Kinetics and Mechanism of Chlorine Exchange between Chloramine-T and Secondary Amines

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Abstract I The kinetics and mechanisms of chlorine transfer from chloramine-T (CAT) to several amines are second order and independent of p-toluenesulfonamide concentration; thus, the reaction does not involve disproportionation of CAT to dichloramine-T. From the profile of pH versus rate, the following mechanisms were proposed: (1) reaction of the ionized species of CAT with the ionized amine (ionic mechanism) and (2) reaction of the un-ionized species of CAT with the un-ionized amine (nonionic mechanism). The second-order, pH-independent rate constants calculated for the ionic and nonionic mechanisms were 1.6 and 5 \times 10⁶ M⁻¹ s⁻¹, respectively. Although these two mechanisms are kinetically indistinguishable, the rate constant for the nonionic mechanism is of the same order of magnitude as those calculated for similar chlorination reactions involving nonionizable chloramines, such as N-chlorosuccinimide, N-chloroquinuclidine, and N-chloro-N-methylbenzenesulfonamide. The proposed mechanism for the chlorine exchange involves a molecule of water in a cyclic, six-membered transition state.

Treatment with gaseous chlorine is still the most widely used method of disinfecting municipal water supplies. Recently, great concern has been raised over such problems as the chemical reactivity of chlorine with industrial pollutants, such as hydrocarbons, to produce carcinogens.¹ As a result, many municipal water systems have begun using chloramines (R-N-Cl) in place of gaseous chlorine, and serious consideration has been given to using chloramine-T (CAT) as a disinfecting agent for water.²

Not much is reported about the reactivities of chlorinating agents, such as CAT, with biomaterials, such as amines, in raw water. Such information about these reactions is extremely important in evaluating the safety and efficacy of these agents. This report presents fundamental data that will be useful in the search for new, safer, and more-effective chlorinating agents.

Chlorination of organic compounds such as imides, amides, amino acids, and phenols by CAT proceeds by either of the following mechanisms: (1) facile disproportion of CAT into free *p*-toluenesulfonamide (TSA) and dichloramine-T (DCT), with DCT participating in the subsequent reaction with the chlorine receptor molecule (Scheme I, route 1),³⁻⁵ or (2) direct transfer of chlorine⁶ from CAT to the chlorine acceptor molecule (Scheme I, route 2). The latter mechanism was recently proposed for the *N*-chlorination of amino acids (Scheme II).^{7,8} In these earlier investigations, however, the hydrolysis of CAT to HOCl and subsequent involvement of HOCl in the chlorination mechanism⁹ (Scheme I, route 3) were ruled out.

The kinetics and mechanisms of chlorination of secondary amines by N-chlorosuccinimide¹⁰ and N-chloro-N-methylbenzenesulfonamide¹¹ have previously been studied. Because these reactions proceed via a direct chlorine exchange mechanism, a study of the kinetics and mechanism(s) of the reaction between CAT and secondary amines will (1) establish whether chlorination of secondary amines at pH 5–12



ROUTE 2



ROUTE 3



Scheme I



proceeds by route 2 and not by route 1 (Scheme I), (2) compare the reactivity of CAT with other structurally related chlorinating agents, and (3) provide information regarding the mechanism(s) by which these positive chlorine agents exert their germicidal action.

Experimental Section

Materials—Commercial CAT was freed from possible contamination with DCT by washing several times with carbon tetrachloride and drying in a vacuum desiccator over phosphorous pentoxide. The final purity of CAT was determined by iodometric titration. TSA was recrystallized from glacial acetic acid prior to use. Dimethylamine hydrochloride (DMA) was recrystallized once from chloroform—ether prior to use. The following amines were purified by distillation before use: 2,6-dimethylpiperidine (DMP), 2,2,6,6-tetramethylpiperidine (TMP), piperidine (PIP), diethylamine (DEA), and diisopropylamine (DIP). Deuterium oxide (minimum purity, 99.5 atom % D) was used as purchased from Norell, Inc. (Landisville, NJ).

