

# THE NOVEL OXIDATION OF 4-HYDROXYACETANILIDE BY N-CHLORO-4-METHYLBENZENESULPHONAMIDE IN AQUEOUS ACIDIC MEDIUM

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## ABSTRACT

The oxidation kinetics of 4-hydroxyacetanilide by N-chloro-4-methylbenzenesulphonamide in aqueous acidic medium has been studied iodometrically at 303 K. The values of  $K_1$  remain unaltered with the variation of N-chloro-4-methylbenzenesulphonamide, indicated the order to be unity with respect to oxidant. Reaction was studied under similar conditions by varying the concentration of substrate. Order was found to be unity at its low concentrations but tending towards zero order at its higher concentrations. The Stoichiometry between reactant and oxidant was confirmed as 1:2. The plot of rate of reaction versus the concentration of the catalyst indicated the order towards catalyst. Thermodynamic parameters were computed by performing the kinetic runs at various temperatures. A mechanism consistent with observed parameters is proposed and rate law is derived. The overall sequence described here is consistent with all the experimental evidence including the product, mechanistic, and kinetic studies.

**Keywords:** 4-hydroxyacetanilide, N-chloro-4-methylbenzenesulphonamide Ru(III)Chloride, Kinetics, Oxidation

## I. INTRODUCTION

4-hydroxyacetanilide or acetaminophen or Tylenol or 4-acetamidophenol is a well-known drug that finds extensive applications in pharmaceutical industries. It is also used as an intermediate for pharmaceuticals (as a precursor in penicillin) and azo dyes, and as a stabilizer for hydrogen peroxide and photographic chemicals. It is used as an alternative to aspirin<sup>[1-4]</sup>.

Aromatic N-halosulfonamides act as mild oxidants in both acid and alkaline solutions due to the presence of strongly polarized N-linked halogen in +1 state. Many organic substrates were oxidized by these sulfonamides and the kinetic and mechanistic aspects of these reactions are well documented<sup>[5-6]</sup>. A prominent member of this group N-chloro-4-methylbenzenesulphonamide Chloramine-T (CAT) is used as halogenating and oxidizing agent in acidic and basic media<sup>[7-11]</sup>. It is a versatile oxidizing agent and has shown a variety of kinetic results due to formation of various oxidizing species depending upon pH of the medium. Recently, use of transition metals as catalyst in various redox processes has attracted considerable interest<sup>[12]</sup>. Ru (III) Chloride is known as a nontoxic and homogenous catalyst<sup>[13]</sup> but a little attention is paid to explore role of Ru(III) as catalyst. In

the present communication we are reporting kinetic, mechanistic and thermodynamic aspects of oxidation of acetaminophen by chloramine-T in alkaline medium at 303 K.

## II. EXPERIMENTAL

All the chemicals were A.R. grade and double distilled water was used throughout the investigations. A solution of 4-hydroxyacetanilide (CDH Ltd, New Delhi) of required strength was freshly prepared every time. The Stock solution of the oxidant was prepared in double distilled water and its concentration was checked idometrically. The stock solution of Ruthenium Chloride was prepared by dissolving the known amount in HCl of known strength in a black coated flask to avoid photochemical effects. KCl,  $\text{HClO}_4$ ,  $\text{Hg}(\text{OAc})_2$  of known strength are also used without further purification. All other reaction vessels were also coated black from outside to avoid any photochemical degradation. A thermostatic water bath was used to maintain the desired temperature. Aliquots of the reaction mixture were placed in the thermostat-controlled water bath, which was per-equilibrated at 313 K. Requisite volume of 4-hydroxyacetanilide solution, also thermo stated at the same temperature was rapidly pipette out and poured into the reaction vessel. The total volume of the reaction mixture was 50 ml each time. 5 ml aliquots of the reaction mixture was pipetted out at different intervals of time and quenched with 4% acidified KI solution. The progress of the reaction was monitored by iodometric estimation of unreacted oxidant in measured aliquots of the reaction mixture withdrawn at regular intervals of time. The kinetic runs were carried out at 303 K.

## III. STOICHIOMETRY AND PRODUCT ANALYSIS

Different sets of the reaction mixture with excess of oxidant were kept for 48 hrs at room temperature. Determination of unconsumed oxidant in each set confirmed 1:2 Stoichiometries between substrate and oxidant. The reaction products were extracted with ether. From the ether layer the oxidation product was identified as quinone oxime. The nature of quinone oxime was confirmed by FTIR ( $1652\text{ cm}^{-1}$  due to C=O stretching,  $1615\text{ cm}^{-1}$  due to C=N stretching of oxime,  $3332\text{ cm}^{-1}$  due to OH stretching). Acetic acid was confirmed by spot test<sup>(14)</sup>.

