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Ruthenium(III) catalysed oxidation of gabapentin (neurontin) by diperiodatonickelate(IV) in aqueous alkaline medium: A kinetic and mechanistic study

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Abstract

The kinetics of Ru(III) catalysed oxidation of neuroleptic drug, gabapentin by diperiodatonickelate(IV) (DPN) in alkaline medium at 298 K and a constant ionic strength of 0.30 mol dm^{-3} was studied spectrophotometrically. The oxidation products are 1-(hydroxymethyl) cyclohexane acetic acid and Ni(II) which are identified by spectral studies. The stoichiometry of the reaction is 1:1 which is similar as in the case of absence of ruthenium(III). The oxidation reaction in alkaline medium has been shown to proceed via a Ru(III)–gabapentin complex, which further reacts with deprotonated form of DPN in a rate determining step, which is followed by other fast steps to give the products. The reaction constants involved in the different steps of the mechanism are calculated. The activation parameters with respect to slow step of the mechanism are computed and discussed and thermodynamic quantities are also determined. The catalytic constant (K_C) was calculated at different temperatures. The probable active species of catalyst and oxidant have been identified.

Keywords: Gabapentin; Ru(III) catalysis; Diperiodatonickelate(IV); Oxidation; Kinetics

1. Introduction

Gabapentin (neurontin) (GBP) is a neuroleptic drug, and is important because of its biological significance and selectivity towards the oxidant. It is sometimes prescribed for the management of neuralgia [1] (nerve pain). It is prescribed usually in combination with other medications for the prevention of seizure in people suffering from seizure disorders. Its anticonvulsant mechanism of action is not known. Gabapentin has been prescribed off-label for the treatment of some mood disorders, anxiety and tardive dyskinesia (a neurological syndrome caused by the long-term use of neuroleptic drugs).

Diperiodatonickelate(IV) (DPN) as an oxidant in alkaline medium is new and restricted to a few cases [2–4] due to the fact of its limited solubility and stability in aqueous medium. Reduction of nickel(IV) complexes have been received a considerable attention in order to understand, the nature of intermediate oxidation states of nickel such as nickel(III). Indeed, stable nickel(III) complexes are known [5,6]. Moreover, when nickel(IV) periodate is oxidant, it needs to be known which of the species is the active form of oxidant, since multiple equilibria between the different nickel(IV) species are involved.

In earlier reports [2,4] on DPN oxidation, periodate had a retarding effect in almost all the reactions and monoperiodatonickelate(IV) (MPN), is considered to be the active species. However, in the present study we have observed entirely different kinetic observations and deprotonated diperiodatonickelate(IV), is found to be active form of the oxidant.

In recent years, the use of transition metal ions such as ruthenium, osmium, and iridium, either alone or as binery mixtures, as catalysts in various redox processes has attracted considerable interest [7]. Ruthenium(III) acts as an efficient catalyst in many redox reactions, particularly in an alkaline medium [8]. The catalysed mechanism can be quite complicated due to the formation of different intermediate complexes, free radicals and different oxidation states of ruthenium. The uncatalysed

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reaction of oxidation of gabapentin by DPN has been studied previously [9]. Ruthenium(III) catalyses the oxidation of gabapentin by diperiodatonickelate(IV) in alkaline medium in micro amounts. In order to investigate the redox chemistry and the active species of oxidant and catalyst in such media and to propose the appropriate mechanism of the reaction on the basis of kinetic and spectral results, the title reaction is investigated in detail.

2. Experimental

2.1. Materials and reagents

All chemicals used were of reagent grade and double distilled water was used throughout the work. Solution of gabapentin (S.D. Fine Chemicals) was prepared by dissolving appropriate amount of recrystallised sample in double distilled water. The purity of GBP sample was checked by comparing its I.R. spectrum with literature data. The required concentration of GBP was used from its aqueous stock solution. A standard stock solution of Ru(III) was prepared by dissolving $RuCl_3$ (S.D. Fine Chemicals) in 0.20 mol dm^{-3} HCl. The concentration was determined [10] by EDTA titration. The nickel(II) solution was made by dissolving weighed amount of nickel sulphate (Thomas Baker) in water. Potassium hydroxide (Thomas Baker) and potassium nitrate (Qualigens) were used to provide the required alkalinity and ionic strength, respectively in the reaction solutions. A stock standard solution of IO_4^- was prepared by dissolving a known weight of KIO_4 (Riedel-de Haen) in hot water and used after keeping for 24 h. Its concentration was ascertained iodometrically [11] at neutral pH maintained using phosphate buffer. The temperature was maintained constant to within ±0.1 °C.

