A Study of Substituent Effect on the Oxidative Strengths of *N*-Chloroarenesulphonamides: Kinetics of Oxidation of Leucine and Isoleucine in Aqueous Acid Medium

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To study the variation of oxidative strengths of *N*-chloro-arenesulphonamides with substitution in the benzene ring, six mono- and five di-substituted *N*-chloro-arenesulphonamides are employed as oxidants for studying the kinetics of oxidation of two neutral amino acids, L-leucine and L-isoleucine in aqueous acid medium. The *N*-chloro-arenesulphonamides studied are of the constitution: $ArSO_2NaNCl{\cdot}H_2O$ (where Ar = C_6H_5, 4-$CH_3C_6H_4$, 4-$C_2H_5C_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 2,3-$(CH_3)_2C_6H_3$, 2,4-$(CH_3)_2C_6H_3$, 2-CH_3-4-ClC_6H_3, 2,4-$Cl_2C_6H_3$, and 3,4-$Cl_2C_6H_3$). The reactions show second order kinetics in [oxidant], fractional order in [amino acid] and inverse dependence on [H^+]. Addition of the reduced product of the oxidants or variation in ionic strength of the medium has no significant effect on the rates of oxidations. A two-pathway mechanism is considered to explain the experimental results. Effective oxidizing species of the oxidants is Cl^+ in different forms. Therefore the oxidising strengths of *N*-chloro-arenesulphonamides depend on the ease with which Cl^+ is released from them. The study reveals that the introduction of substituent in the benzene ring of the oxidant affects both the kinetic and thermodynamic data for the oxidations The electron releasing groups such as CH_3 generally inhibit the rates, while electron-withdrawing groups such as Cl enhance this ability, as the electron withdrawing groups ease the release of Cl^+ from the reagents and hence increase the oxidising strengths. The on E_a and log$A$ and validity of the Hammett and isokinetic relationships for the oxidations are also analysed.

Key words: Kinetics, Oxidation, Leucine, Isoleucine, *N*-Chloroarenesulphonamides

Introduction

The chemistry of *N*-halo-arenesulphonamides is of interest due to their distinct physical, chemical and biological properties. They act as halonium cations, hypohalite species and *N*-anions which behave both as bases and nucleophiles. The diverse properties are due to their oxidising action in aqueous, partial aqueous and non-aqueous media [1 – 11]. Although two members of this class of reagents, commonly known as chloramine-T and chloramine-B have been extensively studied, there are no efforts in altering the electron environment around the nitrogen atom of the sulphonamide group by making appropriate substitution in the benzene ring, to get Cl^+ released either at ease or with difficulty, to produce *N*-chloro-arenesulphonamide of required oxidising capacity. Hence in an effort to introduce *N*-chloro-arenesulphonamides of different oxidizing strengths, we have recently reported the preparation and spectroscopic characterization of several sodium salts of mono- and di-substituted *N*-chloro-arenesulphonamides [12 – 14]. In this paper, we report the results of kinetic studies on the oxidations of two neutral amino acids, L-leucine and L-isoleucine by six mono- and five di-substituted *N*-chloro-arenesulphonamides of the constitution $ArSO_2NaNCl{\cdot}H_2O$.

Results and Discussion

Stoichiometry and product analysis

The stoichiometry of amino acid (AA) – substituted *N*-chloro-arenesulphonamide (NCSBS) oxidations was determined by equilibrating varying ratios of [NCSBS] to [AA] in aqueous $HClO_4$ at room temperature. The major products of oxidations were the corresponding aldehydes. The observed 1:1 stoichiometry may be represented by the following equation.

10^3[NCSBS]$_0$ (mol dm^{-3})	10^2[Leu/Ile]$_0$ (mol dm^{-3})	10^2[$HClO_4$] (mol dm^{-3})	10 k_{obs}(dm^3 mol^{-1} s^{-1}) 4-X-$C_6H_4SO_2NaNCl{\cdot}H_2O$ where X =					
			H	CH_3	C_2H_5	F	Cl	Br
			Leu					
1.0	2.0	1.0	14.8	9.2	21.0	12.0	17.0	41.2
1.0	2.0	2.0	6.7	5.3	9.9	8.5	12.0	29.5
1.0	2.0	3.0	4.5	3.3	5.7	6.0	8.5	13.0
1.0	2.0	5.0	2.6	1.5	2.6	3.3	5.0	7.5
1.0	2.0	10.0	1.4	1.0	1.6	2.3	3.0	4.4
			Ile					
1.0	2.0	1.0	10.8	10.8	17.7	17.8	30.3	40.1
1.0	2.0	2.0	8.3	7.2	12.5	12.0	20.0	30.0
1.0	2.0	3.0	6.8	4.4	7.0	9.6	13.9	22.4
1.0	2.0	5.0	4.0	3.7	3.6	4.7	7.5	11.6
1.0	2.0	10.0	2.5	2.3	2.5	2.7	4.9	6.9
			i-X-j-$YC_6H_3SO_2NaNCl{\cdot}H_2O$, i-X-j-Y =					
			2,3-$(CH_3)_2$	2,4-$(CH_3)_2$	2-CH_3,4-Cl	2,4-Cl_2	3,4-Cl_2	
			Leu					
1.0	2.0	1.0	9.5	9.3	25.6	35.9	30.6	
1.0	2.0	2.0	5.8	6.2	18.7	25.9	19.6	
1.0	2.0	3.0	4.2	4.4	11.7	17.5	13.9	
1.0	2.0	5.0	2.9	2.4	6.3	12.0	7.6	
1.0	2.0	10.0	2.0	1.5	3.8	8.3	3.8	
			Ile					
1.0	2.0	1.0	8.5	8.3	10.1	16.2	22.6	
1.0	2.0	2.0	5.3	5.7	7.4	12.6	14.3	
1.0	2.0	3.0	4.4	4.8	6.1	10.7	8.4	
1.0	2.0	5.0	2.7	3.3	3.4	5.1	3.9	
1.0	2.0	10.0	1.7	1.9	2.4	2.5	2.1	

Table 1. Pseudo-second order rate constants (k_{obs}) for the oxidation of L-leucine (Leu) and L-isoleucine (Ile) by sodium salts of mono- and di-substituted *N*-chloroarenesulphonamides (NCSBS) in aqueous perchloric acid at 303 K (I = 0.30 mol dm^{-3}).

$$ArSO_2NCl^- + RCH(NH_3^+)COO^- + H_2O \rightarrow ArSO_2NH_2 + RCHO + Cl^- + NH_3 + CO_2$$

Ar = C_6H_5 (**1**), 4-CH_3-C_6H_4 (**2**), 4-C_2H_5-C_6H_4 (**3**), 4-F-C_6H_4 (**4**), 4-Cl-C_6H_4 (**5**), 4-Br-C_6H_4 (**6**), 2,3-$(CH_3)_2$-C_6H_3 (**7**), 2,4-$(CH_3)_2$-C_6H_3 (**8**), 2-CH_3-4-Cl-C_6H_3 (**9**), 2,4-Cl_2-C_6H_3 (**10**), and 3,4-Cl_2-C_6H_3 (**11**). R = $(CH_3)_2CHCH_2$ (Leu) and $CH_3CH_2CH(CH_3)$ (Ile).

