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Full Paper

Mechanistic Investigations of Oxidation of Some Dipeptides by Sodium *N*-chloro-*p*-toluenesulfonamide in Alkaline Medium: A Kinetic Study

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The kinetics of oxidation of five dipeptides (DPP) *viz.*, glycylglycine (Gly-Gly), *L*-alanyl-*L*-alanine (Ala-Ala), *L*-valyl-*L*-valine (Val-Val), *L*-leucyl-*L*-leucine (Leu-Leu) and phenylglycyl-phenylglycine (Phg-Phg) by sodium *N*-chloro-*p*-toluenesulfonamide or chloramine-T (CAT) in NaOH medium was studied at 308 K. The reactions follow identical kinetics for all the dipeptides, being first-order dependence each on $[CAT]_o$, $[DPP]_o$ and fractional-order on $[OH^-]$. Addition of *p*-toluenesulfonamide or halide ions (Cl^- or Br^-) has no significant effect on the rate of reaction. The reaction rate was found to increase with increase in ionic strength of the medium. The solvent isotope effect was studied using D_2O. The activation parameters for the reaction were computed from Arrhenius plots. Equilibrium and decomposition constants were evaluated. The oxidation products of the dipeptides were identified as their corresponding aldehydes. An isokinetic relationship was observed with $\beta = 352$ K, indicating that enthalpy factors control the reaction rate. $CH_3C_6H_4SO_2NCl^-$ of the oxidant has been postulated as the reactive oxidizing species. Under comparable experimental conditions, the rate of oxidation of the dipeptides increases in the order: Phg-Phg > Ala-Ala > Val-Val > Leu-Leu > Gly-Gly. The kinetics of oxidation of the dipeptides have also been compared with those of their corresponding monomer amino acids. The observed results have been explained by a plausible mechanism and the related rate law has been deduced.

Keywords oxidation-kinetics, dipeptide, chloramine-T, alkaline medium

Introduction

The chemistry of aromatic sulfonyl haloamines (*N*-haloamines), is of interest due to their diverse behaviour. Their versatile nature is due to their ability to exist as halonium cations and nitrogen anions, which act both as bases and nucleophiles.[1] As a result, these compounds react with a wide range of functional groups and affect a variety of molecular changes. The prominent member of this class of compounds is sodium *N*-chloro-*p*-toluenesulfonamide or chloramine-T (CAT, $p\text{-}CH_3C_6H_4SO_2NClNa\bullet 3H_2O$). The mechanistic aspects of its reactions have been well documented.[1] Although extensive work has been reported on the kinetics of oxidation of amino acids using a variety of oxidants,[2] there is little information in the literature on the oxidation kinetics of dipeptides.

Dipeptides are useful biomaterials in many analytical, biological, pharmaceutical and synthetic applications. Glycylglycine is the first member of the dipeptide series and *L*-valyl-*L*-valine (Val-Val), *L*-alanyl-*L*-alanine (Ala-Ala), *L*-leucyl-*L*-leucine (Leu-Leu) and phenylglycyl-phenylglycine (Phg-Phg) are the other dipeptides of our interest to study the oxidation kinetics. Gly-Gly has been oxidized by manganese(III) and bromamine-T in an acid medium,[3,4] and its hydrolysis kinetics[5,6] has also been reported. However, similar studies with other dipeptides are scanty. The kinetics of oxidation of Gly-Gly, Val-Val, Ala-Ala, Leu-Leu and Phg-Phg by bromamine-B in an acid medium has been reported from our laboratory.[7] Since similar studies in an alkaline medium are not available in the literature, we have undertaken the title reaction.

