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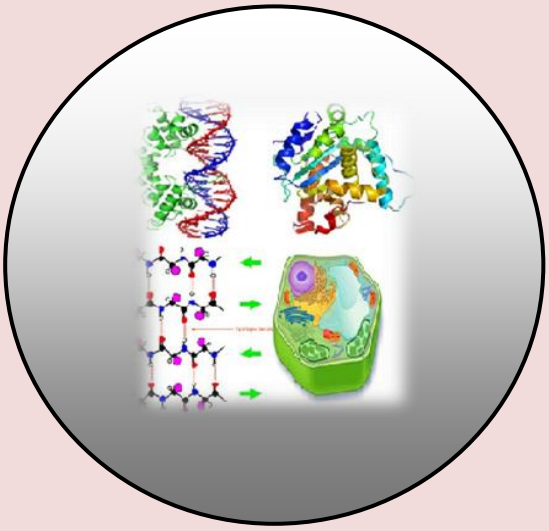

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RESEARCH PAPER

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Kinetics and Mechanistic Studies of Ru(Iii) Catalysed Oxidation of Antibiotic Drug Chloramphenicol by $Kbro_3$ in Acidic Medium

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ABSTRACT

The kinetics of oxidation of chloramphenicol by $KBrO_3$ has been investigated over the temperature range of 308-328 K. The reaction has been found to proceed quantitatively over a wide range of experimental conditions. Oxidation of this antibiotic involves four electron changes and the product of oxidation has been identified. Proposed oxidation reaction exhibits first order kinetics with respect to [$KBrO_3$]. The rate of reaction was found to be independent of the concentration of the substrate. The order dependence of rate on [H^+] suggests complex formation between $KBrO_3$ and [H^+]. The rate of reaction was found to be first order with respect to Ru(III) also. Thermodynamic parameters were evaluated. A suitable reaction scheme is proposed and appropriate rate law is derived to account for the observed kinetic data.

Keywords: Chloramphenicol, $KBrO_3$, Thermodynamic parameters and Ruthenium (III) catalysis.

INTRODUCTION

Transition metals are known to catalyze many redox reactions due to multiple oxidation states. Their higher oxidation states can be generally stabilized with unstable polydentate ligands. A great interest has been shown in using transition metals such as ruthenium, (Little et al. 2005) osmium, palladium and iridium either alone or as binary mixtures. Ruthenium catalysis in redox reactions involves different degrees of complexity, due to formation of different intermediate complexes and different oxidation states of ruthenium. Ruthenium (III) acts as a homogenous catalyst in the oxidation of many organic and inorganic substrates (Sirsalmath Kiran et al. 2006, Adejo et al. 2008). The unanalyzed reaction of oxidation of chloramphenicol and ruthenium (III) catalyzed reaction has been studied (Baralles, et al 2002, Veeraish et al. 2010).

Chloramphenicol undergoes hydrolysis in strong acidic and basic medium at elevated temperature (Gowda Ramachandrappa et al. 2012, Aftab Aslam et al. 2014). Chloramphenicol is effective against a wide variety of gram positive and gram negative bacteria, including anaerobic microorganisms. It is the first broad spectrum antibiotic drug, has been analyzed by spectrophotometric techniques (Singh Ajay et al.2009, Demappa et al. 2009). Aromatic sulphonyl monohaloamines have been used as versatile oxidizing agents (Gupta Madhu et al 2018). Oxidimetric estimation of chloramphenicol has been studied with aromatic sulphonyl monohaloamines (subrahmanayam et al. 2001) but no information has been found for its oxidation with $KBrO_3$using ruthenium (III) as catalyst.