## IV. KINETIC RESULTS AND DISCUSSION

Effect of reactants concentration on the rate: The kinetics measurements were performed by varying the concentration of any one reactant and keeping the concentrations of all other reactants constant. The values of  $K_1$  remain unaltered with the variation of [CAT]. The same was also confirmed by the plot of [CAT] versus  $(-dc/dt)$  was linear passing through the origin (graph-a), indicated a first order dependence of the rate of reaction on [CAT]. The constant K on varying the concentration confirmed the first-order dependence on Ru(III) also. The plot of rate of reaction  $(-dc/dt)$  versus [Ru] indicated first order with respect to catalyst. Reactions were studied under similar experimental conditions by varying the concentration of [PA]. First order dependence on substrate at its low concentrations and tends to zero order at its higher concentrations as seen from the (table-1).

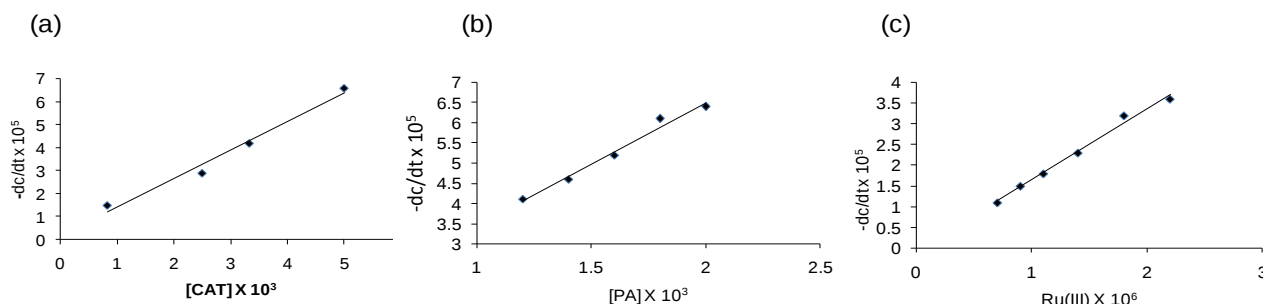
**Effect of ionic strength on the rate:** Effect of ionic strength was studied by adding  $\text{NaClO}_4$ . The rate of reaction did not show any significant change confirming the involvement of non ionic species in the rate determining step.

**Effect of temperature on the rate:** The effect of temperature was studied by carrying out the reaction at different temperatures (303, 308, 313, 318) but keeping other experimental conditions constant (table-3). The activation parameters were computed from the Arrhenius plot of  $\log k$  versus  $1/T$  (plot-e).

**TABLE -1 Effect of variation of substrate, oxidant, catalyst & medium at 303K**

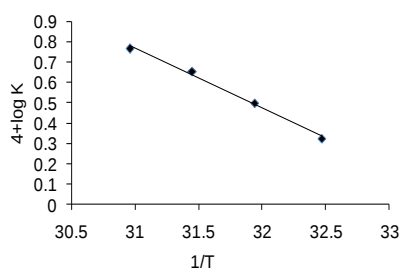
| [PA] X $10^3$ | [CAT] X $10^3$ | Ru(III) X $10^6$ | [H+] X $10^3$ | -dc/dt x $10^5$ |
|---------------|----------------|------------------|---------------|-----------------|
| 1.2           | 1.0            | 2.0              | 1.0           | 4.10            |
| 1.4           | 1.0            | 2.0              | 1.0           | 4.60            |
| 1.6           | 1.0            | 2.0              | 1.0           | 5.20            |
| 1.8           | 1.0            | 2.0              | 1.0           | 6.10            |
| 2.0           | 1.0            | 2.0              | 1.0           | 6.40            |
| 2.2           | 1.0            | 2.0              | 1.0           | 6.60            |
| 2.5           | 1.0            | 2.0              | 1.0           | 6.70            |
| 5.0           | 1.0            | 2.0              | 1.0           | 6.80            |
| 1.0           | 0.83           | 2.0              | 1.0           | 1.50            |
| 1.0           | 1.25           | 2.0              | 1.0           | 2.70            |
| 1.0           | 2.50           | 2.0              | 1.0           | 2.90            |
| 1.0           | 3.33           | 2.0              | 1.0           | 4.20            |
| 1.0           | 5.0            | 2.0              | 1.0           | 6.60            |
| 1.0           | 1.0            | 0.7              | 1.0           | 1.10            |
| 1.0           | 1.0            | 0.9              | 1.0           | 1.50            |
| 1.0           | 1.0            | 1.1              | 1.0           | 1.80            |
| 1.0           | 1.0            | 1.4              | 1.0           | 2.30            |
| 1.0           | 1.0            | 1.8              | 1.0           | 3.20            |
| 1.0           | 1.0            | 2.2              | 1.0           | 3.60            |
| 1.0           | 1.0            | 2.0              | 0.66          | 13.6            |
| 1.0           | 1.0            | 2.0              | 0.83          | 11.0            |
| 1.0           | 1.0            | 2.0              | 1.25          | 8.30            |
| 1.0           | 1.0            | 2.0              | 2.5           | 3.80            |
| 1.0           | 1.0            | 2.0              | 3.33          | 0.58            |

