Kinetics and Mechanism of Decomposition of *N*-Chloro-α-amino Acids

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The kinetics of decomposition of *N*-chloro derivatives of the following amino acids have been studied in phosphate buffer solution in the pH range 6–13: glycine, alanine, 2-aminoisobutyric acid, *N*-methylglycine, *N*-methylalanine, 2-(methylamino)isobutyric acid, proline, *N*-methylvaline, valine, isoleucine, and L-*tert*-leucine. The rates of decomposition of *N*-chloro-α-amino acids were found to be independent of the initial concentrations, ionic strengths, buffer concentrations and pH in the studied range. The first-order rate constants were found to increase as the relative permittivity decreased. The decomposition of *N*-chloroamino acids was followed by either a spectrophotometric method or an iodometric method, and in some cases the reaction was monitored by determining the rate of CO_2 evolution. The three methods gave results that were in good agreement. The effects of both α-carbon substitution and *N*-substitution on the rate of decomposition were investigated. All the kinetic data obtained appear to be consistent with a concerted mechanism in which dechlorination and decarboxylation take place concomitantly, resulting in the formation of an imine intermediate *via* an imine-like transition state. The imine may then be hydrolysed to the corresponding aldehyde or ketone, and amine. The kinetic data suggest that factors which influence the stability of the imine-like transition state affect the rate of decomposition of the *N*-chloro amino acid. The data from the decomposition of *N*-chloro amino acids may be useful in designing chemically stable, biodegradable germicidal agents.

N-Chloro-α-amino acids are not generally stable in solution but readily decompose to ammonia, carbon dioxide, chloride ion, and carboxyl products. Several studies have focused on the mechanism of decomposition of *N*-chloro-α-amino acids.[1–6] Fox and Bullock[1] have put forward a mechanism which involves initial loss of the α-proton followed by dechlorination of the intermediate carbanion, while Becker and Grob[3] suggest that decomposition occurs with concomitant decarboxylation and *N*-dechlorination *via* an E_2-like mechanism. Recent studies by Hand and Margerum[4] appear to support this latter mechanism. We now describe some detailed structure–activity studies carried out on *N*- and *C*-α-substituted *N*-chloro-α-amino acids which were designed to determine in more detail the nature of mechanism of decomposition of *N*-chloro-α-amino acids.

Experimental

Analytical Methodology.—Amino acids were *N*-chlorinated *in situ* utilizing sodium hypochlorite as the *N*-chlorinating agent. The formation and decomposition of the appropriate *N*-chloroamino acid was followed using the following three methods of analysis.

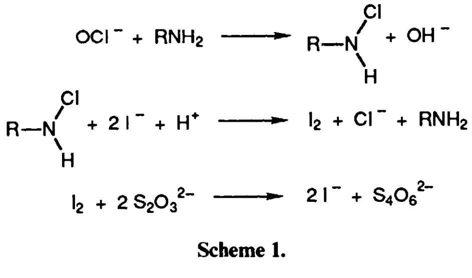
Spectrophotometric analysis. Since hypochlorite has a maximum absorbance at 292.5 nm, whereas *N*-chloroamino acids absorb at 250–254 nm, a rapid increase followed by a gradual decrease in absorbance at 250–254 nm is indicative of the formation followed by the decomposition of the *N*-chloroamino acid.

Reaction mixtures of the amino acid and sodium hypochlorite were prepared by mixing equal volumes of phosphate-buffered solutions of the appropriate amino acid and sodium hypochlorite in a 3 cm^3-cuvette to give the desired concentration of *N*-chloroamino acid. In the case of very fast reactions, hypochlorite solution was injected into a cuvette containing an equivolume of amino acid solution using a long needle syringe. The amino acid concentration was present in excess to prevent the formation of the *N*,*N*-dichloroamino acid as a by-product. Hypochlorite concentrations were determined by the method of Hussain *et al.*[7] After mixing, the decrease in absorbance of the reaction mixture at the wavelength of maximum absorbance was followed as a function of time. The above experiment was repeated using a variety of amino acids with initial concentrations in the range 0.001–0.005 mol dm^{-3}.

To study the effect of the relative permittivity of the medium on the reaction rate, calculated amounts of 1,4-dioxane were added to the reaction mixture at pH 7 immediately after, or just before addition of the hypochlorite solution. Dioxane concentration ranges were 0–50% (v/v) of the final reaction mixture. The effect of the addition of ethanol was also studied utilizing the same procedure. Blank experiments were also performed in which dioxane was added to hypochlorite solution to give final concentrations in the 0–50% (v/v) range.

