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Oxidation of Niacinamide by sodium N-chlorobenzenesulphonamide (CAB) in acid medium catalysed by Ru(III) Ion: Kinetic and Mechanistically

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ABSTRACT

The kinetics of Ru (III) Catalysed oxidation of Niacinamide by sodium-N-chlorobenzene sulphonamide (CAB) has been studied in acidic medium at 303K. The reaction shows first order dependence of the rate on [CAB] [Ru(III)] and an inverse fractional order on [H$^+$] and fractional order shows on [NA]. The addition of halide ions and the reduction product of CAB, benzene sulphonamide and dielectric constant of the medium have no influence on the rate. Thermodynamically parameters were computed by studying the reaction at different temperatures, a mechanism consistent with observed kinetics is presented.

KEYWORDS: Niacinamide, Oxidation, Chloramine-B, Ruthenium catalyst.

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INTRODUCTION

Niacinamide is an important component of vitamin-B complex group. It is water soluble vitamin and is part of the vitamin B group. It is also known as prevents pellagra. This disease is mainly found in those areas where maize is the main dietary component as the grain in deficient in niacin. Niacinamide also have anti-diabetogenic, antioxidant and anti-inflammatory properties[1], anxiolytic (anti-anxiety) agent[2]. and also acts as a chemo and radio sensitizing agent by enhancing tumour blood, thereby reducing tumour hypoxia. Niacinamide is an activator of sirtuins but it inhibits at higer doses. Sharma ashok etal have reported Nicotinamide and Isonicotinamide were oxidized using permanganate ion in acidic medium[3]. Chandrashekar etal have reported oxidation of Nicotinamide by bromamine-T in acidic medium catalysed by Ru (III) ion[4]. Hence, the oxidation of niacinamide adds much to the knowledge of chemistry. These facts promoted us to undertake the study of kinetics of oxidation of Niacinamide by CAB in acidic media catalysed by ruthenium with a view to elucidate the reaction mechanism.

EXPERIMENTAL

Chloramine-B (CAB) was prepared using standard method and its purity checked iodometrically and through IR and NMR spectral data[5] allowance was made for the amount of HCl present in the catalyst solution, while preparing reaction mixtures for kinetics runs. All other chemicals used were of accepted grade of purity. A constant ionic strength of the reaction mixtures was maintained by adding concentrated sodiumperchlorate ($NaClO_4$). A solution of $Rucl_3.3H_2O$ (Arora matthey) in 0.5 M HCl was prepared and used as catalyst solution. Triply distilled water was utilized for preparing aqueous solutions.

KINETIC MEASUREMENT

The kinetic runs were performed under pseudo-first order condition of $[Niacinamide] >> [CAB]_0$ at 303K. Mixtures contains requisite amount of substrate, oxidant, $NaClO_4$, Ru(III) and HCl were taken in stoppered pyrex glass tube, whose outer surface was coated black to eliminate the photochemical effects. A required quantity of water was added to maintain constant total volume for all runs. The reaction vessel was thermo stated in a water bath set at a temperature 303K, to this solution a measured amount of pre-equilibrated CAB solution was added to give a known concentration. The progress of the reaction was monitored iodometrically for two half-lives by withdrawing aliquots of the reaction mixture at regular time intervals. Under pseudo-first order conditions rate constant k′ were reproducible with in ±3%. The regression analysis of experimental data was carried out on an origin 5.0.

STOICHIOMETRY

Reaction mixtures containing different composition of Niacinamide and CAB was equilibrated at 303K in acidic medium catalysed by Ru(III) ion for 24 hours. The analysis showed that one mole of CAB reacted with same mole of substrate is illustrated as in equation (1)

$$C_6H_6N_2O + PhSO_2NCl\text{-}Na+ H_2O \longrightarrow C_6H_6N_2O_2 + PhSO_2NH_2+ Na+ \ Cl\text{-} \ \dots \ (1)$$