Hence, the present investigation aimed to establish the reactivity of chloramphenicol towards chloramines-T in ruthenium (III) catalyzed reactions and to arrive at a plausible mechanism. The optimized structures of reactant and product [Fig. 1] are given as,

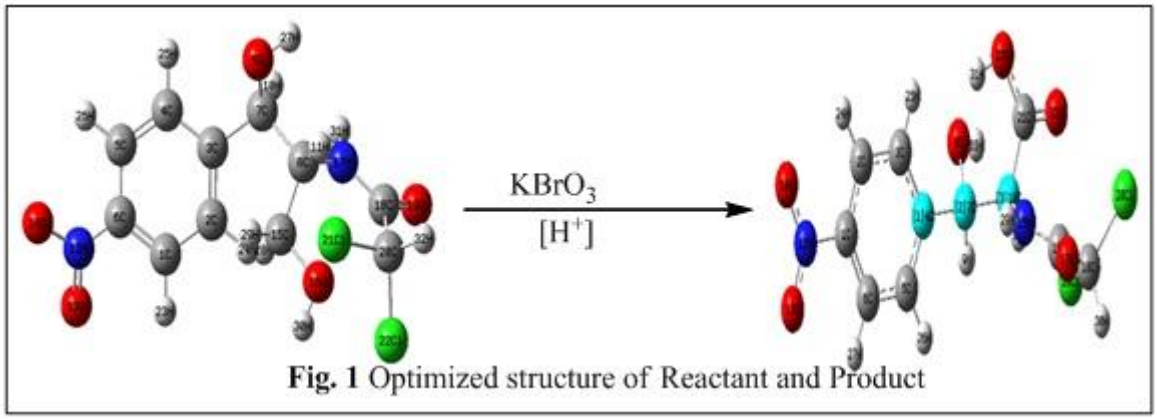


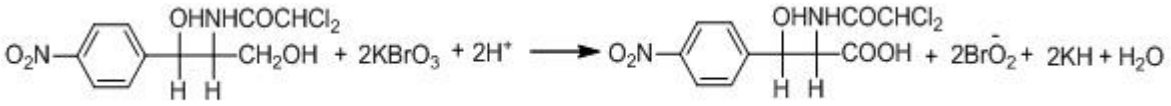
Fig. 1 Optimized structure of Reactant and Product

MATERIALS AND METHODS

A solution of Chloramphenicol (S.D. Fine Chemicals) was prepared by dissolving an appropriate amount in double distilled water. The purity was checked by its melting point i.e. 149°C (literature: 149-153°C). Analytical grade chemicals and double distilled water was used throughout the studies. The oxidation of chloramphenicol by $KBrO_3$ in the presence of Ru(III) catalyst was studied at 308 K. The reaction was initiated by mixing $KBrO_3$ with chloramphenicol solution which also contained required concentrations of $HClO_4$, KCl, $Hg(OAc)_2$ and Ru(III) as catalyst. The progress of the reaction was monitored iodometrically under suitable and desirable reaction conditions. The course of reaction was studied for at least up to seventy percent completion of the reaction. The oxidation of chloramphenicol with $KBrO_3$ is not feasible at pH 1-10. The oxidation was also very slow in aqueous solution and became appreciable only in presence of H^+ ions at higher temperature (Gupta Madhu et al.2019). Hence, detailed kinetic investigations of oxidation of chloramphenicol by $KBrO_3$ were made in presence of perchloric acid using Ru (III) as catalyst.

Stoichiometric and product analysis

Different sets of the reaction mixture in perchloric acid medium (with excess of Chloramphenicol) were kept for over 48 hrs at 313K, keeping other conditions constant. The determination of unconsumed $KBrO_3$ in the reaction mixture showed that 1 mole of chloramphenicol consumed 2 moles of $KBrO_3$. The observed Stoichiometry is shown as-



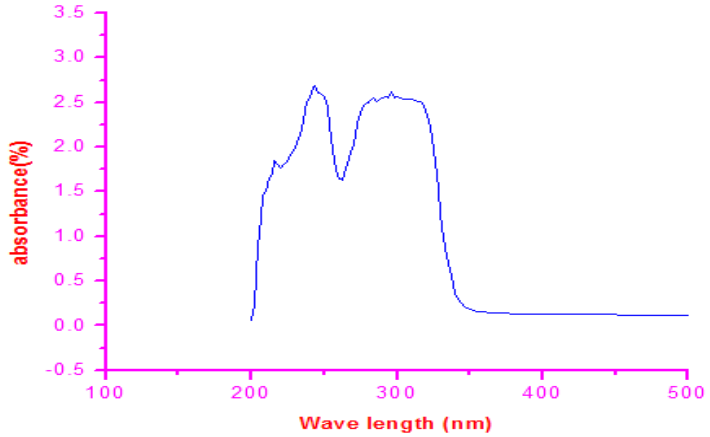


Figure 2. Experimental UV graph of Product.

