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A kinetic and mechanistic study of oxidation of L-lysine by diperiodatonickelate(IV) in aqueous alkaline medium

Basavaraj T, Shivamurthi A. Chimatadar & Sharanappa T. Nandibewoor*
P.G. Department of Studies in Chemistry, Karnatak University, Dharwad- 580 003, India
Email: stnandibewoor@yahoo.com

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The kinetics of oxidation of L-lysine by diperiodatonickelate(IV) (DPN) in aqueous alkaline medium at a constant ionic strength of 0.60 mol dm^{-3} has been studied spectrophotometrically. The reaction shows first order in diperiodatonickelate(IV) and less than unit order dependence each in lysine and OH$^-$ ion concentrations. The addition of periodate retards the reaction, while the product nickel(II) do not show any significant effect on the reaction rate. An increase in ionic strength and decrease in dielectric constant of the medium decreases the rate. A mechanism based on experimental results is proposed. The constants involved in the mechanism are evaluated. The activation parameters with respect to slow step of the mechanism are computed and discussed.

Keywords: L-lysine, Diperiodatonickelate(IV), Oxidation and reduction, Kinetics, Mechanism

The kinetic studies using nickel(IV) complex as an oxidant in the form of nickel(IV) oxime or nickel(IV) periodate are limited to a few cases[1] due to its limited stability and solubility in aqueous medium. In kinetic studies, involving nickel(IV) as an oxidant, the intervention of nickel(III) as an intermediate may occur. Indeed stable nickel(III) complexes are also known[2]. Moreover, when nickel(IV) periodate is the oxidant, since multiple equilibria between the different nickel(IV) species are involved[1], one needs to know which of the species is the active oxidant.

Amino acids act not only as the building block in protein synthesis but they also play a significant role in metabolism and have been oxidised by a variety of oxidising agents[3]. The study of the oxidation of amino acids is of interest because of their biological significance and selectivity towards the oxidant to yield the different products[4]. L-lysine is an essential amino acid and one gets it from food. Some evidence suggests that supplemental L-lysine[5] may be able to help to prevent herpes infections (cold sores and genital herpes). Most people need about 1 g of L-lysine per day. The requirement may be greater for athletes and people recovering from major injuries, especially burns. The richest sources of L-lysine are animal proteins, such as meat and poultry, but it is also found in dairy products, eggs, and beans. A typical therapeutic dosage of L-lysine for herpes infections is one gram three times a day. Due to lack of literature on the oxidation of L-lysine by diperiodatonickelate(IV) and to understand the species of diperiodatonickelate(IV) and to arrive at the mechanism, the study of title reaction is undertaken.

Materials and Method

The chemicals used were of reagent grade and double distilled water was used throughout the study. L-lysine(Fluka) solution was prepared by dissolving appropriate amount in water. The solid diperiodatonickelate(IV) complex (DPN) was prepared by the known method[6]. The complex was characterized[1] by its UV-visible spectrum, which shows a broad absorbance band at 410 nm. The diperiodatonickelate(IV) solution was standardized gravimetrically after reducing nickel(IV) to nickel(II) and precipitating the nickel(II) as dimethylglyoxime complex[7]. Periodate (BDH) solution was prepared in hot water and it was kept for 24 h. Its concentration was ascertained iodometrically[8] at neutral pH maintained by a phosphate buffer. Potassium hydroxide (BDH) and potassium nitrate (BDH) were employed to maintain required alkalinity and ionic strength respectively in the reaction solution.

Kinetic measurments

The kinetic measurements were performed under pseudo-first order conditions, where L-lysine concentration was excess over diperiodatonickelate

(IV) concentration, at a constant ionic strength of 0.60 mol dm^{-3} and at constant temperature, 25 ± 0.1 ºC. The reaction was initiated by mixing the required quantities of previously thermostatted solution of diperiodatonickelate(IV) and L-lysine which also contained the necessary quantities of periodate, potassium hydroxide and potassium nitrate. Here the total concentration of hydroxyl ion was calculated by considering the potassium hydroxide in diperiodatonickelate(IV) as well as the potassium hydroxide additionally added. Similarly, the total metaperiodate concentration was calculated by considering the metaperiodate present in the diperiodatonickelate(IV) solution and that additionally added. The progress of the reaction was monitored by measuring the concentration of diperiodatonickelate(IV) in a 1 cm quartz cell at 410 nm in a Varian Cary-50 Bio UV-visible spectrophotometer, where all other species do not absorb significantly at this wavelength. Diperiodatonickelate(IV) concentration from 1.0×10^{-5} to 1.4×10^{-4} mol dm^{-3} in 0.20 mol dm^{-3} alkali obeyed Beer’s law with molar absorbance index, $\varepsilon = 7500 \pm 375$ dm^3 mol^{-1} cm^{-1} at 410 nm . The first order rate constants, k_{obs}, were obtained by the plots of log[DPN] versus time. The plots were linear over 70% completion of the reaction. Most of the kinetic runs were followed more than 80% completion of the reaction and the rate constants were reproducible within ± 5%.