Niacinamide CAB

The reaction product benzene sulphonamide ($PhSO_2NH_2$) was identified by TLC using light petroleum ether-chloroform-butanol (2:2:1 v/v) as the solvent system for a sending (Rf=0.88), the 6-hydroxyl niacinamide present in the reaction mixture was identified with authenticated sample by TLC method. Further it was confirmed by conventional ferric chloride test[6]. The evolved CO_2 was detected by the conventional lime water test. Attempts to quantitative measure of the CO_2 evolved were unsuccessful. The GC-MS data for 6- hydroxy niacinamideobtained on a 17A shimadzu spectrometer showed a molecular ion peak at 133amu (figure.1), clearly confirming the formation of 6- hydroxy Niacinamide.
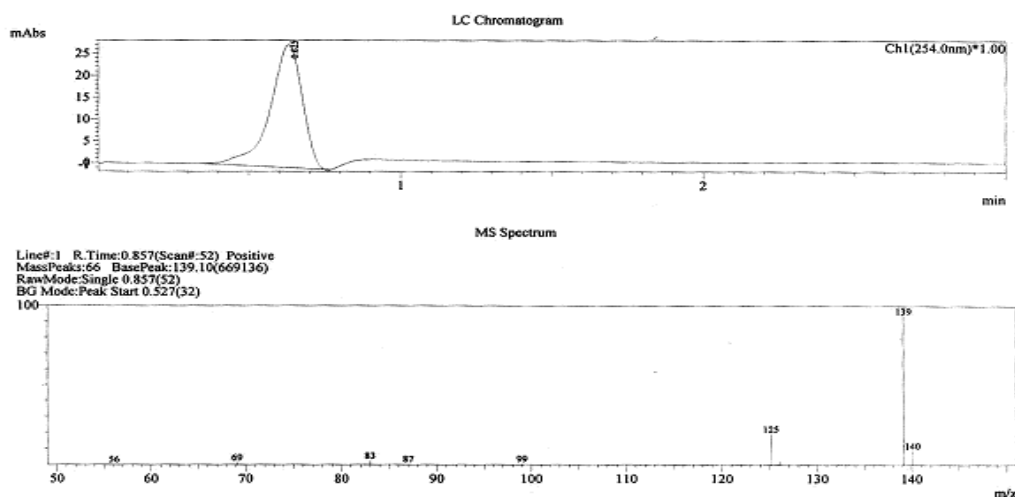

Fig 1: GC Mass Spectra of 6- Hydroxy Niacinamide.

RESULTS

Effect of reactant concentration on the rate

Under pseudo-first order conditions of [Niacinamide] >> [CAB]$_0$ plots of log [titre value] versus time are linear (r= 0.9980) indicating a first order dependence of rate on [CAB]. The pseudo-first order rate constants k′ is given in table 1. The values of k′ remain unaffected with a change in [CAB]. The rate increased with increase in [Niacinamide] (table 1) and a plot of logk′versus log [Niacinamide] was linear with fractional slopes indicating the fractional order dependence of rate on [Niacinamide].

Table-1 Effects of varying reactant concentrations on the reaction rate [HCl] = 2.0 x 10^{-3} mol dm^{-3}; [Ru(III)]= 1.243 x 10^{-6} mol dm^{-3}; Temp. = 303 K ; μ = 0.2 mol dm^{-3}

[CAB] x 10^4 mol dm^{-3}	[Niacinamide] x 10^{3}mol dm^{-3}	k′ x 10^6 sec^{-1}
1.15	2.0	3.00
1.61	2.0	2.90
2.00	2.0	2.80
2.53	2.0	2.85
2.99	2.0	3.15
2.00	1.0	1.25
2.00	1.5	2.00
2.00	2.0	2.80
2.00	3.0	3.70
2.00	4.0	4.60
2.00	5.0	5.40

