Chloraminometric Reactions: Kinetics and Mechanisms of Oxidations of Amino-acids by Sodium *N*-Chlorotoluene-*p*-sulphonamide in Acid and Alkaline Media

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Available data on the kinetics of oxidations of amino-acids by sodium *N*-chloro toluene-*p*-sulphonamide (chloramine T) in acid and alkaline media have been critically examined. General mechanisms have been proposed for both acid and alkaline medium oxidations. The oxidation process in acid media has been shown to proceed *via* two paths, one involving the direct interaction of *N*-chlorotoluene-*p*-sulphonamide (RNHCl) with the neutral amino-acid in a slow step leading to the formation of the monochloroamino-acid which subsequently interacts with another molecule of RNHCl, in a fast step, to give the *NN*-dichloroamino-acid which in turn undergoes molecular rearrangement and elimination to yield the products, and the other involving the interaction of Cl_2 or H_2OCl^+, produced from the disproportionation of RNHCl in the presence or absence of Cl^-, with the substrate to give the products. In the alkaline medium mechanisms involving the interaction of RNHCl, HOCl, $RNCl^-$, and OCl^- with the substrate are proposed. The mechanisms proposed and the derived rate laws are consistent with the observed kinetics. The rate constants predicted by the derived rate laws, as the concentrations of substrate and Cl^- ion change, are in excellent agreement with the observed rate constants thus further verifying the rate laws and hence the proposed mechanisms.

Recently considerable attention has been focused on the chemistry of *N*-halogeno- and *N*-metalo-reagents.[1] The diverse nature of the chemistry of these compounds is due to their ability to act as sources of halogenonium cations, hypohalite species, and nitrogen anions which act both as bases and nucleophiles. The potential applications of these compounds remain largely unrealised as is evident by the scant information available in the literature. Any addition to existing knowledge is useful in exploring the properties of related compounds and is also of interest to those studying the physicochemical aspects of reactions involving halogeno-cations. This paper intends to outline the characteristics of this class of compounds with special emphasis on the physicochemical properties of organic halogenoamines.

Sodium *N*-chlorotoluene-*p*-sulphonamide, $p\text{-}CH_3C_6H_4SO_2NClNa,3H_2O$, generally known as chloramine T (CAT), is a very important member of this class of organic *N*-halogenoamines. It behaves both as a chlorinating and an oxidizing agent in both acidic and alkaline media. Generally CAT undergoes a two-electron change in its reactions, the products being toluene-*p*-sulphonamide (PTS) and sodium chloride.[2] The redox potential of CAT–PTS is pH dependent and decreases with an increase in the pH of the medium (E_{redox} 1.138, 0.778, 0.614, and 0.5 V at pH 0.65, 7.0, 9.7, and 12, respectively). Depending on the pH of the medium CAT furnishes different types of reactive species in solution.[3] *N*-Chlorotoluene-*p*-sulphonamide (monochloramine T, RNHCl, where $R = p\text{-}CH_3C_6H_4SO_2$), dichloramine T ($RNCl_2$), HOCl, and possibly H_2OCl^+ are the predominant species in acid solution and $RNCl^-$ and OCl^- ions are formed in alkaline solution. Free chlorine has also been detected in acid medium when chloride ion is present.[4] Although there are few kinetic investigations reported in the literature [5–13] in many cases the mechanisms proposed to account for the results are inconsistent. So we thought it is worthwhile to re-examine these mechanisms. The main object was to elucidate suitable mechanisms and put forward rate laws consistent with the experimental data with a view to shedding more light on the mechanisms of oxidation reactions involving aromatic sulphonyl-halogenoamines in general and chloramine T in particular. In this paper we discuss oxidation kinetics of amino-acids by CAT in acid and alkaline media.

$$\underset{S^-}{R'CH(NH_2)COO^-} \underset{OH^-}{\overset{H^+}{\rightleftharpoons}} \underset{S^\circ}{R'CH(NH_3^+)COO^-} \underset{OH^-}{\overset{H^+}{\rightleftharpoons}} \underset{SH^+}{R'CH(NH_3^+)COOH} \quad (1)$$

Anion Zwitterion Cation

Several workers have studied the kinetics of oxidation of amino-acids by a number of oxidants.[14–18] Some work on the action of chlorine and hypochlorite on free amino-acids has been reported, but in most cases there is no adequate explanation for the reactions of these compounds with chlorine.[16–18] Although the kinetics of oxidation of a number of amino-acids with chloramine T in both acidic and alkaline media have been reported,[9,12] the mechanisms proposed to account for the experimental results are inconsistent as the results, at that time, were insufficient to permit generalization.

The chemistry of amino-acids $R'CH(NH_2)COOH$ consists of transformations of functional groups already present in these molecules,[19] their (intact) hydrocarbon portions (R') have not been subjected to chemical reactions. The reason for this is obviously the high reactivity of the functional groups relative to the inertness of the hydrocarbon chain.

The dissociation of amino-acids depends on the pH of the medium. In strongly acidic or alkaline media the equilibria (1) exist.

Results

The stoicheiometry of the reactions and available kinetic and thermodynamic data for the oxidation of several amino-acids

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Table 1. Kinetic data for the oxidation of amino-acids by chloramine T in the acid media

Amino-acid [a]	Observed order with respect to [Amino-acid]	Observed order with respect to [H^+]	Thermodynamic parameters * E_a/kJ mol^{-1}	log A	$\Delta S^{\ddagger}$/ J mol^{-1} K^{-1}	$\Delta H^{\ddagger}$/ kJ mol^{-1}	$\Delta G^{\ddagger}$/ kJ mol^{-1}	T/K
Hydrochloric acid medium (*ca.* 0.003—0.10M)								
Alanine	0	1	69	10.7	−44	66	80	303—313
Phenylalanine	0	1	65	10.3	−52	62	78	303—313
Leucine	0	1	76	11.1	−36	73	84	303—318
Glutamine	0	1	71	10.2	−53	68	84	303—318
Glutamic acid	1	1	76	11.4	−31	73	83	298—318
Serine [b]	0	1	91	13.6	11	88	85	303—318
Lysine [b]	0	1	93	13.8	16	90	85	303—318
Histidine	0	1	70	10.5	−84	67	93	303—318
Arginine	1	1	93	14.9	−1	93	93	303—318
Threonine	0.5	−0.4	77	10.3	−57	74	92	303—318
Hydrochloric acid medium (*ca.* 0.06—0.30M)								
Glycine	1	−1	89	11.7	−25	86	94	308—320
Valine	1	−1	110	16.8	73	108	85	306—315
Hydrochloric acid medium (*ca.* 0.14—0.40M)								
Alanine	1	0	101	15.9	56	98	81	303—313
Phenylalanine	1	0	103	16.5	67	100	80	303—313
Arginine	0.6	0	100	15.9	19	97	91	303—318
Histidine	0.7	0	66	10.5	−86	64	90	303—318
Perchloric acid medium (*ca.* 0.01—0.10M)								
Leucine	1	−1	87	11.5	−29	84	93	303—321
Glutamine	1	−1	89	11.7	−23	86	94	303—319
Glutamic acid	1	−1	70	8.2	−22	67	96	303—319
Serine [b]	1	−1	102	14.2	22	99	93	301—309
Arginine	1	−1	47	6.2	−167	45	100	303—318
Histidine	0	0.6	59	8.4	−125	57	95	303—318
Threonine	0.5	−0.6	77	9.8	−67	74	95	303—318
Sulphuric acid medium (*ca.* 0.02—0.20M)								
Leucine	1	−1	71	9.1	−74	69	91	302—314
Glutamine	1	−1	65	7.8	−99	63	94	302—314
Glutamic acid	1	−1	68	8.6	−85	66	92	302—314
Serine [b]	1	−1	68	8.5	−86	66	92	302—314
Arginine	1	−1	43	6.2	−167	40	92	303—318
Threonine	0.5	−0.4	75	9.6	−71	72	94	303—318

[a] Unless stated otherwise, CAT : amino-acid observed stoicheiometry is 2 : 1. Reactions are first order in [chloramine T]. [b] CAT : amino-acid observed stoicheiometry is 3 : 1. Reactions are first order in [Chloramine T].

