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Comparative And Kinetic Investigation Of Oxidation Of 3-Methylindole By Potassium Bromate In Two Different Solvents

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Abstract
This study investigates the kinetics of 3-Methylindole oxidation by potassium bromate ($KBrO_3$) in aqueous ethanol and acetone media. The oxidation follows second-order kinetics first order with respect to both 3-Methylindole and $KBrO_3$. The reaction rate remains unaffected by added H^+, suggesting that the oxidation does not involve protonation-dependent pathways. Variation in ionic strength (μ) does not impact the reaction rate, indicating that charged intermediates may not play a significant role. Increasing the concentration of the solvent (ethanol or acetone) decreases the reaction rate, implying that the solvent polarity significantly influences the oxidation process. The absence of polymerization suggests a non-radical oxidation mechanism. IR and NMR spectral analysis confirm the oxidation product, the oxidation occurs faster in ethanol compared to acetone.
Keywords: *Kinetics, Mechanism, Oxidation, 3-Methylindole, Potassium bromate, Ethanol, Acetone.*

INTRODUCTION

3-Methylindole (C_9H_9N), commonly known as Skatole, is a naturally occurring indole derivative with a methyl ($-CH_3$) group at the 3-position of the indole ring. It is a white crystalline solid with a distinct fecal odor at high concentrations, but in low amounts, it contributes to floral and musky scents. 3-Methylindole itself may not be a strong therapeutic agent, its derivatives have shown promising antitumor, analgesic, anti-inflammatory, antimicrobial and biological activities [1-4]. The indole moiety plays a vital role in natural and synthetic bioactive compounds, making it a key structure in medicinal chemistry [5]. Skatole (3-Methylindole) is a metabolite produced during the microbial fermentation of the amino acid tryptophan in the rumen of cattle and other ruminants [6-7]. The oxidation of 3-methylindole to 3-Methyloxindole can be achieved through chemical, enzymatic, or microbial oxidation using agents like peracetic acid [8] and potassium bromated [9]. The oxidation of 3-Methylindole to Indole-3-Carboxaldehyde via Indole-3-Methanol is a microbial transformation carried out using Pseudomonas species [10]. This pathway involves enzymatic hydroxylation and oxidation reactions that selectively convert 3-Methylindole into valuable indole derivatives. The oxidation of Indole-3-Acetic Acid (IAA) by Peroxomonosulfate (PMS) in aqueous acetonitrile medium was carried out a radical-driven process involving hydroxyl and sulfate radicals [11]. The oxidation of indole by PMS follows pseudo-first or second-order kinetics and is influenced by various solvent (ethanol, acetonitrile and acetone) and various temperature investigated [12-16]. This work and is presented as a first report in this study of the oxidation of 3-Methylindole by potassium bromate in two different solvent (ethanol and acetone) highlights the significant influence of solvent polarity on reaction kinetics and mechanism.

EXPERIMENTAL

Materials and methods

3-Methylindole (3-MI) or Skatole (Sigma Alrdich) was Analytical grade, used as the substrate. Potassium bromate ($KBrO_3$) (E. Merck. AR. Grade) wad a oxidant, prepared in deionizer water and It has an assay value of at least 99.9%. Potassium Iodide (KI) was used for iodometric titration. Sulfuric Acid (H_2SO_4) (Acidic medium for reaction and titration), Starch Solution (Indicator for iodometric titration), Sodium Thiosulfate ($Na_2S_2O_3$) (Titration for determining unreacted bromated), Ethanol and Acetone (Solvents used to compare the reaction in different media), Sodium per chlorate ($NaClO_4$) was used to maintain the ionic strength, Mercuric acetate (E. Merck) and used were of analytical grade with 99.9% purity and Deionised water was used for reagent preparation. The kinetics and mechanism of 3-Methylindole oxidation by $KBrO_3$ were systematically studied by varying substrate, oxidant, solvent, [H^+], and ionic strength. The reaction followed pseudo-first-order or second-order kinetics, depending on reactant concentrations.

