



## Oxidation of P-methoxy Benzoic Acid Hydrazide by Thallium (III) in Acidic Medium (A Kinetic and Mechanistic Study)

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### ABSTRACT

The kinetics of oxidation of p-Methoxy benzoic acid hydrazide by Thallium (III) in a mixture of perchloric and hydrochloric acid media at a constant ionic strength has been planned to study iodometrically. The reaction proceeds through formation of complex with reactant, which decomposes in subsequent steps to give product. Effect of acrylonitrile shows, that there is no formation of free radicals. The increase in  $[H^+]$  and  $[Cl^-]$  decreases the rate of the reaction. The increase in ionic strength does not affect the rate of reaction. The effect of temperature was studied at four different temperatures ranging from 15°C to 30°C. The activation parameters were also determined and a mechanism is predicted.

**Key words:** p-methoxy acid hydrazide, kinetics, thallium (III), oxidation.

### INTRODUCTION

Hydrazides are pharmaceutically important compounds used as antitubercular<sup>1</sup> and antibacterial<sup>2,3</sup> agents, some of them have been reported to possess anti-inflammatory<sup>4</sup> and diuretic<sup>5</sup> activities. Interest in the use of thallium(III) in the oxidation of organic compounds has increased only recently and research in this regard has not been extensive. The redox potential of  $Tl(III)/Tl(I)$  couple is sensitive to the anion present in the solution. In perchloric and sulphuric acid media<sup>6</sup> it has the highest value of 1.23V with either free  $Tl^{3+}$ ,  $TlOH^{2+}$  or thallium(III) sulphate complexes as active species respectively. Therefore, thallium(III) can be utilized

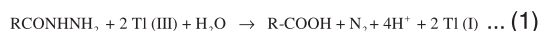
both as a strong (in perchloric acid and sulfuric acid media) and as a mild oxidant<sup>7</sup> (in hydrochloric acid medium) by changing the reactive species.

### MATERIAL AND METHODS

Thallium (III) solution was prepared by dissolving  $Tl_2O_3$  (ACROS) in 1.0 moldm<sup>-3</sup> HCl and the concentration was ascertained by iodometric titration. The p-Methoxy Benzoic acid hydrazide was prepared from reported<sup>[11]</sup> procedure and characterized by determining its melting point. Stock solution of p-Methoxy Benzoic acid hydrazide was prepared in 50 % v/v, 1,4-dioxane. Ionic strength was kept constant.

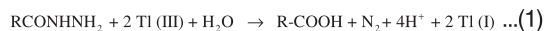
The reactions were carried out in 50 % v/v 1,4-dioxane (s.d.fine.chem) under pseudo first order conditions keeping concentration of hydrazide in large excess over that of the oxidant. The solutions containing the reactants and all other constituents were thermally equilibrated separately, mixed and the reaction mixture was analysed for unreacted thallium (III) iodometrically by titrating against standard thiosulphate. The pseudo-first order rate constants were determined from the slopes of linear  $\log[\text{TI(III)}]$  versus time plots. The results were reproducible up to  $\pm 5\%$ . Kinetic runs were followed to about three half-lives of the reactions<sup>9</sup>. Under the experimental condition oxidation of 1,4-dioxane did not occur.

The stoichiometry of the reaction was determined using a known excess of thallium (III) over hydrazide and determining remaining oxidant iodometrically after 24 hrs. The results consistent with equation-(1) were obtained. The corresponding p-Methoxy Benzoic acid was characterized by determining its MP.



*End product analysis.* For identification of products the reaction was carried out by using aqueous solution of hydrazide, thallium(III), HCl and  $\text{HClO}_4$ . The flask containing reaction mixture was kept in thermostated water bath maintained at 50°C for 24 h to complete the reaction, the residue obtained after filtration was analysed for acid as follows:

- (i) The presence of p-Methoxy acid group was detected by testing with bicarbonate.
- (ii) The formation of acid was confirmed by IR and its melting point.