2.2. Preparation of DPN

The complex diperiodatonickelate(IV), was prepared as follows [12]: a solution of 3.0 g (1.3×10^{-2} mol) of potassium metaperiodate in about 400 cm^3 of boiling water was added to a 100 cm^3 of boiling solution containing 2.0 g (7.0×10^{-3} mol) of nickel sulphate with vigorous stirring. The resultant boiling solution was treated with 4.0 g of potassium peroxydisulfate (1.5×10^{-2} mol) over a period of 25–30 min, added in 0.40 g increments. Boiling was continued for 10 min after complete addition of potassium peroxydisulfate. The reaction takes place as indicated below.

$$NiSO_4 + KIO_4 + K_2S_2O_8 + 2(1/2)H_2O \rightarrow KNiIO_6{\cdot}(1/2)H_2O + 2KHSO_4 + H_2SO_4$$

The dark red coloured, almost black, crystals that formed ($KNiIO_6{\cdot}(1/2)H_2O$) were allowed to settle and were then washed several times by decantation with 1% potassium peroxydisulfate solution. The product was transferred to a G_3 sintered glass crucible and washed repeatedly with boiling water to remove any adsorbed periodate. The moisture was removed by suction and final drying was effected at room temperature over anhydrous calcium chloride. The purity of the complex was checked [3] by its UV–vis spectrum, which shows a broad absorbance band at 410 nm.

A stock solution of diperiodatonickelate(IV) was prepared by dissolving the above compound ($KNiIO_6{\cdot}(1/2)H_2O$) in 1.0 mol dm^{-3} potassium hydroxide solution and 100 mg of KIO_4 is added to it. The resulting solution was stirred vigorously for about 30 min at 50 °C and kept aside over 24 h to get red coloured solution. The dissolved material was filtered through G_4 sintered glass crucible and the filtrate, DPN solution was found to be sufficiently stable. The concentration of nickel(IV) periodate solution was determined gravimetrically [13] after reducing nickel(IV) to nickel(II) as the dimethyl glyoxime complex.

2.3. Kinetic measurements

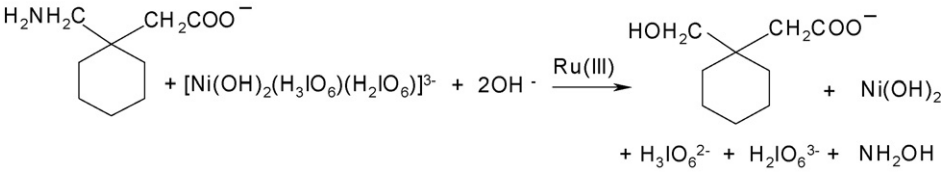
Since the initial reaction was too fast to be monitored by usual methods, kinetic measurements were performed on a Varian CARY 50 Bio UV–vis Spectrophotometer connected to a rapid kinetic accessory (HI-TECH SFA-12). The kinetics was followed under pseudo first order condition where [GBP] > [DPN] at 25 ± 0.1 °C, unless specified. The reaction was initiated by mixing the DPN to GBP solution which also contained required concentration of KNO_3, KOH, Ru(III) and KIO_4. The progress of reaction was followed spectrophotometrically at 410 nm by monitoring decrease in absorbance due to DPN with the molar absorbancy index, 'ε' to be 7500 ± 375 dm^3 mol^{-1} cm^{-1}. It was verified that there is a negligible interference from other species present in the reaction mixture at this wavelength.

The pseudo first order rate constants, 'k_{obs}', were determined from the log(absorbance) versus time plots. 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_{obs} versus respective concentration of species except for [DPN] in which non variation of 'k_{obs}' was observed as expected to the reaction condition. The rate constants were reproducible to within ±5%. 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 Programme.

3. Results

3.1. Stoichiometry and product analysis

Different sets of reaction mixtures containing varying ratios of reactants where [Ni(IV)] was in excess over [gabapentin] at constant ionic strength, alkali and catalyst, were kept for about 2 h at 298 K in nitrogen atmosphere and in a closed vessel. The remaining [DPN] was assayed spectrophotometrically by measuring the absorbance at 410 nm. The product, nickel(II) was analyzed as the dimethyl glyoxime gravimetrically [13]. The results indicated that 1 mol of DPN consumed 1 mol of gabapentin in presence of catalyst as in Eq. (1).