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Kinetic studies

The required volume of all reagents, including the 3-Methylindole (substrate), solvent, and acidic medium, was maintained at a constant temperature between 293–308 K to establish equilibrium. A pre-thermostated solution of potassium bromate ($KBrO_3$) was prepared separately and rapidly added to the reaction mixture to initiate oxidation. The progress of the oxidation reaction was followed iodometrically, using starch as an indicator. Aliquots of the reaction mixture were withdrawn at different time intervals and assayed for unreacted $KBrO_3$. The unused bromate was determined by titration with potassium iodide (KI) in an acidic solution, following the reaction:

$$BrO_3^- + 6I^- + 6H^+ \rightarrow Br^- + 3I_2 + 3H_2O\ (l)$$

The liberated iodine (I_2) was titrated with sodium thiosulfate ($Na_2S_2O_3$) until the disappearance of the blue starch-iodine complex. The rate of oxidation was determined by measuring the decrease in bromate concentration over time. The reaction followed pseudo-first-order kinetics under excess bromate conditions, with the rate equation.

RESULTS AND DISCUSSION

Factors influencing the rate of oxidation of [3-Methylindole] by oxidants such as effects of (i) [3-MI], (ii) [Oxidants], (iii) Ionic strength (μ), (iv) $[H^+]$, and (v) Dielectric constant have been studied. Rate and activation parameters were evaluated.

Effect of $[\text{3-Methylindole}]_0$

Kinetic runs were conducted at 303 K, maintaining constant concentrations of oxidant ($KBrO_3$), Acid concentration ($[H^+]$), Ionic strength (μ), Solvent composition (Ethanol and Acetone) and The concentration of 3-Methylindole (3-MI) was varied within the range (2.0×10^{-2} – 4.0×10^{-2} mol dm^{-3}). The pseudo-first-order rate constant (k') increased with an increase in [3-MI]. The linear relationship between k' and [3-MI] confirmed first-order dependence on [3-MI]. Linear Plots of k' vs. [3-MI] (Fig. 3 & 4 Table 2 & 3) passing through the origin (r = 0.998) (Fig.3 & 4). Such a kinetic behaviour indicate no self-decomposition of $KBrO_3$ in the reaction system. The rate constant k' (s^{-1}) was obtained from kinetic measurements. The second-order rate constant k_2 (mol^{-1} dm^3 s^{-1}) was calculated from the slope of $k'(s^{-1})$ / [3-MI] . Experiments were conducted at different temperatures (293 K – 308 K) to study the temperature dependence.

Effect of [Oxidants]

It is observed that the reaction rate was unaffected as evident from the constant slopes of log $[KBrO_3]$ Vs time plots for various $[KBrO_3]$ (1×10^{-2} – 5×10^{-2} mol dm^{-3}) at fixed [3-MI], $[H^+]$, μ, and percentage of ethanol and acetone (Table 2 & 3). This observation confirms the first-order dependence of rate on $[KBrO_3]$.

Effect of μ

The influence of ionic strength (μ) maintained by the addition of Sodium per chlorate (1×10^{-1} – 5×10^{-1} mol dm^{-3}) on the reaction rate was found to be negligible (Table 2 & 3). This shows that the reaction occurs between a neutral species namely the 3-Methylindole molecule and the negative ion (for $KBrO_3$ mononegative ion BrO_3^-), the active species of the oxidants.

Effect of [H+]

The reaction rates measured at constant [3-MI], $[KBrO_3]$, μ, and percentage of solvent (Ethanol and Acetone) but with various $[H^+]$ (0.5×10^{-2} – 9×10^{-2} mol dm—3) were found to be the same (Table 2 & 3). Such a kinetic behaviour indicates the nonexistence of any protonation equilibrium with respect to both oxidants and 3-Methylindole under the present experimental conditions employed.

Effect of Dielectric Constant

The reaction rate increased with a decrease in the percentage of organic solvents (ethanol or acetone) in the aqueous medium. This indicates that an increase in the dielectric constant (polarity) of the medium enhances the reaction rate. As the dielectric constant increases, solvent polarity increases (3-Methylindole neutral molecule and Bromate ion mononegative ion). The rate enhancement suggests the formation of a highly polar activated complex, which is more polar than the reactants. This indicates an ionic mechanism involving charge development in the transition state. The more negative the $\Delta S^\#$ (entropy of activation), the greater the electrostriction due to increased charge concentration in the transition state. As the concentration of organic solvents (ethanol and acetone) decreases, $\Delta S^\#$ becomes more negative, confirming greater charge development in the activated complex.

