

COMPARATIVE KINETIC AND MECHANISTIC STUDY OF OXIDATION OF BENZOIC, p-CHLORO BENZOIC, p- METHOXY BENZOIC ACID HYDRAZIDES WITH THALLIUM (III) IN ACIDIC MEDIUM

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ABSTRACT

The kinetics and Mechanism of oxidation of benzoic, p-chlorobenzoic and p-methoxy benzoic acid hydrazides by thallium(III) in acidic is carried out iodometrically by keeping ionic strength of reaction mixture constant. The reaction proceeds through formation of complex with reactant, which decomposes in subsequent steps to give product. The increase in $[H^+]$ and $[Cl^-]$ decreases the rate of the reaction. The thermodynamic parameters were also determined and a mechanism is predicted.

KEY WORDS : kinetics, Thallium(III), Oxidation.

1. INTRODUCTION

A detail investigation of oxidation of carboxylic acid hydrazide by thallium(III) have not been received much attention. Therefore, with a view to develop a new method, the present study was carried out. The reaction of hydrazides with most oxidants give the corresponding acids (Ho, 1972; Schnyder, 1975; Tsuji, 1976) and in some cases (Aylward, Norman, 1968; Tsuji, 1975; Hoffman, Kumar, 1984) esters or amides. The hydrazides are pharmaceutically important compounds used as antitubercular (Werner, 1953) and antibacterial (Madzhoyan, 1966; Winterstein, 1956) agents, some of them have been reported to possess anti-inflammatory (Pfister, Soliman, 1968) and diuretic (Jucker, Linde, 1962) 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 thallium(III) oxidations of several other aliphatic, aryl aliphatic and cyclic ketones have been examined (Radhakrishnamurthi, Patil, 1979). The chemical literature has described thallium-induced splitting of carbon-nitrogen bonds (Radhakrishnamurthi, Patil, 1978) no mechanistic investigation has been carried out. The present work deals with kinetic and mechanistic study of oxidation of benzoic, p-chlorobenzoic and p-methoxy benzoic acid hydrazide in hydrochloric acid medium.

2. EXPERIMENTAL

Thallium (III) solution was prepared by dissolving Tl_2O_3 (ACROS) in 1.0 mol dm^{-3} HCl and the concentration was ascertained by iodometric titration.

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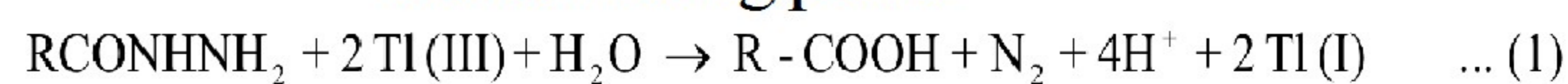
The heterocyclic acid hydrazides were prepared from reported (Vogel, 1975) procedure and characterized by determining their melting points. Stock solution of benzoic, p-chlorobenzoic and p-methoxy benzoic acid hydrazides were prepared in 50 % v/v 1,4-dioxan. Ionic strength was kept constant.

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 $50^\circ C$ for 24 hours to complete the reaction, the residue obtained after filtration was analysed for acid as follows