(1)

The main reaction products were extracted with solvent ether and organic product was submitted to spot tests. The main reaction product was identified as the 1-(hydroxymethyl) cyclohexane acetic acid by spot test [14a] for free carboxyl group and –OH. The product was also confirmed by IR spectra. In gabapentin, the IR spectra [15] shows that it exists as Zwitter ion indicating the absence of $–NH_2$ and –COOH groups; there is no absorption in the usual –NH stretching, i.e., 3500–3300 cm^{-1} but instead the bands are observed in the region of 2800–3100 cm^{-1}, the band due to NH_3^+ stretching and also there is one characteristic band at 1541 cm^{-1} as assignable to NH_3^+ deformation vibration. In addition to this there is one more band at 1607 cm^{-1} which is assignable to ionic carboxyl absorption. At 1485 cm^{-1} a band is appeared which is assignable to NH_3^+ deformation vibration (second band). Where as in the product, 1-(hydroxymethyl) cyclohexane acetic acid, the presence of absorption band at 1681 cm^{-1} indicates the free $–COO^-$ group which was absent in gabapentin (due to Zwitter ion) and there is a broad valley in the region 3098–3500 cm^{-1} indicating the presence of –OH group as well as carboxylic –OH group. There is C–O stretching frequency of alcoholic –OH group (hydroxy methyl group) at 1066 cm^{-1} indicating the formation of $–CH_2–OH$ group, which was absent in gabapentin, and –OH deformation bands occur at 1329–1320 cm^{-1}.

The product was also confirmed by H^1 NMR spectra. From the spectra of gabapentin, it is observed that the two $–CH_2$ peaks appeared at 2.24 and 2.81δ ppm, respectively. The cyclohexyl proton appeared in the region of 1.18–1.31δ ppm and as earlier suggested $–NH_2$ and –COOH peaks are not observed because of Zwitter ion form. In 1-(hydroxymethyl) cyclohexane acetic acid, the cyclohexyl protons appeared in the region of 1.27–1.65δ ppm, and two $–CH_2$ bands appeared at down field to cyclohexyl protons, i.e., 2.19–3.16δ ppm, respectively. Another peak appeared at 4.60δ ppm due to hydroxy methyl group. Another product, hydroxylamine (NH_2OH) was identified by CHN data analysis, H = 08.98%, N = 41.83% and O = 41.12% and further it was identified by spot test [14b]. It was observed that the products do not undergo further oxidation under prevailing kinetic conditions. The products obtained are similar to that for uncatalysed reaction [9].

3.2. Reaction orders

As the diperiodatonickelate(IV) oxidation of gabapentin in alkaline medium proceeds with a measurable rate in the absence of Ru(III), the catalysed reaction is understood to occur in parallel paths with contributions from both the catalysed and unanalyzed paths. Thus, the total rate constant (k_T) is equal to the sum of the rate constants of the catalysed (k_C) and uncatalysed (k_U) reactions, so $k_C = k_T - k_U$. Hence the reaction orders have been determined from the slopes of $\log k_C$ versus log(concentration) plots by varying the concentrations of gabapentin, IO_4^-, OH^- and Ru(III), in turn, while keeping others constant. The DPN concentration was varied in the range of 1.0×10^{-5} to 1.0×10^{-4} mol dm^{-3} and the linearity of the plots of log(absorbance) versus time up to 80% completion of the reaction indicates a reaction order of unity in [DPN] (Fig. 1). This is also confirmed by varying of [DPN], which did not result in any change in the pseudo first order rate constants, k_C (Table 1). The gabapentin concentration was varied in the range 1.0×10^{-4} to 1.0×10^{-3} mol dm^{-3} at 298 K while keeping other reactant concentrations and conditions constant. The k_C values increased with the increase in concentration of gabapentin indicating an apparent less than unit order dependence on [GBP] (Table 1). The effect of alkali on the reaction has been studied in the range of 0.01–0.10 mol dm^{-3} at constant concentrations of gabapentin, DPN, catalyst and a constant ionic strength of 0.30 mol dm^{-3}. The rate constants increased with increasing [alkali] and the order was found to be less than unity (Table 1).

3.3. Effect of [periodate]

The effect of [IO_4^-] was studied by varying the concentration from 1.0×10^{-5} to 1.0×10^{-4} mol dm^{-3} keeping all other reactants concentrations constant. It was found that the added periodate has no significant effect on the rate of reaction.