* Thermodynamic parameters were determined in presence of Cl^- ion in HCl medium and in the absence of Cl^- ion in the other acid media.

by CAT in acid and alkaline media are compiled in Tables 1 and 2. The stoicheiometry of the reactions is given by equations (2) [for glycine, valine, alanine, phenylalanine, leucine, glutamine, glutamic acid, arginine, histidine, serine (alkaline medium), and threonine] and (3) [for serine (acid medium) and lysine]. For proline reaction (4) takes place.

Generally the decrease in dielectric constant by adding methanol retards the rate (except in the case of alanine, phenylalanine, arginine, and histidine in high HCl concentrations and histidine and threonine in alkaline medium where the rate is slightly increased). The variation of the ionic strength of the medium or addition of the product toluene-*p*-sulphonamide has negligible effect. The rates at different temperatures have been measured and the energies of activation, Arrhenius parameters, and enthalpies, entropies, and free energies of activation have been computed in all cases.[9,12] In some cases kinetic isotope effects have also been investigated.[12]

Discussion

In the light of the available data, we try to generalise the mechanism of the oxidation of amino-acids by chloramine T in both acid and alkaline media. It is interesting to note that the rate constants are almost of the same order of magnitude in the acid medium with the exception of two or three amino-acids (Table 3), irrespective of the acid employed and orders observed with respect to each of the reactants. This is not surprising as these amino-acids have almost the same pK values (Table 4). In alkaline medium, as expected, the rate constants are small (except for histidine and threonine) and slightly differ for different amino-acids. All reactions in acid media have been studied at 30 and 35 °C and in the alkaline medium at 35, 40, and/or 45 °C.

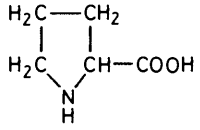
Chloramine T behaves like a strong electrolyte [3] in aqueous solutions and dissociates according to equation (5). The anion picks up a proton in acid solutions to give the free acid

Table 2. Kinetic data for the oxidation of amino-acids by chloramine T in alkaline media

		Stoicheiometry	Observed order with respect to									
Amino-acid	t/°C	[CAT]:[amino-acid]	[CAT]	[Amino-acid]	$[OH^-]$	$[Cl^-]$	E_a/kJ mol^{-1}	log A	$\Delta S^{\ddagger}$/J mol^{-1} K^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta G^{\ddagger}$/kJ mol^{-1}	T/K
Glycine	40	2:1	1	1	−0.90	0	62	6.0	−136	59		308—328
	45	2:1	1	1	−0.92	0						
Valine	40	2:1	1	1	−0.81	0	72	8.0	−96	70		308—333
	45	2:1	1	1	−0.79	0						
Leucine	40	2:1	1	1	−0.98	0	59	5.4	−147	56		308—328
	45	2:1	1	1	−0.97	0						
Alanine	40	2:1	1	1	−0.83	0	69	7.5	−105	67		308—328
	45	2:1	1	1	−0.82	0						
Phenylalanine	40	2:1	1	1	−0.94	0	39	2.0	−212	36	103	308—328
	45	2:1	1	1	−0.96	0						
Serine	40	2:1	1	1	−0.96	0	44	3.2	−188	41	101	308—328
	45	2:1	1	1	−0.98	0						
Proline	35	2:1	1	1	−0.96	0	61	7.7	−103	60	93	303—323
	40	2:1	1	1	−0.94	0						
Arginine	35	2:1	1	1	−0.79	0	125	19.4	86	122	95	303—323
Histidine	35	2:1	1	1	−0.67	0	96	15.2	4	93	92	303—323
Threonine	35	2:1	1	1	0	0	120	18.9	77	117	93	303—323

$$R'CH(NH_2)COOH + 2\ RNNaCl \longrightarrow R'CN + CO_2 + 2\ RNH_2 + 2\ Na^+ + 2\ Cl^- \quad (2)$$

$$R''CH(NH_2)COOH + 3\ RNNaCl + H_2O \longrightarrow R''CNO + 3\ RNH_2 + CO_2 + 3\ Na^+ + 3\ Cl^- \quad (3)$$



$$+ 2RNNaCl \longrightarrow H_2C{=}CHCH_2CN + 2\ RNH_2 + CO_2 + 2\ Na^+ + 2\ Cl^- \quad (4)$$

monochloramine T [reaction (6)].[20] Although the free acid has not been isolated there is experimental evidence for its formation in acid solutions.[3] It undergoes disproportionation giving rise to toluene-*p*-sulphonamide and dichloramine T.[21] Dichloramine T and the free acid hydrolyse to give hypochlorous acid (HOCl).[22] Finally HOCl ionizes according to reaction (10). Free chlorine has also been detected in acid medium in the presence of chloride ion.[4] It may probably be formed through steps (11) or (12). Therefore the possible oxidizing species in acidified CAT solution are RNHCl, $RNCl_2$, HOCl, Cl_2, and probably H_2OCl^+ and in the alkaline solution RNHCl, HOCl, $(RNCl)^-$, and OCl^-. Bishop and Jennings [3] have calculated the order of the concentrations of the various species present at different pH in a 0.05M solution of chloramine T (see Table 5).

As can be seen from Table 5, the RNHCl concentration in acid solutions with pH < 1.5 or $[H^+] > 0.03$M is almost constant and hence insensitive to increases in $[H^+]$ beyond *ca.* 0.03M. Almost all amino-acids reactions with CAT have been studied in the acid medium with $[H^+]$ generally >0.03M. So under these experimental conditions, it is quite unlikely that a slight increase in RNHCl concentration with increase in acid concentration could account for the observed first-order dependence on $[H^+]$. Although, earlier, under particular circumstances we attributed the first-order dependence of $[H^+]$ to the formation of RNHCl [equation (6)] to account for the observed kinetics of the reactions of alcohols with chloramine T,[23] after studying a number of reactions with the latter we found that if this assumption is valid we cannot propose consistent mechanisms for all other reactions.[24] Therefore we looked at different schemes to generalise these mechanistic studies. This we felt was essential as amino-acid reactions are of great interest.

I. *Mechanisms in Acid Media.*—As discussed before, in acid solutions of CAT, RNHCl, $RNCl_2$, and HOCl are the probable oxidizing species. If $RNCl_2$ were to be the reactive species in the oxidation of amino-acids then the rate law predicts a second-order dependence of rate on CAT, which is contrary to the experimental observations. Equation (9) indicates that the hydrolysis of RNHCl to give HOCl takes place to only a small extent and if HOCl is involved, a first-order retardation of rate by the added toluene-*p*-sulphonamide is expected. But no such effect was noticed. First approximation calculations by Bishop and Jennings on 0.1M solutions of CAT have shown that the concentrations of RNHCl and HOCl are *ca.* 10^{-2} and 10^{-7}M, respectively, at pH *ca.* 0—3 (Table 5). Soper *et al.*[22,25] have stated that the direct interaction of RNHCl with the substrate could be slow while HOCl formed by the hydrolysis of RNHCl and $RNCl_2$ would attack at a faster rate. This has been recently disproved by Swain and Crist [26] who have shown that HOCl is relatively unreactive and Cl_2, H_2OCl^+, Cl_2O, and possibly Cl^+ formed from HOCl are relatively more reactive species. So under the experimental conditions in which amino-acid reactions with CAT in acid media were studied, RNHCl is the only probable oxidising species which reacts with the substrates in different pathways depending on the presence or absence of Cl^- in the reaction mixtures. In the presence of Cl^-, Cl_2 formed from RNHCl is the most likely oxidising species. Since it is an effective chlorinating agent [27] it attacks the substrate in a fast step. In the absence of Cl^-, H_2OCl^+ formed from RNH_2Cl^+ attacks the substrate also in a fast step.

