Table V. Reaction of Chlorite with Aldehydes at 26.95°, Ionic Strength 0.20

Aldehyde	Aldehyde concn, M	Chlorite concn, M	pH	k_2, l./mole min
Formaldehyde	1.239×10^{-4}	0.0333	6.60	3.47
	1.239×10^{-4}	0.0333	6.60	3.25
Acetaldehyde	6.66×10^{-5}	0.1000	6.60	0.396

to the induction period gave straight-line plots when submitted to the pseudo-first-order treatment (chlorite was employed in excess). The results are summarized in Table V.

Estimation of Activation Energy for Chlorine Dioxide Reaction with *p*-Nitrobenzyl-N,N-dimethylamine. The reaction of this amine was studied at 26.95 ± 0.2°, at 14.3 ± 0.2°, and at 40.7 ± 0.2°. Although the Arrhenius plot showed some scatter, the Arrhenius activation energy, E_a, was estimated at 12.9 ± 2 kcal/mole, and $\Delta F^{\ddagger}$ was estimated to be 13.3 ± 2 kcal/mole.

Oxidations of Amines. III. Duality of Mechanism in the Reaction of Amines with Chlorine Dioxide[1]

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Abstract: Chlorine dioxide reacts with aliphatic amines to give the products of oxidative dealkylation. Reaction of chlorine dioxide with triethylamine, trimethylamine, and diisopropylamine is retarded by addition of chlorite ion. Analyses of these data substantiate a single mechanism in which formation of an aminium cation radical is rate controlling. Reactions of chlorine dioxide with dibenzylamine, benzyl-*t*-butylamine, and benzylamine are also retarded by addition of chlorite, but analyses of the data isolate an additional reaction component unaffected by addition of chlorite ion. A similar, but extremely minor, reaction component is isolated in the reaction with trimethylamine-d_9. Deuterium isotope effects were studied with trimethylamine-d_9, α,α-d_2-benzyl-*t*-butylamine, and α,α-d_2-benzylamine. The isotope effects substantiate the belief that the retarded reaction is that involving formation of the aminium radical by electron abstraction, whereas the unretarded component represents α-hydrogen atom abstraction.

Previous studies[1] have elucidated the order, products, stoichiometry, and electronic influences for the reaction of chlorine dioxide with some amines. It was strongly suggested that the principal rate-controlling step in the reaction of tertiary amines was an electron-abstraction process rather than a hydrogen-abstraction process.

Further evidence supporting the previously proposed mechanism for tertiary amines has now been obtained. In this report is presented the discovery that kinetics of amine oxidations by chlorine dioxide are influenced by added chlorite ion, and that analysis of the data for several amines provides evidence for two simultaneous mechanisms, either of which may predominate in a given circumstance, depending upon the structure of the amine.

In the mechanism proposed for reaction of chlorine dioxide with amines, at least two steps were considered necessary. This followed from observations of second-order over-all kinetics (first order with respect to each reactant) and a stoichiometric requirement of 2 moles of chlorine dioxide per mole of amine. Reversibility of the first step was not proposed, but this possibility was recognized by analogy of eq 1 with the thoroughly studied SN1 mechanism (in which reversibility is sometimes detected by addition of a common ion).[2] Electronic effects[1b] and product ratios[1b] were in agreement with this proposed dominant mechanism (eq 1), in

$$ClO_2 + RCH_2N<\begin{matrix}R'\\R'\end{matrix} \underset{k_{-1}}{\overset{\text{slow}}{\rightleftharpoons}} ClO_2^- + \underset{A}{RCH_2\overset{+}{N}}<\begin{matrix}R'\\R'\end{matrix} \quad (1)$$

$$A \xrightarrow[k_2]{\text{fast}} H^+ + RCH{\cdots}N<\begin{matrix}R'\\R'\end{matrix}$$

$$B + ClO_2 \xrightarrow[k_3]{\text{fast}} RCH=\overset{+}{N}<\begin{matrix}R'\\R'\end{matrix} + ClO_2^-$$

which the rate-determining step was a reversible one-electron transfer from amine to chlorine dioxide.

