

# Kinetics of oxidation of tripeleennamine hydrochloride by silver periodate complex in presence and absence of ruthenium catalyst

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## ABSTRACT

In this paper author seeks to present kinetics of oxidation of Tripeleennamine hydrochloride (TPH) is a psychoactive drug and member of the pyridine and ethylenediamine classes that is used as an antipruritic and first-generation antihistamine. It is used in the treatment of asthma, hay fever, rhinitis and urticaria. In addition to its antihistamine properties, tripeleennamine also acts as a weak serotonin reuptake inhibitor (SRI) and dopamine reuptake inhibitor (DRI). Because of its inhibitor properties, tripeleennamine is used as the recreational drug. Diperioatoargentate(III) (DPA) is a powerful oxidizing agent in alkaline medium with the reduction potential 1.74 V. It is widely used as a volumetric reagent for the determination of various organic and inorganic species. Jayaprakash Rao et al. have used DPA as an oxidizing agent for the kinetics of oxidation of various substrates. They normally found that order with respect to both oxidant and substrate was unity and  $\text{OH}^-$  was found to enhance the rate of reaction. It was also observed that they did not arrive at the possible active species of DPA in alkali and on the other hand they proposed mechanisms by generalizing the DPA as  $[\text{Ag}(\text{HL})\text{L}]^{(x+1)-}$ . However, Kumar et al. put an effort to give an evidence for the reactive form of DPA in the large scale of alkaline pH. When the Ag(III) species are involved, it would be interesting to know which of the species is the active oxidant. In the present investigation, we have obtained the evidence for the reactive species for the DPA in alkaline medium. The DPA is a metal complex with Ag in 3<sup>+</sup> oxidation state like  $\text{Cu}^{3+}$  in DPC and  $\text{Fe}^{3+}$  in hemoglobin.

Transition metals are known to catalyze many oxidation-reduction reactions since they involve multiple oxidation states. In recent years, the use of transition metal ions such as osmium, ruthenium, palladium, chromium and iridium either alone or as binary mixtures, as catalysts in various redox processes has attracted considerable interest.

**Keywords:** Oxidation, Kinetics, Ruthenium (III) catalyst, Tripeleennamine hydrochloride, Silver (III) periodate complex.

## 1. Introduction

Literature survey reveals that there is no report on the uncatalyzed and catalyzed oxidative mechanism of tripeleennamine hydrochloride by diperioatoargentate(III) in alkaline medium. Such oxidation studies may throw some light on the mechanism of conversions of the compounds in biological systems. In earlier reports of DPA oxidation [18], the order in  $[\text{OH}^-]$  was found to be less than unity and periodate had a retarding effect in most of

the reactions and monoperiodatoargentate(III) (MPA) was considered to be active species. However, in the present study, we have observed entirely different kinetic observations and diperiodatoargentate(III) (DPA) itself is found to be active form of oxidant. In order to understand the active species of oxidant and catalyst, to compute the activity of the catalyst and to propose the appropriate mechanisms, the title reaction is investigated in detail in this present work. An understanding of the mechanism allows the chemistry to be interpreted, understood and predicted.