After completion of the reaction, the reaction mixture was acidified, concentrated and extracted with ether. The ether layer was subjected to column chromatography and various fractions were used for spectral investigations (Kolachana et al. 2012). From the UV (Fig. 2) spectra, the main oxidation product was identified and confirmed.

RESULTS AND DISCUSSION

Reaction orders

The reaction orders have been determined by varying the concentrations of chloramphenicol, $KBrO_3$, H^+, Ruthenium, in turn by keeping the others constant.

Effect of [substrate]

The effect of Chloramphenicol was studied by varying it in the concentration range of 1.25×10^{3} - 10.00×10^{3} mol dm^{-3} keeping all other conditions and variables constant. The value of k_r remained constant (Table1) (Fig. 3) indicating zero order dependence of the reaction on chloramphenicol.

Table 1. Effect of variation of [$KBrO_3$] and Ru (III) on the reaction rate at 40°C.

[$KBro_3$]×10^3Mol dm^{-3}	Ru(lll)×10^6 Mol $dm^{-3}S^{-1}$	[Chloramphenicol]×10^3 M	(-dc/dt)× 10^7
1.25	1.0	1.96	1.6
1.60	1.0	1.96	2.0
2.00	1.0	1.96	2.6
2.50	1.0	1.96	3.0
3.33	1.0	1.96	3.5
5.00	1.0	1.96	5.0
1.0	1.0	1.96	2.0
1.0	2.0	1.96	4.0
1.0	2.5	1.96	5.75
1.0	3.0	1.96	8.15
1.0	4.0	1.96	10
1.0	5.0	1.96	12.05
1.0	1.0	1.25	0.14
1.0	1.0	2.9	0.13
1.0	1.0	3.5	0.14
1.0	1.0	4.5	0.16
1.0	1.0	6.25	0.13
1.0	1.0	10.0	0.14

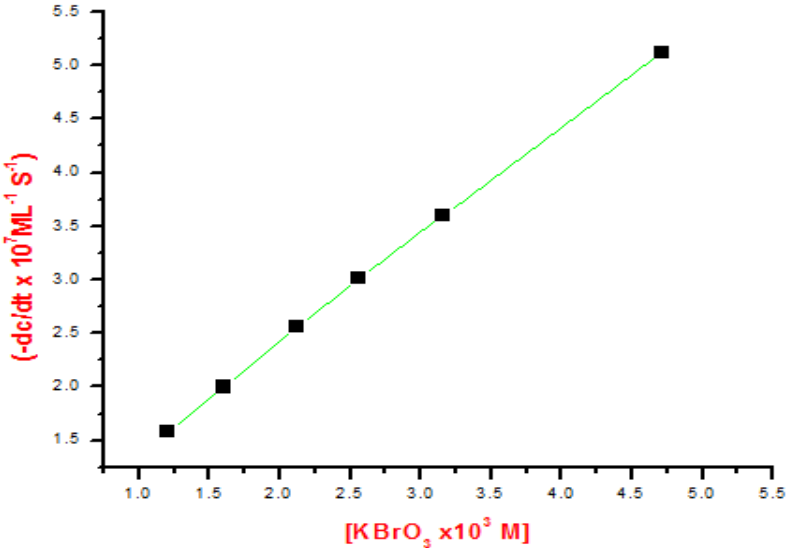


Figure 3. Plot between [$KBrO_3$] ×10^3M Vs (-dc/dt)×$10^7$$ML^{-1}S^{-1}$.

