

Oxidation of Hydroxyzine with Potassium Permanganate: A Kinetic Study

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Abstract:- Hydroxyzine a pharmaceutical used as antihistamine is oxidized with potassium permanganate to study its kinetics at various temperatures. The rate of reaction was observed is first order with respect to substrate and oxidant whereas it is independent on acid medium. There is no effect of salt on the rate of reaction and no polymerization initiated during the reaction. The final product obtained is identified as hydroxyzine N-oxide. The suitable mechanism is proposed and rate law is derived.

Keywords:- Oxidation, Mechanism, Hydroxyzine, Kinetics, Acid.

I. INTRODUCTION

Antihistamines are the drugs used to treat allergic conditions such as itches, hay fever, etc. These chemicals are used to treat excess of histamines produced in the body. Hydroxyzine is an antihistamine working as a blocking agent for histamine produced excessively in the body. Present study deals with the kinetic study of oxidation of hydroxyzine and its mechanistic aspects. The oxidizing agent used is potassium permanganate. It is a strong oxidizing agent used for oxidation of various organic compounds in acid medium. The potassium permanganate is used extensively for oxidation reaction. It does not produce toxic substances after completion of the reaction. Potassium permanganate is used by many workers for oxidation of various organic compounds e.g. ciprofloxacin [1], L-tryptophan [2], naphthalene [3], etc. but no one has studied kinetic study of oxidation of hydroxyzine with potassium permanganate.

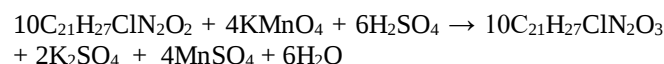
II. MATERIALS & METHODS

All the chemicals used for the study were of analytical grade and used without any purification. Doubly distilled water is used throughout the course of reactions for preparation of solutions. For kinetic study the reaction is run with excess potassium permanganate solution compared to hydroxyzine in the presence of sulphuric acid solution. The reaction is monitored spectrophotometrically by estimating unreacted potassium permanganate with regular intervals at 540 nm.

A. Stoichiometry

For stoichiometric studies solutions of different concentrations of hydroxyzine and same concentration of potassium permanganate and sulphuric acid were reacted and kept the reaction mixture for about five hours. After completion of reaction absorbance of the solutions were

recorded. The graph of absorbance versus the mole ratio is plotted to know the stoichiometry of the reaction. The obtained stoichiometric equation is as follows;



The reaction product is identified by reacting desired quantity of the hydroxyzine, potassium permanganate and sulphuric acid and kept the reaction mixture for two days for completion of the reaction. One of the product is extracted with ether, the organic layer obtained was separated and treated with sodium bicarbonate and washed with distilled water. The ether layer was evaporated and dried to get product. The product obtained is Hydroxyzine N-oxide. It is confirmed by spot tests [4].

III. RESULTS & DISCUSSION

A. Effect of concentration of substrate

Pseudo-first order kinetics is followed for observing the effect of different parameters on the rate of reaction. The pseudo-first order rate constants were determined with various initial concentrations of the hydroxyzine whereas keeping other conditions constant i.e. concentration of potassium permanganate solution, concentration of sulphuric acid solution, temperature, etc. The k_{obs} calculated from the graph of $\log_{\text{obs}}$ versus time. The rate constant is found to be increasing with the increase in the concentration of hydroxyzine. This can be treated as first order kinetics [5].

B. Effect of concentration of oxidant

The pseudo-first order rate constants were determined with various initial concentrations of the potassium permanganate solution whereas keeping other conditions constant i.e. concentration of hydroxyzine solution, concentration of sulphuric acid solution, temperature, etc. The result is obtained from the graph of k_{obs} versus time. The k_{obs} rate constant is found to be increasing with the increase in the concentration of potassium permanganate indicating first order dependence of the rate of the reaction.