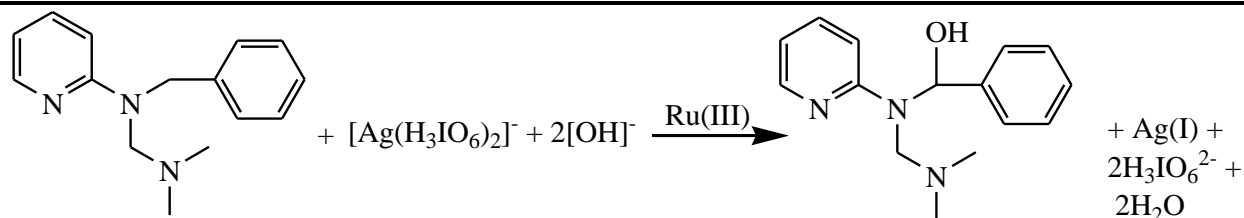
## 2. Experimental

The reaction was followed to more than 85% completion of the reaction. Plots of  $\log(\text{absorbance})$  versus time lead to the first-order rate constants ( $k_U$  or  $k_C$ ). The plots were linear up to 80% completion of reaction. The orders for various species were determined from the slopes of plots of  $\log(k_U$  or  $k_C)$  versus respective concentration of species except for [DPA] in which non-variation of  $k_U$  and  $k_C$  was observed as expected to the reaction condition. The rate constants were reproducible within  $\pm 5\%$ . During the kinetics, a constant concentration viz.  $1.0 \times 10^5 \text{ mol dm}^{-3}$  of  $\text{KIO}_4$  was used throughout the study. The total concentration of  $\text{OH}^-$  and  $\text{IO}_4^-$  was calculated by considering the amount present in the DPA solution and that additionally added. Kinetics runs were also carried out in  $\text{N}_2$  atmosphere in order to understand the effect of dissolved oxygen on the rate of reaction. No significant difference in the results was obtained under a  $\text{N}_2$  atmosphere and in the presence of air. In view of the ubiquitous contamination of carbonate in the basic medium, the effect of carbonate was also studied. The added carbonate had no effect on the reaction rates. In view of the modest concentration of alkali used in the reaction medium, attention was also directed to the effect of the reaction vessel surface on the kinetics. Use of polythene/acrylic wares and quartz or polyacrylate cells gave the same results, indicating that the surface did not have any significant effect on the reaction rates. The spectral changes during the reaction for the standard conditions at 298 K are shown in [figure 2](#). It is evident in the figure that concentration of DPA decreases by observing the absorbance at 362 nm. Regression analysis of experimental data to obtain regression coefficient 'r' and the standard deviation 'S', of points from the regression line, was performed with the Microsoft office Excel-2003 program.

## 3. Results

### 3.1. Stoichiometry and product analysis

Different sets of reaction mixtures containing varying ratios of DPA to TPH in presence of constant amount of  $\text{OH}^-$  and  $\text{KNO}_3$  in uncatalyzed reaction and a constant amount of Ru(III) in catalyzed reaction were kept for 2 h in a closed vessel under nitrogen atmosphere. The remaining concentration of DPA was estimated spectrophotometrically at 362 nm. The results indicated 1:1 stoichiometry (TPH: DPA) for both the reactions as given in [Scheme 1](#).



**Scheme 1.** Stoichiometry of uncatalyzed and Ruthenium(III) catalyzed Tripelennamine hydrochloride and DPA reaction in alkaline medium

The stoichiometric ratio in both the cases suggests the main product as ((di-methyl-amino)-methyl)(pyridin-2-yl)-amino (phenyl) methanol. The product was extracted with ether and recrystallized from aqueous alcohol. It was characterized by FT-IR and GC-MS spectral studies. The nature of the alcoholic -OH was confirmed by the IR spectrum, which shows peaks at  $3383\text{ cm}^{-1}$ ,  $1618\text{ cm}^{-1}$  and  $1293\text{ cm}^{-1}$ , for alcoholic -OH stretching, -NH and -CN stretching respectively<sup>22</sup>. Further, the product was subjected to GC-MS spectral analysis. The mass spectrum showed molecular ion peak at 257 amu, confirming ((di-methyl-amino)-methyl)(pyridin-2-yl)-amino (phenyl) methanol (Figure 3). All other peaks observed in GC-MS can be interpreted in accordance with the observed structure of product.

The formation of free  $\text{Ag}^+$  in solution was detected by adding KCl solution to the reaction mixture, which produced white turbidity due to the formation of AgCl. It was observed that ((di-methyl-amino)-methyl)(pyridin-2-yl)-amino (phenyl) methanol does not undergo further oxidation under the present kinetic conditions.