## RESULTS

The reaction occurs rapidly in perchloric acid medium, but in the presence of hydrochloric acid the rate is measurable. Therefore, the reaction was carried out in a mixture of both the acids. The effect of reactants on the reaction was studied at constant  $[\text{HCl}]$  and  $[\text{HClO}_4]$  of 0.1 mol  $\text{dm}^{-3}$  each and ionic strength of 0.6 mol  $\text{dm}^{-3}$ . Concentration of oxidant was varied from  $6.4 \times 10^{-4}$  to  $6.4 \times 10^{-3}$  mol

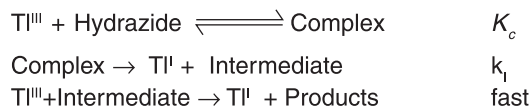
$\text{dm}^{-3}$  keeping [hydrazide] constant at  $1 \times 10^{-1}$  mol  $\text{dm}^{-3}$ . Since the pseudo-first order rate constants were fairly constant ( $6.70 \pm 0.1 \times 10^4 \text{ s}^{-1}$  for p-Methoxy BAH at 25°C) the order with respect to [oxidant] is unity. The effect of [hydrazide] was studied between the concentration range from  $1 \times 10^{-2}$  to  $1 \times 10^{-1}$  mol  $\text{dm}^{-3}$  keeping the [oxidant] constant at  $3.0 \times 10^{-3}$  mol  $\text{dm}^{-3}$ . The pseudo-first order rate constants increase with increase in concentration and the order with respect to hydrazide is found to be fractional<sup>9,10</sup>.

To study the effect of  $[\text{H}^+]$  and  $[\text{Cl}^-]$ , [oxidant], [hydrazide] and ionic strength were kept as  $3.0 \times 10^{-3}$ ,  $1 \times 10^{-1}$  and 0.6 mol  $\text{dm}^{-3}$ , respectively. To vary  $[\text{H}^+]$  and  $[\text{Cl}^-]$ ,  $\text{HClO}_4$  and NaCl were used. Increase in  $[\text{H}^+]$  from 74.20 to  $1.05 \times 10^{-2}$  mol  $\text{dm}^{-3}$  decreases  $k \times 10^{-4} (\text{s}^{-1})$  from 28.71 to 0.21 for p-Methoxy BAH at 25°C. Increase in  $[\text{Cl}^-]$  from 0.13 to 0.60 mol  $\text{dm}^{-3}$  decreases  $k \times 10^{-4} (\text{s}^{-1})$  from 7.35 to 1.05 for p-Methoxy BAH at 25°C. The relative permittivity was varied by changing the 1,4-dioxane content from 5 to 40% v/v. The rate was found to decrease with decrease in relative permittivity<sup>11</sup>.

Added acrylonitrile in the concentration range from 0.5 to 2.5 vol.%, by keeping concentrations of oxidant, reductant, perchloric acid, hydrochloric acid and ionic strength fixed, did not produce any precipitate due to polymerisation of the added acrylonitrile, indicating absence of free radicals.

## DISCUSSION

Since there is no formation of free radicals in the reaction, the reaction proceeds with two-electron transfer step.



### Scheme 1

The order in thallium (III) was found to be unity and the order in hydrazide was found to be fractional. Such fractional order in substrate concentration is due to the prior complex formation equilibrium between the reactants. The Michealis -

Menten plots of  $1/k_{\text{obs}}$  versus  $1/[\text{Hydrazide}]$  were linear with an intercept in support of the complex formation. Therefore, in agreement with the results obtained the mechanism of the reaction can be represented as in Scheme 1. Equation 2 gives the rate according to Scheme 1. Since, total  $[\text{Tl}^{\text{III}}]$  exists in the form of free  $[\text{Tl}^{\text{III}}]$  and the complex (Equation 3) therefore, the  $[\text{Tl}^{\text{III}}]$  free is given by Equation 6. The overall rate law is now expressed by Equation 7 and the Pseudo-first order rate constant  $k_{\text{obs}}$ , by Equation 8.