$[\text{Hg}(\text{OAc})_2] = 1.00 \times 10^{-3} \text{ M}$ ,  $[\text{HClO}_4] = 1.00 \times 10^{-3} \text{ M}$ ,  $[\text{KCl}] = 1.00 \times 10^{-3} \text{ M}$



Plot between (a)  $[CAT] \times 10^{-3}$  (b)  $[PA] \times 10^{-3}$  and (c)  $Ru(III) \times 10^6$  M vs.  $[-dc/dt] \times 10^5 \text{ ML}^{-1}\text{S}^{-1}$

**Effect of dielectric constant on the rate:** The rate of reaction decreased by decreasing dielectric constant of the medium. This was checked by adding and varying  $\text{CH}_3\text{COOH}$  to the reaction mixture.



(e) Plot between  $1/T$  vs.  $\log K$

TABLE-2 Effect of variation of  $\text{KCl}$ ,  $\text{NaClO}_4$  and  $\text{Hg}(\text{OAc})_2$  at 313K

| $[\text{KCl}] \times 10^3 \text{ M}$ | $[\text{Hg}(\text{OAc})_2] \times 10^3 \text{ M}$ | $[\text{NaClO}_4] \times 10^3 \text{ M}$ | $(-dc/dt) \times 10^5$ |
|--------------------------------------|---------------------------------------------------|------------------------------------------|------------------------|
| 1.00                                 | 1.00                                              | -                                        | 2.22                   |
| 1.40                                 | 1.00                                              | -                                        | 2.18                   |
| 2.00                                 | 1.00                                              | -                                        | 2.22                   |
| 2.41                                 | 1.00                                              | -                                        | 2.18                   |
| 1.00                                 | 1.20                                              | -                                        | 1.50                   |
| 1.00                                 | 1.66                                              | -                                        | 1.61                   |
| 1.00                                 | 2.50                                              | -                                        | 1.51                   |
| 1.00                                 | 3.33                                              | -                                        | 1.70                   |
| 1.00                                 | 1.00                                              | 1.1                                      | .27                    |
| 1.00                                 | 1.00                                              | 1.5                                      | .26                    |
| 1.00                                 | 1.00                                              | 2.0                                      | .27                    |

Solution conditions:  $[\text{CAT}] = 1 \times 10^{-3} \text{ M}$ ,  $[\text{PA}] = 1 \times 10^{-3} \text{ M}$ ,  $[\text{Ru(III)}] = 2 \times 10^{-6} \text{ M}$ ,  $[\text{H}^+] = 1 \times 10^{-3} \text{ M}$

TABLE -3 .Effect of temperature and activation parameters on the rate

| Temperature<br>(K)                       | $K_1 \times 10^5$<br>( $S^{-1}$ ) | Activation<br>parameter |
|------------------------------------------|-----------------------------------|-------------------------|
| 303                                      | 2.15                              | -                       |
| 308                                      | 3.10                              | -                       |
| 313                                      | 4.42                              | -                       |
| 318                                      | 5.63                              | -                       |
| $E_a$ (kJ mol $^{-1}$ )                  | -                                 | 52.9                    |
| $\Delta S^*$ (J K $^{-1}$ mol $^{-1}$ )  | -                                 | -96.87                  |
| $\Delta G^*$ (kJ K $^{-1}$ mol $^{-1}$ ) | -                                 | 79.96                   |
| log A                                    | -                                 | 9.15                    |

Solution conditions : [CAT]=  $1 \times 10^{-3}$  M, [PA] =  $1 \times 10^{-3}$  M, [Ru(III)] =  $2 \times 10^{-6}$  M, [H $^{+}$ ] =  $1 \times 10^{-3}$  M, , [KCl] =  $1.00 \times 10^{-3}$  M

the rate of reaction and rate law may be derived as-

$$\text{Rate} = -d \frac{[CAT]}{dt} = 2 K [\text{complex}]$$

The rate law can be written as-

$$\text{Rate} = \frac{2 K_1 K_2 K_3 [Ru] [PA] [CAT]_T}{[TsNH_2][H^+] + K_1 [H^+] + K_1 K_2 [PA]}$$

The above equation is based on the observed kinetic orders with respect to each reactant of the reaction and is in conformity with the derived rate law.

