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Mechanistic study of [RuCl₃(H₂O)₂OH]⁻ catalyzed oxidation of L-leucine by acidic N-bromophthalimide

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Abstract Kinetic studies in homogenous Ru(III) catalyzed oxidation of L-leucine (Leu), by N-bromophthalimide (NBP) in the presence of perchloric acid have been made at 303 K using mercuric acetate as Br⁻ ion scavenger. The reaction follows first-order kinetics with respect to [NBP]. In the lower concentration range of Leu and Ru(III) chloride, the reaction follows first-order kinetics but tends to zero at higher concentration. A positive effect of [Cl⁻] was observed in the oxidation of Leu. An increase in the rate of reaction with the decrease in dielectric constant of the medium was observed while negative effect was observed for [H⁺]. The rate of oxidation is unaffected by the change in [phthalimide (NHP)]. Rate of reaction decreased with increase in ionic strength of the medium. The main oxidation products of the reactions were identified as aldehyde, ammonia and CO₂ for the oxidation of Leu. From the effect of temperature (298-318 K) on the reaction rate, various activation parameters have been calculated and on the basis of these parameters, a suitable explanation for the reaction mechanism has been given.

Keywords Kinetics \cdot Oxidation \cdot L-Leucine \cdot Ru (III) chloride catalysis \cdot *N*-Bromophthalimide

Introduction

A new application of NBP for the oxidation of amino acid to aldehyde and nitrile was observed by Singh et al. [1-3].

Ajaya Kumar Singh ajayaksingh_au@yahoo.co.in The work on the oxidation and halogenations by N-halocompounds has received considerable attention; N-halocompounds, a group of mild oxidizing agents, have been extensively used for the catalyzed and uncatalyzed oxidation of variety of organic compounds [4–16]. Literature survey revealed that there is limited work done on NBP [17, 18]. Oxidation of amino acids is of great importance both from a chemical point of view and also on the mechanism of amino acids metabolism. Amino acids undergo much type of reactions depending on whether a particular amino acid contains a non-polar group or polar constituent and the oxidation products differ from different oxidants [19]. Leu is an essential amino acid. It helps with the regulation of blood sugar levels, the growth and repair of muscle tissue as well as growth hormone production. There is no work reported on the kinetics of oxidation of Leu by NBP so far, there are few reports available for the oxidation of Leu [20].

Formation of hazardous osmates restricts the use of osmium as homogeneous catalyst to the alkaline medium only while; ruthenium compounds get advantage as they can be used in acidic as well as in alkaline medium. Difference among the osmium, palladium and ruthenium is that osmium adds to the double bond while ruthenium and palladium compounds are reported to break the bond [21]. Different metal ion catalysts like chromium (III) [22], ruthenium (III) [23, 24], iridium (III) [25, 26], Pd (II) [27, 28] have been used in the oxidation by different oxidizing agents. Among the different metal ions, ruthenium (III) and iridium (III) are highly efficient. Transition metal ions have been extensively used [29] as catalysts for affecting a number of reactions. In recent times, studies on the use of transition metal ions either alone or as binary mixtures as catalysts in many redox reactions have been gaining interest. Their oxidizing and catalytic activities are due

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to the existence of variable oxidation states, as a consequence of partly filled d- or f-orbital. Their ability to form both σ and π bonds with other moieties or ligands is one of the most important factors for importing catalytic properties to transition metal ions as well as their complexes. Most of the d-block elements show characteristics of inter ligand migration reactions and such a process forms one of the most important types of reactions in homogeneous catalysis. In the modern chemical industry, the higher requirement on catalyst selectivity has been advanced. However, the studies of active center structure by means of physical method only cannot calculate reaction channel about complicated molecules. Reaction mechanism of various elementary reactions must be investigated to analyze the effect on selectivity [30]. Therefore, the basic study of catalytic reaction will prove the scientific basis for improving catalyst selectivity and making highly efficient catalyst. The mechanism of catalysis is quite complicated due to the formation of different intermediate complexes, free radicals and different oxidizing states of Ru (III) [31]. The utility of Ru (III) chloride as a nontoxic and homogenous catalyst has been reported [32, 33], but scant attention has been paid to explore the catalytic role of Ru (III) with N-halocompounds as oxidant. The present investigation describes the results of Ru (III) chloride catalyzed oxidation of Leu by NBP in perchloric acid medium and proposes a new mechanism based partially on experimental results. Objectives of the present study are: (i) to ascertain the reactive species of Ru(III) chloride as catalyst, Leu as substrate and NBP as an oxidant in acidic medium, (ii) to identify the oxidation products, (iii) to elucidate a plausible mechanism, and (iv) to deduce an appropriate rate law.

Experimental

Material

AR grade chemicals and double distilled water are used throughout the investigation. NBP (Lancaster, 98 %) was used as received; solution of NBP was prepared in 80 % acetic acid and stored in a black-coated flask to prevent

of RuCl₃ (S.D. fine chemicals) in HCl of known concentration. Mercury was added to ruthenium (III) chloride solution to reduce any ruthenium (IV) chloride formed during the preparation of ruthenium (III) chloride stock solution and was kept for a day. The ruthenium (III) chloride concentration was assayed by EDTA titration and stored in a black-coated bottle to prevent photochemical decomposition. Standard solution of sodium thiosulphate, KCl, NaClO₄ and phthalimide were prepared with double distilled water and mercuric acetate (Loba chem., Mumbai, India) was acidified with 20 % acetic acid. Perchloric acid (GR) was used as a source of H⁺ ions and acetonitrile as solvent.

