



Oxidation of n-Valeric acid hydrazide to the Corresponding Acid by Thallium (III) in 1, 4-Dioxane Medium - A Kinetic and Mechanistic Approach

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Abstract : The reaction between Thallium (III) and n-Valeric 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 $15^{\circ}C$ to $30^{\circ}C$. The activation parameters were also determined and a mechanism is predicted.

Key words : kinetics, Thallium(III), Oxidation, n-VAH.

Aims and Background

Chemical kinetics, also known as reaction kinetics, is the study of rates of chemical processes. Chemical kinetics includes investigations of how different experimental conditions can influence the speed of a chemical reaction and yield information about the reaction's mechanism and transition states, as well as the construction of mathematical models that can describe the characteristics of a chemical reaction.

During the course of chemical reaction, molecules come closer, atoms change their positions, electron shift takes place and as a result new compounds are formed. A sequence of steps by which the reaction occurs is known as "reaction mechanism". The mechanism of the reaction is known, if the detailed picture of all the individual or elementary processes involving atoms, molecules, radicals, ions and other reactive species are clearly understood.

The mechanism of the reaction gives a detailed picture of the activated complex¹ not only in terms of the constituent molecules but also in terms of geometry.

Therefore, the investigation of reaction mechanism needs the study of reaction rates.

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Thallium(III) salts, which are wellknown oxidants in organic chemistry² have not yet been employed for the oxidation of hydrazides of carbon-nitrogen bonds: 1) Cleavage of oximes and semicarbazones to obtain aldehydes or ketones³ and 2) the preparation of alkynoic esters or allenic esters from 5-pyrazolanes and their condensed analogs⁴. The oxidation of cyclopropane by thallium(III) acetate in acetic acid leads to cleavage of C-H bonds⁵. The reaction is first order in both reactants. Interest in the use of thallium(III) in the oxidation of organic compounds has increased only recently and research in this regard is not been extensive. The potential of this oxidant is realized more and more as is evident from the considerable amount of work that is lately being done. Thus, the selectivity of thallium (III) is higher than its neighbours in the periodic table, mercury(II) and lead (IV) and also thallium (III) is a better oxidant than the other two. The kinetics of oxidation of simple olefins was studied in detail by Henry⁶.

The hydrazides are pharmaceutically important compounds used as antitubercular and antibacterial^{7,8} agents, some of them have been reported to possess anti-inflammatory⁹ and diuretic¹⁰ activities. The reaction of hydrazides with most oxidants give the corresponding acids¹¹ and in some cases¹² esters or amides. Thallium(III) salts are well known oxidants 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 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 and mild oxidizing agent. Hence, the present work deals with the kinetics and mechanism of oxidation of n-Valeric acid hydrazide by thallium(III) in acidic medium.

Experimental

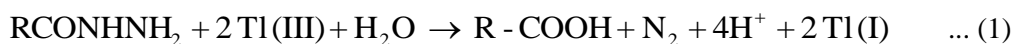
Thallium (III) solution was prepared by dissolving Tl_2O_3 (ACROS) in 1.0 moldm⁻³ HCl and the concentration was ascertained by iodometric titration. The n-Valeric acid hydrazide was prepared from reported¹³ procedure and characterized by determining their melting points. Stock solution of n-Valeric acid hydrazide was prepared in 50 % v/v, 1,4-dioxan. 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-dioxan did not occur.

End Product Analysis

For identification of products the reaction was carried out by using aqueous solution of hydrazide, Thallium(III), HCl and $HClO_4$. The flask containing reaction mixture was kept in thermostated water bath maintained at 50°C for 24 hours to complete the reaction, the residue obtained after filtration was analysed for acid as follows

- i. The presence of n-Valeric acid group was detected by testing with bicarbonate.
- ii. The formation of acid was confirmed by IR and its melting point.