Analytical Methodology—All kinetic experiments were carried out with a Cary 219 spectrophotometer (Varian) connected to a circulating water bath (Haake F.K.) to maintain constant temperature. The pHs of the reaction mixtures were determined with a digital ionizer pH meter (Orion Research, model 501). The reactions between CAT and the secondary amines (forward reactions) and the reactions between TSA and the N-chloramines (reverse reactions) were determined by following the disappearance or appearance, respectively, of CAT at 250 nm with a Cary 219 spectrophotometer with 1-cm cuvettes. This method was based on the fact that CAT has a much higher molar absorptivity than TSA and the N-chlorodialkylamines at this wavelength. Phosphate buffers (0.05 M) were used as the reaction media, and the pH was determined after each kinetic measurement.

Forward Reaction Rates-Experiments were performed under pseudo-first-order conditions (i.e., the amines were used in at least a sixfold molar excess over CAT). Stock solutions (0.1 and 0.2 M) of each amine were prepared either in water or in 0.2 M phosphoric acid. A calculated volume of each stock solution was transferred to a volumetric flask and brought to mark with water and 0.2 M phosphate buffer at the desired pH to produce a solution containing twice the desired amine concentration in 0.1 M buffer. The pHs of the solutions were then readjusted to the original values by using either 0.1 M phosphoric acid or 0.1 M sodium hydroxide. After temperature equilibration, 1.5 mL of 1×10^{-3} M freshly prepared CAT solution in water was placed in a spectrophotometer cuvette in the instrument, and 1.5 mL of temperature-equilibrated amine solution was rapidly injected. The reaction was monitored by following the decrease in absorbance at 250 nm. Blank experiments were performed under identical conditions in the absence of amine. In these cases, no appreciable change in absorbance was observed.

The reaction between CAT and DEA was also followed in the presence of 0.5×10^{-3} and 1.5×10^{-3} M TSA to establish that TSA had no effect on the rates of the forward reactions.

The solvent isotope effect was investigated by preparing all the solutions in D_2O (minimum purity, 99.8 atom % D) instead of H_2O and following the reactions in the previously described manner.

Reverse Reaction Rates—Aqueous solutions of TSA were freshly prepared at a concentration of either 2×10^{-3} or 1×10^{-2} M. A calculated volume of the TSA solution was injected onto a spectrophotometer cell containing a calculated volume of the N-chloramine solution at the desired pH and at a concentration of either 3.6×10^{-4} or 5×10^{-4} M. The concentrations and volumes of the solutions were chosen so that TSA was present in 10- to 20-fold molar excess over N-chloramine. The absorbance due to these relatively high concentrations of TSA was canceled by placing a solution of equivalent sulfonamide concentration in the reference cell. The increase in absorbance corresponding to the appearance of CAT was monitored at 250 nm. All kinetic reactions were carried out in duplicate or triplicate, and the rate constants from individual experiments did not vary by more than $\pm 10\%$.

Results

Chlorine exchange between CAT and secondary amines (Scheme I, route 2) was studied spectrophotometrically as a function of amine, CAT, and TSA concentrations and as a function of pH in the range 5–12. Figure 1 shows the time course of the change in the UV spectrum (190–310 nm) of a system containing DEA and CAT (molar ratio, 1:1) at pH 7.6. On the basis of these spectra, an analytical wavelength of 250 nm was chosen for the kinetic runs, because this wavelength shows the greatest change in absorbance, free from interference by other UV absorbers in the system, as CAT is either formed or lost.