The effect of dissolved oxygen on the reaction mixture was checked by preparing the reaction mixture and following the reaction in an atmosphere of nitrogen. No significant difference in the results was observed in presence and absence of nitrogen. Added carbonate showed no effect on the reaction rate. However, fresh solutions were always used while performing the experiment. In view of the modest concentrations of alkali used in the reaction media, attention was also given to the effect of the surface of the reaction vessels on the kinetics. Use of polythene/acrylic equipment and quartz or polyacrylate cell gave the same results as with the glass vessels and cells.

Stoichiometry and product analysis

Different sets of reaction mixtures containing different amounts of diperiodatonickelate(IV) and L-lysine at constant ionic strength and alkali were allowed to react for about 2 h at 25 ºC in an inert atmosphere and then analyzed. Diperiodatonickelate(IV) was estimated spectrophotometrically at 410 nm and nickel(II) gravimetrically as dimethylglyoxime complex[7]. The results indicated that one mole of L-lysine consumes two moles of diperiodatonickelate(IV) according to the Eqn (1).

$$\begin{aligned}&NH_2CH_2CH_2CH_2CH_2CH(NH_2)COOH + 2Ni(IV) \rightarrow \\ &NH_2CH_2CH_2CH_2CH_2COOH + 2Ni(II) + NH_3 + CO_2 + 4H^+ \end{aligned} \quad (1)$$

The main reaction products were identified as 5-aminovaleric acid by spot test[9], ammonia by Nessler’s reagent test and carbon dioxide by lime water. The product 5-aminovaleric acid was separated by TLC using n- propanol / water (7: 3) upon silica gel with Rf values (0.56 for 5-amino valeric acid and 0.03 for lysine) and its melting point (158 ºC). ^{13}C NMR spectra of lysine shows peaks for C_1 at 183.79 ppm, C_2 at 54.02 ppm, C_3 at 40.28ppm, C_4 at 37.92 ppm, C_5 at 27.68 ppm, C_6 at 23.72 ppm where as 5-amino valeric acid shows peaks for C_1 at 183.79 ppm, , C_2 at 40.28ppm, C_3 at 37.92 ppm, C_4 at 27.68 ppm, C_5 at 23.72 ppm. ^{13}C NMR spectra of 5-amino valeric acid shows one carbon short to lysine (Fig. 1).

Results and Disscussion

Reaction order

The reaction orders with respect to reactive species were determined from the slopes of log k_{obs} verses log(conc.) plots by varying the concentrations of the reductant, alkali and periodate, in turn while keeping the others constant.

Effect of [diperiodatonickelate(IV)]

The diperiodatonickelate(IV) concentration was varied from 1.0×10^{-5} to 1.0×10^{-4} mol dm^{-3} at a constant concentrations of L-lysine, alkali, periodate and at

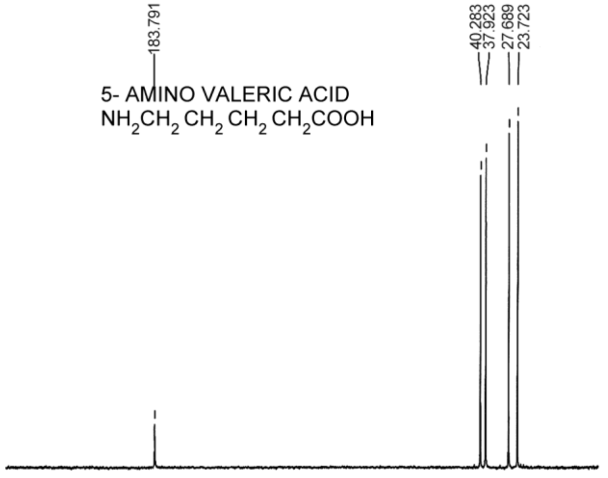


Fig. 1 — ^{13}C NMR spectrum of 5-amino valeric acid in D_2O.

constant ionic strength of 0.6 mol dm^{-3}. The linearity of the plots of log[DPN] versus time, indicates first order in diperiodatonickelate(IV). This was also confirmed by varying the concentration of diperiodatonickelate(IV), which did not show any change in pseudo-first order rate constants, k_{obs} (Table 1).

