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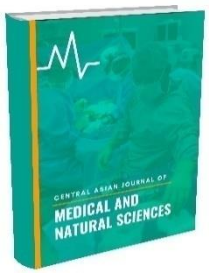

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OXIDATION OF N-ACETYL ALANINE BY CHLORAMINE-T IN PRESENCE OF HYDROCHLORIC ACID: A KINETIC AND MECHANISTIC STUDY

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Abstract: The purpose of this work is to examine the mechanism and kinetics of N-acetyl alanine oxidation by Chloramine-T (CAT) in a hydrochloric acid medium at temperatures between 30 and 50 degrees Celsius. First-order kinetic dependency on both the oxidant [CAT] and [H+] is indicated by the experimental results. On the other hand, there is zero-order dependence on the substrate reactant [S] and chloride ion [Cl-]. The reaction is barely impacted by the medium's ionic strength. The reaction between N-acetyl alanine and Chloramine-T shows a 1:1 stoichiometry in the acidic media. To find the activation parameters, the reaction was examined at five different temperatures, ranging from 30°C to 50°C. Spectroscopic analysis revealed that the ultimate oxidation product of N-acetyl Alanine was N-chloro acetyl Alanine.

Key words: Chloramine-T, N-acetyl Alanine, kinetic, oxidation, Mechanistic.

Introduction:

Sodium N-chloro-4-methylbenzenesulphonamide, or CAT (RNClNa), is another name for chloramine-T, which is expressed as P-CH_3-$C_6H_5SO_2NCl$. Na.$3H_2O$. In both acidic and alkaline conditions, it functions as an oxidizing agent. CAT changes by two electrons during its reactions, resulting in the production of sodium chloride and p-toluenesulphonamide (p-TSA; RNH_2). The pH of the media affects the CAT/RNH_2 pair's reduction potential. (A. R. V. Murthy and B. S. Rao., 1952), diminishing as the pH rises. For example, at pH 0.65 and pH 12, the potential value is 1.14V and 0.5V, respectively. An analysis (M. M. Campbell and G. Johnson., 1978) A number of potential active species in different media are noted in the chapter on chloramine-T chemistry. These include, in acidic solutions, CAT, RNHCl, DCT (dichloramine-T), and HOCl; in alkaline conditions, RNCl and OCl^-ions are mentioned. Chloramine-T has been used to investigate several chemical and inorganic substances, although there haven't been many kinetic investigations using this reagent. One notable difference is the way hydrogen peroxide breaks down. (J. Coull, H. et al., 1935) in HCl presence, oxidation of cyanide(D. S. Mahadevappa and B. T. Gowda., 1979), thiocyanates, sulphoxides(M. S. Ahmed. et .,al 1980), α-hydroxyl acids, hydroxylamines, primary and secondary alcohols, p-cresols, phenols(Nayak, Y. N. et. al., 2022) (Liu, R. et.

al., 2022) (Sowmya, P. T. et. al., 2021), aliphatic aldehydes, ketones, and amino acids (Malini, S. et. al., 2023) (Haydari, A. et. al., 2023) using chloramine-T. Chlorination reactions involving compounds like dialdo-galactose (Zhao, K. et. al., 2023), 1,3,4-oxadiazole (Liu, Y. et. al., 2023), peptides (Morjan, R. Y., 2023), radiolabeled antibodies (Vallabhajosula, S., 2023), P-Nitroaniline & Sulfanilic Acid Sodium Salt(Vallabhajosula, S., 2023) (Al-Niemi, H., & Mahmoud, M., 2023) (Sengupta, P., 2023) (Pareek, D. et. al., 2023) (Pareek, D. et. al., 2023), and water modifications for COVID-19(Curling, E. A. et. al., 2022) (Mahmoud D. Abdulrahman et. al., 2022) (Zhang, A. et. al., 2022) (Elardo, N. et. al., 2022) (Mohammed I. Jameel et. al., 2022) treatment have also been studied. This work aims to examine the mechanistic pathway of N-acetyl Alanine chlorination in an acidic medium.