Preliminary kinetic studies revealed that the reactions between dipeptides and bromamines were too rapid to be measured in an alkaline medium. Hence, to investigate the kinetic and mechanistic aspects of these redox systems, chloramine-T was used as an oxidant in an alkaline medium. In view of this, we have taken up a systematic kinetic study of the oxidation of dipeptides namely, Gly-Gly, Val-Val, Ala-Ala, Leu-Leu and Phg-Phg by CAT in an alkaline medium to explore the mechanistic aspects of these oxidations and also to compare the oxidative behaviour of the dipeptides in the alkaline medium. Attempts have been made to assess the relative rates of oxidation of the dipeptides and to derive an isokinetic relationship with the computed activation parameters. Further, the rates of oxidation of these dipeptides by CAT in NaOH medium were compared with their monomers under identical experimental

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conditions.

Experimental

Materials

Chloramine-T (Merck) was purified by the method of Morris *et al*..[8] Solutions of CAT were preserved in brown bottles to prevent its photochemical deterioration. Chromatographically pure Gly-Gly and Ala-Ala (Merck), Val-Val and Leu-Leu (Bachem AG, Switzerland), were used as received. Phg-Phg was prepared[9] by employing Boc group for *N*-protection and methyl ester as *C*-protecting group. The hydrolysis of the methyl ester followed by removal of Boc group gave the dipeptide. It was confirmed by its NMR data. All other chemicals were of analytical grade. Heavy water (D_2O, 99.4%) employed for solvent isotope studies was supplied by the Bhabha Atomic Research Centre, Mumbai, India. The ionic strength (*I*) of the system was maintained at a constant high value (0.3 mol/L) using a concentrated solution of $NaClO_4$ to swamp the reaction. Triply distilled water was used in the preparation of all aqueous solutions. Regression analysis of the experimental data to obtain the regression coefficient (*r*) was carried out on an FX-100W scientific calculator.

Kinetic measurements

Kinetic runs were performed under pseudo-first-order conditions with a known excess of the $[substrate]_o$ over $[oxidant]_o$ at 308 K. The reactions were carried out in glass stoppered pyrex boiling tubes whose outer surface was coated black to eliminate any photochemical effects. For each run, requisite amounts of solutions of substrate, NaOH, $NaClO_4$ and water (for constant total volume) were introduced into the tube and thermostated at the desired temperature (308 K) for 30 min. A measured amount of CAT solution, also thermostated at the same temperature, was added rapidly to the above mixture to initiate the reaction. The mixture was periodically shaken to ensure uniform concentration and the progress of the reaction was monitored by iodometric determination of unreacted CAT in a measured aliquot of the reaction mixture at different time intervals. The reaction was followed for more than two half-lives. The pseudo-first-order rate constants (*k′*) calculated from the linear plots of log [CAT] vs. time were reproducible within ±3%—5%.

Stoichiometry

Various ratios of CAT to dipeptide were equilibrated at 308 K in the presence of 1.0×10^{-3} mol/L NaOH for 48 h. The iodometric determination of unreacted CAT in the reaction mixture showed that one mole of the dipeptide consumed two moles of CAT to give the corresponding aldehyde. The observed stoichiometry is shown by Eq. (1):

$$NH_2CHRCONHCHRCOOH + 2TsNClNa + 3H_2O \rightarrow 2RCHO + 2TsNH_2 + 2NH_3 + 2CO_2 + 2Na^+ + 2Cl^- \quad (1)$$

where Ts = *p*-$CH_3C_6H_4SO_2$ and R = H for Gly-Gly, CH_3 for Ala-Ala, $CH(CH_3)_2$ for Val-Val, $CH_2CH(CH_3)_2$ for Leu-Leu and C_6H_5 for Phg- Phg.

Product analysis

The reaction mixture was extracted with ether and the corresponding aldehydes (RCHO, oxidation products of the dipeptides) obtained were characterized by their 2,4-DNP derivatives.[10] Formaldehyde, acetaldehyde, isobutyraldehyde, isovaleraldehyde and benzaldehyde are the oxidation products of Gly-Gly, Ala-Ala, Val-Val, Leu-Leu, Phg-Phg and the melting points[10] of the corresponding 2,4-DNP hydrazone derivatives are 164, 168, 186, 122, and 235 ℃ respectively. The reduction product of CAT, $TsNH_2$ was identified[1d] by TLC. Ammonia was detected by Nessler's reagent test. The liberated carbon dioxide was detected by lime water test.