### 3.2. Reaction orders

As the diperiodatoargentate(III) oxidation of tripelennamine hydrochloride in alkaline medium proceeds with a measurable rate in the absence of Ru(III), the catalyzed reaction is understood to occur in parallel paths with contributions from both the catalyzed and uncatalyzed paths. Thus, the total rate constant ( $k_T$ ) is equal to the sum of the rate constants of the catalyzed ( $k_C$ ) and uncatalyzed ( $k_U$ ) reactions, so  $k_C = k_T - k_U$ . Hence, the reaction orders have been determined from the slopes of  $\log(k_U \text{ or } k_C)$  versus  $\log(\text{concentration})$  plots by varying the concentrations of TPH,  $\text{OH}^-$ ,  $\text{IO}_4^-$  and catalyst Ru(III), in turn while keeping others constant.

### 3.3. Effect of varying [DPA]

### 3.4. Effect of initially added products

In both the cases initially added products, ((di-methyl-amino)-methyl)(pyridin-2-yl)-amino (phenyl) methanol and Ag(I) did not have any significant effect on the rate of reaction.

### 3.5. Free radical study

For both uncatalyzed and catalyzed reactions, the intervention of free radicals was tested as follows: to the reaction mixture, a known quantity of acrylonitrile (scavenger) had been added initially, was kept for 2 h in an inert atmosphere. On diluting the reaction mixture with methanol, a white precipitate was formed, indicating the intervention of free radicals in the reactions. The blank experiments of either DPA or TPH alone with acrylonitrile

did not induce any polymerization under the same condition as those induced for the reaction mixture. Also, initially added acrylonitrile decreases the rate of reaction indicating free radical intervention<sup>23</sup>.

### 3.6. Effect of temperature

The influence of temperature on the rate of reaction was studied for both uncatalyzed and catalyzed reaction at four different temperatures (288, 298, 308 and 318 °C) under varying concentrations of [TPH] and [alkali] keeping other conditions constant. The rate constant was found to increase with increase in temperature. The rate constant ( $k_1$ ) of the slow step of the uncatalyzed reaction mechanism was obtained from the slopes and intercepts of plots of  $1/k_U$  versus  $1/[TPH]$  and  $1/k_U$  versus  $[OH^-]$  plots at different temperatures and were used to calculate the activation parameters. The energy of activation corresponding to these constants was evaluated from the Arrhenius plot of  $\log k_1$  versus  $1/T$  ( $r \geq 0.995$ ,  $S \leq 0.002$ ) and other activation parameters obtained are tabulated in Table 3.

Similarly, the rate constant ( $k_2$ ) of the slow step of catalyzed reaction mechanism was obtained from the slopes and the intercept of the plots of  $[Ru(III)]/k_C$  versus  $1/[TPH]$  and  $[Ru(III)]/k_C$  versus  $[OH^-]$  at four different temperatures. The values are given in Table 4. The energy of activation for the rate determining step was obtained by the least square method of plot of  $\log k_2$  versus  $1/T$  and other activation parameters calculated for the reaction are presented in Table 4.

### 3.7. Catalytic activity

It has been pointed out by Moelwyn-Hughes<sup>24</sup> that in presence of the catalyst, the uncatalyzed and catalyzed reactions proceed simultaneously, so that,

$$k_T = k_U + K_C [\text{Catalyst}]^x \quad (1)$$

Here ' $k_T$ ' is the total rate constant, ' $k_U$ ' the pseudo-first-order rate constant for the uncatalyzed reaction, ' $K_C$ ' the catalytic constant and ' $x$ ' the order of the reaction with respect to  $[Ru(III)]$ . In the present investigation,  $x$  value was found to be unity. Then the value of  $K_C$  is calculated using the equation,

$$K_C = \frac{k_T - k_U}{[\text{Catalyst}]^x} = \frac{k_C}{[\text{Catalyst}]^x} \quad (\text{where } k_T - k_U = k_C) \quad (2)$$

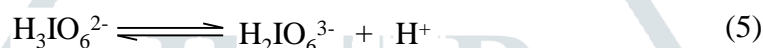
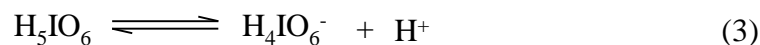
The values of  $K_C$  were evaluated for Ru(III) catalyst at different temperatures and were found to vary at different temperatures. Further, plots of  $\log K_C$  versus  $1/T$  were linear and the values of energy of activation and other activation parameters with reference to catalytic constant were computed. These results are summarized in Table 5.