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



3. RESULTS AND DISCUSSION

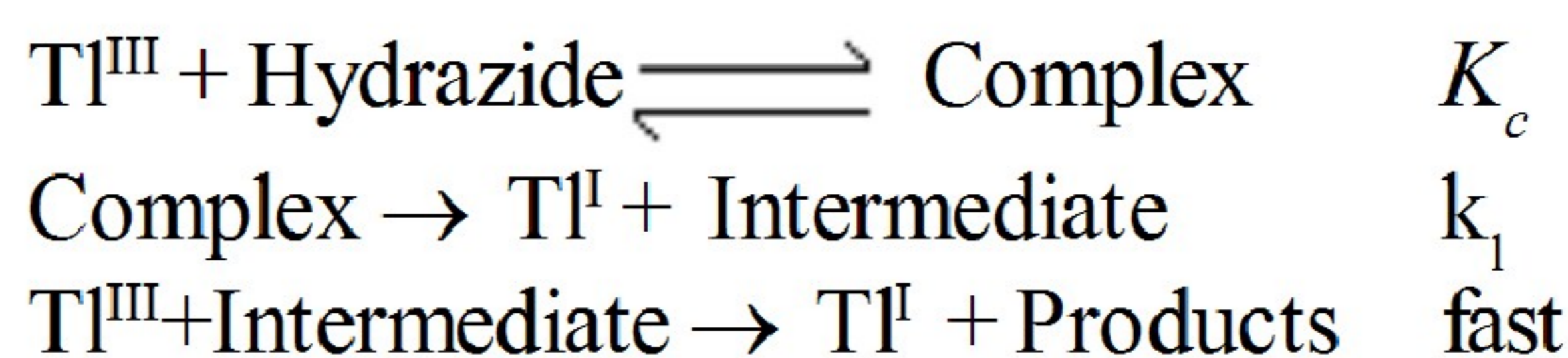
The reaction occurs rapidly in perchloric acid medium but in the presence of hydrochloric acid the rate is measurable. Therefore, the reaction was carried out in a mixture of both the acids. The effect of reactants on the reaction was studied at constant $[H^+]$ and $[Cl^-]$ of 0.23 and 0.13 mol dm⁻³ each and ionic strength of 0.6 mol dm⁻³. Concentration of oxidant was varied from 6.4x10⁻⁴ to 6.4x10⁻³ mol dm⁻³ keeping the [hydrazide] constant at 1x10⁻¹ mol dm⁻³. Since, the pseudo first order rate constants were fairly constant (3.6 ± 0.1x10⁻⁴ s⁻¹ for BAH at 25°C and 6.70 ± 0.1x10⁻⁴ s⁻¹ for p- OCH₃ BAH at 25°C and 2.3 ± 0.1x10⁻⁴ s⁻¹ for p- Cl BAH at 25°C, the order with respect to [oxidant] is unity. The effect of [hydrazide] was studied between the concentration range from 1x10⁻² to 1x10⁻¹ mol dm⁻³ keeping the [oxidant] constant at 3.0x10⁻³ 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 (0.75 for BAH, 0.79 for p-OCH₃ BAH and 0.70 for p-Cl BAH).

To study the effect of $[H^+]$ and $[Cl^-]$, [oxidant], [hydrazide] and ionic strength were kept as 3.0x10⁻³, 1x10⁻¹ 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 4.20 to 0.15 for BAH at 25°C and 74.20 to 1.05 for p-OCH₃ BAH at 25°C and from 2.03 to 0.08 for p-Cl BAH at 25°C. Increase in $[Cl^-]$ from 0.13 to 0.60 mol dm⁻³ decreases 10⁻⁴ k(S⁻¹) from 2.8 to 0.095 for BAH at 25°C and 7.35 to 1.05 for p-OCH₃ BAH at 25°C and from 1.40 to 0.060 for p-Cl BAH 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 2.5 vol.% 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 radicals.

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_{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. Equation 2 gives the rate according to Scheme 1. Since, total $[Tl^{III}]$ exists in the form of free $[Tl^{III}]$ and the complex (Equation 3) therefore, the $[Tl^{III}]$ 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.

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

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

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

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

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

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

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 k₁ 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 (Weast, 1970) and different chloro-complexes (Kazo, 1963; Krishnarao, 1978; Ramaih, 1979) 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 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.

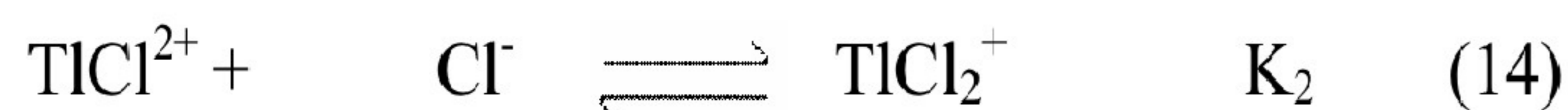


$$[\text{Hydrazide}]_{\text{total}} = [\text{Hydrazide}]_{\text{free}} + [\text{Hydrazide}]_{\text{protonated}} \quad (10)$$

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

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

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 constants (Lee, 1971) are $K_1 = 1.38 \times 10^8$, $K_2 = 3.98 \times 10^{13}$, $K_3 = 6.02 \times 10^{15}$ and $K_4 = 1.0 \times 10^{18} \text{ mol}^{-1} \text{ dm}^3$.



