

Kinetics and mechanism of oxidation of alanine, phenylalanine and valine by *N*-bromosuccinimide in alkaline medium

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The kinetics of oxidation of amino acids (AA), viz. alanine, phenylalanine and valine by *N*-bromosuccinimide (NBS) have been studied in alkaline medium. The reaction is first order in NBS. The order of reaction in amino acid and alkali decreases from unity to zero at higher [AA] and [OH⁻] respectively. The rate is accelerated in presence of succinimide (product of NBS) at lower [succinimide]₀, while that becomes independent to succinimide at higher [succinimide]₀. A mechanism consistent with kinetic data has been proposed.

Oxidative decarboxylation of α -amino acids is a well known biochemical process. The mechanism of oxidative decarboxylation of amino acids by *N*-bromosuccinimide (NBS)¹ in pH < 7 have shown to be significantly influenced by the presence of alkyl group at α -carbon. Most of the investigations of NBS oxidations of organic substances have assumed that the molecular NBS acts only through its positive polar end² producing Br⁺, which is subsequently solvated. Thus H₂O⁺Br has been considered as the effective oxidizing species of NBS in acidic medium. In presence of mercuric acetate protonated form of NBS, i.e. N⁺BSH has also been considered³ as reactive species of NBS in acidic medium. However, there are only few reports on the oxidation reactions of NBS in alkaline medium⁴. Therefore, the title reaction has been studied in detail and the results are presented.

Results and Discussion

The kinetics of oxidation of amino acids by NBS were investigated at several initial concentrations of the reactants. The linear plots of log [NBS] vs time indicate a first order dependence of rate on [NBS]. Therefore, pseudo-first order rate constants (k_{obs}) in NBS at various initial concentrations of reactants have been evaluated from the slopes of these plots. The observed rate constant remained identical at various [NBS]₀ which further confirms the first order dependence of rate with respect of NBS (Table 1).

The rate increases with an increase in [Amino acid]₀ (Table 1). However, from the linear plots of $1/k_{\text{obs}}$ vs $1/[\text{Amino acid}]$ with intercepts, it appears that order in substrate falls from unity to zero at higher [Amino acid].

To study the effect of alkali on the reaction rate, kinetic studies were made over a wide range of alkali concentra-

tions. In order to avoid any variations due to change in ionic strength, the kinetic runs were made at a fixed ionic strength ($\mu = 0.003 \text{ mol dm}^{-3}$ for alanine and valine, $0.015 \text{ mol dm}^{-3}$ for phenylalanine) maintained by sodium perchlorate. An increase in [OH⁻] resulted in increase in the observed rate constant (Table 1) and the linear plot of $1/k_{\text{obs}}$ vs $1/[\text{OH}^-]$ with intercept in each case, suggests that order of reaction in OH⁻ also decreases from unity to zero.

Table 1. Effect of [*N*-bromosuccinimide], [amino acid] and [OH⁻] on rate constant at 35^o

| 10 ³ [NBS] mol dm ⁻³ | 10 ² [AA] mol dm ⁻³ | 10 [OH ⁻] [*] mol dm ⁻³ | K _{obs} , 10 ⁴ s ⁻¹ | | |
|---|--|--|--|------------|-------------------|
| | | | Alanine (A) | Valine (B) | Phenylalanine (C) |
| 1.0 | 2.0 | 5.0 (2.0) | 11.86 | 6.60 | 5.43 |
| 1.5 | 2.0 | 5.0 (2.0) | 12.50 | 7.67 | 5.48 |
| 2.0 | 2.0 | 5.0 (2.0) | 12.70 | 7.67 | 5.11 |
| 3.0 | 2.0 | 5.0 (2.0) | 11.86 | 7.60 | 5.11 |
| 4.0 | 2.0 | 5.0 (2.0) | 12.28 | 7.67 | 5.40 |
| 2.0 | 0.4 | 5.0 (2.0) | 7.82 | 4.82 | 3.00 |
| 2.0 | 0.6 | 5.0 (2.0) | 10.52 | 6.20 | 3.75 |
| 2.0 | 0.8 | 5.0 (2.0) | 12.56 | 6.90 | 4.41 |
| 2.0 | 1.0 | 5.0 (2.0) | 12.70 | 7.20 | 5.01 |
| 2.0 | 3.0 | 5.0 (2.0) | 12.70 | 7.67 | 5.11 |
| 2.0 | 4.0 | 5.0 (2.0) | 12.70 | 7.67 | 5.11 |
| 2.0 | 2.0 | 2.5 (0.5) | 7.12 | 4.09 | 1.77 |
| 2.0 | 2.0 | 5.0 (1.0) | 12.79 | 7.67 | 3.12 |
| 2.0 | 2.0 | 7.5 (1.5) | 16.22 | 9.38 | 3.65 |
| 2.0 | 2.0 | 10.0 (2.0) | 17.54 | 10.23 | 5.11 |
| 2.0 | 2.0 | 15.0 (3.0) | 21.75 | 12.47 | 6.58 |
| 2.0 | 2.0 | 20.0 (4.0) | 23.03 | 13.11 | 7.82 |

*The effect of [OH⁻] was studied at a fixed ionic strength $\mu = 0.003 \text{ mol dm}^{-3}$ for alanine and valine and $0.015 \text{ mol dm}^{-3}$ for phenylalanine; in parenthesis the [OH⁻] in case of phenylalanine are given.

cinimide]/(k_{obs}) vs [Succinimide] should be linear with an intercept.