Rate of Chlorine Transfer from CAT to Secondary Amines (Forward Reaction)—The reaction of CAT with secondary amines was followed by monitoring the decrease in the UV absorbance at 250 nm that corresponds to the disappearance of CAT. Pseudo-first-order conditions were maintained in the pH range 5.0–11.9 by keeping the amine concentration in at least sixfold molar excess over CAT. Plots



WAVELENGTH(nm)

Figure 1—Change in UV absorbance during reaction between CAT and DEA (molar ratio, 1:1) at pH 7.6. Spectra were run every 5 min. The reaction was complete in <2 h.

of $\ln (A_t - A_{\infty})$ versus time (Figure 2) at pH 7.0 and 11.1 were linear, indicating a first-order (and not a second-order) dependency on CAT (where A_t and A_{∞} are absorbances of CAT at time t and infinity, respectively). This conclusion was further supported by determining the rate constant of the reaction between CAT and DEA at pH 7.3, by using the initial rate method, according to the following equations:

$$-dA/dt = k_{sec}A_0[DEA]$$
(1)

In eq 1, A_0 is the absorbance of CAT at t = 0, k_{sec} is the observed second-order rate constant, and [DEA] is the concentration of DEA. By keeping [CAT] constant and changing the amine concentration, eq 1 can be rearranged as follows:

$$-dA/dt/A_0 = k_{sec}[DEA]$$
(2)

A plot of $-dA/dt/A_0$ versus the different amine concentrations (Figure 3) resulted in a straight line with a slope of 1.24 $M^{-1}s^{-1}$, which is in close agreement to the observed second-



Figure 2—Plots of In ($A_t \sim A_{\infty}$) versus *t* for reaction between DEA and CAT in phosphate buffer (0.05 M) at pH 7 (\bullet) and pH 11.1 (\bigcirc).

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Figure 3—Plot of initial rate of reaction between CAT (5 \times 10⁻⁴ M) and DEA versus [DEA] in phosphate buffer (pH 7.4; 0.05 M).

order rate constant $(1.6 \text{ M}^{-1} \text{s}^{-1})$ determined from first-order plots at the same pH.

Effect of Amine and CAT Concentrations—To verify further that the overall reaction was second order, the dependence of the pseudo-first-order rate constant for the forward reaction (k_{obs}) on [CAT] and [DEA] was determined. Figure 4 shows the dependence of k_{obs} on [DEA]; the line in this figure has a slope of +1. Similar results were obtained when [DEA] was held constant and [CAT] was varied, indicating that the reaction is first order with respect to each reactant and is, overall, second order. The pH-dependent k_{sec} (1.6 $M^{-1}s^{-1}$) was calculated with the following equation:

$$k_{\rm obs} = k_{\rm sec} [{\rm DEA}] \tag{3}$$

Effect of TSA Concentration—To rule out the involvement of DCT in the overall reaction between CAT and secondary amines, the reaction was run in the presence of an equal or threefold molar excess of TSA over CAT at pH 7.36. The added TSA was expected to shift the disproportionation equilibrium, if it occurred, away from DCT toward CAT.

The initial rate of disappearance of CAT (expressed as -dA/dt) was calculated for each kinetic measurement. The results clearly indicate that the addition of TSA has no appreciable effect on the initial reaction rate. These results, along with the observations discussed earlier, indicate that disproportionation of CAT to DCT does not occur at appreciable rates in these systems.

Effect of pH—The rate of the reaction between CAT and DEA was studied over the pH range 5–12. The reaction rate was independent of pH between pH 5 and pH 10, but the rate decreased significantly as the pH was increased above 10. The profile of pH versus rate (pH-rate profile) is shown in Figure 5, and values of the pH-independent rate constants (k_{true}) calculated for the ionic and nonionic mechanisms are shown



Figure 4—Plot showing first-order dependence on [DEA] for reaction between CAT (5×10^{-4} M) and DEA in phosphate buffer (pH 7.4, 0.05 M).

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Figure 5—pH-Rate profile for reaction between CAT and DEA. (The line was calculated by using eq 11.)

in Table I.

