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Kinetic Oxidation Studies of Pentoxifylline by *N*-Chlorosuccinimide in Acidic Medium Using Iridium(III) Chloride as Inhibitor

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In present study, the kinetics and mechanism of oxidation of pentoxifylline (PTX) by *N*-chlorosuccinimide (NCS) in acidic conditions at 40 ± 0.1 ºC is reported. The reaction depicts first-order kinetics in regard to [NCS], [PTX] and [$HClO_4$]. The reaction rate goes on decreasing as the concentration of iridium(III) chloride is increased. This shows that iridium(III) chloride plays the role of an inhibitor in the reaction under investigation. Nil impact of [$Hg(OAc)_2$], [NHS] and dielectric constant (D) of the medium on the rate of oxidation of pentoxifylline have been observed. This reaction has been investigated from 308-323 K and the monitored rate of reaction suggests a direct relationship between temperature and the rate of reaction. From the graph between log k and 1/T, value of activation energy (E_a) was numerated and more activation parameters like enthalpy of activation ($\Delta H^{\#}$), entropy of activation ($\Delta S^{\#}$) and free energy of activation ($\Delta G^{\#}$) were calculated with the help of activation energy (E_a). On account of experimentally determined the kinetic orders and activation parameters, a most plausible reaction path has been suggested for the oxidation of pentoxifylline in presence of Ir(III) as an inhibitor.

Keywords: Kinetics, *N*-Chlorosuccinimide, Pentoxifylline, Iridium(III) chloride, Mechanism.

INTRODUCTION

Originally, antibiotics were a product of microorganisms that selectively prevents the growth of another organism. Synthetic antibiotics also perform comparable tasks. Different types of drugs and pharmaceutical contaminants, present in environment are hazardous for many living organism, especially in water ecosystem. Due to specific non-biodegradability and stability nature of many contaminants exhibit bioaccumu-lation and biomagnifications properties. These unwanted compounds spread in many species of earth, including human *via* food chain. Chavoshan *et al*. [1] investigated the kinetics of photocatalytic [UV/ZnO] disintegration of penicillin G from wastewater. Singh *et al*. [2] studied the oxidation of tetracycline by copper(II) complex with bipyridyl in alkaline medium using palladium(II) as homogeneous catalyst. Singh *et al*. [3] also reported the kinetics of tetracycline hydrate by $Cu(Bip)_2^{2+}$ in alkaline medium spectrophotometrically at 35 ºC using $RhCl_3$ as homogeneous catalyst. The catalytic efficiency of two different transition metal catalysts in oxidation process of tetra-cycline was approximately same and exhibits first order kinetics.

Pentoxifylline (PTX) is a class of drug used to treat muscles pain of patients suffering from peripheral artery disease. Ru(III) catalyzed oxidation of pentoxifylline (PTX) in basic medium by diperiodatocuprate(III), (DPC), has been performed [4]. First order kinetics with respect to [DPC] and [Ru(III)], however less than unity order for each [PTX] and [OH^-] were observed. Negative order kinetics for [IO_4^-] was obtained. A different set of reaction have catalyzed, [Os(VIII) catalyst] and uncatalyzed oxidation of pentoxifylline by diperiodatocuprate(III), (DPC), in aqueous alkaline medium has also been investigated [5]. The stoichiometry of reaction was obtained same in both cases, *i.e*. catalyzed and uncatalyzed, are as [PTX]/[DPC] = 1:2. Catalyzed and uncatalyzed reactions exhibit similar kinetic behaviour with respect to the same reactants. It was found that the order of reaction for [DPC] was unity whiles the order with respect to [PTX] and [OH^-] was fractional positive. Rate of reaction decreased smoothly on increase in [IO_4^-] successively in both the cases. Effect of catalyst concentrations, [Os(VIII)], on velocity of reaction is positive first order.

The importance of *N*-halo compounds in organic chemistry is also due to their ability to generate halonium ion (X^+) *in*

situ reaction. This happens because the N-X bond is polar and highly reactive, which reacts with a variety of substances in mild condition. *N*-Chlorosuccinimide (NCS) functions as a source of Cl^+, HOCl and stable succinimide anions, which also behaves as a bases and nucleophiles [6,7]. Due to their oxidizing property for the catalyzed and uncatalyzed reactions [8-16], *N*-halo compounds have extensively been used in organic reactions. In addition to this *N*-halo compounds are also used as halogenating agent for organic compounds [17,18].

