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Comparative Study of Ce(IV) Catalyzed and Uncatalyzed Oxidation of Cefixime Trihydrate using Chloramine-T in Acidic Medium: A Kinetics and Mechanistic Study

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ABSTRACT

The kinetics of oxidation of cefixime trihydrate (CFT) by chloramine-T (CAT) was studied in hydrochloric acid medium at 298 K. The reaction stoichiometry was determined and oxidation products were identified. A first order dependence on [CAT] for both catalyzed and uncatalyzed and the reaction were observed, fractional order dependence on [CFT] for both catalyzed and uncatalyzed, fractional order on [H⁺] of rate for uncatalyzed whereas fractional order for metal catalyzed was observed. The products of reaction have no considerable effect on the rate. There is a slight negative effect by the dielectric constant for both catalyzed and uncatalyzed reaction. The rate remains same with the variation in the ionic strength of the medium indicating the involvement of non-ionic species in the rate determining step. There were no free radicals during the course of reaction. Kinetic runs were performed at different temperatures and thermodynamic parameters were computed for both catalyzed and uncatalyzed reaction. A mechanism consistent with the observed parameters were proposed and rate law were derived.

1. Introduction

The aromatic sulphonyl halo amines have diverse properties and behave both as halogenating and oxidizing agents. These organic halo amines resemble hypohalites in their oxidative behavior and though less familiar, are more stable than hypohalites [1,2]. Oxidation kinetics of numerous organic substrates was studied by aromatic sulphonyl halo amines. They are also used as analytical reagents in estimating a variety of reducing agents in solution. They are mild oxidizing agents both in acidic and basic medium. N-chloro-p-toluene sulfonamide or Chloramine-T (CAT) is a well-known derivative of this class of organic halo amines. It reacts with variety of functional groups performing a wide range of molecular modifications and transformations. Kinetic and mechanistic aspects of many of its reactions have been reported [1-8].

Cefixime trihydrate [CFT] is an oral third generation cephalosporin antibiotic. Chemically, it is (6R,7R)-7-[[2-(2-amino-1,3-thiazole-4-yl)-2-(carboxymethoxyimino)acetyl] amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo-[4.2.0]oct-2-ene-2-carboxylic acid [9-11]. CFT is an antibiotic having bactericidal activity by inhibition of cell wall synthesis and is used in the treatment of uncomplicated UTI, otitis media, pharyngitis and tonsillitis, acute bronchitis and acute exacerbation of chronic bronchitis, uncomplicated gonorrhoea [12]. It is particularly active against many Enterobacteriaceae and haemophilus influenzae. CFT is extensively used for treatment of urinary tract infection (UTI), acute otitis media, upper and lower respiratory tract infection, and gonococcal urethritis [13]. Cefixime trihydrate is very stable in the existence of beta-lactamase enzymes. The antibacterial effect of cefixime trihydrate results from inhibition of mucopeptide synthesis in the bacterial cell wall. It is active against Gram-positive and Gram-negative microorganisms. Cefixime trihydrate is available as oral and parenteral dosage forms in the market. It's on the World Health Organization's List of Essential Medicines [14-16].

Due to the presence of variable valency in empty d and f orbitals, most of transition metal ions and some inner-transition metals exhibits catalytic behaviour. These transition metal ions react with certain organic molecules with their reactants they produce unstable intermediates. Cerium (IV) sulphate in a highly efficient reusable catalyst used for many redox reactions. Early investigation outcomes show that the reaction of cefixime trihydrate (CFT) with chloramine-T in the acidic medium.

A review of the literature provides information about quantitative determination, biodegradation and mechanism of action of cefixime trihydrate drug. Oxidation of cefixime trihydrate by mild oxidants was not reported. This paper reporting kinetics, mechanistic and thermodynamic aspects of cefixime trihydrate oxidation by chloramine-T in hydrochloric acid medium at 298 K.

2. Experimental Methods

2.1 Experimental

The substrate CFT (E. Merck) is of analytical grade purity and was used as received. An aqueous solution of the desired strength of the substrate was prepared freshly each time whenever required. Required weight of the Ce (IV) catalyst is used in the reaction mixture for the catalyzed reaction. A solution of an oxidant CAT (E. Merck) in water was prepared afresh, standardized by the iodometric method and preserved in the brown bottle to prevent any further photochemical degradation effects. Double distilled water was used for the kinetic studies. The dielectric constant was measured by altering the methanol concentration. Concentrated solution of potassium nitrate prepared using distilled water and it was used to maintain ionic strength. An excess of CFT over CAT was maintained to keep pseudo first-order conditions.

