



A Comparative Kinetic Study of Uncatalyzed and Ce(IV) Catalyzed Cetrizine Dihydrochloride Oxidation in Aqueous Acid Medium by Chloramine-T

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A kinetic study of uncatalyzed and Ce(IV) catalyzed cetrizine dihydrochloride oxidation was carried out in aqueous acid medium using chloramine-T. Both uncatalyzed and catalyzed reactions follow first order kinetics with respect to [CAT] and fractional order kinetics with respect to [substrate]. The reaction follows first order dependence on [Ce^{IV}] catalyst. The uncatalyzed reaction shows inverse fractional order for [H⁺] and [Cl⁻] whereas catalyzed reaction follows fractional order. The effect of ionic strength is negligible in both cases. The dielectric constant has negative effect on uncatalyzed reaction and positive effect on catalyzed reaction. To compute the thermodynamic parameters the kinetic runs were studied at different temperatures (293-313 K). The stoichiometry of the reaction was studied and the products of oxidation were analyzed. The rate law was also derived by the proposed mechanism.

Keywords: Chloramine-T, Cetrizine dihydrochloride, Rate law, Oxidation, Mechanism, Cerium(IV) catalyst.

INTRODUCTION

Cetrizine dihydrochloride (CTZ), named as 2-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]acetic acid dihydrochloride is generally more effective H₁ receptor antagonist exhibiting histamine-responsive wheal and flare properties. It is the properly tolerated and effective agent for perennial allergic rhinitis (PAR), seasonal allergic rhinitis (SAR) and chronic idiopathic urticaria (CIU) symptoms treatment in adult, adolescent and pediatric patients. The drug does not cause sedation as it cannot pass through blood-brain barrier [1-3]. Cetrizine exist both in the two optically active forms and marketed as a mixture of dextrocetrizine and levocetrizine. The drug is a second generation H₁ antihistamine and clinically useful for the treatment of seasonal allergies symptoms. Its single R-enantiomer levocetirizine is a newest antihistamine and is recently approved by the FDA [4]. Cetrizine, has a rapid onset of action, orally active, long duration of effects and a very good safety record at recommended doses [5]. It reduces the symptoms of certain allergic reactions and block the action of histamine in human body. The symptoms effectively treated include rhinorrhea, postnasal discharge, sneezing, ocular pruritus, nasal pruritus and tearing. It markedly reduces the occurrence severity and

duration of hives and significantly reduces pruritus [6]. Sleepiness, headache, dry mouth and abdominal pain are the common side effects of the drug [7,8]. The degree of sleepiness is less in second generation of antihistamine than the first-generation antihistamine because it is more selective for the H₁ receptor.

The sodium salt of *N*-chloro-*p*-toluenesulfonamide known as chloramine-T (CAT) is a versatile oxidizing agent. The mild oxidizing capacity of this compound is attributable to its role as a source of hypohalite species, nitrogen anions and halonium ions, which function as nucleophiles and bases. Accordingly, they interact with most of functional groups to cause numerous kinds of molecular transformations. This reagent is a stable, efficient, non-toxic, inexpensive and mild oxidant. Several researchers were studied the mild oxidation kinetics of substrates by chloramine-T [9-18].

Transition metal ions and some inner-transition metals exhibits catalytic behaviour due to their variable valency due to presence of empty *d*- and *f*-orbitals. These metal ions react with certain organic molecules with their reactants they produce unstable intermediates [19,20]. Cerium(IV) sulphate is a highly efficient reusable heterogeneous catalyst used for several redox reactions. Early investigation outcomes show that the reaction of cetrizine (CTZ) with chloramine-T in the acidic medium.

In present paper, the comparative kinetic study of uncatalyzed and Ce(IV) catalyzed cetirizine dihydrochloride oxidation in aqueous acid medium by chloramine-T reagent is described.

EXPERIMENTAL

A solution of chloramine-T (CAT, E. Merck) was prepared in double distilled water and standardized iodometrically. It was preserved in a brown bottle in dark condition to avoid probable photochemical deterioration. Cetirizine (CTZ) in required amount was freshly prepared each time using double distilled water. Ionic strength was maintained using sodium perchlorate solution, while the dielectric constant was altered by using methanol. A solution of cerium(IV) sulphate was prepared using double distilled water. Sodium chloride was added to vary the halide ion concentration and the acidic condition was maintained using hydrochloric acid. The other chemicals used for kinetic runs were of analytical grade and double distilled water was used to freshly prepare their solutions.

Kinetic measurements: All the kinetic runs of oxidation were studied under pseudo-first order concentrations in which $[CTZ] \gg [CAT]$. As other components of the reaction mixture do not significantly absorb at $\lambda_{max} = 260$ nm progress of Ce(IV) catalyzed and uncatalyzed oxidation was studied by measuring decrease in the absorbance maximum for CAT (Fig. 1). All the absorbance values were recorded on a computer-controlled Thermo Scientific spectrophotometer.