Stoichiometry

A solution of 3-Methylindole (3-MI) with an excess of potassium bromate ($KBrO_3$) was prepared and allowed to react overnight at room temperature to ensure complete reaction. The remaining oxidant was determined titrimetrically, and the amount of oxidant consumed was calculated. Assuming that all the 3-MI was completely oxidized, the molar ratio of 3-MI to $KBrO_3$ was found to be 1:2.

Test for Free Radical Intermediates

A freshly distilled acrylonitrile monomer was added to a deaerated reaction mixture to check for free radical formation. If free radical intermediates were involved, they would initiate polymerization of acrylonitrile, forming a polymeric precipitate. In our observation was no polymer formation was detected, suggesting that free radical intermediates [17] are absent in this reaction.

Rate Law

In accordance with the above observations, the rate of disappearance of Br(V) (potassium bromate) is given by

$-d[Br\ (V)] / dt = k_2\ [Br\ (V)][3\text{-MI}]$

rate / $[Br\ (V)] = k'\ (s\text{-}1) = k_2[3\text{-MI}]$

$k' = k_2\ [3\text{-MI}]$

where k' is the pseudo first order rate constant ($mol^{-1}\ dm^3\ s^{-1}$)

By plotting k' vs. [3-MI], a straight line passing through the origin confirms the first-order dependence on 3-Methylindole. The slope of this plot gives the second-order rate constant (k_2).

Product Analysis

Reaction mixtures were prepared using of slight excess of oxidant(0.125 mol dm^{-3}) of $KBrO_3$ and 3-Methylindole (0.06 mol dm^{-3}), using solvent systems(Ethanol or Acetone), Other additives are maintained as in kinetic studies. The reaction was allowed to proceed at room temperature for 48 hours to ensure complete oxidation. Thin Layer Chromatography (TLC) was performed to confirm the disappearance of 3-Methylindole and the formation of new products. The remaining reaction mixture was poured into doubly distilled water to precipitate the product. The solid residue obtained was filtered, washed thoroughly to remove unreached components and dried for analysis.

