

for the methionine sulfoxide complex.

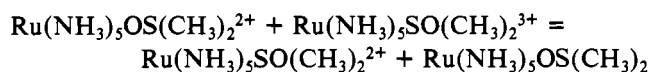
It should be noted that there is significant aquation at zero time in each case, and we conclude that this measures the aquation that accompanies O → S isomerization in the 2+ state.

Discussion

Unexpectedly facile linkage isomerization on pentaammineruthenium(III) has been observed in other cases,^{9,10} and it is therefore not surprising that it is observed in the present instance. To learn the cause of this lability, it would be useful to have a measurement of the rate of this change also for Rh(III). It is likely that the reaction proceeds through a 7-coordinate transition state, and this would have less antibonding character for a d⁵ as compared to a d⁶ system. Rh(III) is the only center that provides a straightforward comparison—the changes in the bond distance would be small as compared to case for Ru(III), and the πd-σd energy separation for the same ligand environment also is as close as can be arranged. The higher stability of the Ru(III)-O bond as compared to the S-bound form is expected from the estimate of the affinity of H₂S for Ru(NH₃)₅H₂O³⁺, $K_{\text{assoc}} = 2.4 \times 10^{-4}$. Though K_{assoc} for (CH₃)₂S is greater than for H₂S, a sharp decrease is expected when the sulfur is oxidized to the dimethyl sulfoxide state, and it is likely therefore that K_{assoc} for the latter ligand ≪ 1. On the other hand, the affinity of Me₂SO acting as an oxygen donor to Cr(H₂O)₆³⁺ has been found to be quite high,¹¹ and Ru(III) and Cr(III) can be expected to show roughly similar affinities.

Though the values of the activation parameters for the linkage isomerization on Ru(III) are not accurate, they do suffice to show that ΔS[‡] for the reaction is quite negative. This is in line with other observations. For the N → O rearrangement of nitrite on Rh(NH₃)₅³⁺, ΔS[‡] = -12 cal/(deg mol), and on Ir(NH₃)₅³⁺, ΔS[‡] = -14 cal/(deg mol).¹²

The marked preference of Me₂SO for the S bonding mode on Ru(II) would be hard to predict from first principles, and the exact magnitude of this preference has not been established. The two values of E_f do lead to the equilibrium quotient for



($K_{\text{eq}} = 5 \times 10^{11}$), but this only gives us the relative preference for the two forms in the two oxidation states.

The lability of Ru(NH₃)₅OS(CH₃)₂²⁺ toward aquation ($k \approx 10 \text{ s}^{-1}$) is a matter of some interest, as providing a rough measure of the exchange rate for water between Ru(NH₃)₅H₂O²⁺ and solvent. Because of the low charge on Ru(II), the preference for oxygen in the two cases, H₂O vs. OS(CH₃)₂, is likely not to be very great. The specific rate of water exchange was estimated elsewhere¹³ as 3 s⁻¹ at 25 °C.

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Registry No. Ru(NH₃)₅Me₂SO²⁺, 44863-54-9; [(NH₃)₅RuSO(CH₃)(CH₂CH₂CH(NH₂)COOH)](BF₄)₂, 81230-34-4; Ru(NH₃)₅OS(CH₃)₂³⁺, 81245-10-5; Ru(NH₃)₅OS(CH₃)(CH₂CH₂CH(NH₂)COOH)³⁺, 81230-41-3; [Ru(NH₃)₅Cl]Cl₂, 18532-87-1.

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Kinetics of Chlorine Transfer from Chloramine to Amines, Amino Acids, and Peptides

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The equilibria and kinetics of chlorine transfer from chloramine to give *N*-chloro derivatives of methylamine, amino acids, and peptides are determined in aqueous solution. The reactions, which are studied from pH 2 to 10, are first order in total chloramine and first order in total amine with rate constants which vary from 0.1 to 7 M⁻¹ s⁻¹ at 25.0 °C. The rates are independent of pH from pH 4 to 7. The results indicate that direct chlorine transfer occurs with NH₃Cl⁺ as a very active chlorinating agent. The rate constants for the reactions of NH₃Cl⁺ increase with the amine basicity but reach a maximum level of 2.4 × 10⁸ M⁻¹ s⁻¹ (25.0 °C, 0.50 M NaClO₄).

Introduction

Chloramine (NH₂Cl) is formed in the process of disinfecting water by chlorination.¹ It results from the reaction of hypochlorous acid with ammonia.^{2,3} Since NH₂Cl is slow to hydrolyze, is not very volatile, and is a less reactive oxidant than Cl₂ or HOCl, it persists as a source of active chlorine.⁴⁻⁷

One series of possible chloramine reactions is the transfer of chlorine to other amine nitrogens (eq 1, where RNH₂ is an



amine, an amino acid, or a peptide). A previous investigation⁸ suggested that the transfer of chlorine from *N*-chloro-D-leucine to α-amino acids and NH₃ did not occur, even with 100-fold

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molar excess of the ammonia (pH 8.3 and 25 °C). Studies in our laboratory have indicated that the reaction in eq 1 is favorable. Hence, we wished to examine the ability of NH₂Cl to transfer chlorine to nitrogenous substrates. Our concern is whether chlorine is transferred directly between nitrogen atoms or if the reaction occurs by hydrolysis of NH₂Cl to give a reactive HOCl molecule which then forms RNHCl.

Higuchi and co-workers^{9,10} have studied the chlorine exchange reactions between nitrogenous centers for several *N*-chloramides, *N*-chlorosuccinimide, and *N*-chloroquinuclidine with dialkylamines in acidic solutions. Direct chlorine transfer was observed with unprotonated amine as the reactive amine species. In the oxidation of phenylalanine to phenylacetaldehyde by *N*-chlorocytosine, Patton et al.¹¹ suggested direct chlorine transfer to form *N*-chlorophenylalanine as an intermediate preceding the oxidation step.

