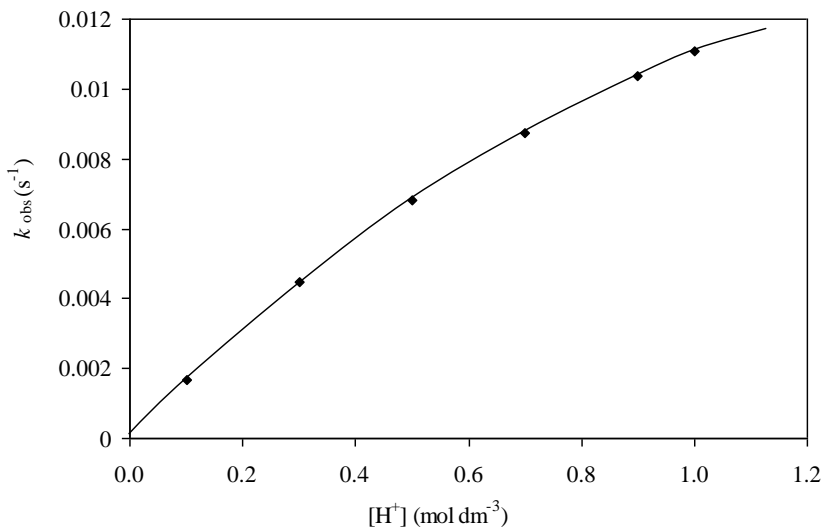


Figure 8. The plot of k_{obs} versus $[\text{H}^+]$, a curve of increasing slope (convex to the rate axis) (Conditions as in Table 2).

reacts with the one mole of etophylline in the rate determining step to give a free radical derived from etophylline and an intermediate Mn^{VI} . In further fast steps the intermediate Mn^{VI} reacts with a free radical derived from etophylline to produce the product, 1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-purin-7yl)-acetaldehyde and an intermediate Mn^{V} . In further fast steps Mn^{V} subsequently reduced to the end product Mn^{II} satisfying stoichiometric observations. The mechanism is proposed as in Appendix 2.

Since none of the intermediate could be detected, Appendix 2 is only one of the possible mechanisms for the reaction in the presence of free radical. Attempts were made to allow spectroscopic detection of intermediate Mn^{V} and Mn^{III} as the reaction proceeded in the oxidation of etophylline by MnO_4^- . Unfortunately, the low concentration of Mn^{III} and Mn^{V} intermediates obtained under our experimental conditions made the detection unsuccessful. However, there are reports in the literature for the existence of Mn^{III} and Mn^{V} (Bailar et al., 1975). Appendix 2 leads to the rate law (8); according to Appendix 2:

$$\begin{aligned} \text{Rate} &= k_1[\text{HMnO}_4] [\text{ETO}] \\ &= k_1 K_1 [\text{MnO}_4^-]_{\text{f}} [\text{ETO}]_{\text{f}} [\text{H}^+]_{\text{f}} \end{aligned} \quad (2)$$

The total concentration of MnO_4^- is given by, (where 't'

and 'f' stands for total and free)

$$\begin{aligned} [\text{MnO}_4]_{\text{t}} &= [\text{MnO}_4^-]_{\text{f}} + [\text{HMnO}_4]_{\text{f}} \\ &= [\text{MnO}_4^-]_{\text{f}} + K_1 [\text{H}^+] [\text{MnO}_4^-]_{\text{f}} \\ &= [\text{MnO}_4^-]_{\text{f}} (1 + K_1 [\text{H}^+]) \end{aligned}$$

Therefore,

$$[\text{MnO}_4^-]_{\text{f}} = \frac{[\text{MnO}_4^-]_{\text{t}}}{1 + K_1 [\text{MnO}_4^-]} \quad (3)$$

Similarly,

$$[\text{H}^+]_{\text{f}} = \frac{[\text{H}^+]_{\text{t}}}{1 + K_1 [\text{MnO}_4^-]} \quad (4)$$

Substituting the Equations (3) and (4) in Equations (2) (and omitting 't' and 'f' subscripts),

$$\text{Rate} = \frac{-d[\text{MnO}_4^-]}{dt} = \frac{k_1 K_1 [\text{MnO}_4^-] [\text{ETO}] [\text{H}^+]}{(1 + K_1 [\text{H}^+]) (1 + K_1 [\text{MnO}_4^-])} \quad (5)$$