$$\text{Rate} = k_1 [\text{Complex}] = k_1 K_c [\text{Hydrazide}]_{\text{free}} [\text{Tl}^{\text{III}}]_{\text{free}} \quad \dots(2)$$

$$[\text{Tl}^{\text{III}}]_{\text{total}} = [\text{Tl}^{\text{III}}]_{\text{free}} + [\text{Complex}] \quad \dots(3)$$

$$[\text{Tl}^{\text{III}}]_{\text{total}} = [\text{Tl}^{\text{III}}]_{\text{free}} + K_c [\text{Hydrazide}] [\text{Tl}^{\text{III}}]_{\text{free}} \quad \dots(5)$$

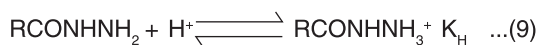
$$[\text{Tl}^{\text{III}}]_{\text{free}} = [\text{Tl}^{\text{III}}]_{\text{total}} / (1 + K_c [\text{Hydrazide}]) \quad \dots(6)$$

$$\text{Rate} = k_1 K_c [\text{Hydrazide}] [\text{Tl}^{\text{III}}]_{\text{free}} \quad \dots(7)$$

$$k_{\text{obs}} = k_1 K_c [\text{Hydrazide}] / (1 + K_c [\text{Hydrazide}]) \quad \dots(8)$$

Rate law 8 is verified by plotting  $1/k_{\text{obs}}$  against  $1/[\text{Hydrazide}]$  at four different temperatures and from the slopes and intercepts of these plots the values of  $k_1$  and  $K_c$  were calculated and are given in Table 1.

The effect of hydrogen and chloride ion concentrations on the reaction is due to the protonation of hydrazides and different chloro-complexes of thallium (III) present in the solution. Hydrazides are known to be protonated in acid medium according to Equation 9.



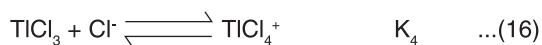
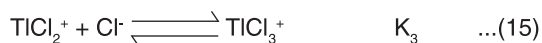
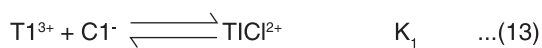
Therefore, total  $[\text{Hydrazide}]$  can be expressed by Equation 10 and thereby the fact that there was no effect of free  $[\text{Hydrazide}]$  by Eq. 12. Since the rates of reaction decreases as the  $[\text{H}^+]$  increases, free hydrazide is the active species. This is in support of ionic strength on the reactions indicating one of the reactant is neutral.

$$[\text{Hydrazide}]_{\text{total}} = [\text{Hydrazide}]_{\text{free}} + [\text{Hydrazide}]_{\text{protonated}} \quad \dots(10)$$

$$[\text{Hydrazide}]_{\text{total}} = [\text{Hydrazide}]_{\text{free}} + K_H [\text{Hydrazide}]_{\text{free}} \quad \dots(11)$$

$$[\text{Hydrazide}]_{\text{free}} = [\text{Hydrazide}]_{\text{total}} / (1 + K_H [\text{H}^+]) \quad \dots(12)$$

Thallium (III) forms strong complexes with chloride ions of the formula  $\text{TlCl}_n^{3-n}$  where  $n$  is the number of chlorides complexes with thallium (III) as represented in equilibrium 13 to 16. The values of respective stability constants are  $K_1 = 1.38 \times 10^8$ ,  $K_2 = 3.98 \times 10^{13}$ ,  $K_3 = 6.02 \times 10^{15}$  and  $K_4 = 1.0 \times 10^{18} \text{ mol}^{-1} \text{ dm}^3$ .



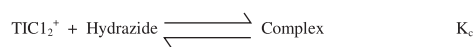
All the thallium(III) will exist as  $\text{TlCl}_2^+$  and its concentration can be expressed by Equation 17. The  $[\text{TlCl}_2^+]_{\text{free}}$  can now be given by eq. 19 where,  $\beta_1 = K_3/K_2 = 151$  and  $\beta_2 = K_4/K_3 = 166$ , further, using Equations 18 and 19 the concentrations of  $[\text{TlCl}_2^+]_{\text{free}}$ ,  $\text{TlCl}_3^+$  and  $\text{TlCl}_4^+$  were calculated at different chloride ion concentrations and compared with the change in rate constant as the chloride ion concentration varied.