2.2 Kinetic Measurements

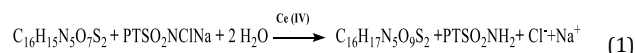
The kinetic experiments for oxidation of cefixime trihydrate by chloramine-T was studied by maintaining pseudo first order conditions with [CFT] >> [CAT]. In a glass-stoppered Pyrex boiling tube mixture of appropriate amounts of solutions of CFT, HCl and NaCl was taken. Requisite amount of distilled water was added to keep total volume constant for all runs. The reaction mixture was thermostatic at 298 K for sufficient time. An equilibrated solution of CAT of required amount was added to the mixture and shaken appropriately. Immediately pipette out and poured into the reaction flask containing ice cold water. The progress of reaction was followed iodometrically by estimating the unreacted CAT in a measured aliquot (2 mL) of the reaction mixture with time up to about two half-lives respectively. The pseudo first order rate constant calculated from the plots of log [CAT] against time are reproducible within ±3%. For each kinetic run the rate of reaction was determined by slope of the tangent drawn at a fixed [CAT]. The order of the reaction in each reactant was measured and calculated with the help of double logarithmic plot of (-dc/dt) versus concentration of reactants.

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2.3 Stoichiometry and Product Analysis

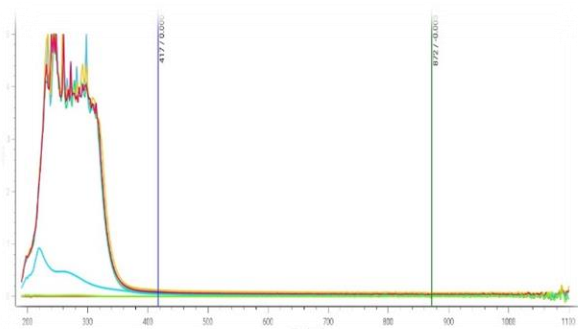
The kinetic runs performed by keeping excess of CFT over CAT at 298K confirm the following stoichiometry as one mole of CFT consume two moles of CAT.



Here PT is $\text{CH}_3\text{C}_6\text{H}_4$. The reaction products were extracted with ether. From the ether layer the oxidation product of substrate was identified as the (E)-2-((2-(2-aminothiothiazol-4-yl)-2-((carboxymethoxy)imino)acetamido) (carboxy)methyl)-5-vinyl-3,6-dihydro-2H-1,3-thiazine-4-carboxylic acid 1-oxide treated with aqueous sodium hydroxide solution and identified by spot test. The presence of peptide bond in it is tested by biuret test. Diethyl amine, the other oxidation product is also confirmed by spot tests [17]. The reduction product of CAT, p-toluene sulfonamide (PTS), was extracted with ethyl acetate and confirmed by TLC using the system of solvent petroleum ether-chloroform-1-butanol (2:2:1 v/v) and the developing reagent iodine (Rf=0.839).

2.4 Spectral Evidence

UV-VIS spectra of cefixime trihydrate, chloramine-T, and a mixture of both catalyzed and uncatalyzed reactions are shown in Fig. 1. The absorption of cefixime trihydrate and progress of Ce (IV) metal catalyzed and uncatalyzed reactions were measured by the decay of CAT absorbance has observed in the absorption maxima (220 nm). The other constituents of reaction mixture were not absorbed in the same wavelength significantly. So, the computer controlled double beam spectrophotometer is used to determine the absorbance of the other constituents.



- a) Blank [CFT] = $2 \times 10^{-3} \text{ mol dm}^{-3}$ [Cl] = $2 \times 10^{-2} \text{ mol dm}^{-3}$ [H⁺] = $2 \times 10^{-2} \text{ mol dm}^{-3}$
 b) [CFT] = $2 \times 10^{-3} \text{ mol dm}^{-3}$
 c) Reaction mixture:- initial reading [CFT] = $2 \times 10^{-3} \text{ mol dm}^{-3}$ [CAT] = $2 \times 10^{-3} \text{ mol dm}^{-3}$ [Cl] = $2 \times 10^{-2} \text{ mol dm}^{-3}$ [H⁺] = $2 \times 10^{-2} \text{ mol dm}^{-3}$
 d) Reaction mixture:- final reading without catalyst [Cl] = $2 \times 10^{-3} \text{ mol dm}^{-3}$, [HCl⁺] = $2 \times 10^{-3} \text{ mol dm}^{-3}$
 e) Reaction mixture with catalyst [Cl] = $2 \times 10^{-3} \text{ mol dm}^{-3}$, [HCl⁺] = $2 \times 10^{-3} \text{ mol dm}^{-3}$
 f) Metal catalyst [Ce(IV)] = $2 \times 10^{-4} \text{ mol dm}^{-3}$
 g) [CAT] = $2 \times 10^{-3} \text{ mol dm}^{-3}$

Fig. 1 UV-Visible spectra for the different combination of reactants.

