J. Indian Chem. Soc.,
Vol. LXV, May 1988, pp. 339-341

# Decarboxylation and Deamination of Amino Acids by *N*-Bromo-*N*-sodio-*p*-toluenesulphonamide in Perchloric Acid Medium. A Kinetic Study

B. THIMME GOWDA* and (MRS.) R. VIJAYALAKSHMI RAO

Department of Post-Graduate Studies and Research in Chemistry, Mangalore University, Mangalagangothri-574-199

*Manuscript received 26 December 1985, revised 14 March 1988, accepted 17 March 1988*

**Kinetics of decarboxylation and deamination of amino acids by *N*-bromo-*N*-sodio-*p*-toluenesulphonamide have been investigated in perchloric acid medium. The reaction followed first order kinetics each in [oxidant] and [substrate] and inverse first order in [$H^+$]. Variation in ionic strength of the medium and addition of the reaction product, *p*-toluenesulphonamide had no effect on the rate of reaction. The effect of variation in dielectric constant of the medium on the rate has also been investigated. The activation parameters have been computed from the Arrhenius plots. A suitable mechanism consistent with observed results has been proposed. Validity of Taft equation has also been tested.**

RECENTLY, the chemistry of *N*-halosulphonamides has attracted the attention of many investigators due to their diverse nature[1-5]. *N*-Bromo-*N*-sodio-*p*-toluenesulphonamide (bromamine-T, BAT) is an important member of these reagents[6]. It is a source of $Br^+$, hypobromite and *N*-anion and acts both as a base and a nucleophile[2,3]. It reacts with a wide range of functional groups both as a brominating agent and an oxidising agent in the presence of acids or bases. It undergoes a two-electron change in its reactions, the end-products being *p*-toluenesulphonamide (PTS) and sodium bromide[6]. In the present investigation, the kinetics of oxidative decarboxylation and deamination of amino acids by bromamine-T have been studied in perchloric acid medium.

## Experimental

Bromamine-T was prepared by the method reported elsewhere[6] and its purity checked by its ir spectra and by estimating the amount of active halogen present. Its aqueous stock solution (~0.05 mol $dm^{-3}$) was standardised iodometrically and stored in dark-coloured bottles. Chromatographically pure L-glycine (Gly), L-alanine (Ala), L-valine (Val), L-leucine (Leu), L-phenylalanine (Phe) and L-serine (Ser) (all Sisco) were used. Aqueous stock solutions of amino acids were standardised by the usual method. All other reagents were of analytical grade. Preliminary investigations showed that the ionic strength of the medium has no significant effect on the rate of oxidation with all the amino acids.

The kinetic studies were carried out under pseudo-first order conditions ([amino acid] >> [BAT]). The reaction was initiated by the quick addition of known quantities of BAT solution (thermally equilibrated at a desired temperature) to a mixture containing requisite amounts of amino acid solution, perchloric acid and water in the boiling tube (pre-equilibrated at the same temperature). The progress of the reaction was monitored iodometrically by determining the unreated BAT in a measured aliquot of the reaction mixture at regular time intervals at least for two half-lives. The pseudo-first order rate constants computed by the method of least-squares were reproducible within ±3%.

*Stoichiometry and product analysis :* The stoichiometry of the reactions was determined in the presence of $H^+$ ions (0.01 – 0.2 mol $dm^{-3}$) by thermally equilibrating varying ratios of [amino acid]/[BAT] at 303 K. The products were identified to be ammonia, carbon dioxide, *p*-toluenesulphonamide and the corresponding aldehyde. The aldehyde was quantitatively estimated by method reported elsewhere. The observed stoichiometry may be represented as

$$R'CH(NH_2)COOH + (RNBr)^-Na^+ + H_2O \rightarrow R'CHO + RNH_2 + NH_3 + CO_2 + Na^+Br^- \quad (1)$$

where, $R = CH_3C_6H_4SO_2$, $R' = H$(Gly), $CH_3$ (Ala), $(CH_3)_2CH$ (Val), $(CH_3)_2CHCH_2$ (Leu), $C_6H_5CH_2$ (Phe), $HOCH_2$ (Ser). It was further observed that the parent aldehydes (HCHO, $CH_3CHO$ etc.) do not undergo further reactions with the oxidant under the present reaction conditions.