Experimental:

Using cm^{-1} quartz ces, absorbance was measured with a CECIL CE 1011 spectrophotometer from the 1000 SERIES. Throughout the studies, the required temperature was controlled and maintained using a Digital EYELA Water Bath SB-11.

Materials:

Morris's approach was used to manufacture and purify chloramine-T. (Mohammed I. Jameel. et .,al 2022). The iodometric method was then used to standardize its aqueous solution. All other reagents, including N-acetyl Alanine, were analytical grade and came from Fluka. A strong sodium perchlorate solution was used to keep the ionic strength of the reaction mixture high.

Kinetic Measurements:

The kinetic investigations were methodically carried out at 30°C. A notable excess of N-acetyl Alanine [N-AA] over [CAT] was maintained in order to guarantee pseudo-first order requirements. Carefully mixing the necessary amounts of [N-AA], $NaClO_3$, HCl, ethanol, and water resulted in the reaction mixture. This made guaranteed that the overall volume was the same for every experiment run. The mixture was put into a Pyrex boiling tube with a glass stopper, and it was thermostatically stabilized at 303 K.

A pre-measured volume of the [CAT] solution, which had already been thermostated at 303K, was quickly added to the mixture to start the reaction. Samples were frequently extracted in order to track the reaction's development. Following that, these samples were promptly placed in a volumetric flask that had been calibrated, containing 5% potassium iodide, 2M sulfuric acid, and water as the quenching solution. Following this reaction, the freed iodine was measured spectrophotometrically at a wavelength of 353 nm. as described in reference(A. I. Vogel, 1978). Through monitoring the reaction for a period of time that included its final two half-lives, the pseudo-first order rate constant, k_1, could be established. The logarithm of [CAT] concentration was plotted against time to achieve this, and the slope of this plot produced the required k_1 value.

Results:

In an acidic medium, the kinetics of [N-AA] oxidation by [CAT] were fully studied at different reactant starting concentrations. Plotting log [CAT] versus time revealed a linear relationship that maintained a constant acid content and guaranteed a significant excess of substrate, as shown by the correlation coefficient ($R^2 > 0.9927$). shown in Figure 1.

Table 1 provides further details on the pseudo-first order constants (k_1) that relate to the rate's dependency on [CAT]. It's interesting to note that changes in k_1 did not change significantly when [N-AA] concentrations increased, indicating that the [N-AA] concentration had no effect on the reaction rate.

Additionally, the behavior of the reaction was examined in relation to various HCl concentrations. Table 2 shows that the reaction rate increased in tandem with the increase in [H+] concentration. With [Cl^-] held constant, a

graph of log k_1 against log $[H^+]$ showed a unitary slope and a linear trend ($R^2 > 0.9626$).

An alternative study approach examined the reaction in various aqueous ethanol compositions. The rate also rose as the amount of ethanol increased. Table 3: Log k_1 plotted against the dielectric constant (1/D) of the medium, as reported in the literature (G. Akerlof, 1932) (Mohammad G. Faraj. et. al., 2022), An advantageous link with ion-dipole interactions was shown by the distinct linear relationship with a positive slope. Table 4 demonstrates that there was no appreciable change in the pace of reaction when sodium perchlorate was added to the medium to increase its ionic strength from 0.03125 M to 0.15625 M. Moreover, introducing the reaction product, p-toluene sulphonamide [p-TSA], up to a concentration of 0.0025 M had a very small effect on the rate constant k_1. Table 4.

Finally, the temperature sensitivity of the reaction was examined throughout a (303–323)K range. Table 5 provides the pseudo-first order rate constants and activation parameters for the oxidation of [N-AV] by [CAT], based on the Arrhenius plot of log k1 against temperature reciprocal (1/T) in Figure 2.