3. Results and Discussion

3.1 Impact of Oxidant Concentration on the Rate

Kinetic runs were performed for both catalyzed and uncatalyzed oxidation of CFT in the presence of Ce (IV) catalyst in pseudo-first order condition ([CFT] >> [CAT]) by varied [CAT], at constant [CFT], acid, Ce (IV) catalyst and temperature. The initial rate of the reaction in each kinetic run was determined by the slope of the tangent drawn at fixed concentration of oxidant (CAT). In the variation of oxidant, tangent has been drawn at fixed time. From the slopes the pseudo first order rate constants (k₁) were calculated. The unchanged k₁ values on varying oxidant concentration in catalyzed and uncatalyzed reaction confirm the first-order dependence of the rate on [CAT]₀ for both catalyzed and uncatalyzed reaction.

3.2 Impact of Substrate Concentration on the Rate

The reaction is studied under similar experimental conditions by varying the concentration of [CFT] for with and without catalyst reactions. The k' values increased with increase in [CFT] (Table 1). The linear plot of log k' versus log [CFT] (Fig. 2) with slope 0.67 and 0.65 for uncatalyzed and catalyzed reactions respectively. These indicates fractional order dependence on [CFT]. But the in the presence of metal catalyst, potency of the reaction rates high.

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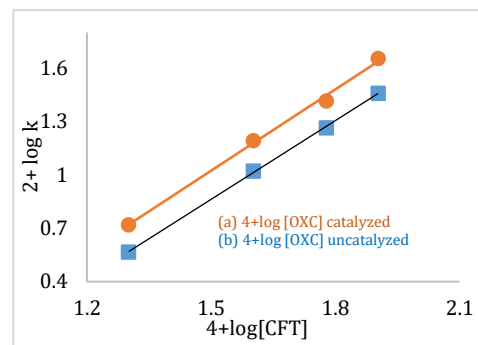


Fig. 2 Impact of substrate concentration on the rate of reaction at 298K. [CAT] = $2 \times 10^{-3} \text{ mol dm}^{-3}$, [Ni (II)] = $2 \times 10^{-4} \text{ mol dm}^{-3}$

3.3 Impact of [H⁺] on the Rate

For uncatalyzed reaction on varying [H⁺] concentration from $2 \times 10^{-3} \text{ mol dm}^{-3}$ to $8 \times 10^{-3} \text{ mol dm}^{-3}$ by keeping all other reaction condition constant, results in the decrease in the rate of reaction. By the graphical calculation it shows the linear plot of log k' versus log [H⁺] with negative slope 0.67 indicate inverse fractional order dependence of rate on [H⁺]. Whereas for catalyzed reaction on changing the [H⁺] concentration from $2 \times 10^{-3} \text{ mol dm}^{-3}$ to $8 \times 10^{-3} \text{ mol dm}^{-3}$ and kept all other condition constant, the reaction rate increases gradually (Fig. 3). By the graphical calculation it shows the linear plot of log k' versus log [H⁺] with positive slope 0.32 indicate fractional order dependence of rate on [H⁺].

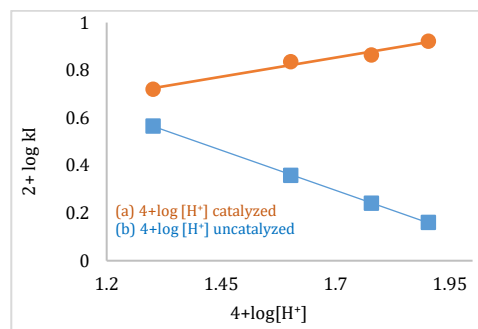


Fig. 3 Influence of [H⁺] on the rate of reaction at 298K. [CAT] = $2 \times 10^{-3} \text{ mol dm}^{-3}$, Ce (IV) = $2 \times 10^{-4} \text{ mol dm}^{-3}$

Table 1 Impact of [CAT], [OXC], [H⁺], [Cl⁻] and catalyzed oxidation of Cefixime trihydrate by chloramine T in acid medium at 298K, μ=0.5 mol/dm³, T=298K, 10²/D=1.66

