Indian Journal of Chemistry
Vol. 26A, December 1987, pp. 1042-1043

Kinetics & Mechanism of Oxidation of Some α-Amino Acids by N-Bromoacetamide

H P PANDA*
Department of Chemistry, M P C College, Baripada (Mayurbhanj) 757 001
and
B D SAHU
Department of Chemistry, Rajendra College, Bolangir 767 002

Received 1 *January* 1987; *revised* 9 *March* 1987; *accepted* 27 *April* 1987

Kinetics of N-bromoacetamide (NBA) oxidation of glycine, L-phenylalanine L-leucine, L-valine and L-alanine in aqueous acetic acid in the presence of perchloric acid at a fixed $Hg(OAc)_2$ concentration have been investigated. The reaction shows first order dependence in [NBA] and fractional order in [substrate], the dependence on $[H^+]$ being inverse fractional. Added acetamide retards the reaction rate. The activation parameters have been computed. The reactivity order is, L-phala > L-leu > L-val > L-ala > gly.

A vast array of reports are available on the kinetics and mechanism of oxidation of amino acids by a variety of oxidants[1-8]. We report herein hitherto unreported results on the kinetics and mechanism of oxidation of glycine (gly, L-alanine (ala), L-valine (val), L-leucine (leu) and L-phenylalanine (phala) by N-bromoacetamide (NBA) in the presence of $Hg(OAc)_2$ in acetic acid-water mixtures containing perchloric acid.

The oxidant, NBA (E. Merck, GR) was preserved in dark in a desiccator. Stock solutions of amino acids (Loba Chemicals) were prepared in doubly distilled water and standardised by Sorensen formol titration. Self decomposition of NBA, in solvent mixtures employed, was negligible. Standard iodometric procedure was adopted for estimating unreacted NBA. All the experiments were carried out in duplicate and the results are reproducible within ± 2% error.

The results of stoichiometric runs revealed that one mol of substrate consumes one mol of oxidant to give one mol of the corresponding aldehydes, viz. formaldehyde, phenylacetaldehyde, isovaleraldehyde, isobutyraldehyde and acetaldehyde respectively alongwith one mol of CO_2 and one mol of acetamide in the oxidation of gly, phala, leu, val and ala. The aldehydes were characterised via their 2,4-DNP derivatives followed by direct comparison with authentic samples.

Under the condition, [amino acid] ≫ [NBA] the order in [NBA] is unity as revealed by the linear plots of log $[NBA]_t$ against time. The pseudo-first order rate constants (k_{obs}) are invariant over a four-fold variation of initial [NBA]. Increase in [substrate] increases the rate constant. Plots of log k_{obs} versus log [substrate] are linear with slopes less than unity pointing to a complex dependence.

Table 1—Activation Parameters at 40°C

Substrate	*Ea* kJ/mol	$\Delta H^{\ddagger}$ kJ/mol	log *A* 10	$\Delta S^{\ddagger}$ $(JK^{-1}\,mol^{-1})$
Gly	73.9	71.3	8.8	−86.1
L-Ala	64.0	61.4	8.3	−95.4
L-Val	54.3	51.7	6.8	−122.8
L-Leu	53.4	50.8	6.8	−124.4
L-Phala	53.4	50.8	6.8	−123.0

Increase in $[HClO_4]$ retards the rate. Plots of log k_{obs} versus log $[H^+]$ are linear with slopes −0.8, −0.38, −0.42, −0.30 and −0.33 respectively for gly, ala, val, leu and phala. This inverse fractional dependence on $[H^+]$ may be traced to the protonation equilibria involving amino acids, the unprotonated molecules being more suitable for attack by NBA.

Variation of $[Hg(OAc)_2]$ as well as the proportion of acetic acid in the solvent medium has only marginal effects. Addition of acetamide retards the rate, the k_{obs} values at 0.02, 0.04 and 0.08 mol dm^{-3} acetamide are 8.73, 5.00 and $2.80 \times 10^{-5}\,s^{-1}$ at [phala] = 0.005 mol dm^{-3}, $HClO_4$ = 0.05 mol dm^{-3} and 40°C.

The activation parameters have been computed from the linear Arrhenius plots (Table 1).