In a typical experiment, a mixture of leucine (0.02 mol dm^{-3}), sodium salt of *N*-chloro-4-chloroarenesulphonamide (NC4CBS) (0.001 mol dm^{-3}) and perchloric acid (0.03 mol dm^{-3}) was made up to 50 ml with water. The mixture was allowed to stand for 24 h to ensure completion of reaction. It was then treated with an excess of saturated solution of 2,4-dinitro-phenylhydrazine and set aside for 10 h. The precipitated 2,4-dinitrophenyl-hydrazone (DNP) was filtered off, dried, recrystallised from ethanol and its melting point was determined. In all the cases, carbon dioxide and ammonia were detected by baryta water and Nessler's reagent, respectively. The presence of aldehydes were also confirmed by the spot tests. The reduced products of the oxidants, the substituted arenesulphonamides ($ArSO_2NH_2$) were identified by TLC [15] using petroleum ether-chloroform-butanol (2:2:1 v/v) as the solvent system and iodine as spray reagent. The R_f values of the reduced arenesulphonamides were virtually identical with the values of the corresponding pure arenesulphonamides.

Kinetic measurements

The kinetics of oxidations were carried out under pseudo-second order conditions with [amino acid] $\gg$ [NCSBS] (by 5 – 50 times). The reactions were initiated by the rapid addition of known amounts of oxidant solution (0.0005 – 0.004 mol dm^{-3}), pre-equilibrated at a desired temperature, to mixtures containing the required amounts of amino acid (0.005 – 0.04 mol dm^{-3}), perchloric acid (0.01 – 0.10 mol dm^{-3}), sodium nitrate and water in the boiling tube, thermostated at the same temperature. The progress of the reactions was monitored for at least two half-lives by the iodometric determination of unreacted oxidant at regular intervals of time. The pseudo-second order rate constants (k_{obs}) were computed by graphical methods and the values were reproducible within $\pm$3% error.

The kinetic data on the oxidations of Leu and Ile by eleven mono- and di-substituted *N*-chloro-

Table 2. Kinetic data for the oxidation of L-leucine (Leu) and L-isoleucine (Ile) by sodium salts of mono- and di-substituted *N*-chloroarenesulphonamides (NCSBS) in aqueous perchloric acid.

$ArSO_2NaNCl·H_2O$, where Ar =	Kinetic orders observed in					
		Leu			Ile	
	[NCSBS]	[Leu]	$[HClO_4]$	[NCSBS]	[Ile]	$[HClO_4]$
C_6H_5	2.0	0.4	−1.1	2.0	0.4	−0.8
4-$CH_3C_6H_4$	2.0	0.3	−1.1	2.0	0.4	−0.7
4-$C_2H_5C_6H_4$	2.0	0.3	−1.1	2.0	0.3	−1.0
4-FC_6H_4	2.0	0.3	−1.0	2.0	0.4	−0.9
4-ClC_6H_4	2.0	0.3	−1.0	2.0	0.3	−1.1
4-BrC_6H_4	2.0	0.3	−1.0	2.0	0.6	−1.1
2,3-$(CH_3)_2C_6H_3$	2.0	0.3	−0.7	2.0	0.4	−0.7
2,4-$(CH_3)_2C_6H_3$	2.0	0.4	−0.9	2.0	0.4	−0.7
2-CH_3-4-ClC_6H_3	2.0	0.4	−0.9	2.0	0.4	−0.7
2,4-$Cl_2C_6H_3$	2.0	0.5	−0.9	2.0	0.5	−1.1
3,4-$Cl_2C_6H_3$	2.0	0.5	−1.0	2.0	0.4	−1.1

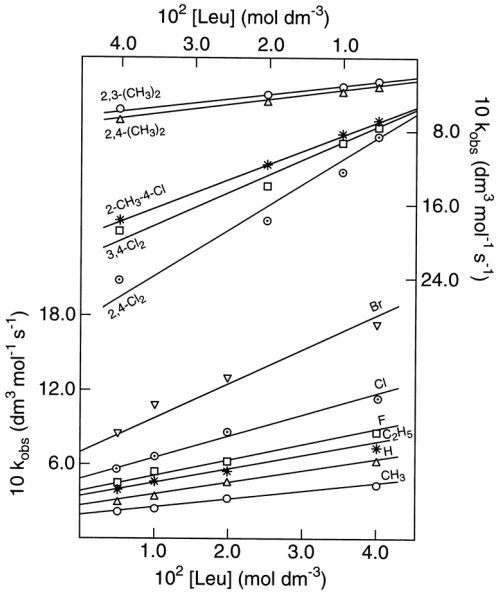

Fig. 1. Plots of k_{obs} *versus* [Leu]; 10^3 [NCSBS] = 33.3 $[HClO_4]$ = 3.33 I = 1.0 mol dm^{-3}; Temp.: 303 K. NCSBS: 4-X-$C_6H_4SO_2NaNCl$, where X = H, CH_3, C_2H_5, F, Cl or Br and i-X-j-Y-C_6H_3 SO_2NaNCl, where i-X-j-Y = 2,3-$(CH_3)_2$, 2,4-$(CH_3)_2$, 2-CH_3-4-Cl, 2,4-Cl_2, 3,4-Cl_2.