Table 3. Rate constants (10^4 k_{obs}/s^{-1}) at various amino-acid concentrations in acid and alkaline media

[Amino-acid]/M	Lysine [a] [CAT] 0.003M [HCl] 0.05M	Leucine [a] [CAT] 0.003M [HCl] 0.05M
0.01	3.78	
0.02	3.87	4.79
0.03	3.75	4.67
0.04	3.81	4.80

[Amino-acid]/M	Serine [a] [CAT] 0.003M [HCl] 0.05M	Glutamine [a] [CAT] 0.003M [HCl] 0.05M
0.03	3.41	5.63
0.04	3.46	5.54
0.05	3.44	5.65
0.06	3.49	5.57

	Arginine [a] [CAT] 0.002M [HCl] 0.05M	Histidine [a] [CAT] 0.002M [HCl] 0.07M
0.01	2.54	5.91
0.02	4.61	6.08
0.03	6.60	6.08
0.04	8.96	6.08

	Arginine [a] [CAT] 0.002M [HCl] 0.3M	Histidine [a] [CAT] 0.002M [HCl] 0.22M
0.01	7.70	14.40
0.02	11.62	22.44
0.03	14.62	28.15
0.04	17.34	32.02

	Glutamic acid [a] [CAT] 0.001M [$HClO_4$] 0.01M	Threonine [b] [CAT] 0.002M [$HClO_4$] 0.05M
0.01		3.78
0.02		5.54
0.03	3.99	6.85
0.04	4.88	7.56
0.05	6.94	7.98
0.06	8.30	

	Leucine [b] [CAT] 0.003M [H_2SO_4] 0.05M	Serine [b] [CAT] 0.003M [H_2SO_4] 0.05M
0.030	3.74	2.60
0.050	6.39	4.39
0.075	9.27	6.52
0.100	12.50	8.73

	Leucine [c] [CAT] 0.001M pH 11.5	Proline [c] [CAT] 0.001M [NaOH] 0.158M
0.006	0.86	1.28
0.010	1.38	2.08
0.014	1.92	3.02
0.020	2.40	4.23
0.030	3.26	

	Histidine [b] [CAT] 0.002M [NaOH] 0.005M	Threonine [b] [CAT] 0.002M [NaOH] 0.005M
0.005	4.70	2.50
0.010	8.31	
0.020	15.57	9.18
0.030	22.18	13.50

[a] At 30 °C. [b] At 35 °C. [c] At 40 °C.

Table 4. Ionization constants and pH values at the isoelectric points of amino acids at 25 °C

Amino-acid	pK_1	pK_2	pK_3	pH_I[a]
Alanine	2.34	9.69		6.01
Arginine [b]	2.17	9.04	12.48	10.76
Glutamic acid	2.16	4.32	9.96	3.24
Glutamine	2.17	9.13		5.65
Glycine	2.34	9.60		5.97
Histidine [b]	1.82	6.00	9.17	7.59
Leucine	2.36	9.60		5.98
Lysine [b]	2.18	9.12	10.53	9.82
Phenylalanine	1.83	9.13		5.48
Proline	1.99	10.60		6.30
Serine	2.21	9.15		5.68
Threonine	2.71	9.62		6.16
Valine	2.32	9.62		5.96

[a] Isoelectric point (or I.P.). This is the pH at which the maximum number of amino-acid molecules are present as zwitterions. For neutral and acidic amino-acids $pH_I = (pK_1 + pK_2)/2$; for basic amino-acids $pH_I = (pK_2 + pK_3)/2$. [b] Basic amino-acid.

(a) *At low hydrochloric acid concentrations* (ca. 0.05M). The rate of oxidation of amino-acids (alanine, phenylalanine, leucine, glutamine, serine, lysine, and histidine) shows first-order dependence on [CAT] and $[H^+]$, fractional order on $[Cl^-]$, and zero order on [amino-acid]. Under these conditions, direct interaction of RNHCl with the substrate is unlikely since the rate is independent of the substrate concentration. It is quite likely that RNHCl picks up a proton to form protonated monochloramine T, which subsequently interacts with Cl^- in a slow step to give molecular chlorine followed by a rapid interaction of the latter with the substrate. The overall reaction may be represented as in Scheme 1.

Addition of the product toluene-*p*-sulphonamide has a negligible effect thus indicating the unimportance of the backward reaction of the rate-determining step. S′ is the *N*-chloro-derivative of the substrate. Many investigators have observed or proposed the formation of *N*-chloro-derivatives as intermediates in their investigations.[17,18,28,29] Kantouch and Abdel-Fattah [18] have observed the formation of such chloro-derivatives as intermediates during their investigations on the oxidation of amino-acids with sodium hypochlorite at pH 2 or 8. By investigating the role of the free amino-group in the reaction with chlorine they showed that only substitution of the free hydrogen atoms of the amino-group takes place. Haberfield and Paul [28] have shown the existence of *N*-chloro-intermediates in their studies of chlorination of anilines. Gassman and Campbell [29] have proposed the formation of *N*-chloro-derivatives as the intermediates to explain the mechanism of chlorination of anilines and related compounds. The rate law is given by equation (16).

$$-d[CAT]/dt = k_1 [CAT][H^+][Cl^-] \qquad (16)$$

The fractional order in $[Cl^-]$ can be accounted by considering that a fraction of the overall reaction proceeds *via* an alternative path independent of $[Cl^-]$ in which protonated monochloramine T undergoes hydrolysis to give H_2OCl^+ which in turn attacks the substrate in a fast step.

Assuming steady-state conditions the rate law (21) can be derived. The observed kinetics can be accounted by the

$$RNClNa \rightleftharpoons (RNCl)^- + Na^+ \quad (5)$$

$$(RNCl)^- + H^+ \rightleftharpoons RNHCl \quad K_a\ 2{\cdot}82 \times 10^{-5} \quad (6)$$

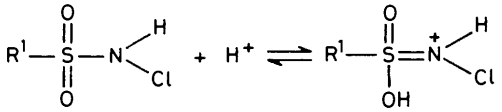
$$2\ RNHCl \overset{K_d}{\rightleftharpoons} RNH_2 + RNCl_2 \quad K_d\ 5{\cdot}8 \times 10^{-2} \text{ at } 25\ ^\circ C \quad (7)$$

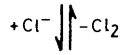
(k_d 10·1 1 mol^{-1} s^{-1} at pH 3·7 and 25 °C)

$$RNCl_2 + H_2O \overset{K_h}{\rightleftharpoons} RNHCl + HOCl \quad K_h\ 8{\cdot}0 \times 10^{-7} \text{ at } 25\ ^\circ C \quad (8)$$

$$RNHCl + H_2O \overset{K'_h}{\rightleftharpoons} RNH_2 + HOCl \quad K'_h\ 4{\cdot}88 \times 10^{-8} \text{ at } 25\ ^\circ C \quad (9)$$

$$HOCl \overset{K_a}{\rightleftharpoons} H^+ + OCl^- \quad K_a\ 3{\cdot}3 \times 10^{-8} \text{ at } 25\ ^\circ C \quad (10)$$