10 ³ [CAT] mol dm ⁻³	10 ³ [CFT] mol dm ⁻³	10 ⁴ Ce (IV) mol dm ⁻³	10 ³ [HCl] mol dm ⁻³	10 ³ [NaCl] mol dm ⁻³	k' 10 ⁴ (S ⁻¹)	k' 10 ⁴ (S ⁻¹)
2	2	2	2	2	3.68	5.25
4	2	2	2	2	3.72	5.32
6	2	2	2	2	3.65	5.28
8	2	2	2	2	3.61	5.26
2	2	2	2	2	3.68	5.25
2	4	2	2	2	10.49	15.57
2	6	2	2	2	18.42	26.66
2	8	2	2	2	28.72	45.23
2	2	2	2	2	3.68	5.25
2	2	2	4	2	2.28	6.85
2	2	2	6	2	1.74	7.31
2	2	2	8	2	1.45	8.35
2	2	2	2	2	3.68	5.25
2	2	2	2	4	3.62	5.24
2	2	2	2	6	3.70	5.30
2	2	2	2	8	3.71	5.22
2	2	2	2	2	-	5.25
2	2	4	2	2	-	5.32
2	2	6	2	2	-	5.21
2	2	8	2	2	-	5.23

3.4 Impact of Halide Ions on the Rate

Reactions were studied by adding NaCl by varying the concentration of NaCl from $2 \times 10^{-3} \text{ mol dm}^{-3}$ to $8 \times 10^{-3} \text{ mol dm}^{-3}$ by keeping all the other variable constant. The rate remains constant with adding Cl⁻ for both uncatalyzed and metal catalyzed, it indicates that there is no significant effect on the rate of reaction.

3.5 Impact of Ionic Strength on the Rate

The effect of ionic strength of the medium on rate was carried out for both uncatalyzed and metal catalyzed reactions by varying $[KNO_3]$ ($0.1-1.0 \text{ mol dm}^{-3}$) by keeping the other variable constant. The experiment shows there is no appreciable variation occur on the rate. It approves for both uncatalyzed and catalyzed reactions. The unchanged rate of reaction indicates the involvement of non-ionic species in the rate determining step of reaction in both of the cases.

3.6 Impact of Para-Toluene Sulfonamide Concentration on the Rate

The reduced product of oxidant para-toluene sulfonamide (PTS) shows that, there is no significant influence on the rate of reaction by the added PTS ($1 \times 10^{-4}-10 \times 10^{-4} \text{ mol dm}^{-3}$) concentration on both metal catalyzed and uncatalyzed reaction. This specifies that it's non-involvement in pre-equilibrium step.

3.7 Impact of Dielectric Constant on the Rate

As shown in Table 2, the dielectric constant of the medium is varied by using methanol by adding different proportions (0-40%) in the reaction mixture. On increasing the dielectric permittivity(D) of the medium by adding the methanol to reaction mixture decreases the kinetics of reaction for uncatalyzed reaction. Plots of $\log k'$ versus $1/D$ is linear with a negative slope. From the Fig. 4, plot shows that for catalyzed reaction also the rate decreases but the rate value increases comparatively. Blank experiments run with methanol indicated negligible oxidation under experimental conditions employed.

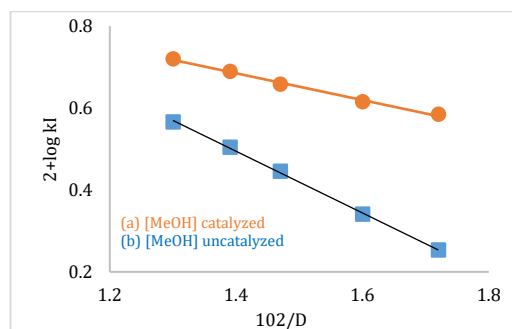


Fig. 4 effect of dielectric constant on the rate at 298K

Table 2 Impact of dielectric constant on rate. $[CAT]=2 \times 10^{-3} \text{ mol dm}^{-3}$, $[CFT]=2 \times 10^{-3} \text{ mol dm}^{-3}$, $[H^+]=2 \times 10^{-3} \text{ mol dm}^{-3}$, $\mu=0.5 \text{ mol dm}^{-3}$, $T=298\text{K}$

MeOH % v/v	D	$102/D$	$k' 10^4 \text{ S}^{-1}$	$k' 10^4 \text{ S}^{-1}$
0	76.7	1.3	3.68	5.25
10	72.4	1.39	3.19	4.88
20	67.4	1.47	2.79	4.55
30	62.7	1.6	2.19	4.12
40	58.1	1.72	1.79	3.85

3.8 Impact of the Temperature on the Rate

As shown in Table 4, the kinetic runs were carried out at varied temperature (293-313 K) for both catalyzed and uncatalyzed reactions by maintaining other variables constant. The measured values in Table 3 shows that rate constant of the reaction increases with raise in temperature for both metal catalyzed and uncatalyzed reactions. From the liner Arrhenius plot of $\log k'$ versus $1/T$ (Fig. 5) the thermodynamic and by using activation energy variables like free energy of activation, enthalpy of activation and entropy of activation of the reaction were measured for both catalyzed and uncatalyzed reactions (Table 4).