## 4. Discussion

In the later period of 20<sup>th</sup> century the kinetics of oxidation of some organic and inorganic substrates have been studied by Ag(III) species which may be due to its strong versatile nature of two electrons oxidant. Among the various species of Ag(III),  $Ag(OH)_4^-$ , diperiodatoargentate(III) and ethylenebis (biguanide) (EBS), silver(III) are of maximum attention to the researchers due to their relative stability [25]. The stability of  $Ag(OH)_4^-$  is very sensitive

towards traces of dissolved oxygen and other impurities in the reaction medium whereupon it had not drawn much attention. However, the other two forms of Ag(III) [26] are considerably stable; the DPA is used in highly alkaline medium and EBS is used in highly acidic medium.

The literature survey [21] reveals that the water soluble diperiodatoargentate(III) has a formula  $[\text{Ag}(\text{IO}_6)_2]^{7-}$  with  $\text{dsp}^2$  configuration of square planar structure, similar to diperiodatocopper(III) complex with two bidentate ligands, periodate to form a planar molecule. When the same molecule is used in alkaline medium, it is unlikely to exist as  $[\text{Ag}(\text{IO}_6)_2]^{7-}$ , since periodate is known to be in various protonated forms [27] depending on pH of the solution as given in following multiple equilibria (3) – (5).



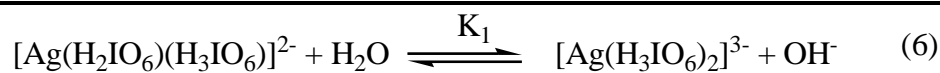
Periodic acid exists as  $\text{H}_5\text{IO}_6$  in acid medium and as  $\text{H}_4\text{IO}_6^-$  near pH 7. Hence, under alkaline conditions as employed in this study, the main species are expected to be  $\text{H}_3\text{IO}_6^{2-}$  and  $\text{H}_2\text{IO}_6^{3-}$ . At higher concentrations, periodate also tends to dimerise. However, formation of this species is negligible under conditions employed for kinetic study. The recent studies have proposed the DPA species as  $[\text{Ag}(\text{HL})_2]^{x-}$  in which 'L' is a periodate with uncertain number of protons and 'HL' is a protonated periodate of uncertain number of protons. This can be ruled out by considering the alternative form [27] of  $\text{IO}_4^-$  at  $\text{pH} > 7$  which is in the form  $\text{H}_3\text{IO}_6^{2-}$  or  $\text{H}_2\text{IO}_6^{3-}$ . Hence, DPA could be as  $[\text{Ag}(\text{H}_3\text{IO}_6)_2]^-$  or  $[\text{Ag}(\text{H}_2\text{IO}_6)_2]^{3-}$  in alkaline medium. Therefore, under the present condition, diperiodatoargentate(III), may be depicted as  $[\text{Ag}(\text{H}_3\text{IO}_6)_2]^-$ . The similar speciation of periodate in alkali was proposed [28] for diperiodatonickelate(IV).