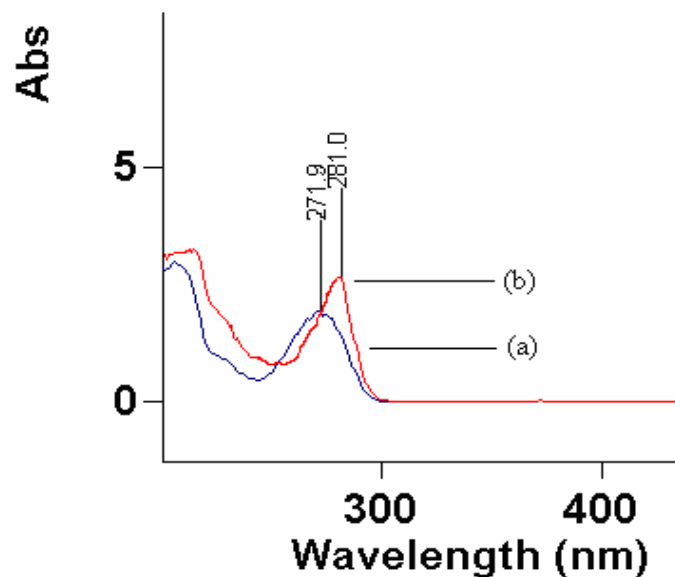


Figure 9. Spectroscopic evidence for the complex formation between etophylline and Manganese (II). (a) UV-vis spectra of etophylline (271 nm); (b) UV-vis spectra of mixture of etophylline and Manganese(II) (281 nm).

$$= \frac{k_1 K_1 [\text{MnO}_4^-][\text{ETO}][\text{H}^+]}{1 + K_1[\text{H}^+] + K_1 [\text{MnO}_4^-] + K_1^2 [\text{H}^+][\text{MnO}_4^-]} \quad (6)$$

The terms, such as $K_1[\text{MnO}_4^-]$ and $K_1^2 [\text{H}^+][\text{MnO}_4^-]$ in the denominator of Equation (6) are neglected in the view of the low concentration of MnO_4^- used in the experiments. Hence the Equation (6) becomes (7)

$$k_{\text{obs}} = \frac{\text{Rate}}{[\text{MnO}_4^-]} = \frac{k_1 K_1 [\text{ETO}][\text{H}^+]}{1 + K_1[\text{H}^+]} \quad (7)$$

The rate law (7) may be verified by rearranging in the form:

$$\frac{[\text{ETO}]}{k_{\text{obs}}} = \frac{1}{k_1 K_1 [\text{H}^+]} + \frac{1}{k_1} \quad (8)$$

where k_{obs} is first order rate constant. According to Equation (8), the plot of $[\text{ETO}]/k_{\text{obs}}$ versus $1/[\text{H}^+]$ is expected to be linear, and is found to be so (Figure 6). The slope and the intercept of such plot lead to the values of K_1 and k_1 at 25°C as $0.59 \text{ dm}^3 \text{ mol}^{-1}$ and 1.49

$\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. The negligible effect of ionic strength and relative permittivity is consistent with reaction between two neutral molecules as in Appendix 2.

The Mn^{II} acts as an auto catalyst in case of oxidation of permanganate is well known (Zahedi et al., 2004). In the present case Mn^{II} was found to auto catalyze the rate of oxidation of etophylline by permanganate. In all the experiments performed, curves with a sigmoid profile (Figures 1 and 5) have been obtained. This characteristic suggests the existence of an autocatalytic mechanism. In order to demonstrate that Mn^{II} species is responsible for the autocatalytic effect, kinetic runs were carried out in the presence of Mn^{II} . As the concentration of Mn^{2+} ions increased, a notable increase in the rate of reaction was observed (Figure 5 and Table 3).

The catalytic effect of Mn^{II} can be interpreted in either of two ways, (a) Mn^{II} may form a complex with the substrate which is then oxidized by HMnO_4 or (b) Mn^{II} first reacts with Mn^{VII} to produce Mn^{III} which accelerates the rate of reaction. The apparent order is less than unity in Mn^{II} ions may be attributed to the complex formation between etophylline and Mn^{II} . The complex (C_1) is then subsequently involved in the interaction with MnO_4^- . These steps in Appendix 3 will form part of Appendix 2. The probable structure of the complex (C_1) is given in Appendix 4.