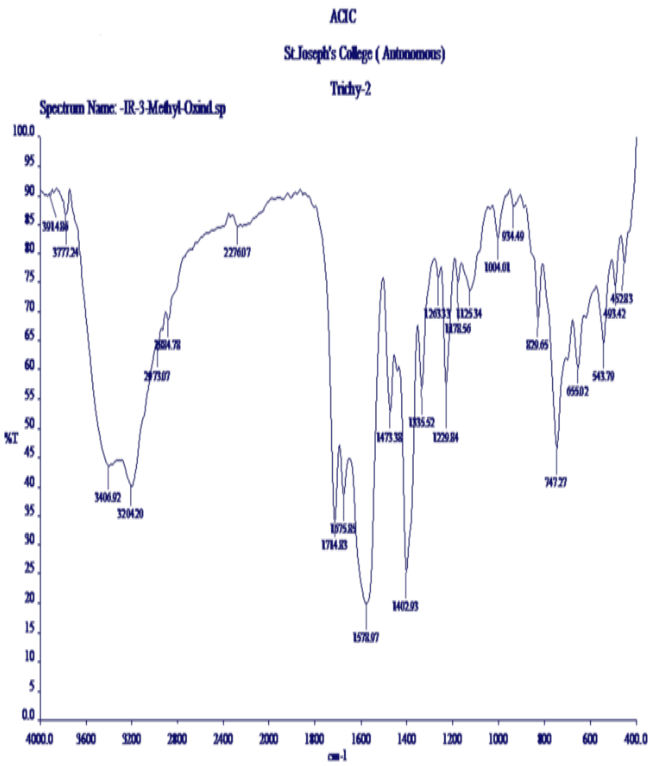

Fig. 1. FT-IR spectrum of product

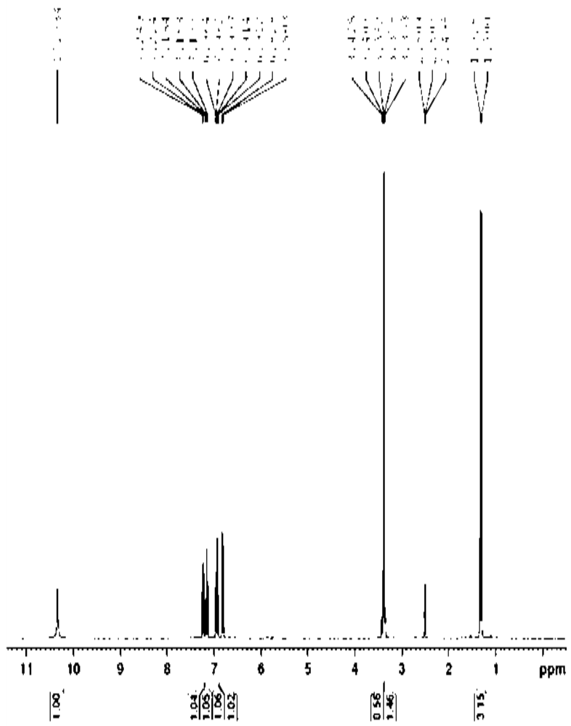

Fig. 2. NMR- spectrum of product

The identity of the product was further confirmed from its FT-IR spectra (Fig .I) and HMNR (Fig .II). FT-IR (KBr) 3406, 1714 and 1675 cm-1, HNMR (DMSO) ppm = 6.0 - 8.0 (m, 5H, ArH, NH), 3.3 (S, 3H, C-H).

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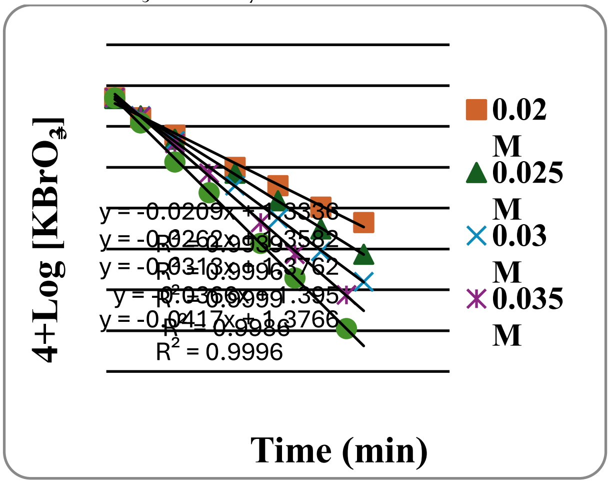
Rate and Activation Parameters

The effect of temperature on k' (s^{-1}) was studied in in the temperature range 293–308 K in both ethanol and acetone solvent systems. The rate constants (k', s^{-1}) at different temperatures were recorded in Table 2 (ethanol) and Table 3 (acetone). The Arrhenius plot of log k_2 vs 1/T was linear (Fig.5). From the above plot, the values of energy of activation (*E*a) was calculated (Table 4 Fig. 5).

The large negative value of entropy of activation ($\Delta S^{\#}$) suggests high solvent organization around the transition state. This supports the idea that the transition state involves a more ordered, polar structure, restricting solvent movement The value of $\Delta S^{\#}$ was computed from Eyring equation. All thermodynamic parameters (Ea, $\Delta H^{\#}$, $\Delta S^{\#}$ $\Delta G^{\#}$) are summarized in Table 4.