An alternative (irreversible) mechanism which would fit the previously observed kinetics (eq 2) was less

$$ClO_2 + RCH_2N<\begin{matrix}R'\\R'\end{matrix} \underset{\text{slow}}{\xrightarrow{k_1'}} RCH{\cdots}N<\begin{matrix}R'\\R'\end{matrix} + HClO_2 \quad (2)$$

$$HClO_2 \rightleftharpoons H^+ + ClO_2^-$$

$$B + ClO_2 \xrightarrow[\text{fast}]{k_2'} RCH=\overset{+}{N}<\begin{matrix}R'\\R'\end{matrix} + ClO_2^-$$

satisfactory on the grounds that it was less likely to give the excellent linear free energy correlations observed,[1b] and was less likely to show the nonselectivity observed in the product-determining step.[1b] In addition, we now propose that eq 2 would not allow for easy reversibility of the first step, since the chlorous acid produced would be immediately dissociated (and neutralized) at the pH ranges under study. The great difference between this mechanism and mechanism 1 is

(1) Papers I and II of this series: (a) D. H. Rosenblatt, A. J. Hayes, B. L. Harrison, R. A. Streaty, and K. A. Moore, *J. Org. Chem.*, **28**, 2790 (1963); (b) D. H. Rosenblatt, L. A. Hull, D. C. De Luca, G. T. Davis, R. C. Weglein, and H. K. R. Williams, *J. Am. Chem. Soc.*, **89**, 1158 (1967).

(2) L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold, and N. A. Taher, *J. Chem. Soc.*, 979 (1940).

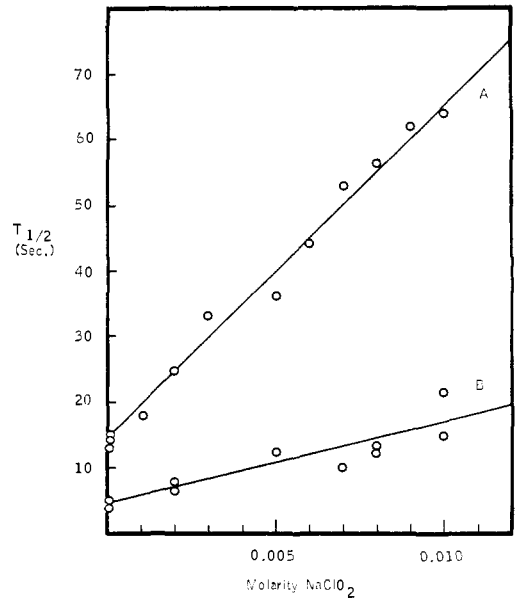

Figure 1. Chlorite retardation of chlorine dioxide oxidation of triethylamine (0.003 *M*) at 25°, 0.20 μ in 0.033 *M* phosphate buffer: A, at pH 6.60; B, at pH 7.10.

that the rate-controlling step of (2) is the abstraction of hydrogen.

These considerations prompted a test for distinguishing mechanisms related to (1) from those related to (2) by addition of chlorite ion. It was anticipated that mechanism 1 might be retarded by addition of chlorite ion whereas mechanism 2 should be insensitive to chlorite addition.

Furthermore, reaction path 1 would be expected to show only small (secondary) kinetic isotope effects in reaction with suitable α-deuterated amines. In contrast, path 2, for the same reactions, should provide large (primary) kinetic isotope effects, for in this route, α-carbon–deuterium bonds would be broken in the rate-determining step. These hypotheses suggested an additional test of mechanism, namely the study of deuterium isotope effects.

Trimethylamine and triethylamine were selected for study as examples of tertiary amines, owing to the commercial availability of the perdeuterated analog of the former, and because of the relative simplicity of the latter structure. (The oxidation product of the latter, *i.e.*, acetaldehyde, is also less subject to reaction with chlorite to produce chlorine dioxide than the reaction of the former.[1b])

Benzyl-*t*-butylamine was selected for study because the *t*-butyl group does not contain α hydrogens; this permitted the easy synthesis of the analogous secondary amine with only two α-deuterium atoms per molecule. Dibenzylamine was chosen to complement the studies of benzyl-*t*-butylamine. (The deuterated analog would not be as readily accessible, requiring two separate deuteration steps in the synthesis of the amine.) Diisopropylamine was selected as an example of a secondary amine not having an activated benzylic position, and as an amine which yields products (acetone and isopropylamine) not interfering with the normal course of the reaction by the regeneration of chlorine dioxide[1] under any conditions of pH and concentration.

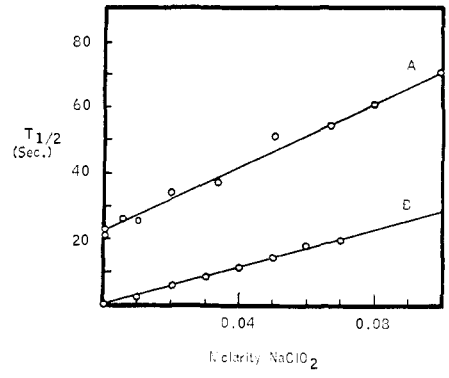

Figure 2. Chlorite retardation of chlorine dioxide oxidation at 25°, 0.200 μ, of: A, diisopropylamine (0.010 *M*), pH 8.93 in 0.01 *M* borate buffer; B, trimethylamine (0.009943 *M*), pH 7.20 in 0.04064 *M* phosphate buffer.