Effect of Steric Hindrance in Amine Structure on Rate of Chlorine Transfer from CAT to Amine (Forward Reaction)—The effect of steric hindrance in the amine structure on the rate of the forward reaction was studied with the amines shown in Table II over the pH range 5–10, at which pH the reaction is independent of pH. In this series of amines, methyl substitution on the carbon adjacent to the nitrogen (i.e., the α -carbon) increases from DMA to DIP and from PIP to TMP. The true second-order rate constants (k_{true}) were calculated (Table III) for both an ionic and a nonionic mechanism (see *Discussion*). For both mechanisms, the values of k_{true} for chlorine transfer from CAT to the secondary amines decreased as the methyl substitution on the α -carbon increased.

Solvent Isotope Effect—The rate of the reaction between DMA and CAT was studied in D_2O with the initial rate method, as described earlier. The value of k_{sec} was $1.2 M^{-1}s^{-1}$ at pD 7.3. This value is significantly lower than the value of $1.95 M^{-1}s^{-1}$ obtained for k_{true} in H_2O (Table III) and suggests that a molecule of water is involved in the transition state of the reaction.

Rate of Chlorine Transfer from N-Chloramine to TSA (Reverse Reaction)—The reaction of N-chloramines with TSA was followed by monitoring the increase in the UV absorbance at 250 nm, which corresponds to the appearance of CAT. The reaction between N-chlorodiisopropylamine and TSA was used as a model reaction to study the influence of pH on the reaction rate. Pseudo-first-order conditions were maintained by keeping [TSA] in at least a 10-fold molar excess over the N-chloramine concentration. The results indicate that the reverse reaction is first order with respect to N-chloramine.

The rate of chlorine transfer from N-chlorodiisopropylamine to TSA was independent of pH in the range 4–9. The pH-independent rate constant $(k'_{true}; 1.0 \text{ M}^{-1}\text{s}^{-1})$ was calcu-

Table I—pH-Independent k_{true} Values for Reaction between CAT and DEA⁴

<i>k_{obs}</i> , M ^{−1} s ^{−1}	$k_{\rm true}, {\rm M}^{-1} {\rm s}^{-1b}$		
	lonic Mechanism	Nonionic Mechanism	
1.74	2.30	6.70 × 10 ⁸	
1.60	1.58	4.78×10^{6}	
1.56	1.56	4.73 × 10 ⁶	
1.54	1.54	4.67×10^{8}	
1.18	1.61	4.90×10^{6}	
0.42	1.71	5.19 × 10 ⁶	
0.21	1.87	5.61 × 10 ⁶	
	K _{obe} , M ⁻¹ s ⁻¹ 1.74 1.60 1.56 1.54 1.18 0.42 0.21	$\begin{array}{c c} & & & & & & \\ \hline k_{\rm obs}, M^{-1} {\rm s}^{-1} & & & & \\ \hline lonic & & & \\ \hline Mechanism & & \\ \hline 1.74 & 2.30 & & \\ 1.60 & 1.58 & & \\ 1.56 & 1.56 & & \\ 1.56 & 1.56 & & \\ 1.54 & 1.54 & & \\ 1.18 & 1.61 & & \\ 0.42 & 1.71 & & \\ 0.21 & 1.87 & & \\ \end{array}$	

[•]Based on eqs 11 (ionic mechanism) and 12 (nonionic mechanism). [•]Average values are 1.74 and 5.20 \times 10⁶ M⁻¹sec⁻¹ for the ionic and nonionic mechanisms, respectively.