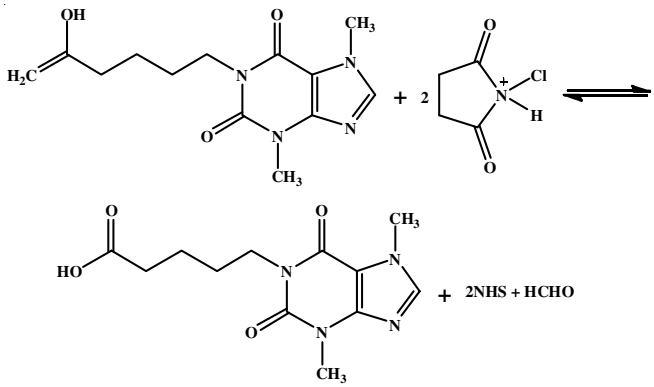
Oxidation of pentoxifylline by various oxidants in different reaction conditions were studied due to their biological importance [4,5,19,20]. In the annihilation of any knowledge about oxidation of pentoxifylline by NCS in acidic medium has motivated to determine the kinetics of the oxidation of pentoxifylline in absence and presence of iridium(III) chloride. In this study, the main aim is to (i) elucidate a plausible mechanism, (ii) derived an appropriate rate equation, (iii) ensure the different reactive species, (iv) test the inhibiting efficiency of Ir(III), (v) calibrate the complexation, (vi) the role of ionic strength (μ) and (v) dielectric constant of medium for the oxidation of pentoxifylline.

EXPERIMENTAL

Iridium(III) chloride (1 g) dissolved in 0.02 M HCl solution in 1000 mL used as stock solution having strength 3.35×10^{-3} mol/L. The concentration of Cl^- associated with iridium(III) chloride solution was identified in kinetic study of reaction. Sodium perchlorate, potassium chloride, *N*-hydrosuccinimide and mercury acetate solution of known strength were prepared in double distilled water. Perchloric acid ($HClO_4$), used as medium of reaction, solution was prepared by diluting its stock solution. To maintain the ionic strength of medium sodium perchlorate solution was used. Standard solution of pentoxifylline (Sigma-Aldrich) was freshly prepared day by day. *N*-Chlorosuccinimide, (Sigma-Aldrich) was used as supplied without further purification. A fresh solution of *N*-chlorosuccinimide (NCS) of required strength formed in doubly distilled water in a black coated flask and ascertained its strength iodometrically. All other reagents used in kinetic study of titled reaction formed in doubly distilled water were of AR grade. The reaction vessels were coated from outside with black paint to avoid any photochemical reaction.

Kinetic procedure: A thermostatic water bath was used to fix the temperature of reaction mixture with ± 0.1 ºC accuracy. The requisite volume of NCS, $HClO_4$, Ir(III), NHS, KCl, $NaClO_4$ taken in a black coated conical flask, which already have calculated amount of water, however pentoxifylline (PTX) solution were taken in another conical flask. Both solutions were kept in same thermostatic water bath. After 0.5 h, when reaction mixture and organic substrate, attain the required temperature, a requisite amount of PTX solution was rapidly pipette out and poured into the mixture of solution. Shake the flask gently to form the homogeneity of solution and immediately pipette out 5 mL aliquot of the reaction mixture and poured in reaction flask, which already have 5 mL of 4% KI along with 5 mL of $HClO_4$ (0.5 M) solution act as reaction quencher. This process was repeated at regular time intervals for iodometric titration to find out the remaining concentration of NCS and hence progress of reaction. The unreacted NCS in the presence of excess of KI and $HClO_4$ release iodine. The amount of liberated iodine was estimated by titrating against a known strength of sodium thiosulphate solution using starch as an indicator. The initial velocity of the reaction (−dc/dt) was determined by the slope of the tangent draw at reaction progress curve of the graph between remaining [NCS] *versus* time at fixed [NCS] in each kinetic run except in oxidant variation when the tangent have fixed position along *x*-axis *i.e.* at a fixed time. The order of reaction was measured by the slop of graph plotting between −dc/dt and concentrations of the reactants. The whole experiment based on Ostwald's isolation method along with van't Hoff differential method to determine the order of reaction with respect to each reactant.

Stoichiometry and product analysis: To find out the stoichiometry of reaction, a number of reaction with changing ratios of [NCS]:[PTX] were occur at 35 ºC for 70 h put reaction mixture as [NCS] much greater than [PTX]. After determined the remaining concentration of NCS for each sets of reaction it is clear that one mole of pentoxifylline consumes two moles of NCS. On the basis of above finding, stoichiometric equation proposed as:



1-(5-carboxypentyl)-3,7-dimethyl,-purine-2,9-dione and formaldehyde were assumed that the products of reaction on the basis of kinetic finding, thermodynamic parameters and also from literature.