The effect of ionic strength was studied by adding calculated volumes of 4 mol dm^{-3} sodium chloride solution to the reaction mixture to give sodium chloride concentrations in the range 0.2–1.6 mol dm^{-3}.

Iodometric analysis. This method is able to determine the active chlorine (*i.e.*, positive chlorine) in the form of the *N*-chloroamino acid present in the reaction mixture, since such species are able to oxidize iodide ion to iodine (see Scheme 1). The liberated iodine is then back-titrated with sodium thiosulphate solution using starch as indicator.



Scheme 1.

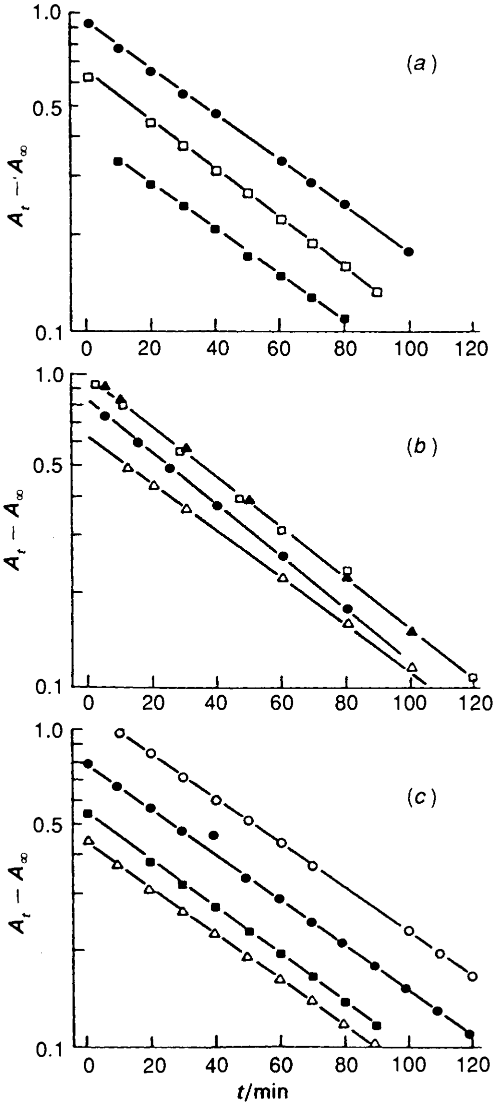


Figure 1. (*a*) Semilogarithmic plots of the change in absorbance at 250 nm *versus* time for solutions of various initial concentrations of *N*-chloroalanine at pH 7 and 25 °C: ■, 3.3×10^{-3} mol dm^{-3}; □, 5.5×10^{-3} mol dm^{-3}; ●, 6.35×10^{-3} mol dm^{-3}. (*b*) Semilogarithmic plots of absorbance *versus* time for the decomposition of *N*-chloro-L-alanine at various phosphate buffer concentrations at pH 7 and 25 °C: ●, 0.05 mol dm^{-3}; □, 0.1 mol dm^{-3}; △ 0.2 mol dm^{-3}; ▲, 0.5 mol dm^{-3}. (*c*) Semilogarithmic plots of the change in absorbance at 250 nm *versus* time for the decomposition of *N*-chloroalanine at various pH values at 25 °C: △, pH 6; ■, pH 7; ●, pH 8; ○, pH 13.

Acid–Base titration. This method of analysis was used to determine the CO_2 evolved during the decomposition reaction. The CO_2 evolved was trapped in a solution containing a known excess of barium hydroxide to form insoluble barium carbonate. The unchanged barium hydroxide was then back-titrated with a standard solution of hydrochloric acid using phenolphthalein as an indicator. The method utilized followed the procedure described by Gallelli and Kostenbauder.[8]

All determinations were carried out in triplicate. Values quoted in Tables 2–7 are means of values which were within ±10%.