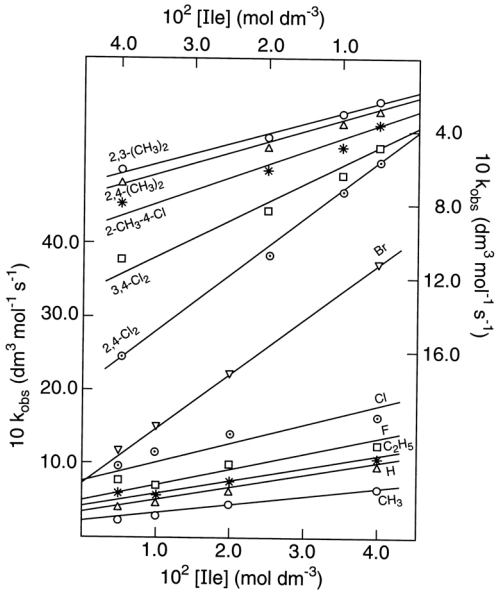

Fig. 2. Plots of k_{obs} *versus* [Ile]; 10^3 [NCSBS] = 33.3 $[HClO_4]$ = 3.33 I = 1.0 mol dm^{-3}; Temp.: 303 K. NCSBS : 4-X-$C_6H_4SO_2NaNCl$, where X = H, CH_3, C_2H_5, F, Cl or Br and i-X-j-Y-C_6H_3 SO_2NaNCl, where i-X-j-Y = 2,3-$(CH_3)_2$, 2,4-$(CH_3)_2$, 2-CH_3-4-Cl, 2,4-Cl_2, 3,4-Cl_2.

arenesulphonamides (NCSBS) (1-11), under varying [NCSBS], [AA], $[HClO_4]$, solution composition, and temperature of the medium, are shown in Tables 1, 2 and Figures 1, 2.

Effect of varying [oxidant]$_0$

At constant $[AA]_0$ (5−50 fold excess over $[oxidant]_0$) and $[H^+]$, the second order plots of 1/[oxidant] *versus* time were linear up to 70% completion of the reactions. The pseudo-second order rate constants computed from the plots remained unaffected by the changes in $[oxidant]_0$, establishing second order dependence of the rate on $[NCSBS]_0$.

Effect of varying [AA]$_0$

At constant $[NCSBS]_0$ and $[H^+]$, the rates increased with increase in [AA] with fractional order dependences in [AA] for all the oxidations. The plots of k_{obs} *versus* [AA] were linear with finite intercepts on the ordinates (Figs. 1 and 2), indicating the operation of a two-pathway mechanism for the oxidation of amino acids by all the reagents.

Effect of varying [H^+]

The rates decreased with increase in [H^+], at fixed [NCSBS]$_0$ and [AA]$_0$, with varying inverse order dependences in [H^+] (Tables 1 and 2).

Effect of varying ionic strength and other parameters of the medium

Variation in either the ionic strength of the medium or addition of the reduced products of the oxidants, substituted arenesulphonamides (SBSA), to the reaction mixtures had no significant effect on the rates of oxidations. The rates were measured at different temperatures under varying [AA]. The constants of both the pathways in the two-pathway mechanism have been calculated at each temperature as described later. Activation parameters corresponding to these constants have also been computed from the Arrhenius and Eyring plots.

Sodium salts of *N*-chloro-benzenesulphonamide and its substituted compounds (NCSBS) are fairly strong electrolytes in aqueous solution. They furnish different reactive species depending upon pH of the medium. The possible oxidising species in acid solutions of NCSBS are $ArSO_2NCl^-$, $ArSO_2NHCl$, HOCl and $ArSO_2NCl_2$ at low [H^+], and $ArSO_2NH_2Cl^+$ and H_2OCl^+ at high [H^+].

Amino acids Leu and Ile exist in the acid/base equilibrium in acidic solutions:

$$\underset{(SH^+)}{RCH_2CH(N^+H_3)COOH} \rightleftharpoons \underset{(S)}{RCH_2CH(N^+H_3)COO^-} + H^+$$

The second order kinetics in [NCSBS], fractional order in [AA] and higher inverse dependence of the rate on [H^+] and other observed effects for the oxidation of Leu and Ile by all the *N*-chloro-arenesulphonamides may be explained by a two-pathway mechanism shown in Scheme 1. It is supported by the fact that the direct plots between the rate constants and [AA] (Figs. 1 and 2) gave better correlations than the double reciprocal plots. Further, in acidic aqueous solutions of *N*-chloroarenesulphonamides, the corresponding *N*,*N*-dichloro compounds are produced, which are insoluble in water but soluble in organic solvents.

Applying the steady state approximation to the intermediate Y in path 1, the rate of the reaction going through path 1 is given by

$$-d[ArSO_2NH_2Cl^+]/dt = k_3[ArSO_2NH_2Cl^+][Y] \quad (1)$$

Path 1

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

$$(ArSO_2NH_2Cl)^+ + S \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \text{Intermediate (Y)} \quad \text{(fast)}$$

$$Y + (ArSO_2NH_2Cl)^+ \overset{k_3}{\longrightarrow} \text{products} \quad \text{(slow)}$$

Path 2

$$2(ArSO_2NH_2Cl)^+ \overset{K_4}{\rightleftharpoons} \text{Intermediate } (Y') + 2H^+ \quad \text{(fast)}$$

$$Y' \overset{k_5}{\longrightarrow} ArSO_2NCl_2 + ArSO_2NH_2 \quad \text{(slow)}$$

$$ArSO_2NCl_2 + H_3O^+ \longrightarrow H_2OCl^+ + ArSO_2NHCl \quad \text{(fast)}$$

$$H_2OCl^+ + S \longrightarrow \text{products} \quad \text{(fast)}$$

$$ArSO_2NHCl + H^+ \longrightarrow (ArSO_2NH_2Cl)^+ \quad \text{(fast)}$$

Scheme 1.

where [Y] = k_2 [$ArSO_2NH_2Cl^+$]$_0$ [S] / {k_{-2} + k_3 $ArSO_2NH_2Cl^+$]$_0$ + k_2 [S]} as [$ArSO_2NH_2Cl^+$] = [$ArSO_2NH_2Cl^+$]$_0$ − [Y] and [S]$_0$ ∼ [S].

