

Kinetic and Mechanistic Study of Oxidation of Salicylic acid Hydrazide by Thallium (III) in Acidic Medium

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Abstract: The reaction between Thallium (III) and Salicylic acid hydrazide is carried out in a mixture of perchloric and hydrochloric acid medium. 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.

Keywords: Salicylic acid hydrazide, kinetics, thallium(III), oxidation.

Introduction

The hydrazides are pharmaceutically important compounds used as antitubercular¹ and antibacterial^{2,3} agents, some of them have been reported to possess anti-inflammatory⁴ and diuretic⁵ activities.

A detail investigation of oxidation of carboxylic acid hydrazide by thallium(III) have not been received much attention. Therefore, 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.

Thallium(III) salts are well known oxidants⁶ in organic synthesis. The oxidation of cyclopropane by thallium(III) acetate in acetic acid leads to cleavage of C-H bonds⁷. The present work deals with kinetic and mechanistic study of oxidation of Salicylic acid hydrazide in hydrochloric acid medium.

Experimental

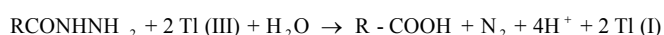
Thallium (III) solution was prepared by dissolving Tl_2O_3 (ACROS) in 1.0 moldm⁻³ HCl and the concentration was ascertained by iodometric titration.

The Salicylic acid hydrazide was prepared from reported⁸ procedure and characterized by determining its melting point. Stock solution of Salicylic 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 $\pm 5\%$. Kinetic runs were followed to about three half-lives of the reactions. 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 carboxylic acid was characterized by determining its MP.



(1)

Results

The reaction was carried out in a mixture of both the acids HCl and HClO₄ 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 [HClO₄] 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 X 10⁻² to 1 X 10⁻¹ mol dm⁻³, keeping the [oxidant] constant at 3.0 X 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 x 10⁻⁴ to 6.5 x 10⁻³ mol dm⁻³ keeping the [hydrazide] constant at 1 x 10⁻¹ mole dm⁻³.

A persual of data shows that the rate of oxidation of Salicylic 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 Salicylic acid hydrazide, the concentration of HCl was varied and also different concentrations of NaCl were added in order to keep ionic strength constant.

A persual of the above data shows that, the rate of oxidation of Salicylic acid decreases as the concentration of H⁺ ion increases.

Effect of Cl⁻ ion concentration

To study the effect of Cl⁻ ion concentration on the rate of oxidation of Salicylic acid hydrazide by thallium (III), the concentration of HCl and HClO₄

were varied keeping the concentration of other reactant constant.

From the above data, it shows that the rate of oxidation of Salicylic acid hydrazide decreases as Cl⁻ ion concentration decreases.

Effect of Temperature

In order to determine the temperature coefficient and thermodynamic parameters, the reaction was studied at four different temperatures ranging from 15^oC to 30^oC and at five different initial concentrations of hydrazide. A persual of the data clearly shows that the rates of oxidation of Salicylic acid hydrazide are approximately doubled for 10^oC rise in temperature.

Effect of NaClO₄ concentration

In order to study the effect of NaClO₄ on the oxidation of Salicylic acid hydrazide, the concentration of NaClO₄ solution was varied keeping the other reactants constant.

A persual of the data from table shows that the oxidation of Salicylic 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 Salicylic 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 rate of oxidation of Salicylic acid hydrazide also decreases.

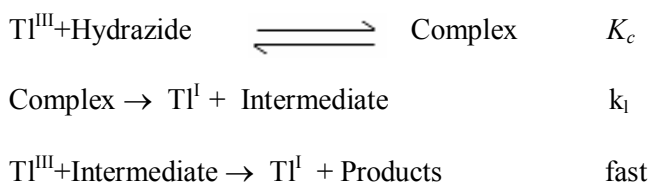
Effect of Acrylonitrile

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 Salicylic acid hydrazide remains practically constant at five different concentrations of acrylonitrile. This shows that there is no formation of free radicals in the reaction.