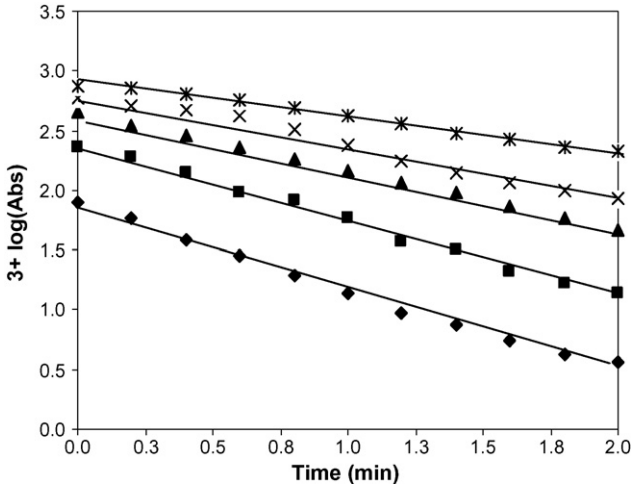


Fig. 1. First-order plots of Ru(III) catalysed oxidation of gabapentin by DPN in aqueous alkaline medium at 298 K. 10^5 [DPN] (mol dm^{-3}); (1) 1.0; (2) 3.0; (3) 6.0; (4) 8.0; (5) 10.0; (10^4 [GBP] = 6.0, [OH^-] = 0.10, 10^5 [IO_4^-] = 1.0 and I = 0.30 mol dm^{-3}).

Table 1
Effect of [DPN], [GBP], [OH^-] and [IO_4^-] on the ruthenium(III) catalysed oxidation of GBP by DPN in alkaline medium at 298 K, [IO_4] = 1.0×10^{-5} mol dm^{-3} and I = 0.30 mol dm^{-3}

[DPN] ($\times 10^5$ mol dm^{-3})	[GBP] ($\times 10^4$ mol dm^{-3})	[OH^-] (mol dm^{-3})	[Ru(III)] ($\times 10^6$ mol dm^{-3})	k_T ($\times 10^2$ s^{-1})	k_U ($\times 10^3$ s^{-1})	k_C ($\times 10^2$ s^{-1})	
						Found	Calculated
1.0	6.0	0.1	6.0	1.88	4.29	1.45	1.45
3.0	6.0	0.1	6.0	1.89	4.28	1.46	1.45
6.0	6.0	0.1	6.0	1.85	4.30	1.42	1.45
8.0	6.0	0.1	6.0	1.87	4.29	1.44	1.45
10	6.0	0.1	6.0	1.84	4.27	1.41	1.45
6.0	1.0	0.1	6.0	1.01	3.92	0.61	0.57
6.0	3.0	0.1	6.0	1.55	4.05	1.15	1.12
6.0	6.0	0.1	6.0	1.88	4.29	1.45	1.45
6.0	8.0	0.1	6.0	2.14	4.75	1.66	1.59
6.0	10	0.1	6.0	2.35	5.11	1.84	1.75
6.0	6.0	0.01	6.0	0.61	2.18	0.39	0.39
6.0	6.0	0.03	6.0	1.10	2.89	0.81	0.86
6.0	6.0	0.05	6.0	1.54	3.25	1.21	1.28
6.0	6.0	0.08	6.0	1.74	4.01	1.34	1.35
6.0	6.0	0.1	6.0	1.88	4.29	1.45	1.45
6.0	6.0	0.1	1.0	0.71	4.29	0.28	0.27
6.0	6.0	0.1	3.0	1.25	4.29	0.82	0.78
6.0	6.0	0.1	6.0	1.88	429	1.45	1.45
6.0	6.0	0.1	8.0	2.45	4.29	2.02	1.94
6.0	6.0	0.1	10	2.97	4.29	2.54	2.43

3.4. Effect of [Ru(III)]

The [Ru(III)] concentrations was varied from 1.0×10^{-6} to 1.0×10^{-5} mol dm^{-3} range, at constant concentration of diperiodatonickelate(IV), gabapentin, alkali and ionic strength (Table 1). The k_C values increased with the increase in concentration of ruthenium(III). The order in [Ru(III)] was found to be unity from the linearity of the plots of log k_C versus log [Ru(III)] ($r \geq 0.9824$, $S \leq 0.076$).

3.5. Effect of added products

Effect of initially added reaction product such as Ni(II) in the form of $NiSO_4$ was studied in the concentration ranges from 1.0×10^{-5} to 1.0×10^{-4} mol dm^{-3}, keeping all other reactant concentrations constant. It was found that the added product had negligible effect on rate of reaction.

3.6. Effect of dielectric constant (D) and ionic strength

Dielectric constant of the medium, '*D*' was varied by varying the *t*-butyl alcohol and water percentage. The decrease in dielectric constant of the reaction medium, decreases the rate and the plot of log k_C versus 1/*D* was linear with negative slope ($r \geq 0.9824$, $S \leq 0.006$) (Fig. 2).

