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Kinetics and Mechanism of Oxidation of Amino Acids by Dichloramine T

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Kinetics of oxidations of several amino acids (alanine, leucine, aspargine, glutamine, and proline) by *N,N*-dichloro-*p*-toluenesulfonamide (generally known as dichloramine-T) have been studied in 1 : 1 (v/v) water-methanol medium in the presence of perchloric acid. The oxidations of alanine and leucine showed second order kinetics in [oxidant], first order in [amino acid] and inverse fractional order in [H^+] over the entire range of [$HClO_4$](0.0005—0.10 mol dm^{-3}) used. But the kinetics of oxidations of aspargine, glutamine, and proline were [H^+] dependent. The rate dependence in [oxidant] was second and first orders in [H^+] ranges 0.0005—0.005 mol dm^{-3} and 0.005—0.10 mol dm^{-3}, respectively. The kinetics in [amino acid] for these oxidations were also different. Variation in ionic strength of the medium or addition of the reduced product of the oxidant had no or negligible effects on the rates of reactions. Decrease in dielectric constant of the medium by increasing the methanol composition of the solvent decreased the rate in all the cases. Activation parameters have been computed from the Arrhenius plots. Plausible mechanisms consistent with the observed kinetics have been discussed.

Although extensive studies have been reported on the kinetics and mechanisms of oxidation of a variety of substrates by *N*-halosulfonamides like *N*-chloro- and *N*-bromobenzene- or toluenesulfonamides,[1-8] studies by *N,N*-dihalosulfonamides have recently been initiated in our laboratories.[7-9]

As a part of these investigations, we report herein the kinetics of oxidation of several amino acids by *N,N*-dichloro-*p*-toluenesulfonamide in 1 : 1 (v/v) water-methanol medium in the presence of perchloric acid. The amino acids studied are alanine, leucine, aspargine, glutamine, and proline.

Materials and Methods

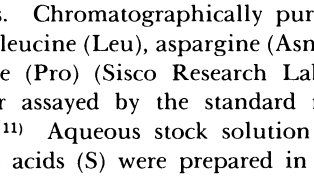
N,N-Dichloro-*p*-toluenesulfonamide, abbreviated as dichloramine-T (DCT) was prepared by the method of Jacob and Nair.[10] The stock solution (ca. 0.05 mol dm^{-3}) of the oxidant in pure methanol was prepared and standardised by iodometric method and preserved in amber colored bottles. Chromatographically pure amino acids: alanine (Ala), leucine (Leu), aspargine (Asn), glutamine (Gln), and proline (Pro) (Sisco Research Laboratories, India) were further assayed by the standard methods reported elsewhere.[11] Aqueous stock solution (0.1 mol dm^{-3}) of the amino acids (S) were prepared in doubly distilled water. Preliminary investigations of the reactions showed that the variations in ionic strength of the medium had no significant effect on the rates of all the oxidations. All other reagents used were of accepted grades of purity.

Kinetic Measurements: Kinetic studies were made in glass stoppered pyrex boiling tubes under pseudo-first-order or pseudo-second-order conditions with [S]≫[DCT]. The reactions were initiated by the quick addition of measured amounts of oxidant solution (0.0005—0.005 mol dm^{-3}), thermostated at a desired temperature, to solutions containing required amounts of amino acid (0.005—0.10 mol dm^{-3}), perchloric acid (0.0005—0.10 mol dm^{-3}), methanol, and water (to maintain 1 : 1 (v/v) water-methanol composition), equilibrated at the same temperature. The progress of the reactions was monitored for two half-lives by iodometric estimation of unreacted oxidant at regular time intervals. The pseudo-first-order or pseudo-second-order rate constants (k_{obs}) were calculated by the graphical methods and the values were reproducible within ±4% error.

Stoichiometry and Product Analysis

The stoichiometries of DCT-amino acid reactions are determined in 1 : 1 (v/v) water-methanol medium in the presence of varying concentrations of perchloric acid (0.0005—0.10 mol dm^{-3}) by equilibrating varying ratios of $[DCT]_0$ to $[S]_0$ at room temperature for different intervals of time. The products were found to be CO_2, ammonia, and the corresponding aldehyde by standard tests.[12,13] *p*-Toluenesulfonamide, the reduced product of DCT, was detected by paper chromatography. The observed stoichiometries may be represented by Eqs. 1 and 2.

$$2RCH(NH_2)COOH + ArSO_2NCl_2 + 2H_2O \longrightarrow 2RCHO + 2CO_2 + 2NH_4^+ + 2Cl^- + ArSO_2NH_2 \quad (1)$$



$$+ ArSO_2NCl_2 + 2H_2O \longrightarrow 2H_2C{=}CHCH_2CHO + 2CO_2 + 2NH_4^+ + 2Cl^- + ArSO_2NH_2 \quad (2)$$

where R=CH_3(Ala), $(CH_3)_2CHCH_2$(Leu), $H_2N(CO)CH_2CH_2$(Gln), $H_2N(CO)CH_2$(Asn).