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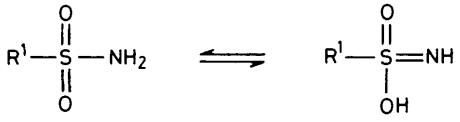


$R^1 = p\text{—}CH_3C_6H_4$

$$HOCl + H^+ + Cl^- \overset{K}{\rightleftharpoons} Cl_2 + H_2O,\ K\ 2{\cdot}15 \times 10^3 \quad (12)$$

(hydrolysis constant of chlorine[30] is $4{\cdot}66 \times 10^{-4}$)

Table 5. Concentrations (M) of various species * present in a 0.05M chloramine T solution over a range of pH values

pH	$RNCl^-$	RNHCl	$RNCl_2 = RNH_2$	HOCl	OCl^-
0	9.60×10^{-5}	4.01×10^{-2}	9.90×10^{-3}	3.95×10^{-7}	1.30×10^{-14}
1	9.60×10^{-4}	4.01×10^{-2}	9.90×10^{-3}	3.95×10^{-7}	1.30×10^{-13}
1.5		3.76×10^{-2}			
2	7.80×10^{-3}	3.24×10^{-2}	7.98×10^{-3}	3.95×10^{-7}	1.30×10^{-12}
3	2.83×10^{-2}	1.18×10^{-2}	2.92×10^{-3}	3.95×10^{-7}	1.30×10^{-11}
4	3.84×10^{-2}	1.60×10^{-3}	3.95×10^{-4}	3.95×10^{-7}	1.30×10^{-10}
5 *	4.00×10^{-2}	1.67×10^{-4}	4.10×10^{-5}	3.95×10^{-7}	1.30×10^{-9}
6 *	4.00×10^{-2}	1.67×10^{-5}	4.10×10^{-6}	3.95×10^{-7}	1.30×10^{-8}
7 *	4.00×10^{-2}	1.67×10^{-6}	4.10×10^{-7}	3.95×10^{-7}	1.30×10^{-7}
8 *	4.00×10^{-2}	1.67×10^{-7}	4.10×10^{-8}	3.95×10^{-7}	1.30×10^{-6}

* Values are obtained through first approximation calculations. There are some apparent discrepancies from the point of view of material balance.

$$RNHCl + H^+ + Cl^- \xrightarrow{k_1} RNH_2 + Cl_2 \quad \text{slow} \quad (13)$$

$$Cl_2 + S \xrightarrow{k_2} S' + H^+ + Cl^- \quad \text{fast} \quad (14)$$

$$n\ Cl_2 + S' \xrightarrow{k_3} \text{products} \quad \text{fast} \quad (15)$$

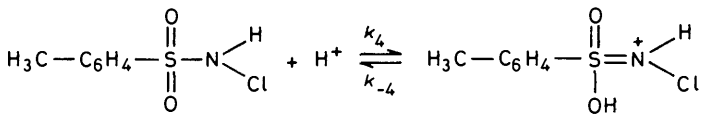
Scheme 1 n = 1 for alanine, phenylalanine, leucine, glutamine, and histidine and 2 for serine and lysine

$$-d[CAT]/dt = k_4k_5[H_2O][CAT][H^+]/(k_{-4} + k_5[H_2O]) \quad (21)$$

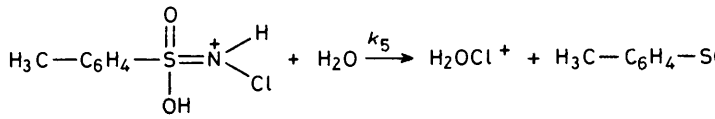
$$-d[CAT]/dt = k_1[CAT][H^+][Cl^-] + k'[CAT][H^+] \quad (22)$$

combined rate law (22) where $k' = k_4k_5[H_2O]/k_{-4} + k_5[HO_2]$. Arginine, glutamic acid, and threonine are exceptions to this rate law. With arginine the rate also has a first-order dependence on the substrate. In this case the mechanistic steps (14) and (19) may probably be slow (rate determining). So the rate law (23) in agreement with the

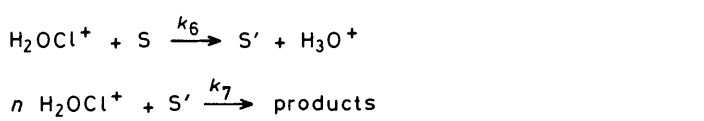
$$-d[CAT]/dt = k_1k_2[CAT][S][H^+][Cl^-] + k''[CAT][S][H^+] \quad (23)$$



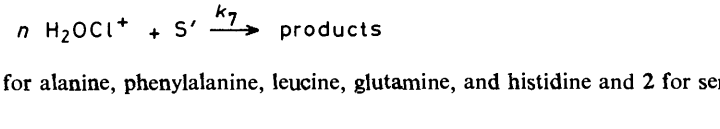
slow (17)



slow (18)

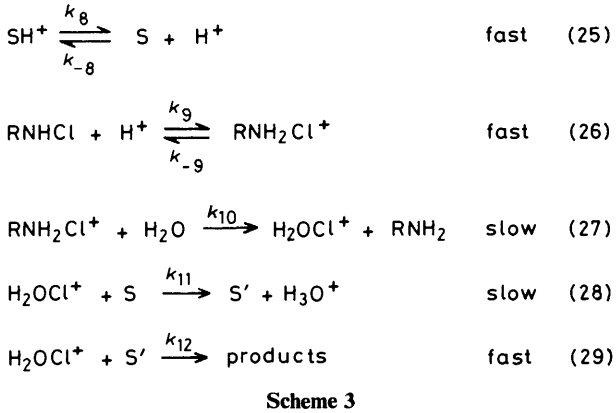


fast (19)



fast (20)

Scheme 2 $n = 1$ for alanine, phenylalanine, leucine, glutamine, and histidine and 2 for serine and lysine



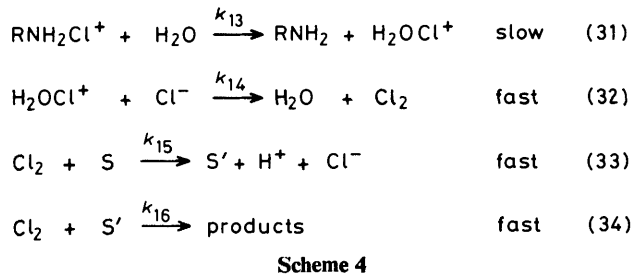
Scheme 3

observed kinetics can be derived where $k'' = k_4k_5k_6[H_2O]/(k_{-4} + k_5[H_2O])$. A detailed mechanism of oxidation is shown in Scheme 13.