Effect of acid on the rate

The reaction was studied with varying [HCl] at constant [CAB], [Niacinamide], [Ru (III)], ionic strength and temperature. The rate of reaction decreased with increase in [HCl] (r= -0.9990), the plot of logk′versus log[HCl] was linear with negative slope equal to less than unity indicating inverse fractional order in HCl as shown in figure 2.
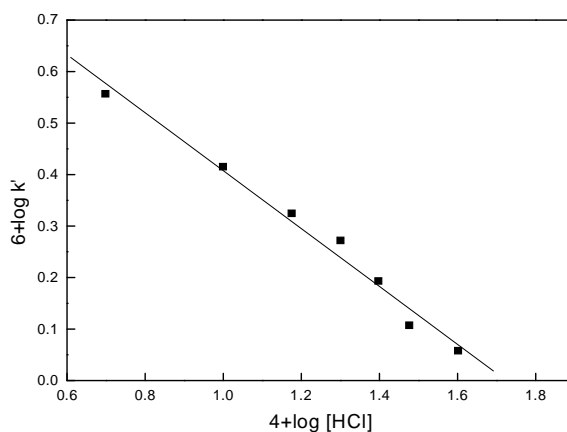

FIG.2. Plot of log k' versus log [HCl]

Effect of [H$^+$] on the rate

At constant [CAB], [Niacinamide] and [Cl$^-$], the rate of reaction decreased with increase in [H$^+$] (r= -0.9910). The plot of logk′versus log [H$^+$] was linear with negative slope equal to less than unity (-0.62) indicating an inverse fractional order in [H$^+$] table 2.

Table:2 Effect of varying [H⁺] ion on the rate of reaction [NA] = 2.0 x 10⁻³mol dm⁻³; [CAB]₀ = 2.0×10⁻⁴ mol dm⁻³; [Ru(III)]= 1.243 x 10⁻⁶ mol dm⁻³ Temp. = 303K; µ= 0.2 mol dm⁻³

$[H^+] \times 10^4$ (mol dm^{-3})	$k' \times 10^6$ (sec^{-1})
2.4	3.04
4.8	2.05
7.2	1.75
9.6	1.40
12.0	1.20
13.4	1.15

Effect of Ru(III) catalysed reaction on the rate

The rate increased with increase in [Ru(III)] and plots of logk′versus log[Ru(III)] was linear with unit slope indicating a first order dependence of rate on [Ru(III)] table.3.

Table : 3. Effects of varying [RuCl₂] on the reaction rate [NA] = 2.0 x 10⁻³mol dm⁻³; [CAB]₀ = 2.0×10⁻⁴ mol dm⁻³; [HCl]= 2.0 x 10⁻³mol dm⁻³ ; Temp. = 303K; µ= 0.2 mol dm⁻³

$[RuCl_2] \times 10^6$ moldm^{-3}	$k' \times 10^6$ sec^{-1}
3.729	2.75
7.458	7.40
11.187	16.24
14.187	20.12
18..640	27.08

Effect of halide ion on the rate on the rate

Addition of Cl⁻ or Br⁻ ions in the form of NaCl or NaBr at constant [H⁺] did not affect the rate, suggesting that chloride or bromide ions were not involved in the reaction rate.

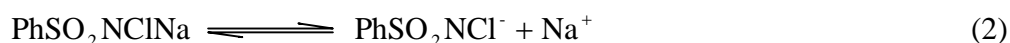## *Effect of benzenesulphonamide and ionic strength on the rate*

The addition of benzenesulphonamide had no affect on the rate indicating that it is not involved in a pre-equilibrium to the rate determining step. The variation of ionic strength of the medium using NaClO₄ had no effect on the rate.

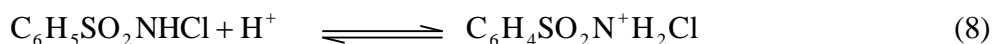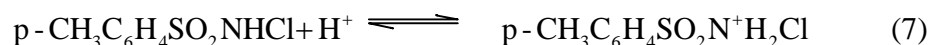## *Effect of dielectric constant and temperature on the rate*

The variation of the solvent composition using methanol (5.0-20% v/v) did not affect the rate. The reaction was studied at varying temperatures 303-318K. The activation parameters namely energy of activation (Ea), enthalpy of activation (ΔH#), entropy of activation and free energy of activation (ΔG#), were obtained from the Arrhenius plots of logk′versus 1/T.

