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OXIDATION OF NICOTINIC ACID HYDRAZIDE BY THALLIUM (III) IN ACIDIC MEDIUM: A KINETIC AND MECHANISTIC STUDY

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ABSTRACT

The kinetics of oxidation of nicotinic acid hydrazide by thallium (III) in a mixture of perchloric and hydrochloric acid media at a constant ionic strength has been studied 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 15ºC to 30ºC. The activation parameters were also determined and a mechanism has been predicted.

Key words: Nicotinic acid hydrazide, Kinetics, Thallium (III), Oxidation

INTRODUCTION

Thallium oxide is one of the versatile available oxidizing agents used for oxidation of hydrazide. The reaction of hydrazide with most oxidants give the corresponding acids[1-3] and in some cases[4-7], esters or amides. Thallium (III) salts are well known oxidants[8] in organic synthesis. The redox potential of Tl (III)/Tl (I) couple is sensitive to the anion present in the solution. In perchloric and sulphuric acid media[9], 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[10-14] (in hydrochloric acid medium) by changing the reactive species. Nicotinic acid or niacin is a vitamin.

EXPERIMENTAL

Thallium (III) solution was prepared by dissolving Tl_2O_3 (ACROS) in 1.0 mol dm^{-3}

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HCl and the concentration was ascertained by iodometric titration. The nicotinic acid hydrazide was prepared from reported procedure[15] and characterized by determining its melting point. Stock solution of nicotinic 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 [Tl (III)] versus time plots. The results were reproducible up to ± 5 %. Kinetic runs were followed to about three half lives of the reactions. Under the experimental conditions, 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 heterocyclic acid was characterized by determining its MP.

$$\text{RCONHNH}_2 + 2\,\text{Tl (III)} + \text{H}_2\text{O} \rightarrow \text{R-COOH} + \text{N}_2 + 4\,\text{H}^+ + 2\,\text{Tl (I)} \quad \dots (1)$$

RESULTS AND DISCUSSION

The reaction was carried out in a mixture of both the acids; HCl and $HClO_4$ because, the reaction occurs rapidly in perchloric acid medium but in the presence of hydrochloric acid, the rate is measurable. The effect of reactants on the reaction was studied at constant [HCl] and [$HClO_4$] of 0.1 mol dm^{-3} each and ionic strength of 0.6 mol dm^{-3}.

Effect of hydrazide concentration

The effect of [hydrazide] was studied between 1.0×10^{-2} to 1.0×10^{-1} mol dm^{-3}, keeping the [oxidant] constant at 3.0×10^{-3} mol dm^{-3}. It is observed that the pseudo-first order rate constant increases, with increase in [hydrazide].

An examination of above result indicates that the value of rate constant k depends on initial concentration of hydrazide and it increases with increase in hydrazide concentration.

Effect of thallium (III) concentration

To study the effect of thallium (III) concentration on reaction rate, concentration of oxidant was varied from 6.5×10^{-4} to 6.5×10^{-3} mol dm^{-3} keeping the [Hydrazide] constant at 1×10^{-1} mole dm^{-3}.

A persual of data shows that the rate of oxidation of isonicotinic acid hydrazide remains practically constant at five different concentrations of thallium (III). Hence, the order with respect to [oxidant] is unity.

Effect of H^+ ion concentration

To study the effect of H^+ ion concentration on the rate of oxidation of isonicotinic acid hydrazide, the concentration of HCl was varied and also different concentrations of NaCl were added in order to keep ionic strength constant.

Effect of Cl^- ion concentration

To study the effect of Cl^- ion concentration on the rate of oxidation of isonicotinic acid hydrazide by thallium (III), the concentration of HCl and $HClO_4$ were varied keeping the concentration of other reactant constant.

From the above data, it shows that the rate of oxidation of isonicotinic acid hydrazide decreases as Cl^- ion concentration increases.

Effect of temperature

In order to determine the temperature coefficient and activation parameters, the reaction was studied at four different temperatures ranging from 15ºC to 30ºC and at five different initial concentrations of hydrazide.

A persual of the data clearly shows that the rates of oxidation of isonicotinic acid hydrazide are approximately doubled for 10ºC rise in temperature.