Effect of [L-lysine]

The substrate, L-lysine concentration was varied in the range 1.0×10^{-4} to 1.0×10^{-3} mol dm^{-3} keeping all other reactant concentrations and conditions constant. The reaction order was determined from the slope of log k_{obs} versus log(conc.) plot. The order in L-lysine concentration was found to be less than unity, *ca* 0.76 (Table 1).

Effect of [alkali]

The effect of OH$^-$ ion concentration on the reaction was studied in the range of 0.1 to 1.0 mol dm^{-3}, at constant diperiodatonickelate(IV) and L-lysine concentrations and at a constant ionic strength of 1.0 mol dm^{-3} at 25 ºC. The rate constants increased with increase in the concentration of alkali. The order with respect to alkali concentration was found to be less than unity, *ca* 0.54 (Table 1).

Table 1 — Effect of diperiodatonickelate(IV), L-lysine, alkali and periodate concentrations on the oxidation of L-lysine by diperiodatonickelate(IV) in an alkaline medium at I = 0.60 mol dm^{-3} and at 25 °C

[DPN]$\times10^5$ (mol dm^{-3})	[L-lysine]$\times10^4$ (mol dm^{-3})	[OH$^-$] (mol dm^{-3})	[IO$_4^-$]$\times10^3$ (mol dm^{-3})	$k_{obs}\times10^3$ (s^{-1})
1.0	8.0	0.2	2.0	7.12
2.0	8.0	0.2	2.0	7.02
4.0	8.0	0.2	2.0	7.39
6.0	8.0	0.2	2.0	7.21
8.0	8.0	0.2	2.0	6.98
10.0	8.0	0.2	2.0	7.33
6.0	1.0	0.2	2.0	1.10
6.0	2.0	0.2	2.0	2.16
6.0	4.0	0.2	2.0	3.82
6.0	6.0	0.2	2.0	5.33
6.0	10.0	0.2	2.0	8.36
6.0	8.0	0.1*	2.0	3.09
6.0	8.0	0.2	2.0	4.45
6.0	8.0	0.4	2.0	6.38
6.0	8.0	0.6	2.0	8.31
6.0	8.0	0.8	2.0	9.13
6.0	8.0	1.0	2.0	10.7
6.0	8.0	0.2	1.0	10.4
6.0	8.0	0.2	4.0	4.85
6.0	8.0	0.2	5.0	2.86
6.0	8.0	0.2	7.0	2.00
6.0	8.0	0.2	10.0	1.12

In the variation of [OH$^-$], the ionic strength was kept constant at I=1.0 mol dm^{-3}

Effect of [periodate]

The concentration of periodate was varied in the range of 1.0×10^{-3} to 1.0×10^{-2} mol dm^{-3} keeping all other reactant concentration and conditions constant. It was found that the added periodate retards the rate of the reaction. The order with respect to periodate concentration was found to be negative and less than unity, *ca* - 0.90 (Table 1).

Effect of added products

The effect of initially added products, 5-aminovaleric acid and nickel(II)sulphate, was studied in the concentration range of 1.0×10^{-4} to 1.0×10^{-2} and 1.0×10^{-5} to 1.0×10^{-4} mol dm^{-3}, respectively, while keeping the reactant concentrations and all other conditions constant. It was observed that, both the products did not show any significant effect on the reaction rate.

Effect of dielectric constant and ionic strength

The relative permittivity (D) effect was studied by varying the t-butyl alcohol-water(v/v) content in the reaction mixture with all other conditions being maintained constant. As the percentage of t-butanol increased, the rate of reaction decreased. Attempts to measure the relative permittivities were not successful. However, they were computed from the values of pure liquids as in earlier studies[8]. There was no reaction of the solvent with the oxidant under the experimental conditions used. The plot of log k_{obs} versus 1/D was linear with a negative slope (Fig. 2).