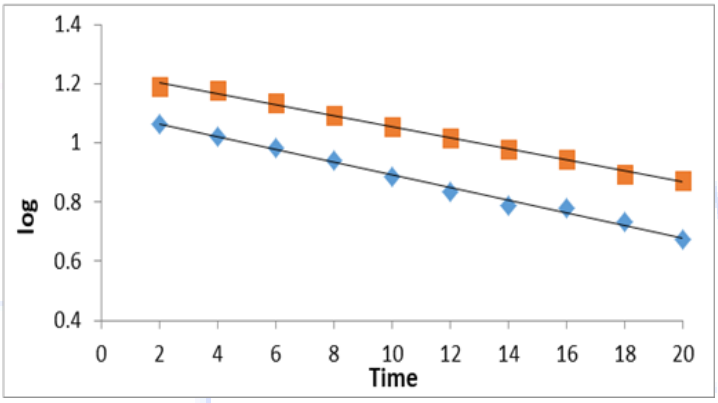


Figure 1: plot of log [CAT] VS Time

[N-AA]= 0.2M ; [HCl]= 1M ; μ= 0.0625 M ; 35 % ethanol ; temp=303°K

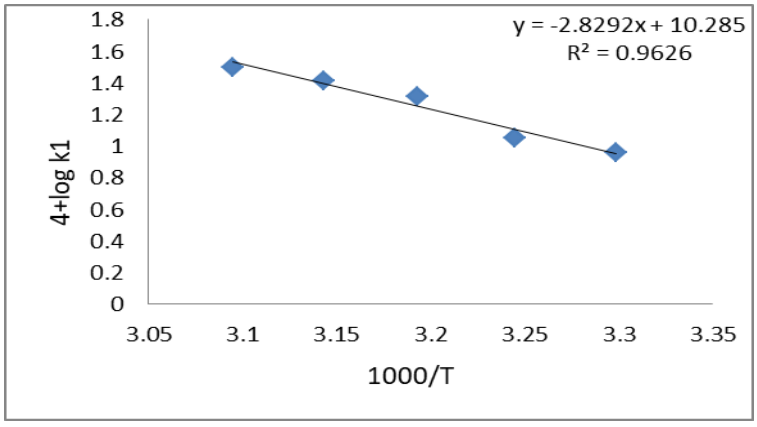


Figure 2: plot of 3+log k1 VS 1/T

[N-AA]= 0.2M ; [CAT]= 0.01M ; [HCl]= 1M ; μ= 0.0625 M ; 35 % ethanol

Table 1: effect of varying reactant concentration on rate of oxidation of N-AA by chloramine – T in acid mediam at 30°C; [HCl]=1 M; μ=0.0625 M; 35% ethanol

10^3[CAT] M	10^3[N-AA] M	$10^4 k_1 Sec^{-1}$
1.25	10.00	8.6172
1.50	10.00	7.4927
1.75	10.00	7.1138
2.00	10.00	6.4685
2.25	10.00	6.0812
1.50	7.50	7.5943
1.50	10.00	7.4927
1.50	12.50	7.4484
1.50	15.00	7.3532
1.50	17.50	7.5190

Table 2: effect of hydrogen ion concentration $[H^+]$ and chloride ion concentration $[Cl^-]$ on reaction rate at 30°C, [CAT] = 0.001 M,[N-AA]= 0.2 M, μ=0.0625 M; 35% ethanol

$[H^+]$ M	$[Cl^-]$ M	$10^4 k_1 [H^+]$
2.50	5.00	3.4001
5.00	5.00	7.4927
7.50	5.00	10.8426
10.00	5.00	15.7175
12.50	5.00	17.0198
5.00	2.50	7.4865
5.00	5.00	7.4927
5.00	7.50	7.5903
5.00	10.00	7.5343
5.00	12.50	7.5944

Table 3: effect of varying dielectric constant (D) on the reaction rate at 30°C; [CAT]=0.01M; [N-AA]=0.2M; $[H^+]$= 1 M; μ =0.0625 M