Results

The kinetics of oxidations of Ala, Leu, Asn, Gln, and Pro by DCT in 1 : 1 (v/v) water-methanol medium were studied under varying conditions: [DCT] (0.0005—0.005 mol dm^{-3}), [S] (0.005—0.10 mol dm^{-3}), and [$HClO_4$] (0.0005—0.10 mol dm^{-3}). The results are shown in Tables 1—4 and Figs. 1—6. The kinetics of oxidations were [H^+] dependent. The order in [oxidant] was two and one in the acid ranges 0.0005—0.005 mol dm^{-3} and 0.005—0.10 mol dm^{-3}, respectively, for the oxidations of Asn, Gln,

Table 1. Pseudo-Second-Order Rate Constants (k_{obs}) for the Oxidation of Amino Acids (S) by *N,N*-Dichloro-*p*-toluenesulfonamide (Dicloramine-T, DCT) in 1 : 1 (v/v) Water-Methanol Medium in the Presence of Perchloric Acid at 303 K (Ala and Leu) and 293 K (Asn, Gln, and Pro)

10^3[DCT]$_0$	10^2[S]$_0$		10^2[$HClO_4$]		$10k_{obs}$/dm^3 mol^{-1}s^{-1}				
mol dm^{-3}	mol dm^{-3}		mol dm^{-3}		Ala	Leu	Asn	Gln	Pro
Effect of varying [DCT]$_0$									
0.5	2.0	(5.0)	1.0	(0.10)	2.1	1.5	12.9	20.6	7.5
1.0	2.0	(5.0)	1.0	(0.10)	1.9	1.6	12.9	20.9	7.6
2.0	2.0	(5.0)	1.0	(0.10)	1.9	1.6	12.3	19.9	7.5
4.0	2.0	(5.0)	1.0	(0.10)	1.9	1.6	—	—	—
5.0	2.0	(5.0)	1.0	(0.10)	—	—	12.7	19.3	7.6
Effect of varying [S]$_0$									
1.0	0.5		1.0	(0.10)	0.35	0.36	1.8	2.6	0.8
1.0	1.0		1.0	(0.10)	0.82	0.79	3.1	4.4	1.8
1.0	2.0		1.0	(0.10)	1.9	1.6	5.8	9.4	3.3
1.0	3.0		1.0	(0.10)	2.7	2.2	—	—	—
1.0	5.0		1.0	(0.10)	4.4	4.5	12.9	20.9	7.6
Effect of varying [$HClO_4$]									
1.0	2.0	(5.0)	0.05		6.0	7.3	22.2	41.0	15.2
1.0	2.0	(5.0)	0.10		5.2	5.3	12.9	20.9	7.6
1.0	2.0	(5.0)	0.20		3.9	3.3	6.4	9.8	3.8
1.0	2.0	(5.0)	0.30		—	—	4.9	6.9	2.6
1.0	2.0	(5.0)	0.50		3.3	2.3	—	—	—
1.0	2.0	(5.0)	1.0		1.9	1.6	—	—	—
1.0	2.0	(5.0)	2.0		1.4	1.3	—	—	—
1.0	2.0	(5.0)	5.0		1.1	0.7	—	—	—
1.0	2.0	(5.0)	10.0		0.7	0.5	—	—	—

Values in parentheses are for Asn, Gln, and Pro.

Table 2. Pseudo-First-Order Rate Constants (k_{obs}) for the Oxidation of Amino Acids (S) by *N,N*-Dichloro-*p*-toluenesulfonamide (Dichloramine-T, DCT) in 1 : 1 (v/v) Water-Methanol Medium in the Presence of Perchloric Acid at 303 K

10^3[DCT]$_0$	10^2[S]$_0$	10^2[$HClO_4$]	10^4k_{obs}/s^{-1}		
mol dm^{-3}	mol dm^{-3}	mol dm^{-3}	Asn	Gln	Pro
Effect of varying [DCT]$_0$					
0.5	5.0	1.0	5.8	7.5	3.3
1.0	5.0	1.0	5.4	7.2	3.2
2.0	5.0	1.0	5.4	7.2	3.2
3.0	5.0	1.0	5.4	7.3	3.2
4.0	5.0	1.0	—	—	—
Effect of varying [S]					
1.0	1.0	1.0	—	—	—
1.0	2.0	1.0	1.3	1.9	0.7
1.0	3.0	1.0	2.6	3.4	—
1.0	4.0	1.0	—	—	2.4
1.0	5.0	1.0	5.4	7.2	3.2
1.0	7.0	1.0	8.9	10.1	6.4
1.0	10.0	1.0	13.4	15.8	9.7
Effect of varying [$HClO_4$]					
1.0	5.0	0.2	—	—	—
1.0	5.0	0.5	10.0	17.7	4.8
1.0	5.0	1.0	5.4	7.2	3.2
1.0	5.0	2.0	4.8	4.3	1.4
1.0	5.0	5.0	2.2	2.8	—
1.0	5.0	10.0	—	—	0.51

and Pro. The dependence in [S] for these oxidations was also different (Table 4). But the oxidations of Ala and Leu showed second-order dependence in [oxidant], first order in [S] and inverse fractional order in [H^+] over the entire range of [$HClO_4$](0.0005—0.10 mol dm^{-3}).