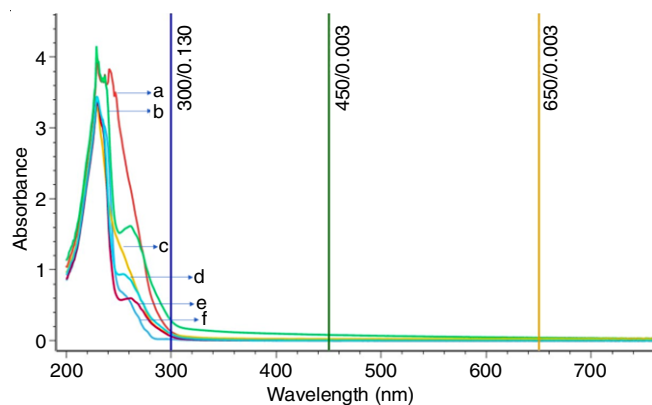


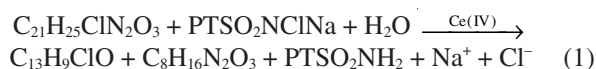
Fig. 1. Visible spectra for the different combination of reactants: (a) $[CAT] = 10 \times 10^{-5} \text{ mol dm}^{-3}$; (b) $[Ce(IV)] = 10 \times 10^{-6} \text{ mol dm}^{-3}$ and $[CTZ] = 10 \times 10^{-4} \text{ mol dm}^{-3}$; (c) $[CAT] = 10 \times 10^{-5} \text{ mol dm}^{-3}$ and $[CTZ] = 10 \times 10^{-4} \text{ mol dm}^{-3}$; (d) $[Ce(IV)] = 10 \times 10^{-6} \text{ mol dm}^{-3}$ and $[CAT] = 10 \times 10^{-5} \text{ mol dm}^{-3}$; (e) Reaction mixture with out catalyst $[Cl^-] = 10 \times 10^{-4} \text{ mol dm}^{-3}$, $[H^+] = 10 \times 10^{-4} \text{ mol dm}^{-3}$; (f) Reaction mixture with catalyst $[Cl^-] = 10 \times 10^{-4} \text{ mol dm}^{-3}$, $[H^+] = 10 \times 10^{-4} \text{ mol dm}^{-3}$

The cerium(IV) catalyzed and uncatalyzed oxidation of cetirizine in aqueous acid media by CAT was determined in a parallel path. It has been determined from the slope of $\log k_c$ versus $\log(\text{conc.})$ plots by varying the concentration of $[CTZ]$, $[CAT]$, $[H^+]$, $[Cl^-]$ and catalyst, in turn, keeping others concentration constant.

The kinetic runs were studied within ± 0.1 °C. The reaction mixture for the kinetic runs containing calculated amounts of acid, NaCl and substrate solutions with appropriate volume of water to keep the total volume constant in a boiling tube were kept in a thermostates at 298 K. The required amount of CAT

was added rapidly to initiate the reaction with shaken appropriately. The unreacted CAT determined by iodometrically while monitoring the reaction progress with time approximately up to two half-lives. The pseudo first order rate constants were calculated by the plot graph of $\log [CAT]$ versus time. The values of k are reproducible within $\pm 3\%$.

Reaction stoichiometry: The reaction stoichiometry was carried out in a different set of varying ratios of CAT to CTZ reaction mixture containing a constant amount of H^+ and Cl^- , in uncatalyzed reaction and requisite amount Ce(IV) in the catalyzed reaction. The reaction mixture were kept 48 h in a closed vessel. Unreacted CAT concentration was determined iodometrically with starch as an indicator. The stoichiometry reaction shows that one mole of CTZ was consumed by one mole of CAT.



where, $PT = CH_3C_6H_4$.

Ether was used to extract the reaction product, one of the oxidation product of substrate (2-piperazine-1-yl-ethoxy)acetic acid. From ether layer, it was extracted with aqueous NaOH solution and that conformed by esterification and spot test. 2,4-DNP (2,4-dinitrophenylhydrazine) test was conducted for the qualitative identification of product 4-chlorobenzophenone. The *p*-toluenesulfonamide (PTS), a reduction product was conformed by using TLC system of solvent petroleum ether: chloroform:1-butanol (2:2:1 v/v/v) and ethyl acetate.

RESULTS AND DISCUSSION

Effect of varying reactants concentration: The oxidation of cetirizine (CTZ) by chloramine-T (CAT) was carried out in a catalyzed as well as uncatalyzed path while keeping concentrate other variables constant such as cerium, acid, halide and substrate and also the temperature kept constant.

Effect of rate on the variation of oxidant concentration: At different concentrations of oxidant (8×10^{-5} to $40 \times 10^{-5} \text{ mol dm}^{-3}$) by keeping other variables such as concentration of Ce(IV) catalyst, reductant and acid constant. The temperature were also keeping constant during reaction. The unaffected values of k^1 on varying oxidant concentration shows that rate of the reactant was independent of oxidant concentration and the reactions follows first order dependence on rate of $[CAT]$.

Effect of rate on substrate concentrations: The kinetic oxidation of CTZ by CAT was determined for different concentrations of CTZ in uncatalyzed aqueous acid medium at 298 K. The rate of reaction increased along the increasing cetirizine concentration in Table-1, which shows that fractional order kinetic with respect to $[CTZ]$. In catalyzed reaction, the concentration of $[CTZ]$ was varied from (8×10^{-4} to $40 \times 10^{-4} \text{ mol dm}^{-3}$) while keeping the other variables constant. The rate was increased with increase concentration of CTZ, thus, the rate of reaction follows fractional with respect to CTZ (Fig. 2).