$$[\text{Tl}(\text{III})]_{\text{total}} = [\text{TlCl}_2^+]_{\text{total}} = [\text{TlCl}_2^+]_{\text{free}} + [\text{TlCl}_3^+] + [\text{TlCl}_4^+] \quad \dots(17)$$

$$[\text{TlCl}_2^+]_{\text{total}} = [\text{TlCl}_2^+]_{\text{free}} (1 + \beta_1 [\text{Cl}^-] + \beta_2 [\text{Cl}^-]^2) \quad \dots(18)$$

$$[\text{TlCl}_2^+]_{\text{free}} = [\text{TlCl}_2^+]_{\text{total}} / (1 + \beta_1 [\text{Cl}^-] + \beta_2 [\text{Cl}^-]^2) \quad \dots(19)$$

The concentration of both of  $[\text{TlCl}_2^+]_{\text{free}}$  and  $\text{TlCl}_3^+$  parallel the values of rate constants as  $[\text{Cl}^-]$  changes but the order  $[\text{Cl}^-]$  is  $-1.5$ , which makes  $[\text{TlCl}_2^+]_{\text{free}}$  as the only active species.



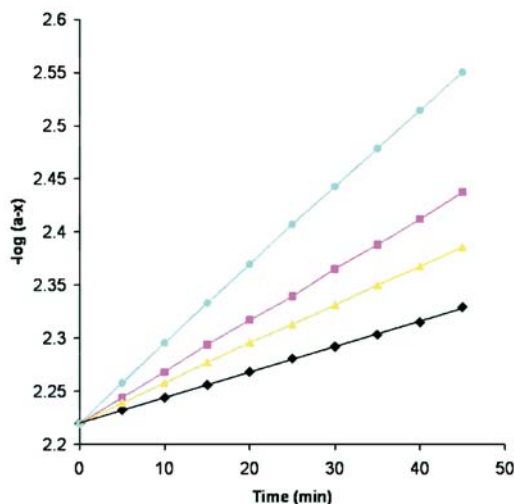
where R = C<sub>5</sub>H<sub>4</sub> for p-Methoxy Benzoic acid hydrazide

### Scheme 2:

The mechanism considering TlCl<sub>2</sub><sup>+</sup> of oxidant and free hydrazide of the substrate as the active species can now be represented by scheme 2 with respective rate law and the expression for the pseudo-first order rate constants by Equations

### Effect of temperature

[BAH] = 5 × 10<sup>-2</sup>M                      [H<sup>+</sup>] = 0.23 M  
 [TI (III)] = 3 × 10<sup>-3</sup>                      [Cl<sup>-</sup>] = 0.13 M  
 Temperature = 30°C                      μ = 0.6 M  
 [Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> · 5H<sub>2</sub>O] = 1.1 × 10<sup>-3</sup> M      Dioxan(v/v) % = 5



From graph,  
 $k = 2.86 \times 10^{-4} \text{ sec}^{-1}$

The results of four different temperatures for the same concentration of benzoic and aromatic acid hydrazides are given below,

[Hyd] = 5 × 10<sup>-2</sup>M                      [H<sup>+</sup>] = 0.23 M  
 [TI (III)] = 3 × 10<sup>-3</sup>                      [Cl<sup>-</sup>] = 0.13 M  
 μ = 0.6 M                                      Dioxan(v/v) % = 5

Temperature	$k \times 10^4 \text{ s}^{-1}$			
	BAH	p-OCH <sub>3</sub> BAH	p-Cl BAH	p-NO <sub>2</sub> BAH
15	0.93	2.45	0.64	0.36
20	1.53	3.34	1.10	0.50
25	1.87	4.24	1.56	0.70
30	2.86	6.98	2.42	1.10

20 and 21. The rate law 21 was verified by plotting  $1/k_{\text{obs}}$  against  $1/[\text{Hydrazide}]$  and  $1/k_{\text{obs}}$  against  $[\text{H}^+]$  which were found to be linear. From the slopes and intercepts of these plots the values of  $K_c$  and  $K_H$  were determined.