Effect of $NaClO_4$ concentration

In order to study the effect of $NaClO_4$ on the oxidation of isonicotinic acid hydrazide, the concentration of $NaClO_4$ solution was varied keeping the other reactants constant.

A persual of the data from table shows that the oxidation of isonicotinic acid hydrazide remains practically constant at five different concentrations of sodium perchlorate.

Effect of dielectric constant

The effect of dielectric constant (D) of the medium on the rate of oxidation of isonicotinic acid hydrazide was studied by the addition of different volumes of ethanol (5% to 40%) to the reaction mixture, keeping the concentration of other reactants constant.

A persual of the data shows that as dielectric constant of the reaction mixture decreases, the rate of oxidation of isonicotinic acid hydrazide also decreases.

Effect of acrylonitrile

In order to determine, whether free radical formation takes place during the course of oxidation, it was necessary to determine the effect of acrylonitrile concentration on the rate of oxidation. The reaction was carried out at five different initial concentrations of acrylonitrile.

A persual of the data from table shows that the rate of oxidation of isonicotinic acid hydrazide remains practically constant at five different concentrations of acrylonitrile. This shows that there is no formation of free radicals in the reaction.

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

$$\mathrm{Tl^{III}} + \text{Hydrazide} \rightleftharpoons \text{Complex} \qquad K_c$$

$$\text{Complex} \rightarrow \mathrm{Tl^{I}} + \text{Intermediate} \qquad \mathrm{k_1}$$

$$\mathrm{Tl^{III}} + \text{Intermediate} \rightarrow \mathrm{Tl^{I}} + \text{Products} \qquad \text{fast}$$

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 $1/k_{obs}$ versus 1/[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**. Eq. (2) gives the rate according to **Scheme 1.**

Since, total [Tl^{III}] exists in the form of free [Tl^{III}] and the complex, Eq. (3); therefore, the [Tl^{III}] free is given by Eq. (6). The overall rate law is now expressed by Eq. (7) and the pseudo-first order rate constant k_{obs}, by Eq. (8).

$$\text{Rate} = k_1\,[\text{Complex}] = k_1K_c\,[\text{Hydrazide}]_{\text{free}}\,[TI^{III}]_{\text{free}} \qquad \ldots(2)$$

$$[TI^{III}]_{\text{total}} = [T1^{III}]_{\text{free}} + [\text{Complex}] \qquad \ldots(3)$$

$$[TI^{III}]_{\text{total}} = [T1^{III}]_{\text{free}} + K_c\,[\text{Hydrazide}]\,[TI^{III}]_{\text{free}} \qquad \ldots(5)$$

$$[T1^{III}]_{\text{free}} = [TI^{III}]_{\text{total}}/\,(1 + K_c\,[\text{Hydrazide}]) \qquad \ldots(6)$$

$$\text{Rate} = k_1K_c\,[\text{Hydrazide}]\,[TI^{III}]_{\text{free}} \qquad \ldots(7)$$

$$k_{obs} = k_1K_c\,[\text{Hydrazide}]/\,(1 + K_c\,[\text{Hydrazide}]) \qquad \ldots(8)$$

Rate law (8) is verified by plotting $1/k_{obs}$ against 1/[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.

Table 1 : Values of Kc and k_1

Temperature (ºC)	K_C ($mol^{-1}dm^3$) [NAH]	$k_1 \times 10^{-4}$ (s^{-1}) [NAH]
15	6.17	10.0
20	7.52	14.3
25	8.1	20.0
30	9.7	33.34

The effect of hydrogen and chloride ion concentrations on the reaction is due to the protonation of hydrazides[16-19] and different chloro – complexes of thallium (III) present in the solution. Hydrazides are known to be protonated in acid medium according to Eq. (9).

$$RCONHNH_2 + H^+ \rightleftharpoons RCONHNH_3^+ \qquad K_H \quad \ldots(9)$$

Therefore, total [Hydrazide] can be expressed by Eq. (10) and thereby, the fact that there was no effect of free [Hydrazide] by Eq. (12). Since the rates of reaction decreases as the [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.