RESULTS AND DISCUSSION

The oxidation of pentoxifylline (PTX) was studied in acidic solution using *N*-chlorosuccinimide (NCS) as an oxidant at 40 ºC. The above titled reaction was investigated in the presence and absence of iridium(III) chloride. In the first scheme of reaction NCS, PTX, $HClO_4$ and Ir(III) were taken as main reactants along with NHS, $Hg(OAc)_2$, $NaClO_4$ and KCl as complementary reactants of reaction. In the second scheme, all the above mentioned reactants were taken as same, except Ir(III) was excluded. These two sets of reactions for convenience are called "reaction with Ir(III) and reaction without Ir(III)". The velocity of reaction shows first order kinetics with respect to [NCS], [PTX] (Figs. 1 and 2) and [H^+] throughout its variation. However, no effect on (-dc/dt) on varying concentrations of NHS, KCl, $Hg(OAc)_2$ and dielectric constant of medium. On comparing the velocity of reaction with respect

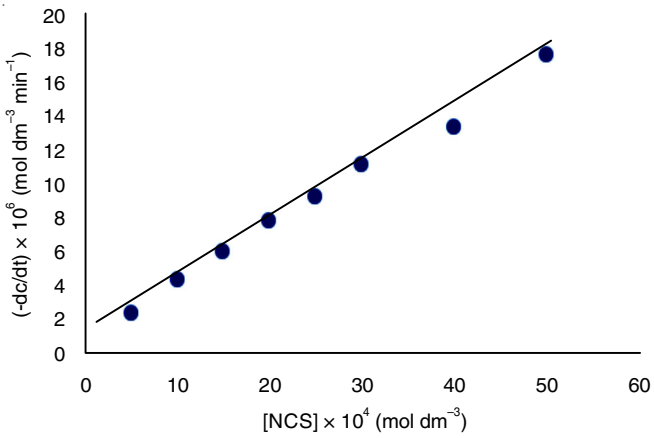


Fig. 1. Plot between (-dc/dt) and [NCS]; Solution condition: [PTX] = 1.00 × 10^{-2} M, [$HClO_4$] = 20.00 × 10^{-3} M, [$IrCl_3 \cdot 3H_2O$] = 3.35 × 10^{-5} M, [$Hg(OAc)_2$] = 1.20 × 10^{-3} M, [NHS] = 1.20 × 10^{-3} M, m = 0.15 M

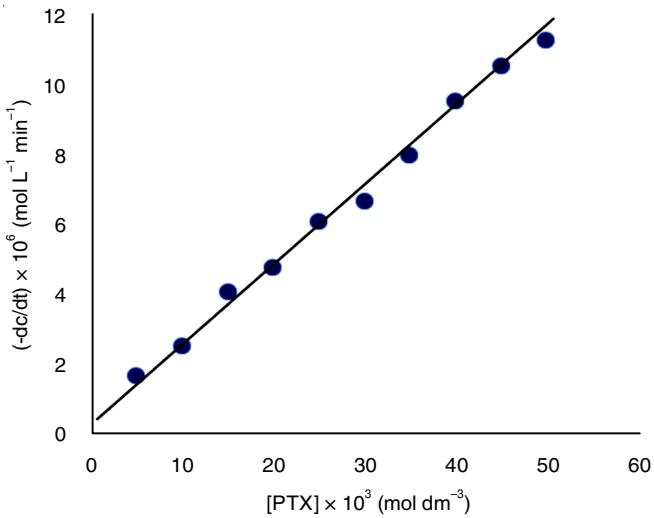


Fig. 2. Plot between (-dc/dt) and [PTX]; Solution condition: [NCS]= 1.00 × 10^{-3} M, [$IrCl_3 \cdot 3H_2O$] = 3.35 × 10^{-5} M, [$HClO_4$] = 20.00 × 10^{-3} M, [$Hg(OAc)_2$] = 1.20 × 10^{-3} M, [NHS] = 1.20 × 10^{-3} M, [KCl] = 5.00 × 10^{-4} M, m = 0.15 M

to [H^+] for reactions "with Ir(III) and without Ir(III)", we find that the values of (-dc/dt) is greater when Ir(III) was absent from reaction mixture (Table-1 and Fig. 3). The negative effect of iridium(III) chloride on the velocity of reaction was further verified when concentration of iridium(III) chloride was increased successively the value of (-dc/dt) decreases smoothly while keeping concentration of all other reactants constant (Fig. 4). On increasing the ionic strength of medium (-dc/dt) also increases smoothly.