(i) Pseudo-Second-Order Kinetics: At fixed [S]$_0$ and [$HClO_4$], the plots of 1/[DCT] versus time were linear at least for two-half lives (Figs. 1 and 2). The pseudo-second-order rate constants (k_{obs}), computed from the plots, were unaffected by changes in [DCT]$_0$ (Table 1), establishing second-order kinetics in [DCT] for the oxidations of Ala and Leu over the entire acid range studied and for Asn, Gln, and Pro in the acid range 0.0005—0.005 mol dm^{-3}. At constant [DCT]$_0$ and [$HClO_4$], the rates increased with increase in [S]$_0$ (Table 1) and the plots of log k_{obs} versus log[S]$_0$ were linear with varying slopes (Table 4), showing nearly first-order to first-order kinetics in [S]. The rates decreased with increase in [$HClO_4$], at fixed [DCT]$_0$ and [S]$_0$, with inverse fractional order to inverse first-order dependences in [H^+]. Variation in ionic strength of the medium or addition of the reduced product of the oxidant, *p*-toluenesulfonamide (TSA), had negligible effects on the rates of oxidations. But the decrease in dielectric constant of the medium by increasing the methanol composition of the solvent

Table 3. Effect of Varying Dielectric Constant of the Reaction Medium and Addition of the Reaction Product, *p*-Toluenesulfonamide (TSA) on the Rates of Oxidations of Amino Acids by *N,N*-Dichloro-*p*-toluenesulfonamide (DCT) in 1 : 1 (v/v) Water-Methanol Medium

% MeOH	$10K_{obs}$[a,b]/dm³mol⁻¹s⁻¹					10^4k_{obs}[c]/s⁻¹		
	Ala	Leu	Asn	Gln	Pro	Asn	Gln	Pro
40	4.6	3.2	19.0	28.8	17.0	7.0	12.6	5.6
45	2.9	2.3	—	—	—	—	—	—
50	1.9	1.6	12.9	19.9	7.5	5.4	7.2	3.2
60	0.8	0.9	8.9	13.4	5.0	3.9	4.8	2.0
10^3[TSA] (mol dm⁻³)								
0	1.9	1.6	12.9	19.9		5.4	7.2	3.2
1.0	1.9	1.6	11.8	18.8		—	—	—
2.0	1.9	1.6	—	—		—	—	—
3.0	1.9	1.6	12.0	19.6		5.3	7.2	3.3
4.0	—	—	—	—		5.4	7.0	3.3

a) $10^3[DCT]_0=50[S]_0=10^2[HClO_4]=1.0$ mol dm⁻³, temp 303 K for Ala and Leu. b) $10^3[DCT]_0=20[S]_0=10^3[HClO_4]=1.0$ mol dm⁻³, temp 293 K for Asn, Gln, and Pro under pseudo-second-order conditions. c) $10^3[DCT]_0=20[S]_0=10^2[HClO_4]=1.0$ mol dm⁻³, temp 303 K for Asn, Gln, and Pro under pseudo-first-order conditions.

Table 4. Kinetic and Activation Parameters for the Oxidation of Amino Acids by *N,N*-Dichloro-*p*-toluenesulfonamide (DCT) in 1 : 1 (v/v) Water-Methanol Medium in the Presence of Perchloric Acid

Orders observed	Ala	Leu	$[HClO_4]$=0.0005—0.005 mol dm⁻³			$[HClO_4]$=0.005—0.10 mol dm⁻³		
			Asn	Gln	Pro	Asn	Gln	Pro
[DCT]	2.0	2.0	2.0	2.0	2.0	1.0	1.0	1.0
[S]	1.0	1.0	0.94	0.98	0.91	1.57	1.65	1.59
$[H^+]$	−0.41	−0.52	−0.85	−1.0	−0.96	−0.66	−0.60	−0.75
Activation parameters								
$\log A$	3.93	4.48	6.28	7.13	9.69	6.47	8.59	5.70
E_a/kJ mol⁻¹	27.0	30.6	35.4	38.4	55.1	56.5	68.1	53.3
$\Delta H^{\neq}$/kJ mol⁻¹	23.7	28.0	31.7	38.3	52.4	55.1	65.1	52.1
$\Delta S^{\neq}$/J K⁻¹	−180.6	−167.9	−134.9	−107.7	−68.4	−125.6	−87.5	−139.9
$\Delta G^{\neq}$/kJ mol⁻¹	78.5	78.9	71.2	69.8	72.5	93.2	91.6	94.5

decreased the rates of oxidations for all the amino acids. The plots of $\log k_{obs}$ versus % methanol (by volume) were linear with negative slopes (Fig. 6). The rates were measured at different temperatures (293—313 K) and the activation parameters computed from the Arrhenius plots (Table 4).

(ii) Pseudo-First-Order Kinetics: Oxidations of Asn, Gln, and Pro in the acid range ≥ 0.005 mol dm⁻³ showed pseudo-first-order kinetics in [oxidant]. At fixed $[DCT]_0$ and $[S]_0$, the plots of log[DCT] versus time were linear for at least two-half lives (Fig. 3) and the pseudo-first-order rate constants calculated from the plots were insensitive to the variations in $[DCT]_0$, showing first-order kinetics in [DCT]. The rates increased with increase in $[S]_0$ and the plots of $\log k_{obs}$ versus $\log[S]_0$ were linear with varying slopes, indicating varying kinetic orders in [S] (Table 4). At constant $[DCT]_0$ and $[S]_0$ the rates decreased with increase in $[HClO_4]$ with inverse fractional order dependences in $[H^+]$ for oxidations of all the amino acids. Variations in ionic strength of the medium or the addition of *p*-toluenesulfonamide had no effect on the rates. Decrease in dielectric constant of the medium by increasing the methanol composition of the solvent decreased the rates even under these conditions (Table 3). The plots of $\log k_{obs}$ versus % methanol (by volume) were also linear with negative slopes (Fig. 6). The rates of oxidations were also measured at different temperatures (283—313 K) and activation parameters were computed from the plots of $\log k_{obs}$ versus $1/T$ and $\log(k_{obs}/T)$ versus $1/T$ (Table 4).