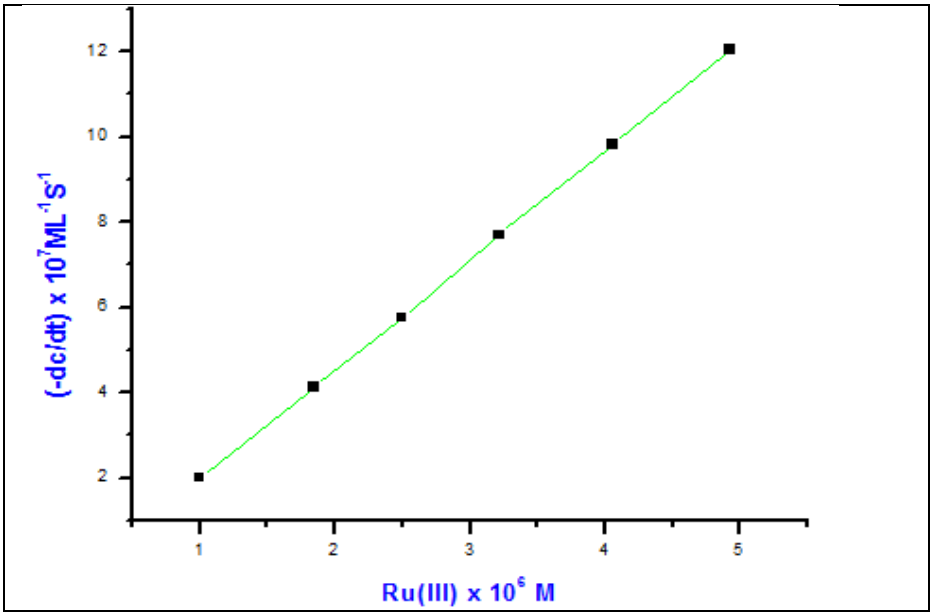


Figure 4. Plot between [Ru(III)×10⁶ ML⁻¹S⁻¹ and (-dc/dt)×10⁷ML⁻¹S⁻¹.

Table 2. Effect of $HClO_4$, KCI and $Hg(OAc)_2$ on the reaction rate at 40⁰C.

[$HClO_4$]×10³ Mol	[KCI] × 10³ Mol	[$Hg(OAc)_2$] ×10³ Mol	(-dc/dt) ×10⁷ ML⁻¹S⁻¹
1.66	1.0	1.0	2.50
2.0	1.0	1.0	2.51
2.5	1.0	1.0	2.51
3.33	1.0	1.0	2.50
5.0	1.0	1.0	2.63
10.0	1.0	1.0	2.53
1.0	1.25	1.0	2.60
1.0	1.66	1.0	2.55
1.0	2.0	1.0	2.56
1.0	3.3	1.0	2.60
1.0	5.0	1.0	2.57
1.0	5.5	1.0	2.57
1.0	1.0	1.0	2.58
1.0	1.0	2.0	2.56
1.0	1.0	3.0	2.55
1.0	1.0	4.0	2.57
1.0	1.0	5.0	2.56
1.0	1.0	6.0	2.56

Effect of [oxidant]

The oxidation concentration was varied in the range of 1.25 × 10^{-3}- 5.00 ×10^{-3} mol dm^{-3}.The fairly constant value of K indicates the order with respect to $KBrO_3$ is unity in Ru(III) catalyzed reactions (Table 1).

Effect of [Ru(III)]

The catalyst concentration was varied in the range of 1.00×10^{-6}- 5.00 × 10^{-6} mol dm^{-3}. The rate of reaction increased with increase in concentration of Ru (III) confirming first order dependence on it (Table 1) (Fig. 4).

Effect of ionic strength on the reaction rate

The ionic strength of the medium was varied by the addition of $NaClO_4$ (0.1 – 0.5 mol dm^{-3}). The rate of reaction was not changed confirming the involvement of non ionic species in the rate limiting step.

Effect of temperature on the rate of reaction

The value of k were evaluated at different temperatures and found to vary at different temperatures. Plot of log k versus 1/T was found to be linear and the values of activation parameters with reference to catalyst were computed and results are summarized in (Table 3), (Fig.5).

Table 3. Effect of temperature on the rate of reaction.

Parameters	Values
Ea (KJmol-1)	42.0
Log A	12.4
ΔS* ($K^{-1}Jmol^{-1}$)	-56.08
ΔH*($KJmol^{-1}$)	60.5
ΔG*(KJmol)	54.88

Table 4. Activation parameters.

