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***Research Article***

# Oxidative deamination and decorboxylation of leucine by 1-chlorobenzimidazole in acid medium - A kinetic approach

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## Abstract

The oxidation of leucine (amino acid) by 1-chlorobenzimidazole (CBI) has been studied in 80% (v/v) acetic acid – water medium. The reactions were followed potentiometrically up to 70% completion, by following the potentials of the reaction mixture containing varying concentrations of [CBI]/[BI] couple (BI=benzimidazole) at regular time intervals using a platinum-saturated calomel electrode assembly. The pseudo first order rate constants, $k_1$, were evaluated from the linear plots ($r>0.999$) of log ($E_t$ - Eα) Vs time. The reaction exhibits first order dependence each in [CBI] and [leucine] and inverse fractional order in [$H^+$] ions. Decrease in dielectric constant of the solvent medium decreases the rate of reaction suggesting dipole–dipole type of reaction. The rate of reaction is not influenced by the addition of electrolyte like sodium perchlorate. The reaction rate was retarded by added benzimidazole, one of the reaction products. Polymerization was not observed when acrylonitrile is added to the reaction mixture. The kinetic runs were carried out at four different temperatures and thermodynamic parameters have been evaluated. Product analysis showed the formation of carboxylic acid, ammonia and carbon-dioxide. Carboxylic acid formation was confirmed by TLC, ammonia by Nessler's reagent test and carbon-dioxide by lime water test. HOCl has been postulated as the most probable oxidizing species. A plausible mechanism in accordance with observed kinetic data has been proposed.

**Keywords**: Kinetics; Deamination; Decarboxylation; 1-Chlorobenzimidazole; Leucine.

## Introduction

The chemistry of N- halo compounds has evoked considerable interest, as they are sources of halonium cations which act as oxidizing agents (Anil Kumar et al., 2007; Mohamed Farook, 2007; Jagdish Bharad et al., 2008; Kabilan et al., 2006; Priya et al., 2011). 1–chlorobenzimidazole (CBI) is gaining importance as a mild oxidant and utilized as oxidizing agent against various kinetic studies (Ramkumar, 2003; Rukmangathan et al., 2011; Rukmangathan et al., 2012). In addition, its utility as an oxidimetric titrant against some common reductants had already been proved (Rukmangathan et al., 2010).

Essential amino acids serve important functions in our biological system especially in metabolic activities. These amino acids find uses in a variety of fields such as bio chemical, micro biological and nutrition investigation. Oxidation of amino acids has been reported earlier. (Alhaji et al., 2011; Singh et al., 2003; Kutti Rani et al., 2009; Puttasamy et al., 2004; Pushpalatha et al., 2009).

N-halo compounds also play a vital role in the oxidation kinetics of amino acids. Many N- halo oxidants have been successfully utilized for the oxidation of amino acids (Mohamed Farook et al., 2004; Singh et al., 2010; Demappa, 2001; Alhaji et al., 2011).

## Materials and methods

CBI was prepared and purified by literature method (Ramkumar, 2001). Acetic acid was refluxed over chromic oxide for 6 hours and the fraction distilling at 118°C was collected and used. Chromatographically pure leucine was further assayed by acetous perchloric acid method (Vogel A. 1958). All other chemicals are of AnalaR grade from E merck brand (Global Manufacturers, Germany).

### *Kinetic measurements*

All the kinetic reactions were carried out under pseudo-first order conditions, keeping [Leucine] >> [CBI] in solvent system 80% (v/v) acetic acid-water medium at 308K and the courses the reactions were followed potentiometrically (Ramkumar, 2003).

In a typical experiment, the required quantities of the substrate solution, perchloric acid and acetic acid-water mixture were pipetted out in a double walled beaker provided with an inlet and outlet for circulating water from the thermostat set at the desired temperature and the solution were kept in the beaker for nearly half an hour to attain the desired temperature. The reaction was started by pipetting out the required quantity of CBI solution which had also been thermostated for nearly half an hour. The total volume of the reaction mixture was always 25 ml. A stop-watch was started when half the amount of oxidant was added.

$[Pt|BI^{(+)}—CBI||^{(-)}SCE]$---------- (1)

The reaction was followed by setting up a cell made up of the reaction mixture into which the platinum electrode and saturated calomel electrode (SCE) were dipped. The emf of the cell was measured periodically using Equip-Tronics Digital potentiometer while the reaction mixture was continuously stirred using a magnetic stirrer. The pseudo-first order rate constant, $k_1$, was computed from the linear ($r>0.999$) plots of log ($E_t$- $E_\infty$) Vs time.

where, $E_t$ - potential at time 't' and

$E_\infty$ - potential at infinity.