Kinetic procedure

All the kinetic measurements were carried out in a black-coated vessel at constant temperature (303 K) and performed under pseudo-first-order condition with [Leu] \gg [NBP]. The reaction was initiated by the rapid addition of known amounts of oxidant to the reaction mixture containing the required amounts of Leu, perchloric acid, Ru(III) chloride, mercuric acetate, acetic acid, KCl, NaClO₄ and water in glass stoppered Pyrex boiling tubes, thermostated at the same temperature. Progress of reaction was monitored by iodometric determination of unconsumed [NBP] in known aliquots of the reaction mixtures at different time intervals. Each kinetic run was studied for ~75 % reaction. Runs were repeated twice and had <4 % standard deviation. The rate of reaction (-d[NBP]/dt) in each kinetic run was determined by the slope of tangent drawn at fixed [NBP].

Stoichiometry and product analysis

Varying different ratio of NBP to Leu were equilibrated at 303 K in presence of requisite amount of perchloric acid, mercuric acetate, acetic acid and KCl under the condition of [NBP] \gg [Leu], for 48 h. Determination of unconsumed NBP revealed that for the oxidation of each mole of Leu, one mole of NBP was required. Accordingly, the following stoichiometric equation could be formulated:

$$\operatorname{RCH} \left\langle \begin{array}{c} \operatorname{COOH} \\ \operatorname{NH}_2 \end{array} \right| (\operatorname{aq}) + \operatorname{C}_8\operatorname{H}_4\operatorname{NO}_2\operatorname{Br}(\operatorname{aq}) + \operatorname{H}_2\operatorname{O} \longrightarrow \operatorname{R-CHO}(\operatorname{aq}) + \operatorname{C}_8\operatorname{H}_5\operatorname{NO}_2(\operatorname{aq}) + \operatorname{HBr} \\ (\operatorname{aq}) + \operatorname{NH}_3 \not + \operatorname{CO}_2 \not + \operatorname{H}_2\operatorname{O}$$
(1)

photochemical deterioration. The prepared solution of NBP was standardized iodometrically. Stock solution of Leu was prepared by dissolving appropriate amount of sample in double distilled water. The ruthenium (III) chloride solution was prepared by dissolving a known weight

where,

$$R = -CH_2 - HC \begin{pmatrix} CH_3 \\ CH_3 \end{pmatrix}$$

I

The oxidation product was indentified as aldehyde and was confirmed by its infra red (IR) spectrum [34], carbonyl stretching was found at 1729 cm⁻¹ and a band at 2928 was found due to aldehydic –CH stretching, and CO₂ was identified by bubbling N₂ gas through the reaction mixture and passing liberated gas through a U-shaped tube containing a saturated Ba(OH)₂ solution. Formation of BaCO₃ indicated the liberation of CO₂ in the oxidation of Leu by NBP and was later confirmed by GC–MS techniques. It was also observed that there was no further oxidation of this product under the present kinetic investigation.

Kinetic measurements and results

Kinetics

Initially, the kinetics of the oxidation of Leu by NBP in the presence of Ru(III) chloride under all acidic conditions were studied at several initial concentrations of all the reactants at 30° C. For the variation of [NBP], the reaction rate was calculated by the slope of tangent drawn at fixed time. In the variation of concentration of other reactants, tangents were drawn at constant [NBP] ([NBP]*) (Fig. 1). The pseudo-first-order rate constant k_1 was calculated as:



Fig. 1 Plot between unconsumed [NBP] versus Time at T = 303 K. [Leu] = 2.00×10^{-3} mol dm⁻³, [H⁺] = 0.50 mol dm⁻³, I = 1.00 [Ru (III)] = 4.84×10^{-5} mol dm⁻³, [KCl] = 1.00×10^{-4} mol dm⁻³, [Hg (OAc)₂] = 3.00×10^{-4} mol dm⁻³ and CH₃COOH = 20 %

concentration and tends to zero-order at high concentration range. This result was further confirmed by the plot of -dc/dt versus [Ru(III)] (Fig. 3; Table 1). The reaction rate decreased with increasing [HClO₄]. This may be related to protonation equilibrium of Leu, which has two forms in the acidic region of the study (Eq. 4).

$$k_1 = \frac{\text{rate}}{[\text{NBP}]^*} \tag{2}$$

The order of reaction in each reactant was determined using log–log plot of rate versus concentration of reactant. Considering NBP, Leu, H^+ , Ru(III) chloride as the main reactants, the general form of the rate equation for the oxidation of Leu by NBP can be written as:

rate =
$$k_1 [\text{NBP}]^{\alpha} [\text{Leu}]^{\beta} [\text{Ru}(\text{III})]^{\gamma} [\text{H}^+]^{\delta}$$
 (3)

Uniform pseudo-first-order rate constant (k_1) values for the variation of [NBP] clearly indicate that the order with respect to [NBP] is unity. This is also obvious from the plot of (-dc/dt) versus [NBP] (Fig. 2; Table 1). The reactions have been studied for Leu from 0.5×10^{-3} to 5×10^{-3} mol dm⁻³ at fixed concentration of all reactants at constant temperature. The rate of reaction calculated at different [Leu] was showing fractional order kinetics with respect to [Leu] (Fig. 2; Table 1). The reaction follows first-order kinetics with respect to [Ru(III)] chloride at a low range of The equilibrium of Eq. (4) suggests that the positive species of Leu increases with increase in the proton concentration while the neutral species of Leu decreases. If positive species of Leu was involved in the reaction, the rate was expected to increase with increase in $[H^+]$. This is contrast to the results shown in Fig. 3 and given in Table 1. Hence, the neutral species of Leu is possibly involved in the oxidation by NBP.