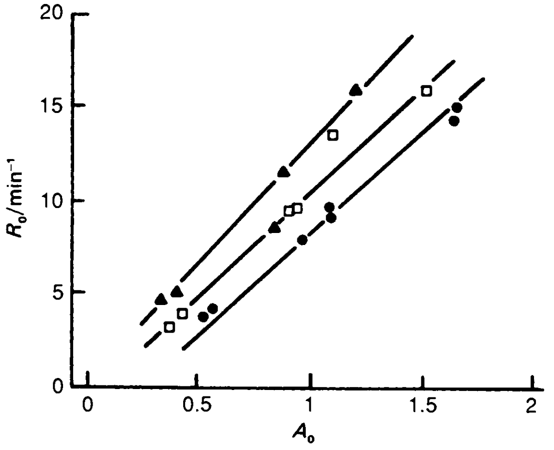


Figure 2. Plot of initial rates of decomposition of *N*-chloro-L-alanine in systems of varying initial concentrations of the compound at 25 °C and various pH values: ●, pH 6; □, pH 7; ▲, pH 8.

Results

In monitoring spectrophotometrically the decomposition of *N*-chloroamino acids, each reaction was allowed to proceed to completion and semilogarithmic plots of $(A_t - A_\infty)$ *versus* time were constructed (Figure 1). All plots afforded a straight line, which indicates first order kinetics, and first order rate constants that were independent of the initial concentration of *N*-chloro-α-amino acid, phosphate buffer concentration, and ionic strength of the medium. The rates of decomposition of the *N*-chloro-L-amino acids (see Table 1) studied were also found to be independent of pH over the range studied (*i.e.* 6–13). Typical results are illustrated in Figure 1(*a–c*) and Table 2 for *N*-chloro-L-alanine (**8**). The first order rate constant for this reaction was also determined by the initial rate method to ensure that only the decomposition of the monochloroalanine was being followed. Figure 2 shows semilogarithmic plots of initial rates (R_0) *versus* the initial absorbances of *N*-chloroalanine (A_0) for three pH values. The slopes of the lines, which correspond to the first order rate constants, were found to be in a good agreement with the value of 0.016 min^{-1} obtained from the semilogarithmic plots of $(A_t - A_\infty)$ *versus* time. The first-order rate constant can also be obtained from a plot of log R_0 *versus* log A_0. This plot of the data from Figure 2 was found to be a straight line with a slope of 0.98 (corresponding to the order of the reaction), and the first order rate constant was calculated from the intercept and found to be 0.015 min^{-1}.

The decomposition of *N*-chloroalanine was also followed by determination of the rate of evolution of CO_2. Figure 3 illustrates the semilogarithmic plot of $(V_\infty - V_t)$ *versus* time, where V_∞ is the volume of 0.05 mol dm^{-3} HCl equivalent to the CO_2 evolved up to the end of the reaction and V_t is the volume of 0.05 mol dm^{-3} HCl equivalent to the CO_2 evolved at a specified time. The first-order rate constant calculated from the slope of the straight line was found to be 0.014 min^{-1}, which is comparable to the value of 0.015 min^{-1} obtained by the iodometric method and 0.016 min^{-1} obtained by the spectrophotometric method. Table 3 illustrates the consistency obtained in the determination of first order rate constants for the decomposition of a number of *N*-chloro-α-amino acids by four different methods of analysis.

The effect of ionic strength of the medium on the rate of decomposition of *N*-chloroalanine was studied by the spectrophotometric method in the presence of 0.2, 0.4, 0.8, and 1.6 mol dm^{-3} sodium chloride. The results, shown in Table 4, indicate that ionic strength (*viz.* addition of chloride ion) had no effect on the rate of the reaction.

The effect of temperature on the first-order rate constant for decomposition of *N*-chloro-L-alanine was also studied by the spectrophotometric method. The results are shown in Table 5. An

Table 1. Structures of α-amino acids and their *N*-chloro derivatives.

	$R^1R^2C(NR^3X)CO_2H$			
Compound	R^1	R^2	R^3	X
(1)	H	H	H	H
(2)	H	CH_3	H	H
(3)	CH_3	CH_3	H	H
(4)	H	$(CH_3)_2CH$	H	H
(5)	H	$C_2H_5(CH_3)CH$	H	H
(6)	H	$(CH_3)_3C$	H	H
(7)	H	H	H	Cl
(8)	H	CH_3	H	Cl
(9)	CH_3	CH_3	H	Cl
(10)	H	$(CH_3)_2CH$	H	Cl
(11)	H	$C_2H_5(CH_3)CH$	H	Cl
(12)	H	$(CH_3)_3C$	H	Cl
(13)	H	H	CH_3	H
(14)	H	CH_3	CH_3	H
(15)	CH_3	CH_3	CH_3	H
(16)	H	$(CH_3)_2CH$	CH_3	H
(17)	H	H	CH_3	Cl
(18)	H	CH_3	CH_3	Cl
(19)	CH_3	CH_3	CH_3	Cl
(20)	H	$(CH_3)_2CH$	CH_3	Cl