When the kinetic run was also done by iodometry, the same results were obtained within $\pm 2\%$. Preliminary experiments showed that the rate of oxidation is not sensitive to change in ionic strength and hence no attempt was made to keep it constant.

***Stoichiometry and product analysis***

The stoichiometry of the reaction was determined by equilibrating varying ratios of [CBI] Vs [leucine] at 303K for 48 hours under kinetic conditions. Estimation of unconsumed CBI revealed that 2 moles of CBI was required to oxidize 1 mole of the leucine.

$$2\ CBI + H_2NCH(R)COOH \longrightarrow BI + RCOOH + 2HCl + NH_3 + CO_2 \quad .....(2)$$

where $R = -CH_2 – CH(CH_3)_2$

The reaction mixture from the actual kinetic run after sufficient time was then evaporated with ether. The layer was then separated and dried. The formation of carboxylic acid was confirmed by spot tests (Feigl, 1954) and ammonium ions by Nessler's reagent. The liberated $CO_2$ was predicted by lime test.

**Results and discussions**

The kinetics of oxidation of leucine by CBI was investigated at several initial concentrations of leucine. The oxidation of leucine by CBI proceeds smoothly at 303K in aqueous acetic acid medium. The order of the reaction with respect to CBI (oxidant) was found to be unity as shown by the linearity of log ($E_t – E_\infty$) Vs time plots, over 70% of the reaction.

The reaction was found to be first order dependent with respect to substrate as evidenced by the unit slope of log $k_{obs}$ Vs log[S] (Table 1). The increase in $[H^+]$ decreases the reaction rate and shows an inverse fractional order dependence on $[H^+]$ as indicated in Table.1. The rate of the reaction increases with increase in percentage of acetic acid. The plot of log $k_{obs}$ Vs 1/D was found to be linear with positive slope (Table 2).

Table 1. Effect of varying [substrate], [oxidant] and $[H^+]$ on the reaction rate (Acetic acid= 70%; Temperature = 303K)

| [CBI] X $10^3$ mol.dm$^{-3}$ | [leucine] X $10^2$ mol.dm$^{-3}$ | [$HClO_4$] X $10^2$ mol.dm$^{-3}$ | $k_{obs}$ X $10^4$ ($s^{-1}$) |
|---|---|---|---|
| 1.50 | 3.00 | 3.25 | 5.33 |
| 2.25 | 3.00 | 3.25 | 5.25 |
| 3.00 | 3.00 | 3.25 | 5.30 |
| 3.75 | 3.00 | 3.25 | 5.38 |
| 4.50 | 3.00 | 3.25 | 5.23 |
| 3.00 | 1.50 | 3.25 | 2.45 |
| 3.00 | 3.00 | 3.25 | 5.30 |
| 3.00 | 4.50 | 3.25 | 7.76 |
| 3.00 | 6.00 | 3.25 | 10.96 |
| 3.00 | 7.50 | 3.25 | 13.80 |
| 3.00 | 3.00 | 1.30 | 8.91 |
| 3.00 | 3.00 | 3.25 | 5.30 |
| 3.00 | 3.00 | 5.20 | 3.98 |
| 3.00 | 3.00 | 7.80 | 3.09 |
| 3.00 | 3.00 | 9.75 | 2.83 |

Table 2. Effect of varying [acetic acid] on the reaction rate ([CBI] = 6.0 X $10^{-3}$ mol.dm$^{-3}$; [leucine] = 6.0 X $10^{-2}$ mol.dm$^{-3}$; Temperature = 303K)

| Acetic acid (%) | D | 1/D X $10^2$ | $k_{obs}$ X $10^4$ ($s^1$) |
|---|---|---|---|
| 90 | 12.80 | 7.8 | 1.64 |
| 80 | 20.00 | 5.0 | 5.30 |
| 70 | 27.00 | 3.7 | 9.49 |
| 60 | 34.50 | 2.8 | 13.71 |

The reaction mixture when allowed to stand with acrylonitrile does not induce polymerization suggesting the absence of free radical mechanism. Added nickel (II) chloride has no appreciable effect on the reaction rate. The rate constants were measured at three different temperatures (Table 3) and the activation parameters have been calculated from the linear Eyring's plot by least square method.