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

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

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

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[20] are $K_1 = 1.38 \times 10^8$, $K_2 = 3.98 \times 10^{13}$, $K_3 = 6.02 \times 10^{15}$ and $K_4 = 1.0 \times 10^{18}$ mol^{-1}dm^3.

$$\text{T1}^{3+} + \text{C1}^- \rightleftharpoons \text{TICl}^{2+} \qquad K_1 \quad \ldots(13)$$

$$\text{TlCl}^{2+} + \text{Cl}^- \rightleftharpoons \text{TlCl}_2^{\;+} \qquad K_2 \quad \ldots(14)$$

$$\text{TlCl}_2^{\;+} + \text{Cl}^- \rightleftharpoons \text{TlCl}_3 \qquad K_3 \quad \ldots(15)$$

$$\text{TlCl}_3 + \text{Cl}^- \rightleftharpoons \text{TlCl}_4^{\;-} \qquad K_4 \quad \ldots(16)$$

All the thallium (III) will exist as $\text{TlCl}_2^{\;+}$ and its concentration can be expressed by Eq. (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 Eq. (18) and (19), the concentrations of $[\text{TlCl}_2]^+_{\text{free,}}$ 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.

$$[\text{Tl (III)}]_{\text{total}} = [\text{T1Cl}_2^{\;+}]_{\text{total}} = [\text{T1C1}_2^{\;+}]_{\text{free}} + [\text{T1C1}_3] + [\text{T1C1}_4^{\;-}] \quad \ldots(17)$$

$$[\text{T1C1}_2^{\;+}]_{\text{total}} = [\text{T1C1}_2^{\;+}]_{\text{free}}\,(1+\beta_1[\text{Cl}^-] + \beta_2[\text{Cl}^-]^2) \quad \ldots(18)$$

$$[\text{T1C1}_2^{\;+}]_{\text{free}} = [\text{T1Cl}_2^{\;+}]_{\text{total}} / (1 + \beta_1[\text{Cl}^-] + \beta_2[\text{Cl}^-]^2) \quad \ldots(19)$$

The concentration of both $[\text{TlCl}_2^{\;+}]_{\text{free}}$ and TlCl_3 parallel the values of rate constants as [Cl$^-$] changes but the order [Cl$^-$] is – 1.5, which makes $[\text{TlCl}_2^{\;+}]_{\text{free}}$ as the only active species.

$$\text{TIC1}_2^{\;+} + \text{Hydrazide} \rightleftharpoons \text{Complex} \qquad K_c$$

$$\text{Complex} \rightarrow \text{RCONNH} + \text{T1C1}_2^{\;-} + \text{H}^+ \qquad k_1$$

$$\text{RCONNH} + \text{H}_2\text{O} + \text{T1C1}_2^+ \rightarrow \text{RCOOH} + \text{N}_2 + 2\ \text{H}^+ + \text{T1C1}_2^- \qquad \text{fast}$$

where R = C_5H_4 for nicotinic acid hydrazide

Scheme 2

The mechanism considering $TlCl_2^+$ 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 Eq. (20) and (21).The rate law (21) was verified by plotting $1/k_{obs}$ against 1/[Hydrazide] and $1/k_{obs}$ against $[H^+]$, which were found to be linear. From the slopes and intercepts of these plots, the values of K_c and K_H were determined.