Results

Addition of chlorite ion to reaction media (at constant pH and constant amine concentration) of triethylamine and chlorine dioxide resulted in a pronounced decrease[3] in the observed pseudo-first-order rate constant (increase in reaction half-life). The reaction continued to follow first-order kinetics. Similar effects were observed for trimethylamine and diisopropylamine. The plots of the reaction half-lives (Figures 1 and 2) *vs.* concentration of added sodium chlorite were linear. The steady-state approximation for eq 1 gives the result

$$k_0/[R_3N] = k_1k_2/(k_{-1}[ClO_2^-] + k_2) \quad (3)$$

$$t_{1/2}[R_3N]/0.693 = (k_{-1}/k_1k_2)[ClO_2^-] + 1/k_1 \quad (4)$$

where k_0 = observed first-order rate constant, $t_{1/2}$ = reaction half-life, and $[R_3N]$ = amine free base concentration. Results of dissection of the data according to eq 4 are given in Table I.

Similar experiments with benzyl-*t*-butylamine and dibenzylamine gave the results shown in Figure 3 when the data were treated according to mechanism 1 and eq 4. The asymptotic approach to a limiting value suggested the presence of a second component such as eq 2 which is *unaffected* by chlorite addition. When the mathematical expression included both mechanisms, the steady-state approximation allowed derivation of a new equation for analysis of the data. Derivation of this equation is presented since its development may not be obvious.

The pseudo-first-order rate-constant dependency for simultaneous operation of the two mechanisms on the presence of added chlorite is, by use of the steady-state treatment (eq 5) for mechanism 1 and previously employed symbols

$$k_0/[R_3N] = \{k_1k_2/(k_{-1}[ClO_2^-] + k_2)\} + k_1' \quad (5)$$

where k_1' has the same significance as depicted in eq 2. (The steady-state treatment is not used for mechanism 2, all steps being assumed irreversible.) We define k_0^0 to be the observed rate constant in the absence of added chlorite ion, with the following relationship (and assuming no significant reversibility of mech-

(3) This effect was specific for chlorite ion, as similar concentrations of chloride ion did not retard the rate.

Table I. Constants for Reaction of Amines with Chlorine Dioxide[a]

Amine	pK_a	k_1,[b] M^{-1} sec^{-1}	k_1',[b] M^{-1} sec^{-1}	k_2/k_{-1},[b] M^{-1}	% H abst	pH	Temp, °C	Amine molarity	Corr coeff[c]
Triethylamine	10.78	1.99×10^5	...	0.00283	0	6.60	26.5 ± 0.2	0.0030	...
		2.16×10^5	...	0.0035	0	7.14	26.5 ± 0.2	0.0030	...
Diisopropylamine	11.01	3.61×10^2	...	0.0474	0	8.93	25.0 ± 0.2	0.0100	...
Benzyl-*t*-butylamine	10.19	$2.27 \pm 0.30 \times 10^2$	68 ± 4	0.0057 ± 0.0006	25.4	8.40	25.0 ± 0.2	0.0050	0.958
		2.54×10^2	50 ± 4	0.00782 ± 0.0006	16.4	7.07	25.0 ± 0.2	0.0050	0.992
	9.79	4.47×10^2	197.6 ± 30	0.011 ± 0.0014	30.7	7.07	40.7 ± 0.2	0.0050	0.936
Dibenzylamine	8.43	5.30×10	29.7 ± 0.6	0.0259 ± 0.0015	35.1	7.08	40.7 ± 0.2	0.0050	0.990
Trimethylamine	9.92	1.00×10^5	...	0.00125 ± 0.0013	...	7.20	25.2 ± 0.2	0.00943	0.994
Piperidine[d]	11.20[e]	2.43×10^3	...	0.00888	...	8.95	25.0 ± 0.2	0.002394	...
Benzylamine	9.60	1.12×10^{-2}	3.00×10^{-2}	...	72.8	8.96	25.0 ± 0.2	0.00833	...