#### 4.1. Mechanism for uncatalyzed reaction

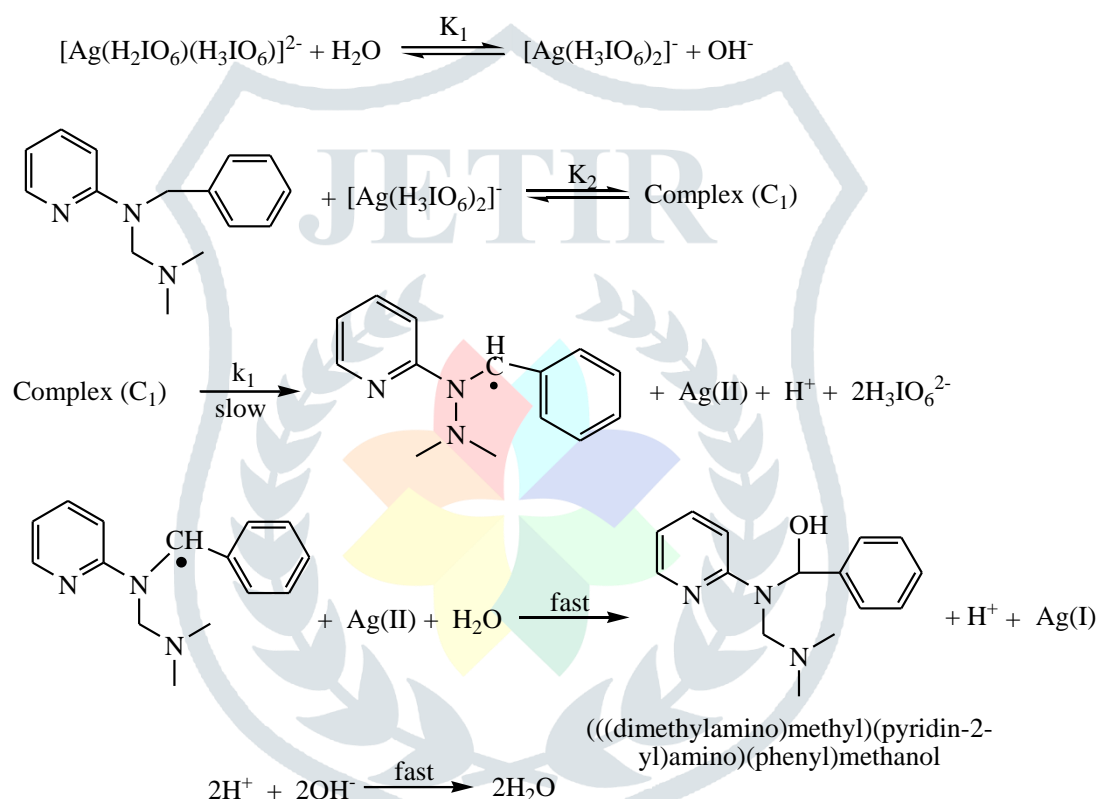
The reaction between DPA and TPH in alkaline medium has the stoichiometry 1:1 (TPH: DPA) with a first order dependence on [DPA] and an apparent order of less than unit order in [substrate], a negative fractional order dependence on [alkali]. No effect of added products was observed. Based on the experimental results, a mechanism is proposed for which all the observed orders in each constituent such as [DPA], [TPH],  $[\text{OH}^-]$  and  $[\text{IO}_4^-]$  may be well accommodated.

In the DPA oxidation mechanism of earlier work [18],  $\text{OH}^-$  had a increasing effect on the rate of the reaction, while periodate has retarding effect on the rate of reaction and DPA itself was considered as active species. However, in the present kinetic study, different kinetic results have been obtained. The result of decrease in rate of reaction with increase in alkalinity can be explained in terms of prevailing equilibrium of formation of  $[\text{Ag}(\text{H}_3\text{IO}_6)_2]^-$  from  $[\text{Ag}(\text{H}_2\text{IO}_6)(\text{H}_3\text{IO}_6)]^{2-}$  hydrolysis as given in the following equation(6).