The disproportionation reactions of chloramines to form dichloramines also occur by direct chlorine transfer between nitrogens.^{7,12} The protonation of chloramine (log $K_H = 1.5$)⁷ occurs much more readily than had been previously thought.¹³ One pathway for the disproportionation reaction is given in eq 2 and 3. However, Granstrom¹² reported a second pathway



which involved hydrolysis and subsequent chlorination of another molecule of chloramine by the liberated hypochlorous acid.

The present work shows that chlorine is transferred directly from chloramine to other amine species. The results indicate that protonated chloramine is a very reactive chlorinating agent. These types of reactions are possible pathways for the disinfecting properties and toxicity of chloramine.

Experimental Section

Reagents. Glycine and β -alanine (Eastman) were purified by recrystallization from a 20% methanol-water solution. Glycylglycine, glycylglycine ethyl ester hydrochloride (Sigma), and L-threonine (Cyclo, allo free) were chromatographically pure as obtained. Methylamine hydrochloride (Baker) was purified by sublimation (1 mmHg, ~200 °C), and the crystals were dissolved in CO₂-free water. The methylamine concentration was determined by passing 1 aliquot of this stock solution down an anion-exchange column (BioRad AG1-X10, 200-400 mesh) in the hydroxide form and titrating the released base with standardized perchloric acid. Ammonia solutions (Mallinckrodt) were titrated with standardized acid.

The distribution of amine species in solution was calculated from the protonation constants in Table I. The proton-independent equilibrium constant, K_Z , between the zwitterionic amino acid or dipeptide and the neutral form (eq 4) was calculated by assuming



that the amine protonation constant of the neutral form is equal to the protonation constant of the alkyl ester of the amino acid or peptide.¹⁴ Under these conditions $K_Z = K_H^{\text{ester}}/K_H^{\text{RCOO}^-}$, where $K_H^{\text{RCOO}^-}$ is the protonation constant of the carboxyl terminus for the amino acid or dipeptide. All protonation constants are reported for 0.5 M ionic strength unless noted otherwise.

Reagent grade sodium hypochlorite solution (5%, Baker) was diluted to give stock solutions. Hypochlorite concentrations were checked spectrophotometrically. The molar absorptivity at 292 nm of iodometrically standardized NaOCl was confirmed to be 350 M⁻¹ cm⁻¹.¹⁵

Table I. Protonation Constants of Amines, Amino Acids, and Dipeptides^{a, b}

amine	log $K_H^{\text{RNH}_2}$	log $K_H^{\text{RCOO}^-}$	log K_Z^c	ref
NH ₃	9.43			<i>d</i>
CH ₃ NH ₂	10.80			<i>d, e</i>
β -Ala	10.15	3.56	5.70	<i>f</i>
β -AlaEE	9.26 ^g			<i>h</i>
Gly	9.65	2.41	5.24	<i>f, i</i>
GlyEE	7.65 ^g			<i>j</i>
Thr	8.98 ^g	2.20 ^g	(4.83) ^{g, h}	<i>l</i>
ThrEE	(7.03) ^{g, h}			
Gly ₂	8.11	3.17	4.53	<i>m</i>
Gly ₂ EE	7.70 ^g			<i>n</i>

^a 25.0 °C, $\mu = 0.50$ M. ^b Abbreviations: β -Ala, β -alanine; Gly, glycine; Thr, L-threonine; Gly₂, glycylglycine; EE, ethyl ester. ^c $\log K_Z = \log K_H^{\text{ester}} - \log K_H^{\text{RCOO}^-}$. ^d Gray, E. T., Jr. Ph.D. Thesis, Purdue University, 1977. ^e Partridge, J. A.; Christiansen, J. J.; Izatt, R. M. *J. Am. Chem. Soc.* **1968**, *90*, 1543-1552. ^f Leussing, D. L.; Hanna, E. M. *Ibid.* **1966**, *88*, 693-696. ^g $\mu = 0.10$ M (NaClO₄ or KCl). ^h Hopgood, D.; Angelici, R. J. *J. Am. Chem. Soc.* **1968**, *90*, 2508-2513. ⁱ Thiers, G. F.; van Poncki, L. C.; Herman, M. A. *J. Inorg. Nucl. Chem.* **1968**, *30*, 1543-1552. ^j Connor, W. A.; Jones, M. M.; Tuleen, D. L. *Inorg. Chem.* **1965**, *4*, 1129-1133. ^k Estimated from data for serine in ref 1. ^l Raki, E. V.; Mathur, B. *J. Inorg. Nucl. Chem.* **1968**, *30*, 2181-2188. ^m Biester, J. L.; Ruoff, P. M. *J. Am. Chem. Soc.* **1959**, *81*, 6517-6521. ⁿ Martin, R. B.; Chamberlain, M.; Edsall, J. T. *Ibid.* **1960**, *82*, 495-498.