Effect of catalyst on rate: The catalyst concentration was varied from (8×10^{-6} to $40 \times 10^{-6} \text{ mol dm}^{-3}$) all other reaction condition such as $[CTZ]$, $[CAT]$ and acid kept constant. The temperature of the reaction was also kept constant. The reaction

TABLE-1
EFFECT OF [CTZ], [CAT], [H⁺], [Cl⁻] AND Ce(IV) ON THE CATALYZED OXIDATION OF
CETRIZINE DIHYDROCHLORIDE BY CAT IN ACID MEDIUM AT 27 °C, I = 0.20 mol dm⁻³

10 ⁵ × [CAT] (mol dm ⁻³)	10 ⁴ × [CTZ] (mol dm ⁻³)	10 ⁴ × [H ⁺] (mol dm ⁻³)	10 ⁴ × [Cl ⁻] (mol dm ⁻³)	10 ⁶ × [Ce(IV)] (mol dm ⁻³)	10 ⁴ × k _v (s ⁻¹)	10 ³ × k _c (s ⁻¹)	
						Found	Calcd.
8	10	10	10	10	3.830	0.635	0.639
10	10	10	10	10	3.269	0.698	0.736
20	10	10	10	10	3.198	0.680	0.675
40	10	10	10	10	3.198	0.699	0.693
10	8	10	10	10	2.878	0.880	0.895
10	10	10	10	10	3.269	1.023	1.053
10	20	10	10	10	6.00	1.155	1.172
10	40	10	10	10	10.46	1.215	1.230
10	10	8	10	10	3.760	0.950	0.913
10	10	10	10	10	3.269	1.045	1.053
10	10	20	10	10	2.600	1.165	1.177
10	10	40	10	10	2.000	1.392	1.421
10	10	10	8	10	3.800	0.964	0.959
10	10	10	10	10	3.260	1.049	1.053
10	10	10	20	10	2.191	1.477	1.492
10	10	10	40	10	1.391	1.657	1.663
10	10	10	10	8	–	0.880	0.895
10	10	10	10	10	–	1.050	1.053
10	10	10	10	20	–	1.380	1.395
10	10	10	10	40	–	1.965	1.968

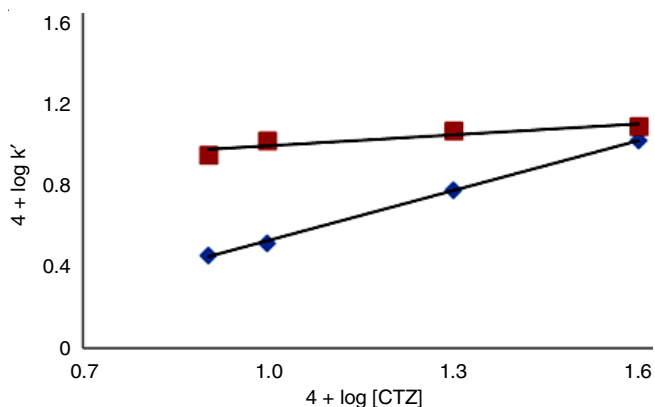


Fig. 2. Effect of rate on variation of [CTZ] concentration at 298 K. [CAT] = 10 × 10⁻⁵, [Ce(IV)] = 10 × 10⁻⁶ and [H⁺] = 10 × 10⁻⁴

rate increases with increasing the concentration of catalyst, it indicates the rate of reaction shows first order with respect to [Ce^{IV}] (Fig. 3).

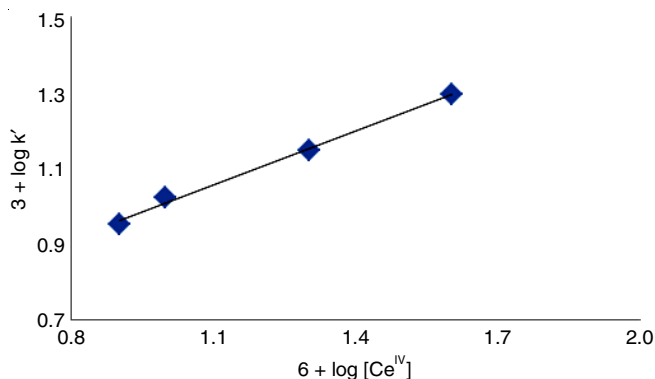


Fig. 3. Effect of rate on varying the concentration of catalyst on rate for the oxidation of cetrizine by chloramine-T at 298 K; [CAT] = 10 × 10⁻⁵, [H⁺] = 10 × 10⁻⁴ and [CTZ] = 10 × 10⁻⁴ mol dm⁻³

Effect of rate on [H⁺]: The rates of uncatalyzed reaction were determined by changing the [HCl] concentration from (8 × 10⁻⁴ to 40 × 10⁻⁴ mol dm⁻³), while the remaining reaction conditions kept constant. There is decrease rate of reaction with constantly increase in the [H⁺] (Table-1). Fig. 4 shows that there is a negative slope of 0.3775, which indicate that rate of reaction follows the inverse fractional order on [H⁺].