Table II—Structures, Nomenclature, and Acid Dissociation Constants (pK_a) of Amines Used in N-Chlorination Studies

Structure	Name (Abbreviation)	pK.
(CH ₃) ₂ NH	Dimethylamine (DMA)	10.72
(CH ₂ CH ₂) ₂ NH	Diethylamine (DEA)	10.98
(CH_)_CHNHCH(CH_)_	Diisopropylamine (DIP)	11.05
CH2CH2NHCH2CH2CH2	Piperidine (PIP)	11.28
CH ₂ CH(CH ₃)NHCH(CH ₃)CH ₂ CH ₂	2,6-Dimethylpiperidine	11.14
CH ₂ C(CH ₃) ₂ NHC(CH ₃) ₂ CH ₂ CH ₂	2,2-6,6-Tetramethyl- piperidine (TMP)	11.10

Table III—pH-Independent k_{true} Values for Reactions between CAT and Secondary Amines

A main a	$k_{\rm true}, {\rm M}^{-1} {\rm s}^{-1}$				
Amine	Ionic Mechanism ^e	Nonionic Mechanism ^b			
DMA	1.95	3.25 × 10 ⁶			
DEA	1.58	4.80 × 10 ⁸			
DIP	0.35	1.25 × 10 ⁸			
PIP	2.70	16.3 × 10 ⁶			
DMP	0.83	3.60 × 10 ⁸			
TMP	0.22	0.88 × 10 ⁶			

Equation 11. ^b Equation 12.

lated on the basis that the rate of the reverse reaction depends on the un-ionized form of TSA.

Effect of Steric Hindrance in Chloramine Structure on Rate of Reverse Reaction—The effect of steric factors described previously for the forward reaction were also investigated for the reverse reaction. The N-chloro derivatives of the amines listed in Table II were used in this study, and TSA was used in large excess to maintain pseudo-first-order conditions.

The k'_{true} values for the N-chloramines studied are summarized in Table IV. In contrast to results for the forward reaction, the rate of the reverse reaction increased with increasing methyl substitution on the α -carbon of the N-chloramine. This trend is more evident with the N-chlorosubstituted, piperidines (Table IV).

Discussion

The reactions between CAT and several secondary amines were followed spectrophotometrically at 250 nm. Chlorine transfer from CAT to DEA is clearly first order with respect to both reactants. The pH-rate profile for the forward reaction exhibited a pH-independent region (pH 5-10), after which the rate of the reaction decreased with increasing pH. To identify the reactive species of CAT and DEA, all the ionic forms of CAT and the amine that can exist in solution must be considered, and then the rate equations accounting for all the ionized and un-ionized species in the reactions must be constructed.

Table IV—pH-independent k'_{true} Values for Reaction between TSA and N-Chioramines

N-Chloramine	K'rue, M ⁻¹ s ⁻¹
N-Chioro-DMA	0.22
N-Chloro-DEA	0.15
N-Chloro-DIP	0.97
N-Chloro-PIP	0.05
N-Chloro-DMP	0.27
N-Chioro-TMP	1.81

The overall rate of disappearance of CAT at any given pH and amine concentration may be written as follows:

$$-d[CAT]/dt = k_{sec}[CAT]_{T}[amine]_{T}$$
(4)

In eq 4, k_{sec} is the pH-dependent, second-order rate constant describing the overall reaction between all CAT species and all amine species, and the subscript T indicates total concentration (i.e., ionized species + un-ionized species).

In the pH range 5–12, both the amine and CAT can exist in both their ionized and un-ionized forms, and the fraction of each species is related to its total concentration by the following relationships:

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$$[R_1R_2NH]_f = K_a 1/([H^+] + K_a 1) \cdot [amine]_T \quad (5)$$

$$[R_1 R_2 N H_2]_f = [H^+]/([H^+] + K_a 1) \cdot [amine]_T \quad (6)$$

$$[\mathbf{TsSO}_2\mathbf{NC}]_{\mathbf{f}} = K_{\mathbf{a}} / ([\mathbf{H}^+] + K_{\mathbf{a}}) \cdot [\mathbf{CAT}]_{\mathbf{T}}$$
(7)

$$[T_{s}SO_{2}NHCl]_{f} = [H^{+}]/([H^{+}] + K_{a}) \cdot [CAT]_{T}$$
(8)

In eqs 5–8, K_a and K_a1 are the ionization constants for CAT and the amine, respectively; TsSO₂NCl and TsSO₂NHCl are ionized and un-ionized CAT, respectively; and the subscript f indicates the fraction of each species.