Discussion

(i) Pseudo-Second-Order Kinetics in [DCT]: The kinetics of second order in [DCT], nearly first-order in [S] and inverse fractional order in $[H^+]$ observed for the oxidations of Ala, Leu, Asn, Gln, and Pro may be explained by a mechanism shown in Scheme 1.

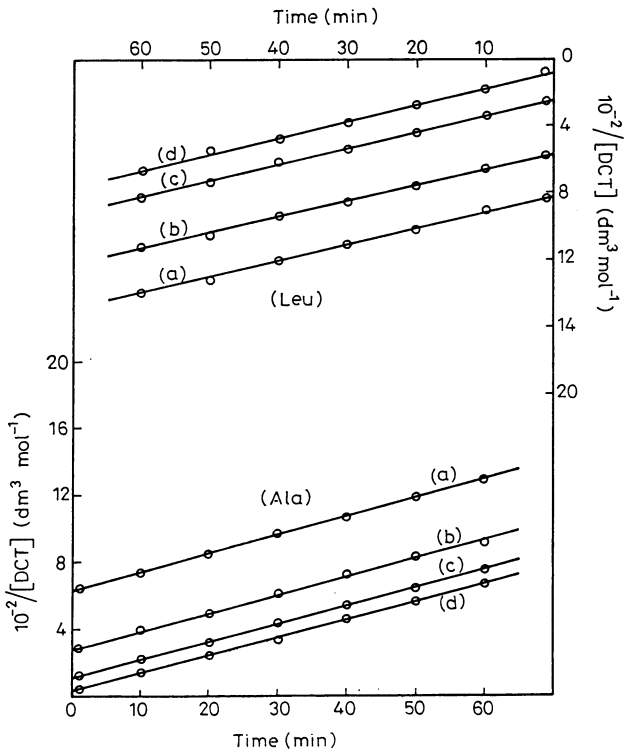


Fig. 1. Plots of 1/[DCT] versus time (Ala and Leu)
$10^2[S]_0$=2.0 mol dm^{-3}, $10^2[HClO_4]$=1.0 mol dm^{-3}, temp 303 K.
$10^3[DCT]_0$(mol dm^{-3}): 0.5(a), 1.0(b), 2.0(c), 4.0(d).

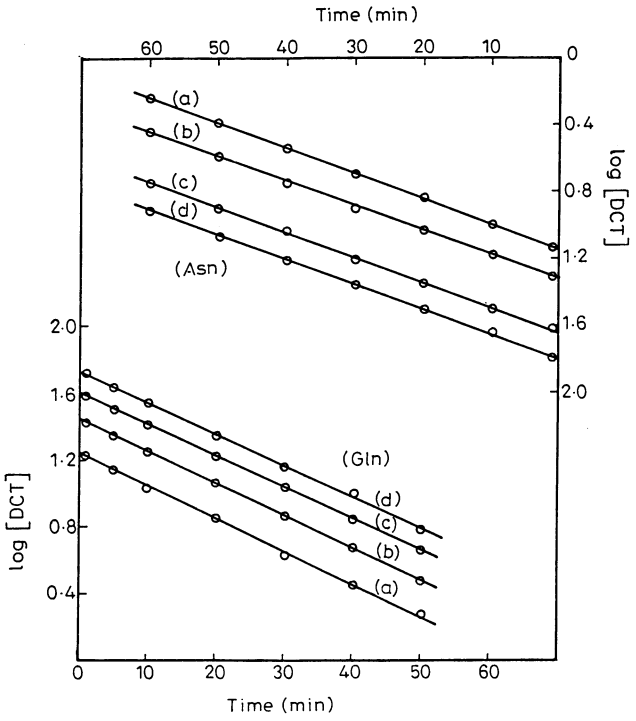


Fig. 3. Plots of log [DCT] versus time (Asn and Gln)
$10^2[S]_0$=5.0 mol dm^{-3}, $10^2[HClO_4]$=1.0 mol dm^{-3}, temp 303 K.
$10^3[DCT]_0$(mol dm^{-3}): 0.5(a), 1.0(b), 2.0(c), 3.0(d).

