Kinetics of Oxidative Cleavage of Amino Acids by N-Bromosuccinimide in Aqueous Perchloric Acid Medium

P S RADHAKRISHNAMURTI*, B M SASMAL & D P PATNAIK

Department of Chemistry, Berhampur University, Berhampur 760 007

Received 9 April 1985; revised and accepted 4 July 1985

The kinetics of oxidation of glycine, alanine, leucine and arginine by N-bromosuccinimide (NBS) in aqueous perchloric acid (0.025 to 0.2 mol dm⁻³) has been studied at 30°C. The reaction is first order in [NBS], fractional order in [amino acid] and inverse fractional order in [H⁺]. Variation in ionic strength has no effect on the reaction rate. Although there is pronounced acceleration by the added bromide ion, effect of dielectric constant has been studied. Activation parameters have been evaluated. Suitable mechanism and rate law are proposed to account for the observed kinetics.

The present note deals with the kinetics and mechanism of oxidation of glycine, alanine, leucine and arginine by N-bromosuccinimide (NBS) in aqueous perchloric acid medium.

The amino acids used were of AR (BDH) grade and were recrystallised before use. Acetic acid (BDH), acetonitrile (E Merck), perchloric acid (E Merck) and N-bromosuccinimide (E Merck) were used as such. NBS oxidation of all the four amino acids studied exhibit similar kinetic behaviour. A first order dependence of reaction rate on [NBS] is observed. The first order rate constants (k₁) are almost same at all initial [oxidant].

The first order rate constants increase with increase in [amino acid] (Table 1) and the order of the reaction in [amino acid] is fractional, since the slope of the plot of log k₁ versus log [amino acid] is less than unity. Further the plots of k₁ versus log [amino acid] (Table 2) are negative.

The decomposition constants (kₒ) of the complexes formed between the substrate and the oxidant at [H⁺] = 0.05 mol dm⁻³, [Hg(OAc)₂] = 5 × 10⁻⁴ mol dm⁻³ and temp. = 30°C, in aqueous medium are: 10⁴ × kₒ = 1.56 (glycine); 8.33 (alanine), 12.5 (leucine) and 25.0 (arginine).

The dependence on [H⁺] is found to be inverse fractional (Table 2) as indicated by the slopes of the plots of log k₁ versus log [HClO₄] which are negative and less than unity. Further the plots of k₁ versus 1/[H⁺] yield a negative intercept. While addition of NaClO₄ does not influence the rate, that of Br⁻ has a pronounced accelerating effect on the rate; the latter may be due to formation of more reactive molecular bromine species.

An attempt has also been made to study the effect of varying Hg(OAc)₂ concentration in the range 0.0005 and 0.001 mol dm⁻³ on the rate constants. The k₁ values at these two concentrations of Hg(OAc)₂ are: 1.67.92 × 10⁻⁵ s⁻¹ and 159.83 × 10⁻⁵ s⁻¹ respectively. The possibility of mercuration is ruled out as it would have caused a remarkable change of reaction rate.

The reaction rate increases linearly with increase in HOAc content of the reaction medium. The plots of log k₁ versus 1/D are linear with positive slopes. In a polar solvent like acetonitrile the reaction rate is retarded with increase in acetonitrile content of the solvent medium and the plots of log k₁ versus 1/D are linear with negative slopes.

Increase in pH increases the rate constant. For example at [glycine] = 0.0005 mol dm⁻³, [NBS] = 0.00125 mol dm⁻³, [Hg(OAc)₂] = 0.0005 mol
Table 3—Activation Parameters at 30°C

<table>
<thead>
<tr>
<th>Substrate</th>
<th>$E_a$ (kJ mol⁻¹)</th>
<th>$\Delta H^\ddagger$ (kJ mol⁻¹)</th>
<th>$\log_{10} A$ (mol⁻¹ sec⁻¹)</th>
<th>$\Delta S^\ddagger$ (JK⁻¹ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycine</td>
<td>95.8</td>
<td>92.8</td>
<td>15.4</td>
<td>41.2</td>
</tr>
<tr>
<td>Alanine</td>
<td>123.5</td>
<td>121.0</td>
<td>19.3</td>
<td>117.6</td>
</tr>
<tr>
<td>Leucine</td>
<td>109.4</td>
<td>106.9</td>
<td>19.3</td>
<td>115.5</td>
</tr>
<tr>
<td>Arginine</td>
<td>106.4</td>
<td>103.9</td>
<td>18.9</td>
<td>107.7</td>
</tr>
</tbody>
</table>

and 30°C, the rate constant ($10^5 k_1 = 112.8$ s⁻¹) at pH 3.4 increases to 234.56 at pH 6.85 and thereafter it decreases to 57.57 at pH 8.65. No reaction occurs at pH 12.0.

The activation parameters at 30°C for different amino acids under study have been evaluated (Table 3) from the slopes of linear plots of log $k_o$ versus $1/T$.

The LEFR has been applied for the three mono amino acids, except arginine. The plots of log $k_1$ versus $\sigma$ is linear with $\rho = -6$, in consonance with oxidation reactions involving halogens. Application of isokinetic relationship ($\Delta H = C + \beta \Delta S$) by plotting $\Delta H$ versus $\Delta S$ leads to the values of $C$ as 80 kJ mol⁻¹ and $\beta$ as 301 K.

Stoichiometric runs with large excess of NBS in the presence of perchloric acid at 30°C for 24 hr reveal that 1 mol of each amino acid consumes 2 mol of NBS, in accordance with Eq. (1).

$$R'\text{CH}_2\text{CH}_2\text{NHCOOH} + 2\text{NBS} \rightarrow$$

$$2\text{HBr} + \text{CO}_2 + R'\text{CH}_2\text{CN} + 2\text{succimide} \quad \ldots (1)$$

The products have been identified by TLC as succinimide and corresponding nitrile.²⁰

The mechanism consistent with the kinetic observations is expressed by Eqs (2-4).

$$\text{[Amino acid]H}^+ \xrightarrow{k_{fast}} \text{[Amino acid] + [H+] \quad \ldots (2)}$$

$$\text{[Amino acid] + [NBS]} \xrightarrow{k_{fast}} \text{complex \quad \ldots (3)}$$

$$\text{Complex} \xrightarrow{k_{slow}} \text{products \quad \ldots (4)}$$

The rate law is given by Eq. (5).

$$\frac{d[NBS]}{dt} = K_1K_2K_3[NBS][\text{amino acid}]_T \quad \ldots (5)$$

References