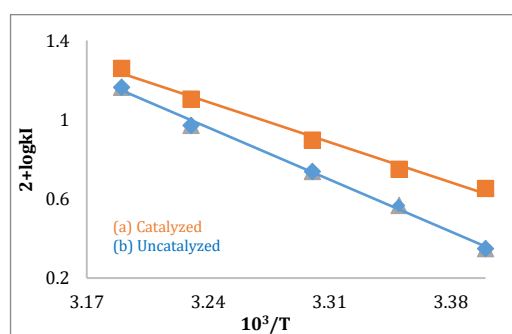


Fig. 5 Temperature dependence on reaction rate.

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Table 3 Impact of temperature and activation parameters on rate. $[CAT]=2 \times 10^{-3} \text{ mol dm}^{-3}$, $[CFT]=2 \times 10^{-3} \text{ mol dm}^{-3}$, $[H^+]=2 \times 10^{-3} \text{ mol dm}^{-3}$, $\mu=0.5 \text{ mol dm}^{-3}$, $102/D=1.33$

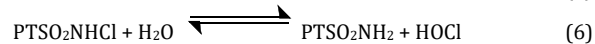
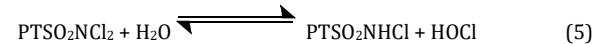
Temperature (K)	$k' 10^4 \text{ (S}^{-1})$ uncatalyzed	$k' 10^4 \text{ (S}^{-1})$ Catalyzed
293	2.99	4.71
298	3.68	5.25
303	6.44	7.89
308	16.83	18.89

Table 4 Thermodynamic parameters for uncatalyzed and catalyzed reactions

Activation parameters	Uncatalyzed	Catalyzed
E_a (kJ mol ⁻¹)	71.26	94.26
ΔS^\ddagger (JK ⁻¹ mol ⁻¹)	-41.37	42.11
ΔH^\ddagger (kJ mol ⁻¹)	68.82	91.82
ΔG^\ddagger (kJ mol)	81.15	78.25

3.9 Derivation of Rate Law and Mechanism for the Uncatalyzed Reaction

Chloramine-T behaves as mild oxidant in both acid and alkali solutions to give reduced products with a change in two electrons. It behaves as a strong electrolyte in aqueous solution. It exhibits following equilibria furnishing different ionic species in aqueous acidic medium [18,19].



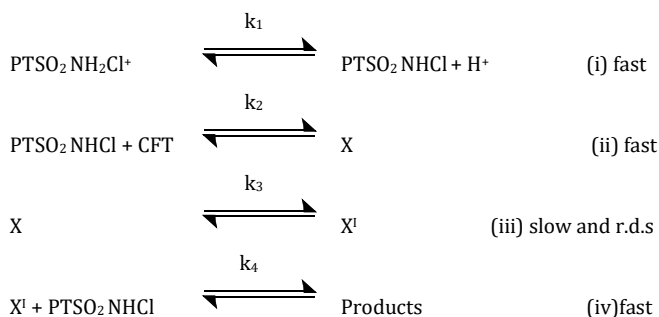
where $\text{PT} = \text{CH}_3\text{C}_6\text{H}_4$.

Hence PTSO_2NHCl , $\text{PTSO}_2\text{NCl}_2$ and HOCl are the possible oxidizing species of CAT in aqueous acid mixture. As the rate is not second order with respect to $[\text{CAT}]_0$ as from Eq.(4) the possibility of $\text{PTSO}_2\text{NCl}_2$ as reactive species was ruled out. Further the rate does not show first order retardation by the added p-toluenesulfonamide. Hence HCl is not primarily involved in oxidation. Thus, PTSO_2NHCl is considered as the active oxidising species. In acid medium ($\text{pH} < 2$) PTSO_2NHCl is protonated to give $\text{PTSO}_2\text{NH}_2\text{Cl}^+$ [21,22].



The protonation constant for Eq.(7) at 298K is 1.02×10^2 . The rate is retarded by added H^+ ions confirming the deprotonation of $\text{PTSO}_2\text{NH}_2\text{Cl}^+$ leading to formation of unprotonated active oxidizing species PTSO_2NHCl .