At higher concentrations of alkali, substrate and succinimide, the approximations,

$$[\text{OH}^-]\{K_1 + K_2K_3 [\text{AA}][\text{Succ}]\} \gg [\text{Succ}]$$

$$\text{and } K_2K_3[\text{AA}][\text{Succ}] \gg K_1$$

the rate law (6) reduces to

$$-\frac{d[\text{NBS}]}{dt} = k_4[\text{NBS}]_0 \quad (7)$$

The experimental results are in agreement with rate laws (6) and (7). Eqn. (7) is valid only at high values of K_2 and K_3 and this indicates that steps (2) and (3) would be very fast and irreversible in nature.

The entropy of activation in each case was found to be negative (reduction of entropy of system) suggesting the compactness of the transition state as compared to the ground state. The nearly same value of ΔG^\ddagger (Table 3) also suggests a common mechanism in case of all the amino acids studied.

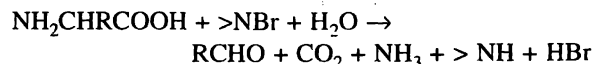
Experimental

Alanine, valine and phenylalanine (Loba, A.R.), *N*-bromosuccinimide (Thomas Baker, A.R.), NaOH, NaClO₄, succinimide (all AnalaR) were used. All the solutions were prepared in double-distilled water. NBS solution was prepared afresh and standardized iodometrically⁵.

To a reaction mixture containing the appropriate quantities of solutions of NBS and NaOH, requisite amount of double-distilled water was added so that the total volume of the mixture was 50 dm³ after adding the amino acid. The mixture and amino acid solution of desired concentration were kept separately at the desired temperature ($\pm 0.1^\circ$). The reaction was started by adding the requisite amount of amino acid solution to the mixture. The progress of reaction was followed by estimating the unconsumed NBS iodometrically.

Stoichiometry and product analysis : Varying ratios of

amino acid to NBS were mixed in the presence of NaOH for 72 h at 35°. The unreacted NBS was estimated iodometrically. The results indicate that 1 mol of amino acid consumes 1 mol of NBS,



where, R represent CH₃, CH(CH₃)₂ and C₆H₅CH₂ for alanine, valine and phenylalanine, respectively. The presence of aldehyde as the oxidation product was confirmed⁶ by converting it into 2,4-dinitrophenylhydrazone and comparing it with an authentic sample (m.p. and TLC).

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References

1. G. Gopalkrishnan and J. L. Hogg, *J. Org. Chem.*, 1985, **50**, 1206.
2. P. F. Jr. Kruse, K. L. Grist and T. A. McCoy, *Anal. Chem.*, 1954, **26**, 1319; J. Lecomte and H. C. R. H. Gault, *Seances Acad. Sci.*, 1952, **234**, 1887; N. Venkatasubramanian and V. Thiagarajan, *Can. J. Chem.*, 1969, **47**, 694; *Indian J. Chem.*, 1970, **8**, 809.
3. A. Shukla and S. K. Upadhyay, *J. Indian Chem. Soc.*, 1992, **69**, 745; P. G. Reddy, Y. Ramesh and S. Kandlikar, *Oxid. Commun.*, 1984, **7**, 89; J. P. Sharma, R. N. P. Singh, A. K. Singh and B. Singh, *Tetrahedron*, 1986, **42**, 2739; A. K. Singh, B. Rahmani, V. K. Singh, V. Gupta, K. Kesarwani and B. Singh, *Indian J. Chem., Sect. A*, 2001, **40**, 519; A. K. Singh, T. Gupta, V. Kumar, D. Kesarwani and B. Singh, *Oxid. Commun.*, 2000, **23**, 416.
4. D. L. Kamble, G. H. Hugar and S. T. Nandibewoor, *Indian J. Chem., Sect. A*, 1996, **35**, 144; S. K. Mavalangi, S. M. Desai and S. T. Nandibewoor, *Oxid. Commun.*, 2000, **23**, 617.
5. N. K. Mathur and C. K. Narang, "The Determination of Organic Compounds with *N*-Bromosuccinimide", Academic, New York, 1975.
6. P. G. Reddy, T. Kistayya, J. A. Khan and S. Kandlikar, *Z. Phys. Chem. (Leipzig)*, 1998, **269**, 1253.