[a] Ionic strength 0.20; aqueous solution. [b] Reported deviations are standard deviations. Others are estimated to be ±10%. [c] Linear regression values reported at 99.9% confidence level. See text for equations applied to date. [d] Determined by only three points. [e] G. Bredig, *Z. Physik. Chem.*, **13**, 289 (1894).

anism 1 in the *absence* of added chlorite ion)

$$k_0^0/[R_3N] = k_1 + k_1' \quad (6)$$

Equation 6 can be used to eliminate k_1 from (5) by substitution, giving on simplification

$$k_0/[R_3N] = [(k_0^0k_2/[R_3N]) + k_1'k_{-1}[ClO_2^-])/(k_{-1}[ClO_2^-] + k_2) \quad (7)$$

Multiplication by the right-hand denominator followed by rearrangement, factoring, division by $[ClO_2^-]/k_{-1}$, and final rearrangement gives the expression

$$k_0/[R_3N] = ((k_0^0 - k_0)/[R_3N][ClO_2^-])(k_2/k_{-1}) + k_1' \quad (8)$$

According to this equation, the experimentally accessible values, $k_0/[R_3N]$ and $(k_0^0 - k_0)/[R_3N][ClO_2^-]$,

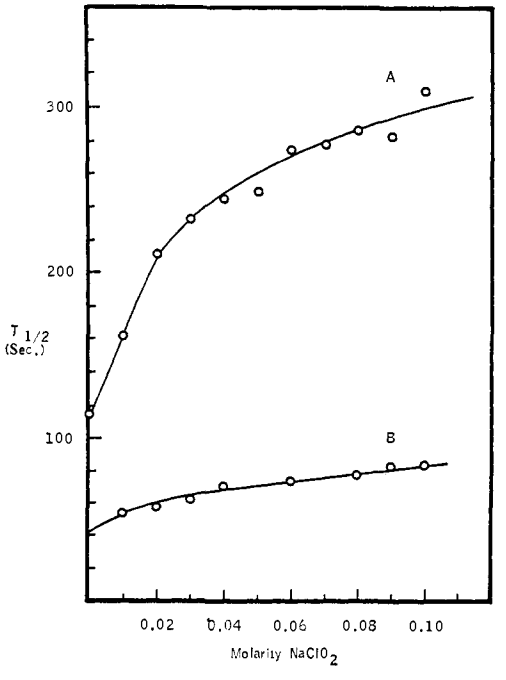

Figure 3. Chlorite retardation of chlorine dioxide oxidation at 40.7°, 0.200 μ, pH 7.1, 0.032 M phosphate buffer: A, benzyl-*t*-butylamine; B, dibenzylamine.

when plotted as the ordinate and abscissa, respectively, would fall on a straight line of slope k_2/k_{-1} and intercept k_1'. Thus, eq 8 and 6 allow the separation of the data into the components of electron abstraction and hydrogen abstraction. In Figure 4 is presented the linearization of data for benzyl-*t*-butylamine and for dibenzylamine according to the *dual mechanism* model given by eq 8. Results for dissection of these data using this model are shown in Table I.

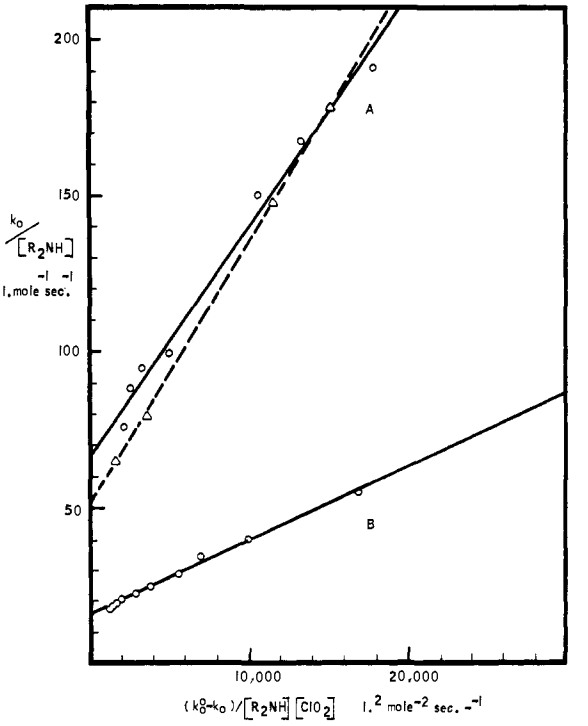

Figure 4. Chlorite retardation of chlorine dioxide oxidation at 25°, 0.200 μ: A, benzyl-*t*-butylamine, pH 8.4 in 0.01 M borate buffer, pH 7.1 in 0.033 M phosphate buffer; B, α,α-d_2-benzyl-*t*-butylamine, pH 8.4 in 0.01 M borate buffer.