## Results

The kinetics of oxidative decarboxylation and deamination of amino acids by BAT in perchloric acid medium was investigated at several initial concentrations of the reactants and $H^+$. At constant [$HClO_4$] with the [substrate] in excess, plots of log

TABLE 1—PSEUDO-FIRST ORDER RATE CONSTANTS ($k_{obs}$) FOR OXIDATION OF AMINO ACIDS (AA) BY BROMAMINE-T (BAT) IN ACID MEDIUM AT 303 K

| $[AA]_0$ $\times 10^3$ mol dm$^{-3}$ | $[BAT]_0$ $\times 10^3$ mol dm$^{-3}$ | $[HClO_4]$ $\times 10^3$ mol dm$^{-3}$ | $k_{obs}$ ($\times 10^4$ s$^{-1}$) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Gly | Ala | Val | Leu | Phe | Ser |
| 5.0 | 5.0 | 2.0 | 13.33 | — | — | — | 9.58 | 6.09 |
| 5.0 | 5.0 | 3.0 | 7.68 | 9.78 | 11.10 | 4.89 | 7.85 | — |
| 5.0 | 5.0 | 4.0 | — | 6.50 | 8.23 | 4.26 | 5.21 | — |
| 5.0 | 5.0 | 5.0 | 5.33 | 5.45 | 6.47 | 3.21 | 4.06 | 2.84 |
| 5.0 | 5.0 | 7.5 | 3.21 | 3.99 | 4.91 | 2.19 | 2.67 | — |
| 5.0 | 5.0 | 10.0 | 2.03 | 2.43 | 4.02 | 1.60 | 2.24 | 1.47 |
| 5.0 | 5.0 | 20.0 | — | 1.71 | 2.10 | 0.82 | 1.16 | 0.87 |
| 5.0 | 1.0 | 5.0 | 5.24 | 5.42 | 6.89 | 3.18 | 4.08 | 2.88 |
| 5.0 | 2.0 | 5.0 | 5.48 | 5.49 | 7.02 | 3.29 | 4.16 | 2.69 |
| 5.0 | 4.0 | 5.0 | 5.32 | 5.45 | 6.93 | 3.23 | 3.98 | 2.78 |
| 5.0 | 5.0 | 5.0 | 5.33 | 5.45 | 6.47 | 3.21 | 4.06 | 2.84 |
| 5.0 | 10.0 | 5.0 | 5.38 | 5.38 | 6.98 | 3.15 | 4.12 | 2.89 |
| 0.75 | 5.0 | 5.0 | — | — | — | 1.10 | 1.63 | — |
| 1.0 | 5.0 | 5.0 | 1.02 | 0.94 | 1.38 | 1.39 | 2.28 | — |
| 2.0 | 5.0 | 5.0 | 2.07 | 1.97 | 2.59 | 3.21 | 4.06 | 1.26 |
| 4.0 | 5.0 | 5.0 | — | 4.17 | — | 5.42 | 8.70 | 2.21 |
| 5.0 | 5.0 | 5.0 | 5.33 | 5.45 | 6.47 | 6.45 | 10.10 | 2.84 |
| 7.5 | 5.0 | 5.0 | 8.70 | 9.58 | 9.05 | 9.64 | 14.86 | 4.45 |
| 10.0 | 5.0 | 5.0 | 10.85 | 12.47 | 11.44 | — | — | — |

TABLE 2—EFFECT OF ADDITION OF REACTION PRODUCT AND VARIATION IN DIELECTRIC CONSTANT OF THE MEDIUM ON THE RATE OF OXIDATION OF AMINO ACIDS BY BROMAMINE-T IN ACID MEDIUM AT 303 K