MECHANISM

Chloramine-B (PhSO$_2$NClNa) like chloramine-T behaves as a strong electrolyte in aqueous solutions forming different species as shown in Equation 2-6 [7,8,9].

$$PhSO_2NClNa \rightleftharpoons PhSO_2NCl^- + Na^+ \quad\quad (2)$$

$$PhSO_2NCl^- + H^+ \rightleftharpoons PhSO_2NHCl \quad\quad (3)$$

$$PhSO_2NHCl + H_2O \rightleftharpoons PhSO_2NH_2 + HOCl \quad\quad (4)$$

$$2PhSO_2NHCl \rightleftharpoons PhSO_2NH_2 + PhSO_2NCl_2 \quad\quad (5)$$

$$HOCl + H^+ \rightleftharpoons H_2O^+Cl \quad\quad (6)$$

In acid solutions, the probable oxidizing species are the free acid PhSO$_2$NHCl, PhSO$_2$NHCl$_2$, HOCl and H$_2$O$^+$Cl. The involvement of PhSO$_2$NCl$_2$ in mechanism leads to a second-order rate law according to equation (5), which is contrary to the experimental observations. The monohaloamines can be further protonated at p^H < 2 as in equation (7) and (8) for chlroamine-T and chlroamine-B respectively.[10,11].
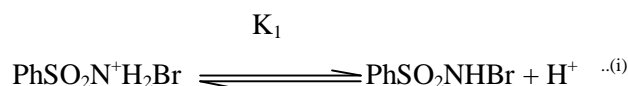
$$p\text{-}CH_3C_6H_4SO_2NHCl + H^+ \rightleftharpoons p\text{-}CH_3C_6H_4SO_2N^+H_2Cl \quad\quad (7)$$
$$C_6H_5SO_2NHCl + H^+ \rightleftharpoons C_6H_4SO_2N^+H_2Cl \quad\quad (8)$$

Therefore in acidic conditions, for chloramine-B, PhSO$_2$NHCl is expected to protonate as follows.

$$C_6H_5SO_2NHCl + H^+ \rightleftharpoons C_6H_5SO_2N^+H_2Cl \quad\quad (9)$$
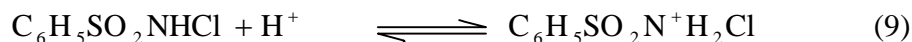
Electronic spectral studies have shown that coordination species such as [RuCl$_5$(H$_2$O)]$^{-2}$, [RuCl$_4$(H$_2$O)$_2$]$^-$, [RuCl$_3$(H$_2$O)$_3$], [RuCl$_2$(H$_2$O)$_4$]$^+$ and [RuCl$_5$(H$_2$O)$_5$]$^{2+}$ do not exist in the aqueous solution of RuCl$_3$. Ruthenium (III) however exists in the following ligand substitution equilibrium in acid medium

$$[Ru(III)Cl_6]^{3-} + H_2O \rightleftharpoons [Ru(III)Cl_5(H_2O)]^{2-} + Cl^- \quad\quad (10)$$

In the present study the oxidation of Niacinamide in the presence of Ru(III) as catalyst, the inverse fractional order in [H$^+$] suggest that, the deprotonation of PhSO$_2$N$^+$H$_2$Cl in step (i) results in the formation of regeneration of PhSO$_2$NHCl. A retardation by the added benzenesulphonamides (PhSO$_2$NH$_2$) i.e. an inverse fractional order on [PhSO$_2$NH$_2$] indicates hydrolysis of monobromamine [PhSO$_2$NHCl] to form HOCl in step (ii) which act as the active species in fast pre-equilibrium step. The reaction rate shows fractional order in Ru(III) concentration and first order on [Niacinamide]. Based on the preceding discussion a mechanism scheme 1 is proposed to account for the experimental observation.