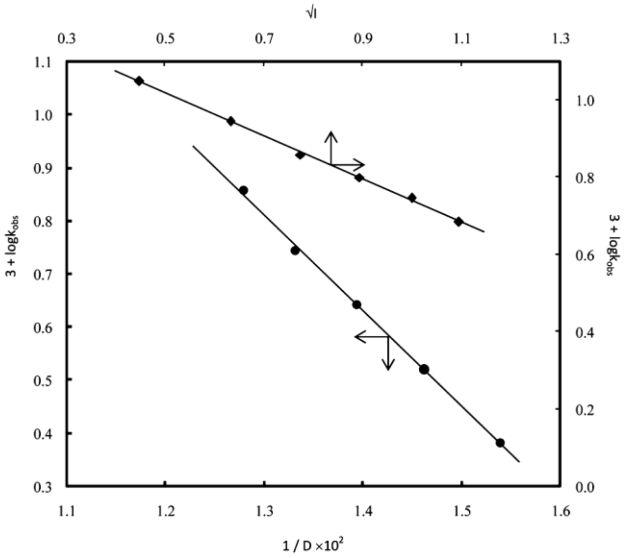


Fig. 2 — Effect of variation of dielectric constant (D) and ionic strength (I) on the oxidation of L-lysine by diperiodatonickelate(IV) in an aqueous alkaline medium at 25 °C.

The effect of ionic strength was studied by varying the potassium nitrate concentration. The ionic strength in the reaction medium was varied from 0.2 to 1.2 mol dm^{-3} at constant concentrations of diperiodatonickelate(IV), L-lysine and alkali. It was found that the rate constants decreased with increasing concentration of potassium nitrate and the plot of log k_{obs} versus $I^{1/2}$ was linear with a negative slope (Fig. 2).

Test for free radicals

To test for free radicals, the reaction mixture containing acrylonitrile scavenger was kept for 24 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 reaction. The blank experiments of either diperiodatonickelate(IV) or L-lysine alone with acrylonitrile did not induce any polymerisation under the similar reaction conditions.

Effect of temperature

The rate of the reaction was measured at four different temperatures with varying L-lysine concentrations keeping other conditions constant. The rate was found to increase with increase in temperature. The rate constants k, of the slow step of Scheme 1 were obtained from the intercepts of the plots of $1/k_{obs}$ versus 1/[L-lysine] at four different temperatures. The data were subjected to least square analysis. The activation parameters were evaluated from the plot of log k versus 1/T are listed in Table 2.

The water soluble nickel(IV) periodate complex was reported[10] as $[Ni(HIO_6)_2(OH)_2]^{6-}$. However in aqueous alkaline medium and in high pH range employed in this study, periodate is unlikely to exist as $H_4IO_6^{4-}$ (as present in the complex) as is evident from its involvement in the multiple equillibria[11] Eqn (2) to (4) depending on the pH of the solution.

$$H_5IO_6 \rightleftharpoons H_4IO_6^- + H^+ \qquad K_1 = 5.1 \times 10^{-4} \tag{2}$$

$$H_4IO_6^- \rightleftharpoons H_3IO_6^{2-} + H^+ \qquad K_2 = 4.9 \times 10^{-9} \tag{3}$$

$$H_3IO_6^{2-} \rightleftharpoons H_2IO_6^{3-} + H^+ \qquad K_3 = 2.5 \times 10^{-12} \tag{4}$$

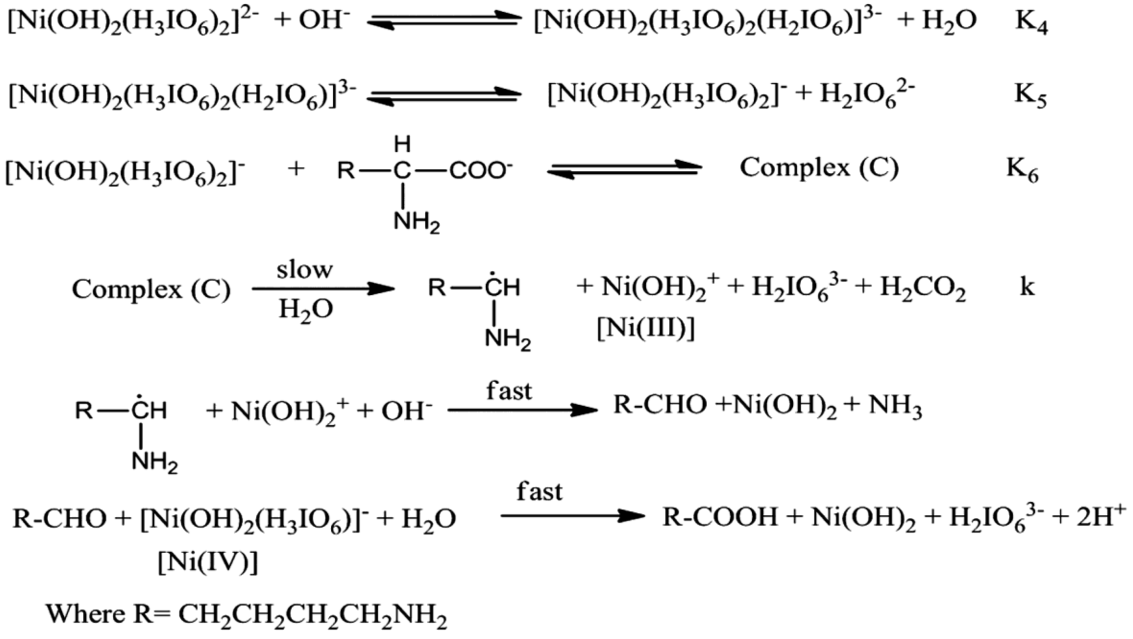
Table 2 — (a) Effect of variation of temperature on the oxidation of L-lysine by diperiodatonickelate(IV) in an aqueous alkaline medium