The decrease in ionic strength decreased the rate of reaction and the plot of log k_C versus $I^{1/2}$ was linear with negative slope.

3.7. Test for free radicals (polymerization study)

To test the intervention of free radicals, the reaction mixture was mixed with acrylonitrile monomer and kept for 4 h under nitrogen atmosphere. On dilution with methanol, white precipitate of polymer was formed, indicating the presence of intervention of free radicals in the reaction. The blank experiment of either DPN or gabapentin with acrylonitrile alone did not induce polymerization under the same condition as those induce with reaction mixture. Initially added acrylonitrile decreases the rate indicating the free radical intervention, which is the case in earlier work [16].

3.8. Effect of temperature (T)

The influence of temperature on the rate of reaction were studied at 25, 30, 35 and 40 °C. The rate constants, *k*, of the slow step of Scheme 1 were obtained from the slopes and the intercepts of the plots of [Ru(III)]/k_C versus

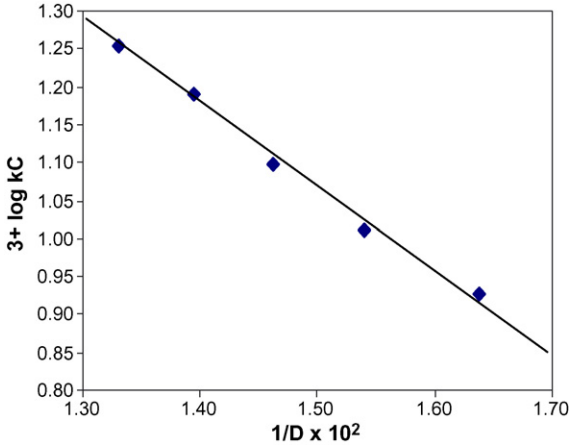
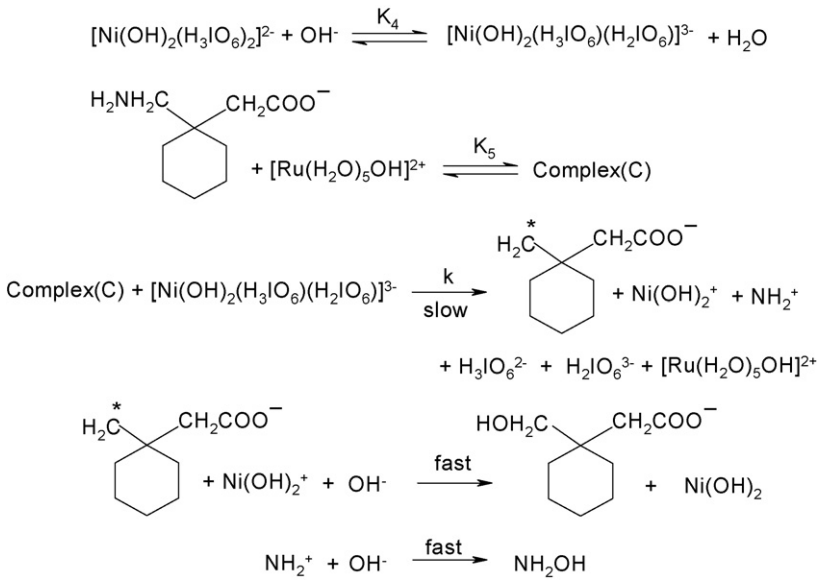


Fig. 2. Effect of dielectric constant of the medium on Ru(III) catalysed oxidation of gabapentin by diperiodatonickelate(III) at 298 K.



Scheme 1.

1/[GBP] ($r \geq 0.9924$, $S \leq 0.024$)and [Ru(III)]/k_C versus 1/[OH] ($r \geq 0.9784$, $S \leq 0.012$) plots at four different temperatures. The values are given in Table 2. The activation parameters for the rate determining step were obtained by the least square method of plot of log k versus $1/T$ ($r \geq 0.96994$, $S \leq 0.016$) and are presented in Table 2.