Since k_3 is small and [S] ≫ [$ArSO_2NH_2Cl^+$]$_0$, k_3 [$ArSO_2NH_2Cl^+$]$_0$ is negligibly small compared to other terms in the denominator, and eq. (1) becomes:

$$-d[ArSO_2NH_2Cl^+]/dt = K_2k_3[ArSO_2NH_2Cl^+]_0[ArSO_2NH_2Cl^+]\frac{[S]}{(1+K_2[S])}$$

where $K_2 = k_2/k_{-2}$. (2)

With [$ArSO_2NH_2Cl^+$]$_0$[$ArSO_2NH_2Cl^+$] ≈ [$ArSO_2$-NH_2Cl^+]^2, the rate law in eq. (2) becomes:

$$-d[ArSO_2NH_2Cl^+]/dt = K_2k_3[ArSO_2NH_2Cl^+]^2[S]/(1 + K_2[S]) \quad (3)$$

Rearranging eq. (3), we obtain eq. (4):

$$-\{d[NCSBS]/[NCSBS]^2\}/dt = K_2k_3[S]/(1+K_2[S]) \quad (4)$$

The left-hand side of eq. (4) may be written as:

$$-\{d[NCSBS]/[NCSBS]^2\}/dt = d\{1/[NCSBS]\}/dt = k_{p1}$$

Hence eq. (4) becomes eq. (5):

$$k_{p1} = K_2k_3[S]/(1+K_2[S]) \quad (5)$$

We also have:

$$[S] = K_1[SH^+]/[H^+] \quad (6)$$

Therefore eq. (5) takes the form:

$$k_{p1} = K_1K_2k_3[SH^+]/\{[H^+] + K_1K_2[SH^+]\} \quad (7)$$

Table 3. The calculated constants k and k' for paths 1 and 2 of the mechanism at different temperatures for the oxidation of L-leucine (Leu) and L-isoleucine (Ile) by sodium salts of mono- and di-substituted *N*-chloro-arenesulphonamides in aqueous perchloric acid.

$ArSO_2NaNCl{\cdot}H_2O$, where Ar =	$10\,k$ ($dm^3\ mol^{-1}\ s^{-1}$) at Temp. (K)							
	Leu				Ile			
	298	303	308	313	298	303	308	313
C_6H_5	1.1	2.8	3.3	4.0	3.0	4.8	6.0	11.0
4-$CH_3C_6H_4$	1.0	1.8	2.1	3.3	2.4	3.1	4.3	6.3
4-$C_2H_5C_6H_4$	1.3	2.6	3.8	4.7	3.1	3.9	6.7	11.6
4-FC_6H_4	2.5	3.6	4.2	5.2	3.6	5.7	7.9	11.6
4-ClC_6H_4	5.7	6.5	7.7	8.5	7.7	10.8	13.2	16.9
4-BrC_6H_4	5.4	7.0	10.1	13.3	6.2	13.6	14.5	16.9
2,3-$(CH_3)_2C_6H_3$	2.0	2.4	3.1	4.4	2.2	3.0	4.1	5.7
2,4-$(CH_3)_2C_6H_3$	1.8	2.8	6.3	9.3	2.3	2.7	3.7	5.3
2-CH_3-4-ClC_6H_3	6.5	8.8	11.3	16.9	2.7	3.7	5.9	8.0
2,4-$Cl_2C_6H_3$	9.3	14.6	17.0	18.0	5.3	8.9	11.3	14.5
3,4-$Cl_2C_6H_3$	5.3	10.7	13.0	15.4	4.5	5.3	6.2	10.3
	$10^4\,k'$ ($dm^3\ mol^{-1}\ s^{-1}$)							
C_6H_5	1.1	2.2	2.5	2.9	2.5	3.1	5.2	7.0
4-$CH_3C_6H_4$	1.5	1.7	2.3	3.5	1.6	2.0	3.1	3.5
4-C_2H_5 C_6H_4	2.2	3.4	4.5	5.0	2.2	3.6	5.0	6.5
4-F C_6H_4	2.0	2.8	3.3	3.8	3.2	4.3	5.0	6.5
4-ClC_6H_4	1.9	3.5	5.4	8.8	4.6	5.9	9.4	11.6
4-BrC_6H_4	5.0	7.2	10.2	14.2	5.4	9.4	13.2	15.1
2,3-$(CH_3)_2C_6H_3$	1.2	2.2	3.7	4.3	1.6	2.0	2.5	3.4
2,4-$(CH_3)_2C_6H_3$	1.9	2.4	2.7	4.6	1.5	2.3	2.9	3.8
2-CH_3-4-ClC_6H_3	4.5	5.4	6.8	7.9	2.2	2.8	4.2	5.8
2,4-$Cl_2C_6H_3$	4.5	5.6	7.4	10.8	3.1	4.3	6.1	7.2
3,4-$Cl_2C_6H_3$	3.1	5.0	5.6	7.9	3.2	4.0	4.7	6.5

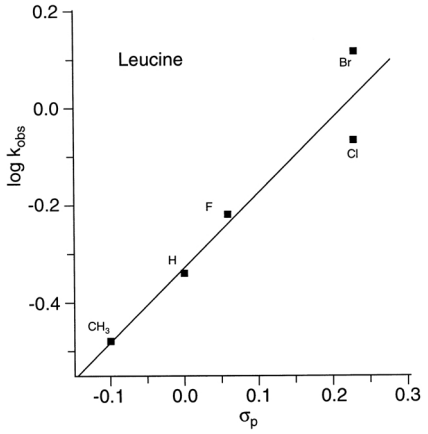

Fig. 3a. Plot of log k_{obs} *versus* σ_p (NCSBS) for leucine oxidation. 10^3 [NCSBS] = 33.3 [$HClO_4$] = 3.33 I = 1.0 mol dm^{-3}; Temp.: 303 K. NCSBS: 4-X-$C_6H_4SO_2NaNCl$, where X = H, CH_3, C_2H_5, F, Cl, or Br.

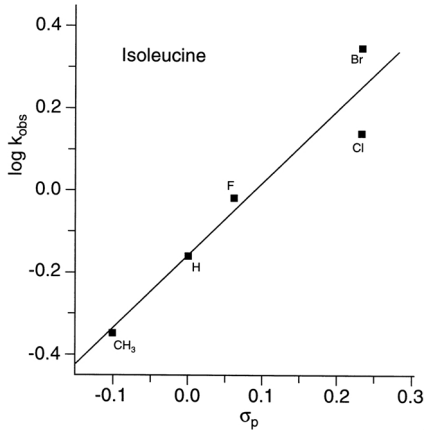

Fig. 3b. Plot of log k_{obs} *versus* σ_p (NCSBS) for isoleucine oxidation. 10^3 [NCSBS] = 33.3 [$HClO_4$] = 3.33 I = 1.0 mol dm^{-3}; Temp.: 303 K. NCSBS: 4-X-$C_6H_4SO_2NaNCl$, where X = H, CH_3, C_2H_5, F, Cl, or Br.