The variation of [Cl⁻] had a positive effect on the reaction rate (Fig. 4; Table 2). The rate of reaction increases with decrease in dielectric constant (*D*) of the medium (Fig. 5; Table 2). The effect of ionic strength (*I*) of the medium on the rate was studied using NaClO₄ solution keeping the other experimental conditions constant. A negative effect of ionic strength of the medium was observed for Ru(III) catalyzed reaction (Fig. 6; Table 2). Mercuric acetate and [NHP] did not affect the reaction rate (Table 3). The effect of temperature on the reaction rate was determined by keeping constant concentration of other constituents of the solution (Table 4; Fig. 7). The values of different activation parameters such as activation energy, E_a ,



Fig. 2 Plot between rate of reaction (-dc/dt) versus [NBP] and [Leu] at T = 303 K. [H⁺] = 0.50 mol dm⁻³, [Ru(III)] = 4.84×10^{-5} mol dm⁻³, [KCI] = 1.00×10^{-4} mol dm⁻³, I = 1.00, [Hg(OAc)₂] = 3.00×10^{-4} mol dm⁻³ and CH₃COOH = 20 %

enthalpy of activation, $(\Delta H^{\#})$, and entropy of activation $(\Delta S^{\#})$ were determined from the temperature effect on rates.

Test for free radicals

To test the presence of free radicals in the reaction, the reaction mixture containing NBP, Leu, Ru(III) chloride, KCl, NaClO₄, Hg(OAc)₂, acetic acid and perchloric acid with acryl amide was placed in an inert atmosphere for 24 h. When the reaction mixture was diluted with methanol, it was found that there was no precipitate in the reaction mixture. This clearly showed free radicals were not formed in the redox reaction under investigation.

Discussion

Reactive species of NBP

Similar to N-halo imides, free NBP, protonated NBP (NBPH⁺), Br⁺, HOBr, and $(H_2OBr)^+$ species of NBP may exist in the acidic medium through the following equilibria [35–37] (Eqs. 5–8).

$$NBP + H_2O \rightleftharpoons HOBr + NHP$$
(5)

 $NBP + H^+ \rightleftharpoons NHP + Br^+ \tag{6}$

 $NBP + H^+ \rightleftharpoons (NPPH)^+ \tag{7}$

$$HOBr + H^+ \rightleftharpoons (H_2OBr)^+ \tag{8}$$

In consideration of $(H_2OBr)^+$ as the reactive species of the oxidation of Leu by NBP, the rate law obtained had a first-order proportionality with respect to the proton concentration. This is contrary to observed inverse proton dependence in rates, hence involvement of the $(H_2OBr)^+$ as the reactive species was ruled out. Similar argument could also be made for non-participation of Br⁺ as the reactive species. If HOBr was the reactive species, there would have been effect of [NHP] on the rates of the oxidation of Leu by NBP; suggested by Eq. 5. Since this was not the case in our experiments (see Table 3), the possibility of the HOBr as the reactive species was also ruled out. Based on elimination of species other than NBP, it was to assume that the NBP is the only reactive species.

Reactive species of Ru(III) chloride

A study for the chloro-complexes of Ru(III) in 0.1 M KCl at pH 0.4–2.0 at 25 °C reported four major species, i.e. $[RuCl_4(H_2O)_2]^-$, $[RuCl_3(H_2O)_3]$, $[RuCl_2(H_2O)_4]^+$ and $[RuCl(H_2O)_5]^{2+}$ [37]. Except $[RuCl_2(H_2O)_4]^+$, the stability of the species decreased with increase in pH with high instability at pH 2.0. The $[RuCl_2(H_2O)_4]^+$ species was quite stable at pH 2.0, which goes through the equilibrium with its hydrolyzed form, $[RuCl_2(H_2O)_3OH]$ (C₁) [38]

$$\left[\operatorname{RuCl}_{2}(\operatorname{H}_{2}\operatorname{O})_{4}\right]^{+} + \operatorname{H}_{2}\operatorname{O} \rightleftharpoons \left[\operatorname{RuCl}_{2}(\operatorname{H}_{2}\operatorname{O})_{3}\operatorname{OH}\right] + \operatorname{H}_{3}\operatorname{O}^{+}$$
(9)

 Table 1
 Effect of variation of [NBP], [Leu], [Ru(III)], and [H⁺] on the rate of oxidation of Leu at 303 K