Benzylamine, the only primary amine investigated, was studied as a consequence of the results obtained for benzyl-*t*-butylamine and dibenzylamine, it being postulated that this amine would react preponderantly by mechanism 2 in contrast to the secondary and tertiary amines. When the data were treated according to eq 4, the results plotted in Figure 5 were obtained, showing that a component such as reaction 2 dominated the reaction for this amine. Hence, the anticipated result (Table I) was obtained, *i.e.*, 73% reaction by the hydrogen-abstraction path.

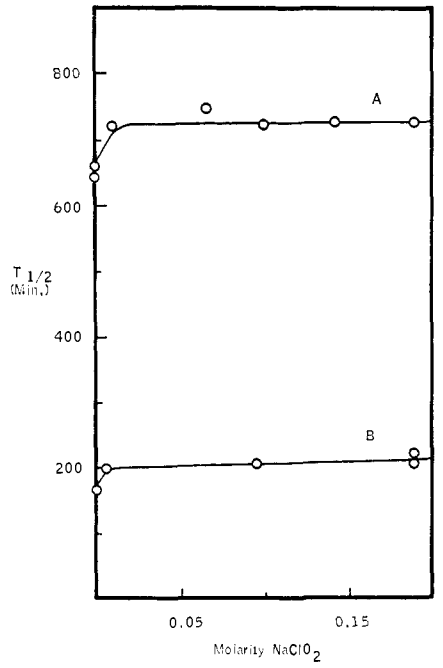

Figure 5. Chlorite retardation of chlorine dioxide oxidation at 25°, 0.2083 μ, pH 8.96, 0.01 M borate buffer: A, 0.00833 M α,α-d_2-benzylamine; B, 0.00833 M benzylamine.

Alternative nonkinetic explanations can be advanced for the retardation of these reaction kinetics by addition of chlorite ion. Of particular concern to us was the possibility that chlorine dioxide might be tied up by chlorite ion as a new, relatively inactive species, perhaps $Cl_2O_4^-$. This species can be postulated as the intermediate in the known and rapid electron interchange between chlorine dioxide and chlorite ion.[4] For the equilibrium eq 9, it can be shown that, with a

$$K = [Cl_2O_4^-]/[ClO_2][ClO_2^-] \quad (9)$$

high ratio of chlorite to chlorine dioxide, as in our experimental conditions, the dependency of the pseudo-first-order rate constant on chlorite concentration would be as follows:

$$k_0/[R_3N] = k_1/(K[ClO_2^-] + 1) \quad (10)$$

since $[ClO_2] = [ClO_2]_t/(K[ClO_2^-] + 1)$, where $[ClO_2]$ = free chlorine dioxide, and $[ClO_2]_t$ = concentration of chlorine dioxide before complexation. Clearly eq 10 is mathematically equivalent to eq 3, insofar as it predicts the same retardation by chlorite ion. No evidence for strong complexation could be found (see Experimental Section). Thus, the vapor pressure of chlorine dioxide in aqueous solution at 25° is sufficient to allow examination of the vapor–solution equilibrium. This vapor–solution equilibrium was not detectably altered by addition of a large excess of chlorite. With the reasonable assumption that the complex $Cl_2O_4^-$ would not have an appreciable vapor pressure, we concluded that any quantities of complex formed in this equilibrium were too small to account for the large kinetic effects observed in these studies.[5]

(4) H. Dodgen and H. Taube, *J. Am. Chem. Soc.*, 71, 2501 (1949).

(5) The complex, $Cl_2O_4^-$, has actually been spectrophotometrically observed by G. Gordon and co-workers at the University of Maryland (private communication), but its formation constant, *ca.* 4, is too small to account for our kinetic observations.

A second, if remote, possible explanation of the retardation would be formation of a complex between amine and chlorite ion, diminishing the availability of free amine for reaction. In this case, two simultaneous equilibria would determine the concentration of free amine.

$$K_a = [R_3N'][H^+]/[R_3NH^+] \quad (11)$$

$$K = [R_3N \cdot ClO_2^-]/[R_3N'][ClO_2^-] \quad (12)$$

where $[R_3N']$ would be the free amine concentration determined by these equilibria. When chlorite is present in large excess over amine, such that initial added chlorite concentration is substantially unaffected by complex formation, an expression mathematically equivalent to (3) can be obtained. (If this assumption is not made, a mathematically equivalent formula is not obtained, but a much more complex result is achieved.) Let the total amine be

$$[R_3N] = [R_3N'] + [R_3NH^+] + [R_3N \cdot ClO_2^-] \quad (13)$$

Solving (11) for $[R_3NH^+]$, substitution in (13), and rearranging give

$$[R_3N \cdot ClO_2^-] = [R_3N]_{total} - [R_3N']\{1 + ([H^+]/K_a)\} \quad (14)$$