C. Effect of H^+ concentration

The pseudo-first order rate constants were determined with various initial concentrations of the sulphuric acid solution whereas keeping other conditions constant i.e. concentration of hydroxyzine solution, concentration of potassium permanganate solution, temperature, etc. The result is obtained from the graph of $\log_{\text{obs}}$ versus time. The k_{obs} rate constant does have much impact indicating rate of the reaction is not depending on the concentration of H^+ .

D. Effect of temperature

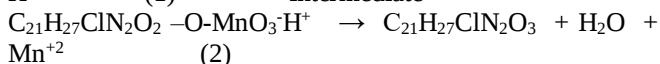
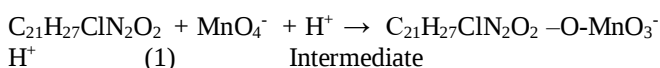
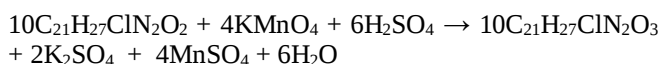
The oxidation of hydroxyzine was carried out at different temperatures from 303K to 323K whereas the concentration of the hydroxyzine, potassium permanganate and sulphuric acid were kept constant. The result shows the rate of the reaction increases with rise in temperature indicating first order dependence on temperature. From the linear Arrhenius plots of $\log k_{obs}$ versus $1/T$ activation parameters were calculated. The Arrhenius activation energy values calculated as 23.6kJ/mole. The other thermodynamic parameters are $\Delta H = -13\text{kJ/mole}$ & $\Delta S = -32\text{ J/Kmole}$ and $-\Delta G = -1.2\text{ kJ/mole}$.

E. Effect of salt

To study the effect of salts on the rate of reaction NaCl, KCl, KBr, MgCl_2 these salts were added in the reaction mixture keeping all other conditions constant at 298K temperature. There is no effect of addition of salt observed on the rate of reaction indicating no interaction of charged species during the reaction.

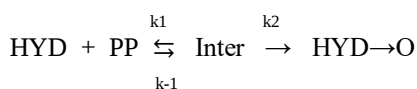
F. Free radical test

Acrylonitrile is used to test the presence of polymerization. It is added to the solution of substrate, oxidant and acid in proper proportion. There is no initiation of polymerization indicating there are no free radicals formed during the reaction [6].

G. Proposed Mechanism of the reaction

The rate equation can be proposed on the basis of the results obtained as

$$-\frac{d[\text{MnO}_4^-]}{dt} = -\frac{d[\text{Mn}^{+2}]}{dt} = k_2 [\text{Inter}]$$



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We can apply steady state approximation to Inter

$$\frac{d[\text{Inter}]}{dt} = 0 = k_1[\text{HYD}] [\text{PP}] - k_{-1}[\text{Inter}] - k_2 [\text{Inter}]$$

$$[\text{Inter}] = \frac{k_1}{k_{-1} + k_2} [\text{HYD}] [\text{PP}]$$

The overall rate is the rate of formation of $\text{HYD} \rightarrow \text{O}$

$$\frac{d[\text{HYD} \rightarrow \text{O}]}{dt} = k_2 [\text{Inter}] = \frac{k_1 k_2}{k_{-1} + k_2} [\text{HYD}] [\text{PP}]$$

Since k_{-1} is much smaller than k_2 , $k_{-1} \ll k_2$ neglecting k_{-1} in the above equation, rate equation is reduced to

$$\text{Rate} = k_1[\text{HYD}] [\text{PP}]$$

IV. CONCLUSION

The kinetics of oxidation of hydroxyzine with potassium dichromate in acid medium was studied. The reaction undergoes to give an intermediate which on decomposition in the rate determining step gives the oxidized product. The proposed mechanism and rate law is suggested for the reaction. The reaction is found to be first order with respect to substrate i.e. hydroxyzine and potassium permanganate whereas it is independent on the concentration of acid. There is no effect on the rate of reaction of addition of salt showing no interaction of charged species during the reaction [7].

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