Results and discussion

Kinetic Orders

The kinetics of oxidation of the dipeptides (DPP) by CAT was investigated at several initial concentrations of the reactants in NaOH medium. The same oxidation behavior was observed for all the five dipeptides studied. Under pseudo-first-order conditions of $[substrate]_o >> [oxidant]_o$ at constant $[DPP]_o$, [NaOH] and temperature, plots of log[CAT] vs. time were linear ($r > 0.9935$), indicating a first-order dependence of the reaction rate on $[CAT]_o$. The pseudo-first-order rate constant (*k′*) was not affected by a change in $[CAT]_o$, confirming the first-order dependence of the rate on $[CAT]_o$ (Table 1). Values of *k′* increased with increase in $[DPP]_o$ (Table 1). Plots of log *k′* vs. log [DPP] are linear ($r > 0.9909$) with unit slopes, indicating a first-order dependence of the rate on $[DPP]_o$. Furthermore, the second-order rate constants $k'' = k'/[DPP]_o$ are nearly the same for all the dipeptides establishing a first-order dependence on $[DPP]_o$ (values are not reported). Furthermore, plots of *k′* vs. [DPP] were linear ($r > 0.9892$), passing through the origin, confirming the first-order dependence on $[DPP]_o$ and also the intermediates formed were of transient existence. The reaction rate increased with increase in [NaOH] (Table 1) and plots of log *k′* vs. log[NaOH] were linear ($r > 0.9921$) with slopes less than unity (0.5—0.7), showing fractional order dependence of rate on $[OH^-]$ in each case.

The effect of ionic strength (*I*) of the medium on the reaction rate was studied by varying the $NaClO_4$ concentration in a range of 0.10—0.50 mol/L, keeping the other experimental conditions constant. The rate was found to increase with increase in ionic strength of the medium (Table 2) and plots of log *k′* vs. $I^{1/2}$ were linear ($r > 0.9948$) with positive slopes (0.40 to 0.60). Hence,

Table 1 Effect of varying oxidant, substrate and NaOH concentrations on the reaction rate at 308 K

10^3 [CAT]$_o$/ (mol•L^{-1})	10^2 [DPP]$_o$/ (mol•L^{-1})	10^3 [NaOH]/ (mol•L^{-1})	10^4 k'/s^{-1}				
			Gly-Gly	Leu-Leu	Val-Val	Ala-Ala	Phg-Phg
0.5	1.0	1.0	1.95	5.28	8.44	10.5	12.9
0.7	1.0	1.0	1.98	5.20	8.38	10.4	12.7
1.0	1.0	1.0	1.90	5.25	8.42	10.5	12.8
2.0	1.0	1.0	1.92	5.30	8.35	10.6	12.8
4.0	1.0	1.0	1.85	5.32	8.32	10.4	12.7
1.0	0.3	1.0	0.47	1.30	2.10	2.24	2.92
1.0	0.5	1.0	0.90	2.64	4.22	5.02	6.04
1.0	1.0	1.0	1.90	5.25	8.42	10.5	12.8
1.0	2.0	1.0	3.82	10.4	16.9	20.6	25.2
1.0	4.0	1.0	7.59	21.0	32.9	40.4	47.9
1.0	1.0	0.3	0.96	2.61	4.02	5.31	6.05
1.0	1.0	0.5	1.31	3.57	5.71	7.30	8.70
1.0	1.0	1.0	1.90	5.25	8.42	10.5	12.8
1.0	1.0	2.0	2.51	7.46	11.8	14.5	19.0
1.0	1.0	4.0	3.54	10.5	16.6	20.7	28.2

I=0.3 mol•L^{-1}.