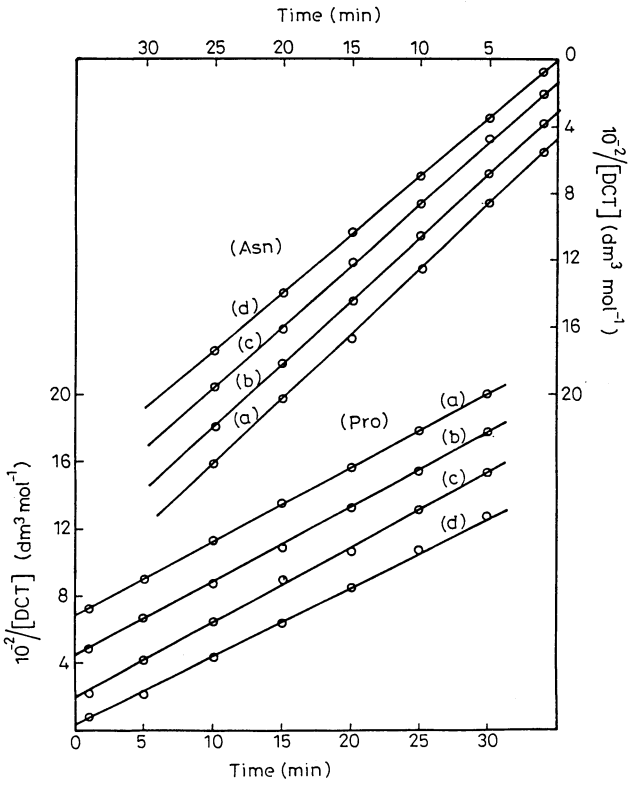


Fig. 2. Plots of 1/[DCT] versus time (Asn and Pro)
$10^2[S]_0$=5.0 mol dm^{-3}, $10^3[HClO_4]$=1.0 mol dm^{-3}, temp 293 K.
$10^3[DCT]_0$(mol dm^{-3}): 0.5(a), 1.0(b), 2.0(c), 5.0(d).

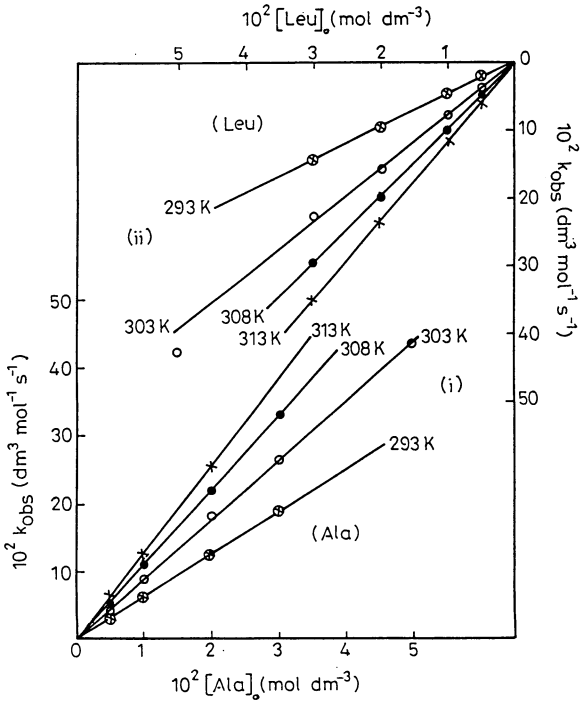


Fig. 4. Plots of (i) k_{obs} versus $[Ala]_0$ and (ii) k_{obs} versus $[Leu]_0$.
$10^3[DCT]_0$=$10^2[HClO_4]$=1.0 mol dm^{-3}.

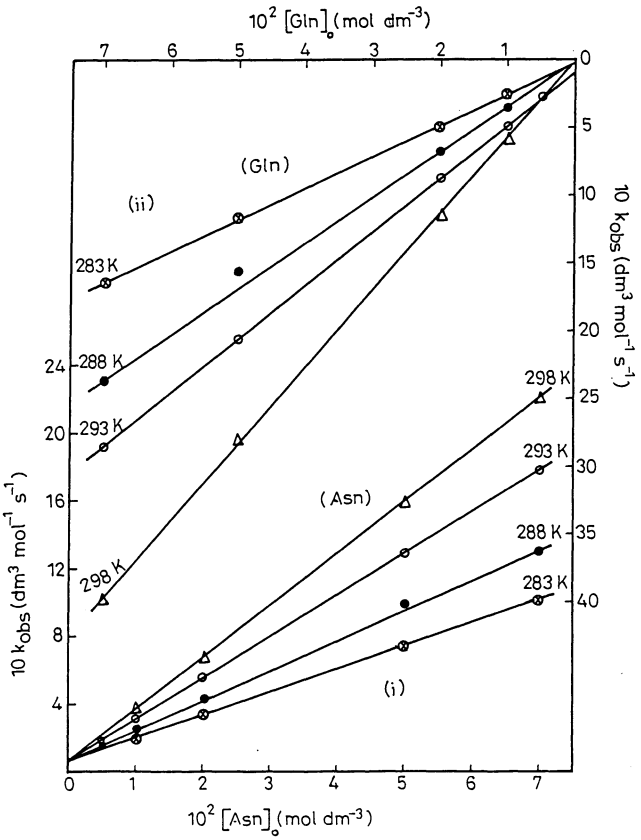


Fig. 5. Plots of (i) k_{obs} versus $[Asn]_0$ and (ii) k_{obs} versus $[Gln]_0$.
$10^3[DCT]_0=10^3[HClO_4]=1.0$ mol dm^{-3}.

$$SH^+ \overset{K_1}{\rightleftharpoons} S + H^+ \qquad \text{(fast)}$$

$$ArSO_2NCl_2 + S \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \underset{(X)}{\text{Intermediate}} \qquad \text{(fast)}$$
(DCT)

$$ArSO_2NCl_2 + X \xrightarrow{k_3} \text{Products} \qquad \text{(slow)}$$

where SH^+: Protonated amino acid

Scheme 1.