To account for the experimental results of CFT oxidation by CAT the following Scheme 1 is proposed. Let PTSO_2NHCl represent the active oxidant, CFT represent the substrate and X and X' represent the intermediate complex species. The reaction is initiated through the formation of PTSO_2NHCl which attacks the substrate to give an intermediate complex X which dissociates in the rate determining step to give the complex cation X' eliminating PTSO_2NH_2 . X' on hydrolysis give X'' which reacts with another molecule of PTSO_2NHCl to give products. The detailed plausible reaction mechanism is illustrated in Scheme 2.



Scheme 1 Determination of rate determining step with uncatalyzed

$$\text{The differential rate equation is } \frac{d[\text{CAT}]}{dt} = k_3[\text{X}] \quad (8)$$

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

$$[\text{CAT}]_t = [\text{PTSO}_2\text{NH}_2\text{Cl}^+] + [\text{PTSO}_2\text{NHCl}] + [\text{X}] \quad (9)$$

$$[\text{CAT}]_t = \frac{[\text{PTSO}_2\text{NHCl}][\text{H}^+]}{k_1} + \frac{[\text{X}]}{k_2[\text{CFT}]} + [\text{X}] \quad (10)$$

On solving for X,

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

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

The deduced rate law Eq.(12) agrees with the experimental results that a first, fractional and inverse fractional order dependence of reaction rate on $[\text{CAT}]_0$, $[\text{CFT}]_0$ and $[\text{H}^+]$ respectively.

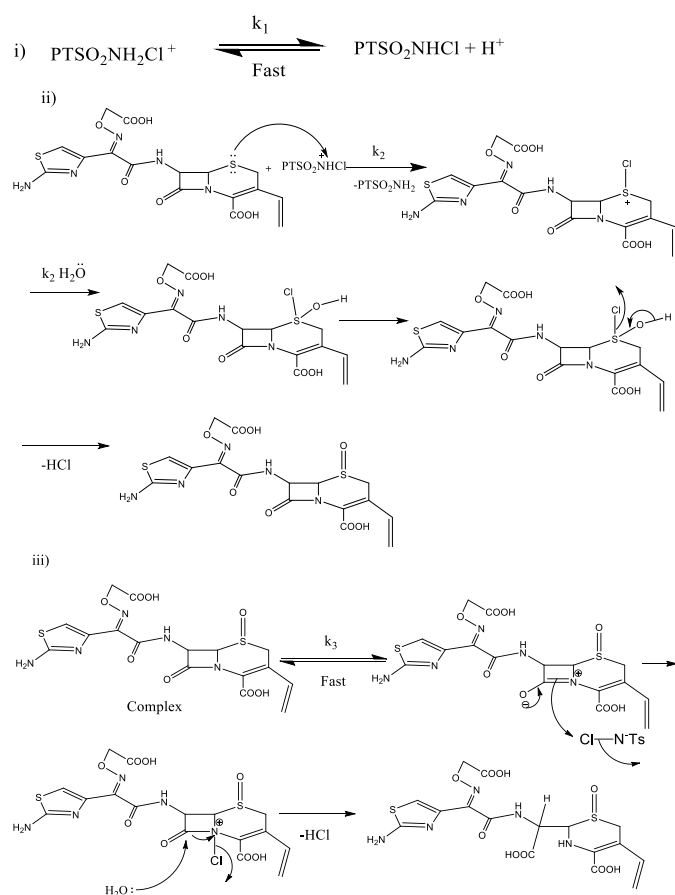
Since rate = $k^l [\text{CAT}]_0$, from Eq.(12), it can be rearranged as,

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

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

Considering Eqs.(13) and (14), indicates the linear plot of $1/k^l$ versus $1/[\text{CFT}]$ and $1/k^l$ versus $[\text{H}^+]$ were linear. From the slopes and intercepts the values of k_1, k_2, k_3 were calculated. Different proportions (0 – 40%, v/v) of methanol is added to influence the dielectric constant of the medium. The negative dielectric effect as seen from the plot of $\log k^l$ versus $1/D$ reveals the presence of dipole-dipole interaction in the reaction.

Addition of reduction product PTS fails to change the rate indicating its non- involvement in pre-equilibrium. From the plot k^l v/s $1/D$, indicates that the presence of dipole-dipole interaction in reaction and it was revealed by the negative dielectric effect. In the rate determining step on varying the ionic strength of the reaction medium, the rate remains unchanged, shows the involvement of the non-ionic species [20-24]. Halide ion concentration has slightly negative effect on the reaction rate. Further the computed thermodynamic parameters support the proposed mechanism. A large negative value of entropy of activation and moderate positive values of free energy of activation and entropy of activation indicates the formation of properly ordered compact transition state complex which has lesser degree of freedom.