With glutamic acid the rate has first-order dependence on the substrate concentration but zero order on chloride concentration. Hence the observed kinetics can be accounted for by the rate law (24). The observed kinetics with threonine will be explained later.

$$-d[CAT]/dt = k''[CAT][S][H^+] \quad (24)$$

(b) *At high hydrochloric acid concentrations* (ca. 0.2M). The rate of oxidation of alanine and phenylalanine at high [HCl] shows first-order dependence on both the oxidant and substrate concentrations and is independent of $[H^+]$ and $[Cl^-]$. But the rate shows fractional dependence on the substrate concentration with arginine and histidine. Variation of ionic strength of the medium and addition of the product toluene-*p*-sulphonamide have negligible effects on the rate. Addition of methanol slightly increases the rate. At high $[H^+]$ most of the amino-acid is in the cationic form. Thus the reaction of the latter with the positive halogen source is expected to be the rate-determining step. But the experimental observation that the rate is zero order in substrate at lower acidity and first order at higher acidity indicates that a neutral form of the amino-acid is reacting, as at the higher acidity [neutral substrate (S)] $\propto [H^+]^{-1}$. Under these conditions Scheme 2 will be transformed into Scheme 3. This is supported by the fact that the rate constants at higher acidity are 2—4 times larger than those at lower acidity (Table 3). The rate law is (30).



Scheme 4

$$-d[CAT]/dt = \frac{k_8k_9k_{10}k_{11}[H_2O][CAT][SH^+]}{k_{-8}(k_{-9} + k_{10}[H_2O])} \quad (30)$$

Scheme 3 and the rate law (30) accounts for the observed kinetics with alanine and phenylalanine. The observed fractional dependence on the substrate concentration with arginine and histidine can be accounted by assuming that a fraction of the reaction goes through steps (31)—(34) and the combined rate law is (35) where $k''' = k_8k_9k_{10}k_{11}[H_2O]/\{k_{-8}(k_{-9} + k_{10}[H_2O])\}$ and $k'_{13} = k_{13}[H_2O]$.

$$-d[CAT]/dt = k'''[CAT][SH^+] + k'_{13}[CAT] \quad (35)$$

(c) *Perchloric and sulphuric acid media* (ca. 0.1M). Rate of oxidation of leucine, glutamine, glutamic acid, serine, and arginine in perchloric or sulphuric acid medium shows first-order dependence on [CAT] and [substrate] and inverse first-order dependence on $[H^+]$. Variations of ionic strength of the medium or addition of the reaction product, toluene-*p*-sulphonamide, have virtually no effect on the rate, while the decrease in dielectric constant of the medium retards the rate. Under these conditions the direct interaction of RNHCl and the substrate is quite likely to form a reaction intermediate which in turn undergoes further reactions to give the products. Scheme 5 may be proposed to account for the experimental results. The rate law is given by (39). The same rate law and

$$-d[CAT]/dt = k_{17}k_{18}[CAT][SH^+]/k_{-17}[H^+] \quad (39)$$

mechanism account for the observed kinetics with glycine and valine in hydrochloric acid medium.

(d) *Effect of chloride ion.* It is interesting to note that the chloride ion catalyses the rate even under these acid conditions. Scheme 6 can be suggested to account for it.

$$SH^+ \underset{k_{-17}}{\overset{k_{17}}{\rightleftharpoons}} S + H^+ \quad \text{fast} \quad (36)$$

$$RNHCl + S \xrightarrow{k_{18}} S' + RNH_2 \quad \text{slow} \quad (37)$$

$$S' + n\ RNHCl \xrightarrow{k_{19}} \text{products} \quad \text{fast} \quad (38)$$

Scheme 5 $n = 1$ for leucine, glutamine, glutamic acid, and arginine and 2 for serine

$$SH^+ \underset{k_{-20}}{\overset{k_{20}}{\rightleftharpoons}} S + H^+ \quad \text{fast} \quad (40)$$

$$RNHCl + Cl^- \underset{k_{-21}}{\overset{k_{21}}{\rightleftharpoons}} R{-}N(H)(Cl \cdots Cl^-) \quad \text{fast} \quad (41)$$

X

$$X + S \xrightarrow{k_{22}} S' + RNH_2 + Cl^- \quad \text{slow} \quad (42)$$

$$S' + n\ X \xrightarrow{k_{23}} \text{products} \quad \text{fast} \quad (43)$$

Scheme 6 $n = 1$ for leucine, glutamine, glutamic acid, and arginine and 2 for serine

The rate expression may be derived from equations (44) and (45) giving the rate laws (46) and (47).

$$[CAT]_T = [RNHCl] + [X]$$

$$= \frac{k_{-21}[X]}{k_{21}[Cl^-]} + [X] \quad (44)$$

$$[X] = k_{21}[CAT]_T[Cl^-]/(k_{-21} + k_{21}[Cl^-]) \quad (45)$$

$$-d[CAT]/dt = \frac{k_{20}k_{22}[X][SH^+]}{k_{-20}[H^+]} \quad (46)$$

$$-d[CAT]/dt = k_{20}k_{21}k_{22}[CAT]_T[SH^+][Cl^-]/\{k_{-20}(k_{-21} + k_{21}[Cl^-])[H^+]\} \quad (47)$$

The observed kinetics with threonine in hydrochloric, perchloric, and sulphuric acid media can be explained by the Schemes 5, 7, and 8 and the related rate laws (39), (52), and (57).

$$-d[CAT]/dt = k_{24}[CAT][Cl^-] \quad (52)$$

In the absence of Cl^- ion Scheme 7 involves the interaction of hypochlorous acidium ion ' which is formed when water attacks RNHCl '. Scheme 8 explains these interactions.

$$-d[CAT]/dt = k_{28}[CAT][H_2O] = k'_{28}[CAT] \quad (57)$$

The observed kinetics in the presence of Cl^- ion can be accounted by the combined rate law (58) from equations (39)

$$-d[CAT]/dt = k_1k_{18}[CAT][SH^+]/k_{-17}[H^+] + k_{24}[CAT][Cl^-] \quad (58)$$

and (52). In the absence of Cl^- ion, the combined rate law becomes (59) from equations (39) and (57). Equations (58) and

$$-d[CAT]/dt = k_1k_{18}[CAT][SH^+]/k_{-17}[H^+] + k'_{28}[CAT] \quad (59)$$

$$RNHCl + Cl^- \underset{k_{-24}}{\overset{k_{24}}{\rightleftharpoons}} RNH^- + Cl_2 \quad \text{Forward reaction is slow} \quad (48)$$

$$Cl_2 + S \xrightarrow{k_{25}} S' + H^+ + Cl^- \quad \text{fast} \quad (49)$$

$$Cl_2 + S' \xrightarrow{k_{26}} \text{products} \quad \text{fast} \quad (50)$$

$$RNH^- + H^+ \xrightarrow{k_{27}} RNH_2 \quad \text{fast} \quad (51)$$

Scheme 7

$$RNHCl + H_2O \underset{k_{-28}}{\overset{k_{28}}{\rightleftharpoons}} RNH^- + H_2OCl^+ \quad \text{Forward reaction is slow} \quad (53)$$

$$H_2OCl^+ + S \xrightarrow{k_{29}} S' + H_3O^+ \quad \text{fast} \quad (54)$$

$$S' + H_2OCl^+ \xrightarrow{k_{30}} \text{products} \quad \text{fast} \quad (55)$$

$$RNH^- + H^+ \xrightarrow{k_{31}} RNH_2 \quad \text{fast} \quad (56)$$

Scheme 8

$$RNCl^- + H_2O \rightleftharpoons RNHCl + OH^- \quad (61)$$

$$RNCl^- + H_2O \rightleftharpoons RNH_2 + OCl^- \quad (62)$$

$$OCl^- + H_2O \rightleftharpoons HOCl + OH^- \quad (63)$$

(59) clearly indicate the fractional orders observed in $[H^+]$, $[Cl^-]$, and [substrate] with threonine both in the presence and absence of Cl^- ion.

