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Research Article

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A Kinetic Study of Oxidation of Cetirizine Hydrochloride by Potassium Dichromate in Acid Medium

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ABSTRACT

Kinetics of oxidation of cetirizine hydrochloride using potassium dichromate as oxidizing agent in acid medium was studied spectrophotometrically at 520 nm. The result interprets that rate of oxidation is first order with respect to potassium dichromate and cetirizine hydrochloride where as it does not depend on the concentration of acid. The stoichiometry of the reaction was found that one mole of oxidant is consumed for oxidation of three moles of cetirizine hydrochloride and the product found is cetirizine N-oxide. From the results of kinetic studies, reaction stoichiometry and product analysis with suitable mechanism of the reaction was proposed. Based on results of the reaction at different temperatures, the activation parameters with respect to the slow step of the proposed mechanism were calculated.

Keywords: Kinetics; Cetirizine hydrochloride; Oxidation; Potassium dichromate

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INTRODUCTION

The Cetirizine Hydrochloride is a second generation antihistamine, orally active and selective H_1 receptor antagonist used for the treatment of allergy symptoms [1]. It is used for the prevention and treatment of hay fever, itchy eyes, sneezing and running nose, watery eyes and other allergic symptoms. Oxidation of cetirizine hydrochloride with potassium dichromate is studied kinetically. Chromium, permanganate ions in various forms are used as powerful oxidizing agent in organic and inorganic oxidation in polar media [2]. Chromium has frequently and extensively been employed as an oxidizing agent both for preparative as well as analytical methods in chemistry [3,4]. Chromic acid, aqueous dichromate, chromyl chloride, chromyl acetate and other substituted chromates have been employed in oxidation of organic as well as inorganic compounds in aqueous acid and alkaline media [5-7]. It is the reason for which the analytical chemists in general and kineticists in particular are attracted to know more about such an interesting chemistry of this reagent. Oxidation of cetirizine hydrochloride has been studied by different researchers with other oxidizing agents. J Panda et al. studied oxidation of cetirizine hydrochloride by Mn (VII) [8], Rangaraju P.R. studied using Bromamine-T in HCl medium.

MATERIALS AND METHODS

Potassium dichromate and cetirizine hydrochloride is of analytical grade of purity supplied by local company. The stock solution of potassium dichromate was obtained by dissolving a known weight of it in double distilled water. The standard solution of cetirizine hydrochloride was freshly prepared with double distilled water. The oxidation of cetirizine hydrochloride by potassium dichromate was followed under pseudo-first order conditions where concentration of cetirizine hydrochloride was excess over concentration of dichromate at 30^{o}C [9]. The reaction was initiated by mixing the required quantities of solutions of substrate and reagents with sulphuric acid. The unreacted dichromate was analyzed spectrophotometrically.

Stoichiometry and Product Analysis

Different reaction mixtures containing different concentrations of cetirizine hydrochloride with excess concentration of potassium dichromate in sulphuric acid were kept for 48 hours for completion of reaction. The unreacted potassium dichromate was determined spectrophotometrically at 520 nm. The stoichiometry of the reaction was found that one mole of oxidant is consumed for oxidation of three moles of cetirizine hydrochloride. Hence following equation is confirmed.

$$K_2Cr_2O_7 + 4H_2SO_{4(aq)} + 3C_{21}H_{25}ClN_2O_3 \rightarrow 3C_{21}H_{25}ClN_2O_3 \rightarrow O + K_2SO_4 + (Cr_2SO_4)_3 + 4H_2O$$

The reaction product was confirmed by using reaction mixture containing 0.1 mol dm^{-3}, 0.2 mol dm^{-3} potassium dichromate and 0.1 mol dm^{-3} sulphuric acid. The reaction mixture was allowed to stand for 48 hours for completion of the reaction. The reaction mixture was extracted with ether. The ether layer was neutralized using sodium bicarbonate and washed with distilled water. The ether layer was evaporated and dried to get product. The product was identified as cetirizine N-oxide ($C_{21}H_{25}ClN_2O_3 \rightarrow O$). It is confirmed by spot tests [10].