Table II. Ultraviolet Spectral Characteristics of Chloramines in Aqueous Solution

RNHCl	λ_{max} , nm	ϵ_{max} , M ⁻¹ cm ⁻¹	ϵ_{290} , M ⁻¹ cm ⁻¹
NH ₂ Cl	243	450	82
CH ₃ NHCl	252	354	120
<i>N</i> -Cl- β -Ala	250	358	142
<i>N</i> -Cl-Gly	254	375	187
<i>N</i> -Cl-Thr	256	357	185
<i>N</i> -Cl-Gly ₂	254	357	157
<i>N</i> -Cl-Gly ₂ EE	254	357	156

Chloramines were prepared at an initial pH between 8 and 10. Solutions of hypochlorite were reacted with solutions containing an excess of the corresponding amine in a double twin-jet tangential mixer. With this technique, the formation of dichloramines could be prevented, particularly when the final amine to chlorine ratio was high. Molar absorptivities of the chloramines, which were determined for iodometrically standardized solutions (Table II), were in good agreement with previously determined values.^{1,16}

Sodium perchlorate (prepared from Na₂CO₃ and HClO₄) was used to control solution ionic strength at 0.50 M. A glass electrode (Corning) and a NaCl saturated calomel reference electrode were used for pH measurements. All pH values above 2 and below 11 were corrected to $-\log [\text{H}^+]$ by titration of the electrodes with standard HClO₄ and NaOH solutions. Hydrogen ion concentrations outside this range were calculated from the standard HClO₄ concentration used.

Mono- and disodium phosphates (Mallinckrodt) were used to buffer solutions for measurement of equilibrium constants. Acetate buffer was prepared by mixing acetic acid with a carbonate free solution of sodium hydroxide to give the desired buffer concentration.

Methods. Equilibrium constants for mixtures of the chloramines of ammonia and amines were determined spectrophotometrically with a Hewlett Packard 8450A spectrophotometer with a cell thermostated at 25.0 \pm 0.1 °C. Phosphate-buffered solutions of hypochlorous acid were reacted with phosphate-buffered solutions of mixtures of ammonia and amine. An equilibrium spectrum was obtained when the spectral maximum of the reaction solution reached a constant value and the ratio of absorbance at the spectral maximum to the isobestic absorbance became constant. Analysis of equilibrium absorbances was performed in the 240-290-nm region.

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Table III. Chlorine-Transfer Equilibrium and Rate Constants^a

amine	K_{TR}	$k,^b$ $M^{-1} s^{-1}$	$k_{Cl},^c$ $M^{-1} s^{-1}$	$k^o_{Cl},^d$ $M^{-1} s^{-1}$
CH ₃ NH ₂	35 ^e	0.110	$(2.4 \pm 0.1) \times 10^8$	
β -Ala	48 ^e	0.510	$(2.3 \pm 0.1) \times 10^8$	$(1.3 \pm 0.2) \times 10^8$
Gly	51 \pm 4	1.58	$(2.4 \pm 0.1) \times 10^8$	$(1.8 \pm 0.1) \times 10^7$
Thr	100 \pm 9	2.90	$(9.5 \pm 0.3) \times 10^7$	$(1.8 \pm 0.2) \times 10^6$
Gly ₂	400 \pm 25	5.91	$(3.3 \pm 0.2) \times 10^7$	$(1.7 \pm 0.2) \times 10^7$
Gly ₂ EE		7.02	$(1.4 \pm 0.1) \times 10^7$	

^a 25.0 °C, $\mu = 0.50$ M (NaClO₄), 0.002 M phosphate buffer.

^b These values are averaged apparent rate constants from Table IV for the region where the reaction is independent of hydrogen ion concentration ($-\log [H^+] = 5.5 \pm 0.5$). ^c These are the resolved second-order rate constants for the reaction of NH₂Cl⁺ with unprotonated amine, RNH₂. ^d These are the resolved second-order rate constants for the reaction of NH₂Cl⁺ with the neutral form of the amino carboxylic acids, H₂NRCOOH. Values of k_{Cl} and k^o_{Cl} are calculated from eq 13 and 17. ^e Calculated from ref 7.

Kinetic studies for the reaction of NH₂Cl with amine compounds were performed with at least a 50-fold excess of amine concentration over chloramine. The solutions were unbuffered with the exception of the buffering capacity supplied by the reagent amines. Spectra of reactants and products were obtained with a Cary 14 spectrophotometer. Absorbance vs. time data at 280 nm were obtained with a computer-interfaced Durrum stopped-flow spectrophotometer¹⁷ or a Cary 16 spectrophotometer with thermostated cell compartments. Linear plots of $\log (A_\infty - A_t)$ vs. time were obtained, where A_∞ and A_t represent the final absorbance and the absorbance at any time. The slope of these plots yielded pseudo-first-order rate constants, k_{obsd} , for the rate expression $-d[NH_2Cl]_T/dt = k_{obsd}[NH_2Cl]_T$. A second-order rate constant, k , was calculated from the expression $k = k_{obsd}/[RNH_2]_T$, where T refers to total species in solutions. Most kinetic studies were performed at 25.0 \pm 0.1 °C. In studies of the effect of temperature on the rate of chlorine transfer, solutions were allowed to equilibrate at the reaction temperature for 20 min before the reaction was started. The rate constants from the kinetic studies have been averaged for at least three kinetic runs and have a relative error of 1–4%.

The protonation constants of NH₂Cl were determined as a function of temperature by pH-jump experiments. Solutions of standardized perchloric acid and monochloramine were allowed to equilibrate thermally for 20 min before being mixed in the stopped-flow spectrophotometer with a thermostated cell compartment. Initial absorbances at 243 nm were obtained after the pH jump but before the loss of NH₂Cl due to disproportionation became significant (eq 2 and 3). A chloramine solution mixed with 0.50 M NaClO₄ at pH 8.0 confirmed the chloramine stability at each temperature and gave the NH₂Cl absorbance.

Results

Chlorine-Transfer Equilibria. Hypochlorous acid was reacted with solutions containing ammonia and the amine of interest. A mixture of NH₂Cl and RNHCl was obtained, and the reaction proceeded rapidly to an equilibrium position through two isobestics. The measurement of the equilibrium spectrum for *N*-chloro-L-threonine was complicated by the oxidative decarboxylation^{18,19} of the chloramino acid. This chloramino acid decomposed more rapidly than is the case for the other amines. Analysis of the ratio of the isobestic absorbance to the absorbance at the spectral maximum indicated that the decay reaction proceeded from an equilibrium position. The equilibrium constant was calculated from the isobestic absorbance for measurement of total chlorine in solution.