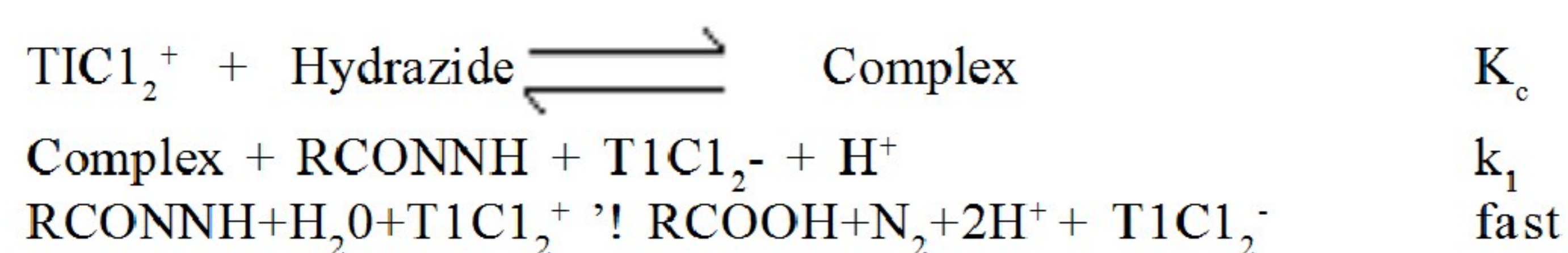
All the thallium(III) will exist as $TlCl_2^+$ and its concentration can be expressed by Equation 17. The $[TlCl_2^+]_{\text{free}}$ can now be given by eq. 19, where, $\beta_1 = K_3/K_2 = 151$ and $\beta_2 = K_4/K_3 = 166$, further, using Equations 18 and 19 the concentrations of $[TlCl_2^+]_{\text{free}}$,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

$$[Tl(III)]_{\text{total}} = [TlCl_2^+]_{\text{total}} = [TlCl_2^+]_{\text{free}} + [TlCl_3] + [TlCl_4] \quad (17)$$

$$[TlCl_2^+]_{\text{total}} = [TlCl_2^+]_{\text{free}} (1 + \beta_1[Cl^-] + \beta_2[Cl^-]^2) \quad (18)$$

$$[TlCl_2^+]_{\text{free}} = [TlCl_2^+]_{\text{total}} / (1 + \beta_1[Cl^-] + \beta_2[Cl^-]^2) \quad (19)$$