Table 2 Effect of varying ionic strength of the medium on the reaction rate at 308 K

I/ (mol•L^{-1})	10^4 k'/s^{-1}				
	Gly-Gly	Leu-Leu	Val-Val	Ala-Ala	Phg-Phg
0.1	1.02	4.10	6.0	8.08	9.21
0.2	1.41	4.70	7.44	9.11	10.9
0.3	1.90	5.25	8.42	10.5	12.8
0.4	2.31	5.72	9.03	11.5	14.2
0.5	4.05	6.21	9.90	12.6	15.6

[CAT]$_o$=1.0×10^{-3} mol•L^{-1}; [DPP]$_o$=1.0×10^{-2} mol•L^{-1}; [NaOH]=1.0×10^{-3} mol•L^{-1}.

the ionic strength of the medium was maintained at a high concentration of 0.30 mol/L of $NaClO_4$ for all kinetic runs in order to swamp the reaction.

Addition of *p*-toluenesulfonamide, a reduction product of CAT ($TsNH_2$; 5.0×10^{-4}—5.0×10^{-3} mol/L) to the reaction mixture did not affect the rate significantly. This indicates that *p*-toluenesulfonamide is not involved in any step prior to the rate limiting step in the scheme proposed. Addition of Cl^- or Br^- ions in the form of NaCl or NaBr (1.0×10^{-3}—5.0×10^{-3} mol/L) had no effect on the rate, signifying that no interhalogen or free chlorine is formed in the reaction sequence.

As the rate was dependent on [OH^-], solvent isotope studies were made using D_2O as the solvent medium. The values of k' (H_2O) are 1.90×10^{-4}, 5.25×10^{-4}, 8.42×10^{-4}, 10.5×10^{-4}, 12.8×10^{-4} s^{-1} and those of k' (D_2O) are 2.42×10^{-4}, 6.44×10^{-4}, 9.85×10^{-4}, 13.2×10^{-4}, 15.3×10^{-4} s^{-1}, leading to solvent isotope effect, $k'(H_2O)/k'(D_2O)$, of 0.78, 0.81, 0.85, 0.80, 0.84 for Gly-Gly, Leu-Leu, Val-Val, Ala-Ala and Phg-Phg, respectively.

The effect of temperature on the rate was studied by performing the kinetic runs at various temperatures (298—318 K), keeping other experimental conditions constant. From the Arrhenius plots of log k' vs. 1/T, values of activation parameters (E_a, $\Delta H^{\neq}$, $\Delta G^{\neq}$ and $\Delta S^{\neq}$) were computed and these results are summarized in Table 3. Addition of reaction mixture to acrylamide did not initiate polymerization showing the absence of free radicals.

Reactive oxidizing species

Chloramine-T acts as an oxidizing agent in both acidic and alkaline media. In general, CAT undergoes a two-electron change in its reactions. The reduction potential of CAT/$TsNH_2$ is pH dependent and decreases with increase in the pH of the medium, having values of 1.14 V at pH 0.65 and 0.5 V at pH 12. Chloramine-T (TsNClNa) behaves like a strong electrolyte[11] in aqueous solution and depending on the pH, it furnishes different types of reactive species [Eqs. (2)—(7)], such as TsNHCl, $TsNCl_2$, HOCl, and possibly H_2OCl^+ in acid solutions.[8,11-13]

$$TsNClNa \rightleftharpoons TsNCl^- + Na^+ \quad (2)$$

$$TsNCl^- + H_2O \rightleftharpoons TsNHCl + OH^- \quad (3)$$

$$2TsNHCl \rightleftharpoons TsNCl_2 + TsNH_2 \quad (4)$$

$$TsNHCl + H_2O \rightleftharpoons TsNH_2 + HOCl \quad (5)$$

$$HOCl \rightleftharpoons H^+ + OCl^- \quad (6)$$

$$HOCl + H^+ \rightleftharpoons H_2OCl^+ \quad (7)$$

In alkaline solutions of CAT, $TsNCl_2$ does not exist, and the possible oxidizing species are $TsNCl^-$ and

Table 3 Effect of varying temperature on the reaction rate and values of activation parameters for the oxidation of dipeptides by CAT in NaOH medium