$\frac{[\text{NBP}] \times 10^4}{\text{mol dm}^{-3}}$	$[\text{Leu}] \times 10^3 \\ \text{mol } \text{dm}^{-3}$	$[\mathrm{Ru(III)}] \times 10^5$ mol dm ⁻³	$[\mathrm{H^+}] \mathrm{mol} \mathrm{dm}^{-3}$	Rate $\times 10^8$ mol dm ⁻³ s ⁻¹	$k_1 \times 10^4 \mathrm{s}^{-1} \mathrm{(obs)}$	$k_1 \times 10^4 \mathrm{s}^{-1} \mathrm{(cal)}$
0.50	2.00	4.84	0.50	2.81 ± 0.42	6.12	_
1.00	2.00	4.84	0.50	5.63 ± 0.18	6.19	_
1.50	2.00	4.84	0.50	7.42 ± 0.25	6.14	_
2.00	2.00	4.84	0.50	11.11 ± 0.20	6.07	_
3.00	2.00	4.84	0.50	16.79 ± 0.18	6.15	_
2.00	0.50	4.84	0.50	3.24 ± 0.11	1.80	1.65
2.00	1.00	4.84	0.50	6.61 ± 0.09	3.67	3.26
2.00	1.50	4.84	0.50	9.24 ± 0.13	5.13	4.72
2.00	2.00	4.84	0.50	11.10 ± 0.04	6.12	5.57
2.00	3.00	4.84	0.50	17.29 ± 0.37	9.61	8.72
2.00	4.00	4.84	0.50	18.90 ± 0.31	10.50	10.90
2.00	5.00	4.84	0.50	19.21 ± 0.21	10.67	12.14
2.00	2.00	0.60	0.50	1.31 ± 0.15	0.72	0.85
2.00	2.00	1.21	0.50	2.67 ± 0.05	1.48	1.52
2.00	2.00	2.42	0.50	5.23 ± 0.07	2.90	3.50
2.00	2.00	3.63	0.50	7.82 ± 0.16	4.34	4.72
2.00	2.00	4.84	0.50	11.14 ± 0.11	6. 19	5.57
2.00	2.00	9.67	0.50	20.14 ± 0.14	11.18	10.87
2.00	2.00	12.00	0.50	22.65 ± 0.25	12.58	12.81
2.00	2.00	4.84	0.10	31.21 ± 0.24	17.33	18.70
2.00	2.00	4.84	0.20	23.24 ± 0.20	12.91	11.75
2.00	2.00	4.84	0.30	17.82 ± 0.21	9.90	8.59
2.00	2.00	4.84	0.50	11.37 ± 0.30	6.32	5.57
2.00	2.00	4.84	0.80	7.76 ± 0.16	4.32	3.91
2.00	2.00	4.84	1.00	6.67 ± 0.14	3.71	3.65

Solution conditions: $[Hg(OAc)_2] = 3.00 \times 10^{-4} \text{ mol dm}^{-3}$, $[KCI] = 1.00 \times 10^{-4} \text{ mol dm}^{-3}$, $CH_3COOH = 20\%$ and I = 1.00



Fig. 3 Plot between rate of reaction (-dc/dt) versus [H⁺] and [Ru(III)] at T = 303 K. [NBP] = 2×10^{-4} mol dm⁻³ [Leu] = 2.00×10^{-3} mol dm⁻³, [KCI] = 1.00×10^{-4} mol dm⁻³, I = 1.00, [Hg(OAc)₂] = 3.00×10^{-4} mol dm⁻³ and CH₃COOH = 20 %



Fig. 4 Plot between rate of reaction (-dc/dt) versus [KCl] at T = 303 K [NBP] $= 2 \times 10^{-4}$ mol dm⁻³ [Leu] $= 2.00 \times 10^{-3}$ mol dm⁻³, [H⁺] = 0.50 mol dm⁻³, [Ru(III)] $= 4.84 \times 10^{-5}$ mol dm⁻³, I = 1.00, [Hg(OAc)₂] $= 3.00 \times 10^{-4}$ mol dm⁻³ and CH₃COOH = 20 %

$\rm [KCl] \times 10^4 \ mol \ dm^{-3}$	NaClO ₄ (I)	Acetonitrile (% by volume)	Rate $\times 10^8$ mol dm ⁻³ s ⁻¹	$k_1 \times 10^4 \mathrm{s}^{-1}$ (obs)	$k_1 \times 10^4 \mathrm{s}^{-1} \mathrm{(cal)}$
1.00	1.00	_	11.08 ± 0.16	6.16	6.95
2.00	1.00	-	23.40 ± 0.12	13.00	12.39
3.00	1.00	-	29.52 ± 0.19	16.44	16.97
4.00	1.00	_	35.10 ± 0.11	19.50	20.33
6.00	1.00	_	43.56 ± 0.25	24.22	25.84
8.00	1.00	_	56.50 ± 0.31	31.39	30.17
10.00	1.00	_	59.94 ± 0.29	33.30	33.27
1.00	0.80	_	12.79 ± 0.20	7.11	_
1.00	1.00	_	11.01 ± 0.34	6.12	_
1.00	1.50	_	8.10 ± 0.31	4.50	_
1.00	1.80	-	6.30 ± 0.21	3.50	_
1.00	2.80	-	1.89 ± 0.10	1.05	_
1.00	1.00	5	11.09 ± 0.19	6.16	_
1.00	1.00	10	13.55 ± 0.10	7.53	_
1.00	1.00	15	15.19 ± 0.23	8.43	_
1.00	1.00	20	16.88 ± 0.41	9.38	_
1.00	1.00	25	20.95 ± 016	11.64	_
1.00	1.00	30	25.61 ± 0.20	14.23	-

Table 2 Effect of ionic strength (I) by using NaClO₄, chloride ion and solvent on the rate of oxidation of Leu at 303 K

Solution conditions: [NBP] = 2.00×10^{-4} mol dm⁻³, [Leu] = 2.00×10^{-3} mol dm⁻³, [Ru(III)] = 4.84×10^{-5} mol dm⁻³, [H⁺] = 0.50 mol dm⁻³ [Hg(OAc)₂] = 3.00×10^{-4} mol dm⁻³ and CH₃COOH = 20 %



Fig. 5 Plot between rate of reaction log k_1 versus 1/D at T = 303 K. [NBP] = 2 × 10⁻⁴ mol dm⁻³ [Leu] = 2.00 × 10⁻³ mol dm⁻³, [H⁺] = 0.50 mol dm⁻³, [Ru(III)] = 4.84 × 10⁻⁵ mol dm⁻³ [KCl] = 1.00 × 10⁻⁴ mol dm⁻³, I = 1.00 and [Hg(OAc)₂] = 3.00 × 10⁻⁴ mol dm⁻³