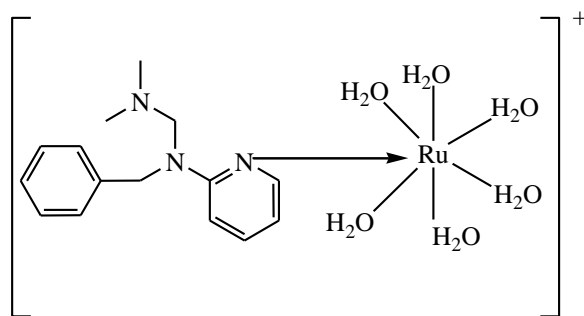




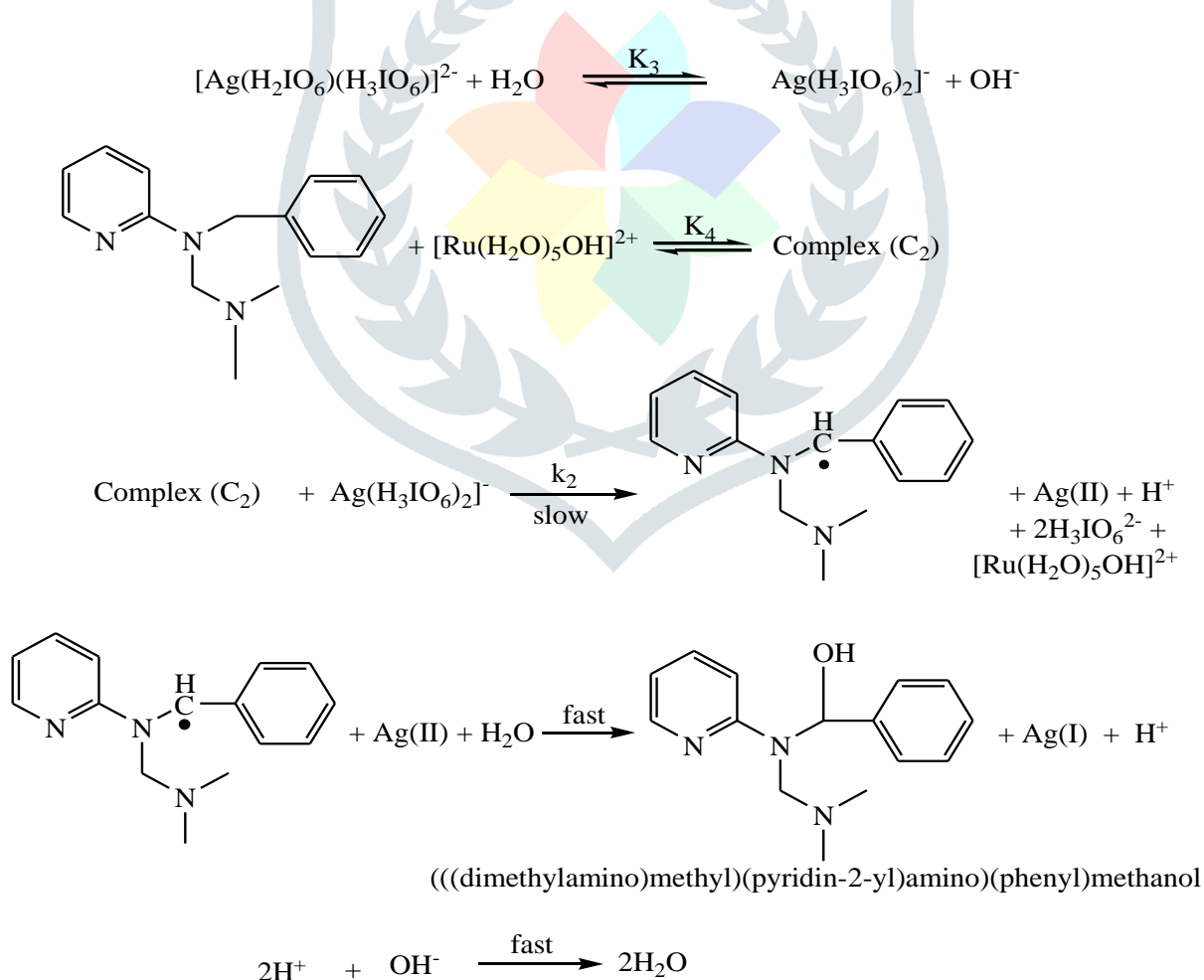
Such type of equilibrium (6) has been well noticed in literature [29]. Because of this reaction and fact that  $k_U$  values are inverse function of hydroxyl ion concentration with fractional order in  $\text{OH}^-$  concentration, the main oxidant species is likely to be  $[\text{Ag}(\text{H}_3\text{IO}_6)_2]^-$  and its formation by the above equilibrium is important in the present study. The less than unit order in  $[\text{TPH}]$  presumably results from formation of a complex ( $C_1$ ) between the DPA species and TPH prior to the formation of the products. This complex ( $C_1$ ) decomposes in a slow step to form a free radical derived from TPH. This free radical species further reacts with  $\text{Ag}(\text{II})$  in a fast step to form products such as ((di-methyl-amino)-methyl)(pyridin-2-yl)-amino (phenyl) methanol and  $\text{Ag}(\text{I})$  as given in Scheme 2.