Temperature/K	$10^4\ k'/s^{-1}$				
	Gly-Gly	Leu-Leu	Val-Val	Ala-Ala	Phg-Phg
298	0.62	1.92	3.15	5.50	6.35
303	1.05	3.22	5.22	8.08	9.55
308	1.90	5.25	8.42	10.5	12.8
313	3.72	9.72	12.7	18.4	19.8
318	6.95	15.6	21.6	28.2	29.2
E_a/(kJ•mol^{-1})	99.3	83.0	75.8	66.9	60.7
$\Delta H^{\neq}$/(kJ•mol^{-1})	96.7	80.4	73.2	64.3	58.1
$\Delta S^{\neq}$/(J•K^{-1}•mol^{-1})	−41.9	−46.5	−66.3	−92.4	−111
$\Delta G^{\neq}$/(kJ•mol^{-1})	95.3	94.8	93.5	93.7	93.5

$[CAT]_o = 1.0\times10^{-3}$ mol•L^{-1}; $[DPP]_o = 1.0\times10^{-2}$ mol•L^{-1}; $[NaOH] = 1.0\times10^{-3}$ mol•L^{-1}; $I = 0.3$ mol•L^{-1}.

OCl^- anions, which could be transformed into more reactive species, TsNHCl and HOCl, during the course of the reaction in alkali retarding steps. Several workers have observed the retarding influence of OH^- ions on the rate of haloamine reactions with a number of substrates[13-20] and have suggested that the reactivity of weakly alkaline solutions of haloamines is due to the formation of the conjugate acid TsNHCl from $TsNCl^-$ in the OH^- retarding step. But in the present investigations, OH^- increases the rate of the reaction which clearly indicates that $TsNCl^-$ is the reactive oxidizing species. The positive influence of OH^- ion on the rate of haloamine reactions with a number of substrates has been observed and RNX^- (R = Ts or $PhSO_2$; X = Cl or Br) has been postulated as the reactive oxidizing species in our earlier work.[21-24] Bearing these facts in mind, the following general mechanism (Scheme 1) was proposed for the oxidation of the dipeptides by CAT in NaOH medium to account the observed kinetics.

Scheme 1 A general mechanistic path way for the oxidation of dipeptides by CAT in alkaline medium

(i) fast

$$TsNHCl + OH^- \underset{}{\overset{K_1}{\rightleftharpoons}} TsNCl^- + H_2O$$

(ii) slow and rate determining step (rds)

$$TsNCl^- + DPP \xrightarrow{k_2} X_{(Complex)}$$

(iii) fast

$$X + TsNCl^- \xrightarrow{k_3} Products$$

Scheme 2 indicates the electron flow during the oxidation of the dipeptides by CAT in the alkaline medium.

If $[CAT]_t$ represents the total effective concentration of CAT, then

$$[CAT]_t = [TsNHCl] + [TsNCl^-] \quad (8)$$

From step (i) of Scheme 1,

$$[TsNHCl] = \frac{[TsNCl^-][H_2O]}{K_1[OH^-]} \quad (9)$$

By substituting for [TsNHCl] from Eq. (9) into Eq. (8) and solving for $[TsNCl^-]$, one obtains,

$$[TsNCl^-] = \frac{K_1[CAT]_t[OH^-]}{[H_2O] + K_1[OH^-]} \quad (10)$$

From the slow and rate determining step of Scheme 1, the rate of reaction is given as

$$Rate = k_2[DPP][TsNCl^-] \quad (11)$$

By substituting for $[TsNCl^-]$ from Eq. (10) into Eq. (11), the following rate law is obtained:

$$Rate = \frac{K_1k_2[DPP][CAT]_t[OH^-]}{[H_2O] + K_1[OH^-]} \quad (12)$$

Since rate $= k'[CAT]_t$, Eq. (12) can be transformed into Eqs. (13) and (14):

$$k' = \frac{K_1k_2[DPP][OH^-]}{[H_2O] + K_1[OH^-]} \quad (13)$$

$$\frac{1}{k'} = \frac{[H_2O]}{K_1k_2[DPP][OH^-]} + \frac{1}{k_2[DPP]} \quad (14)$$

Based on Eq. (14), plots of $1/k'$ vs. $1/[OH^-]$ were found to be linear ($r > 0.9899$) and from the slopes and intercepts of such plots, the values of equilibrium constant (K_1) and decomposition constant (k_2) have been evaluated for each dipeptide. The values of K_1 and k_2 have been listed in Table 4. Scheme 1 and rate law (12) is in accordance with the experimental kinetic findings and are substantiated by the following factors.