Applying the steady state approximation to the intermediate X, we have

$$[X] = \frac{k_2[ArSO_2NCl_2]_0\,[S]}{k_{-2}+k_3[ArSO_2NCl_2]+k_2[S]} \tag{3}$$

where $[ArSO_2NCl_2]=[ArSO_2NCl_2]_0-[X]$ and $[S]_0\approx[S]$. Since k_3 is small and $[S]\gg[ArSO_2NCl_2]$, $k_3[ArSO_2NCl_2]$ is negligibly small compared with other terms in the denominator, then Eq. 3 becomes,

$$[X]=\frac{k_2[ArSO_2NCl_2]_0[S]}{k_{-2}+k_2[S]}=\frac{K_2[DCT]_0[S]}{1+K_2[S]} \tag{4}$$

where $K_2=k_2/k_{-2}$.
The rate of the reaction is then given by Eq. 5

$$-\frac{d[DCT]}{dt} = k_3[DCT]\,[X] = \frac{K_2k_3[DCT]_0[DCT][S]}{1+K_2[S]}. \tag{5}$$

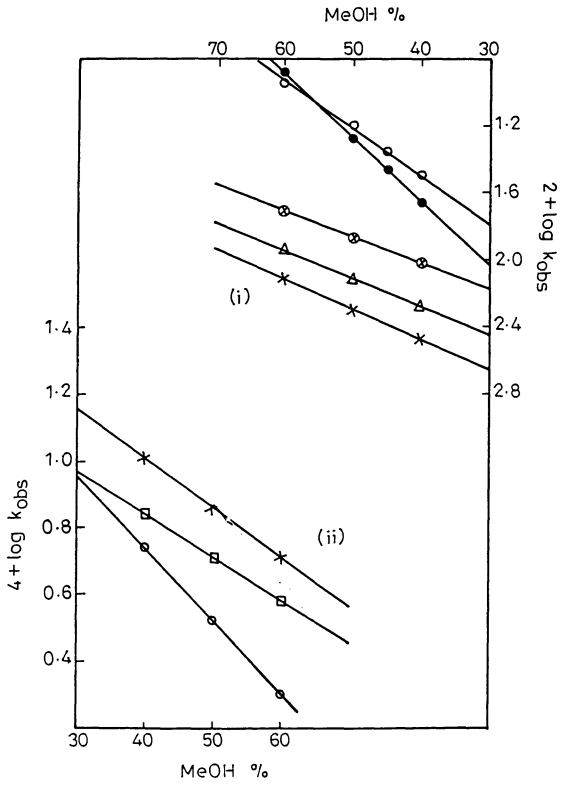


Fig. 6. Plot of log k_{obs} versus % MeOH
(i) Pseudo-second-order rate constants
$10^3[DCT]_0=50[S]_0=10^2[HClO_4]=1.0$ mol dm^{-3}, temp 303 K (Ala and Leu).
$10^3[DCT]_0=20[S]_0=10^3[HClO_4]=1.0$ mol dm^{-3}, temp 293 K (Asn, Gln, and Pro).
● Ala, ○ Leu, △ Asn, × Gln, ○ Pro.
(ii) Pseudo-first-order rate constants
$10^3[DCT]_0=[S]_0=10^2[HClO_4]=1.0$ mol dm^{-3}, temp 303 K.
□ Asn, ×Gln, ○ Pro.

If we now make further assumption that $[DCT]_0\times[DCT]\approx[DCT]^2$ then the rate law (5) becomes

$$-\frac{d[DCT]}{dt} = \frac{K_2k_3[DCT]^2[S]}{1+K_2[S]}, \tag{6}$$

rearranging Eq. 6, we have Eq. 7

$$-\frac{1}{[DCT]^2}\frac{d[DCT]}{dt} = \frac{K_2k_3[S]}{1+K_2[S]}. \tag{7}$$

But LHS of Eq. 7 may be written as

$$-\frac{1}{[DCT]^2}\frac{d[DCT]}{dt} = \frac{d\{1/[DCT]\}}{dt} = k_{obs}$$

hence Eq. 7 becomes Eq. 8

$$k_{obs} = \frac{K_2k_3[S]}{1+K_2[S]}. \tag{8}$$

We also have

$$[S]=K_1[SH^+]/[H^+]. \tag{9}$$

Therefore Eq. 8 takes the form

$$k_{obs} = \frac{K_1K_2k_3[SH^+]}{[H^+] + K_1K_2[SH^+]} . \quad (10)$$

If K_2 is small, the rate law (8) will take the form

$$k_{obs}=K_2k_3[S]=K_1K_2k_3[SH^+]/[H^+]. \quad (11)$$

The plots of k_{obs} versus [S] (amino acid) gave straight lines passing through the origin with most of the amino acids (Figs. 4 and 5), in conformity with the rate law (11).

The rate laws (Eqs. 10 and 11) explain the observed inverse fractional to nearly inverse first-order in $[H^+]$. The plots of either k_{obs} versus $1/[H^+]$ or $1/k_{obs}$ versus $[H^+]$ were non-linear in most cases (figure not shown).