$$\overset{K_1}{PhSO_2N^+H_2Br \rightleftharpoons PhSO_2NHBr + H^+} \quad ..(i)$$

$$PhSO_2NHCl + S \xrightleftharpoons{K_2} X \qquad \qquad ....(ii)$$

$$X + Ru(III) \xrightleftharpoons{k_3} X' \qquad slow \qquad ...(iii)$$

$$X' \longrightarrow X'' + Ru(III) \qquad fast \qquad ...(iv)$$

$$X'' \longrightarrow product \qquad ...(v)$$
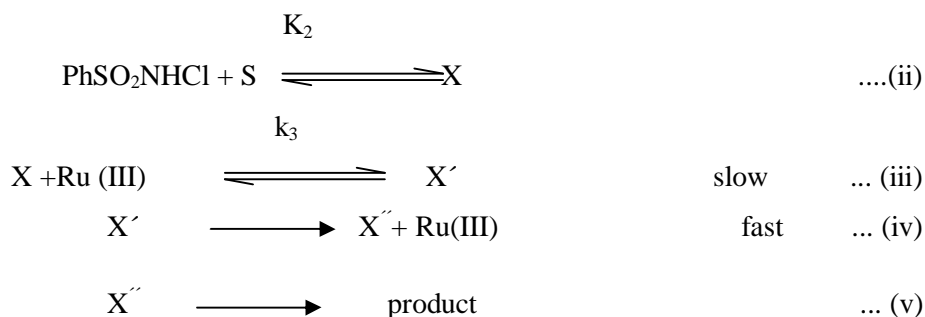
Scheme – 1

$$Rate = -\frac{d[CAB]_t}{dt} = k_3\,[X]\,[Ru(III)] \qquad \qquad ...(11)$$

From step (ii)

$$[PhSO_2NHCl] = \frac{[X]}{K_2[S]} \qquad \qquad ...(12)$$

From step (i)

$$[PhSO_2N^+H_2Cl] = \frac{[PhSO_2NHCl]\,[H^+]}{K_1}$$

$$\therefore [PhSO_2N^+H_2Cl] = \frac{[X][H^+]}{K_1\,K_2[S]} \qquad \qquad ...(13)$$

Total effective concentration of $[CAB]_t$

$$[CAB]_t = [PhSO_2N^+H_2Cl] + [PhSO_2NHCl] + [X] \qquad \qquad ...(14)$$

$$[CAB]_t = \frac{[X]\,[H^+]}{K_1\,K_2\,[S]} + \frac{[X]}{K_2[S]} + [X] \qquad \qquad ...(15)$$

$$[CAB]_t = [X]\left\{ \frac{[H^+]}{K_1\,K_2\,[S]} + \frac{1}{K_2[S]} + 1 \right\}$$

$$= [X]\left\{ \frac{[H^+] + K_1 + K_1\,K_2[S]}{K_1\,K_2\,[S]} \right\}$$

$$\therefore [X] = \frac{K_1\,K_2\,[S]\,[CAB]_t}{[H^+]\,K_1 + K_1\,K_2[S]} \qquad \qquad ...(16)$$

$$\therefore Rate = \frac{K_1\,K_2\,k_3[S][CAB][Ru(III)]}{[H^+] + K_1 + K_1\,K_2\,[S]} \qquad \qquad ...(17)$$

This rate law equation (17) is in good agreement with the experimental observations, including first order in [CAB], [Ru(III)] and inverse fractional order in [H⁺] and fractional order on [Niacinamide].

This is in good agreement with the experimental results. A detailed mechanism of Ru(III) catalyzed oxidation of niacinamide by CAB in HCl medium is given in Scheme 2.

$$PhSO_2\overset{+}{N}H_2Cl \rightleftharpoons PhSO_2NHCl + H^+$$

(X)

$$+ [RuCl_6]^{3-} \longrightarrow$$

(X')

$$+ PhSO_2\overset{-}{NH}$$

(X')   (X'')