Table 2. Effect of phosphate buffer concentration on the first-order rate constant for the decomposition of *N*-chloro-L-alanine at pH 7 and 25 °C.[a]

Buffer concentration/mol dm^{-3}	K/min^{-1}	Half-life/min
0.05	0.018	38.50
0.10	0.018	38.50
0.20	0.019	36.67
0.50	0.018	39.38

[a] Values are means of triplicate determinations which did not vary by more than ±10%.

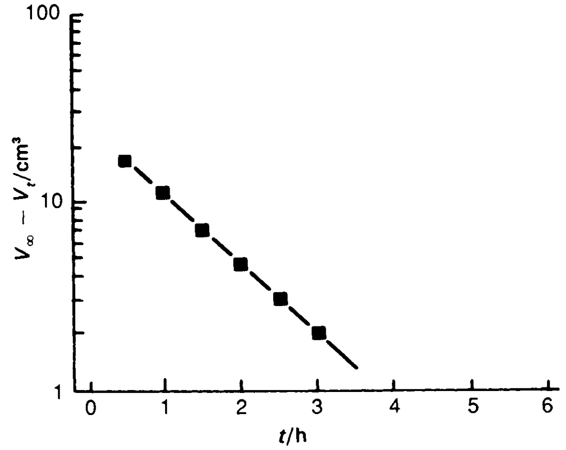


Figure 3. Semilogarithmic plot of volume of 0.05 mol dm^{-3} HCl *versus* time for the decarboxylation of *N*-chloro-L-alanine at pH 7 and 25 °C. V = volume of 0.05 mol dm^{-3} HCl.

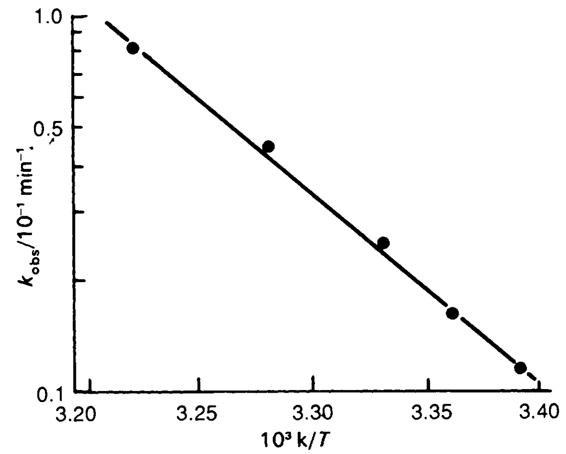


Figure 4. Semilogarithmic plot of $k_{obs.}$ *versus* reciprocal of absolute temperature (Arrhenius plot) for the decomposition of *N*-chloro-L-alanine at pH 7.

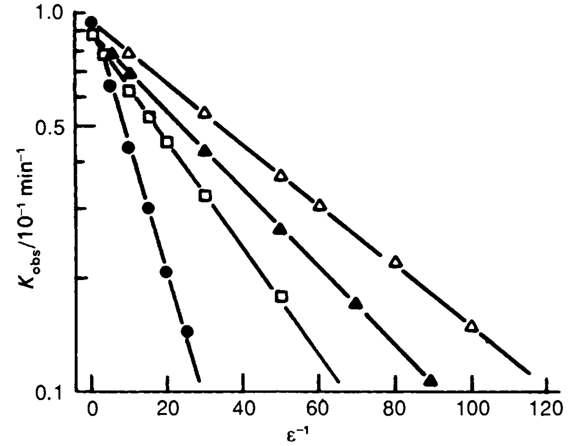


Figure 5. Semilogarithmic plot of the observed rate constant *versus* reciprocal of relative permittivity for the decomposition of 2.7 × 10^3 mol dm^{-3} *N*-chloro-L-alanine in various dioxane concentrations and 25 °C: △, 0%; ▲, 5%; □, 10%; ●, 25% dioxane.