(ii) Pseudo-First-Order Kinetics in [DCT]: The observed kinetic data (Table 4) for the oxidations of Asn, Gln, and Pro may be accounted for by a mechanism shown in Scheme 2 (modified Scheme 1).

$$SH^+ \underset{}{\overset{K_1}{\rightleftharpoons}} S + H^+ \quad \text{(fast)}$$

$$\underset{(DCT)}{ArSO_2NCl_2} + S \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} \underset{(Y)}{\text{Intermediate}} \quad \text{(fast)}$$

$$Y + S \xrightarrow{k_5} \text{Products} \quad \text{(slow)}$$

Scheme 2.

Application of the steady state approximation to the intermediate Y, through a procedure similar to the previous one, we have

$$[Y] = \frac{k_4[ArSO_2NCl_2]_0[S]}{k_{-4} + k_5[S] + k_4[S]} \quad (12)$$

or

$$[Y] = \frac{K_4[DCT]_0[S]}{1 + K_4[S]} \quad (13)$$

as $k_5[S](k_5$ is very small) in the denominator is negligible compared to other terms and $K_4=k_4/k_{-4}$.

The rate of reaction is then given by Eq. 14

$$-\frac{d[DCT]}{dt} = k_5[Y][S] = \frac{K_4k_5[DCT]_0[S]^2}{1+K_4[S]} \quad (14)$$

or

$$k_{obs} \approx \frac{-1}{[DCT]_0}\frac{d[DCT]}{dt} \approx \frac{K_4k_5[S]^2}{1+K_4[S]} , \quad (15)$$

introducing Eq. 9 into Eq. 15 we have

$$k_{obs} = \frac{K_1^2K_4k_5[SH^+]^2}{[H^+]\{[H^+] + K_1K_4[SH^+]\}} . \quad (16)$$

Thus the rate laws (15) and (16) explain the kinetic data for the oxidations of Asn, Gln, and Pro.

A typical detailed mechanism of oxidation of amino acids is shown in Scheme 3.

Similarly monochlorosulfonamide and HOCl formed further react with amino acids in fast steps to give products.

$$RCH(NH_3^+)COO^- + ArSO_2NHCl + H_2O \xrightarrow[\text{(fast)}]{}$$

$$RCHO + ArSO_2NH_2 + CO_2 + NH_4^+ + Cl^-$$

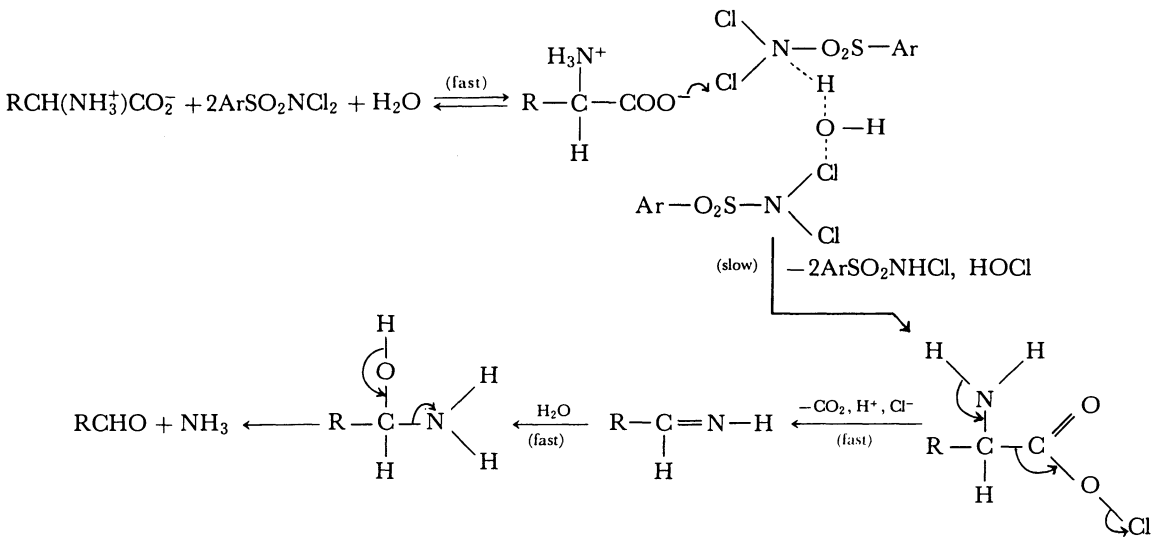
Table 5. Pseudo-First-Order Rate Constants (k_{obs}) for the Oxidation of Amino Acids (S) by *N*-Chloro-*N*-sodio-*p*-toluenesulfonamide (Chloramine-T, CAT) in 1 : 1 (v/v) Water-Methanol Medium in the Presence of Perchloric Acid at 303 K