Thus, the following rate laws are required to describe the reactions between all CAT species and all amine species:

$$-d[CAT]/dt = k_1[TsSO_2NCl]_f[R_1R_2NH]_f \qquad (9a)$$

$$-d[CAT]/dt = k_2[T_8SO_2NCI]_f[R_1R_2NH_2]_f \quad (9b)$$

$$-d[CAT]/dt = k_3[TsSO_2NHCl]_f[R_1R_2NH]_f \quad (9c)$$

$$-d[CAT]/dt = k_4[T_8SO_2NHCl]_t[R_1R_2NH_2]_f \quad (9d)$$

1

In eqs 9a-9d, k_1 , k_2 , k_3 , and k_4 are the pH-independent, second-order rate constants for the reactions between all the ionized and un-ionized species of CAT and amine.

Substituting eqs 5-8 into eqs 9a-9d and equating to eq 4 give the following:

$$k_{\rm obs} = k_1 \cdot K_{\rm a} / ([{\rm H}^+] + K_{\rm a}) \cdot K_{\rm a} 1 / ([{\rm H}^+] + K_{\rm a} 1)$$
 (10)

$$k_{\rm obs} = k_2 \cdot K_{\rm a} / ([{\rm H}^+] + K_{\rm a}) \cdot [{\rm H}^+] / ([{\rm H}^+] + K_{\rm a})$$
(11)

$$k_{obs} = k_3 \cdot [H^+]/([H^+] + K_a) \cdot K_a 1/([H^+] + K_a 1)$$
 (12)

$$k_{obs} = k_4 \cdot [H^+]/([H^+] + K_a) \cdot [H^+]/([H^+] + K_a 1) \quad (13)$$

For the reaction between CAT and DEA, the pHindependent, second-order rate constants k_1 , k_2 , k_3 , and k_4 were calculated at different pHs. Equations 11 and 12 give the best fit to the pH-rate profile, a fact suggesting that the chlorination reaction occurs either by reaction of the ionized species of CAT with the ionized species of the amine or by reaction of the un-ionized species of CAT with the un-ionized species of the amine. The values of k_2 and k_3 , calculated for the reaction between CAT and DEA by using eqs 11 and 12 were 1.7 and $5 \times 10^{6} \text{ M}^{-1} \text{s}^{-1}$, respectively. As the preceding discussion indicates, two kinetically

equivalent mechanisms can explain the chlorine exchange kinetics: (1) the ionic mechanism, in which a positively charged amine molecule reacts with a negatively charged CAT molecule, and (2) the nonionic mechanism, in which an uncharged amine molecule reacts with an uncharged CAT molecule. Because the two mechanisms differ so greatly with respect to the electrical charges on the reactive species, they may be differentiated by studying the primary salt effect.

The rate equation for the chlorination reaction for the ionic and nonionic mechanisms can be written as shown in eqs 14 and 15, respectively:

$$-d[CAT]/dt = k_1[R_1R_2\vec{N}H_2][TsSO_2\vec{N}Cl] \cdot f_{R_1R_2}\vec{N}H_2 \cdot f_{TsSO_2}\vec{N}cl/f_x$$
(14)

$$-d[CAT]/dt = k_1[R_1R_2NH][T_sSO_2NHCl] \cdot f_{R_1R_2NH_2} \cdot f_{T_sSO_2NH}Cl/f_x$$
(15)

The terms $f_{R_1R_2NH_2}$, $f_{T_8SO_2NC1}$, $f_{R_1R_2NH}$, and $f_{T_8SO_2NHC1}$ represent the activity coefficients of the various species, and f_x represents the activity coefficient for the activated complex.