Fig.3.Variation of [3-MI] @ 303 K

3-MI-KBrO$_3$-EtOH system **3-MI-KBrO$_3$-AC system**



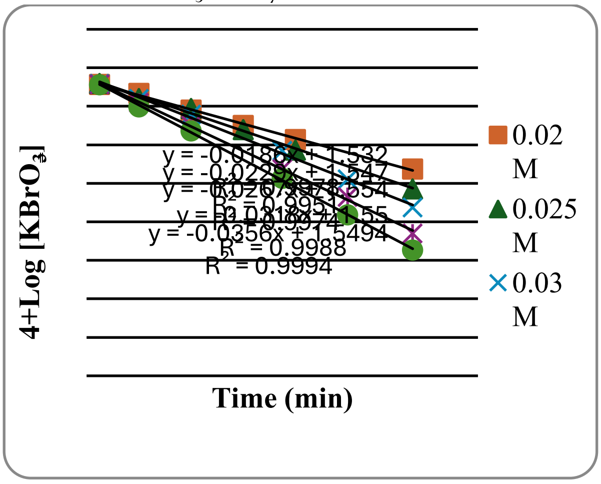
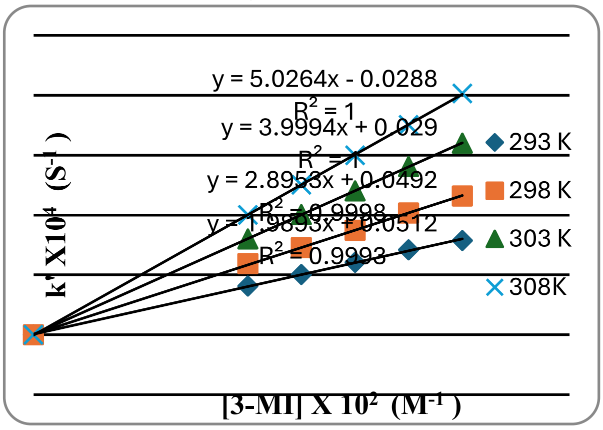


Fig. 4. Evaluation of k_2

3-MI-KBrO$_3$-EtOH system **3-MI-KBrO$_3$-AC system**



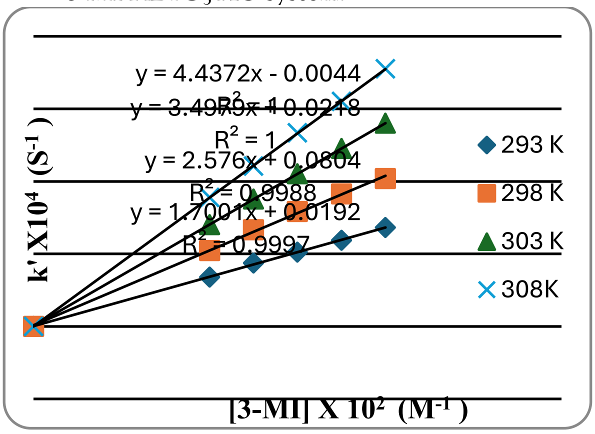


Table 1. Effect of temperature on the reaction rate

Temp (K)	k_2 (103 , s−1)	
	Ethanol Solvent	Acetone Solvent
293	2.01428	1.70926
298	2.92026	2.61425
303	4.01815	3.50550
308	5.01257	4.43452

Table 2. Pseudo-First Order Rate Constant for the oxidation of 3-MI by KBrO$_3$ in Ethanol Solvent

[3-MI] X10^2 (mol dm−3)	[KBrO$_3$] X10^3 (mol dm−3)	[H$^+$] (mol dm−3)	[μ] (mol dm−3)	EtOH % (v/v)	k' (104 s−1) 293 K	298 K	303 K	308K
2.0	2.0	0.02	0.3	50	4.08	5.95	8.01	10.01
2.5	2.0	0.02	0.3	50	5.04	7.27	10.05	12.52
3.0	2.0	0.02	0.3	50	6.05	8.72	12.01	15.00
3.5	2.0	0.02	0.3	50	7.09	10.17	14.04	17.52