[DPN] = 6.0 × 10^{-5} ; [L-lysine] = 8.0 × 10^{-4} ; [OH^-] = 0.20; [IO_4^-] = 2.0 × 10^{-3} ; I = 0.60 / mol dm^{-3}

Temperature (K)	1/T × 10^3 (K^{-1})	k × 10^{-2} (dm^3 $mol^{-1}s^{-1}$)
293	3.4130	2.00
298	3.3557	2.86
303	3.3003	4.00
308	3.2468	5.56

(b) Activation parameters with respect to slow step of Scheme 1

Parameters	Values
E_a	48 ± 1 kJ mol^{-1}
$\Delta H^\#$	46 ± 2 kJ mol^{-1}
$\Delta S^\#$	- 120 ± 15 JK^{-1} mol^{-1}
$\Delta G^\#$	82 ± 5 kJ mol^{-1}
log A	7.0 ± 0.4



Scheme 1 — The detailed mechanism of oxidation of lysine by DPN

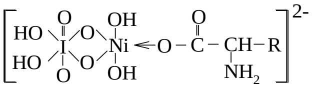
Periodic acid (H_5IO_6) exists in acid medium as $H_4IO^-_6$ and also at pH 7. Thus, under the alkaline conditions, the main species are expected to be $H_3IO_6^{2-}$ and $H_2IO_6^{3-}$. At higher concentrations, periodate also tends to dimerise. Hence, the soluble nickel(II) periodate complex exists as $[Ni(OH)_2(H_3IO_6)]^{2-}$ in aqueous alkaline medium, a conclusion also supported by earlier studies[1].

The reaction between diperiodatonickelate(IV) and L-lysine in alkaline medium has 2:1 stoichiometry of oxidant to reductant with first order dependence in diperiodatonickelate(IV) concentration and less than unit order each in L-lysine and alkali concentrations. Increase in the rate of reaction with increase in the alkali concentration and the decrease in the rate of reaction with increase in periodate concentration, suggests the equillbria of different nickel(IV) periodate complexes as given in Eqns (5) and (6) are possible.

$$[Ni(OH)_2(H_3IO_6)_2]^{2-} + OH^- \rightleftharpoons [Ni(OH)_2(H_3IO_6)(H_2IO_6)]^{3-} + H_2O \quad K_4 \quad (5)$$

$$[Ni(OH)_2(H_3IO_6)(H_2IO_6)]^{3-} \rightleftharpoons [Ni(OH)_2(H_2IO_6)_2]^{-} + H_3IO_6^{2-} \quad K_5 \quad (6)$$

Such types of eqillibria are also found in literature[12]. It may be expected that lower nickel(IV) periodate complex such as monoperiodatonickelate(IV) (MNP) is more important in the reaction than the diperiodatonickelate(IV) (DPN). The inverse fractional order in $[IO_4^-]$ might also be due to this reason. Therefore monoperiodatonickelate(IV) may be the main reactive form of the oxidant. Added acrylonitrile undergoes polymerization under inert atmosphere, indicating the formation of free radical in the reaction mixture. The fractional order in the substrate, L-lysine presumably results a complex formation between the oxidant and substrate, which then decomposes in a slow step to give the free radical derived from L-lysine and intermediate nickel(III) species. This free radical further reacts with nickel(III) species in a fast step to give intermediate aldehyde of L-lysine with nickel(II) product. Further this aldehyde reacts with another molecule of monoperiodatonickelate(IV) in a fast step to give products. The formation of nickel(III) intermediate species is in accordance with earlier study[1]. Indeed, it is to be noted that Michaelis-Menten plot, $1/k_{obs}$ versus 1/[L-lysine] shows a non zero intercept which indicates the complex formation. Such complex formation between substrate and oxidant has been reported in the literature[13]. These experimental results can be accommodated in terms of the Scheme 1. The probable structure of the complex is