Spectroscopic evidence for the complex formation between  $\text{Ru}(\text{III})$  and TPH was obtained from UV-vis spectra of TPH ( $5.0 \times 10^{-4} \text{ mol dm}^{-3}$ ),  $\text{Ru}(\text{III})$  ( $1.0 \times 10^{-6} \text{ mol dm}^{-3}$ ,  $\text{OH}^- = 0.1 \text{ mol dm}^{-3}$ ) and a mixture of both. A hypsochromic shift of 8 nm from 269 nm to 264 nm-in the spectra of  $\text{Ru}(\text{III})$  to the mixture of  $\text{Ru}(\text{III})$  and TPH was observed. Attempts to separate and isolate the complex were not successful. The Michaelis-Menten plot proved the complex formation between catalyst and substrate, which explains less than unit order in  $[\text{TPH}]$ . The possible structure of the complex( $C_2$ ) is given as



In the prior equilibrium step 1, the hydroxyl ion concentration with negative fractional order in  $\text{OH}^-$  concentration, the main oxidant species is likely to be  $[\text{Ag}(\text{H}_3\text{IO}_6)_2]^-$  and its formation by the above equilibrium is important in the present study. The less than unit order in  $[\text{TPH}]$  presumably results from formation of a complex ( $\text{C}_2$ ) between the  $\text{Ru}(\text{III})$  species and TPH. This complex ( $\text{C}_2$ ) reacts with one mole of DPA in a slow step to give the free radical species of TPH,  $\text{Ag}(\text{II})$  with the regeneration of catalyst,  $\text{Ru}(\text{III})$ . Further this free radical species of TPH reacts with  $\text{Ag}(\text{II})$  in a fast step to form the products such as ((di-methyl-amino)-methyl)(pyridin-2-yl)-amino (phenyl) methanol (phenyl) methanol and  $\text{Ag}(\text{I})$  as given in Scheme 3. The reduction of  $\text{Ru}(\text{III})$  to lower oxidation state and then regeneration of  $\text{Ru}(\text{III})$  by oxidant was not possible under the experimental conditions due to observed orders in different constituents of reaction.



**Scheme 3.** Detailed mechanism for  $\text{Ru}(\text{III})$  catalyzed oxidation of TPH by diperiodatoargentate(III) with aqueous alkaline medium.

The Michaelis-Menten plot proved the complex formation between catalyst and substrate, which explains less than unit order in [TPH]. Such a complex between a catalyst and substrate has also been observed in earlier studies <sup>35</sup>.

From Scheme 3, the rate law (10) is obtained as,

$$\text{rate} = \frac{-d[\text{DPA}]}{dt} = \frac{k_2 K_3 K_4 [\text{TPH}] [\text{Ru(III)}] [\text{DPA}]}{K_3 + [\text{OH}^-] + K_3 K_4 [\text{TPH}] + K_4 [\text{TPH}] [\text{OH}^-]} \quad (10)$$

$$\frac{\text{rate}}{[\text{DPA}]} = k_C = k_T - k_U = \frac{k_2 K_3 K_4 [\text{TPH}] [\text{Ru(III)}] [\text{DPA}]}{K_3 + [\text{OH}^-] + K_3 K_4 [\text{TPH}] + K_4 [\text{TPH}] [\text{OH}^-]} \quad (11)$$