With increase in concentration of Cl^- ion in our experiments, the hydrolysed form may form $[RuCl_3(H_2O)_2OH]^-$ (C₂) through equilibrium with Cl^- ion (Eq. 10).

$$\left[\operatorname{RuCl}_{2}(\operatorname{H}_{2}\operatorname{O})_{3}\operatorname{OH}\right] + \operatorname{Cl}^{-} \rightleftharpoons \left[\operatorname{RuCl}_{3}(\operatorname{H}_{2}\operatorname{O})_{2}\operatorname{OH}\right]^{-} + \operatorname{H}_{2}\operatorname{O}$$
(10)

The $[RuCl_3(H_2O)_2OH]^-$ may be the most likely reactive species in the reaction of Leu with NBP, catalyzed by



Fig. 6 Plot between rate of reaction log k_1 versus $I^{1/2}$ at T = 303 K. [NBP] = 2 × 10⁻⁴ mol dm⁻³ [Leu] = 2.00 × 10⁻³ mol dm⁻³, [H⁺] = 0.50 mol dm⁻³, [Ru(III)] = 4.84 × 10⁻⁵ mol dm⁻³, [KCI] = 1.00 × 10⁻⁴ mol dm⁻³, [Hg(OAc)₂] = 3.00 × 10⁻⁴ mol dm ⁻³ and CH₃COOH = 20 %

Ru(III) chloride species because of positive increase in rate with increase in [Cl⁻] in acidic medium.

Reaction scheme

The observed stoichiometry and effect of various parameters on the kinetics of the oxidation of Leu by NBP allowed us to propose a reaction scheme 1. In this scheme, the

$[\text{NHP}] \times 10^4 \text{ mol } \text{dm}^{-3}$	$[\mathrm{Hg(OAc)}_2] \times 10^4 \mathrm{mol} \mathrm{dm}^{-3}$	Rate $\times 10^8$ mol dm ⁻³ s ⁻¹	$k_1 \times 10^4 \mathrm{s}^{-1} \mathrm{(obs)}$
1.00	_	11.45 ± 0.19	6.19
3.00	_	11.56 ± 0.27	6.25
5.00	_	11.28 ± 0.14	6.10
7.00	_	12.26 ± 0.15	6.63
9.00	_	11.96 ± 0.14	6.47
10.00	_	10.80 ± 0.28	6.00
-	3.00	11.56 ± 0.37	6.25
-	6.00	11.56 ± 0.27	6.25
-	9.00	11.84 ± 0.25	6.58
-	12.00	11.02 ± 0.21	5.96
-	18.00	11.82 ± 0.11	6.39
-	30.00	12.32 ± 0.19	6.66

Table 3 Effect of [NHP] and [Hg(OAc)₂ on the rate of oxidation of Leu at 303 K

Solution conditions: [NBP] = 2.00×10^{-4} mol dm⁻³, [Leu] = 2.00×10^{-3} mol dm⁻³, [Ru(III)] = 4.84×10^{-5} mol dm⁻³, [H⁺] = 0.50 mol dm⁻³, CH₃COOH = 20 % and I = 1.00

 Table 4
 Effect of temperature and corresponding activation parameter on the rate of oxidation of Leu

Temperature K	$k_1 \times 10^4 \mathrm{s}^{-1} \mathrm{(obs)}$
298	3.32 ± 0.21
303	6.19 ± 0.26
308	7.70 ± 0.15
313	15.48 ± 0.19
318	19.04 ± 0.12
Ea (kJ mol ^{-1)}	51.69
$\Delta H^{\#}$ (kJ mol ⁻¹)	49.17 ± 0.048
$\Delta S^{\#}$ (JK mol ⁻¹)	121.21 ± 1.24
$\Delta G^{\#}$ (kJ mol ⁻¹)	12.42 ± 0.28
log A	11.35 ± 0.36
log k _r	2.44

Solution conditions: [NBP] = 2.00×10^{-4} mol dm⁻³, [Leu] = 2.00×10^{-3} mol dm⁻³

 $[Ru(III)] = 4.84 \times 10^{-5} \text{ mol dm}^{-3}, [H^+] = 0.50 \text{ mol dm}^{-3}$

 $[\text{KCI}] = 1.00 \times 10^{-4} \, \text{mol dm}^{-3}, \, [\text{Hg}(\text{OAc})_2] = 3.00 \times 10^{-4} \, \text{mol d} \, \text{m}^{-3}$

 $CH_3COOH = 20 \%$ and I = 1.00

species C_2 is formed from the reaction of C_1 with chloride ion and species C_1 and C_2 are in equilibrium having a constant K_1 (Eq. 11). The species C_2 reacts with S (Leu) to give species C_3 having an equilibrium constant K_2 (Eq. 12). In step (12), the formation of species, C_3 occurs with the liberation of H_3O^+ . The positive entropy of activation in the oxidation of Leu by NBP supports such a step. Then species C_3 reacts with NBP to give species C_4 having an equilibrium constant K_3 (Eq. 13). The species C_4 slowly decomposes to give species C_5 , phthalimide (NHP) (Eq. 14). The species C_5 gives back the original species, C_1 and C_6 with release of the chloride ion (Eq. 15). The species C_5 is unstable and rapidly decomposes to Leu oxidized product (C_6) (Eq. 15). The species C_6 forms aldemine (RCH=NH), CO₂ and HBr and in Eq. (17), aldemine further hydrolysed to form final product aldehyde, CO₂ and other products of the reaction by a fast step (Eq. 16). From Eqs. (11)-(17), it is concluded that one molecules of NBP is consumed for per molecule of Leu. This is consistent with the observed stoichiometry of the oxidation of Leu by NBP. Furthermore, the proposed reaction scheme is also supported by the moderate values of energy of activation and other thermodynamic parameters. The fairly high positive values of the free energy of activation and enthalpy of activation suggest that the transition state is highly solvated. The order of frequency factor (A) and values of free energy of activation ($\Delta G^{\#}$) for the redox system also supports the reaction Scheme 1.