Although one might expect similar kinetic behaviour for threonine and serine, we observed fractional orders in substrate and H^+ concentrations with threonine in all acid media, while for serine the rate is zero and unity in [substrate] and $[H^+]$ in HCl medium. The kinetic order is 1 and −1 in $HClO_4$ and H_2SO_4 media for this compound. These differences are also reflected in the values of the thermodynamic parameters. With the present data it is difficult to explain the differences in the kinetic behaviour of these two amino-acids.

The observed kinetics with histidine, first order in [CAT], zero order in [substrate], and fractional order in $[H^+]$ and $[Cl^-]$ (Table 1), can be accounted by Schemes 1, 7, and 8 and the combined rate law (60) from equations (16), (52), and (57).

$$-d[CAT]/dt = k_1[CAT][H^+][Cl^-] + k_{24}[CAT][Cl^-] + k'_{28}[CAT] \quad (60)$$

II. *Mechanism in Alkaline Medium.*—In alkaline medium the kinetics of oxidation of amino-acids with chloramine T shows first-order dependence on [CAT] and [substrate] and nearly inverse first order or inverse fractional order in $[OH^-]$ (except threonine). With threonine the rate is independent of $[OH^-]$.

The possible species in alkaline CAT solutions are $RNCl^-$ and OCl^- which would be transformed into more reactive oxidising species RNHCl and HOCl, in the course of the reaction by steps (61)—(63) retarded by OH^- ion. Several workers have observed the retarding influence of OH^- ions on the rate of chloramine T reactions with *p*-cresol,[31] succini-

$$RNCl^- + H_2O \underset{k_{-32}}{\overset{k_{32}}{\rightleftharpoons}} RNHCl + OH^- \quad \text{fast} \quad (64)$$

$$RNHCl + R'CH(NH_2)COO^- \xrightarrow{k_{33}} RNH_2 + R'CH(NHCl)COO^- \quad \text{slow} \quad (65)$$

$$R'CH(NHCl)COO^- + RNHCl \xrightarrow{k_{34}} \text{products} \quad \text{fast} \quad (66)$$

Scheme 9

$$RNCl^- + H_2O \xrightarrow{k_{35}} OCl^- + RNH_2 \quad \text{fast} \quad (68)$$

$$OCl^- + H_2O \underset{k_{-36}}{\overset{k_{36}}{\rightleftharpoons}} HOCl + OH^- \quad \text{fast} \quad (69)$$

$$HOCl + R'CH(NH_2)COO^- \xrightarrow{k_{37}} R'CH(NHCl)COO^- + H_2O \quad \text{slow} \quad (70)$$

$$R'CH(NHCl)COO^- + HOCl \xrightarrow{k_{38}} \text{products} \quad (71)$$

Scheme 10

$$RNCl^- + H_2O \xrightarrow{k_{39}} OCl^- + RNH_2 \quad \text{fast} \quad (73)$$

$$OCl^- + R'CH(NH_2)COO^- \xrightarrow{k_{40}} R'CH(NHCl)COO^- + OH^- \quad \text{slow} \quad (74)$$

$$R'CH(NHCl)COO^- + OCl^- \xrightarrow{k_{41}} \text{products} \quad \text{fast} \quad (75)$$

Scheme 11

mide,[21] 3-aminonaphthaldehyde,[32] α-hydroxy-acids,[33] ketones,[34] and sulphides [35-37] and have suggested that the reactivity of weakly alkaline solutions of chloramine T is due to the formation of the conjugate acid RNHCl from $RNCl^-$ in an OH^- retarding step. Recently, Hardy and Johnston [38] have reported that in the bromination of *p*-nitrophenol using *N*-bromo-*N*-sodiobenzenesulphonamide (Bromamine B) in dilute alkali, two reactive brominating species, the conjugate acid R_2NHBr ($R_2 = PhSO_2$) and HOBr, may be involved. They also observed the retarding effect of OH^-. So in alkaline oxidations it is expected that there are two competitive reactions, one involving RNHCl as the reactive species and the other involving HOCl. In very dilute alkali solutions (pH < 11) the reaction involving RNHCl is probable and at higher alkali concentrations (pH > 11) the most likely reactive species is HOCl or $RNCl^-$ and OCl^- (Figure 2 in ref. 38). This argument is strengthened by the fact that the rate is almost unaffected by the addition of the product toluene-*p*-sulphonamide and the order with respect to $[OH^-]$ is changing from nearly inverse first order to zero.

Schemes 9—12 can be proposed to account for the observed kinetics for the oxidation of amino-acids by chloramine T in alkaline solution.

The conjugate acid RNHCl, formed from $RNCl^-$, interacts with the substrate by the steps in Scheme 9. The rate law is given by equation (67). Alternatively, Scheme 10 which

$$-d[CAT]/dt = k_{32}k_{33}[CAT][R'CH(NH^z(COO^-][H_2O]/k_{-32}[OH^-] \quad (67)$$

involves the interaction of HOCl and amino acid, may be proposed. Assuming steady-state conditions the rate law (72) can be derived where $k^{iv} = k_{35}k_{36}k_{37}[H_2O]^2/k_{-36}$. Scheme 11

$$-\frac{d[CAT]}{dt} = k_{35}k_{36}k_{37}[CAT][R'CH(NH_2)COO^-][H_2O]^2/k_{-36}[OH^-] = k^{iv}[CAT][R'CH(NH_2)COO^-]/[OH^-] \quad (72)$$

envisages a direct interaction between the amino-acid and OCl^- ion. The rate is given by equation (76) where $k^v =$

$$-d[CAT]/dt = k_{39}k_{40}[CAT][R'CH(NH_2)COO^-][H_2O] = k^v[CAT][R'CH(NH_2)COO^-] \quad (76)$$

$k_{39}k_{40}[H_2O]$. The reaction steps involving the interaction of $RNCl^-$ and amino acid are shown in Scheme 12. The rate is given by equation (80).

$$-d[CAT]/dt = k_{42}[CAT][R'CH(NH_2)COO^-] \quad (80)$$

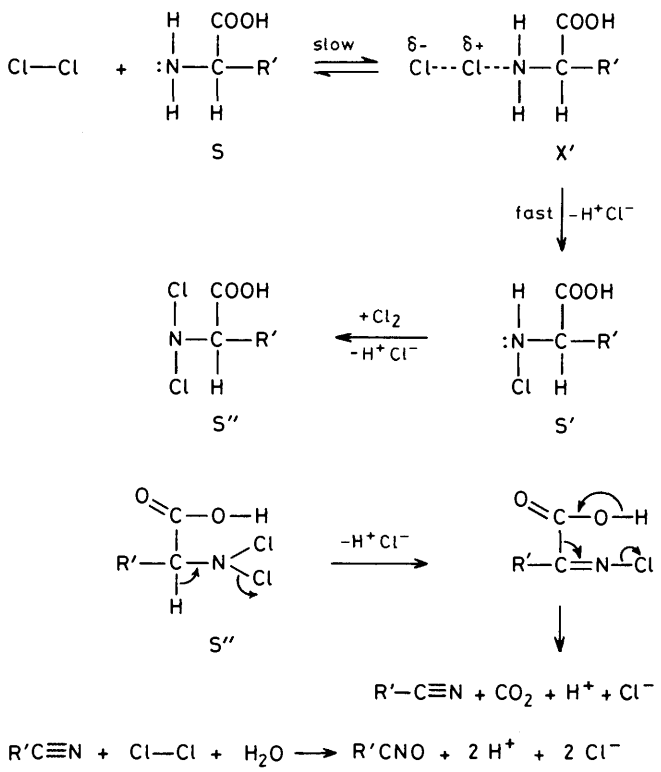
As Hardy and Johnston [38] pointed out, in lower alkali concentrations (pH up to 11) RNHCl is the most likely reactive species (Figure 2 in ref. 38) and hence Scheme 9 is operative. But under our experimental conditions ($[OH^-]$ 0.002—0.03M, pH > 11), it is quite likely that Scheme 10 is operative, *i.e.* HOCl formed from OCl^- in the alkali-retarding step interacts with the substrate in the rate-determining step (pK_a of RNHCl and HOCl are 4.55 and 7.48, respectively, see also Figure 2 in