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 for acid hydrazides

Scheme 2

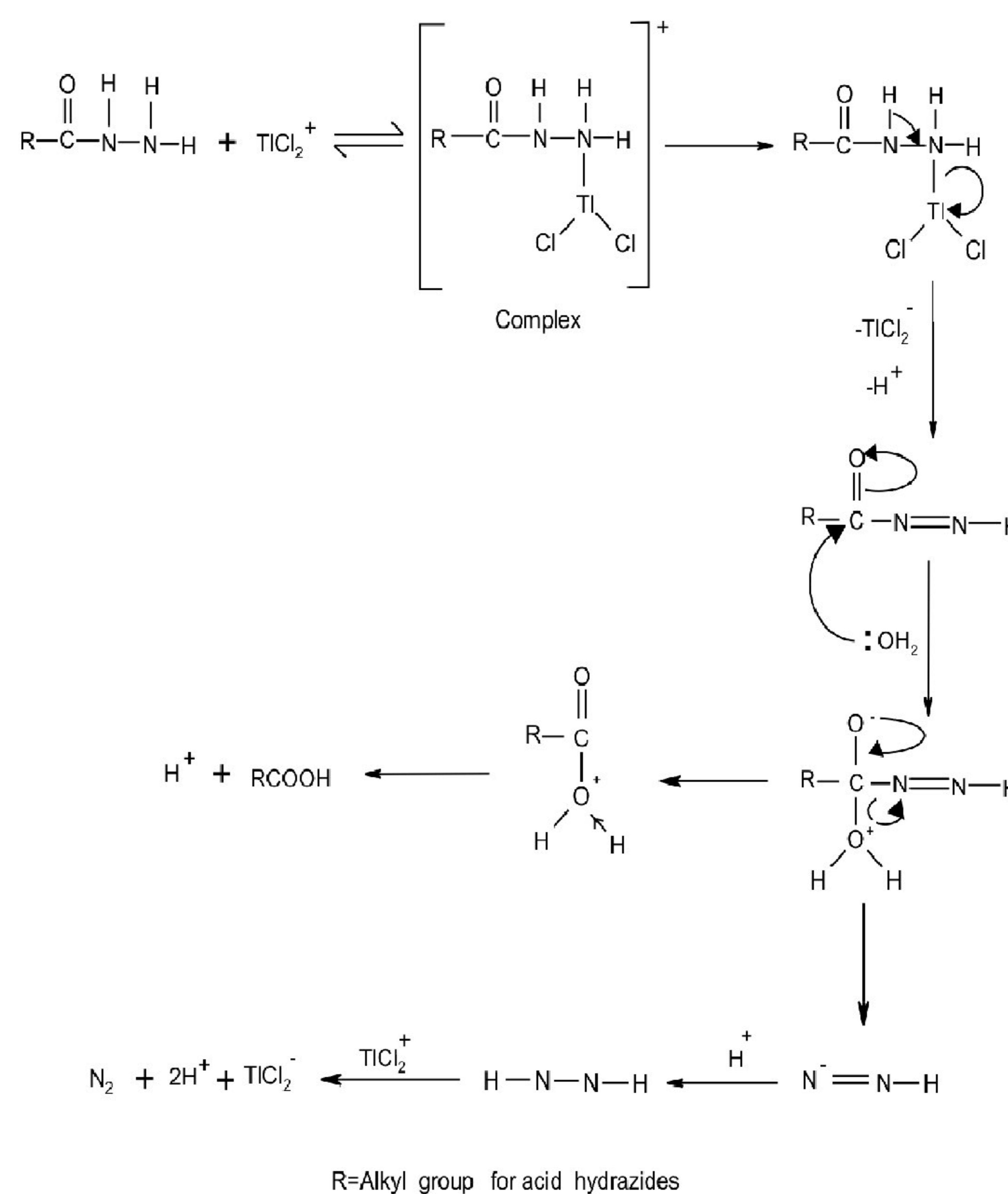
The mechanism considering $TlCl_2^+$ of oxidant and free hydrazide of the substrate as the active species can now be represented by scheme 2 with respective rate law and the expression for the pseudo-first order rate constants by Equations 20 and 21. The rate law 21 was verified by plotting $1/k_{\text{obs}}$ 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 I and those of K_H were found to be 13 and 16 $\text{mol}^{-1} \text{ dm}^3$ for heterocyclic acid hydrazides respectively.

$$\text{Rate} = \frac{k_1 K_c [\text{Hydrazide}]_{\text{total}} [TlCl_2^+]_{\text{total}}}{(1 + K_c [\text{Hydrazide}]) (1 + K_H [H^+]) (1 + \beta_1 [Cl^-] + \beta_2 [Cl^-]^2)} \quad (20)$$

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

The electrophilic character of $TlCl_2^+$ among the thallium (III) chloro complexes is highest thus making it the reactive species.

**Table 1 – K_c ($\text{mol}^{-1} \text{ dm}^3$) and k_1 ($\text{mol}^{-1} \text{ dm}^3$)
T = 288 K to 303 K**



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 nitrogen (Mckillop, 1971; Buttler, 1981) 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, 97.69 and -94.64 respectively for benzoic acid hydrazide (BAH) and 36.78, 78.11 and -204.38 for p-methoxy benzoic acid hydrazide (p-OCH₃BAH) and 71.82, 98.80 and