The evidence for the complex (C_1) formation was obtained from UV-vis spectra etophylline and mixture of etophylline and Mn^{II} , which indicates the bathochromic shift of 10 nm from 271 to 281 nm (Figure 9). Indeed such complex formation is observed in the literature (Kim et al., 1997; Farokhi and Nandibewoor, 2004). MnO_4^- ions are primarily responsible for the oxidation of substrate etophylline. The intermediate complex subsequently undergoes decomposition to give the reaction products.

According to Appendix 3:

$$\begin{aligned} \text{Rate} &= k_2 [\text{C}_1] \\ &= k_2 K_2 [\text{Mn}^{\text{II}}]_{\text{f}} [\text{ETO}]_{\text{f}} \end{aligned}$$

The total concentration of Mn^{II} is given as:

$$\begin{aligned} [\text{Mn}^{\text{II}}]_{\text{t}} &= [\text{Mn}^{\text{II}}]_{\text{f}} + [\text{C}_1] \\ &= [\text{Mn}^{\text{II}}]_{\text{f}} \{ 1 + K_2 [\text{ETO}] \} \end{aligned} \quad (9)$$

$$[\text{Mn}^{\text{II}}]_{\text{f}} = \frac{[\text{Mn}^{\text{II}}]_{\text{t}}}{1 + K_2 [\text{ETO}]} \quad (10)$$

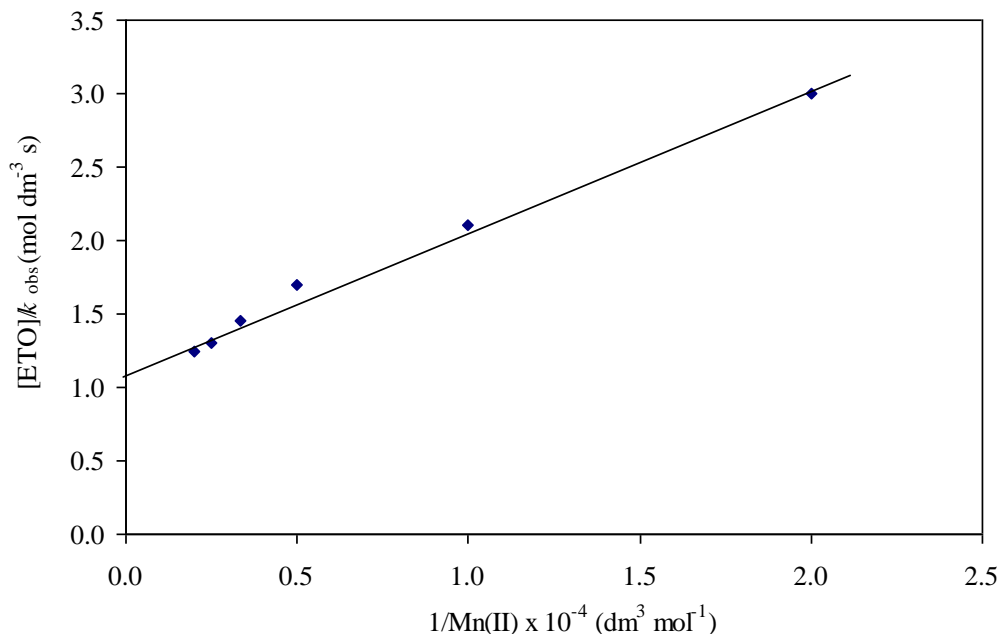


Figure 10. Verification of rate law (16) (Conditions as in Table 3).

Similarly,

$$[\text{ETO}]_f = \frac{[\text{ETO}]_t}{1 + K_2 [\text{Mn}^{\text{II}}]} \quad (11)$$

Substituting Equations (10) and (11) in Equation (9) and omitting the subscripts 't' and 'f'

$$k_{\text{autocat}} = \frac{k_2 K_2 [\text{Mn}^{\text{II}}] [\text{ETO}]}{\{1 + K_2 [\text{ETO}]\} \{1 + K_2 [\text{Mn}^{\text{II}}]\}} \quad (12)$$