Considering the reactive species of catalyst, oxidant and with the help of above experimental findings, the probable reaction mechanism is proposed (Scheme 1) and considering the fact that 1 mole of Leu is oxidised by one of NBP.

Since Eq. (14) is a slow process in the proposed Scheme 1, hence rate can be written as

$$rate = k[C_4] \tag{18}$$

On the basis of steps (i) to (vii), Eqs. (2)–(5) can be obtained in the following forms, respectively:

$$[\mathbf{C}_2] = K_1[\mathbf{C}_1][\mathbf{C}\mathbf{I}^-] \tag{19}$$

$$[C_3] = \frac{K_2[C_2][S]}{[H^+]}$$
(20)

$$[C_4] = K_3[C_3][NBP]$$
(21)

$$= K_2 K_3 \frac{[\text{NBP}][\text{C}_2][\text{S}]}{[\text{H}^+]}$$
(22)

$$=\frac{K_1K_2K_3[C_1][Cl^-][NBP][S]}{[H^+]}$$
(23)

Substitution of Eq. (23) into Eq. (17) gives

rate =
$$\frac{2kK_1K_2K_3[C_1][Cl^-][NBP][S]}{[H^+]}$$
 (24)

At any time of the reaction, the total concentration of NBP, i.e. $[NBP]_T$ can be shown as:



Fig. 7 Plot between rate of reaction log k_1 versus 1/T. [NBP] = 2 × 10⁻⁴ mol dm⁻³ [Leu] = 2.00 × 10⁻³ mol dm⁻³, [H⁺] = 0.50 mol dm⁻³, [Ru(III)] = 4.84 × 10⁻⁵ mol dm⁻³ [KCI] = 1.00 × 10⁻⁴ mol dm⁻³, I = 1.00, [Hg(OAc)₂] = 3.00 × 10⁻⁴ ⁴ mol dm⁻³ and CH₃COOH = 20 %

 $[NBP]_{T} = [NBP]_{f} + [C_4]$ (25)

On substituting the value of $[C_4]$ in Eq. (25) we get Eq. (26)

$$[NBP] = \frac{[NBP]_{T}[H^{+}]}{[H^{+}] + K_{1}K_{2}K_{3}[C_{1}][Cl^{-}][S]}$$
(26)

But

$$[C_1] = [Ru(III)]$$

$$rate = \frac{2kK_1K_2K_3[Ru(III)][Cl^-][Leu][NBP]_T}{[H^+] + K_1K_2K_3[Ru(III)][Cl^-][Leu]}$$
(27)

The rate expression obtained in Eq. (28) can be re-written as:

$$\frac{[\text{NBP}]_{\text{T}}}{\text{rate}} = \frac{[\text{H}^+]}{2kK_1K_2K_3[\text{Ru}(\text{III})][\text{Cl}^-][\text{Leu}]} + \frac{1}{2k}$$
(28)

Equation (28), indicates that if a plot is made between $[NBP]_T]$ /rate and 1/[Leu] or $[H^+]$ or 1/[KCl], a straight line with positive intercept on *y*-axis will be obtained. Straight line with positive intercepts on *y*-axis obtained by the plots of $[NBP]_T$ /rate versus 1/[Leu], $[H^+]$, 1/[KCl] (Fig. 8) on one hand proves the validity of the rate law (26) and on the other hand, the proposed reaction scheme, on the basis of which the rate law (26) has been derived. The value of *k* and $K_1 K_2 K_3$ calculated from the slope and intercept of the plot were $2.84 \times 10^{-3} \text{ s}^{-1}$ and $7.72 \times 10^9 \text{ mol dm}^{-3}$, respectively. Utilizing these value of constants, the reaction rates were

Fig. 8 Plot between [NBP]_T/ rate versus [H⁺] and 1/[Leu] and 1/[KCI] at 303 K [Ru(I II]] = 4.84×10^{-5} mol dm $^{-3}$, I = 1.00, [Hg(OAc)₂] = 3.00×10^{-4} mol dm⁻³ and CH₃COOH = 20 %



$[\text{Leu}] \times 10^4 \text{ mol } \text{dm}^{-3}$	$[NBP] \times 10^4 \text{ mol } \text{dm}^{-3} \text{ initial}$	$[NBP] \times 10^4 \text{ mol dm}^{-3} \text{ final}$	$[NBP] \times 10^4 \text{ mol dm}^{-3} \text{ consumed}$	[NBP]:[Leu]
2.00	20.00	14.78	5.22	1:2.61
4.00	40.00	29.64	10.36	1:2.59
6.00	60.00	44.34	15.66	1:2.61

Table 5 Consumption of NBP in the oxidation of Leu with NBP at 303 K

Solution conditions: $[Ru(III)] = 4.84 \times 10^{-5} \text{ mol dm}^{-3}$, $[H^+] = 0.50 \text{ mol dm}^{-3}$, $[KCI] = 1.00 \times 10^{-4} \text{ mol dm}^{-3}$, $[Hg(OAc)_2] = 3.00 \times 10^{-4} \text{$