## V. CONCLUSION

The reaction has been carried out HClO $_4$  medium. The reaction stoichiometry of 1:2 (PA:CAT) involving the oxidation of PA by CAT has been observed. Quinone oxime has been identified as the reaction product. The effect of dielectric constant and halide ion on the reaction was studied. From the Arrhenius plots the thermodynamic parameters have been computed and a mechanism has been proposed which was in conformity with the observed rate law.

## VI. ACKNOWLEDGEMENT

We would like to thank our Head of Department Prof. Sudha Jain for all the facilities. We would also like to thank our colleagues and anonymous reviewer and editor for their critical and useful comments which refined the manuscript a lot.

## REFERENCES

- [1] Sirsalmath Kiran T, Hiremath Chanabasayya V, Nandibewoor Sharanappa T (2006) Appl Catal A Gen 305:79 CrossRef
- [2] Kiran TS, Hiremath DC, Nandibewoor ST (2007) Z Phys Chem 221:501

- [3] 2. S. O. Adejo, R. A. Wuana, S. G. Yiase, and M. M. Ekwonchi, Kinetics of the dichromate ion oxidation of simple aliphatic aldehydes. *Int'l J. of Chemistry*.18(2): (2008) 63-70.
- [4] P.O. Baralles, R.P. Weigand, and A. M. Dias, Simultaneous determination of paracetamol and caffeine by flow injection-solid phase spectrometry using C18 silica gel as a sensing support, *Analytical Sci. J.* 18 (2002) 1241-1246.
- [5] Veeraiah, M.K., Ananda Murthy, A.S., and Made Gowda, N.M., Oxidation of n-propylamine and n-butylamine by chloramines-B and chloramine-T in basic medium: A kinetic study, *Synth. React. Inorg. Met.-Org. Nano- Met. Chem.*, 2010, 40(4), 225-230
- [6] Mahadevappa D.S., Ananda S., Murthy A.S.A. and Rangappa K.S., Oxidation of dimethylsulphoxide by sodium m-bromobenzene- sulphonamide: A kinetic and mechanistic study, *Tetrahedron*, 1984, 40(10), 1673
- [7] Singh Ajay, Negi Reena, Jain Bhavana, Katre Yokraj, Surya P. Sharma, Virandr(Kinetics and Mechanism of Ru(III)-Catalyzed Oxidation of Paracetamol by Chloramine-T in Aqueous Acidic Medium), 2009 *Catalysis Letters*- 1/2, 285-291
- [8] Singh Ajay, Negi Reena, Jain Bhavana, Katre Yokraj, Surya Prakash sisngh, Virandr. K.(Pd(II) Catalyzed Oxidative Degradation of Paracetamol by Chloramine-T in Acidic and Alkaline Media). *American Chemical Society*; 2011; 50(14): 8407-8419.
- [9] Aftab Aslam, Abdullah Asiri, Naved, Malik, Anish, Abdulrahman(Kinetics and Mechanistic Investigation of Decarboxylation for the Oxidation of Levofloxacin by Chloroamine-T in Acidic Medium) *American Chemical Society*, 2012; 51(13): 4819- 4824.
- [10] T. Demappa and S.Ananda(Kinetics and mechanism of Oxidation of Methionine by Chloramine-T in Alkaline Medium in presence of OsO<sub>4</sub> Catalyst).*Asian Journal of Chemistry*, 2009; 11/2: 376-383.
- [11] Gowda Ramachandrappa, Diwya, Iyengar Pushpa (Oxidation of Propanolol using Chloramine-T in HClO<sub>4</sub> medium: A Kinetic and Mechanistic Study) *International Research Journal of Pharmacy*, 2012; 3(6): 122-125.
- [12] Hiremath CV, Kiran TS, Nandibewoor ST(2006) *J Mol Catalysis A Chem* 248: 163
- [13] Aslam, Anish Khan, Abdulla Ansari, Naved Azum, Malik Abdul (Micro concentrations of Ru(III) used as homogenous catalyst in the oxidation of levothyroxine by N-bromosuccinimide and the mechanistic pathway).*Journal of Taiwan Institute of Chemical Engineers*, 2014; 45/1: 127-133.
- [14] Feig F. *Spot Tests in organic analysis*, 5<sup>th</sup> ed. Elsevier, Amsterdam, 1956, 376