$10^3[CAT]_0$	$10^2[S]_0$	$10^3[HClO_4]$	$10^4k_{obs}/s^{-1}$		
mol dm^{-3}	mol dm^{-3}	mol dm^{-3}	Ala	Leu	Asn
Effect of varying $[CAT]_0$					
0.5	2.0	5.0(2.0)	6.5	5.7	3.9
1.0	2.0	5.0(2.0)	6.5	5.9	4.0
2.0	2.0	5.0(2.0)	6.4	6.3	4.0
Effect of varying $[S]_0$					
1.0	0.5	5.0(2.0)	2.3	1.8	—
1.0	1.0	5.0(2.0)	3.8	3.2	1.8
1.0	2.0	5.0(2.0)	6.5	5.9	4.0
1.0	3.0	5.0(2.0)	9.0	8.8	6.1
1.0	4.0	5.0(2.0)	—	—	8.1
1.0	5.0	5.0(2.0)	13.0	12.1	10.6
1.0	10.0	5.0(2.0)	16.4	—	—
Effect of varying $[HClO_4]$					
1.0	2.0	0.1	17.2	—	—
1.0	2.0	0.2	17.2	—	—
1.0	2.0	0.5	17.2	29.6	52.8
1.0	2.0	1.0	17.3	27.5	2.3
1.0	2.0	2.0	10.7	19.3	4.0
1.0	2.0	5.0	6.5	5.9	5.8
1.0	2.0	10.0	3.5	2.9	—
1.0	2.0	20.0	1.3	—	—

Values in the parentheses are for aspargine.

Table 6. Pseudo-Second-Order Rate Constants (k_{obs}) for the Oxidation of Amino Acids (S) by HOCl in the Presence of Perchloric Acid at 303 K

$10^3[HOCl]_0$	$10^2[S]_0$	$10^2[HClO_4]$	$10k_{obs}/dm^3\,mol^{-1}\,s^{-1}$		
mol dm^{-3}	mol dm^{-3}	mol dm^{-3}	Ala	Val	Phe
Effect of varying $[HOCl]_0$					
0.5	2.0	5.0	9.9	9.8	10.3
1.0	2.0	5.0	10.3	10.1	10.7
2.0	2.0	5.0	10.1	10.1	10.5
4.0	2.0	5.0	10.2	10.3	10.5
5.0	2.0	5.0	10.0	10.5	10.8
Effect of varying $[S]_0$					
2.0	0.5	5.0	10.1	10.2	10.5
2.0	1.0	5.0	10.5	10.0	10.7
2.0	2.0	5.0	10.1	10.1	10.5
2.0	4.0	5.0	9.9	10.3	10.5
2.0	5.0	5.0	10.1	10.1	10.7
Effect of varying $[HClO_4]$					
2.0	2.0	1.0	5.0	6.7	5.1
2.0	2.0	2.0	6.9	7.9	7.0
2.0	2.0	5.0	10.1	10.1	10.5
2.0	2.0	10.0	14.1	12.6	14.7
2.0	2.0	20.0	19.4	15.4	20.3



Scheme 3. Where R=CH_3 (Ala), $(CH_3)_2CHCH_2$ (Leu), $H_2N(CO)CH_2$ (Asn), and $H_2N(CO)CH_2CH_2$ (Gln).

$$RCH(NH_3^+)COO^- + HOCl \xrightarrow[(fast)]{} RCHO + CO_2 + NH_4^+ + Cl^-$$

This is supported by investigations with *N*-chloro-*N*-sodio-*p*-toluenesulfonamide (Chloramine-T, $ArSO_2NHCl$) and HOCl under identical conditions (Tables 5 and 6). The rates with these species showed first-order kinetics in [oxidant] and varying orders in [S] and $[H^+]$. The rates for these oxidations are much higher than those for dichloramine-T oxidations.

Aspargine and glutamine are the amides of acidic amino acids, aspartic and glutamic acids, respectively. Proline is a cyclic amino acid. It is evident from the kinetic data that the kinetic behavior of these amino acids is different from that of simple amino acids (alanine and leucine). The former exhibit different kinetic orders in [DCT] and [S] depending upon $[H^+]$ of the reaction medium, whereas the latter (simple amino acids) show same kinetics over the entire range of $[H^+]$. This difference in behavior is obvious from the comparison of pK_a values of the amino acids. Asparagine, glutamine, and proline have relatively large values for dissociation constants (Table 7) (smaller pK_a's) and hence are more susceptible to change in $[H^+]$ than the simple amino acids. Hence it is not quite unexpected that they show different kinetic behavior at different $[H^+]$(Table 4).

The observed negligible effect of added reduced product of the oxidant, TSA, and of varying ionic strength of the medium on the rates of oxidations are in agreement with the proposed mechanisms. The latter are also supported by the moderate values of the activation parameters (Table 4).

The observed dielectric effect on the rates of oxida-

Table 7. Ionization Constants and pH Values at the Isoelectric Points of Amino Acids at 25 °C

Amino acid	pK_1	pK_2	pH_i
Alanine	2.34	9.69	6.01
Leucine	2.36	9.60	5.98
Aspargine	2.02	8.80	5.41
Glutamine	2.17	9.13	5.65
Proline	2.00	10.60	6.30

Isoelectric point (or IP): This is the pH at which the maximum number of amino acid molecules are present as zwitter ions, $pH_i=(pK_1+pK_2)/2$.

tions (Table 3), is in conformity with Amis-Jaffee equation for dipolar molecule-dipolar molecule interaction.[14,15]

$$\log k_D = \log k_\infty - \frac{2\mu_1\mu_2}{2.303\, k_B T r^3 D} \quad (17)$$

Where k_D and k_∞ are the rate constants in media of dielectric constant D and ∞, respectively, k_B is the Boltzmann constant, μ_1 and μ_2 are the permanent moments on the dipoles, r is the distance of approach for the dipoles, and T *is* the absolute temperature.

The plots of $\log k_{obs}$ versus $1/D$ were linear (Fig. 6) with negative slopes in accordance with Eq. 17.

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