RESULTS AND DISCUSSION

To study the effect of concentration change of cetirizine hydrochloride, potassium dichromate and sulphuric acid on oxidation at room temperature using UV-Visible spectrophotometer different concentrations of these substances were used and results were analyzed to calculate kinetic parameters.

Effect of Cetirizine Hydrochloride Concentration

In this study the concentration of cetirizine hydrochloride was varied from 1×10^{-2} to 5×10^{-2} mol dm^{-3} keeping all other conditions constant. Figure 1 represents plot of concentration of cetirizine hydrochloride verses $k_{obs.}$ The rate constant was found to be increasing with increase in concentration of cetirizine hydrochloride with other conditions remaining constant indicating first order rate of the reaction [11] (Table 1).

Table 1: [CTZ] mol $dm^{-3}$and k

[CTZ] mol dm^{-3}	0.01	0.02	0.03	0.04	0.05
k_{obs}	0.04689	0.0497	0.05301	0.05953	0.06531

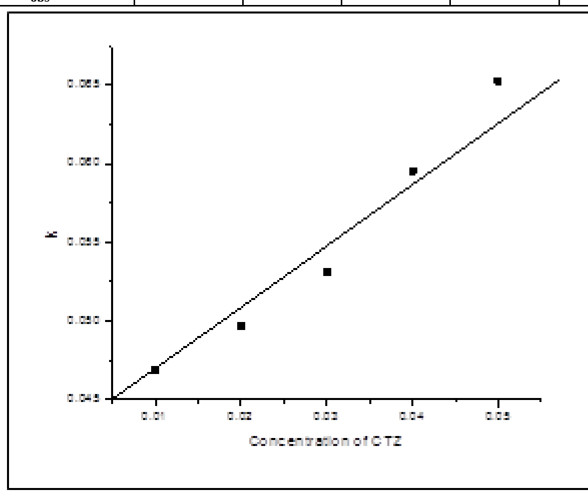

Figure 1: Graph of concentration verses k_{obs} of cetirizine hydrochloride

Effect of Potassium Dichromate Concentration

Concentration of potassium dichromate was varied from 1×10^{-3} to 5×10^{-3} mol dm^{-3} keeping all other conditions constant. The k_{obs} values showed a sharp increase with the increase in concentration of potassium dichromate and giving a linear graph (Figure 2) with line passing nearly through origin indicating first order dependence of the rate of the reaction on concentration of potassium dichromate (Table 2).

Table 2: [PDF] mol $dm^{-3}$and k_{obs}

[PD] mol dm^{-3}	0.01	0.02	0.03	0.04	0.05
k_{obs}	0.04689	0.0497	0.05301	0.05953	0.06531

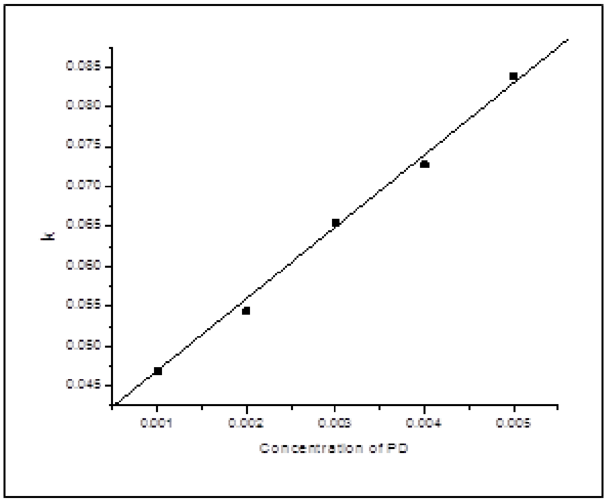

Figure 2: Graph of concentration verses k of potassium dichromate

Effect of Temperature

Variation of temperature change on the rate of oxidation of cetirizine hydrochloride was studied by conducting kinetic runs at different temperatures ranging from 30°C, 35°C, 40°C, 45°C and 50°C keeping all other experimental conditions constant i.e. [CTZ], [PD] and $[H^+]$. The result shows increase in rate of reaction with the increase in temperature (Table 3). From the linear Arrhenius plots of 3+logk verses 1/T activation parameters were calculated and tabulated in Table 4 (Figure 3).