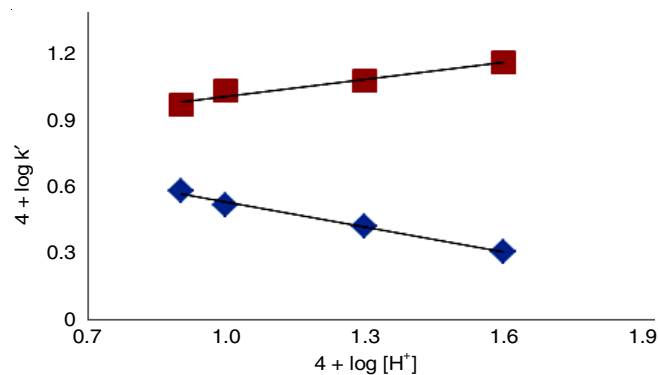


Fig. 4. Effect of concentration of [H⁺] for oxidation of cetrizine by chloramine-T at 298 K; [CAT] = 10 × 10⁻⁵, [Ce(IV)] = 10 × 10⁻⁶ and [CTZ] = 10 × 10⁻⁴ mol dm⁻³, [Cl⁻] = 10 × 10⁻⁴ mol dm⁻³

The oxidation of catalyzed reaction rates were determined by varying the acid concentration, while other variables kept constant. The reaction rate increases with increase in the concentration of [H⁺]. It shows the positive slope of 0.2513 indicating fractional order kinetics on rate of [H⁺].

Effect of ionic strength: NaClO₄ was added for the variation of ionic strength uncatalyzed and catalyzed condition from (0.1-1.0 mol dm⁻³). It was found that the reactions of uncatalyzed and catalyzed paths does not affect of the reaction rate, which shows the involvement of non-ionic species in the rate limiting step.

Effect of rate on halide ion: The chloride ion concentration for uncatalyzed reaction was varied from $(8 \times 10^{-4}$ to $40 \times 10^{-4} \text{ mol dm}^{-3}$), while keeping the other reaction conditions constant. The rate of the reaction decreases with increasing chloride ion concentration (Table-1). A linear plot of $\log k^1$ versus $\log [\text{Cl}^-]$ (Fig. 5) indicate the negative fractional order dependence of rate on $[\text{Cl}^-]$. In catalyzed reaction the concentration of chloride ion was varied from $(8 \times 10^{-4}$ to $40 \times 10^{-4} \text{ mol dm}^{-3}$) with all other such as $[\text{H}^+]$, $[\text{CTZ}]$, $[\text{CAT}]$ and $[\text{Ce}^{\text{IV}}]$, kept constant. The rate of the reaction increases with increasing the chloride ion concentration, which indicates the fractional order dependence of rate on $[\text{Cl}^-]$.

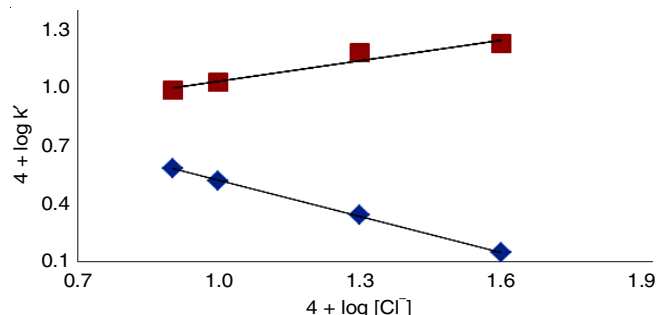


Fig. 5. Effect of concentration of $[\text{Cl}^-]$ on rate for oxidation cetirizine by chloramine-T at 298 K. $[\text{CAT}] = 10 \times 10^{-5}$, $[\text{Ce}(\text{IV})] = 10 \times 10^{-6}$ and $[\text{CTZ}] = 10 \times 10^{-4} \text{ mol dm}^{-3}$, $[\text{H}^+] = 10 \times 10^{-4} \text{ mol dm}^{-3}$

Effect of dielectric constant: The dielectric permittivity of the medium for uncatalyzed reaction was varied at different proportion of methanol (0-40% v/v). From plot of $\log k^1$ versus $1/D$ is linear with a negative slope (Fig. 6) and shows that an increase in dielectric permittivity (D) of medium while decreasing the reaction rate (Table-2). In catalyzed reaction, the rate of reaction increased with increasing the dielectric permittivity of the medium. The plot of $\log k^1$ against $1/D$ is linear with a positive slope.

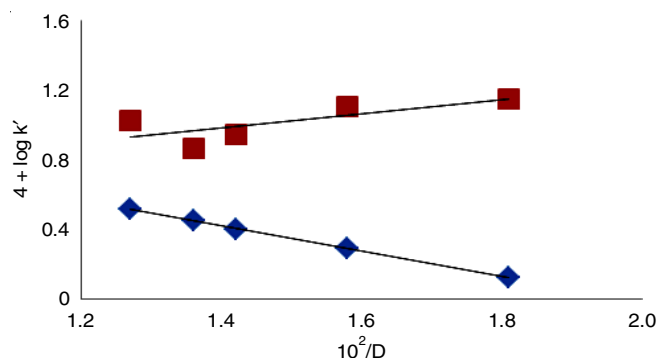


Fig. 6. Effect of varying dielectric constant concentration on rate

TABLE-2
EFFECT OF RATE ON DIELECTRIC CONSTANT

MeOH (%)	D	$10^2/D$	$k_u^1 \times 10^4 (\text{S}^{-1})$	$K_c^1 \times 10^4 (\text{S}^{-1})$
0	76.7	1.30	3.26	6.90
5	72.4	1.39	2.81	7.26
10	67.4	1.47	2.59	8.79
20	62.7	1.60	1.95	12.79
40	58.1	1.72	1.32	14.07

$[\text{CAT}] = 10 \times 10^{-5}$, $[\text{CTZ}] = 10 \times 10^{-4}$, $[\text{H}^+] = 10 \times 10^{-4}$, $[\text{Ce}(\text{IV})] = 10 \times 10^{-6} \text{ mol dm}^{-3}$ and $T = 298 \text{ K}$, $\mu = 0.5 \text{ mol dm}^{-3}$.