The equilibrium constants for the major species in neutral pH solution (eq 5) are given in Table III. These values of



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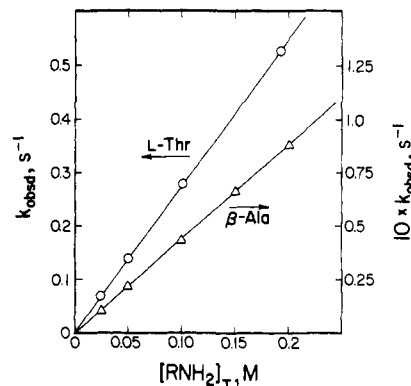


Figure 1. Amine concentration dependence of the observed first-order rate constant for chlorine-transfer reactions of NH₂Cl with amine nitrogen: reaction of NH₂Cl with (O) L-threonine and (Δ) β-alanine (25.0 °C, $\mu = 0.50$ M (NaClO₄), $[NH_2Cl] = [NH_3]_T = 7.0 \times 10^{-4}$ M, $-\log [H^+] = 6.00 \pm 0.03$).

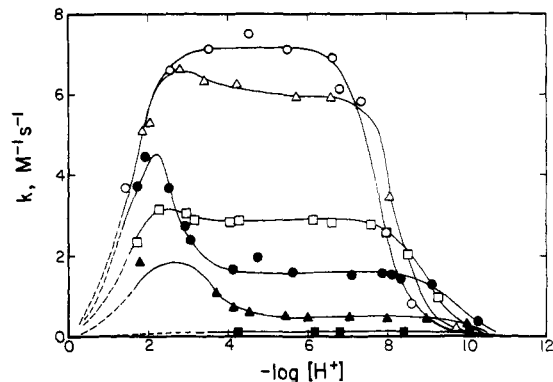


Figure 2. pH profile for chlorine transfer from NH₂Cl to amine nitrogen. The reactions are NH₂Cl with (O) glycylglycine ethyl ester, (Δ) glycylglycine, (□) L-threonine, (●) glycine, (▲) β-alanine, and (■) methylamine (25.0 °C, $\mu = 0.50$ M (NaClO₄)). The solid line is the calculated fit from eq 13, 18, and 19 and data from Tables I and II.

K_{TR} are determined from data in a region where the reaction rate is independent of hydrogen ion concentration. The transfer of chlorine from NH₂Cl to the amine nitrogen is favorable thermodynamically. The equilibrium constants become larger as the amines become less basic because K_{TR} is written in terms of the protonated amines.

Kinetic Studies. The reaction of $(4.0\text{--}7.5) \times 10^{-4}$ M NH₂Cl with excess amine, amino acid, or dipeptide gave excellent fits to a pseudo-first-order kinetic model for all conditions used in this study. The reaction rates are unaffected by changes in ionic strength ($\mu = 0.10\text{--}1.0$ M (NaClO₄)) or buffer concentrations (0.025–0.40 M total acetate, $-\log [H^+] = 4.2$; or 0.05–0.20 M total phosphate, $-\log [H^+] = 6.5$). The observed first-order rate constants, k_{obsd} , have a linear dependence on the excess amine concentration (Figure 1). Thus, the chlorine-transfer reaction of NH₂Cl is first order in total amine and total chloramine.

Kinetic data for the effect of hydrogen ion concentration on the reaction at 25.0 °C are given in Table IV and Figure 2. The reactions of the amines, amino acids, and dipeptides with NH₂Cl are independent of hydrogen ion concentration from pH 4 to 7. The second-order rate constants decrease in more basic solutions. The rate constant for glycylglycine reactions reaches a maximum value when the pH is between 2 and 2.5 and then decreases in more acidic solutions. The methylamine rate constants are invariant down to $-\log [H^+] = 4.2$.

The wavelength for following the chlorine-transfer reaction (280 nm) is very close to the NH₂Cl–NHCl₂ isobestic (277

Table IV. Kinetics Data for Reactions of NH_2Cl with Amines, Amino Acids, and Dipeptides^a

amine	$T, ^\circ\text{C}$	$-\log [\text{H}^+]$	$k, ^b \text{M}^{-1} \text{s}^{-1}$	amine	$T, ^\circ\text{C}$	$-\log [\text{H}^+]$	$k, ^b \text{M}^{-1} \text{s}^{-1}$
CH_3NH_2	25.0	4.20 ^{c,d}	0.115	Thr	25.0	9.14	1.32
		6.25 ^c	0.110			10.36	0.280
		6.85 ^c	0.110			1.71 ^d	2.35
		7.60 ^c	0.106			2.28 ^d	3.14
		8.32 ^c	0.100			2.90 ^d	3.00
	10.00 ^c	0.0927	3.13 ^d			2.90	
	15.3	8.0	0.0668			4.02 ^d	2.82
	25.1	8.00	0.113			4.30	2.88
	36.1	8.0	0.203			6.15	2.90
	42.6	8.0	0.261			6.64	2.84
	48.9	8.0	0.370			7.60	2.77
$\beta\text{-Ala}^e$	25.0	1.80 ^d	1.90	Gly ₂	25.0	7.97	2.55
		3.70 ^d	1.12			8.49	1.98
		4.20	0.755			9.30	0.946
		4.50	0.570			1.80	5.16
		5.45	0.512			2.09	5.32
	6.00	0.450	2.84			6.57	
	7.07	0.502	3.42			6.36	
	8.00	0.434	4.28			6.26	
	9.00	0.384	5.74			5.91	
	10.00	0.240	6.58			5.95	
	$\beta\text{-Ala}^f$	15.3	8.0			0.277	8.08
25.1		8.00	0.548	9.70	0.216		
36.1		8.0	0.836	8.0	3.82		
42.6		8.0	1.15	25.1 ^g	7.95	6.84	
48.9		8.0	1.63	36.1 ^g	8.0	12.5	
Gly	25.0	1.71 ^d	3.72	42.6 ^g	8.0	17.4	
		1.90 ^d	4.46	48.9 ^g	8.0	24.0	
		2.50 ^d	3.66	Gly ₂ EE	25.0	1.43 ^b	3.66
		2.95 ^d	2.74			2.54 ^b	6.63
		3.05 ^d	2.49			3.50 ^b	7.16
	4.12	1.70	4.62			7.46	
	4.78	2.02	5.50			7.02	
	5.62	1.58	6.62			6.90	
	7.10	1.50	6.75	6.10			
	7.85	1.50	7.35	5.85			
	8.02	1.52	8.63	0.811			
8.36	1.42						