If K_2 is small, then the rate law in eq. (5) will take the form:

$$k_{p1} = K_2 k_3[S] = K_1 K_2 k_3[SH^+]/[H^+] \quad (8)$$

The rate law for the reaction in path 2 has been deduced in a similar way:

$$-\{d[NCSBS]/[NCSBS]^2\}/dt = K_4 k_5/[H^+]^2$$

or

$$k_{p2} = K_4 k_5/[H^+]^2 \quad (9)$$

The combined rate law for both pathways is therefore given by eq. (10) or (11):

$$k_{obs} = \{K_1 K_2 k_3[SH^+]/[H^+]\} + \{K_4 k_5/[H^+]^2\} \quad (10)$$

$ArSO_2NaNCl{\cdot}H_2O$, where Ar =	Values calculated from *k*					Optimised values		
	E_a (kJ mol^{-1})	log*A*	$\Delta H^{\#}$ (kJ mol$^{-1'}$)	$\Delta S^{\#}$ (J K^{-1} mol^{-1})	$\Delta G^{\#}$ (kJ mol$^{-1'}$)	E_a (kJ mol^{-1})	log*A*	$\Delta S^{\#}$ (J K^{-1} mol^{-1})
				Leu				
C_6H_5	79.8	13.2	77.1	−1.3	77.5	79.8	13.2	−1.3
4-$CH_3C_6H_4$	59.6	9.5	59.2	−46.4	78.6	80.9	13.0	−4.9
4-$C_2H_5C_6H_4$	77.9	12.8	77.8	+7.0	77.7	79.9	13.2	−2.0
4-FC_6H_4	45.5	7.4	44.4	−107.0	76.8	79.1	13.3	+0.8
4-ClC_6H_4	38.7	6.5	35.3	−132.0	75.3	77.6	13.6	+5.8
4-BrC_6H_4	42.6	7.2	42.0	−98.9	75.1	77.0	13.6	+6.4
2,3-$(CH_3)_2C_6H_3$	46.0	7.3	41.5	−120.0	77.9	80.1	13.1	−2.6
2,4-$(CH_3)_2C_6H_3$	86.2	14.3	82.6	+16.9	77.5	79.8	13.2	−1.3
2-CH_3-4-ClC_6H_3	49.4	8.6	47.9	−87.9	74.6	76.9	13.7	+8.3
2,4-$Cl_2C_6H_3$	47.9	8.4	46.8	−87.5	73.3	75.6	13.9	+12.5
3,4-$Cl_2C_6H_3$	63.8	11.0	62.7	−37.3	74.0	76.5	13.8	+9.8
				Ile				
C_6H_5	66.8	11.2	60.7	−50.9	77.5	66.8	11.2	−50.9
4-$CH_3C_6H_4$	51.7	8.4	49.7	−90.6	77.2	67.1	11.0	−54.5
4-$C_2H_5C_6H_4$	66.0	11.0	65.4	−27.0	76.6	67.3	11.1	−52.6
4-FC_6H_4	62.3	10.5	61.0	−48.4	75.7	66.4	11.3	−49.4
4-ClC_6H_4	44.9	7.8	43.5	−100.8	74.0	64.8	11.5	−44.0
4-BrC_6H_4	59.6	10.4	59.4	−38.3	73.5	64.2	11.6	−42.1
2,3-$(CH_3)_2C_6H_3$	50.1	8.1	45.7	−104.3	77.3	68.0	11.0	−54.7
2,4-$(CH_3)_2C_6H_3$	44.3	7.1	39.4	−125.7	77.5	68.2	11.0	−55.7
2-CH_3-4-ClC_6H_3	56.4	9.3	55.0	−71.4	76.6	67.5	11.1	−53.0
2,4-$Cl_2C_6H_3$	57.4	9.9	53.0	−70.2	74.3	65.3	11.5	−45.7
3,4-$Cl_2C_6H_3$	50.0	8.3	41.0	−114.9	75.8	66.5	11.2	−49.9

Table 4. Activation parameters for path 1 of the mechanism for the oxidation of L-leucine (Leu) and L-isoleucine (Ile) by sodium salts of mono- and di-substituted *N*-chloro-arenesulphonamides in aqueous perchloric acid.

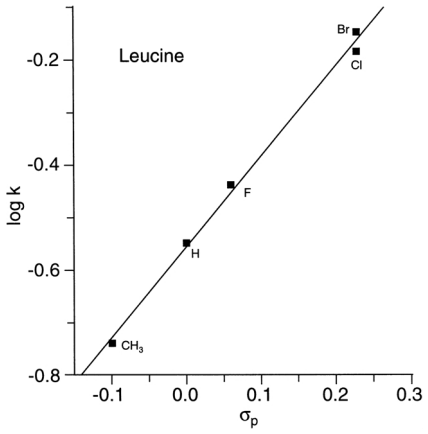

Fig. 4a. Plot of log k *versus* σ_p (NCSBS) for leucine oxidation. NCSBS: 4-X-$C_6H_4SO_2NaNCl$, where X = H, CH_3, C_2H_5, F, Cl, or Br.

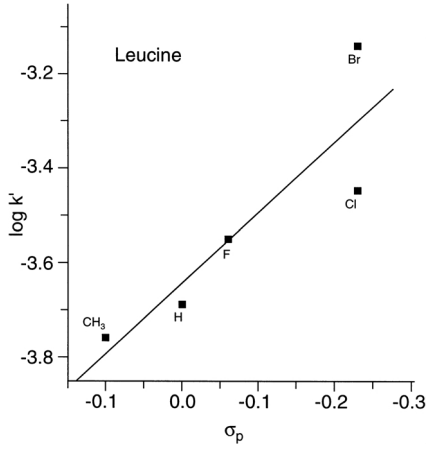

Fig. 4b. Plot of log k′ *versus* σ_p (NCSBS) for leucine oxidation. NCSBS : 4-X-$C_6H_4SO_2NaNCl$, where X = H, CH_3, C_2H_5, F, Cl, or Br.

or

$$k_{obs} = \{k[SH^+]/[H^+]\} + \{k'/[H^+]^2\}, \qquad (11)$$

where $k = K_1K_2k_3$ and $k' = K_4k_5$.