Effect of product *p*-toluene sulfonamide (PTS) concentration: The addition of PTS (1×10^{-4} – $10 \times 10^{-4} \text{ mol dm}^{-3}$), the reduced product of oxidant CAT had no significant effect on the rate of reaction on both catalyzed and uncatalyzed reactions. This indicates the non-involvement of it in pre-equilibrium step.

Effect of temperature on the rate: The uncatalyzed and catalyzed reactions of rate constant were measured at different temperature ranging from 293 K to 313 K while keeping other conditions constant (Table-3). The rate of reaction increases with increase in temperature. The thermodynamic parameters, viz. entropy of activation (ΔS^\ddagger), free energy of activation (ΔG^\ddagger) and enthalpy of activation (ΔH^\ddagger) of the reaction were also evaluated from the plot of $\log k^1$ versus $1/T$ (Fig. 7) and the values are shown in Table-4.

TABLE-3
TEMPERATURE VARIATION ON THE RATE OF OXIDATION OF CTZ BY CAT IN AQUEOUS ACID MEDIUM AT 298 K

Temp. (K)	$k_u \times 10^4 (\text{S}^{-1})$	$k_c \times 10^4 (\text{S}^{-1})$
293	2.52	9.95
298	3.26	10.53
303	4.15	15.23
308	5.42	18.27
313	6.86	23.03

$[\text{CAT}] = 10 \times 10^{-5} \text{ mol dm}^{-3}$, $[\text{CTZ}] = 10 \times 10^{-4} \text{ mol dm}^{-3}$, $[\text{H}^+] = 10 \times 10^{-4} \text{ mol dm}^{-3}$, $[\text{Ce}(\text{IV})] = 10 \times 10^{-6} \text{ mol dm}^{-3}$, $T = 298 \text{ K}$, $\mu = 0.5 \text{ mol dm}^{-3}$.

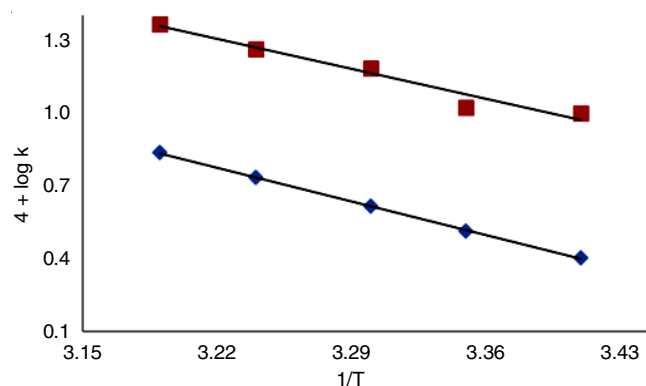


Fig. 7. Temperature dependence for uncatalyzed and catalyzed reactions

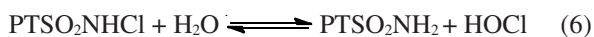
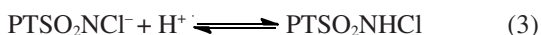
TABLE-4
THERMODYNAMIC PARAMETERS FOR OXIDATION OF CTZ BY CAT IN AN AQUEOUS ACID MEDIUM

Activation parameters	Uncatalyzed	Catalyzed
Ea (kJ mol ⁻¹)	37.754	33.496
ΔH^\ddagger (kJ mol ⁻¹)	35.155	30.976
ΔS^\ddagger (kJ mol ⁻¹)	-193.571	-196.459
ΔG^\ddagger (kJ mol ⁻¹)	93.627	91.688
Log A	1.9718	1.7494

Free radicals test: When the mixture of reaction was added a solution of aqueous acrylamide there was no initiation of polymerization. This indicates the absence of any free radical entities in the course of uncatalyzed reaction. In catalyzed reaction, the free radical species involvement was examined by adding a known amount of the monomer acryl nitrile to the reaction mixture in the inert atmosphere. Formation of white

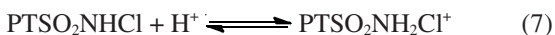
precipitate in the reaction mixture indicates the free radical formation during the course of reaction.

Deduction of rate law and mechanism for uncatalyzed reaction: In the absence of catalyst oxidation of CTZ by CAT occurs in a slow rate in acidic medium. The reaction stoichiometry was 1:1, hence one mole of CTZ consumes one mole of CAT. The first order dependence of reaction rate with respect to CAT and CTZ whereas inverse fractional order for $[H^+]$ were observed. Chloramine-T acts as a strong oxidizing agent in acidic and basic media with a change of two electron to give reduction product. It acts as a powerful electrolyte in aqueous solution forming different ionic species as follows [14,21-23].

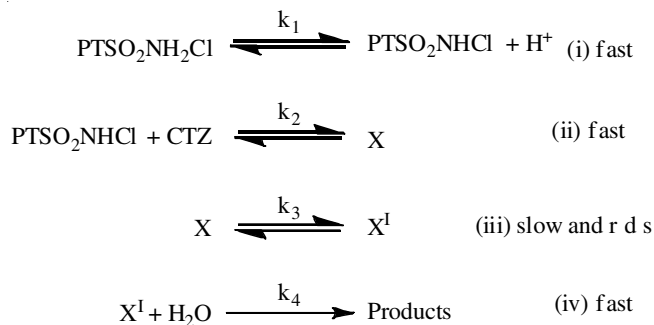


where, PT = $CH_3C_6H_4$.