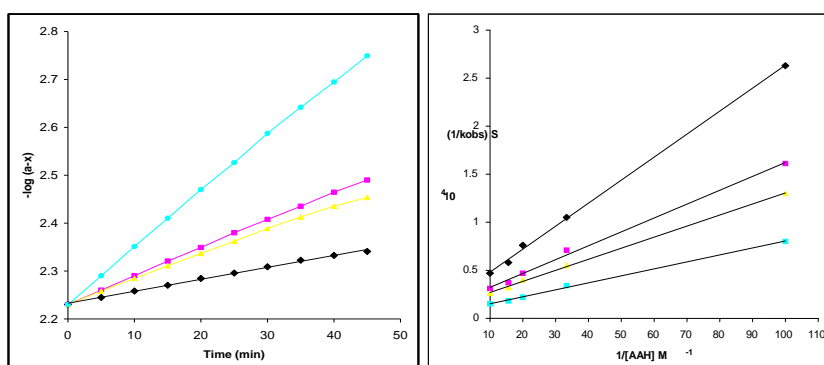
Results and Discussion

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 $[HCl]$ and $[HClO_4]$ of 0.1 mol dm⁻³ each and ionic strength of 0.6 mol dm⁻³. Concentration of oxidant was varied from 6.4×10^{-4} to 6.4×10^{-3} mol dm⁻³ keeping the [hydrazide] constant at 1×10^{-1} mol dm⁻³. Since, the pseudo first order rate constants were fairly constant ($3.4 \pm 0.1 \times 10^{-4} s^{-1}$ for n-VAH) at the order with respect to [oxidant] is unity. The effect of [hydrazide] was studied between the concentration

range from 1×10^{-2} to 1×10^{-1} mol dm⁻³ keeping the [oxidant] constant at 3.0×10^{-3} mol dm⁻³. The pseudo first order rate constants increases with increase in concentration and the order with respect to hydrazide is found to be fractional.

To study the effect of [H⁺] and [Cl⁻],[oxidant], [hydrazide] and ionic strength were kept as 3.0×10^{-3} , 1×10^{-1} and 0.6 mol dm⁻³ respectively. To vary [H⁺] and [Cl⁻], HClO₄ and NaCl were used. Increase in [H⁺] from 0.13 to 0.60 mol dm⁻³ decreases 10^{-4} k(s⁻¹) from 35.85 to 0.40 for n-VAH at 25°C. Increase in [Cl⁻] from 0.13 to 0.60 mol dm⁻³ decreases 10^{-4} k(S⁻¹) from 6.10 to 0.28 for n-VAH at 25°C. The relative permittivity was varied by changing the 1,4-dioxan content from 5 to 40 % v/v. The rate was found to decrease with decrease in relative permittivity.

Added acrylonitrile in the concentration range 0.5 to 2.5vol.% by keeping concentrations of oxidant, reductant, perchloric acid, hydrochloric acid and ionic strength fixed did not produce any precipitate due to polymerization of the added acrylonitrile on the pseudofirst order rate constants indicating absence of free radical



Effect of Temperature

Michaelis-Menten plot

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. Such fractional order in substrate concentration is due to the prior complex formation equilibrium between the reactants.



Scheme 1

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.

$$\text{Rate} = k_1 [\text{Complex}] = k_1 K_c [\text{Hydrazide}]_{\text{free}} [\text{Tl}^{\text{III}}]_{\text{free}} \quad (1)$$

$$[\text{Tl}^{\text{III}}]_{\text{total}} = [\text{Tl}^{\text{III}}]_{\text{free}} + [\text{Complex}] \quad (2)$$

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

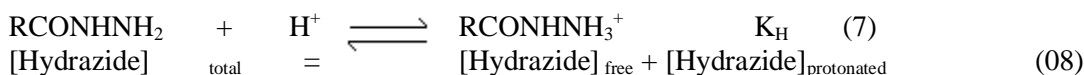
$$[\text{Tl}^{\text{III}}]_{\text{free}} = [\text{Tl}^{\text{III}}]_{\text{total}} / (1 + K_c [\text{Hydrazide}]) \quad (4)$$

$$\text{Rate} = k_1 K_c [\text{Hydrazide}] [\text{Tl}^{\text{III}}]_{\text{free}} \quad (5)$$

$$k_{\text{obs}} = k_1 K_c [\text{Hydrazide}] / (1 + K_c [\text{Hydrazide}]) \quad (6)$$