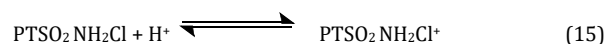
Scheme 2 Degradation mechanism of drug

<https://doi.org/10.30799/jpmr.063.25090101>

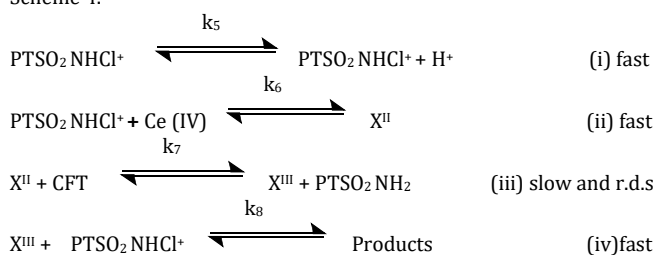
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3.10 Deduction of Rate Law and Mechanism in Presence of Catalyst

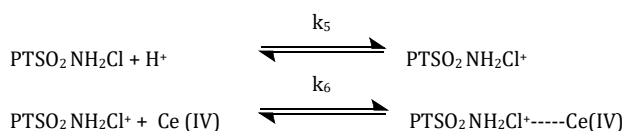
On the basis of kinetics information for the Ce (IV) metal catalyzed reaction oxidation of oxcarbapenem by chloramine-T in aqueous medium is similar to the uncatalyzed reaction with respect to stoichiometry. In the reaction rate chloramine-T follows first order dependence. The rate of reaction increases with increasing the concentration of substrate so it follows fractional order dependence. The rate of reaction increases with increasing the concentration of the Ce (IV) metal concentration, the order shows fractional dependence on the rate. The rate decreases while increasing the concentration of $[\text{H}^+]$ ion in the reaction medium. It indicates that rate of reaction the acid is inverse fractional order dependence. The dielectric permittivity of the medium on the rate of the reaction, the rate has been studied with varied dielectric constant (D) it shows that slightly positive slope. The entropy of the reaction is negative. The observed fractional order dependence with respect to $[\text{CFT}]$ apparently results from the complex formation between the substrate, CAT and the Ce (IV) metal catalyst in the pre-equilibrium step during the reaction course.



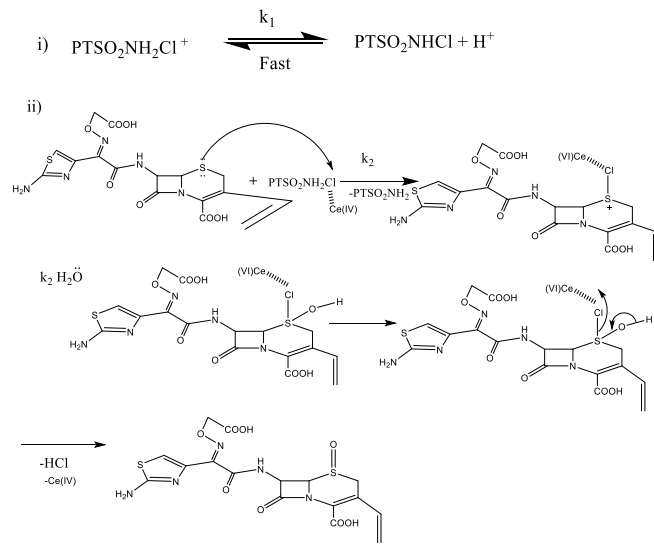
The retardation of rate by added H^+ ions manifest the protonation of $\text{PTSO}_2\text{NH}_2\text{Cl}$ leads to formation of protonated active oxidising species $\text{PTSO}_2\text{NH}_2\text{Cl}^+$. The view of experimental evidence to predict the reaction mechanism for the Ce (IV) metal catalyzed oxidation of CFT by CAT the following Scheme 3 is suggested. Let the $\text{PTSO}_2\text{NH}_2\text{Cl}$ indicates the active oxidant and substrate is represented by CFT. The CAT combine with the catalyst to form intermediate complex X^{II} . Prior to the rate determining step. After that the substrate CFT combines with the formed complex in the rate determined slow step to yield X^{III} and PTSO_2NH_2 complex with again regeneration of the Ce (IV) metal catalyst. After that the complex hydrolysis to yield products. The reaction mechanism is illustrated in the Scheme 4.