Using this result in (12)

$$[R_3N'] = [R_3N]_{total}/\{K[ClO_2^-] + (1 + [H^+]/K_a)\} \quad (15)$$

$$k_0 = k_1[R_3N]_{total}/\{K[ClO_2^-] + (1 + [H^+]/K_a)\} \quad (16)$$

If this expresion is divided by $[R_3N]_{total}/([H^+] + K_a) = [R_3N]$ to obtain a rate constant, as we have done in eq 3, there is obtained

$$k_0/[R_3N] = k_1([H^+] + K_a)/\{K[ClO_2^-] + ([H^+] + K_a)/K_a\} \quad (17)$$

This expression, *at constant pH*, is mathematically equivalent to (3) and would afford a linear plot when rearranged as (4). (However, it should be noted that the constants obtained by dissection as in expression 3 would be pH dependent.) This second alternative was eliminated from further consideration by two experiments designed to detect the phenomenon of amine complexation by chlorite. Thus, the potentiometric titration curve for triethylamine was the same in sodium chloride electrolyte as in sodium chlorite electrolyte. Also, the partition coefficient of triethylamine between buffered water and cyclohexane was changed very little by addition of excess sodium chlorite. Hence, the extent of any complexation of amine by chlorite ion must be very small, if it exists at all.

The data in Table I allowed calculation of the activation parameters for both electron abstraction and hydrogen abstraction in the case of benzyl-*t*-butylamine. For hydrogen abstraction, $\Delta H^{\pm} = 13.7$ kcal/mole, as compared with $\Delta H^{\pm} = 6.8$ kcal/mole for electron abstraction. For hydrogen abstraction $\Delta S^{\pm} = -4$ eu as compared with $\Delta S^{\pm} = -25$ eu for electron abstraction.

The postulated mechanisms were further tested using deuterium-labeled amines for the determination of kinetic isotope effects. Specifically labeled trimethylamine-d_9, α,α-d_2-benzyl-*t*-butylamine, and α,α-d_2-benzylamine were employed. Data for trimethylamine-d_9

Table II. Deuterium Isotope Effects for Reaction of Amines with Chlorine Dioxide[a]

Amine	pK_a	pH	k_1, M^{-1} sec^{-1}	k_1', M^{-1} sec^{-1}	k_2/k_1, M^{-1}	Temp, °C	% H abst	$(k_1)_H/(k_1)_D$	$(k_1')_H/(k_1')_D$	$(k_2/k_{-1})_H/(k_2/k_{-1})_D$
α,α-d_2-Benzylamine	9.68	8.96	...	1.07×10^{-2}	...	25.0	...	...	3.0	...
α,α-d_2-Benzyl-*t*-butylamine	10.18	8.44	122.6	15.1 ± 1.5	$2.40 \times 10^{-3} \pm 0.00$	25.0	10.9	1.8	4.97	2.5
Trimethylamine-d_9	10.155	7.22	7.50×10^4	100 ± 7	$2.3 \times 10^{-9} \pm 0.0$	25.2	0.13	1.3	...	5.43

[a] Deviations reported are standard deviations from linear regression. All other values are estimated to be precise within ±10%.

showed a very minor hydrogen-abstraction component (less than 1%), and was treated according to eq 8 to give the results of Figure 6 and Table II. The secondary deuterium isotope effect on the electron-abstraction portion was 1.3. The deuterium isotope effect for α-hydrogen abstraction was not obtained, as the undeuterated amine did not yield a hydrogen-abstraction component in the experimentally accessible range. (Calculation shows that with a hydrogen-abstraction component five times as large as the deuterium-abstraction component, only slight curvature would be observed, if at all, with the undeuterated amine in the experimentally studied range.) Data for the trimethylamines were obtained using a modified stopped-flow rapid-injection system as described by Thompson and Gordon.[6] This technique was necessary at the pH range selected for experimentation. The particular pH range was chosen to avoid competition by the chlorite–formaldehyde reaction.[1b]

Analysis of the data for deuterium-labeled benzyl-*t*-butylamine according to eq 8 gave the results of Figure 4 and Table II. An isotope effect $(k_1)_H/(k_1)_D$ of 1.8 was obtained for electron abstraction, and an isotope effect $(k_1')_H/(k_1')_D$ of 4.97 was obtained for hydrogen abstraction. It was not possible to ascertain the isotope effect for electron abstraction with α,α-d_2-benzylamine, inasmuch as the electron-abstraction reaction component was too small with this amine. Furthermore, kinetic results were obtained only with difficulty (see Experimental Section), since this amine reacted only very slowly with chlorine dioxide. (The competing base-catalyzed decomposition of chlorine dioxide was appreciable compared with the consumption of chlorine dioxide by amine oxidation.) A semiquantitative estimation of the isotope effect for mechanism 2 (hydrogen abstraction) was possible, however, the value being $(k_1')_H/(k_1')_D = 3.0$.