The plots of k_{obs} *versus* [AA] were linear with finite intercepts on the ordinate (Figs. 1 and 2), in conformity with the rate law in eq. (11). The constants *k* and *k'* were calculated from the slopes and intercepts of the plots, respectively. These constants were used to recalculate the rate constants from the rate law in eq. (11), as $[H^+]$ was varied. The recalculated values agreed reasonably well with the experimental constants (Table not shown) testing the validity of the rate law and providing support to the suggested mechanism. Further, the values of *k* and *k'* were calculated at different temperatures by varying [substrate] at each temperature

Table 5. Activation parameters for path 2 of the mechanism for the oxidation of L-leucine (Leu) and L-isoleucine (Ile) by sodium salts of mono- and di-substituted *N*-chloro-arenesulphonamides in aqueous perchloric acid.

$ArSO_2NaNCl{\cdot}H_2O$, where Ar =	Values calculated from k'					Optimised values		
	E_a (kJ mol^{-1})	log$A$	$\Delta H^{\#}$ (kJ mol$^{-1'}$)	$\Delta S^{\#}$ (J K^{-1} mol^{-1})	$\Delta G^{\#}$ (kJ mol$^{-1'}$)	E_a (kJ mol^{-1})	log$A$	$\Delta S^{\#}$ (J K^{-1} mol^{-1})
				Leu				
C_6H_5	66.0	7.7	65.9	−97.6	95.4	66.0	7.7	−97.6
4-$CH_3C_6H_4$	53.1	5.4	53.0	−142.4	96.1	66.7	7.6	−99.9
4-$C_2H_5C_6H_4$	52.2	5.5	52.1	−139.3	94.3	64.9	7.9	−94.0
4-FC_6H_4	45.5	4.3	45.2	−163.9	94.9	65.4	7.8	−95.7
4-ClC_6H_4	75.1	9.5	75.0	−63.6	94.2	64.9	7.9	−93.8
4-BrC_6H_4	55.8	6.5	55.3	−122.7	92.5	63.1	8.2	−87.8
2,3-$(CH_3)_2C_6H_3$	70.4	8.5	70.3	−83.3	95.5	65.9	7.7	−97.8
2,4-$(CH_3)_2C_6H_3$	48.9	4.8	42.2	−175.2	95.3	65.6	7.8	−97.0
2-CH_3-4-ClC_6H_3	37.1	2.8	36.3	−188.0	93.3	63.6	8.1	−90.3
2,4-$Cl_2C_6H_3$	46.8	4.8	43.9	−162.5	93.1	63.5	8.1	−90.0
3,4-$Cl_2C_6H_3$	49.4	5.2	46.0	−156.6	93.4	63.8	8.1	−90.9
				Ile				
C_6H_5	66.1	7.9	63.8	−101.8	94.7	66.1	7.9	−101.8
4-$CH_3C_6H_4$	47.0	4.4	47.0	−160.8	95.7	67.2	7.7	−105.5
4-$C_2H_5C_6H_4$	55.7	6.2	53.9	−133.0	94.2	65.8	8.0	−100.5
4-FC_6H_4	42.7	4.8	47.0	−154.3	93.7	65.3	8.0	−99.0
4-ClC_6H_4	44.8	4.5	40.2	−174.2	93.0	64.5	8.2	−96.5
4-BrC_6H_4	47.3	5.7	50.7	−135.7	91.8	63.4	8.4	−92.4
2,3-$(CH_3)_2C_6H_3$	42.0	3.6	41.0	−180.7	95.8	67.2	7.7	−105.5
2,4-$(CH_3)_2C_6H_3$	46.6	4.4	42.1	−175.7	95.3	66.9	7.8	−104.1
2-CH_3-4-ClC_6H_3	53.3	5.6	45.8	−161.9	94.8	66.4	7.8	−102.6
2,4-$Cl_2C_6H_3$	44.6	4.3	38.9	−181.1	93.8	65.3	8.0	−99.0
3,4-$Cl_2C_6H_3$	40.2	3.5	39.3	−180.5	94.0	65.5	8.0	−99.5

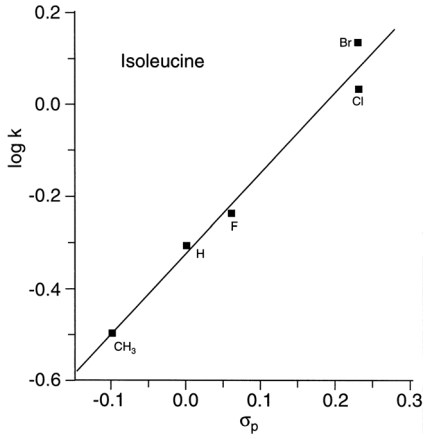

Fig. 5a. Plot of log k *versus* σ_p (NCSBS) for isoleucine oxidation. NCSBS: 4-X-$C_6H_4SO_2NaNCl$, where X = H, CH_3, C_2H_5, F, Cl, or Br.

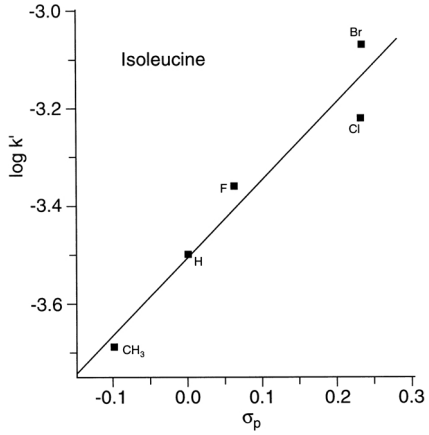

Fig. 5b. Plot of log k′ *versus* σ_p (NCSBS) for isoleucine oxidation. NCSBS: 4-X-$C_6H_4SO_2NaNCl$, where X = H, CH_3, C_2H_5, F, Cl, or Br.

(Table 3). The activation parameters for both the pathways corresponding to these constants have also been computed from the plots of $\log k$ or $\log k'$ *versus* $1/T$ and $\log(k/T)$ or $\log(k'/T)$ *versus* $1/T$ (Table 4 and 5).

Applicability of the Hammett equation has also been tested for the oxidation of both Leu and Ile by all the mono-substituted oxidants. The plots of $\log k_i$ *versus* σ_p were reasonably linear (Figs. 3–5) and the following relations were found to be valid. The oxidant with the p-ethyl group in the ring (**3**) showed deviations from the linearity. Hence the correlations are shown with and without reagent **3**.