Ehanol V%	D	$10^4 k_1 sec^{-1}$
35.00	56.55	7.4927
40.00	53.33	10.7197
45.00	50.29	11.2121
50.00	47.42	13.6601
55.00	44,73	15.7240

Table 4: effect of ionic strength and p-toluenesulphonamide [p-TSA] concentration on reaction rate at 30°C; [CAT]=0.01 M; [N-AA]=0.2M; $[H^+]$ = 1 M; 35% ethanol

10^2 [$NaClO_4$] M	$10^4 k_1 Sec^{-1}$	10^3 [p-TSA] M	$10^4 k_1 Sec^{-1}$
3.125	7.4204	2.50	7.2279
6.250	7.4927	3.75	7.1985
9.375	7.5704	5.00	7.1774
12.500	7.4163	6.25	7.1368
15.625	7.5816	7.50	7.1088

Table 5:effect of varying temperature on reaction rate; [CAT]=0.01M; [N-AA]=0.2M; [H^+]= 1 M; μ=0.0625 M,

35% ethanol

T °K	10^4 k_1 Sec^{-1}	$\Delta H^{\neq}$ KJ/mole	$\Delta S^{\neq}$ J/mole.°K	$\Delta G^{\neq}$ KJ/mole	Log A Sec^{-1}
303	7.4927	50.12396	-318.45	96.5406	6.015073
308	9.3679	50.08239	-319.035	98.31278	5.977441
313	15.7516	50.04082	-316.194	99.01872	6.118845
318	19.6204	49.99925	-317.197	100.9185	6.059586
323	28.5357	49.95768	-317.982	102.7582	6.011772

Ea= 52.6431× 10^3 KJ/mole

$\Delta H^{\neq}$ (average) = 50.04028 KJ/mole

$\Delta S^{\neq}$ (average) = -317.772 J/mole.°K

$\Delta G^{\neq}$ (average) = 99.50976 KJ/mole

Log A (average) = 6.036543 Sec^{-1}

Discussion:

Chloramine-T (CAT) behaves like a strong electrolyte in aqueous solution and it dissociates as(Y. I. Hassan and A. A. AL-Hatim, Mutah.,1995):

$$R\backslash N\dot{.}NaCl \leftrightharpoons R\backslash N\dot{.}Cl^- \ (1)$$

Where (R=P-CH_3-$C_6H_5SO_2$)

The anion picks up a proton in acid solution to give the free acid mono chloramine-T, ŔNHCL.(N-chloro-p-toluene sulphonamide) (Y. I. Hassan and N. H. M. Saeed, 2009).

$$R\backslash N\dot{.}Cl^- + H^+ \leftrightharpoons R\backslash NHClKa = 2.82\times10^{-5}\ at\ 25^oC(2)$$

The free acid undergoes giving rise to p-toluene sulphonamide (R'NH_2) and dichloramine-T ($RNCl_2$):

$$2R\backslash NHCl \leftrightharpoons R\backslash NCl_2 + R\backslash NH_2Kd = 6.1\times10^{-2}\ at\ 25^oC(3)$$

The dichloramine_T and the free acid –hydrolyse to give hypochlorous acid (HOCl) (M. Natarajan and V. Thiagarajan, 1975)

$$R\backslash NCl_2 + H_2O \leftrightharpoons R\backslash NHCl + HOClKh = 8\times10^{-7}\ at\ 25^oC(4)$$

$$R\backslash NHCl + H_2O \leftrightharpoons R\backslash NH_2 + HOClKh = 4.88\times10^{-8}\ at\ 25^oC(5)$$

In addition,protonaion of the free acid in (pH less 2.8) give ($R\backslash H_2Cl$)

$$R\backslash NHCl + H^+ \leftrightharpoons R\backslash N^+H_2ClKa = 1.02\times10^{2}\ at\ 25^oC(6)$$