Hence, the oxidizing species possible by the CAT in acidic aqueous solution are $PTSO_2NHCl$, $PTSO_2NCl_2$ and $HOCl$. Here, $PTSO_2NCl_2$ as the reactive oxidizing species was ruled out since the rate is not second order dependent on CAT as indicated by eqn. 4. Also, $HOCl$ is not primarily involved in oxidation as the rate was not retarded first order by the added *p*-toluenesulphonamide. Hence the possible active oxidizing species is $PTSO_2NHCl$ in acidic condition ($pH < 2$) $PTSO_2NHCl$ is protonated to $PTSO_2NH_2Cl$ [24].



The retardation of rate by the H^+ ions added confirm the deprotonation of $PTSO_2NH_2Cl^+$ from the unprotonated active oxidizing entities $PTSO_2NHCl$. In view of experimental evidence to predict mechanism for the reaction and oxidation of CTZ by CAT in **Scheme-I** was proposed. Now consider the $PTSO_2NHCl$ indicate the active oxidant, CTZ represent the substrate and X and X^1 represents the complex intermediate species. Here course of reaction was initiated by the formation of $PTSO_2NHCl$, which inturn attacks the substrates to give an intermediates X. This complex dissociates in the rate determining step to give complex cation X^1 by eliminating $PTSO_2NH_2$. On hydrolysis, X^1 give products and the mechanism is indicated in **Scheme-II**.



Scheme-I

The differential rate equation is:

$$\frac{d[CAT]}{dt} = k_3[X] \quad (8)$$

Let $[CAT]_t$ be the effective total concentration of CAT, then

$$[CAT]_t = [PTSO_2NH_2Cl^+] + [PTSO_2NHCl] + [X] \quad (9)$$

$$[CAT]_t = \frac{[PTSO_2NHCl][H^+]}{k_1} + \frac{[X]}{k_2[CTZ]} + [X] \quad (10)$$

$$[X] = \frac{k_1 k_2 [CAT]_t [CTZ]}{[H^+] + k_1(1 + k_2)[CTZ]} \quad (11)$$

$$\frac{d[CAT]}{dt} = \frac{k_1 k_2 k_3 [CAT]_t [CTZ]}{[H^+] + k_1(1 + k_2)[CTZ]} \quad (12)$$

The deduced rate law (eqn. 12) is in good agreement with the experimental results.

Since rate = k' $[CAT]_0$ eqn. 12 can be rearranged as:

$$k' = \frac{k_1 k_2 k_3 [CTZ]}{[H^+] + k_1(1 + k_2)[CTZ]} \quad (13)$$

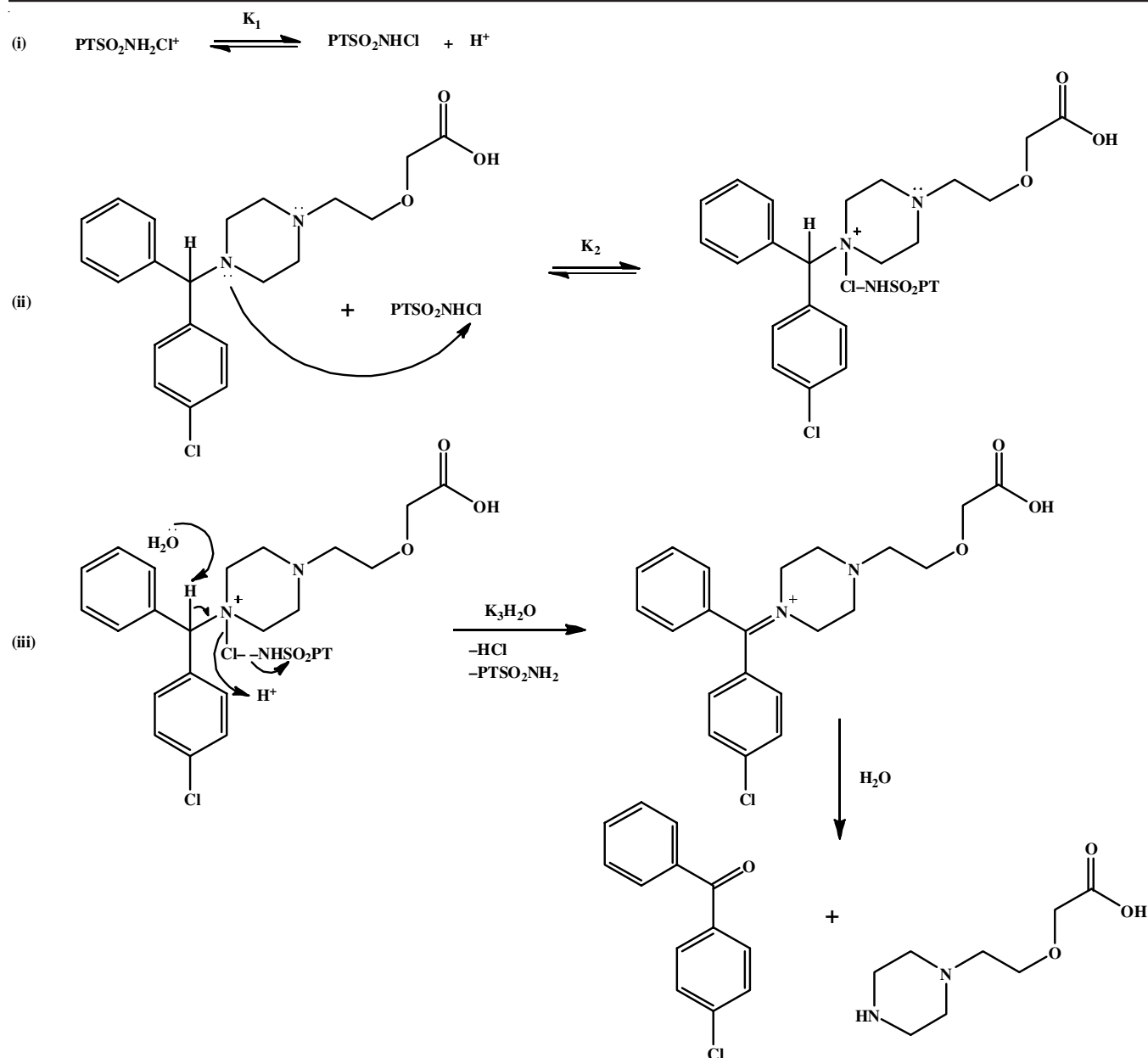
$$\frac{1}{k'} = \frac{1}{k_2 k_3 [CTZ]} \left\{ \frac{[H^+]}{k_1} + 1 \right\} + \frac{1}{k_3 [CTZ]} \quad (14)$$