Discussion

Since there is no formation of free radicals in the reaction, the reaction proceeds with two-electron transfer step. The order in thallium (III) was found to be unity and the order in hydrazide was found to be fractional.



Scheme 1

Table 1 – values of K_c and k_1

$[\text{HCl}] = 0.1 \text{ mol dm}^{-3}$, $[\text{HClO}_4] = 0.1 \text{ mol dm}^{-3}$
 $[\text{Tl}^{\text{III}}] = 3.0 \times 10^{-3} \text{ mol dm}^{-3}$,
 $I = 0.6 \text{ mol dm}^{-3}$ in 50% v/v 1,4-Dioxane

Temperature ⁰ C	$K_c(\text{mol}^1\text{dm}^3)[\text{SAH}]$	$k_1 \times 10^{-4} (\text{S}^{-1})[\text{SAH}]$
15	18.27	1.82
20	18.27	3.20
25	18.28	3.64
30	18.28	6.71

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_{obs} , by Equation 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 hydrazides⁹ and different chloro – complexes of thallium (III) present in the solution. Hydrazides are known to be protonated in acid medium according to Equation 9.

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

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

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

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

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

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



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

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

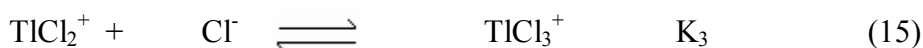
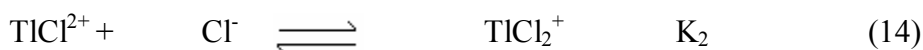
$$[\text{Hydrazide}]_{\text{free}} = [\text{Hydrazide}]_{\text{total}} / (1 + K_H [\text{H}^+]) \quad (12)$$

Therefore, total [Hydrazide] can be expressed by Equation 10 and thereby the fact that there was no effect of Free [Hydrazide] by Eq. 12. Since the rates of reaction decreases as the $[\text{H}^+]$ increases, free hydrazide is the active species.

Thallium (III) forms strong complexes with chloride ions of the formula 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 constants¹⁰ are $K_1 = 1.38 \times 10^8$, $K_2 = 3.98 \times 10^{13}$, $K_3 = 6.02 \times 10^{15}$ and $K_4 = 1.0 \times 10^{18} \text{ mol}^{-1} \text{ dm}^3$. The presence of $3.0 \times 10^{-2} \text{ mol dm}^{-3}$

chloride ion concentration (which is the minimum $[\text{Cl}^-]$ used in the present study).

All the thallium (III) will exist as 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 $[\text{TlCl}_2^+]_{\text{free}}$, TlCl_3 and TlCl_4^+ were calculated at different chloride ion concentrations and compared with the change in rate constant as the chloride ion concentration varied.