The expressions for the dissociation constants of CAT (K_a) and the secondary amine (K_b) may be written as follows:

$$K_{a} = [H^{+}][T_{s}SO_{2}NCl]/[T_{s}SO_{2}NHCl] \cdot f_{H^{+}} \cdot f_{T_{s}SO_{2}NCl}/f_{T_{s}SO_{2}NHCl}$$
(16)

$$K_{\rm b} = [\mathbf{R}_1 \mathbf{R}_2 \dot{\mathbf{N}} \mathbf{H}_2] [\bar{\mathbf{O}} \mathbf{H}] / [\mathbf{R}_1 \mathbf{R}_2 \mathbf{N} \mathbf{H}] \cdot f_{\bar{\mathbf{O}}_1} \cdot f_{\mathbf{R}_1 \mathbf{R}_2} \dot{\mathbf{M}}_{\mathbf{H}_2} / f_{\mathbf{R}_1 \mathbf{R}_2 \mathbf{N} \mathbf{H}}$$
(17)

If eqs 16 and 17 are substituted into eq 15, the following rate equation results:

$$-d[CAT]/dt = k'_1 K_w/K_a K_b \cdot [R_1 R_2 NH_2][TsSO_2 NCl] \cdot f_{R_1 R_2} NH_2 \cdot f_{TsSO_2 NCl}/f_x$$
(18)

In eq 18, K_w is the activity product of water.

By using eqs 14 and 18, it can be shown that:

$$\boldsymbol{k}_1 = \boldsymbol{k}_1' \boldsymbol{K}_{\mathbf{w}} / \boldsymbol{K}_{\mathbf{a}} \boldsymbol{K}_{\mathbf{b}} \tag{19}$$

Therefore, changes in ionic strength will have the same influence whichever mechanism is operating, and the effect of ionic strength cannot be used to determine the nature of the reacting species.

However, when the rate constants for the two mechanisms calculated from eqs 11 and 12 are compared with the rate constants for similar reactions (such as chlorination of amines by N-chlorosuccinimide, N-chloro-N-methylbenzenesulfonamide, or hypochlorous acid; Table V), the molecular (nonionic) mechanism (eq 12) is favored for reactions between CAT and secondary amines, because the rate constants (k_{obs}) are of the same order of magnitude as the rate constants calculated for the other reported chlorination reactions. The fact that the

Table V-Rate Constants for Reactions between DMA and Chlorinating Agents

Chlorinating Agent	ksec, M ⁻¹ s ⁻¹	k _{true} , M ⁻¹ s ⁻¹	Reference
HOCI	830	5.3 × 10 ⁸	13
		2.28 × 10 ⁵⁶	
N-Chlorosuccinimide	25.1	1.53 × 10 ⁷	10
N-Chloroquinuclidine	22	1.15 × 10 ⁷	11, 12
N-Chloro-N-methylbenze- nesulfonamide	0.72	3.7 × 10 ⁵	11, 12

^a Value based on a nonionic mechanism. ^b Value based on an ionic mechanism.

$$R_1NH \rightarrow Hoci + H_2O \longrightarrow R_N R_N R_N R_NCI + 2H_2O$$

 $H Ci$
 $H O H^{O} H$



ionic mechanism requires a higher energy level for the reactants than does the molecular mechanism¹³ further supports the molecular or nonionic mechanism. Consistent with the proposed mechanism, the rank order of the reverse reaction in relation to α -substitution shows that the more sterically hindered amine has the higher k_{true} value (Table IV).

The reaction between CAT and secondary amines is chemically very similar to the reaction between hypochlorous acid and amines13; the latter reaction proceeds through an energetically stable, six-membered transition state (Scheme III). A similar mechanism could be proposed for the reaction between CAT and secondary amines, whereby CAT combines with the amine, and a water molecule in a six-membered transition state assists chlorine displacement from the strong nitrogen-chlorine bond. In our studies, a deuterium isotope effect of 1.6 was observed, indicating involvement of a water molecule in the transition state.

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