^a $\mu = 0.50 \text{ M}$ (NaClO_4). The concentration of NH_2Cl and total ammonia are each $7.5 \times 10^{-4} \text{ M}$, unless stated otherwise. Amino acid or dipeptide total concentrations are 0.0340 M except when noted. ^b The apparent rate constants, k , are the average of at least three kinetic runs and have a relative error of 1–4%. ^c $[\text{CH}_3\text{NH}_2]_{\text{T}} = 0.0440 \text{ M}$. ^d $[\text{NH}_2\text{Cl}] = [\text{NH}_3]_{\text{T}} = 4.5 \times 10^{-4} \text{ M}$. ^e $[\beta\text{-Ala}]_{\text{T}} = 0.050 \text{ M}$. ^f $[\beta\text{-Ala}]_{\text{T}} = 0.0250 \text{ M}$. ^g $[\text{Gly}_2]_{\text{T}} = 0.0125 \text{ M}$.

Table V. Enthalpies and Entropies of Activation for the Resolved Second-Order Rate Constants for Chlorine Transfer from NH_2Cl to Methylamine, β -Alanine, and Glycylglycine

amine	$\Delta H^\ddagger(\text{obsd}),$ kcal mol^{-1}	$\Delta H^\circ_{\text{H}(\text{RNH}_2)},$ kcal mol^{-1}	$\Delta H^\ddagger_{\text{NH}_3\text{Cl}}$ $(\text{RNH}_2),$ kcal mol^{-1}	$\Delta S^\ddagger(\text{obsd}),$ eu	$\Delta S^\circ_{\text{H}(\text{RNH}_2)},$ eu	$\Delta S^\ddagger_{\text{NH}_3\text{Cl}}$ $(\text{RNH}_2), \text{eu}$
methylamine	8.7	-13.2 ^a	1.0	-47	4 ^a	-32
β -alanine	8.8	-11.3 ^b	3.0	-45	8.6 ^b	-25
glycylglycine	9.2	-10.6 ^c	~4.0	-40	1.5 ^c	~-27
NH_2Cl		-5.5 ^d			-11.4 ^d	

^a Partridge, J. A.; Christiansen, J. J.; Izatt, R. M. *J. Am. Chem. Soc.* 1966, 88, 1649–1653. ^b Boyd, S.; Brannan, J. R.; Dunsmore, H. S.; Nancollas, G. H. *J. Chem. Eng. Data* 1967, 12, 601–605. ^c Burnett, A. P.; Lin, M. C.; Nancollas, G. H. *J. Am. Chem. Soc.* 1968, 90, 5120–5126. ^d This work.

nm).⁷ Hence the disproportionation of NH_2Cl to NHCl_2 in acidic solution does not interfere with the kinetic determinations but does provide an alternate path for loss of NH_2Cl . Thus, the observation of the chlorine-transfer reaction becomes limited by smaller signal changes in acidic solutions.

The general shape of the hydrogen ion dependence profile (Figure 2) indicates that at least two proton equilibria, which involve amine and chloramine, precede the chlorine-transfer step. The increasing rate in acid solutions is observed only for the NH_2Cl reactions with amino acids and glycylglycine. These amino carboxylates have multiple-proton equilibria as opposed to the single-proton equilibria for methyl amine and glycylglycine ethyl ester. The ratio of the rate at the maximum to the pH-independent rate constant ($\text{Gly}_2 = 1.1$, $\text{Thr} = 1.1$, $\text{Gly} = 2.8$, $\beta\text{-Ala} = 4.2$) is correlated with the basicity of the amine nitrogen (Table I). Thus, the increasing rates in acid

Table VI. Protonation Constants of NH_2Cl as a Function of Temperature^a

$T, ^\circ\text{C}$	$K_{\text{H}}^{\text{NH}_2\text{Cl}}, \text{M}^{-1}$	$T, ^\circ\text{C}$	$K_{\text{H}}^{\text{NH}_2\text{Cl}}, \text{M}^{-1}$
14.1	42.0 ± 1.5	25.2	29.3 ± 1.2
19.4	36.2 ± 1.1	36.8	21.4 ± 0.2

^a $\mu = 0.50 \text{ M}$ (NaClO_4); T to $\pm 0.1 ^\circ\text{C}$.

are due to an alternate amine species reacting with NH_2Cl .