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 hydrazides¹⁴ and different chloro – complexes¹⁵ of thallium (III) present in the solution. In acid medium according to Equation 9. Hydrazides are known to be protonated, 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 decrease 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.



$$[\text{Hydrazide}]_{\text{total}} = [\text{Hydrazide}]_{\text{free}} + K_H [\text{Hydrazide}]_{\text{free}} \quad (09)$$

$$[\text{Hydrazide}]_{\text{free}} = [\text{Hydrazide}]_{\text{total}} / (1 + K_H [H^+]) \quad (10)$$

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 constants¹⁶ are $K_1 = 1.38 \times 10^8$, $K_2 = 3.98 \times 10^{13}$, $K_3 = 6.02 \times 10^{15}$ and $K_4 = 1.0 \times 10^{18} \text{ mol}^{-1} \text{ dm}^3$.



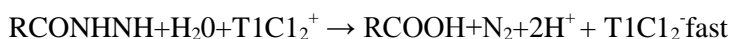
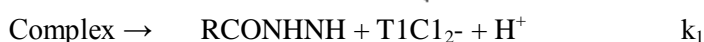
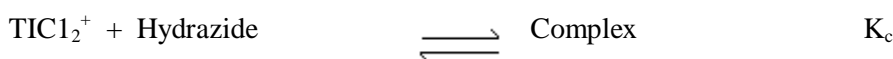
All the thallium(III) will exist as $TlCl_2^+$ and its concentration can be expressed by Equation 17. The $[TlCl_2^+]_{\text{free}}$ can now be given by eq. 19 where, $\beta_1 = K_3/K_2 = 151$ and $\beta_2 = K_4/K_3 = 166$, further, using Equations 18 and 19 the concentrations of $[TlCl_2^+]_{\text{free}}$, $TlCl_3$ and $TlCl_4$ were calculated at different chloride ion concentrations and compared with the change in rate constant as the chloride ion concentration varied.

$$[Tl(III)]_{\text{total}} = [TlCl_2^+]_{\text{total}} = [TlCl_2^+]_{\text{free}} + [TlCl_3] + [TlCl_4] \quad (15)$$

$$[TlCl_2^+]_{\text{total}} = [TlCl_2^+]_{\text{free}} (1 + \beta_1 [Cl^-] + \beta_2 [Cl^-]^2) \quad (16)$$

$$[TlCl_2^+]_{\text{free}} = [TlCl_2^+]_{\text{total}} / (1 + \beta_1 [Cl^-] + \beta_2 [Cl^-]^2) \quad (17)$$

The concentration of both of $[TlCl_2^+]_{\text{free}}$ and $TlCl_3$ parallel the values of rate constants as $[Cl^-]$ changes but the order $[Cl^-]$ is -1.5 , which makes $[TlCl_2^+]_{\text{free}}$ as the only active species.



where R – Alkyl group **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 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 $[H^+]$ 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 heterocyclic acid hydrazides respectively.