The linear plot of $1/k'$ against $1/[CTZ]$ and $1/k'$ versus $1/[H^+]$ were plotted according to Eqns. 13 and 14. The values of k_1 , k_2 and k_3 were evaluated from the intercepts and slopes.

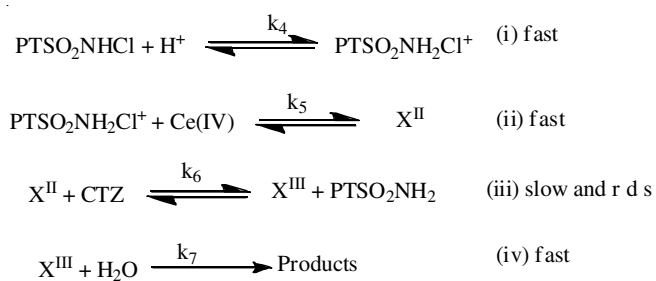
Dielectric constant of the medium varied by adding a different proportion of methanol. The plot of $\log k'$ versus $1/D$ shows the negative dielectric effect which indicate the presence of dipole-dipole interaction in the medium. The reduced product (PTS) did not alter the reaction rate, indicating the absence of ion involvement in the pre-equilibrium step. The rate of the reaction remains same with variation of ionic strength of the medium indicates that the non-ionic species were involved in rate limiting step. However, halide ion has a slight negative effect on the reaction rate. The represented mechanism was supported by the computed thermodynamic variables. The large negative value of entropy of activation and moderate positive values of enthalpy of activation and free energy of activation represents the establishment of a compact transition state complex with lesser degrees of freedom.

Deduction of rate law and mechanism for catalyzed reaction: The stoichiometry of uncatalyzed and catalyzed reactions of oxidation of CTZ by CAT in aqueous acid medium were identical on the basis of kinetic experimental data. CAT follows first-order whereas substrate follows the fractional order dependence on rate determining step. While increasing concentration of $[H^+]$ ion on the rate of reaction gradually increases. It has been observed the fractional order kinetics with respect to $[H^+]$ and the dielectric permittivity of the medium shows the positive slope, while the reaction entropy was negative.

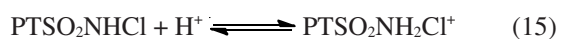
Scheme-III as shows the complexation formed between CAT and catalyst in a pre-equilibrium step before reacting with substrate, which indicate the fractional order dependence on $[CTZ]$.



Scheme-II



Scheme-III



The retardation of rate by the using H^+ ions proves the protonation of PTSO_2NHCl accompanies to the formation of protonated reactive oxidizing entities $\text{PTSO}_2\text{NH}_2\text{Cl}^+$. **Scheme-III** is proposed based on experimental data to predict the reac-