Mechanism and rate law

On the basis of results obtained the mechanism shown in Scheme 1 is proposed for the oxidation of presently studied amino acids by NBA.

$$RCH(\overset{+}{N}H_3)COOH \overset{K_1}{\rightleftharpoons} RCH(NH_2)COOH + \overset{+}{H}$$

$$NBA + H_2O \overset{K_2}{\rightleftharpoons} HOBr + ACETAMIDE(Acm)$$

$$RCH(NH_2)COOH + HOBr \overset{K_3}{\rightleftharpoons} (COMPLEX)$$

$$(COMPLEX) \xrightarrow[Slow]{k_d} RC^{+}HNH_2 + CO_2 + H_2O + Br^-$$

$$RC^{+}HNH_2 \xrightarrow{-H^+} RCH{=}NH \xrightarrow{H_2O} RCHO + NH_3$$

Scheme 1

Scheme 1 leads to rate law (1) in which k_d is the decomposition constant.

$$\frac{1}{k_{obs}} = \left\{\frac{([Acm]+K_2)(K_1+[\overset{+}{H}])}{k_d K_1 K_2 K_3}\right\} \times \frac{1}{(Substrate)_T} + \frac{1}{k_d}$$

Table 2—Decomposition Constants at Various Temperatures in the NBA Oxidation of α-Amino Acids

$[HClO_4] = 0.1$ mol dm^{-3}; $[Hg(CAc)_2] = 0.01$ mol dm^{-3}; [NBA] = 0.0011 mol dm^{-3}; HOAc, 10% (v/v)

Substrates	$10^3 \times k_d$ (s^{-1}) at		
	30°	40°	50°C
Gly	0.140	0.312	0.784
L-Ala	1.90	4.54	9.10
L-Val	3.50	6.25	12.70
L-Leu	4.20	8.00	15.00
L-Phala	4.64	9.52	17.80

The double reciprocal plots of $1/k_{obs}$ against 1/[substrate] are linear with intercepts on the reciprocal rate axis from which the decomposition constants (k_d) have been calculated and the values are given in Table 2.

The order of reactivities of the substrates based on the decomposition constants is phala > leu > val > ala > gly. When the log k_d values of all these amino acids are plotted against their respective σ* values, a linear plot is obtained only when computed values of −0.44 and −0.29 are used for $C_6H_5CH_2$ and $(CH_3)_2CHCH_2$ groups because in these groups it is the electron releasing nature rather than the inductive effect which controls the reactivity[7]. The ρ* value of −1.9 obtained from the plot is similar to the value obtained for phenyliodosyl acetate and lead tetraacetate oxidations of the same substrates.

Frequency factors much less than that expected for a simple bimolecular reaction point to the formation of a complex prior to the reaction proper. The high negative $\Delta S\ddagger$ values further suggest the transition state to be considerably rigid. The plot of $\Delta H\ddagger$ versus $\Delta S\ddagger$ is also linear with isokinetic temperature $\beta = 522$ K and parameter C = 126.5 kJ/mol, pointing the reaction to be enthalpy-controlled.

The authors are indebted to Prof P S Radhakrishnamurti, Department of Chemistry, Berhampur University for encouragement and enlightening discussion.

References

1 Beg M A & Uddin K, *Indian J Chem*, **13** (1975) 1167.
2 Usha A V, Sethuram B & Navaneeth Rao T, *Indian J Chem*, **15A** (1977) 528.
3 Chandra G & Srivastava S N, *Indian J Chem*, **11** (1973) 773; *J inorg nucl Chem*, **11** (1972) 197.
4 Upadhyaya S K & Agrawal M C, *Indian J Chem*, **15A** (1977) 416.
5 Mahadevappa D S, Ahmad M S & Gowda N M M, *Indian J Chem*, **19A** (1980) 325.
6 Verma R S, Reddy M J & Shastry V A, *J chem Soc, Perk II*, (1976) 469.
7 Radhakrishnamurti P S, Panda H P & Pradhan D C, *Indian J Chem*, **24A** (1985) 586.
8 Adinarayan M, Sethuram B & Navaneeth Rao T, *J Indian chem Soc*, **53** (1976) 877.