Thus, when Mn^{II} was initially present, a composite Scheme involving all the steps of the Appendix 2 and 3 operates and rate law becomes

$$k_{\text{gross}} = k_{\text{obs}} + k_{\text{autocat}}$$

$$k_{\text{autocat}} = k_{\text{gross}} - k_{\text{obs}}$$

$$k_{\text{gross}} = \frac{k_1 K_1 [\text{ETO}][\text{H}^+]}{1 + K_1 [\text{H}^+]} + \frac{k_2 K_2 [\text{Mn}^{\text{II}}] [\text{ETO}]}{\{1 + K_2 [\text{ETO}]\} \{1 + K_2 [\text{Mn}^{\text{II}}]\}} \quad (13)$$

$$k_{\text{autocat}} = \frac{k_2 K_2 [\text{Mn}^{\text{II}}] [\text{ETO}]}{\{1 + K_2 [\text{ETO}]\} \{1 + K_2 [\text{Mn}^{\text{II}}]\}} \quad (14)$$

$$k_{\text{autocat}} = \frac{k_2 K_2 [\text{Mn}^{\text{II}}] [\text{ETO}]}{1 + K_2 [\text{ETO}] + K_2 [\text{Mn}^{\text{II}}] + K_2^2 [\text{ETO}] [\text{Mn}^{\text{II}}]} \quad (15)$$

The term $K_2^2 [\text{ETO}] [\text{Mn}^{\text{II}}]$ can be neglected. The rate law (15) may be verified by rearranging in the form:

$$\frac{[\text{ETO}]}{k_{\text{autocat}}} = \frac{1}{k_2 [\text{Mn}^{\text{II}}]} + \frac{1}{k_2 K_2 [\text{Mn}^{\text{II}}]} + \frac{1}{k_2} \quad (16)$$

where k_{autocat} is first order rate constant. According to Equation (16), the plot of $[\text{ETO}]/k_{\text{autocat}}$ versus $1/[\text{Mn}^{\text{II}}]$ (Figure 10) is expected to be linear, and is found to be so (Figure 10). The slope and the intercept of such plot lead to the values of K_1 and k_1 at 25°C as $0.65 \text{ dm}^3 \text{ mol}^{-1}$ and $8.11 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. The value of K_2 is in agreement with the literature (Farokhi and Nandibewoor, 2004). Indeed it is to be noted that the plot shows an intercept which is in agreement with complex formation as in Appendix 3.

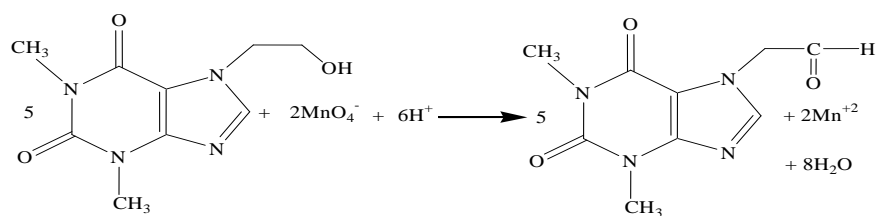
Conclusion

In acid medium, the title reaction exhibits autocatalytic nature by one of the products, Mn^{II} . The sigmoid profile observed for permanganate absorption variation versus time at 525 nm was completely transformed to a line under the condition $[Mn^{II}]_0 = [KMnO_4]$. Thus we report the first conclusive evidence of autocatalytic oxidation process of etophylline in acid medium in which Mn^{II} species are responsible for such effect. Mn^{II} is the reduced product of Mn^{VII} in the reaction may be that, etophylline shows a strong reducing character in H_2SO_4 solution. The interventions of free radicals were observed, and the mechanisms satisfying the experimental observations for the autocatalysed pathways were presented.