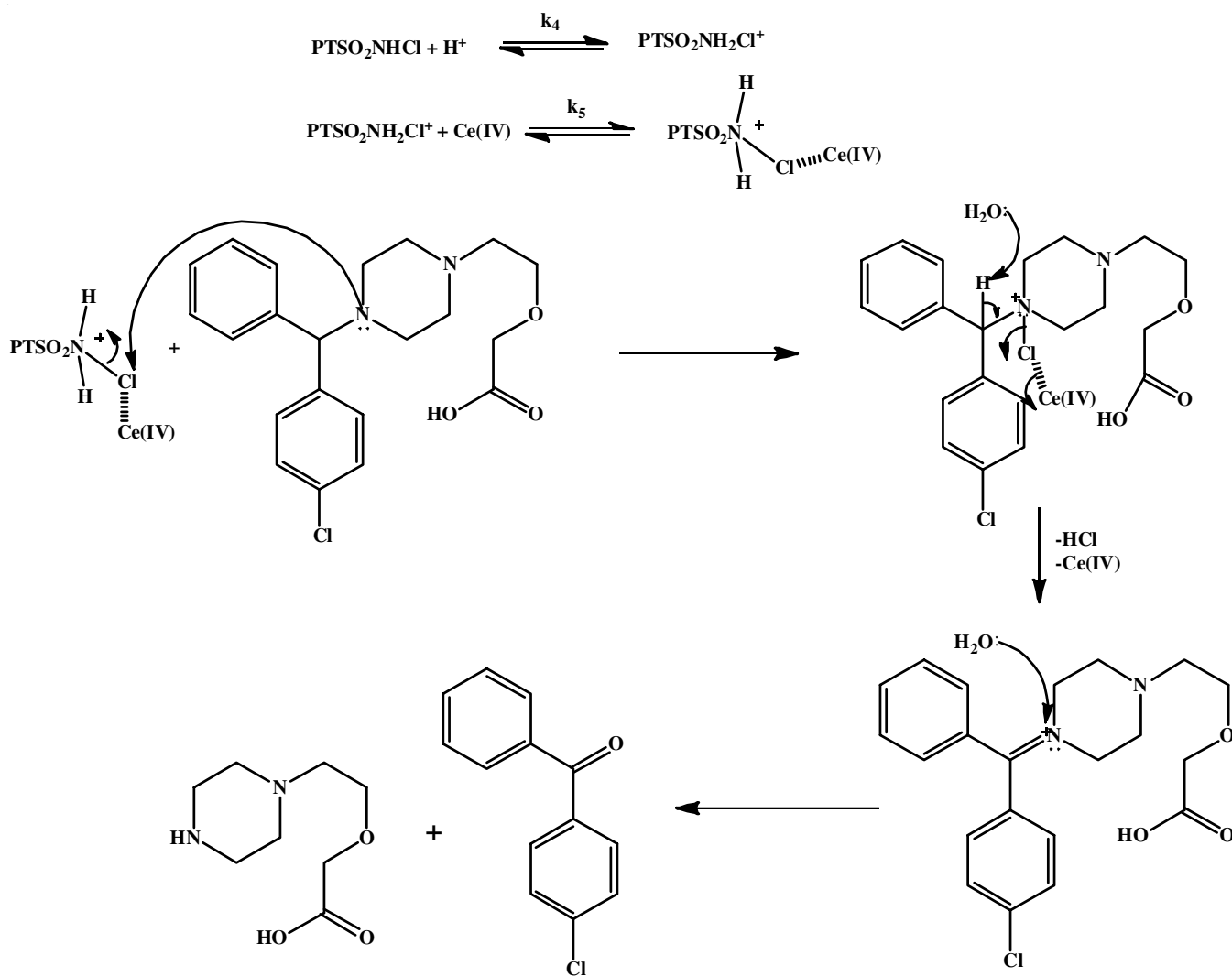
tion mechanism for the reaction of Ce(IV) catalyzed by CTZ by CAT. It is recommended that PTSO_2NHCl be used as active oxidant and CTZ be used as substrate. The CAT reacts with catalyst to form X^{II} intermediate complex, which precedes to the rate determining step. Then, the substrate CTZ reacts with the formed complex in a slow step to yield X^{III} and PTSO_2NH_2 complex with recovery of Ce(IV) catalyst. Then, the complex on hydrolysis yield products and the reaction mechanism is demonstrated in **Scheme-IV**.

The differential rate equation is:

$$\frac{d[\text{CAT}]}{dt} = k_6[\text{X}^{\text{II}}] \quad (16)$$

Let $[\text{CAT}]_t$ be the effective total concentration of CAT, then

$$[\text{CAT}]_t = [\text{PTSO}_2\text{NH}_2\text{Cl}^+] + [\text{PTSO}_2\text{NHCl}] + [\text{X}^{\text{II}}] \quad (17)$$



$$[X^{II}] = \frac{k_5 k_6 [CAT]_t [CTZ] [H^+] [Ce^{IV}]}{[PTSO_2NH_2] + \{1 + k_4 [H^+] + k_4 k_5 [H^+] [Ce^{IV}]\} + k_4 k_3 k_6 [H^+] [Ce^{IV}] [CTZ]} \quad (18)$$

The deduced rate law is in good agreement with the experimental results.

Since rate = $k_7 [X^{III}]$ eqn. 18 can be rearranged as:

$$\text{Rate} = \frac{k_4 k_5 k_6 k_7 [CTZ] [H^+] [Ce^{IV}]}{[PTSO_2NH_2] + \{1 + k_4 [H^+] + k_4 k_5 [H^+] [Ce^{IV}]\} + k_4 k_5 k_6 [H^+] [Ce^{IV}] [CTZ]} \quad (19)$$

Using eqns. 18 and 19, the linear plot of $1/k'$ versus $1/[CTZ]$ and $1/k'$ versus $1/[H^+]$ were plotted. The values of k_5 , k_6 and k_7 were evaluated from slopes and intercepts.

Conclusion

The comparative study of oxidation of uncatalyzed and catalyzed reaction of cetrizine dihydrochloride (CTZ) by chloramine-T (CAT) in aqueous acidic medium was illustrated. The reaction of cerium(IV) catalyzed and uncatalyzed oxidation of CTZ-CAT redox reaction has been carried out in HCl

medium. Stoichiometry of the reaction for both catalyzed and uncatalyzed oxidation of CTZ by CAT was 1:1 as observed in this study. The oxidation products are (2-piperazine-1-yl-ethoxy) acetic acid and 4-chlorobenzophenone. The effect of halide ions and dielectric constant on the rate were examined. The thermodynamic variables E_a , ΔH^\ddagger , ΔG^\ddagger and ΔS^\ddagger have been evaluated from the Arrhenius plots.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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