$$RNCl^- + R'CH(NH_2)COO^- \xrightarrow{k_{42}} R'CH(NHCl)COO^- + RNH^- \quad \text{slow} \quad (77)$$

$$R'CH(NHCl)COO^- + RNCl^- \xrightarrow{k_{43}} \text{products} \quad \text{fast} \quad (78)$$

$$RNH^- + H_2O \xrightarrow{k_{44}} RNH_2 + OH^- \quad \text{fast} \quad (79)$$

Scheme 12



$$R'C{\equiv}N + Cl{-}Cl + H_2O \longrightarrow R'CNO + 2H^+ + 2Cl^-$$

Scheme 13. The further reaction of R'C≡N is for serine and lysine. Similar mechanisms can be written for the oxidation of amino-acids by H_2OCl^+, RNHCl, HOCl, OCl^-, and $RNCl^-$

ref. 38). This mechanism explains the first-order dependence in [CAT] and [amino-acid] and the inverse first order in $[OH^-]$. But the observed order in $[OH^-]$ is inverse fractional or zero. This is due to a fraction of the overall reaction proceeding *via* an alternative path involving either $RNCl^-$ or OCl^- [Scheme 11 or 12 and rate law (76) or (80)] showing the rate to be independent of $[OH^-]$. We think that Scheme 11 is probable. This is supported by the fact that Hardy and Johnston [38] have confirmed the presence of hypohalite at higher pH. The net outcome of the two paths (Schemes 10 and 11) is a fractional order in $[OH^-]$. The combined rate law (81) from equations (72) and

$$-d[CAT]/dt = k^{iv}[CAT][R'CH(NH_2)COO^-]/[OH^-] + k^{v}[CAT][R'CH(NH_2)COO^-] \quad (81)$$

(76) accounts for the observed kinetics for all the amino-acids except threonine. Scheme 11 and rate law (76) explain the kinetic observations for threonine.

The detailed mechanism of oxidation is shown in Scheme 13.

III. *Prediction of Rate Constants from the Derived Rate Laws.*—To check the validity of the combined rate laws they were employed to calculate the rate constants as we changed the concentrations of substrate and Cl^- ion in the acid media in the cases where fractional orders were observed with respect to [substrate] and $[Cl^-]$. The rate law (35) suggests a term of the form $a + b[S]$ for substrate variation, *i.e.*, rate $\propto a + b[S]$. Therefore, the rates with arginine and histidine at higher acidity were plotted against substrate concentrations to extract the values of a and b. The plots are straight lines (Figure 1) with intercepts a and slopes b. The extracted values are shown in Table 6. These values were used to compute the substrate dependent term ($b[S]$) and hence the total rate constant ($a + b[S]$), as the concentration of substrate changes. The calculated values, along with the experimental rate constants are shown in Table 6.

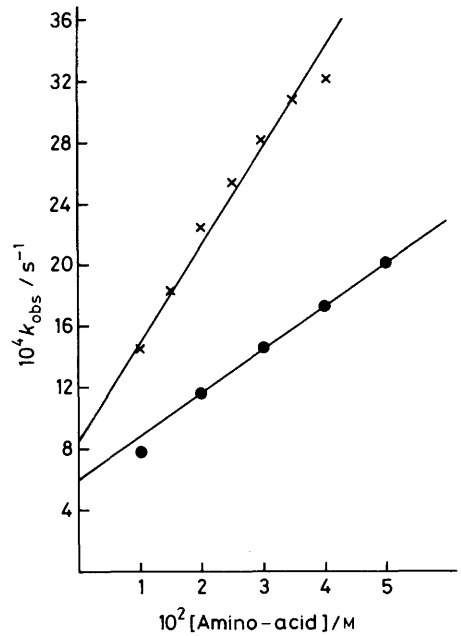


Figure 1. Plots of k_{obs} *versus* [amino-acid]: ●, arginine, [CAT] 0.002M, [HCl] 0.30M, μ 0.5M, 30 °C; ×, histidine, [CAT] 0.002M, [HCl] 0.22M, μ 0.5M, 30 °C

Similarly the rate laws (22), (23), and (58) suggest a term of the form $a' + b'[Cl^-]$ for chloride variation. So the observed rates were plotted against $[Cl^-]$. The plots are again straight lines (Figure 2) with intercepts a' and slopes b'. The derived values of a' and b' in typical cases are given in Tables 6 and 7. The $[Cl^-]$ dependent term in the rate laws and the total rate constant were derived from the values of a' and b' for variation of $[Cl^-]$. The calculated and the experimental rate constants are compared in Tables 6 and 7.

As can be seen from Tables 6 and 7 the agreement between the calculated and the experimental rate constants is excellent, thus indicating the consistency and validity of the proposed

Table 6. Calculated and the observed rate constants for the variation of [amino-acid (S)] and [Cl^-] in hydrochloric acid medium [c]

	Arginine a 6.0 × 10^{-4} s^{-1} b 2.82 × 10^{-2} l mol^{-1} s^{-1}			Histidine a 8.4 × 10^{-4} s^{-1} b 6.47 × 10^{-2} l mol^{-1} s^{-1}		
10^2 [S]/M	10^4 b [S]/s^{-1}	10^4 $k_{calc.}$/s^{-1}	10^4 $k_{obs.}$/s^{-1}	10^4 b [S]/s^{-1}	10^4 $k_{calc.}$/s^{-1}	10^4 $k_{obs.}$/s^{-1}
1.0	2.82	8.82	7.70	6.47	14.87	14.40
1.5	4.23	10.23		9.70	18.10	18.32
2.0	5.64	11.64	11.62	12.93	21.33	22.44
3.0	8.46	14.46	14.62	19.40	27.80	28.15
4.0	11.28	17.28	17.34	25.87	34.27	32.02
5.0	14.10	20.10	20.10	32.33	40.73	
	Arginine a' 4.70 × 10^{-4} s^{-1} b' 0.416 × 10^{-2} l mol^{-1} s^{-1}			Histidine a' 2.80 × 10^{-4} s^{-1} b' 0.55 × 10^{-2} l mol^{-1} s^{-1}		
10^2 [Cl^-]/M	10^4 b' [Cl]$^-$/s^{-1}			10^4 b' [Cl^-]/s^{-1}		
5.0 (7.0) [f]	2.08	6.78	4.61	3.85	6.65	6.08
10.0 (12.0) [f]	4.16	8.86	8.60	6.60	9.40	9.37
15.0 (17.0) [f]	6.24	10.94	11.47	9.35	12.15	11.44
20.0 (22.0) [f]	8.32	13.02	13.32	12.10	14.90	14.44
25.0 (27.0) [f]	10.40	15.10	14.85	14.85	17.65	16.98
	Threonine a' 13.3 × 10^{-4} s^{-1} b' 1.20 × 10^{-2} l mol^{-1} s^{-1}			Threonine [e] a' 5.0 × 10^{-4} s^{-1} b' 1.76 × 10^{-2} l mol^{-1} s^{-1}		
2.0	2.40	15.70		3.52	8.52	8.68
5.0	6.00	19.30	19.20	8.80	13.80	14.39
6.0	7.20	20.50	20.40	10.56	15.56	
7.0	8.40	21.70	22.10	12.32	17.32	
8.0	9.60	22.90	23.10	14.08	19.08	18.72
10.0	12.00	25.30	25.20	17.60	22.60	21.65

[c] The constants a, b, a', and b' were extracted from plots of rate *versus* [S] or rate *versus* [Cl^-] (see Figures 1 and 2). [d] $k_{calc.} = a + b$[S] or $a' + b'$[Cl^-]. [e] In $HClO_4$ medium. [f] Values in parentheses refer to histidine.