The protonated monochloramine -T (ŔNH_2Cl) can also hydrolyzed to give hypochlorous acidium ion (D. S. Mahadevappa. et. al., 1985) ,H_2O^+Cl:

$$R\backslash N^+H_2Cl + H_2O \leftrightharpoons RNH_2 + H_2O^+Cl\ (7)$$

Finally, HOCl ionizes to

$$HOCl \rightleftharpoons H^+ + OCl^-Ki = 3.3\times10^{-8}\ at\ 25^oC(8)$$

Free chlorine has also been detected in acid medium in the presence of chlorine ion (D. S. Mahadevappa et. al., 1981):

$R\backslash NH_2Cl + Cl^- \leftrightharpoons RNH_2 + Cl_2$ (9)

$HOCl + H^+ + Cl^- \rightleftharpoons Cl_2 + H_2OK = 2.15\times10^5$(10)

Chlorine's hydrolysis constant is $4.66*10^4$. Therefore, $RNCl_2$, RNHCl, HOCl, and HO_2Cl^+ are the likely oxidizing species in the acidified chloramine_T solution. The rate law predicts a second-order dependence on chloramine_T if $RNCl_2$ is the reactive species; nevertheless, experimentally clean first-order graphs were obtained for the elimination of chloramine-T figure 1. Bishop and Jennings' approximation calculations on decinornial solutions of chloramine_T have revealed that the concentrations of HOCl and RNHCl around PH 0 are roughly 10-7 M and 10^{-2} M, respectively. Despite the higher number of extinct species, Pryde and Soper (L. R. Pryed and F. G. Soper, 1931) have demonstrated that whereas HOCl might attack more quickly, RNHCl's interaction with the substrate may be sluggish. from Soper's prior work (F. G. Soper, 1929) (T. Higuchi and A. Hussain, 1967) as well as from the observation made during the experiment.the speed at which HOCl forms (Schemes I and II, step II in both schemes), which interacts with N-acetyl Valine quickly. Furthermore, as noted by C. G. Swain and D. R. Grist (1940), protonation transforms the latter into a stronger electrophil (H_2O^+Cl) than the precursor HOCl. Furthermore, because H_2OCl^+ is more reactive than HOCl, it will attack the N-acetyl Alanine more quickly. Ionic involvement in a rate-determining step is ruled out in the absence of a discernible ionic strength effect on the rate. The reaction rate is further increased by altering the solvent composition by changing the ethanol content in ethanol-water.A general equation (11) (E. S. Amis, 1972) relate the rate with the dielectric constant is give by

$Ln\, K_D^{/} = Ln\, K_D^{/} - 2\mu_1\mu_2/DKTr^3$(11)

where the dielectric constant functions as k/D. The reactant dipole moments are denoted by D, μ1 and μ2, the approach distance between the two dipoles is r, the Boltzman constant is k, and the absolute temperature is T. Log k(obs) and 1/D have a linear relationship, as implied by equation (10). When two dipolar molecules react, the line's slope should be negative; instead, when ion-dipole reactions occur, a positive slope is obtained.

Scheme I and II for the oxidation of N-acetyl Alanine by chloramine_T; may be propose as follows:

i $RNCl + H^+ \underset{k_2}{\overset{k_1}{\rightleftharpoons}} RNHCl$ ..... fast

ii $RNHCl + H_2O \underset{k_4}{\overset{k_3}{\rightleftharpoons}} HOCl + RNH_2$ .....fast

iii $HOCl + H^+ \xrightarrow{k_5} H_2OCl^+$ ..... slow

iv $H_2OCl^+ + N\text{-}AA \underset{}{\overset{k_6}{\rightleftharpoons}} N\text{-}AACl + H_2O$ ..... fast