Data for the effect of temperature on the reaction of NH_2Cl with methylamine and β -alanine are given also in Table IV. The apparent rate constants, k , at $25.0 ^\circ\text{C}$ are determined at $-\log [\text{H}^+] = 8.00 \pm 0.03$ where the reaction rates show little sensitivity to fluctuations in hydrogen ion concentration. Activation plots ($\ln(K/T)$ vs. $1/T$) of the data gave excellent linear fits. The observed enthalpies and entropies of activation

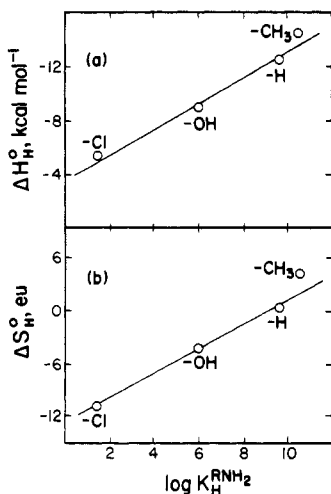


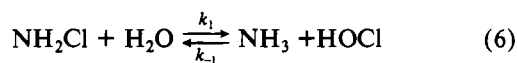
Figure 3. Effect of amine nucleophilicity on the enthalpy and entropy of protonation; methylamine ($-\text{CH}_3$), $\log K_{\text{H}}(25.0\text{ }^\circ\text{C}) = 10.6$, $\Delta H_{\text{H}}^{\circ} = -13.2\text{ kcal mol}^{-1}$, $\Delta S_{\text{H}}^{\circ} = 4\text{ eu}$ (Partridge, J. A.; Christiansen, J. J.; Izatt, R. M. *J. Am. Chem. Soc.* **1966**, *88*, 1649–1653); ammonia ($-\text{H}$), $\log K_{\text{H}}(25.0\text{ }^\circ\text{C}) = 9.29$, $\Delta H_{\text{H}}^{\circ} = -12.43\text{ kcal mol}^{-1}$, $\Delta S_{\text{H}}^{\circ} = 0.8\text{ eu}$ (Paoletti, P.; Stern, J. H.; Vacca, A. *J. Phys. Chem.* **1965**, *69*, 3759–3762); hydroxylamine ($-\text{OH}$), $\log K_{\text{H}}(25.0\text{ }^\circ\text{C}) = 5.95$, $\Delta H_{\text{H}}^{\circ} = -9.3\text{ kcal mol}^{-1}$, $\Delta S_{\text{H}}^{\circ} = -3.8\text{ eu}$ (Lumme, P.; Lahermo, P.; Tummavuori, J. *Acta Chem. Scand.* **1965**, *19*, 2175–2188); chloramine ($-\text{Cl}$), $\log K_{\text{H}}(25.0\text{ }^\circ\text{C}) = 1.47$, $\Delta H_{\text{H}}^{\circ} = -5.5\text{ kcal mol}^{-1}$, $\Delta S_{\text{H}}^{\circ} = -11.4\text{ eu}$, $\mu = 0.50\text{ M}$ (NaClO_4) (this work).

are given in Table V. The activation parameters for the glycyglycine reactions are an approximation because of the pH dependence of the rate constants in this region.

Protonation Constants of NH_2Cl . The addition of acid to solutions of NH_2Cl causes a rapid absorbance drop at its spectral maximum due to the formation of protonated chloramine, NH_3Cl^+ (eq 2).⁷ Table VI gives the protonation constants of NH_2Cl determined by pH-jump experiments at several temperatures. The protonation constant at 25 $^\circ\text{C}$ agrees with the kinetically determined value.⁷ A least-squares linear regression of $\log K_{\text{H}}^{\text{NH}_2\text{Cl}}$ vs. $1/T$ yields the enthalpy, $\Delta H_{\text{H}}^{\circ}(\text{NH}_2\text{Cl})$, and entropy, $\Delta S_{\text{H}}^{\circ}(\text{NH}_2\text{Cl})$, of protonation as $-5.5 \pm 0.2\text{ kcal mol}^{-1}$ and $-11.4 \pm 0.5\text{ eu}$ ($\mu = 0.50\text{ M}$ NaClO_4), respectively. Figure 3 shows that these values follow trends in accord with the increasing electron-withdrawing ability of a donor on the amine nitrogen. The small enthalpy of protonation for NH_2Cl reflects the weak basicity of chloramine. The entropy of protonation for NH_2Cl is more negative than other nitrogen bases. This result suggests that NH_2Cl is relatively poorly solvated compared to NH_3 , which is to be expected for their relative hydrogen-bonding interaction with water.

Discussion

A possible mechanism for chlorine transfer is the hydrolysis of NH_2Cl to form HOCl , which reacts rapidly with other amines (eq 6 and 7). In the presence of excess amine, HOCl



would be a steady-state species and the rate expression is given by eq 8. Under the conditions used, $k_2[\text{RNH}_2] \gg k_{-1}[\text{NH}_3]$

$$\frac{-d[\text{NH}_2\text{Cl}]}{dt} = \frac{k_1 k_2 [\text{NH}_2\text{Cl}][\text{RNH}_2]}{k_{-1}[\text{NH}_3] + k_2[\text{RNH}_2]} \quad (8)$$

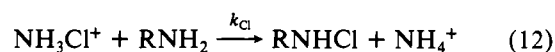
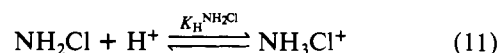
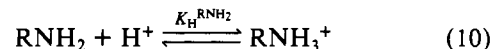
from known rate constants.³ Hence, eq 8 simplifies to eq 9

$$-d[\text{NH}_2\text{Cl}]/dt = k_1[\text{NH}_2\text{Cl}] \quad (9)$$

and $k_1 = 1.5 \times 10^{-5}\text{ s}^{-1}$ at 25.0 $^\circ\text{C}$.⁷ However, the observed first-order rate constants are larger than k_1 by factors as great as 10^3 – 10^5 , and, as seen in Figure 1, there is a first-order dependence in the RNH_2 concentration. Hence, the chlorine transfer is direct, as given in eq 1, with a negligible amount occurring by the hydrolysis pathway.