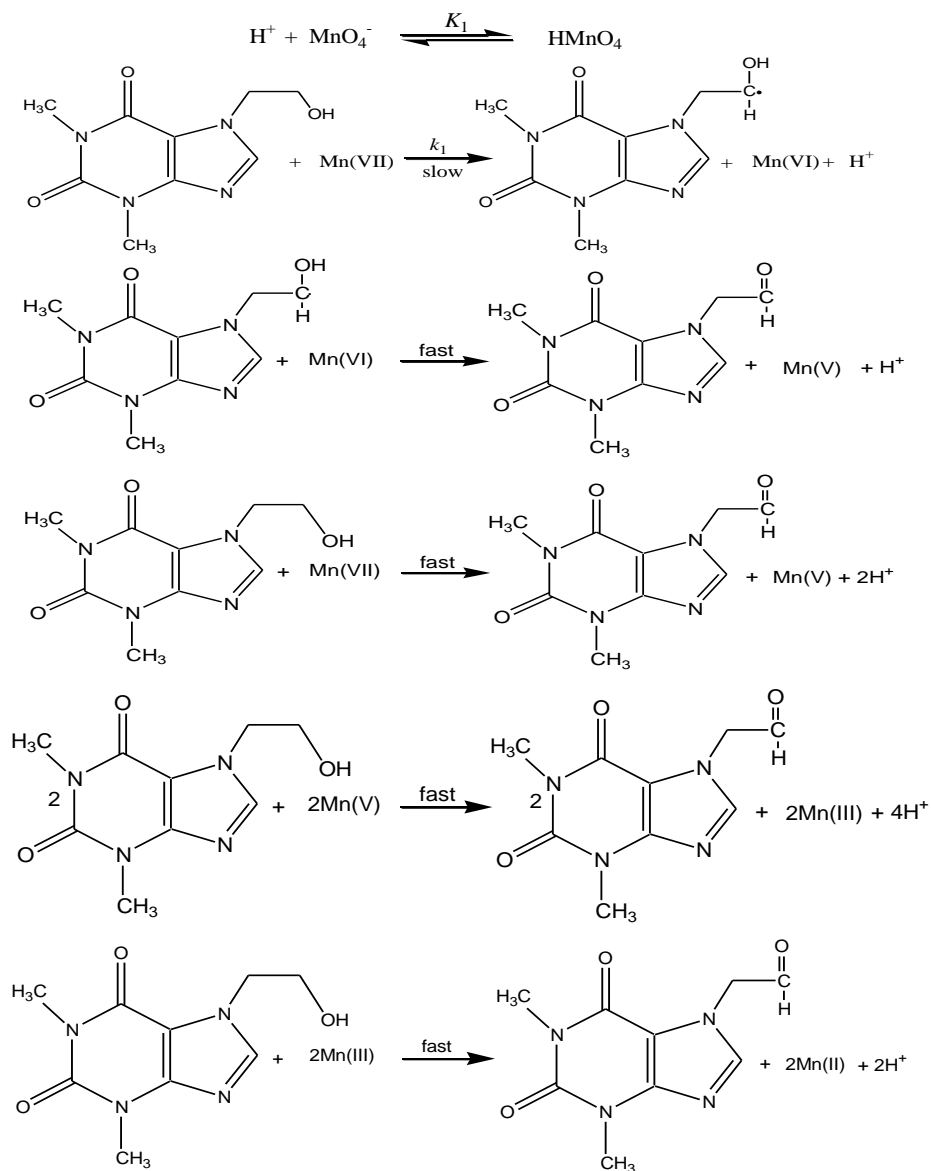
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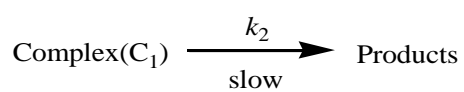
APPENDIX



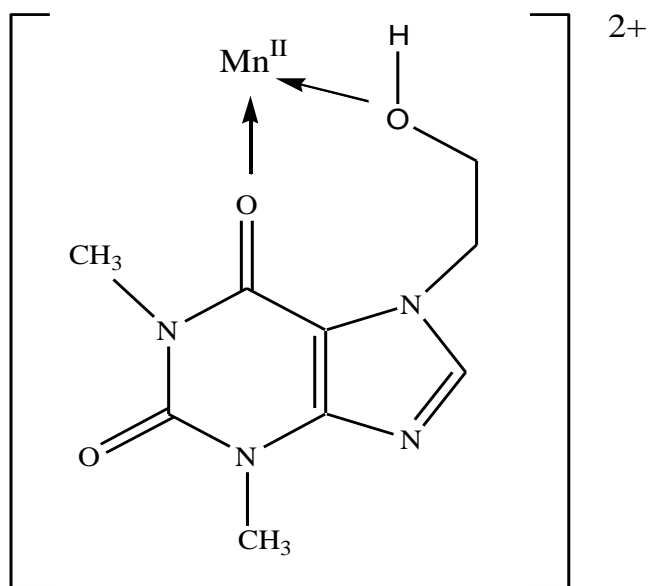
Appendix 1.



Appendix 2.



Appendix 3.



Appendix 4.