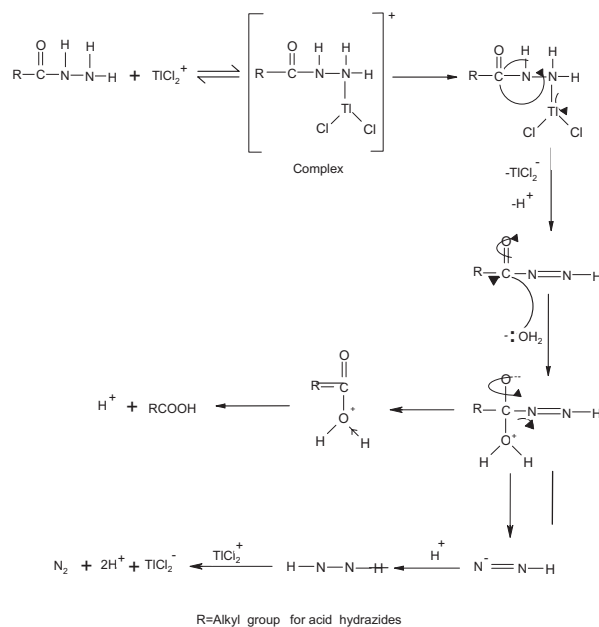
$$\text{Rate} = \frac{k_1 K_c [\text{Hydrazide}]_{\text{total}} [\text{TlCl}_2^+]_{\text{total}}}{(1 + K_c [\text{Hydrazide}]) (1 + K_H [\text{H}^+]) (1 + \beta_1 [\text{Cl}^-] + \beta_2 [\text{Cl}^-]^2)} \dots (20)$$

$$k_{\text{obs}} = \frac{k_1 K_c [\text{Hydrazide}]_{\text{total}}}{(1 + K_c [\text{Hydrazide}]) (1 + K_H [\text{H}^+]) (1 + \beta_1 [\text{Cl}^-] + \beta_2 [\text{Cl}^-]^2)} \dots (21)$$

The values of  $K_c$  are given in Table 1 and those of  $K_H$  were found to be 13 and 16 mol<sup>-1</sup> dm<sup>3</sup> for p-Methoxy Benzoic acid. The electrophilic character of TlCl<sub>2</sub><sup>+</sup> among the thallium (III) chlorocomplexes is highest thus making it the reactive species.

From the above results, it shows that the rates of the oxidation of benzoic and substituted benzoic acid hydrazides are approximately doubled for 10°C rise in temperature.

The detailed mechanism involves electrophilic substitution on the nitrogen of the hydrazide with the formation of N-Tl bond, which decomposes in the subsequent step with direct two-electron transfer from hydrazide to thallium to give an intermediate followed by fast steps. (Scheme 3). Such N-Tl bond formation has been postulated during thallium (III) oxidation of nitrogen containing compounds.



Scheme 3

Table 1: Values of  $K_c$  and  $k_1$ 

Temperature °C	$K_c$ (mol <sup>-1</sup> dm <sup>3</sup> ) [o-TAH]	$k_1 \times 10^4$ (S <sup>-1</sup> ) [o-TAH]
15	14.00	2.38
20	09.52	5.00
25	09.23	8.33
30	07.05	16.66

The activation parameters, with respect to slow step,  $k_1$ ,  $\Delta H^\ddagger$  (KJ mol<sup>-1</sup>),  $\Delta G^\ddagger$  (KJ mol<sup>-1</sup>) and  $\Delta S^\ddagger$  (JK<sup>-1</sup>mol<sup>-1</sup>) were found to be 32.76, 107.04 and -249.26 respectively for p-Methoxy Benzoic acid hydrazide. Considerable decrease in the entropy of activation is due to formation of more ordered

transition state as shown in scheme 3. The mechanism involves neutral hydrazide as the active substrate thus the reaction is unaffected by the change in the ionic strength. The increase in 1,4-dioxane content in the reaction medium decreases; the rate such an effect of the solvent is due to the stabilization of the complex formed between reactants in a medium of low relative permittivity.

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