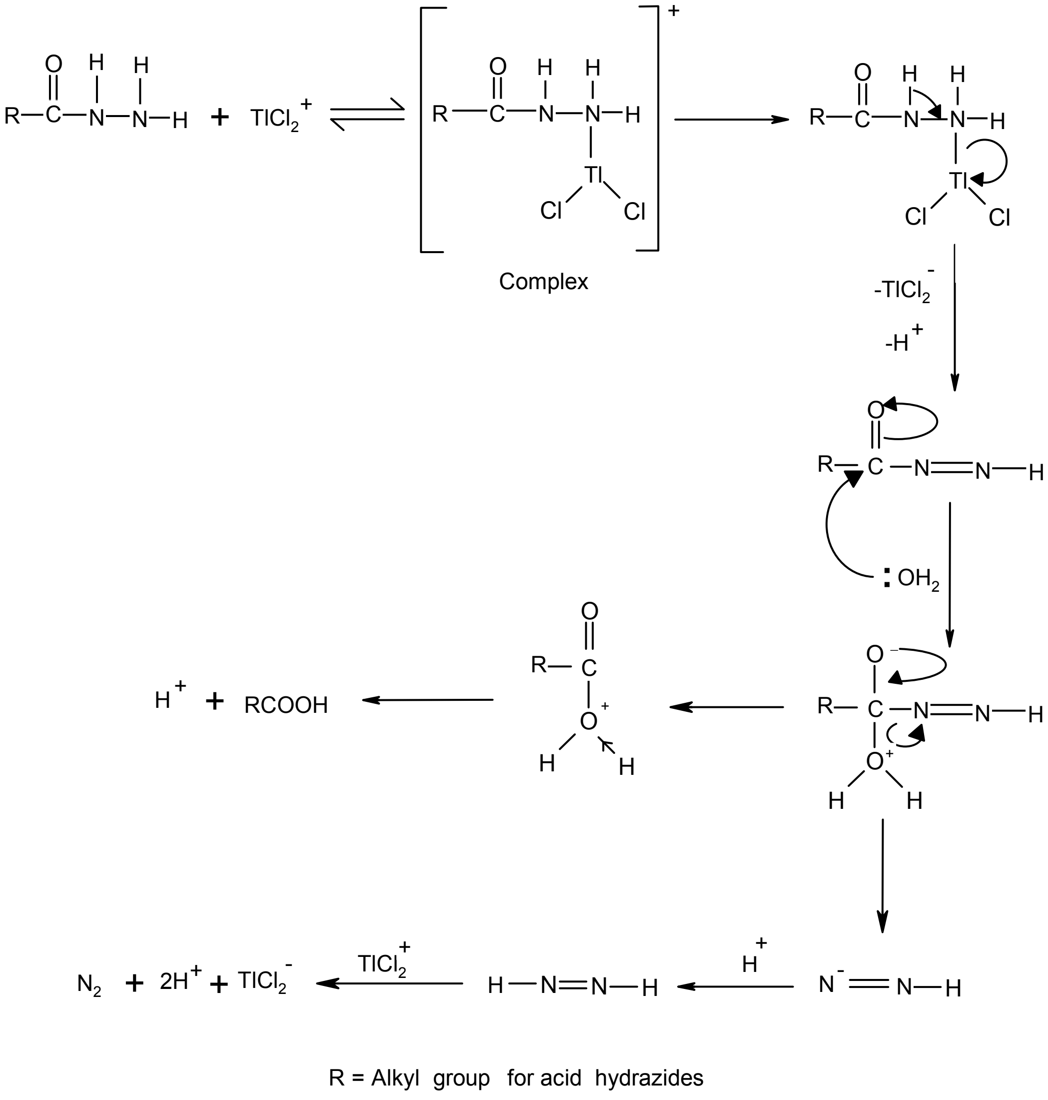
$$\text{Rate} = \frac{k_1 K_c\ [\text{hydrazide}]_{\text{total}}\ [\text{TlCl}_2^+]_{\text{total}}}{(1 + K_c\ [\text{Hydrazide}])\ (1 + K_H[\text{H}^+])\ (1 + \beta_1\ [\text{Cl}^-] + \beta_2\ [\text{Cl}^-]^2} \qquad ...(20)$$

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

The values of K_c are given in Table 1 and those of K_H were found to be 13 and 16 $mol^{-1}\ dm^3$ for isonicotinic acid. The electrophilic character of $TlCl_2^+$ among the thallium (III) chloro complexes is highest; thus, making it the reactive species.

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–T1 bond formation has been postulated during thallium (III) oxidation of nitrogen containing compounds[21,22].

The activation parameters, with respect to slow step, k_1, $\Delta H^\#$ (KJ mol^{-1}), $\Delta G^\#$ (KJ mol^{-1}) and $\Delta S^\#$ ($JK^{-1}mol^{-1}$) were found to be 59.74, 90.42 and -102.96, respectively for isonicotinic 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 and 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[23] in a medium of low relative permittivity.



R = Alkyl group for acid hydrazides

Scheme 3

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