The protonation constant for NH_2Cl is $10^{1.5}$ while the protonation constants for the various amines range from 10^7 to 10^{11} (Table I). Therefore, NH_2Cl and RNH_3^+ are the main species in neutral solutions and the lack of a pH dependence from pH 4 to 7 would fit these reactants. However, RNH_3^+ is not a logical reactant since it has no electron pairs available to react with chlorine. The more likely reactive pair are NH_3Cl^+ and RNH_2 . This reactant pair would also be expected to have a wide range of pH independence.

The proposed general mechanism is given by eq 10–12. The



apparent second-order rate constant, k , based on $[\text{NH}_2\text{Cl}]_{\text{T}}$ and $[\text{RNH}_2]_{\text{T}}$ is given by eq 13. From pH 4 to 7, this ex-

$$k = \frac{k_{\text{Cl}} K_{\text{H}}^{\text{NH}_2\text{Cl}} [\text{H}^+]}{(1 + K_{\text{H}}^{\text{RNH}_2} [\text{H}^+])(1 + K_{\text{H}}^{\text{NH}_2\text{Cl}} [\text{H}^+])} \quad (13)$$

pression simplifies to eq 14 for all amines studied. At higher

$$k = k_{\text{Cl}} (K_{\text{H}}^{\text{NH}_2\text{Cl}} / K_{\text{H}}^{\text{RNH}_2}) \quad (14)$$

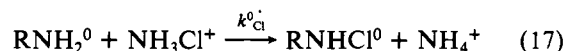
pH the value of k decreases as $[\text{H}^+]$ decreases in accordance with eq 15, as seen in Figure 2. Values of k_{Cl} (eq 12) cal-

$$k = k_{\text{Cl}} K_{\text{H}}^{\text{NH}_2\text{Cl}} [\text{H}^+] / (1 + K_{\text{H}}^{\text{RNH}_2} [\text{H}^+]) \quad (15)$$

culated from neutral and basic solution data are given in Table III.

The reaction of NH_2Cl with glycyglycine ethyl ester has a plateau-shaped dependence upon pH as expected from eq 13. At low pH, the k value decreases in accordance with eq 16 as the percentage of NH_3Cl^+ becomes appreciable. Methylamine would be expected to behave similarly, but the reactions below pH 4 were not studied because of NH_2Cl loss by its disproportionation to NHCl_2 . The disproportionation of the *N*-chloramino acids and *N*-chloropeptides⁷ did not interfere under the conditions used in this study.

Figure 2 shows that additional kinetic factors enter into the chlorine-transfer reactions for the amino acids and dipeptides in the vicinity of $-\log [\text{H}^+] = 2$ –4. This results from the protonation of the amino acid to give the zwitterion ($^+\text{H}_3\text{NCHRCOO}^-$) or the neutral form ($\text{NH}_2\text{CHRCOOH}$). Although K_2 in eq 4 is quite large, the neutral form (RNH_2^0) is reactive toward NH_3Cl^+ (eq 17) while the zwitterion is not.



The second-order rate constant for the reaction is given by eq 18 and 19. Values of k_{Cl}^0 (eq 17) calculated from the acid

$$k = k_{\text{Cl}} + k_{\text{Cl}}^0 (K_{\text{H}}^{\text{RNH}_2} [\text{H}^+] / K_2) C \quad (18)$$

$$C = K_{\text{H}}^{\text{NH}_2\text{Cl}} [\text{H}^+] / \{(1 + K_{\text{H}}^{\text{RNH}_2} [\text{H}^+] + K_{\text{H}}^{\text{RNH}_2} K_{\text{H}}^{\text{RCOO}^-} [\text{H}^+]^2) (1 + K_{\text{H}}^{\text{NH}_2\text{Cl}} [\text{H}^+])\} \quad (19)$$

solution data are given in Table III. The solid curves in Figure 2 are generated from eq 13, 18, and 19 and the data in Tables

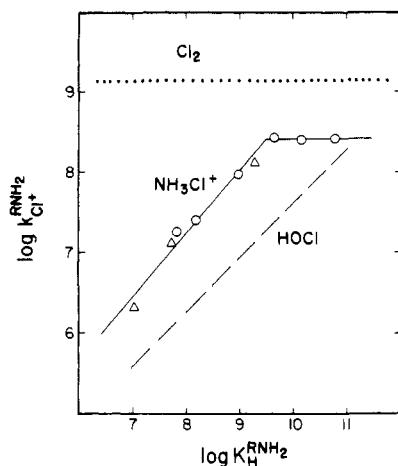
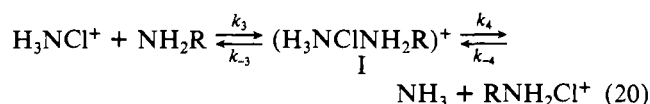


Figure 4. Effect of amine nucleophilicity on chlorine transfer from NH_2Cl to amine nitrogen. Solid line is for NH_2Cl reactions with (O) fully unprotonated amine compound, RNH_2 , and (Δ) the neutral form of the amino acids and glycylglycine, RNH_2^0 . Dotted line is for chlorine data, and dashed line is for hypochlorous acid data for their chlorination reactions with the same or similar amine compounds.³

I and III. The maxima in the vicinity of pH 2–3 are due to the relatively high reactivity of the two protonated forms in eq 17. At lower pH values, the neutral form reacts with another proton to give the fully protonated amino acid or dipeptide ($\text{H}_3\text{N}^+\text{RCOOH}$). Hence, the rate constant, k , decreases as $[\text{H}^+]$ increases further due to depletion of all free amine nitrogen forms.