Arrhenius plot is shown in Figure 4. The slope of the line, which represents the activation energy, was found to be 24 kcal mol^{-1}.*

The effect of the relative permittivity of the medium on the reaction rate was studied by adding different proportions of dioxane to the amino acid–hypochlorite reaction mixture. The results, shown in Table 6, indicate that the rate constant increases as the relative permittivity decreases. A plot of the reciprocal of the relative permittivity (ε) *versus* the logarithm of the first-order rate constant is shown in Figure 5. The relative permittivity of the medium was also varied by adding various proportions of ethanol to the reaction mixture. The results also indicate that the addition of ethanol had the same effect on the rate constant as addition of dioxane, but to a lesser degree. Blank experiments showed that neither dioxane nor ethanol was oxidized by the *N*-chloroamino acid under the experimental conditions.

In order to gain insight into the detailed mechanism of *N*-chloroamino acid decomposition, the kinetics of decomposition of a variety of *N*-chloro-α-amino acids and the nitrogen and α-carbon substituted derivatives were also examined in this study (see Table 7). The data indicate that the rate of decomposition generally increases as the number of substituents on the α-carbon increases, and are in line with previously reported studies by Hand *et al.*[6] These studies also showed that an increase in the steric bulk of the α-substituent results in a small but significant decrease in the rate of decomposition of the *N*-chloramino acid. In addition, it was found that the introduction of a methyl group onto the nitrogen of *N*-chloroamino acids that are either mono- or di-substituted at the α-carbon,

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* 1 cal = 4.184 J.

Table 3. First order rate constant values for the decomposition of a number of *N*-chloro-α-amino acids determined by four different methods.

Amino acid	First order rate constant/min^{-1} at pH 7, 25 °C Spectrophotometric method	Iodometric method	Acid–base titration method	Initial rate method
N-Chloroglycine	0.002	0.002	—	0.01
N-Chloro-*N*-methylglycine	0.005	0.005	0.005	0.005
N-Chloroalanine	0.016	0.015	0.014	0.015
2-Amino-*N*-chloroisobutyric acid	0.63	0.70	—	0.65

Table 4. Effect of ionic strength on the first-order rate constant for the decomposition of *N*-chloro-L-alanine at pH 7 and 25 °C.[a]

Sodium chloride/mol dm^{-3}	k/min^{-1}	$t_{1/2}$/min
0	0.018	39.15
0.2	0.016	42.65
0.4	0.017	41.75
0.8	0.015	45.50
1.2	0.016	42.50
1.6	0.016	42.78

[a] Values are means of triplicate determinations which did not vary by more than ±10%.

Table 5. Effect of temperature on the first-order rate constant for the decomposition of *N*-chloro-L-alanine at pH 7.0.[a]

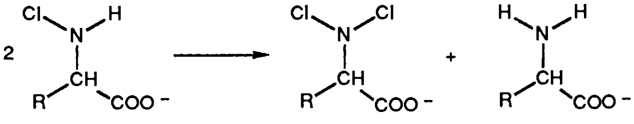
Temperature/°C	k/min^{-1}	$t_{1/2}$/min
22	0.012	60.26
25	0.016	43.31
27	0.025	27.72
32	0.045	15.40
37	0.083	8.35

[a] Values are means of triplicate determinations which did not vary by more than ±10%.

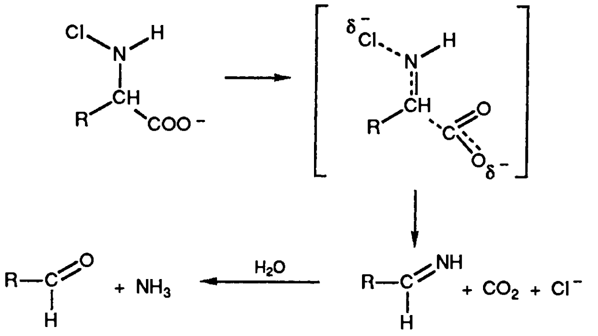
enhances the rate of decomposition of *N*-chloroamino acid by a factor of 30–38.