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4.0	2.0	0.02	0.3	50	7.87	11.59	16.01	20.16
3.0	1.0	0.02	0.3	50	-	-	12.44	-
3.0	1.5	0.02	0.3	50	-	-	12.55	-
3.0	2.0	0.02	0.3	50	-	-	12.01	-
3.0	4.0	0.02	0.3	50	-	-	12.02	-
3.0	5.0	0.02	0.3	50	-	-	12.15	-
3.0	2.0	0.005	0.3	50	-	-	12.54	-
3.0	2.0	0.02	0.3	50	-	-	12.01	-
3.0	2.0	0.05	0.3	50	-	-	12.26	-
3.0	2.0	0.09	0.3	50	-	-	12.28	-
3.0	2.0	0.02	0.1	50	-	-	12.14	-
3.0	2.0	0.02	0.2	50	-	-	12.37	-
3.0	2.0	0.02	0.3	50	-	-	12.01	-
3.0	2.0	0.02	0.5	50	-	-	12.22	-
3.0	2.0	0.02	0.3	40	12.00	16.11	20.19	25.43
3.0	2.0	0.02	0.3	45	9.87	12.61	16.06	21.14
3.0	2.0	0.02	0.3	50	6.81	8.01	12.01	17.82
3.0	2.0	0.02	0.3	55	3.18	4.21	8.12	13.61
3.0	2.0	0.02	0.3	60	0.98	1.61	4.46	9.881

Table 3. Pseudo-First Order Rate Constant for the oxidation of 3-MI by $KBrO_3$ in Acetone Solvent

[3-MI] X10^2 (mol dm−3)	[$KBrO_3$]X10^3 (mol dm−3)	[H^+] (mol dm−3)	[μ] (mol dm−3)	Acetone % (v/v)	*k'* (104 s−1) 293 K	298 K	303 K	308K
2.0	2.0	0.02	0.3	50	3.41	5.22	7.00	8.88
2.5	2.0	0.02	0.3	50	4.35	6.65	8.78	11.04
3.0	2.0	0.02	0.3	50	5.11	7.92	10.51	13.33
3.5	2.0	0.02	0.3	50	5.93	9.13	12.27	15.50
4.0	2.0	0.02	0.3	50	6.80	10.18	14.01	17.76
3.0	1.0	0.02	0.3	50	-	-	10.54	-
3.0	2.0	0.02	0.3	50	-	-	10.51	-
3.0	3.0	0.02	0.3	50	-	-	10.47	-
3.0	4.0	0.02	0.3	50	-	-	10.46	-
3.0	5.0	0.02	0.3	50	-	-	10.11	-
3.0	2.0	0.005	0.3	50	-	-	10.46	-
3.0	2.0	0.02	0.3	50	-	-	10.51	-
3.0	2.0	0.05	0.3	50	-	-	10.48	-
3.0	2.0	0.09	0.3	50	-	-	10.44	-
3.0	2.0	0.02	0.1	50	-	-	10.52	-
3.0	2.0	0.02	0.2	50	-	-	10.82	-
3.0	2.0	0.02	0.3	50	-	-	10.51	-
3.0	2.0	0.02	0.5	50	-	-	10.20	-
3.0	2.0	0.02	0.3	40	12.88	15.10	17.64	19.33
3.0	2.0	0.02	0.3	45	9.98	11.82	13.60	15.21
3.0	2.0	0.02	0.3	50	6.28	8.14	10.51	12.95
3.0	2.0	0.02	0.3	55	3.14	5.61	8.24	10.62
3.0	2.0	0.02	0.3	60	1.84	2.98	5.60	7.74