Scheme 2 A detailed mechanistic interpretation for the oxidation of the dipeptides by CAT in NaOH medium

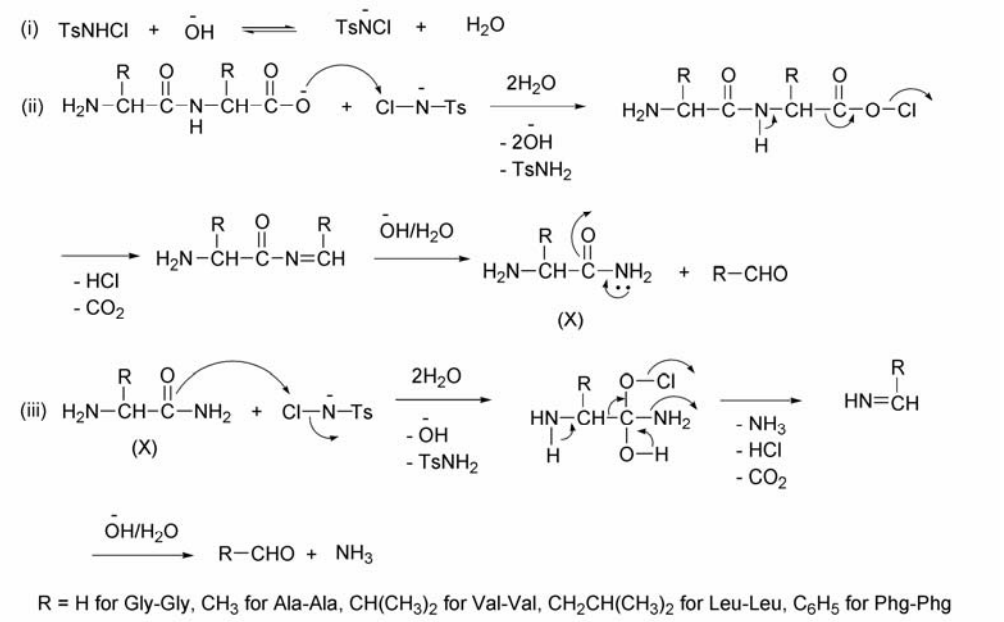

Table 4 Values of equilibrium constants (K_1) and decomposition constants (k_2) calculated from Eq. (14)

Dipeptide	$10^{-3}\,K_1$	k_2/(L•mol^{-1}•s^{-1})
Gly-Gly	4.70	0.10
Leu-Leu	2.34	0.25
Val-Val	1.80	0.33
Ala-Ala	1.12	0.40
Phg-Phg	0.90	0.50

Effect of solvent isotope

It is interesting to note that the rate is only slightly increased in D_2O medium [$k'(H_2O)/k'(D_2O) = 0.78$—0.85]. For a reaction involving a fast equilibrium of H^+ or OH^- ion transfer, the rate increases in D_2O medium since D_3O^+ and OD^- are a stronger acid and a stronger base respectively, than H^+ and OH^- ions[25,26] by a factor of 2 to 3 and a solvent isotope effect of this magnitude is to be expected. In the present investigations, the only slight increase of rate in D_2O medium probably indicates that OH^- ion is involved in an equilibrium (Scheme 1) and only a part of the reaction proceeds through a pH dependent path. Also, the observed magnitude of solvent isotope effect can be attributed to the fractional-order dependence of rate on [OH^-].