6 - hydroxy nicotinamide

$$PhSO_2N\overset{-}{H} + H^+ \longrightarrow PhSO_2NH_2$$
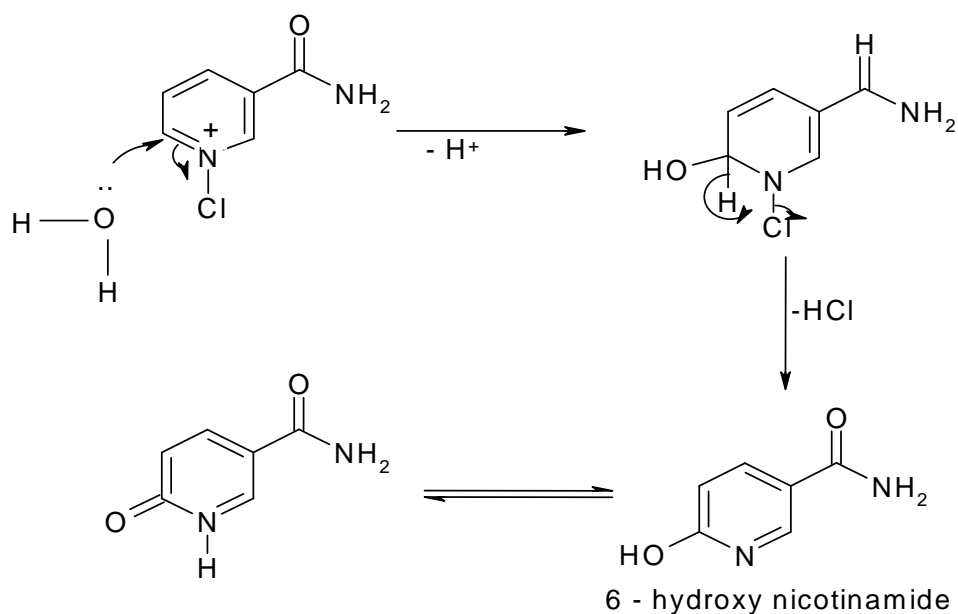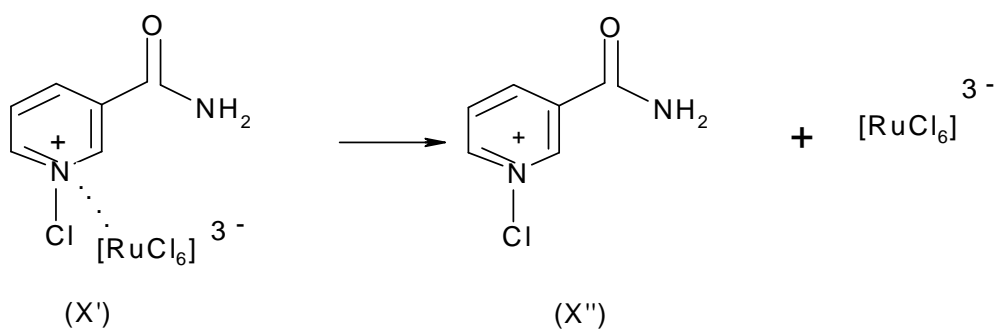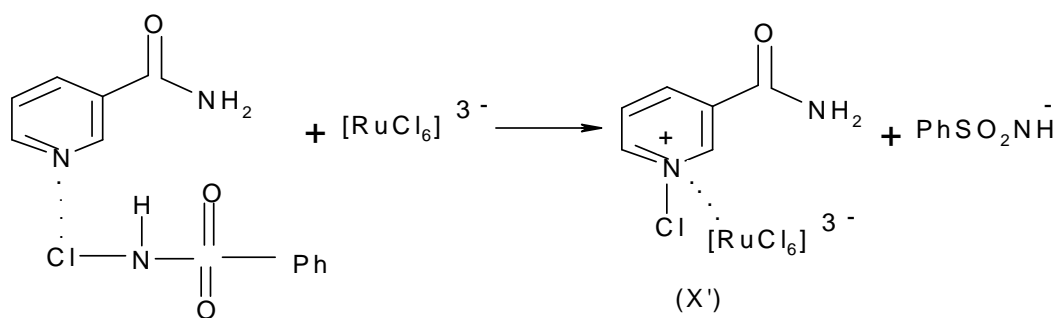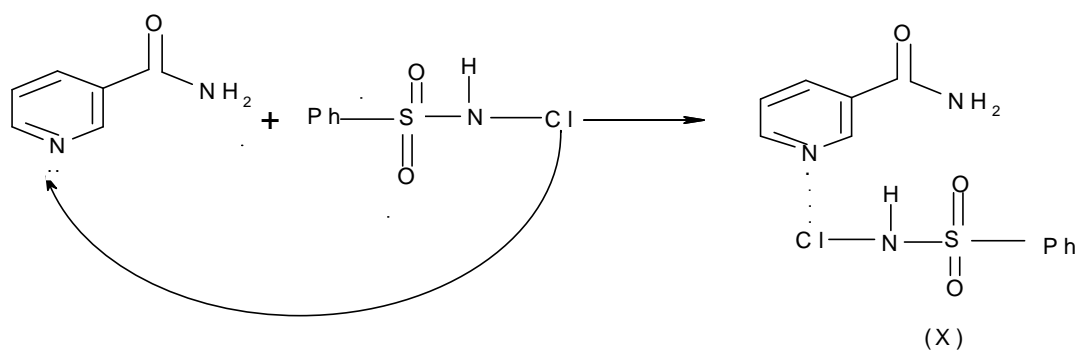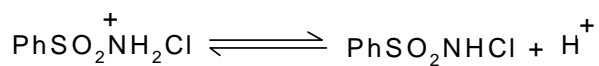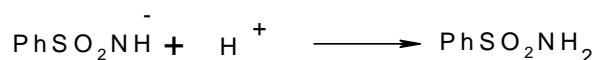
Since rate = $k^\prime$ under pseudo first order condition of [Niacinamide] >> [CAB], the rate equation (17) can be transformed into equation