Scheme I

i $RNCl + H^+ \xrightarrow{k_1} RNHCl$ ..... slow

ii $RNHCl + H_2O \underset{k_3}{\overset{k_2}{\rightleftharpoons}} HOCl + RNH_2$ .....fast

iii $N\text{-}AA + H^+ \xrightarrow{k_4} N\text{-}AVH^+$ ..... fast

iv $N\text{-}AAH^+ + HOCl \xrightarrow{k_5} N\text{-}AACl + H_2O$ .....fast

Scheme II

Both schemes involve the hydrolysis of RNHCl, which is followed by a fast reaction with N-acetyl Valine (Scheme I, step iii) to yield HOCl. Alternatively, it can be protonated to produce H_2OCl^+, which reacts quickly with the substrate. Using the steady state approximation for VIZ.$k_4\{k_{-1}+k_2H_2O\}$ [S]>>k-1k-3[TSA], CAT, and HOCl

One obtains the following equation.

$$\frac{-d}{dt}[CAT] = \frac{K_1}{K_{-1}+K_2[H_2O]}\frac{K_2[H_2O]}{K_2[H_2O]}[CAT][H^+] \quad (12)$$

Thus, the equation becomes Where

$$\frac{-d}{dt}[CAT] = K[CAT][H^+] \quad (13)$$

$HOCl + Na \rightleftharpoons NaOCl + H^+$ (14)

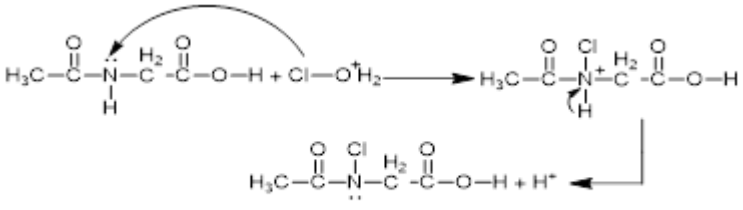
or

$H_2OCl + Na \rightleftharpoons NaOCl + H^+$ (15)

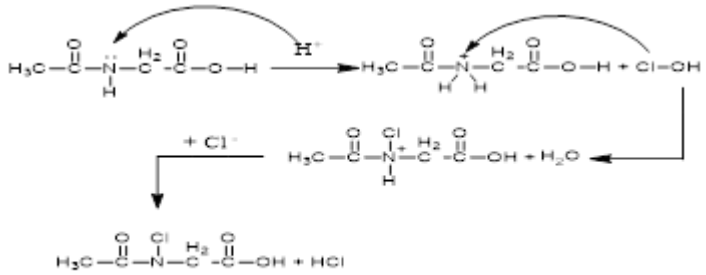
$3NaOCl \longrightarrow NaClO_3 + 2NaCl$ (16)

The derive rate law –equation (13) is not fully consistent with the kinetic outcomes of the experiment. A slight decrease in the first-order constant is observed when the initial concentration of chloramine-T, Table 1, is increased. This decrease could be attributed to deactivation brought on by the formation of trace amounts of $NaClO_3$ in side reactions, as reported by S. P. Mushran et al. (1974). This further establishes that HOCl or H_2OCl^+ is the reactive species.

A detailed mechanism of oxidation of N-acetyl Alanine by CAT in acid medium is shown in Scheme III and IV



Scheme III



Scheme IV

Scheme III involves an electrophilic attack on the nitrogen atom of N-acetyl Valine by the partly positive chlorine of H_2OCl^+, followed by the elimination of H^+ to yield N-chloro acetyl Valine (product).

Lastly, the large negative value of the entropy of activation, which indicates a stiff arrangement of the transition state and a more-ordered activated complex than the reactant, supports the hypothesized mechanism. (Y. I. Hussain, 2003) with fairly high positive value of free energy of activation (Laider K. J., 1965).

Conclusion:

- This study proved that the oxidation depends on the [CAT] and [H^+], as it was found that the reaction follows the first order.
- it does not depend on the [S] or on the [Cl^-], and that changing the ionic strength does not affect the k_1, and the effect of di-Electric Constant was studied, as was found.
- The value of Ea and the values of thermodynamic activation functions by changing temperature.

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