Effect of ionic strength

The ionic strength (I) effect on the reaction rates has been described according to the theory of Bronsted and Bjerrum,[27] which postulates the reaction through the formation of an activated complex. According to this theory, the effect of ionic strength on the rate of a reaction involving two ions is given by the relationship

$$\log k' = \log k_o + 1.02 Z_A Z_B I^{1/2} \quad (15)$$

Here Z_A and Z_B are the valencies of the ions A and B, and k and k_o are the rate constants in the presence and absence of the added electrolyte, respectively. A plot of log k' against $I^{1/2}$ should be linear with a slope of 1.02 Z_AZ_B. If Z_A and Z_B have similar signs, the quantity Z_AZ_B is positive and the rate increases with the ionic strength, having a positive slope, while if the ions have dissimilar charges, the quantity Z_AZ_B is negative and the rate would decrease with the increase in ionic strength, having a negative slope. In the present case, a primary salt effect was observed (Table 2) as the rate increases with increase in ionic strength of the medium,[27] supporting the involvement of ions of similar sign in the rate determining step (Scheme 2). The Debye-Huckel plots (log k' against $I^{1/2}$) gave straight lines with slopes between 0.4 to 0.6. In the present system, two negative ions are involved in the rate determining step (Scheme 2) and the expected value of slope = 1 has not been found. This may be due to the fact that the ionic strength employed is beyond the formal Debye-Huckel limiting range. Alternatively, there could be formation of ion pairs in concentrated solutions, as suggested by Bjerrum.[27]

Reactivity of dipeptides

From the inspection of rate data (Table 3), the rate of oxidation of the dipeptides follows the order Phg-Phg > Ala-Ala > Val-Val > Leu-Leu > Gly-Gly. In case of Phg-Phg, the formation of the intermediate complex (X) by ready decarboxylation is favoured due to resonance stabilization and extended conjugation. In cases of Ala-Ala, Val-Val and Leu-Leu, the presence of alkyl groups due to an inductive effect (+I) facilitates these dipeptides to react more readily with the oxidant. However, a steric interaction between the alkyl chain and the oxidant greatly affects the rate of decarboxylation and

hence the order has been found to be: Ala-Ala＞Val-Val ＞Leu-Leu. In the case of Gly-Gly because the $+I$ and resonance effects are at a minimum, it was found to be least reactive among all the dipeptides studied, and the overall reactivity of these dipeptides has been found to be Phg-Phg＞Ala-Ala＞Val-Val＞Leu-Leu＞Gly-Gly.

Isokinetic relationship

It is seen from Table 3 that the activation energy is highest for the slowest reaction and *vice-versa*, indicating that the reaction is enthalpy controlled. This was verified by calculating the isokinetic temperature (β) from the slope of a linear plot of $\Delta H^{\neq}$ vs. $\Delta S^{\neq}$ (r= 0.9917). The β value of 352 K, which is higher than the temperature range (298—318 K) used in the present study, implies that the dipeptide oxidation is enthalpy controlled. A further confirmation of the existence of isokinetic relationship was inferred from the Exner criterion[28] by plotting log $k'_{(298\ K)}$ vs. log $k'_{(308\ K)}$ which yielded a linear plot (r=0.9955). The value of β was calculated from the equation $\beta=T_1(1-q)/[(T_1/T_2)-q]$, where q is the slope of the Exner plot; β was found to be 354 K. The moderate energy of activation supports the proposed mechanism. The negative values of entropy of activation point towards the formation of a more ordered activation complex while the near constant values of free energy of activation indicate that all the five dipeptides are oxidized by a similar mechanism.