This explains all the observed kinetic orders of different species. The above equation can be written as below which is suitable for verification.

$$\frac{[\text{Ru(III)}]}{k_C} = \frac{[\text{OH}^-]}{k_2 K_3 K_4 [\text{TPH}]} + \frac{[\text{OH}^-]}{k_2 K_3} + \frac{1}{k_2 K_3 [\text{TPH}]} + \frac{1}{k_2} \quad (12)$$

According to equation (12), other conditions being constant, the plots of  $[\text{Ru(III)}]/k_C$  versus  $1/[\text{TPH}]$  ( $r \geq 0.998$ ,  $S \leq 0.003$ ) and  $[\text{Ru(III)}]/k_C$  versus  $[\text{OH}^-]$  ( $r \geq 0.992$ ,  $S \leq 0.005$ ) should be linear and found to be so (Figure 7). The intercepts and slopes of such plots lead to the values of  $k_2$ ,  $K_3$  and  $K_4$  (Table 4).

The thermodynamic quantities for the different equilibrium steps, in Scheme 3 can be evaluated as follows. The slopes and intercepts, the values of  $k_2$ ,  $K_3$  and  $K_4$  were calculated at four different temperatures and are in good agreement with literature [18]. Using these constants, the rate constants were calculated over different experimental conditions, and there is reasonable agreement between the calculated and the experimental values, which fortifies the proposed mechanism (Scheme 3) and these values are listed in Table 4. A van't Hoff plots were made for the variation of  $K_3$  and  $K_4$  with temperature ( $\log K_3$  versus  $1/T$  and  $\log K_4$  versus  $1/T$ ). The values of enthalpy of reaction  $\Delta H$ , entropy of reaction  $\Delta S$  and free energy of reaction  $\Delta G$  were calculated for the first and second equilibrium steps. These values are also given in (Table 4). A comparison of the  $\Delta H$  value of second step ( $16.1 \text{ kJ mol}^{-1}$ ) of Scheme 3 with that of  $\Delta H^\ddagger$  ( $12.9 \text{ kJ mol}^{-1}$ ) obtained for the slow step of the reaction shows that these values mainly refer to the rate limiting step, supporting the fact that the reaction before rate determining step is fairly slow and involves high activation energy [18]. The negative value of  $\Delta S^\ddagger$  suggests that the intermediate complex is more ordered than the reactants [32] involving distribution of charges as given in Scheme 3.

The negligible effect of ionic strength and dielectric constant might be due to the presence of neutral species in both catalyzed and uncatalyzed reactions (Scheme 2 and 3). The moderate  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  values are favorable for electron transfer reaction. The value of  $\Delta H^\ddagger$  was due to energy of solution changes in the transition state. The observed modest enthalpy of activation and a higher rate constant for the slow step indicates that the oxidation presumably occurs via an inner-sphere mechanism. This conclusion is supported by earlier observations [36]. The activation parameters evaluated for the catalyzed and uncatalyzed reactions explain the catalytic effect on the



reaction. The catalyst Ru(III) forms the complex (C<sub>2</sub>) with substrate which enhances the reducing property of the substrate than that without catalyst. Further, the catalyst Ru(III) modifies the reaction path by lowering the energy of activation.

## Conclusion

The comparative study of uncatalyzed and ruthenium (III) catalyzed oxidation of tripeleennamine hydrochloride by diperiodatoargentate(III) was studied. Oxidation products were identified and were same in both cases. Among the various species of Ag(III) in alkaline medium, DPA itself, i.e., [Ag(H<sub>3</sub>IO<sub>6</sub>)<sub>2</sub>]<sup>-</sup> is considered as active species for the title reaction. Active species of Ru(III) is found to be [Ru(H<sub>2</sub>O)<sub>5</sub>OH]<sup>2+</sup>. The reaction constants of individual steps in the mechanisms were evaluated for uncatalyzed and Ru(III) catalyzed reactions at different temperatures. The catalytic constants and the activation parameters with reference to catalyst were also computed.

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