Discussion

Kinetic analysis of the decomposition of the *N*-chloroamino acids studied afforded results that were consistent with a first-order hydrolysis reaction. There was no evidence to support second order disproportionation of any of the *N*-chloroamino acids studied (see Scheme 2). The rate of CO_2 evolution determined for the *N*-chloroalanine (**8**) and *N*-chlorosarcosine (**17**) decomposition reactions afforded first-order rate constants that were similar to those obtained by spectrophotometric analysis and iodometric titration. This observation, together with several studies that report the isolation of the appropriate aldehyde as a major decomposition product,[1,2,9] appears to indicate that the decomposition occurs *via* a concerted E_2-like mechanism in which decarboxylation and *N*-dechlorination occur in a single step, through a transient imine-like intermediate (see Scheme 3), as has been suggested by Becker and Grob.[5] In addition, the above data does not support the proposal by Fox and Bullock[4] that the decomposition proceeds *via* α-proton loss as the rate-limiting step followed by dechlorination of the intermediate carbanion and hydrolysis of the resulting imino acid [Scheme 4(*a*)]. It is also important to note that the rate of decomposition of all the *N*-chloroamino acids studied were found to be first order and independent of pH in the range 6–13, and that *N*-chloro-2-aminoisobutyric acid (**9**), an α-amino acid bearing no α-proton, decomposes 35 times faster than *N*-chloroalanine. Neither of these data support a mechanism involving α-proton loss. The first order rate constants for the decomposition of a series of *N*-chloroamino acids was found to be in the following (increasing) order: *N*-chloroglycine < *N*-chloroalanine < 2-amino-*N*-chloroisobutyric acid. A mechanism involving α-proton loss would predict the reverse order, since the formation of the carbanion would be the rate-limiting step, and one would expect a faster reaction with the compound that is able to form a more stable carbanion (*i.e.*, glycine), which is contrary to the experimental observations. Based upon the above observations, the Fox and Bullock mechanism[4] is not a feasible pathway for the decomposition of *N*-chloro-α-amino acids.



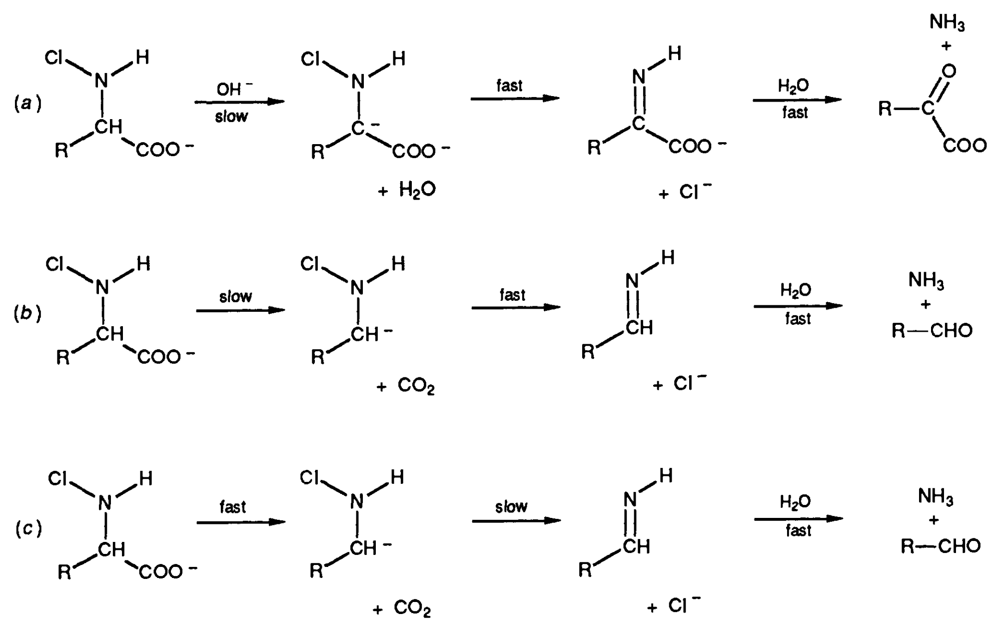
Scheme 2.



Scheme 3.

Formation of a carbanion during the decomposition of *N*-chloroamino acids may also be possible by a first-step decarboxylation. One can propose this step to be a slow step followed by a rapid dechlorination [Scheme 4(*b*)], or a fast step followed by a slow dechlorination step [Scheme 4(*c*)].

Thus, in accordance with Scheme 4(*b*), one would expect to observe a first-order reaction with a rate constant independent of pH and a rate of CO_2 evolution comparable to the rate of loss of active chlorine, as is observed in this present work. However, since the carbanion intermediate is formed in the rate limiting step, one would predict that *N*-chloroglycine would decompose faster than *N*-chloroalanine, since the former compound is able to form a less substituted and hence more stable carbanion, which is contrary to the observed data (see Table 7). In addition, the carbanion intermediate is obviously more charged than the reactant molecule, and one would, therefore, expect the rate of this reaction to decrease in less polar systems. However, the results show that the rate of the reaction actually increases as the relative permittivity decreases; *i.e.*, a decrease in the polarity of the medium increases the rate of the reaction. This



Scheme 4.