Leucine:

$$\log k_{obs} = -0.253 + 1.05\sigma_p \text{ (r = 0.82)}$$

$$\log k_{obs} = -0.327 + 1.53\sigma_p \text{ (r = 0.96) (except ethyl)}$$

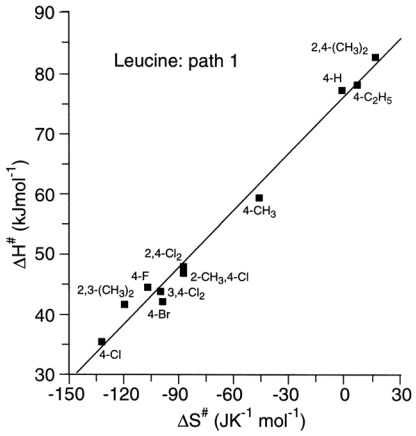

Fig. 6a. Plot of $\Delta H^{\neq}$ *versus* $\Delta S^{\neq}$ (leucine: Path 1). i-X-$C_6H_4SO_2NaNCl$, where i-X = 4-H, 4-CH_3, 4-C_2H_5, 4-F, 4-Cl or 4-Br and i-X-j-Y-$C_6H_3SO_2NaNCl$, where i-X-j-Y = 2,3-$(CH_3)_2$, 2,4-$(CH_3)_2$, 2-CH_3-4-Cl, 2,4-Cl_2, 3,4-Cl_2.

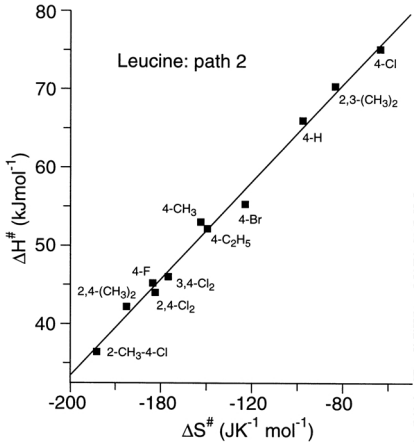

Fig. 6b. Plot of $\Delta H^{\neq}$ *versus* $\Delta S^{\neq}$ (leucine: Path 2). i-X-$C_6H_4SO_2NaNCl$, where i-X = 4-H, 4-CH_3, 4-C_2H_5, 4-F, 4-Cl or 4-Br and i-X-j-Y-$C_6H_3SO_2NaNCl$, where i-X-j-Y = 2,3-$(CH_3)_2$, 2,4-$(CH_3)_2$, 2-CH_3-4-Cl, 2,4-Cl_2, 3,4-Cl_2.

$$\log k = -0.502 + 1.36\sigma_p \text{ (r = 0.94)}$$
$$\log k = -0.550 + 1.70\sigma_p \text{ (r = 0.97) (except ethyl)}$$
$$\log k' = -3.641 + 1.48\sigma_p \text{ (r = 0.89) (except ethyl)}$$

Isoleucine:

$$\log k_{obs} = -0.094 + 1.37\sigma_p \text{ (r = 0.89)}$$
$$\log k_{obs} = -0.159 + 1.79\sigma_p \text{ (r = 0.96) (except ethyl)}$$
$$\log k = -0.281 + 1.47\sigma_p \text{ (r = 0.96);}$$
$$\log k = -0.322 + 1.75\sigma_p \text{ (r = 0.99) (except ethyl)}$$
$$\log k' = -3.503 + 1.61\sigma_p \text{ (r = 0.97) (except ethyl)}$$

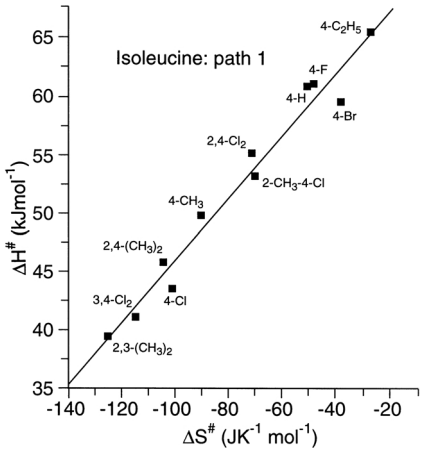

Fig. 7a. Plot of $\Delta H^{\neq}$ *versus* $\Delta S^{\neq}$ (isoleucine: Path 1). i-X-$C_6H_4SO_2NaNCl$, where i-X = 4-H, 4-CH_3, 4-C_2H_5, 4-F, 4-Cl or 4-Br and i-X-j-Y-$C_6H_3SO_2NaNCl$, where i-X-j-Y = 2,3-$(CH_3)_2$, 2,4-$(CH_3)_2$, 2-CH_3-4-Cl, 2,4-Cl_2, 3,4-Cl_2.

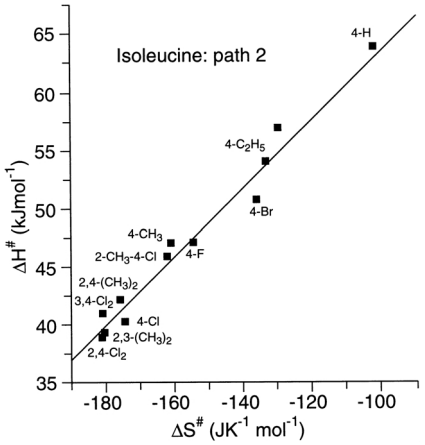

Fig. 7b. Plot of $\Delta H^{\neq}$ *versus* $\Delta S^{\neq}$ (isoleucine: Path 2). i-X-$C_6H_4SO_2NaNCl$, where i-X = 4-H, 4-CH_3, 4-C_2H_5, 4-F, 4-Cl or 4-Br and i-X-j-Y-$C_6H_3SO_2NaNCl$, where i-X-j-Y = 2,3-$(CH_3)_2$, 2,4-$(CH_3)_2$, 2-CH_3-4-Cl, 2,4-Cl_2, 3,4-Cl_2.

The enthalpies and the free energies of activations for the oxidations of Leu and Ile by all the *N*-chloroarenesulphonamides have been correlated. The plots of $\Delta H^{\neq}$ (kJ mol^{-1}) *versus* $\Delta S^{\neq}$ (J K^{-1} mol^{-1}) corresponding to both k and k' were reasonably linear (Figs. 6 and 7) with iso-kinetic temperatures of 311 and 310 K (Leu), and 266 and 294 K (Ile), respectively, which are within the temperature ranges employed or closer to the range used in the present investigations (293 – 313 K).