Table 2
Thermodynamic activation parameters for the Ru(III) catalysed oxidation of GBP by DPN in alkaline medium with respect to the slow step of Scheme 1

Temperature (K)	k_C ($\times 10^{-3}$ s^{-1})
(A) Effect of temperature	
298	4.90
303	5.44
308	5.86
313	6.30

Parameters	Values
(B) Activation parameters (Scheme 1)	
E_a (kJ mol^{-1})	12.9 ± 0.2
$\Delta H^{\#}$ (kJ mol^{-1})	10.4 ± 0.2
$\Delta S^{\#}$ (J K^{-1} mol^{-1})	−139 ± 12
$\Delta G^{\#}$ (kJ mol^{-1})	51.8 ± 2.0
log A	5.9 ± 0.2

Temperature (K)	K_4 (dm^3 mol^{-1})	K_5 ($\times 10^{-3}$ mol dm^{-3})
(C) Effect of temperature to calculate K_4 and K_5 for the oxidation of gabapentin by diperiodatonickelate(IV) in alkaline medium		
298	23.7 ± 1.1	3.97 ± 0.15
303	28.3 ± 1.4	4.95 ± 0.20
308	38.2 ± 1.8	6.54 ± 0.26
313	45.3 ± 2.1	8.95 ± 0.42

Thermodynamic quantities	Values from K_4	Values from K_5
(D) Thermodynamic quantities using K_4 and K_5		
ΔH (kJ mol^{-1})	34.7 ± 1.0	42.3 ± 0.8
ΔS (J K^{-1} mol^{-1})	143 ± 8	209 ± 10
ΔG_{298} (kJ mol^{-1})	−7.8 ± 0.1	−20.5 ± 0.9

[DPN] = 6.0×10^{-5}; [GBP] = 3.0×10^{-4}; [OH$^-$] = 0.10; [Ru(III)] = 6.0×10^{-6} mol dm^{-3}; [IO$_4$] = 1.0×10^{-5} mol dm^{-3}.

3.9. Catalytic activity

It has been pointed out by Moelwyn-Hughes [17] that in presence of the catalyst, the uncatalysed and catalysed reactions proceed simultaneously, so that

$$k_T = k_U + K_C[\text{catalyst}]^x \quad (2)$$

here k_T is the observed pseudo first-order rate constant in the presence Ru(III) catalyst, k_U the pseudo first-order rate constant for the uncatalysed reaction, K_C the catalytic constant and 'x' the order of the reaction with respect to [Ru(III)]. In the present investigations, x values for the standard run were found to be unity for Ru(III). Then the value of K_C is calculated using the equation,

$$K_C = \frac{k_T - k_U}{[\text{catalyst}]^x} = \frac{k_C}{[\text{catalyst}]^x} \quad (\text{where } k_T - k_U = k_C) \quad (3)$$

The values of K_C were evaluated at different temperatures and found to vary at different temperatures. Further, plot of log K_C versus $1/T$ was linear and the value of energy of activation and other activation parameters with reference to catalyst were computed. These results are summarized in Table 3. The value of K_C is 1.04×10^3 at 298 K.

4. Discussion

The water soluble [5,6] nickel periodate complex is reported [4,18] to be $[Ni(HIO_6)_2(OH)_2]^{6-}$. However, in an aqueous alkaline medium and at a high pH range as employed in the study, periodate is unlikely to exist as HIO_6^{4-} (as present in the complex) as is evident from its involvement in multiple equilibria

Table 3
Values of catalytic constant (K_C) at different temperatures and activation parameters calculated using K_C values

Temperature (K)	K_C ($\times 10^{-3}$)
298	1.04
303	1.34
308	1.76
313	2.11
E_a (kJ mol^{-1})	36.8 ± 1.0
$\Delta H^{\#}$ (kJ mol^{-1})	34.3 ± 0.8
$\Delta S^{\#}$ (J K^{-1} mol^{-1})	−71.5 ± 2.0
$\Delta G^{\#}$ (kJ mol^{-1})	55 ± 2
log A	9.5 ± 0.3

[DPN] = 6.0×10^{-5}; [GBP] = 6.0×10^{-4}; [OH$^-$] = 0.10 mol dm^{-3}; [IO_4] = 1.0×10^{-5} mol dm^{-3}; [Ru(III)] = 6.0×10^{-6} mol dm^{-3}. I = 0.30 mol dm^{-3}.

[19] (4)–(6) depending on the pH of the solution.

$$H_5IO_6 \overset{K_1}{\rightleftharpoons} H_4IO_6^- + H^+, \quad K_1 = 5 \times 10^{-4} \tag{4}$$

$$H_4IO_6^- \overset{K_2}{\rightleftharpoons} H_3IO_6^{2-} + H^+, \quad K_2 = 4.9 \times 10^{-9} \tag{5}$$

$$H_3IO_6^{2-} \overset{K_3}{\rightleftharpoons} H_2IO_6^{3-} + H^+, \quad K_3 = 2.5 \times 10^{-12} \tag{6}$$

Periodic acid (H_5IO_6) exists in acid medium and also as $H_4IO_6^-$ around a pH of 7. Thus, under the conditions employed in the alkaline medium, the main species are expected to be $H_3IO_6^{2-}$ and $H_2IO_6^{3-}$. At higher concentrations, periodate also tends to dimerise [20]. Hence the pH employed in the study, the Ni(IV) periodate complex exists as DPN, $[Ni(H_3IO_6)_2(OH)_2]^{2-}$, a conclusion also supported by earlier work [4].