Table 6. Dependency of the first-order rate constant for the decomposition of *N*-chloro-L-alanine on the relative permittivity of the medium in various concentrations of dioxane and ethanol at pH 7 and 25 °C.[a]

Solvent % (v/v)	Relative permittivity (ε)	k/min^{-1}	$t_{\frac{1}{2}}$/min
Dioxane			
0	78.6	0.018	38.08
5	74.0	0.024	24.49
10	70.0	0.033	21.13
25	56.3	0.075	9.26
Ethanol			
0		0.025	27.72
20		0.039	17.77
30		0.061	11.36

[a] Values are means of triplicate determinations which do not vary by more than ±10%.

Table 7. First-order rate constants for the decomposition of *N*-chloro-α-amino acids at pH 7 and 25 °C.

N-Chloro-α-amino acid	k/min^{-1} [a]	$t_{\frac{1}{2}}$/min
N-Chloroalanine	0.016	43.31
N-Chloro-*N*-methylalanine	0.52	1.33
N-Chlorovaline	0.012	57.75
N-Chloro-*N*-methylvaline	0.46	1.51
2-Amino-*N*-chloroisobutyric acid	0.61	1.14
N-Chloro(methylamino)isobutyric acid	18.1	0.038
N-Chloroglycine	0.003	277.20
N-Chloro-*N*-methylglycine	0.005 (0.005)[b] (0.005)[c]	128.33
N-Chloroisoleucine	0.01	69.3
N-Chloro-L-tert-leucine	0.008	92.4

[a] Values obtained by spectrophotometric analysis. [b] Values obtained by iodometric analysis. [c] Values obtained by acid–base titration method.

observation would be more consistent with the mechanism given in Scheme 4(*c*). In this mechanism, the disappearance of the carbanion, rather than the formation, is the rate-determining step. Hence the more stable the anion, the slower the reaction would be, which is consistent with the observation that *N*-chloroglycine is more stable than *N*-chloroalanine. However, the fact that the rate of decarboxylation of *N*-chloroaniline is equal to its rate of dechlorination, cannot be rationalized based upon this mechanism.

Effect of α-Carbon Substituents.—The rates of decomposition of *N*-chloroglycine (**7**), *N*-chloroaniline (**8**), and *N*-chloro-2-aminoisobutyric acid (**9**) were investigated both spectrophotometrically and iodometrically and at different pH values. In each case, the rate constants determined at pH 7 by the two methods were very similar. The results in Tables 7 and 8 show that the rate constants for the decomposition of the *N*-chloroamino acids in the series increase as the number of substituents on the α-carbon increases. These results are in agreement with those obtained by Hand and Margerum.[6]

The fact that *N*-chloro-2-aminoisobutyric acid decomposes faster than *N*-chloroalanine and *N*-chloroglycine indicates that α-protons are not necessary for the decomposition of the corresponding *N*-chloro-α-amino acid, and that the reaction most likely proceeds through an imine-like transition state or intermediate which is increasingly stabilized by the introduction of methyl groups on the α-carbon, and results in a lowering of the energy of the transition state and an enhancement of the rate of the reaction.

The effect of the relative permittivity of the medium on the rates of decomposition of both *N*-chloroalanine and *N*-chloro-2-aminoisobutyric acid showed that in each case the first-order rate constant increased as the relative permittivity decreased, which indicates that the reaction rate increased as the polarity of the medium decreased and suggests that the reaction most likely proceeds through a non-charged or less charged transition state which has greater stability in less polar media.

Effect of Nitrogen Substituents.—The effect of *N*-methylation on the decomposition of *N*-chloro-α-amino acids was investigated by studying the following pairs of amino acids: alanine (**2**) and *N*-methylalanine (**14**), valine (**4**) and *N*-methylvaline (**16**), 2-aminoisobutyric acid (**3**) and 2-(methylamino)isobutyric acid

Table 8. Effect of α-carbon substitution and pH on the first-order rate constants for the decomposition of some *N*-chloro-α-amino acids.

	First-order rate constants/min^{-1} [a,b]			
Amino acid	pH 6	pH 7	pH 8	pH 13
N-Chloroglycine	0.003	0.002 (0.002)[c]	0.002	0.003
N-Chloroalanine	0.016	0.016 (0.02)[c]	0.016	0.016
2-Amino-*N*-chloroisobutyric acid	0.68	0.63 (0.70)[c]	0.64	0.65

[a] Experiments were carried out at 25 °C. [b] Values obtained by spectrophotometric analysis. [c] Values obtained by iodometric analysis.