Table 6 Activation parameters for amino acids in the presence of Ru(III) chloride (for isokinetic temperature)

Amino acid + catalyst	$k_1 \times 10^4 ({ m s}^{-1})$ at 303 K	$k_2 \times 10^4 ({ m s}^{-1})$ at 308 K	$\Delta H^{\#} (\text{kJ mol}^{-1})$	$\Delta S^{\#}$ (JK mol ⁻¹)	$\Delta G^{\#} (\text{kJ mol}^{-1})$	References
Gly	6.00	8.78	52.40	130.00	12.14	[31]
Ala	1.15	1.82	95.13	247.94	20.04	[32]
Val	1.62	2.80	57.32	126.32	19.10	[3]
Leu	6.19	7.70	49.17	121.21	12.42	Present work

calculated for the variations of [Leu], [Ru(III)], $[H^+]$ and [KCl] and are presented in the Tables 1 and 2 along with calculated rates. Almost the same values of two rates, i.e. the calculated and observed, further proves the validity of the rate law (26) and hence the proposed reaction scheme.

Effect of ionic strength

The ionic strength (I) effect on the reaction rate has been described according to the theory of Bronsted and Bjerrum [39], which postulates the reaction through the formation of an activated complex. According to this theory, the effect of ionic strength on the rate for a reaction involving two ions is given by the relationship:

$$\log k_1 = \log k_0 + 1.02 Z_A Z_B I^{1/2} \tag{29}$$

Here, $Z_A Z_B$ are the valency of the ions A and B, and k_1 and k_0 are the rate constant in the presence and absence of the added electrolyte, respectively. A plot of log k_1 against $I^{1/2}$ should be linear with a slope of $1.02 Z_A Z_B$. If $Z_A Z_B$ have similar signs, the quantity $Z_A Z_B$ should be positive and the rate increases with the ionic strength, having a positive slope, while if the ions have dissimilar charges, the quantity $Z_A Z_B$ should be negative and the rate would decrease with increase in ionic strength, having a negative slope. In the present case, a negative effect was observed with respect to the ionic strength of the medium, supporting the involvement of ionic species in the rate-determining step.

Effect of dielectric constant and calculation of the size of an activated complex (d_{AB})

The change in dielectric constant (D) of the medium has been made by addition of acetonitrile to the reaction

mixture. It was found that the rate of reaction increased with increase in % of solvent. To calculate the size of the activated complex (d_{AB}) and also to study the effect of *D* on the rate of oxidation, the percentage concentration of acetonitrile has been varied from 5 to 30 % at constant concentration of all other reactant and at a constant temperature of 303 K. For each set, pseudo first order rate constant (k_1) is calculated and found that there is an increase in rate constant with decrease in *D*. The effect of *D* of the medium on the rate constant of a reaction between two ions has been described by the well known equation given below:

$$\log k_{1} = \log k_{0} - \frac{Z_{A} Z_{B} e^{2} N}{2.303 (4\pi\varepsilon_{0}) d_{AB} R T} \frac{1}{D}$$
(30)

where, k_0 is the rate constant in a medium of infinite dielectric constant, Z_A and Z_B are the charges of reacting ion, d_{AB} refers to the size of activated complex, T is absolute temperature and D is dielectric constant of the medium. This equation shows that if a plot is made between $\log k_1$ versus 1/D, straight line having slope equal to $Z_A Z_B e^2 N/2.303($ 4π Co) $d_{AB}RT$ will be obtained. From the slopes of straight line, the value of d_{AB} have been calculated and found 1.39Å for Leu. It is necessary to verify whether acetonitrile is oxidized by NBP under our experimental condition or not? To ascertain the real role of acetonitrile, few experiments were performed by taking acetonitrile as organic substrate in place of Leu under our experimental condition and it has been found that the acetonitrile is not oxidized by NBP. Thus, the observed rate of reaction with the addition of acetonitrile in reaction mixture is only due to the change in the D (Table 5).

The activation parameters for the oxidation of different amino acids with Ru (III) chloride catalyst by NBP are summarized in Table 6. The entropy of activation for the title reaction changed within the observed range. Variation in the rate within a reaction series may be caused by changes in the enthalpy and entropy of activation. Changes in the rate are caused by change in both $\Delta H^{\#}$ and $\Delta S^{\#}$, but these quantities vary extensively in a parallel fashion. A plot of $\Delta H^{\#}$ versus $\Delta S^{\#}$ is linear according to equation:

$$\Delta H \# = \beta \times \Delta S^{\#} + \text{constant.}$$
(31)

 β is called isokinetic temperature. We have calculated the isokinetic temperature by plotting graph $\Delta H^{\#}$ versus $\Delta S^{\#}$ (Fig. 9). The value of isokinetic temperature (β) is 348.22 K. It has been asserted that apparently linear



Fig. 9 Plot between $\Delta S^{\#}$ versus $\Delta H^{\#}$

Reaction scheme (I)