$[AA]_0 = 5.0 \times 10^{-3}$ mol dm$^{-3}$, $[BAT]_0 = 5.0 \times 10^{-3}$ mol dm$^{-3}$, $[HClO_4] = 5.0 \times 10^{-3}$ mol dm$^{-3}$, Temp. = 303 K

| $D$ | $k_{obs}$ ($\times 10^4$ s$^{-1}$) | | | | | |
|---|---|---|---|---|---|---|
| | Gly | Ala | Val | Leu | Phe | Ser |
| 72.1 | 5.63 | 8.69 | 5.83 | 4.54 | 5.18 | 2.98 |
| 67.6 | 6.14 | 9.77 | 4.21 | 4.58 | 4.48 | 3.23 |
| 63.1 | 6.91 | 11.66 | 3.51 | 4.60 | 3.32 | 3.69 |
| $10^3$[PTS](mol dm$^{-3}$) | | | | | | |
| 1.0 | 5.33 | 5.38 | 6.54 | 3.21 | 4.16 | 2.88 |
| 2.0 | 4.42 | 5.45 | 6.41 | 3.18 | 4.02 | 2.84 |
| 5.0 | 5.38 | 5.39 | 6.47 | 3.25 | 4.21 | 3.03 |
| 10.0 | 5.35 | 5.42 | 6.52 | 3.23 | 4.06 | 2.98 |

TABLE 3—ACTIVATION PARAMETERS FOR OXIDATION OF AMINO ACIDS BY BROMAMINE-T IN ACID MEDIUM

| | | | | | | |
|---|---|---|---|---|---|---|
| $\Delta H^{\neq}$ (kJ mol$^{-1}$) | 89.8 | 54.3 | 54.9 | 54.2 | 78.1 | 50.6 |
| $\Delta S^{\neq}$ (JK$^{-1}$ mol$^{-1}$) | 4.31 | −120.4 | −117.1 | −124.7 | −44.1 | −60.2 |
| $\Delta G^{\neq}$ (kJ mol$^{-1}$) | 88.5 | 91.3 | 91.0 | 92.6 | 91.6 | 68.6 |

$[BAT]_0/[BAT]$ vs time were linear for all the amino acids, showing first order kinetics in $[BAT]_0$. The pseudo-first order rate constants increased with the increase in [amino acid] (Table 1) in all the cases. Plots of log $k_{obs}$ vs log [amino acid] were linear with almost unit slopes, establishing first order kinetics in [amino acid]. But the rate decreased with the increase in $[H^+]$ and the log–log plots were linear with negative unit slopes for all the amino acids, showing inverse first order kinetics in $[H^+]$. The rates were unaffected by the variation of ionic strength of the medium (0.10–1.0 mol dm$^{-3}$). Addition of the reaction product, viz. *p*-toluenesulphonamide (~0.01 mol dm$^{-3}$) had no effect on the rate of oxidation. Variation in dielectric constant of the medium by changing the solvent composition with methanol had little effect on the rate (Table 2). The activation parameters have been computed for all the amino acids by measuring rates at different temperatures and dielectric constant of the medium (Table 3). The absence of free radicals in the reaction mixture was confirmed by adding aqueous acrylamide solution as the latter did not initiate polymerisation.

## Discussion

*Mechanism of oxidations:* Bromamine-T, like chloramine-T and bromamine-B[2] is moderately a strong electrolyte in aqueous solutions. *N*-Bromo-*p*-toluenesulphonamide (monobromamine-T, RNHBr), dibromamine-T ($RNBr_2$) and HOBr are the probable reactive species under the present experimental conditions ($[H^+] = 0.01 - 0.2$ mol dm$^{-3}$). Amino acids

also exist in different forms in aqueous solution[7]. In strongly acid solutions they exist mostly in the cationic forms, $R'CH(NH_3^+)COOH(SH^+)$ which are resistant to the attack by the oxidant as is evidenced by the inverse dependence of the rate on $[H^+]$. Thus the neutral species (S) may be controlling the rate of reaction,

$$SH^+ \rightleftharpoons S + H^+ \qquad (2)$$

Hence, the observed kinetics of first order each in [BAT] and [amino acid] and inverse first order in $[H^+]$ and non-influence of the added PTS and variation in ionic strength of the medium on the rate may be explained through Scheme 1.