Table 3. Effect of varying temperature on the reaction rate ([CBI] = 3.0 X $10^{-3}$mol.dm$^{-3}$; [leucine] = 3.0 X $10^{-2}$mol.dm$^{-3}$; Acetic acid= 70%; [$HClO_4$] = 3.25 X $10^{-2}$mol.dm$^{-3}$)

| Temperature (K) | $k_{obs}$ X $10^4$ ($s^1$) |
|---|---|
| 293 | 3.63 |
| 303 | 5.30 |
| 313 | 7.82 |
| 323 | 11.33 |

$\Delta H^{\#}$ = 26.72 KJ mol$^{-1}$
$\Delta S^{\#}$ = -218.73 JKmol$^{-1}$
$\Delta G^{\#}$ = 92.99 KJ mol$^{-1}$

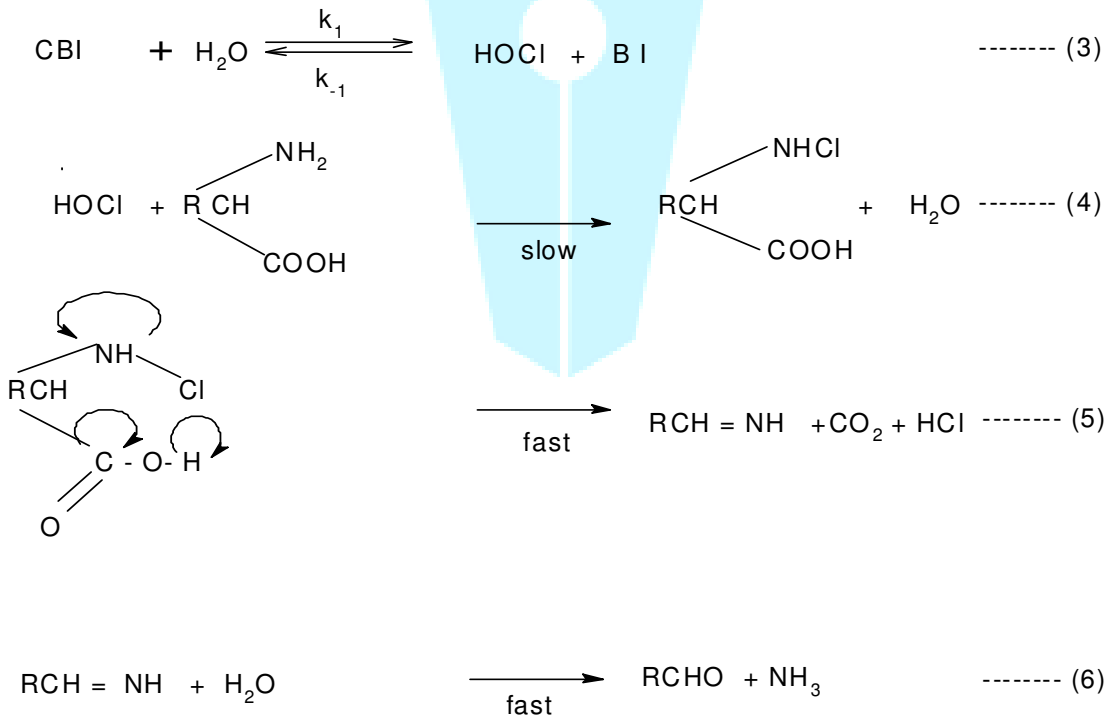
Initial addition of one of the products, viz. benzimidazole, to the reaction mixture does not affect the rate. The reaction rate is not altered significantly with the addition of nickel chloride, a typical chlorine scavenger. Polymerization is not observed when acrylonitrite is added to the reaction mixture.

***Mechanism and rate law***

The possible oxidizing species in acidified solution of CBI are $Cl_2$, HOCl, $H_2OCl^+$, $CBIH^+$ and CBI. Molecular chlorine may not be the oxidizing species, since the rate is not influenced by added nickel (II) chloride which is a well known chlorine scavenger. The involvement of $CBIH^+$ as the oxidizing species can be ruled out on the basis that the reaction shows a negative dependence on [$H^+$].

The retarding effect of benzimidazole suggest that the pre equilibrium step involves a process in which benzimidazole is one of the products. Therefore, it can be assumed that HOCl is the most likely oxidizing species in this present reaction. Based on the above discussions, the following mechanism has been proposed.

The similar kind of mechanism has also been documented in the oxidation of amino acids chloramine–T (Gowda et al., 1983) and N- bromoacetamide (Bishnoi et al., 1985). Aldehyde thus formed on further oxidation gives carboxylic acid in excess of oxygen. The mechanism is also supported by the moderate value of energy of activation and other thermodynamic parameters.



## Conclusions

The kinetics of oxidation of leucine by 1-chlorobenzimidazole (CBI) in perchloric acid medium clearly shows that the order of the reaction with respect to [CBI], [Leucine] are unity and inverse fractional order with respect to $[H^+]$. The product analysis also shows the formation of carboxylic acid as the major product. The mechanism proposed for oxidation kinetics is in accordance with the observed kinetic facts.

## Conflict of Interest

Authors declare there are no conflicts of interest.

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