 $\begin{bmatrix} \operatorname{RuCl}_2(\operatorname{H}_2\operatorname{O})_3\operatorname{OH} \end{bmatrix} + \operatorname{Cl}^{-} \qquad \underbrace{K_1}_{C_1} \begin{bmatrix} \operatorname{RuCl}_3(\operatorname{H}_2\operatorname{O})_2\operatorname{OH} \end{bmatrix}^{-} + \operatorname{H}_2\operatorname{O}_{C_1} \\ C_1 \\ C_2 \\ C_3 \\ C_4 \\ C_4 \\ C_4 \\ C_4 \\ C_5 \\$ (11) $[\operatorname{RuCl}_{3}(\operatorname{H}_{2}\operatorname{O})_{2}\operatorname{OH}]^{-} + \operatorname{H}_{3}^{+} - \operatorname{CH}_{CH}^{-} \operatorname{COO}^{-} \underbrace{K_{2}}_{R} [\operatorname{RuCl}_{3}(\operatorname{H}_{2}\operatorname{O})(\operatorname{OH})\operatorname{NH}_{2}\text{-}\operatorname{CH}_{2}\operatorname{COO}]^{2-} + \operatorname{H}_{3}\operatorname{O}^{+}_{R}$ (12) C_3 S C_2 Where $R = \begin{array}{c} CH_3 \\ CH_3 \end{array} HC - H_2C$ $\frac{\operatorname{RuCl_{3}(H_{2}O)(OH)NH_{2}\text{-}CH\text{-}COO]^{2-}}_{R} + \operatorname{NBP} \xleftarrow{K_{3}}_{R} [\operatorname{RuCl_{3}(NBP)(OH)NH_{2}\text{-}CH\text{-}COO]^{2-}}_{R} + \operatorname{H_{2}O}_{R}$ (13) C_3 $\operatorname{RuCl_{3}(NBP)(OH)NH_{2}-CH-COO}^{2-} \xrightarrow{k}_{H_{2}O} [\operatorname{RuCl_{3}(OBr)(H_{2}O)NH_{2}-CH-COO}]^{2-} + \operatorname{NHP}_{R}$ (14) C_4 $[\operatorname{RuCl}_{3}(\operatorname{OBr})(\operatorname{H}_{2}\operatorname{O})\operatorname{NH}_{2}\text{-}\operatorname{CH}\text{-}\operatorname{COO}] \xrightarrow{2^{-}} \operatorname{Fast}}_{\operatorname{R}} \qquad [\operatorname{RuCl}_{3}(\operatorname{H}_{2}\operatorname{O})_{2}\operatorname{OH}]^{-} + \begin{array}{c} \stackrel{+}{\operatorname{NH}}_{2} - \operatorname{CH}\text{-}\operatorname{COO}^{-} \\ \stackrel{+}{\operatorname{H}}_{3}\operatorname{O}^{+} \\ \stackrel{+}{\operatorname{Br}} \operatorname{R} \\ \operatorname{Br} \\ \operatorname{R} \end{array}$ (15) C_5 Fast R-CH=NH + CO₂ + HBr (16)Br Ŕ C_6 Fast R-CH=NH RCHO + NH₃ (17)H₂O

aldehyde

Scheme 1 Reaction path for the oxidation of Leu by NBP in the presence of Ru(III) chloride

correlation of $\Delta H^{\#}$ with $\Delta S^{\#}$ is sometimes misleading and the evaluation of β by means of the above equation lacks statistical validity. *Exner* advocates an alternative method for the treatment of experimental data [40], he proposed that β can be evaluated from the equation:

$$\beta = T_1 T_2 (b-1) / T_2 b - T_1.$$
(32)

A plot of log k_2 at 303 K versus log k_1 at 308 K gave isokinetic temperature as 348.22 K. Higher values of β (348.22 K) than the experimental temperature (303 K) indicates that the rate is governed by the enthalpy of activation [41].

Comparative study

The title reaction exhibited first-order dependence on NBP for all amino acid and followed zero-order kinetics for glycine (Gly), alanine (Ala), valine (Val) while, leucine (Leu) showed fractional order dependence on the rate of reaction. The Ru(III) chloride showed a catalytic effect on the reaction and followed first-order kinetics with respect to [Ru (III)] at a low concentration range in each case, and negative effect of perchloric acid were observe for the oxidation of Gly, Ala, Val and Leu. Addition of KCl positively influenced the rate of oxidation of Gly, Ala, Val and Leu, while effect of added electrolyte (ionic strength) for the oxidation of Gly, Val, Ala, show negligible effect, whereas negative effect was observed for the oxidation of Leu. D had no significant effect on the rate for the oxidation of Gly, Ala, Val, while the rate of oxidation of leu increases with decrease in dielectric constant of the medium. Addition of reduced product of oxidant, i.e. NHP, had no significant effect on oxidation velocity of Gly, Ala, Leu, but in case of Val it showed negative effect [3, 36, 37].

Conclusions

Oxidation of Leu by NBP in perchloric acid medium was found to be very sluggish, but oxidation became facile in the presence of Ru (III) chloride catalyst. NBP without proton attached and RCH(NH₃⁺)COO⁻ were the reactive species of oxidant and Leu, respectively. Among the various species of Ru(III) chloride in an acidic medium, [RuCl₃(H₂O)₂OH]⁻ was determined to be the catalyzed species. In the proposed reaction scheme, the equilibrium of [RuCl₃(H₂O)₂OH]⁻ and Leu gave C₃, which on reaction with NBP give C₄, which on further reaction gives C₅ through a slow rate-determining step. The species formed was responsible for oxidation of Leu. In the Scheme 1, each molecule of Leu consumed more than two moles of NBP to give aldehyde, NHP, CO_2 , and Br⁻, in agreement with the experimental observed stoichiometry. The deduced rate law from the reaction scheme was also consistent with kinetics of the reaction. Future studies on the Ru(III) chloride catalyzed oxidation of other biological relevant amino acids and peptides by NBP would also be of interest.

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