The role of mercury acetate in this reaction was chloride ion scavenger. However in some cases, $Hg(OAc)_2$ behaves itself as a mild oxidant, but in present case oxidative role of mercury was examine at different temperature and come at a conclusion that there was no parallel oxidation occurred by mercury acetate. In present study, potassium chloride was used to fix the chloride ion concentration because from the different concentration of iridium(III) chloride solution the value of [Cl^-] altered in reaction mixture. However in present investigation, $NaClO_4$ is employed to fix the ionic strength of the reaction medium.

TABLE-1

[H^+] × 10^3 (mol/L)	(-dc/dt) × 10^8 (mol L^{-1} s^{-1})	
	With Ir(III)	Without Ir(III)
10.0	2.06	3.00
20.0	4.16	6.40
30.0	6.50	9.52
40.0	8.33	12.50
50.0	10.50	15.40
60.0	12.28	18.50
80.0	16.60	23.90
100.0	20.00	28.50

Solution condition : 1 = with Ir(III)-[NCS] = 1.00 × 10^{-3} M, [$IrCl_3 \cdot 3H_2O$] = 3.35 × 10^{-5} M, [PTX] = 1.00 × 10^{-2} M, [$Hg(OAc)_2$] = 1.20 × 10^{-3} M, [NHS] = 1.20 × 10^{-3} M, [KCl] = 5.00 × 10^{-4} M, m = 0.15 M; 2 = (without Ir(III)- reaction have same reactant of same strength as above except iridium chloride which is absent)

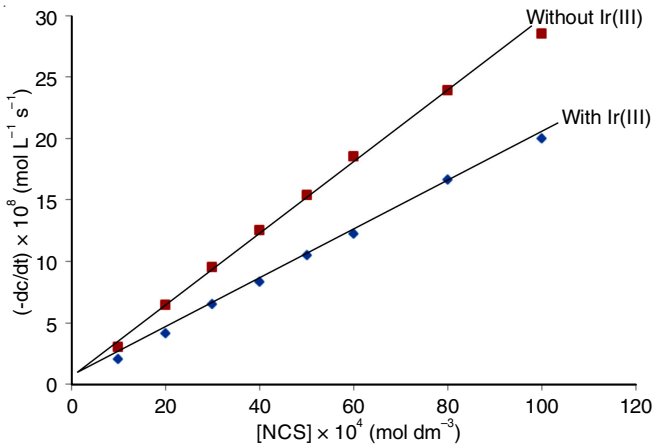


Fig. 3. Plot between (-dc/dt) and [H^+] at 40 °C; Solution condition: (With Ir(III)- [NCS] = 1.00 × 10^{-3} M, [$IrCl_3 \cdot 3H_2O$] = 3.35 × 10^{-5} M, [PTX] = 1.00 × 10^{-2} M, [$Hg(OAc)_2$] = 1.20 × 10^{-3} M, [NHS] = 1.20 × 10^{-3} M, [KCl] = 5.00 × 10^{-4} M, m = 0.15 M; (Without Ir(III)- [NCS] = 1.00 × 10^{-3} M, [PTX] = 1.00 × 10^{-2} M, [$Hg(OAc)_2$] = 1.20 × 10^{-3} M, [NHS] = 1.20 × 10^{-3} M, [KCl] = 5.00 × 10^{-4} M, m = 0.15 M

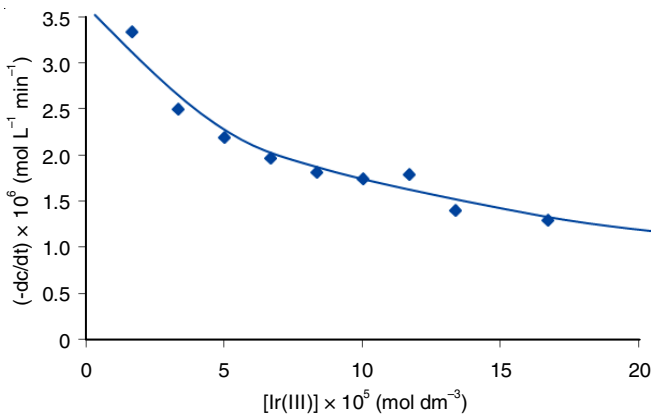


Fig. 4. Plot between (-dc/dt) and [Ir(III)]; Solution conditions: [NCS] = 1.00 × 10^{-3} M, [PTX] = 1.00 × 10^{-2} M, [$HClO_4$] = 20.00 × 10^{-3} M, [$Hg(OAc)_2$] = 1.20 × 10^{-3} M, [NHS] = 1.20 × 10^{-3} M, [KCl] = 1.00 × 10^{-2} M, m = 0.15 M