(**15**), and glycine (**1**) and *N*-methylglycine (sarcosine) (**7**). The first-order rate constants for the decomposition of these *N*-chloroamino acids are given in Table 7. The results indicate that the introduction of a methyl group on the nitrogen of the amino acids, which is either mono- or di-substituted at the α-carbon, enhances the rate of decomposition of the *N*-chloro derivative by a factor of 30–38. This enhancement can be explained with the same argument put forward for the α-carbon substituent effect, *i.e.*, the methyl group on the nitrogen increases the stability of the transition state leading to the formation of the imine intermediate. It is of interest to note that 2-amino-*N*-chloroisobutyric acid (which has two methyl groups on the α-carbon) and *N*-chloro-*N*-methylalanine (which has one methyl group on the nitrogen and one methyl group on the α-carbon) decomposed at comparable rates. This suggests that, as far as the stability of these *N*-chloroamino acids is concerned, one cannot differentiate between the effect of a methyl group on the nitrogen, and a methyl group on the α-carbon. The rate constant for the dechlorination of *N*-chloroproline, a related cyclic amino acid, was found to be almost identical with that of *N*-chloro-*N*-methylalanine (*i.e.* 0.52 min^{-1} by spectrophotometric, and 0.55 min^{-1} by iodometric analysis). 2-(Methylamino)isobutyric acid was the most unstable *N*-chloroamino acid examined.

Steric Effects in the Decomposition of N-*Chloroaminoacids*.—Hand and Margerum[6] have concluded that, among amino acids with the same number of substituents on the α-carbon, the larger the α-carbon substituent, the faster the rate of decomposition of the corresponding *N*-chloroamino acid. This conclusion was based on a comparison of the rate constant for the decomposition of *N*-chloroproline (0.5 min^{-1}) with that of *N*-chloroalanine (0.016 min^{-1}), and assumes that proline is a monosubstituted amino acid structurally similar to alanine, but bearing a larger α-substituent than alanine. However, the present studies have clearly shown that alkyl substitution on the nitrogen of the *N*-chloroamino acid is just as influential as substitution on the α-carbon, with regard to effect on decomposition rate, and hence one should consider proline to be a disubstituted amino acid. Thus comparing proline with a monosubstituted amino acid such as alanine, is unjustified. In other words, the large rate constant for the decomposition of *N*-chloroproline, which was confirmed by the current work, is attributable to the second substituent group on the nitrogen and not to the size of the substituent group on the α-carbon.

In order to investigate further steric effects on the rate of decomposition of *N*-chloroamino acids and to establish whether a larger substituent on the α-carbon would enhance or inhibit this rate, a structural modification on the α-carbon substituent was made in such a way that the size of the substituent was increased while still maintaining almost the same electronic effect. This was accomplished by studying the *N*-chloro derivatives of the following amino acids: L-alanine (**2**), L-valine (**4**), isoleucine (**5**), and L-*tert*-leucine (**6**). The first-order rate constants for the decomposition of these compounds are given in Table 7. The results indicate that among amino acids with the same number of substituents on the α-carbon, the larger the α-carbon substituent, the slower the rate of decomposition of the *N*-chloro derivative will be. However, it is important to note that the steric effect is not very pronounced, since replacing the methyl group on the α-carbon with a t-butyl group decreases the rate constant only by one half. It is known that the most favourable geometry for E_2-type elimination reactions is with the CO_2^- and Cl groups in the *anti*- or *trans*-position. Thus, a bulky group, such as t-butyl, may hinder one of the several possible *anti*-positions. Another possible explanation for the decrease in the rate constant as the size of the group on the α-carbon increases is based on the ability of the α-group to stabilize the transition state. This can be achieved by either a hyperconjugative or an inductive effect, or both. The inductive effect of alkyl groups is normally found to be in the order $CH_3 < CH_3CH_2 < (CH_3)_2CH < (CH_3)_3C$ while the hyperconjugative effect is in the reverse order. In the case of the *N*-chloroamino acids, the stabilization effect of the alkyl group may be attributed to both inductive and hyperconjugative effects, with the latter being predominant. If this argument is valid, then the primary effect of the t-butyl group is not a steric one.

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