It is interesting to identify the probable ruthenium(III) chloride species in alkaline media. Electronic spectral studies [21] have confirmed that ruthenium(III) chloride exists in hydrated form as $[Ru(H_2O)_6OH)]^{3+}$. In the present study, it is quite probable that the $[Ru(H_2O)_5OH)]^{2+}$ species might assume the general form $[Ru(III)(OH)_x]^{3-x}$. The x-value would always be less than six because there are no definite reports of any hexahydroxy ruthenium species. The remainder of the coordination sphere would be filled by water molecules. Hence, under the conditions employed, e.g. [OH$^-$] ≫ [Ru(III)], ruthenium(III) is mostly present as the hydroxylated species [22], $[Ru(H_2O)_5OH)]^{2+}$.

It is known that gabapentin exists in the form of Zwitter ion [23] in aqueous medium. In acidic medium, it exists in the protonated form, whereas in basic medium, it is in the fully deprotonated form [23] according to the following equilibria.

$$RCH_2(NH_2)CH_2COOH \overset{\text{aqueous}}{\rightleftharpoons} RCH_2(\overset{+}{N}H_3)CH_2COO^-$$

$$RCH_2(NH_2)CH_2COOH + H^+ \rightleftharpoons RCH_2(\overset{+}{N}H_3)CH_2COOH$$

$$RCH_2(NH_2)CH_2COOH + OH^- \rightleftharpoons RCH_2(NH_2)CH_2COO^- + H_2O$$

where R = C_6H_{10}.

The reaction between gabapentin and DPN in alkaline medium in the presence of ruthenium(III) presents a 1:1 stoichiometry of oxidant to reductant, with first-order dependence on both [DPN] and [Ru(III)] and an apparent order of less than unity in [GBP] and [OH$^-$]. No products effect was observed.

In most of the reports [2–4] on DPN oxidation, periodate had a retarding effect and order in the [OH$^-$] was found to be less than unity and monoperiodatonickelate(IV) (MPN) is considered to be the active species. However, in the present kinetic study, different kinetic observations have been obtained, i.e., periodate has no effect on the rate of reaction and accordingly deprotonated form of DPN itself is considered to be the active species of oxidant. The results indicate that DPN species reacts with OH$^-$ in prior equilibrium step to form deprotonated form of DPN, which also explains the fractional order in [OH$^-$]. The anionic species of gabapentin reacts with ruthenium(III) species to form a complex (C). The complex (C) reacts with 1 mol of deprotonated form of DPN in a slow step to give a anionic free radical derived from gabapentin with formation of Ni(III) species, this anionic free radical further reacts with Ni(III) species in a fast step to yield the products. The formation of Ni(III) is in accordance with earlier work [24,25]. The formation of anionic free radical is also supported in earlier work [26]. The experimental results can be accommodated in Scheme 1.

Spectral evidence for such a catalyst–substrate complex was obtained from the UV–vis spectra of gabapentin (6.0×10^{-4}), Ru(III) (6.0×10^{-6}), [OH$^-$] = 0.1 mol dm^{-3} and mixture of both. A bathochromic shift, λ_{max}, of ca. 6 nm from 308 to 313.9 nm was observed. Such a complex formation between the catalyst and substrate has been observed in other studies [27]. However, the Michelis–Menten plot also proved the complex formation between catalyst and reductant, which explains less than unit order in [GBP].

The thermodynamic quantities for the different equilibrium steps, in Scheme 1 can be evaluated as follows. The gabapentin and hydroxide ion concentrations (Table 2) were varied at different temperatures. The plots of [Ru(III)]/k_C versus 1/[gabapentin] ($r \geq 0.9799$, $S \leq 0.016$) and [Ru(III)]/k_C versus 1/[OH$^-$] ($r \geq 0.9924$, $S \leq 0.096$) should be linear as shown in Fig. 3. From the slopes and intercepts, the values of K_4 are calculated at different temperature. A vant hoff's plot was made for the variation of K_4 with temperature [i.e., log K_4 versus $1/T$ ($r \geq 0.9847$, $S \leq 0.038$)] and the values of the enthalpy of reaction enthalpy of the reaction, ΔH, entropy of the reaction, ΔS, and free energy reaction, ΔG, were calculated and tabulated in Table 2. A comparison of the latter values with those 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 the rate determining step is fairly slow and involves high activation energy [28]. In the same manner, K_5 values were calculated at different temperatures and the corresponding values of thermodynamic quantities are given in Table 2. Scheme 1 leads to rate law (7) as