$$k^\prime = \frac{K_1\,K_2\,k_3\,[S][Ru(III)]}{K_1 + [H^+] + K_1\,K_2[S]} \qquad \dots(18)$$

$$\frac{1}{k^\prime} = \frac{1}{K_2\,k_3[S][Ru(III)]} + \frac{[H^+]}{K_1\,K_2 k_3\,[S][Ru(III)]} + \frac{1}{k_3[Ru(III)]} \qquad \dots(19)$$

$$\frac{1}{k^\prime} = \frac{1}{[S]K_2 k_3[Ru(III)]}\left\{\frac{K_1 + [H^+]}{K_1}\right\} + \frac{1}{k_3[Ru(III)]} \qquad \dots(20)$$

$$\frac{1}{k^\prime} = \frac{[H^+]}{K_1\,K_2\,k_3[S][Ru(III)]} + \left\{\frac{1}{K_2\,k_3[S][Ru(III)]} + \frac{1}{k_3\,[Ru(III)]}\right\} \dots(21)$$

Plots $^1/_{k^\prime}$ versus $\frac{1}{[S]}$ at constant [H$^+$] and [Ru(III)] from equation (20) and 1/k′ versus [H$^+$] at constant [S] and [Ru(III)] from equation (21) were found to be linear (Figure 3). From the intercepts and slopes of the plots, the values of K_1, K_2 and k_3 were evaluated. The protonation constant ($K_P = ^1/_{K_1}$) value obtained, 18.20 for the species PhSO$_2$NHBr is in good agreement with the previously published work[12,13]. This gives indirect evidence for the proposed mechanism of the scheme 1. The thermodynamic parameters Ea, $\Delta H^{\neq}$, $\Delta S^{\neq}$, and $\Delta G^{\neq}$ were calculated as shown in Table 3. The moderate value of enthalpy of activation is supportive for the proposed mechanism in scheme 1. The high negative value of entropy of activation ($\Delta S^{\neq}$) indicates the formation of a rigid transition state by associative process
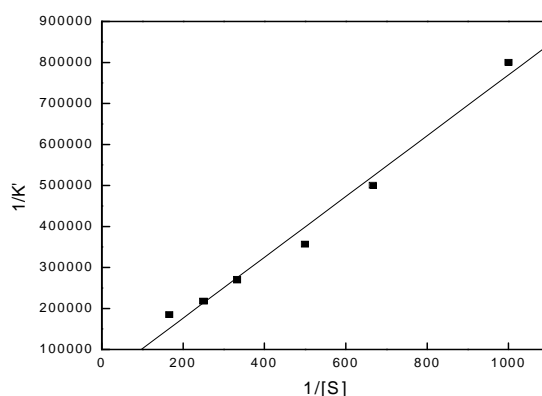

Fig.3.Plot of1/[S] versus 1/k'

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