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

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

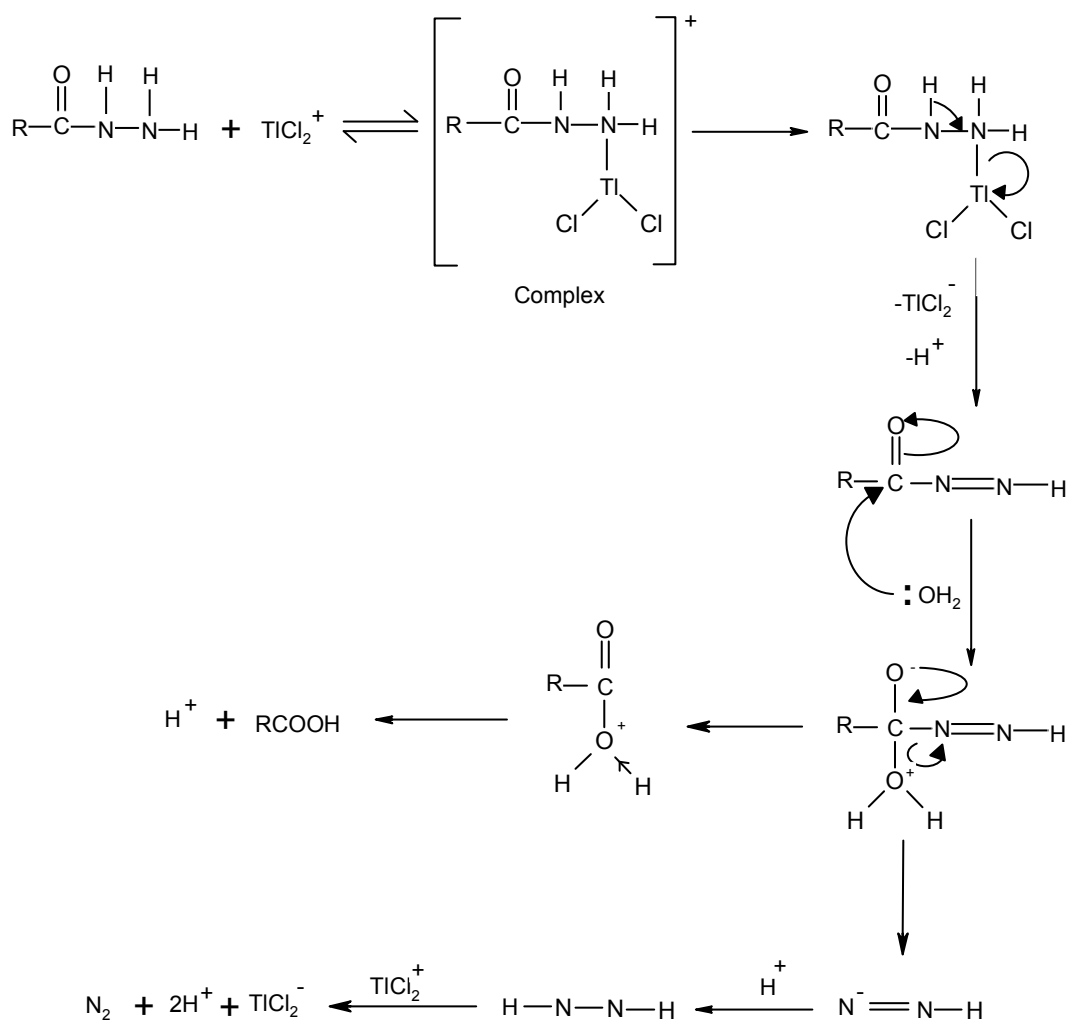
$$[\text{TlCl}_2^+]_{\text{free}} = [\text{TlCl}_2^+]_{\text{total}} / (1 + \beta_1 [\text{Cl}^-] + \beta_2 [\text{Cl}^-]^2) \quad (19)$$

The concentration of both of $[\text{TlCl}_2^+]_{\text{free}}$ and 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 = C₅H₄ for Salicylic acid hydrazide

Scheme 2



R=Alkyl group for acid hydrazides

Scheme 3

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

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

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 Equations 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.

The values of K_c are given in Table 1 and those of K_H were found to be 13 and 16 $\text{mol}^{-1} \text{dm}^3$ for Salicylic acid. The electrophilic character of TlCl_2^+ among the thallium (III) chlorocomplexes 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-Tl bond formation

has been postulated during thallium (III) oxidation of nitrogen¹¹ containing compounds.

The activation parameters, with respect to slow step, k_1 , ΔH^\ddagger (KJ mol^{-1}), ΔG^\ddagger (KJ mol^{-1}) and ΔS^\ddagger ($\text{JK}^{-1} \text{mol}^{-1}$) were found to be 59.74, 90.42 and -102.96 respectively for Salicylic 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 ethanol content in the reaction medium decreases; the rate such an effect of the solvent is due to the stabilization of the complex formed between reactants¹² in a medium of low relative permittivity.

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