Scheme 3 Determination of rate determining step with catalyzed



3.11 Deduction of Rate law and Mechanism in the Presence of Catalyst



Scheme 4 Determination of Rate law and mechanism in the Presence of Catalyst

$$\text{The differential rate equation is } \frac{d[\text{CAT}]}{dt} = k_7[X^{II}] \quad (16)$$

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

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

$$k_5 = \frac{[\text{PTSO}_2\text{NH}_2\text{Cl}^+]}{[\text{PTSO}_2\text{NHCl}][\text{H}^+]} \quad \text{Or} \quad \text{PTSO}_2\text{NHCl} = \frac{[\text{PTSO}_2\text{NH}_2\text{Cl}^+]}{k_5[\text{H}^+]} \quad (18)$$

From Scheme 3,

$$k_6 = \frac{X^{II}}{[\text{PTSO}_2\text{NH}_2\text{Cl}^+][\text{Ce(IV)}]} \quad \text{or} \quad [\text{PTSO}_2\text{NH}_2\text{Cl}^+] = \frac{X^{II}}{k_6[\text{Ce(IV)}]} \quad (19)$$

By substituting for Eq.(17) from equation into one obtains,

$$\text{PTSO}_2\text{NH}_2\text{Cl}^+ = \frac{X^{II}}{k_5 k_6 [\text{Ce(IV)}][\text{H}^+]} \quad (20)$$

$$[\text{CAT}]_t = \frac{X^{II}}{k_5 k_6 [\text{Ce(IV)}][\text{H}^+]} + \frac{X^{II}}{k_6 [\text{Ce(IV)}]} + X^{II}$$

$$X^{II} = \frac{k_5 k_6 [\text{Ce(IV)}][\text{H}^+] [\text{CAT}]_t}{1 + k_5 k_6 [\text{H}^+] + k_5 k_6 [\text{Ce(IV)}][\text{H}^+]}$$

$$\text{Since rate is } \frac{-[\text{CAT}]_t}{dt} = k_7[X^{III}]$$

$$\text{Rate} = \frac{k_5 k_6 k_7 [\text{Ce(IV)}][\text{H}^+] [\text{CAT}]_t}{1 + k_5 [\text{H}^+] + k_5 k_6 [\text{Ce(IV)}][\text{H}^+]} \quad (21)$$

The deduced rate law is in good agreement with the experimental result
Since rate = $k^1 [\text{CAT}]_0$ Eq.(21) can be rearranged as

$$\text{Rate} = \frac{k_5 k_6 k_7 [\text{Ce(IV)}][\text{H}^+]}{1 + k_5 [\text{H}^+] + k_5 k_6 [\text{Ce(IV)}][\text{H}^+]} \quad (22)$$

$$\frac{1}{k_c} = \frac{1}{k_5 k_6 [\text{Ce(IV)}]} \left\{ \frac{1}{k_5 [\text{H}^+]} + 1 + \frac{1}{k_7} \right\} \quad (26)$$

From the Eqs.(25) and (26), indicates that the linear plot of $1/k$ versus $1/[\text{CFT}]$ and $1/k$ versus $1/[\text{H}^+]$. From the slopes and intercept the values of k_5 , k_6 , and k_7 were calculated.

Different proportions (0 – 40%, v/v) of methanol is added to influence the dielectric constant of the medium. The negative dielectric effect as seen from the plot of $\log k^1$ versus $1/D$ reveals the presence of dipole-dipole interaction in the reaction. Adding of reduction product PTS fails to change the rate indicating its non-involvement in pre-equilibrium. From the plot k^1 v/s $1/D$, indicates that the presence of dipole-dipole interaction in reaction and it was revealed by the negative dielectric effect [23].

In the rate determining step on varying the ionic strength of the reaction medium, the rate remains unchanged showing the involvement of the non-ionic species. Halide ions has slightly negative effect on the reaction rate. Further the computed thermodynamic parameters support the proposed mechanism. A large negative value of entropy of activation and moderate positive values of free energy of activation and entropy of activation indicates the formation of properly ordered compact transition state complex has lesser degree of freedom.

4. Conclusion

The cerium catalyzed and uncatalyzed oxidation of CFT-CAT redox reaction has been carried out in acidic medium. A 1:2 (equation) reaction stoichiometry for both catalyzed and uncatalyzed oxidation potency of CFT oxidation by CAT has investigated. The oxidation product was identified as (E)-2-((2-(2-aminothiothiazol-4-yl)-2-((caboxy methoxy) imino)acetamido)(carboxy)methyl)-5-vinyl-3,6-dihydro-2H-1,3-thiazine-4-carboxylic acid 1-oxide. The effect of halide ions and dielectric constant on the rate were observed. The thermodynamic parameters E_a , ΔH^\ddagger , ΔG^\ddagger and ΔS^\ddagger have been calculated from the Arrhenius plots by the observed

parameters. A mechanism consistent has been proposed and rate law was derived.

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