Fig. 5. Evaluation of Ea for Ethanol and Acetone solvent System

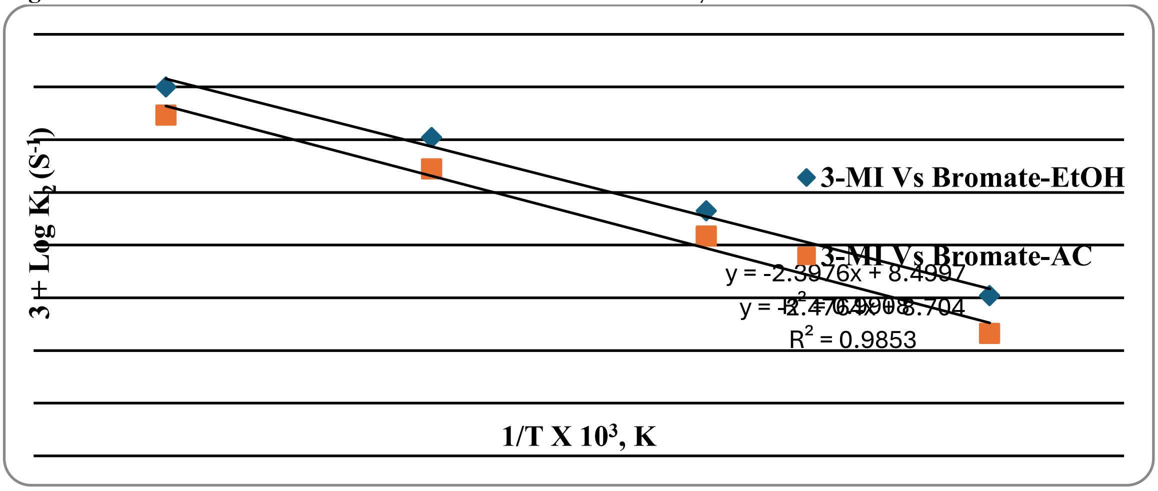
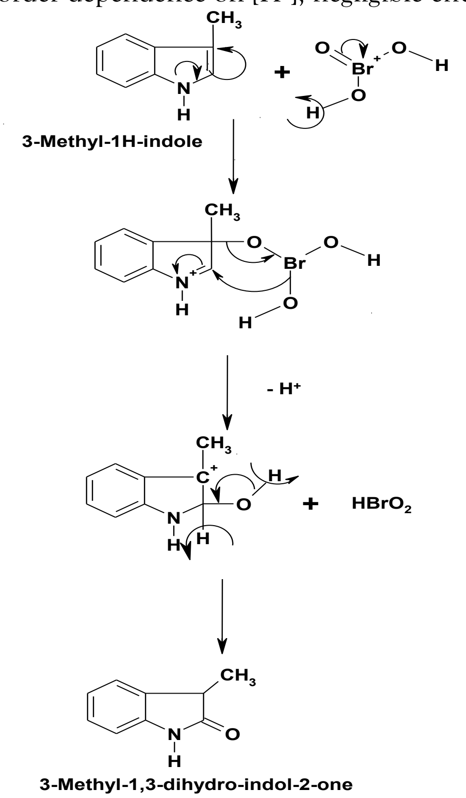


Table 4. Thermodynamic parameters

Thermodynamic parameters of Oxidation of 3-MI vs $KBrO_3$ in two solvent	Activation Parameters	
	Ethanol	Acetone
Energy of Activation (Ea) kJmol-1	53.7387	47.4134
Enthalpy (ΔH#) kJ mol-1	51.2195	44.8962
Entropy (ΔS#) J K-1 mol-1	-284.4568	-284.3994
Free Energy (ΔG#) kJ mol-1	137.4099	131.0692

Mechanism

Based on the foregoing observations such as first-order dependence of rate each on [3-MI], [$KBrO_3$], zero-order dependence on [H^+], negligible effect of [μ], and the stoichiometry, the following mechanism is suggested:



In acidic medium, potassium bromate ($KBrO_3$) forms bromic acid ($HBrO_3$), which further undergoes protonation. The $H_2BrO_3^+$ species acts as an electrophile, facilitating electrophilic attack on 3-Methylindole. The C-3 position of 3-MI is highly nucleophilic due to the electron-releasing methyl (-CH_3) group. $H_2BrO_3^+$ attacks C-3, leading to the formation of a bromated ester intermediate [18]. This step involves a nucleophilic displacement of the bromate ion. The bromated ester undergoes hydrolysis, leading to the formation of 3-Methyloxindole: $HBrO_2$ can further decompose into Br^- and oxygenated species, completing the reaction cycle.

The methyl group at C-3 increases electron density, enhancing the nucleophilicity of the indole ring. This makes C-3 more reactive towards electrophilic attack, accelerating the reaction compared to unsubstituted indole.

CONCLUSION

The reaction is faster in ethanol than in acetone due to better solvation of transition states and stronger radical formation. The rate constant (k') is higher in ethanol, confirming the role of solvent polarity in oxidation kinetics. Activation energy is lower in ethanol, making the reaction more favorable. The mechanism was supported by the observed rate laws, follows first order with respect to 3-Methylindole and $KBrO_3$ and overall follows second order reaction.

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