Magnitudes of the isotope effect on the ratio $k_2/k_{-1} = R$ were $(R_H/R_D) = 5.43$ for trimethylamine and 2.5 for benzyl-*t*-butylamine (Table II).

Chlorine dioxide directly oxidized N,N,N′,N′-tetramethyl-*p*-phenylenediamine to the deep blue cation radical with an observable electron paramagnetic resonance spectrum distinct from chlorine dioxide. Likwise, chlorine dioxide oxidized tris(*p*-N,N-dimethylaminotriphenyl)amine to a deep green free radical,[7] also detected by its electron spin resonance signal.[8]

(6) R. Thompson and G. Gordon, *J. Sci. Instr.*, **41**, 480 (1964).
(7) O. Neunhoeffer and P. Heitmann, *Chem. Ber.*, **92**, 245 (1959).
(8) (a) A future communication (W. Giordano, *et al.*, these laboratories) will describe detection of the diazabicyclooctane amine cation radical as generated by the action of chlorine dioxide on diazabicyclooctane. (This radical was reported by T. M. McKinney and D. H. Geske, *J. Am. Chem. Soc.*, **87**, 3013 (1965).) (b) Electron paramagnetic resonance studies on tris-*p*-N,N-dimethylaminotriphenylamine cation radicals were performed by W. Giordano of these laboratories, and will be the subject of a future communication.
(9) (a) R. I. Walter, *J. Am. Chem. Soc.*, 77, 5999 (1955); (b) K. Kuwata and D. H. Geske, *ibid.*, **86**, 2101 (1964); (c) A. J. Tench, *J. Chem. Phys.*, **38**, 593 (1963); (d) T. Cole, *ibid.*, **35**, 1169 (1961); (e) O. Neunhoeffer and P. Heitmann, *Chem. Ber.*, **96**, 1027 (1963).

Discussion

It is useful to consider the uniqueness of the separate mechanistic steps postulated, especially those which we have proposed in (1). Reversibility of the first step, which is the likeliest explanation for the chlorite retardation phenomenon, is strong evidence for the intermediate cation radical. The existence of analogous radicals has been amply demonstrated.[7,8a,9]

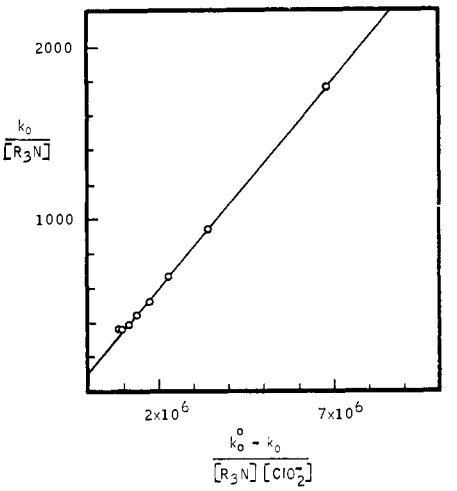

Figure 6. Chlorite retardation of chlorine dioxide oxidation of trimethylamine-d_9 (0.009943 *M*) at 25°, 0.20 μ, pH 7.22, 0.04064 *M* phosphate buffer.

In addition, the direct demonstration of production of some of these radicals by chlorine dioxide lends further credence for the first step of mechanism 1.

The second step following the rate-determining step depicts loss of a proton. If this step were omitted, the mechanism might be formulated as

$$ClO_2 + RCH_2N<_{R'}^{R'} \underset{k_{-1}}{\overset{\text{slow } k_1}{\rightleftharpoons}} ClO_2^- + RCH_2\overset{+}{N}<_{A}^{R'} \quad R'$$

$$A + ClO_2 \xrightarrow[k_2]{\text{fast}} HClO_2 + RCH{=}\overset{+}{N}<_{R'}^{R'}$$

$$H^+ + ClO_2^-$$

However, the steady-state treatment yields the following dependency for the kinetic expression

$$-d[ClO_2]/dt = 2k_1k_2[ClO_2]^2[R_3N]/(k_{-1}[ClO_2^-] + k_2[ClO_2])$$

First-order kinetics with respect to chlorine dioxide would only be obtained at insignificant levels of added chlorite. Since deviations from first-order kinetics were not observed (except for minor curvature in some runs with diisopropylamine), mechanism 18 is eliminated. (The possibility of base-catalyzed dependency of the second step is not eliminated by our results. We note, however, that the effect of pH on slope at two pH values for triethylamine and two pH values for benzyl-*t*-butylamine is not large nor are the changes in a uniform direction. Any hydroxide-catalyzed term must, therefore, be small.) In a similar way, we eliminate the possibility for *reversibility* of step 2 in eq 1, for such a postulation would result in kinetics of the type

$$d[ClO_2]/dt = 2k_1k_2k_3[ClO_2]^2[R_3N]/k_{-1}k_{-2}[H^+][ClO_2^-] + k_{-1}k_{-3}[ClO_2][ClO_2^-] + k_2k_3[ClO_2]$$