$$\underset{(SH^+)}{R'CH(NH_3^+)COOH} \underset{(slow)}{\overset{K_1}{\rightleftharpoons}} \underset{(S)}{R'CH(NH_2)COOH} + H^+ \qquad (3)$$

$$R'CH(NH_2)COOH + RNHBr \xrightarrow[(slow\ and\ r.d.s.)]{k_2} R'CH(NH_2)COOBr + RNH_2 \qquad (4)$$

$$R'CH(NH_2)COOBr \xrightarrow[(fast)]{k_3} R'CH(NH) + CO_2 + H^+Br^- \qquad (5)$$

$$R'CH(NH) + H_2O \xrightarrow[(fast)]{k_4} R'CH(OH)NH_2 \qquad (6)$$

$$R'CH(OH)NH_2 \xrightarrow[(fast)]{k_5} R'CHO + NH_3 \qquad (7)$$

Scheme 1

The related rate law is

$$-\frac{d[BAT]}{dt} = \frac{K_1 k_2 [BAT][SH^+]}{[H^+]}$$

or

$$k_{obs} = \frac{K_1 k_2 [SH^+]}{[H^+]} = k_2[S] \qquad (8)$$

The plots of $k_{obs}$ vs [S] were linear with no intercept on the ordinate in conformity with rate law (8). Applicability of Taft equation was tested[8,9]. The following expressions were found to be valid for the amino acids (with the exception of glycine and phenylalanine).

$$\log k_{obs} = -0.48\,\sigma^* + 0.74 \qquad (9)$$

$$\log k_{obs} = -0.074\,E_s + 0.75 \qquad (10)$$

A negative value of polar constant ($\sigma^*$) indicates that electron-donating centres increase the rate of reaction. It is evident from equations (9) and (10) that the steric effects are relatively smaller.

The isokinetic temperature was evaluated from the linear plots of $\Delta H^{\neq}$ vs $\Delta S^{\neq}$. The $\beta$ value of 282 K is closer to the temperature range employed in the present investigations (298–313 K). Fairly negative $\Delta S^{\neq}$ values indicate the formation of a more ordered activated complex. The $\Delta G^{\neq}$ values are nearly constant (with the exception of serine) showing the operation of similar mechanisms for the reaction of these amino acids with BAT.

The detailed mechanism of reaction envisages the formation of acyl hypobromite derivative of the respective amino acid which undergoes subsequent decarboxylation and deamination processes in fast steps to give the reaction products.

**Acknowledgement**

One of the authors (R.V.R.) is grateful to the Mangalore University, Mangalore, for the award of a research fellowship.

**References**

1. M. M. CAMPBELL and G. JOHNSON, *Chem. Rev.*, 1978, 78, 65.
2. F. E. HARDY and J. P. JOHNSTON, *J. Chem. Soc., Perkin Trans. 2*, 1973, 742.
3. F. RUFF and A. KUCSMAN, *J. Chem. Soc., Perkin Trans. 2*, 1982, 1075.
4. B. T. GOWDA and D. S. MAHADEVAPPA, *J. Chem. Soc., Perkin Trans. 2*, 1983, 323, *Talanta*, 1983, 30, 359, *Microchem. J.*, 1983, 28, 374 and references therein.
5. B. T. GOWDA and R. V. RAO, *Indian J. Chem., Sect. A*, 1985, 24, 1021 and references therein.
6. C. G. R. NAIR, R. L. KUMARI and P. INDRASENAN, *Talanta*, 1978, 25, 525.
7. H. D. JAKUBKE and H. JESCHKEIT, "Amino Acids, Peptides and Proteins", Wiley, New York, 1977.
8. K. B. WIBERG, "Physical Organic Chemistry", Wiley, New York, 1964.
9. R. D. GILLIOM, "Introduction to Physical Organic Chemistry", Addison Wesley, London, 1970.