Comparison of reactivity of dipeptides with their monomers

It was thought necessary to compare the rate of oxidation of these dipeptides with the oxidation of their monomers (phenylglycine, valine, alanine, leucine and glycine) under identical experimental conditions. The rate of oxidation of amino acids increased in the order phenylglycine ＞ alanine ＞ valine ＞ leucine ＞ glycine (Table 5), while in the case of the dipeptides the order was found to be Phg-Phg ＞ Ala-Ala ＞ Val-Val ＞ Leu-Leu＞Gly-Gly. It was also found that the rates of oxidation of the amino acids were about 9-fold faster than those of the dipeptides, under identical experimental conditions. The change in each case can be attributed to the increased distance between the functional groups and consequently weaker electrostatic effects in the dipeptides. In the case of the dipeptides, a lone pair of electron on nitrogen [Scheme 2; (X)] is involved in resonance with the carbonyl group. Therefore, its nucleophilic character will decrease and hence the rate decreases, whereas in the case of monomer amino acids there is no decrease in nucleophilic character and hence the rate is much faster than those of the dipeptides. The decrease in the rate for the dipeptides compared to their monomers may also be due to decreased ionization of COOH group, which is evidenced by the increase in pK_1 values (*eg*. glycine pK_1=2.4; Gly-Gly pK_1=3.4). Since the availability of the COOH group for this reaction is trivial to determine the rate, the rate concurrently decreases due to lower acidity, resulting from the decrease of the dissociative ability of the COOH group and, hence, a decrease in the rate of the reaction was observed in case of the dipeptides. The same argument also holds good for the other four dipeptides studied.

The zero effect of halide ions on the rate indicates that no interhalogen or free chlorine is formed. The reduction product of oxidant, *p*-toluenesulfonamide, does not influence the rate, showing that it is not involved in a pre-equilibrium. These observations are also in conformity with the proposed mechanism.

Conclusion

The kinetics of oxidation of five dipeptides *viz.*, glycylglycine, *L*-alanyl-*L*-alanine, *L*-valyl-*L*-valine, *L*-leucyl-*L*-leucine and phenylglycyl-phenylglycine by chloramine-T in NaOH medium follows the identical kinetics with a rate law: $-\mathrm{d[CAT]}/\mathrm{d}t=k[\mathrm{CAT}]_o[\mathrm{DPP}]_o[\mathrm{OH}^-]^x$ where x is less than unity. The reaction rate was found to increase with increase in ionic strength of the medium. Activation parameters and the equilibrium and decomposition constants have been determined. The anion $CH_3C_6H_4SO_2NCl^-$ has been postulated as the oxidizing reactive species. The rate of

Table 5 Effect of varying temperature on the reaction rate and values of activation parameters for the oxidation of amino acids (AA) by CAT in NaOH medium

Temperature/K	$10^3\ k'/s^{-1}$				
	Gly-Gly	Leu-Leu	Val-Val	Ala-Ala	Phg-Phg
298	0.72	2.15	4.10	5.05	7.10
303	1.10	3.20	6.05	6.90	9.50
308	1.75	4.80	8.20	9.85	11.6
313	2.89	7.92	12.3	14.0	16.5
318	4.30	11.8	18.1	18.2	22.2
E_a/(kJ•mol^{-1})	73.9	68.1	56.8	53.0	46.5
$\Delta H^{\neq}$/(kJ•mol^{-1})	71.1	65.5	54.2	50.4	43.9
$\Delta S^{\neq}$/(J•K^{-1}•mol^{-1})	−67.0	−76.5	−109	−120	−139
$\Delta G^{\neq}$/(kJ•mol^{-1})	91.8	89.2	87.7	87.3	86.7

$[\mathrm{CAT}]_o=1.0\times10^{-3}$ mol•L^{-1}; $[\mathrm{AA}]_o=1.0\times10^{-2}$ mol•L^{-1}; $[\mathrm{NaOH}]=1.0\times10^{-3}$ mol•L^{-1}; I=0.3 mol•L^{-1}.

oxidation of the dipeptides has been found to be in the order: Phg-Phg > Ala-Ala > Val-Val > Leu-Leu > Gly-Gly. The kinetics of oxidation of the dipeptides have also been compared with those of their corresponding monomer amino acids and it was found that the rates of oxidation of amino acids were about 9-fold faster than those of their corresponding dipeptides. The observed results have been explained by a plausible mechanism and the related rate law has been deduced.

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