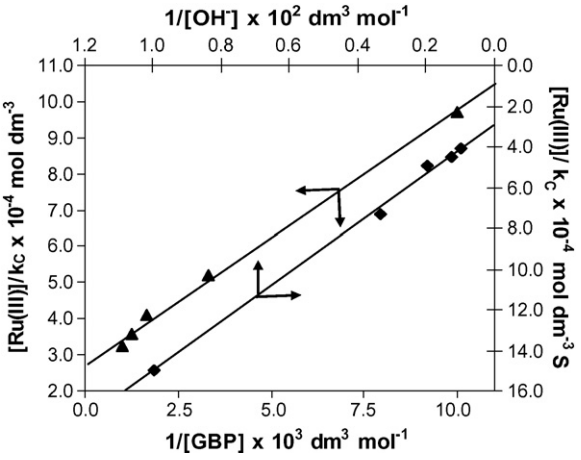


Fig. 3. Verification of rate law (9) of Ru(III) catalysed oxidation of gabapentin by diperiodatonickelate(IV) at 298 K.

follows:

$$\text{Rate} = \frac{-[\text{DPN}]}{\text{d}t} = \frac{kK_4K_5[\text{DPN}][\text{GBP}][\text{OH}^-][\text{Ru(III)}]}{1 + K_5[\text{GBP}] + K_4[\text{OH}^-] + K_4K_5[\text{OH}^-][\text{GBP}]} \quad (7)$$

$$\frac{\text{Rate}}{[\text{DPN}]} = k_\text{C} = k_\text{T} - k_\text{U} = \frac{kK_4K_5[\text{GBP}][\text{OH}^-][\text{Ru(III)}]}{1 + K_5[\text{GBP}] + K_4[\text{OH}^-] + K_4K_5[\text{OH}^-][\text{GBP}]} \quad (8)$$

Eq. (8) can be rearranged to Eq. (9), which is suitable for verification.

$$\frac{[\text{Ru(III)}]}{k_\text{C}} = \frac{1}{kK_4K_5[\text{GBP}][\text{OH}^-]} + \frac{1}{kK_4[\text{OH}^-]} + \frac{1}{kK_5[\text{GBP}]} + \frac{1}{k} \quad (9)$$

According to Eq. (9), the plots of $[\text{Ru(III)}]/k_\text{C}$ versus 1/[gabapentin] ($r \geq 0.9799$, $S \leq 0.016$) and $[\text{Ru(III)}]/k_\text{C}$ versus $1/[\text{OH}^-]$ ($r \geq 0.9924$, $S \leq 0.096$) should be linear as shown in Fig. 3. From the slope and intercept, the values of K_4, K_5 and k at 298 K could be derived as $23.7 \pm 1.3\ \text{dm}^3\ \text{mol}^{-1}$, $(3.9 \pm 0.1) \times 10^3\ \text{dm}^3\ \text{mol}^{-1}$ and $(4.9 \pm 0.2) \times 10^3\ \text{dm}^3\ \text{mol}^{-1}\ \text{s}^{-1}$, respectively. Using these constants, the rate constants were evaluated over different experimental conditions and there is a reasonable agreement between the calculated and experimental values (Table 1), which verifies the proposed mechanism. The value of K_4 is in the neighbourhood of earlier work [9]. The effect of solvent on the reaction rate is described in detail literature [29]. In our present study, a plot of $\log k_\text{C}$ versus $1/D$ ($r \geq 0.9974$, $S \leq 0.004$) is linear with negative slope (Fig. 2), which is in accordance the involvement of ions as given in Scheme 1. The ionic strength is also in the right direction as seen in scheme.

The negative value of $\Delta S^\#$ indicates that the complex (C) is more ordered than the reactants. The observed modest enthalpy of activation and higher rate constant of the slow step indicate that the oxidation presumably occurs by inner-sphere mechanism. This conclusion is supported by earlier work [30].

5. Conclusion

Among various species of diperiodatonickelate(IV) in alkaline medium, in earlier reports the monoperiodatonickelate(IV) was the active species, whereas, deprotonated form of diperiodatonickelate(IV) itself is considered to be the active species for the title reaction. The pH of the medium is crucial. Activation parameters with respect to slow step of reaction were computed. Catalytic constants and the activation parameters with reference to catalyst were also computed.

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