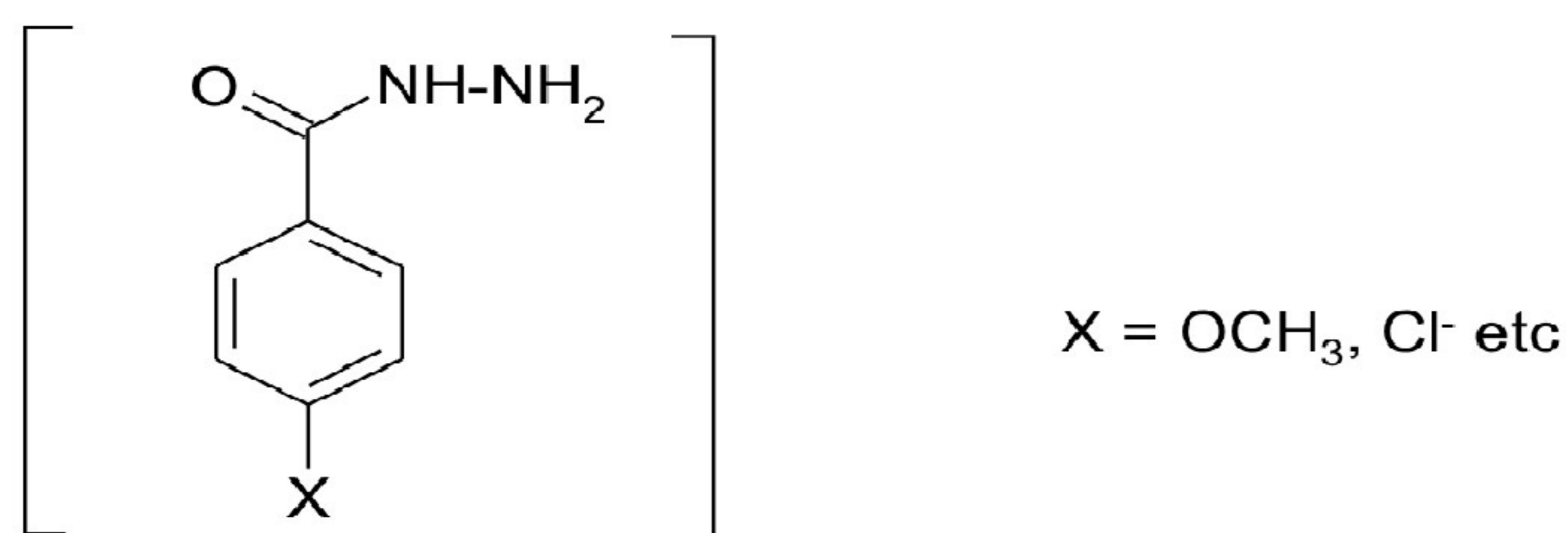
90.54 respectively for benzoic, p- methoxy benzoic and p- chloro benzoic acid hydrazide (p-Cl BAH). Considerable decrease in the entropy of activation is due to formation of more ordered transition state as shown in scheme 3. The mechanism involves neutral hydrazide as the active substrate thus the reaction 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 reactants (Amis, 1966) in a medium of low relative permittivity.

4. CONCLUSION

The order of reactivities of Benzoic and substituted benzoic acid hydrazides under investigation is – p – Cl BAH < BAH < p-OCH₃ BAH

The observed sequence can be attributed to various possibilities and factors. The highest rate of p-OCH₃ BAH is due to strong electron donating mesomeric effect of -OCH₃ group since it is in the para position, the unsubstituted benzoic acid hydrazide has intermediate stability.

Chlorine has electron withdrawing inductive effect but an electron-donating mesomeric effect since it is in the para position.



Hence, it is evident that the rate of reaction is enhanced by electron donating group(s) at para position and retarded by electron withdrawing group(s).

5. ACKNOWLEDGEMENT

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Table 1: K_c (mol⁻¹dm³) and k₁ (mol⁻¹dm³) T = 288 K to 303 K

Temp °C	K _c (mol ⁻¹ dm ³) BAH	k x 10 ⁴ s ⁻¹ BAH	K _c (mol ⁻¹ dm ³) p-OCH ₃ BAH	k x 10 ⁴ s ⁻¹ p-OCH ₃ BAH	K _c (mol ⁻¹ dm ³) p-Cl BAH	k x 10 ⁴ s ⁻¹ p-Cl BAH
15	59.09	1.23	7.42	0.10	16.66	1.25
20	55.50	2.05	8.00	0.12	17.50	2.38
25	47.69	2.58	7.00	0.16	15.00	3.33
30	40.00	4.44	7.57	0.22	17.50	10.00

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