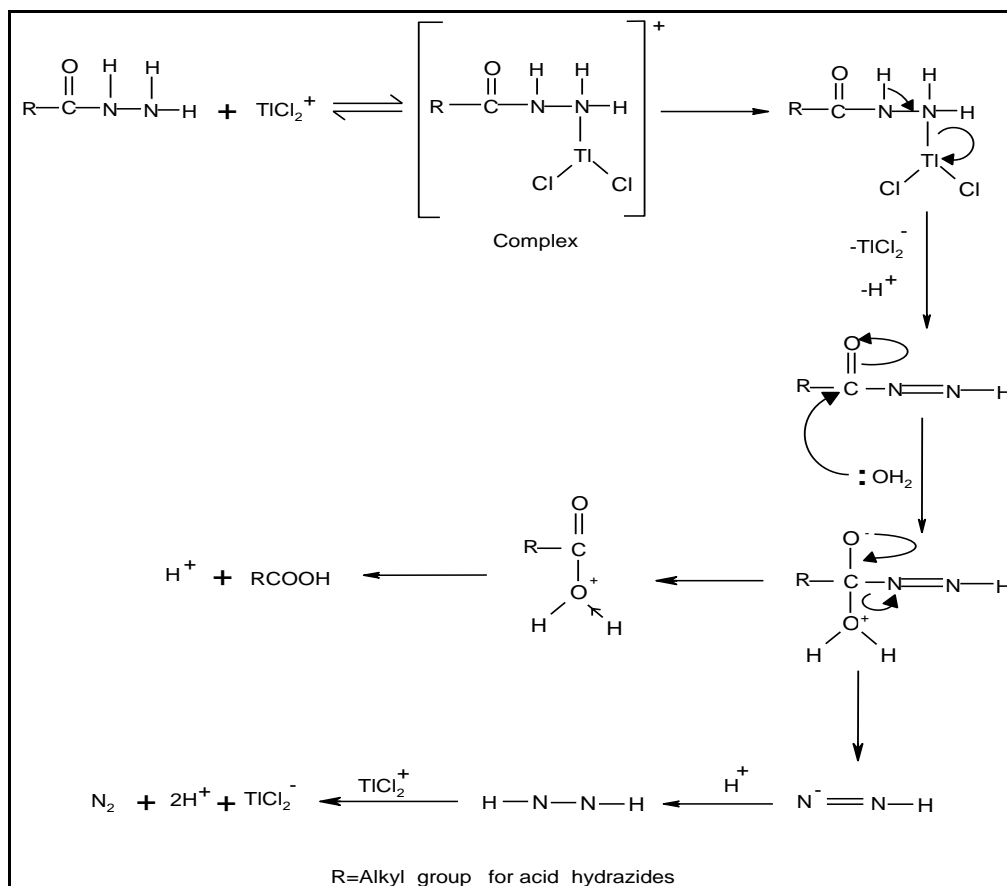
$$\text{Rate} = \frac{k_1 K_c [\text{Hydrazide}]_{\text{total}} [TlCl_2^+]_{\text{total}}}{(1 + K_c [\text{Hydrazide}]) (1 + K_H [H^+]) (1 + \beta_1 [Cl^-] + \beta_2 [Cl^-]^2)} \quad (18)$$

$$k_{\text{obs}} = \frac{k_1 K_c [\text{Hydrazide}]_{\text{total}}}{(1 + K_c [\text{Hydrazide}]) (1 + K_H [H^+]) (1 + \beta_1 [Cl^-] + \beta_2 [Cl^-]^2)} \quad (19)$$

The electrophilic character of $TlCl_2^+$ among the thallium (III) chlorocomplexes is highest thus making it the reactive species. Table 1 – values of K_c and k_1 $[HCl] = 0.1 \text{ mol dm}^{-3}$, $[HClO_4] = 0.1 \text{ mol dm}^{-3}$ $[Tl^{III}] = 3.0 \times 10^{-3} \text{ mol dm}^{-3}$, $I = 0.6 \text{ mol dm}^{-3}$

Hydrazide	$K_c. (\text{mol dm}^{-3})$			
	15°C	20°C	25°C	30°C
n-VAH	9.45	9.48	9.48	9.46

Mechanism



Scheme 3

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 nitrogen¹⁷ 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 (JK⁻¹mol⁻¹) were found to be 48.44, 127.16 and -115.50 respectively for n-VAH. 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-dioxan content in the reaction medium decreases; the rate such an effect of the solvent is due to the stabilization of the complex formed between reactants¹⁸ in a medium of low relative permittivity¹⁹⁻²².

Conclusion

The order of reactivity of n-Valeric acid hydrazide under investigation is -

VAH <BAH.

In case of n-Valeric acid hydrazide, the electron donating inductive effect of alkyl group is weaker and has negligible effect on reactivity.

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