The reaction was examined at different temperatures (35, 40, 45 and 50 ºC) for two different sets of reaction (Table-2). A graph plot between log k_1 and 1/T (Fig. 5) and from the slop of the graph the value of energy of activation calculated by using formula (slope = $-E_a/2.303R$). By the use of value of

TABLE-2
VALUES OF (-dc/dt) AND RATE CONSTANT (k_1) AT FOUR DIFFERENT TEMPERATURES FOR TWO DIFFERENT CONCENTRATIONS OF PENTOXIFYLLINE

Temp. (K)	[PTX] = 1.5×10^{-2} M		[PTX] = 2.5×10^{-2} M	
	$(-dc/dt) \times 10^8$ (mol L^{-1} s^{-1})	$k_1 \times 10^4$ (s^{-1})	$(-dc/dt) \times 10^8$ (mol L^{-1} s^{-1})	$k_1 \times 10^4$ (s^{-1})
308	6.11	6.11	9.59	9.59
313	6.79	6.79	10.10	10.10
318	15.90	15.90	25.69	25.69
323	31.25	31.25	51.28	51.28

Solution condition: [NCS] = 1.00×10^{-3} M, [NHS] = 1.20×10^{-3} M, [$Hg(OAc)_2$] = 1.20×10^{-3} M, [$HClO_4$] = 20.00×10^{-3} M, [$IrCl_3$] = 3.35×10^{-5} M

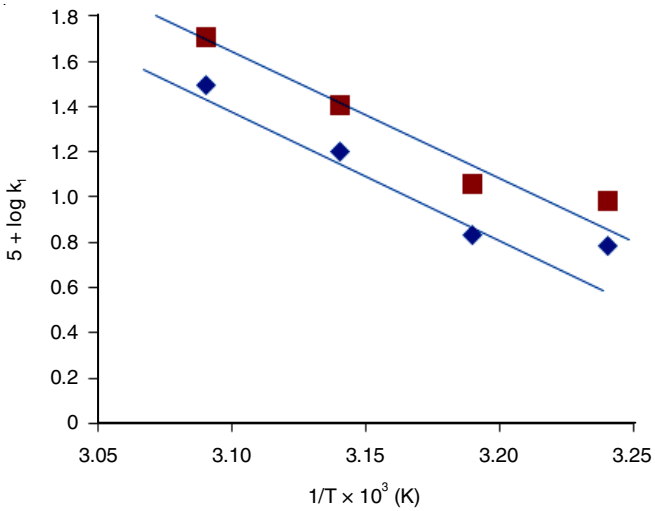
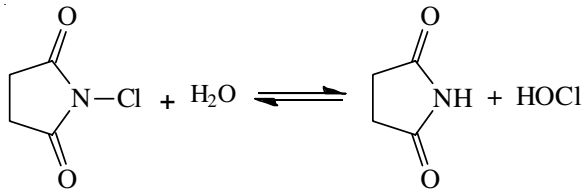


Fig. 5. Plots between k_1 and 1/T; Solution condition: [NCS] = 1.00×10^{-3} M, [NHS] = 1.20×10^{-3} M, [$Hg(OAc)_2$] = 1.20×10^{-3} M, [$HClO_4$] = 20.00×10^{-3} M, [$IrCl_3$] = 3.35×10^{-5} M

rate constant k_r (calculated by using Eyring's equation), the other activation quantities such as $H^{\#}$, $S^{\#}$, $G^{\#}$ and A were obtained (Table-3).

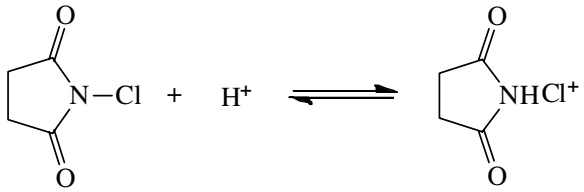
Reactive species of NCS in acidic solution

Aqueous solution of NCS shows following equilibrium:

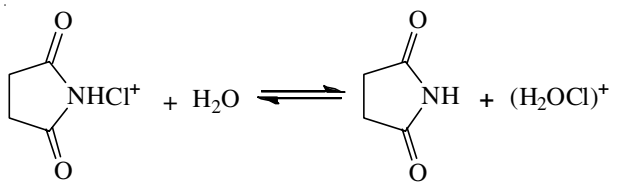


(a)

However, in acidic solution it exist as below:



(b)



(c)