1/T°K	(-dc/dt)× 10^4S^{-1}
33.0	0.5
32.4	1.5
31.9	3.4
31.4	5.6
30.9	8.4

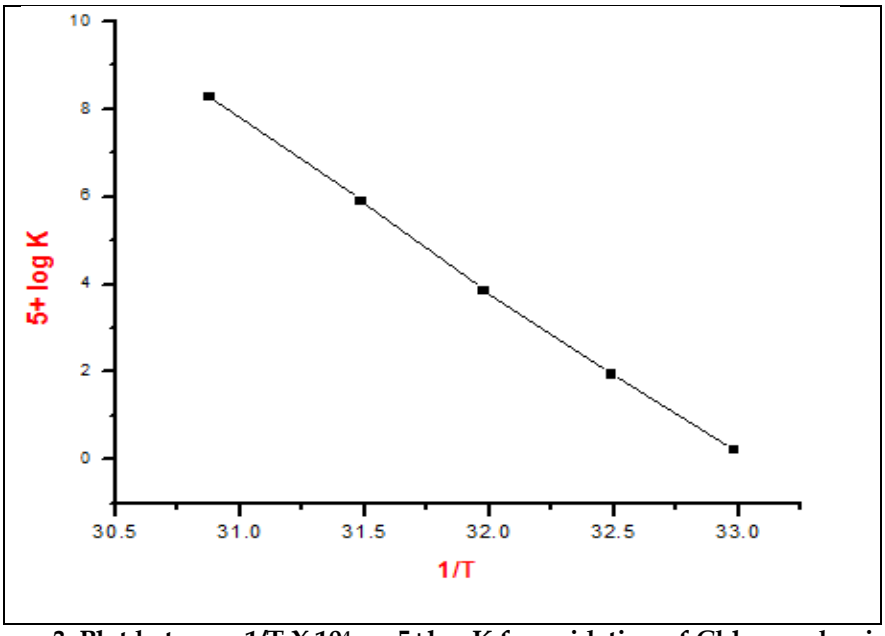
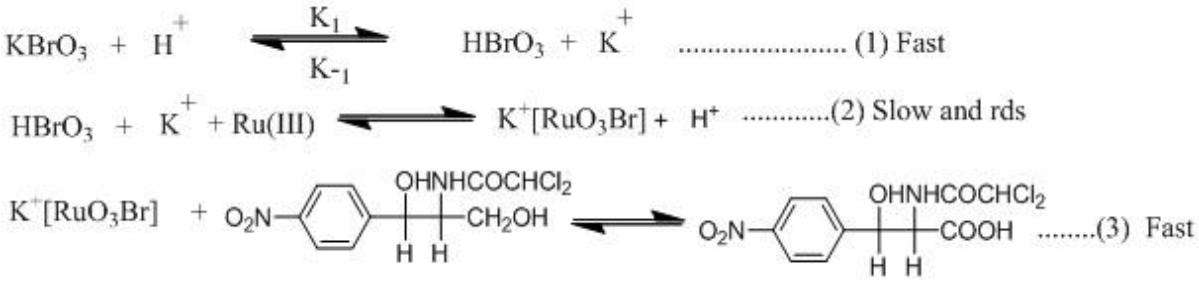


Figure 3. Plot between 1/T X 10^4 vs. 5+log K for oxidation of Chloramphenicol.

Mechanism and rate law

The concentration of each species depends upon the concentration of $KBrO_3$, the nature and pH of the medium the oxidant can exist in protonate from in an aqueous acidic solution. $KBrO_3$ ionizes in aqueous acidic medium as –



From the slow step the rate law can be written as –

$-\frac{d[KBrO_3]}{dt} = K_1[HBrO_3] + [Ru(III)]$ …….. (4)

The total effective concentration of $KBrO_3$ can be written as –

$[KBrO_3]_T = [KBrO_3] + [HBrO_3]$ …… (5)

From equation (1)

$$[KBrO_3]_T = \frac{[HBrO_3]}{K_1[H^+]}$$

By substituting for [CAT] in equation (5)

$[KBrO_3]_T = \frac{[HBrO_3]}{K_1[H^+]} + [HBrO_3]$

$[KBrO_3]_T = \frac{K_1[KBrO_3][H^+]}{1 + K_1[H^+]}$…….. (6)

By substituting for $[HBrO_3]$ from equation (5)

Rate $= -\frac{d[KBrO_3]}{dt} = \frac{K_1K_1[KBrO_3]_T[Ru(III)][H^+]}{1+K_1[H^+]}$

Reaction isotopic studies in heavy water indicated the increase in rate reaction.

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