Table 6. Melting points of mono- and di-substituted arenesulphonamides and sodium salts of their N-chloro compounds **1 – 11**.

Substituted arenesulphonamides	M.p.(°C) obs (lit.)	Sodium salts of *N*-chloro-arenesulphonamides	M.p.(°C) obs (lit.)
$C_6H_5SO_2NH_2$	152-152	$C_6H_5SO_2NaNCl{\cdot}H_2O$ (**1**)	172-173
4-$CH_3C_6H_4$ SO_2NH_2	138-139	4- $CH_3C_6H_4SO_2NaNCl{\cdot}H_2O$ (**2**)	167-170
4-$C_2H_5C_6H_4SO_2NH_2$	99-101 (99-100)	4- $C_2H_5C_6H_4SO_2NaNCl{\cdot}H_2O$ (**3**)	194
4-$FC_6H_4SO_2NH_2$	125 (124-125)	4-$FC_6H_4SO_2NaNCl{\cdot}H_2O$ (**4**)	198
4-$ClC_6H_4SO_2NH_2$	143 (142-143)	4-$ClC_6H_4SO_2NaNCl{\cdot}H_2O$ (**5**)	191(190)
4-$BrC_6H_4SO_2NH_2$	162 (162)	4-$BrC_6H_4SO_2NaNCl{\cdot}H_2O$ (**6**)	179(178)
2,3-$(CH_3)_2C_6H_3SO_2NH_2$	138-140	2,3-$(CH_3)_2C_6H_3SO_2NaNCl{\cdot}H_2O$ (**7**)	167
2,4-$(CH_3)_2C_6H_3SO_2NH_2$	140-142	2,4-$(CH_3)_2C_6H_3SO_2NaNCl{\cdot}H_2O$ (**8**)	154
2-CH_3,4-$ClC_6H_3SO_2NH_2$	158-160	2-CH_3,4-$ClC_6H_3SO_2NaNCl{\cdot}H_2O$ (**9**)	172
2,4-$Cl_2C_6H_3SO_2NH_2$	178-180 (179-180)	2,4-$Cl_2C_6H_3SO_2NaNCl{\cdot}H_2O$ (**10**)	210
3,4-$Cl_2C_6H_3SO_2NH_2$	141-143 (134-135)	3,4-$Cl_2C_6H_3SO_2NaNCl{\cdot}H_2O$ (**11**)	192

Leucine:

$$\text{Path 1: } \Delta H^{\#} = 75.8 + 311\Delta S^{\#} \text{ (r = 0.99)}$$

$$\text{Path 2: } \Delta H^{\#} = 95.4 + 310\Delta S^{\#} \text{ (r = 0.996)}$$

Isoleucine:

$$\text{Path 1: } \Delta H^{\#} = 72.6 + 266\Delta S^{\#} \text{ (r = 0.98)}$$

$$\text{Path 2: } \Delta H^{\#} = 92.8 + 294\Delta S^{\#} \text{ (r = 0.99)}$$

Further, the effect of substitution in the *N*-chloro-arenesulphonamides, on the energy of activation, (E_a) has been analysed by optimising E_a values with reference to log$A$ value of the parent oxidant, *N*-chloro-benzenesulphonamide, through the equation,

$$E_a = 2.303\ \mathrm{RT}(\log A - \log k_i),$$

where k_i is the constant for the oxidant with a substituent. As may be seen (Tables 4 and 5), the energies of activation for the oxidation of either Leu or Ile by the oxidants with electron releasing groups in the benzene ring are slightly higher than that of the parent oxidant, while the E_a values are lower with the oxidants with electron withdrawing groups in the benzene ring. Enthalpies of activations have similar trends. Similarly log$A$ values were optimised with reference to E_a value of the parent oxidant for both Leu and Ile through the equation $\log A = \log k_i + E_a/2.303\ \mathrm{RT}$ (Tables 4 and 5). The log$A$ values have the reverse trend as anticipated. They are little higher for oxidants with the electron withdrawing groups in the benzene ring, while the effect of electron releasing groups on log$A$ is negligible. The free energies of activation for both the pathways remain almost the same in both the optimisations indicating the operation of similar mechanisms in all the cases. The formation of more ordered activated complexes is evident from the negative entropies of activations.

Conclusion

Effective oxidising species of the oxidants employed in the present oxidations is Cl^+ in different forms, released from the oxidant. The introduction of different substituents into the benzene ring of the oxidant affects the ability of it to release Cl^+ and hence its capacity to oxidise the substrate. The study revealed that the introduction of electron releasing groups such as CH_3, C_2H_5 *etc*. into the benzene ring inhibit the ease with which Cl^+ is released from the oxidant, while electron withdrawing groups such as Cl, Br *etc.* enhance this ability and and hence increased the oxidising strengths of the *N*-chloro-arenesulphonamides.

Experimental Section

Materials and methods

The substituted arenesulphonamides, were prepared by the chloro-sulphonation of the respective substituted benzenes to the corresponding sulphonylchlorides and subsequent conversion of the latter to the respective amides by the procedures reported earlier [12]. The sulphonamides were recrystallised to constant melting point (Table 6) from dilute ethanol. The sodium salts of *N*-chloro-arenesulphonamides were then prepared by bubbling pure chlorine gas through clear aqueous solutions of substituted arenesulphonamides in 4M NaOH at 70 °C for about 1 h [13]. The precipitated *N*-chloro compounds were filtered, washed, dried and recrystallised from water. Purity of all the reagents was checked by determining their melting points (Table 6) and by estimating the amounts of active chlorine present in them. Both the sulphonamides and their *N*-chloro compounds were characterized by their infrared and NMR spectra.

Aqueous stock solutions of sodium salts of substituted *N*-chloro-arenesulphonamides (0.01 mol dm^{-3}) were prepared in double distilled water, standardized by the iodometric method and preserved in dark coloured bottles to prevent their photochemical deteriorations.

Pure samples of amino acids (AA), L-leucine (Leu) and L-isoleucine (Ile) (CDH, India) were employed. They were further assayed by the standard method [16]. Aqueous stock solutions of these compounds (0.10 mol dm^{-3}) were used. All other reagents employed were of the accepted grades of purity. Ionic strength of the medium was maintained at 0.30 mol dm^{-3} using concentrated aqueous solution of sodium nitrate (E. Merck).

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