Table 3: 3+log k_{obs} at different temperatures

Temperature °C	30	35	40	45	50
3+log k_{obs}	1.671	1.8357	1.8975	1.9662	2.0044

Table 4: Activation Parameters

Activation Parameters	**Ea**	**ΔH**	**ΔS**	**ΔG**
	30.917 $kJmol^{-1}$	28.272 $kJmol^{-1}$	-178.33 $JK^{-1}mol^{-1}$	84.09 $kJmol^{-1}$

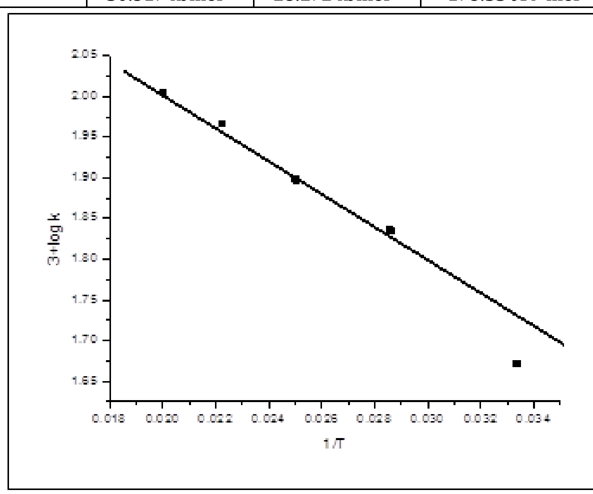

Figure 3: Graph of 1/T verses 3+log k

Effect of Acid Concentration

The oxidation of cetirizine hydrochloride with potassium dichromate was studied with different concentrations of sulphuric acid keeping all other conditions of the reaction constant. There is increase in the rate constant with increasing sulphuric acid concentrations indicating first order rate of the reaction.

Free Radical Test

In the reaction mixture aqueous solution of acrylonitrile was added. It does not show initiation of polymerization reaction indicating non-involvement of free radical in the reaction sequences [12,13].

Mechanism of the Oxidation of Cetirizine Hydrochloride

$$K_2Cr_2O_7 + 4H_2SO_{4(aq)} + 3CTZ \rightarrow 3CTZN{\rightarrow}O + K_2SO_4 + (Cr_2SO_4)_3 + 4H_2O$$

$$Cr_2O_7^{2-} + H_2O \rightarrow 2HCrO_4^{-} \text{ (Cr VI)}$$

$$C_{21}H_{25}ClNO_3N + O = CrO_3^{-2} \rightarrow C_{21}H_{25}ClNO_3N{\rightarrow}O{-}CrO_3^{-2} \text{ (Complex Intermediate)}$$

(Chromate Ester CE)

$$C_{21}H_{25}ClNO_3N{\rightarrow}O{-}CrO_3^{-2} \rightarrow C_{21}H_{25}ClNO_3N{\rightarrow}O + CrO_3^{-2} \text{ (Cr IV)}$$

(Cetirizine N-Oxide)

The probable rate equation for the above reaction can be expressed as follows:

$$\frac{d}{dt}[Cr_2O_7^{-2}] = \frac{d}{dt}[HCrO_4^{-}] = k_2[CE]$$

$$CTZ + PD \underset{k_{-1}}{\overset{k_1}{\leftrightarrows}} CE \xrightarrow{k_2} CTZN \rightarrow O$$

We can apply steady state approximation to CE [13]

$$\frac{d[CE]}{dt} = 0 = k_1[CTZ][PD] - k_{-1}[CE] - k_2[CE]$$

$$[C] = \frac{k_1}{k_{-1} + k_2}[CTZ][PD]$$

The overall rate is the rate of formation of CTZN → O

$$\text{Rate} = \frac{d[CTZN{\rightarrow}O]}{dt} = k_2[CE] = \frac{k_1 k_2}{k_{-1} + k_2}[CTZ][PD]$$

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

Rate = k_1 [CTZ] [PD]

CONCLUSION

The kinetic study of oxidation of cetirizine hydrochloride with potassium dichromate shows that cetirizine undergoes oxidation in acid medium in which the nitrogen which is sterically less hindered undergoes oxidation to yield cetirizine N-oxide as the main product. The rate of the reaction is first order with respect to substrate, oxidant and acid.

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