The resolved second-order rate constants, k_{Cl} and k_{Cl}^0 , are plotted as a function of amine nitrogen basicity in Figure 4. The neutral amino acid protonation constants are assumed to be the same as the protonation constants of the corresponding alkyl esters of the amino acid or dipeptide. The rate constants increase linearly as a function of amine nucleophilicity and reach a limiting value at $(2.4 \pm 0.1) \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ for amines more basic than ammonia. This limiting rate constant is approximately a factor of 10 lower than the expected diffusion-controlled rate constant ($\sim 2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$) seen with the Cl_2 reaction.³

This behavior suggests that an intermediate is formed by nucleophilic attack and that the rate of decomposition of the intermediate is independent of amine nucleophilicity. Equation 20 shows the direct chlorine transfer between NH_3Cl^+ and an



unprotonated amine nitrogen in terms of the intermediate, I. The step k_3 represents the nucleophilic attack of the amine nitrogen on the chlorine atom, and k_3 increases as the nucleophilic character of RNH_2 increases. Step k_4 represents the electrophilic bond breaking of the $\text{NH}_3\text{--Cl}$ bond. This step is dependent upon the NH_3 nitrogen electrophilicity, which is constant for the series of reactions studied. Thus, the rate-determining step shifts from nucleophilic attack for amines less basic than ammonia to electrophilic bond breaking for

amines more basic than ammonia.

Figure 4 also shows that protonated chloramine, NH_3Cl^+ , is a more effective chlorinating agent than HOCl and is only 1–3 orders of magnitude less effective than Cl_2 . However, the small protonation constant of NH_2Cl ($\log K_{\text{H}}^{\text{NH}_2\text{Cl}} = 1.5$, 25.0°C , $\mu = 0.5 \text{ M}$) means that NH_3Cl^+ is not a major species in solution above pH 2. Thus, the apparent second-order rate constants are small ($0.1\text{--}7 \text{ M}^{-1} \text{ s}^{-1}$).

The enthalpies and entropies of chlorine transfer for the resolved second-order rate constants for chlorine transfer can be determined from eq 21–23 by using the data from Table

$$k_{\text{Cl}} = k(K_{\text{H}}^{\text{RNH}_2}/K_{\text{H}}^{\text{NH}_2\text{Cl}}) \quad (21)$$

$$\Delta H_{\text{NH}_3\text{Cl}}^*(\text{RNH}_2) = \Delta H^*(\text{obsd}) - \Delta H_{\text{H}}^0(\text{NH}_2\text{Cl}) + \Delta H_{\text{H}}^0(\text{RNH}_2) \quad (22)$$

$$\Delta S_{\text{NH}_3\text{Cl}}^*(\text{RNH}_2) = \Delta S^*(\text{obsd}) - \Delta S_{\text{H}}^0(\text{NH}_2\text{Cl}) + \Delta S_{\text{H}}^0(\text{RNH}_2) \quad (23)$$

V. These resolved thermodynamic parameters are given also in Table V. The observed enthalpies of activation, $\Delta H^*(\text{obsd})$, for these reactions average 9 kcal mol^{-1} although the apparent second-order rate constants range from $0.1 \text{ M}^{-1} \text{ s}^{-1}$ for the methylamine reaction to $6.6 \text{ M}^{-1} \text{ s}^{-1}$ for the glycylglycine reaction. The resolved enthalpies of activation, $\Delta H_{\text{NH}_3\text{Cl}}^*(\text{RNH}_2)$, are small, 1–4 kcal mol^{-1} , and are typical of activation enthalpies for large rate constants, as in the HOCl –amine chlorination reactions.¹ The 3-kcal difference between these numbers cannot be taken as significant because ionic strengths for the protonation enthalpies of the amines are not the same as that used in this study. The $\Delta S_{\text{NH}_3\text{Cl}}^*(\text{RNH}_2)$ values are very negative, which agrees with the ΔS^* value of -19 eu for the chlorination of NH_3 by HOCl (calculated from data of Morris¹).

Conclusions

The transfer of chlorine from NH_2Cl to amine nitrogen is a direct reaction which is thermodynamically favorable over a pH range that is environmentally significant for water and waste-water systems. The reaction proceeds by nucleophilic attack of the unprotonated amine nitrogen on the chlorine of the protonated chloramine and shifts to a rate-limiting step of electrophilic bond breaking in NH_3Cl^+ as the amine nitrogen becomes more basic than ammonia. The large separation of the chloramine and amine nitrogen protonation constants prevents the reactive forms of these species from reaching significant concentration levels in solution. Consequently, the apparent rate constants are small and the less basic amines appear to react more readily. In neutral pH solutions, chlorine transfer to amine nitrogen present at 10^{-5} M or higher concentration is more favorable than alternate paths for the loss of NH_2Cl such as hydrolysis or disproportionation.

Acknowledgment. This investigation was supported by the National Science Foundation under Grant CHE-7822456.

Registry No. NH_2Cl , 10599-90-3; CH_3NH_2 , 74-89-5; β -Ala, 107-95-9; Gly, 56-40-6; Thr, 72-19-5; Gly₂, 556-50-3; Gly₂EE, 627-74-7; CH_3NHCl , 6154-14-9; *N*-Cl- β -Ala, 69619-04-1; *N*-Cl-Gly, 35065-59-9; *N*-Cl-Thr, 81555-07-9; *N*-Cl-Gly₂, 53090-33-8; *N*-Cl-Gly₂EE, 81584-02-3.