Singh *et al.* [21] reported reactive species of NCS in perchloric acid medium was itself NCS because reaction rate is not influenced by varying [NHS] and [H^+]. Nanda *et al.* [22] studied oxidation of norfloxacin by NCS in hydrochloric acid medium and assumed hydrogenated *N*-chlorosuccinimide (N^+HCS) as reactive species of oxidant. Mohan [23] investigated oxidation of organic substrate by NCS in acidic reaction mixture and found H_2OCl^+ as reactive species of NCS. On the basis of the above equilibrium equation (a, b & c), NCS can be exist in either four forms *i.e.* NCS itself, HOCl, >$NHCl^+$ and $(H_2OCl)^+$. Using kinetic findings, it is possible to identify the active species of NCS in acidic solution of aforesaid reaction. No effect of [NHS] on the velocity of reactions indicates that the HOCl and H_2O^+Cl cannot be exist as reactive species. However, positive effect of [H^+] on velocity of reactions shows that NCS itself does not behaves as reactive species of oxidant. Finally, we come to this conclusion that if consider protonated form of NCS *i.e.* >$NHCl^+$ is the active species of oxidant then first order kinetics of [H^+] will easily be explained and all other kinetic findings can be easily explained by derived rate law for oxidation of pentoxifylline NCS in acidic reaction condition.

In acidic solution reactive moieties of iridium(III) chloride: Singh *et al.* [24,25] studied oxidation of some organic compounds in acidic solution using iridium(III) chloride as homogeneous catalyst and reported reactive moiety of Ir(III) accordingly strength of acid and the role of [Cl^-] on the rate of reaction. It is also reported that on aquation of $[IrCl_6]^{3-}$ gives green aqua complexes of $[IrCl_5(H_2O)]^{2-}$, $[IrCl_4(H_2O)_2]^-$ and possibly $[IrCl_3(H_2O)_3]$ depends on degree of hydration (in solution only) [26]. In present investigation, $[IrCl_3(H_2O)_3]$ is taken as the reactive species of Ir(III) due to its dilution in the range of 10^{-5} M and no more Cl^- released by perchloric acid in solution and zero effect of [Cl^-] variation on the rate of reaction.

Reaction scheme for titled reaction: On the basis of above findings, a general reaction mechanism is draw in **Scheme-I** for the Ir(III) inhibited oxidation of pentoxifylline (PTX) by *N*-chlorosuccinimide (NCS) in $HClO_4$ medium.

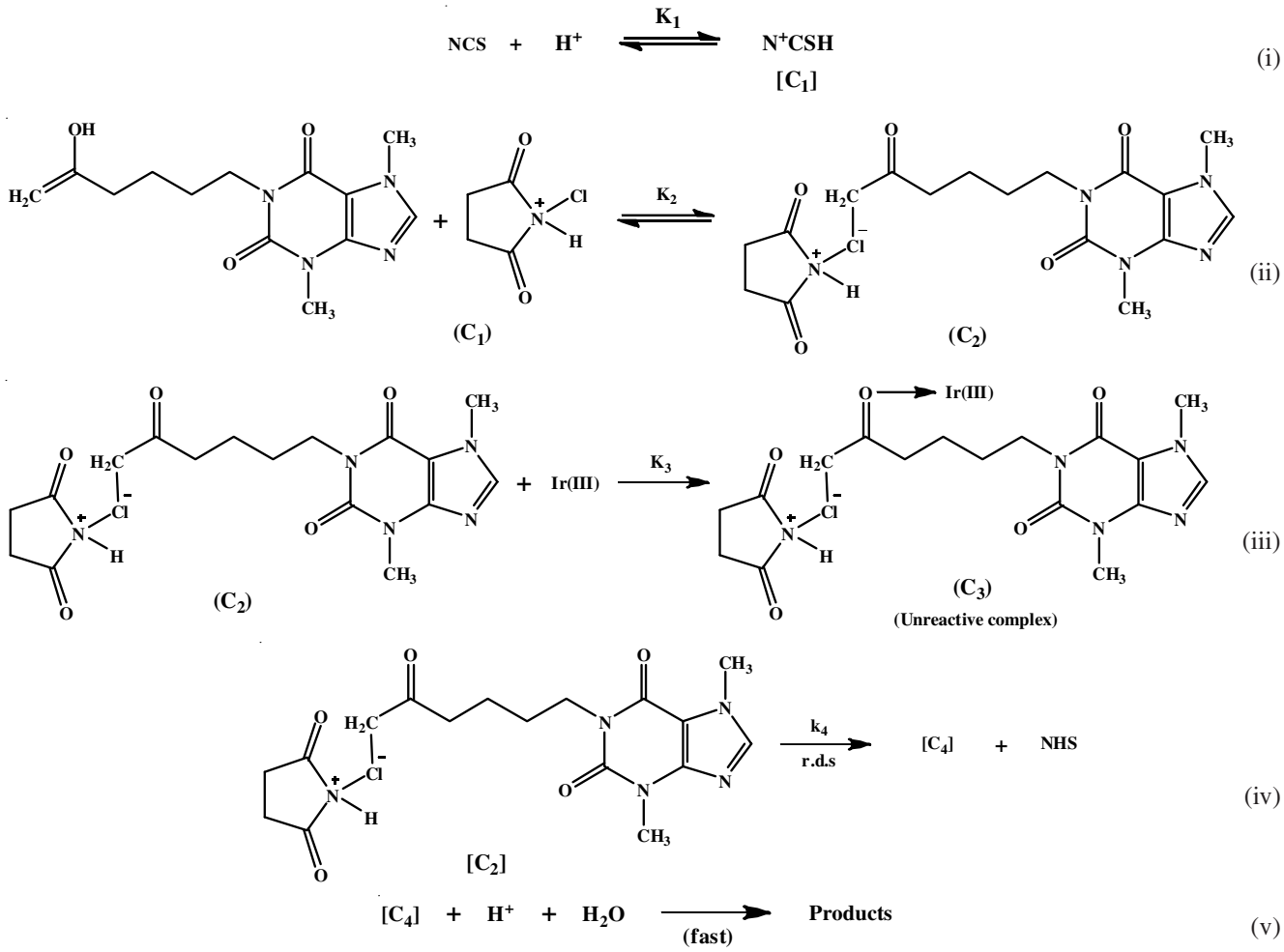
The velocity of oxidation of pentoxifylline may be represented in terms of disappearing [NCS], considering the reaction stoichiometry and mechanistic steps given above for the titled reaction as:

$$\text{Rate} = \frac{-d[NCS]}{dt} = nk_4[C_2] \quad (1)$$

where n = 2, (stoichiometry of reaction).

TABLE-3
VALUE OF ACTIVATION PARAMETERS FOR THE OXIDATION OF PTX AT 40 °C

Substrate	k_r (M^{-3} s^{-1})	$\Delta H^{\#}$ (kJmol^{-1})	$\Delta G^{\#}$ (kJmol^{-1})	$\Delta S^{\#}$ (J/Kmol)	A (M^{-3} s^{-1})	E_a (kJ mol^{-1})
Pentoxifylline	0.51×10^{-1}	81.19	84.39	4.43	1.55×10^{12}	83.82



Scheme-I

The value of chemical equilibrium obtained from step (i) we get eqn. 2:

$$K_1 = \frac{[N^+CSH]}{[NCS][H^+]}$$

or

$$[N^+CSH] = K_1[NCS][H^+] \quad (2)$$

By using the steady-state approximation the value of $[C_2]$ are obtained as

$$d[C_2]/dt = 0$$

$$\frac{d[C_2]}{dt} = k_2[N^+CSH][PTX] - k_{-2}[C_2] - k_3[C_2][Ir(III)] - k_4[C_2]$$

or

$$0 = k_2[N^+CSH][PTX] - k_{-2}[C_2] - k_3[C_2][Ir(III)] - k_4[C_2] \quad (3)$$

Putting the value of $[N^+CSH]$ from eqns. 2 and 3, we get

$$0 = K_1k_2[NCS][H^+][PTX] - k_{-2}[C_2] - k_3[C_2][Ir(III)] - k_4[C_2]$$

or

$$[C_2] = \frac{K_1k_2[NCS][H^+][PTX]}{k_{-2} + k_3[Ir(III)] + k_4} \quad (4)$$

The above value of $[C_2]$ puts in parents rate eqn. 1, we get

$$\text{Rate} = \frac{-d[NCS]}{dt} = \frac{nK_1k_2k_4[NCS][H^+][PTX]}{k_{-2} + k_3[Ir(III)] + k_4} \quad (5)$$

Eqn. 5 is the final rate law derived from the proposed reaction scheme for the iridium(III) chloride inhibited oxidation of pentoxifylline by NCS. Above rate law fully satisfy the experimental observation obtained for prime reactants that is first order reaction with respect to $[H^+]$, [NCS] and [PTX] throughout their variation and negative order kinetics with respect to Ir(III).