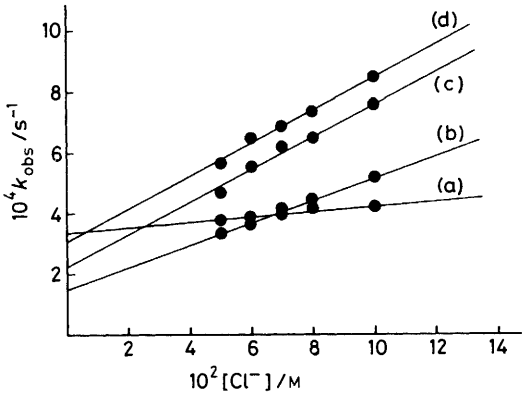


Figure 2. Plots of k_{obs} *versus* [Cl^-]: (a) lysine, [CAT] 0.003M, [amino-acid] 0.05M, [H^+] 0.05M, μ 1.0M, 30 °C; (b) serine, [CAT] 0.003M, [amino-acid] 0.03M, [H^+] 0.05M, μ 1.0M, 30 °C; (c) leucine, [CAT], [amino-acid] *etc.* as (b); (d) glutamine, [CAT], [amino-acid] *etc.* as (b)

mechanisms and derived rate laws in accounting for the experimental results.

The observed solvent isotope effects in acid media [12] support the proposed mechanisms and the derived rate expressions. Since D_3O^+ is about three times stronger than H_3O^+ [39,40] for acid-catalysed reactions the inverse isotope effect k_{D_2O}/k_{H_2O} should be greater than unity. But for reactions retarded by H^+ ion, this ratio should be less than unity. This argument is also valid for alkaline media. That is, for reactions retarded by OH^-, the ratio k_{D_2O}/k_{H_2O} should be less than unity. The isotopic effects observed in alkaline media conform to the above theory.

The effect of solvent on the reaction kinetics has been described in detail by Benson,[41] Frost and Pearson,[42] Laidler,[43] Amis,[44] and Entelis and Tiger.[45] For limiting case of zero angle of approach between two dipoles or an ion–dipole system, Amis [44] has shown that a plot of log $k_{obs.}$ *versus* $1/D$ gives a straight line, with a positive slope for a reaction between a positive ion and a dipole and a negative slope for negative ion–dipole or dipole–dipole interactions. The proposed mechanisms are in accord with the observed dielectric effects with most of the amino-acids in both acid and alkaline media, conforming to Amis' theory.[44]

The observed increase in rate with decrease in the dielectric constant of the medium with histidine and threonine cannot be explained by Amis' theory [44] as the presence of a positive ion in the rate-determining step is unlikely in the alkaline medium employed. Applying the Born equation, Laidler and Eyring [42] have derived equation (82) where k_0 is the rate

$$\ln k = \ln k_0 + \frac{NZ^2e^2}{2DRT}\left(\frac{1}{r} - \frac{1}{r_*}\right) \qquad (82)$$

Table 7. Calculated and the observed rate constants for the variation of $[Cl^-]$ in hydrochloric acid medium [c]

	Alanine a' 3.20×10^{-4} s^{-1} b' 0.44×10^{-2} l mol^{-1} s^{-1}			Phenylalanine a' 1.47×10^{-4} s^{-1} b' 0.576×10^{-2} l mol^{-1} s^{-1}		
10^2 $[Cl^-]$/M	10^4 b' $[Cl^-]/s^{-1}$	10^4 $k_{calc.}$ [d]$/s^{-1}$	10^4 $k_{obs.}/s^{-1}$	10^4 b' $[Cl^-]/s^{-1}$	10^4 $k_{calc.}$ [d]$/s^{-1}$	10^4 $k_{obs.}/s^{-1}$
5.0	2.20	5.40	4.09	2.88	4.35	4.35
7.5	3.30	6.50	6.40	4.32	5.79	5.92
10.0	4.40	7.60	7.79	5.76	7.23	7.35
15.0	6.60	9.80	9.98	8.64	10.11	10.36
20.0	8.80	12.00	11.92	11.52	12.99	12.06
	Leucine a' 2.25×10^{-4} s^{-1} b' 0.53×10^{-2} l mol^{-1} s^{-1}			Glutamine a' 3.23×10^{-4} s^{-1} b' 0.517×10^{-2} l mol^{-1} s^{-1}		
5.0	2.65	4.90	4.67	2.59	5.82	5.63
6.0	3.18	5.43	5.47	3.10	6.33	6.50
7.0	3.71	5.96	6.20	3.62	6.85	6.88
8.0	4.24	6.49	6.42	4.14	7.37	7.32
10.0	5.30	7.55	7.54	5.17	8.40	8.42
	Serine a' 1.45×10^{-4} s^{-1} b' 0.373×10^{-2} l mol^{-1} s^{-1}			Lysine a' 3.38×10^{-4} s^{-1} b' 0.082×10^{-2} l mol^{-1} s^{-1}		
5.0	1.87	3.32	3.41	0.41	3.79	3.75
6.0	2.24	3.69	3.60	0.49	3.87	3.92
7.0	2.61	4.06	4.07	0.57	3.95	3.94
8.0	2.98	4.43	4.49	0.66	4.04	4.15
10.0	3.73	5.18	5.13	0.82	4.20	4.16

[c] The constants a' and b' were extracted from a plot of rate *versus* $[Cl^-]$ (see Figure 2). [d] $k_{calc.} = a' + b'[Cl^-]$.

constant in a medium of infinite dielectric constant and r refers to radius of the reactant species and activated complex. It is seen that the rate should be greater in a medium of lower dielectric constant when $r_* > r$. It is likely that with histidine and threonine the radius of the activated complex form is greater than the radius of the reactant and this fact could explain the experimental observations.

A detailed mode of oxidation of amino-acids by CAT is shown in Scheme 13. The complex intermediates (X′) formed by the electrophilic attack of Cl_2, H_2OCl^+, RNHCl, $RNCl^-$, HOCl, and OCl^- respectively on the nitrogen atom of the amino-acid (S) undergo disproportionation to give the mono-*N*-chloro-derivative of the amino acid (S′) which in turn interacts with a second molecule of the oxidant to form the *NN*-dichloro-derivative (S″). The latter undergoes molecular rearrangement and elimination processes to yield the reaction products.

The negligible influence of variations of the ionic strength and addition of the product toluene-*p*-sulphonamide are in agreement with the proposed mechanisms.

The proposed mechanisms are also supported by the moderate values of energy of activation and thermodynamic parameters (Tables 1 and 2). The fairly high positive values of the free energy of activation $\Delta G^{\ddagger}$ and enthalpy of activation $\Delta H^{\ddagger}$ indicate that the transition state is highly solvated while the negative $\Delta S^{\ddagger}$ suggests the formation of an activated complex with a reduction in the degrees of freedom of molecules.

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