From Scheme 1, including the observed orders in L-lysine, diperiodatonickelate(IV), alkali and periodate, leads to the rate law

$$\text{Rate} = \frac{k\,K_4K_5K_6[\text{Ni(IV)}][\text{OH}^-][\text{L}-\text{lysine}]}{[\text{H}_3\text{IO}_6^{2-}] + K_4[\text{H}_3\text{IO}_6^{2-}][\text{OH}^-] + K_4K_5[\text{OH}^-] + K_4K_5K_6[\text{OH}^-][\text{L}-\text{lysine}]} \quad (7)$$

The rate law (7) can be rearranged to (8), which is suitable for verification.

$$\frac{1}{k_{obs}} = \frac{[\text{H}_3\text{IO}_6^{2-}]}{k\,K_4K_5K_6[\text{OH}^-][\text{L}-\text{lysine}]} + \frac{[\text{H}_3\text{IO}_6^{2-}]}{k\,K_5K_6[\text{L}-\text{lysine}]} + \frac{1}{kK_6[\text{OH}^-]} + \frac{1}{k} \quad (8)$$

According to Eqn (8) other conditions being constant, the plots of $1/k_{obs}$ versus 1/[L-lysine], $1/k_{obs}$ versus $1/[OH^-]$ and $1/k_{obs}$ versus $[H_3IO_6^{2-}]$ should be linear and found to be so as in Fig. 3. From the slopes and intercepts of such plots, the values of K_4, K_5, K_6 and k are obtained as (1.55±0.06) $dm^3\ mol^{-1}$; (2.8±0.1) $\times 10^{-4}$ $moldm^{-3}$; (87.4±4.0)$\times$ 10^2 $dm^3\ mol^{-1}$ and (2.9 ± 0.1) $\times$ 10^{-2} sec^{-1}, respectively. The values of K_4 and K_5 are in good agreement with the literature values[1,10].

The effect of ionic strength is difficult to interpret in view of various ions involved in Scheme 1 and high ionic strength used in the experiment. The effect of solvent on the reaction kinetics has been described in the literature[14]. For the limiting case of a zero angle approach between two dipoles or an ion-dipole

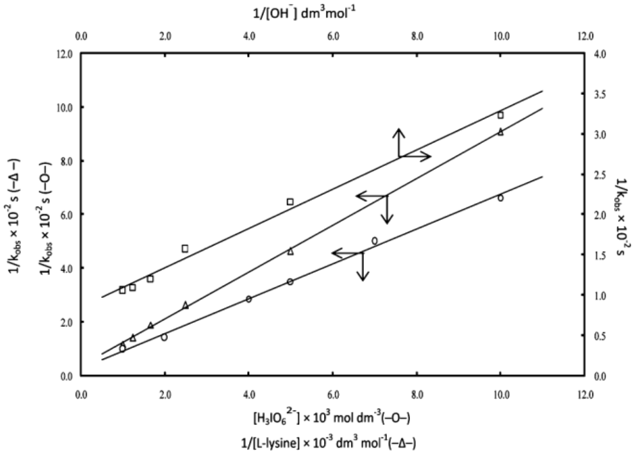


Fig. 3 — Verification of rate law (7) in the form of (8) for the oxidation of L-lysine by diperiodatonickelate(IV) in an aqueous alkaline medium at 25 °C.

system, Amis has shown that a plot of logk_{obs} versus 1/D gives a straight line with negative slope for a reaction between a negative ion and dipole or two dipoles and with positive slope for a positive ion and a dipole interaction. In the present study, the decrease in rate with decrease in the dielectric constant of the medium was observed, which is similar to Amis explanation. The mechanism is also supported by moderate values of thermodynamic activation parameters. High negative value of $\Delta S^{\#}$ suggests that the complex is more ordered than the reactants.

Conclusions

The basic amino acid, L-lysine can be converted into a neutral amino acid, 5-aminovaleric acid by diperiodatonickelate(IV) $[Ni(OH)_2(H_2IO_6)]^-$ in an alkaline medium. Among various species of Ni(IV) in alkaline medium, monoperiodatonickelate is considered as the active species for the title reaction.

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