The value of composite rate constant (k′) for above mentioned reaction have been calculated by putting kinetic data of [NCS], $[H^+]$, [Ir(III)] and [PTX] at constant temperature (40 ºC) in eqn. 5 (Table-4). Table-4 shows that approximate same value of k′ for the variation of [NCS] and $[H^+]$ supports the validity of equation (5) *i.e.* rate law equation and also the proposed reaction scheme.

In the present study of the oxidation of pentoxifylline by *N*-chlorosuccinimide in $HClO_4$ medium using iridium(III) chloride as a reaction inhibitor, **Scheme-I** have been proposed. *In situ* reaction, the activated complex $[C_2]$ is formed, in step-(ii) of the reaction scheme, by the combination of a neutral and a charged moiety (*i.e.* PTX and NH^+CS). This transition state complex bears same electronic charge on sphere as reactants

TABLE-4
VALUE OF COMPOSITE RATE CONSTANT FOR THE VARIATION OF [NCS] AND [H^+] FOR THE TITLE REACTION AT 40 °C

[NCS] × 10^4 (mol/L)	[H^+] × 10^3 (mol/L)	Composite rate constant (mol^{-2} L^2 s^{-1})
1	20	0.38
2	20	0.38
3	20	0.36
4	20	0.37
5	20	0.39
6	*20*	0.38
7	20	0.37
8	20	0.35
10	20	0.33
10	10	0.20
10	20	0.20
10	30	0.21
10	40	0.21
10	50	0.20
10	60	0.21
10	80	0.20
10	100	0.20

Solution condition: [PTX] = 2.00 × 10^{-2} M, [$IrCl_3.3H_2O$] = 3.35 × 10^{-5} M, [$Hg(OAc)_2$] = 1.20 × 10^{-3} M, [NHS] = 1.20 × 10^{-3} M, [KCl]= 5.00 × 10^{-4} M, μ = 1.5 M

but spread over a large volume of adduct. This consequence gives a less polar transition state than reactants. This would facilitate the increase in entropy of the reaction. The calculated positive entropy of activation for aforesaid reaction also supports the proposed reaction scheme.

Comparative analysis: The results of present investigations *i.e.* oxidation of pentoxifylline by protic solution of NCS in the presence and absence of iridium(III) chloride complex give some important information about reaction intermediates. Retarding the effect of iridium(III) chloride on velocity of reaction was assumed that the formation of unreactive complex between (C_2) and Ir(III) in step (iii) of reaction scheme. The amount of unreactive complex becomes more and more by increasing molar strength of iridium chloride regularly and hence value of (-dc/dt) successively decreases. Order of reaction for each individual reactant (*i.e.* NCS, PTX, H^+, NHS, *etc*.) are same in both conditions *i.e.* with and without Ir(III).

Further results of present investigation were compared with results reported for oxidation of glycine [27] by NCS in the presence of Ir(III) in acidic medium and oxidation of pentoxifylline [28] by KIO_3 in alkaline medium using Rh(III) as catalyst. When the present study and Ir(III)-catalyzed oxidation of glycine [27] are compared, it is seen that the order of reaction regarding NCS is unity for both reaction. Reaction order regarding glycine [27] and pentoxifylline [28] was unity, which also unity in present investigation. The role of reaction medium ($HClO_4$) in present work are reaction enhancing while in case of oxidation of glycine [27] effect of medium on rate of reaction was negative however, nil effect was obtained on varying concentration of medium in rhodium(III)-catalyzed [28] oxidation of PTX. The role of iridium(III) chloride in present investigation and reported in oxidation of glycine [27] shows retarding effect on (-dc/dt) value, however order of reaction for rhodium(III) chloride was observed first.

Conclusions

On the behaves of the above analysis based on observed kinetic data regarding reaction of pentoxifylline (PTX) by protic solution of *N*-chlorosuccinimide (NCS) in the presence of iridium(III) chloride complex acting as a reaction inhibitor the following conclusions are drawn:

(1) NH^+CS have been assumed the active moiety of *N*-chlorosuccinimide (NCS) in protonated reaction mixture.

(2) [PTX:$NCSH^+$] (*i.e.* C_2) have been proposed the transition state complex with highest energy level of the reaction and hence most unstable complex.

(3) Formation of adduct [C_2] in step (ii) of the reaction is reasonable because positive entropy of activation of reaction are obtained by the combination of a neutral and a charged species.

(4) The mechanism of inhibition of rate of reaction by iridium chloride are assumed that they act either by forming a stable complex before rate determining step or by decreasing concentration of reactive species of reaction from reaction mixture. In the present study, unreactive complex, [C_3], formed by coordinating reactive intermediate [C_2] with Ir(III) complex in step (iii) of scheme is assumed stable and responsible to slow down the velocity of reaction.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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