Clearly, this expression would not yield first-order kinetics with respect to chlorine dioxide, as is demanded by our results.

The intermediate B, with a three-electron π bond, seems reasonable, in view of consideration arguments advanced for relative stability of three-electron and five-electron bonded systems.[10] (Many stable three-electron bonded systems are known. Even benzene has been modeled after a structure containing six equivalent three-electron bonds.)

The final step is required as a consequence of reaction stoichiometry[1a] and the observed products.[1a,b] We therefore believe that mechanism 1, as depicted, has the minimum detail needed to explain the obtained experimental data. All of the results obtained can be unified in the dual mechanism concept based on eq 1 and 2. The good linearity of plots based on (1) alone for triethylamine and trimethylamine shows that the favored mechanism for tertiary amines has electron abstraction as the rate-determining step. Similarly, aliphatic secondary amines such as diisopropylamine, in which there is no phenyl activation of an α hydrogen, react principally by an electron-abstraction process in which the transition state resembles the intermediate aminium cation radical. However, aliphatic secondary amines such as benzyl-*t*-butylamine and dibenzylamine, in which the α-hydrogen atoms are "activated benzylic" hydrogens, react significantly by both the electron-abstraction mechanism and the hydrogen-abstraction mechanism. Thus, benzyl-*t*-butylamine reacts with chlorine dioxide *via* 16–25% α-hydrogen abstraction at 25°. At 41°, benzyl-*t*-butylamine reacts by 31% hydrogen abstraction and 69% electron abstraction. Dibenzylamine reacts *via* 35% α-hydrogen abstraction and 65% electron abstraction at 40.7°. Finally, primary amines, such as benzylamine, containing phenyl-activated, α-hydrogen atoms react principally by α-hydrogen abstraction, benzylamine going 73% by hydrogen abstraction and 27% by electron abstraction at 25°. (A barely detectable amount of hydrogen abstraction was observed in the reaction of trimethylamine-d_9. This component was rendered observable by the powerful isotope effect on the ratio k_2/k_{-1}, Table II.)

The enthalpies of activation for reaction of chlorine dioxide with benzyl-*t*-butylamine ($\Delta H^{\ddagger}$ = 13.7 kcal/mole for hydrogen abstraction as compared with 6.8 kcal/mole for electron abstraction) favor reaction by electron abstraction, but the entropies of activation ($\Delta S^{\ddagger}$ = −4 eu for hydrogen abstraction as compared with −25 eu for electron abstraction) favor reaction by hydrogen abstraction. The favorable enthalpy for electron abstraction may be in part due to the release of energy on solvation of charges created in the transition state. In a similar way, this solvation of the transition state would constrict solvent molecules, causing them to lose degrees of freedom, and this would cause the reaction to be less favorable from the entropy standpoint. The two effects of solvation would act to minimize the change in free energy, thus favoring, somewhat, the formation of ions in the transition state.

These facts can be rationalized by considering some of the detailed structural bases for reactivity in each of the two mechanisms. For reaction *via* electron abstraction, the order tertiary > secondary > primary is followed.[1b] This order is probably dictated for the most part by the ionization potentials of the amines (which follow the inverse order[11]). Competition by α-hydrogen abstraction is ineffective so long as the bond dissociation energy for the α hydrogen is high. When, however, this bond dissociation energy is lowered by about 24 kcal[12] by phenyl activation, hydrogen abstraction occurs at an increased rate, and is sufficiently competitive with electron abstraction to be significant in the reaction of secondary amines containing the benzyl group. When the ionization potential is high, as in primary amines, and the α-hydrogen dissociation energy is lowered by phenyl activation, as in benzylamine, α-hydrogen abstraction predominates as the rate-controlling step. The absolute rate of hydrogen abstraction is probably not structurally independent of the ionization potential of the adjacent nitrogen atom, for the nitrogen electronegativity should affect the stability of the intermediate, B (structurally similar to the transition state for (2)), and its effective electronegativity can be related to its valence state ionization potential.[13] Further, the intermediate for α-hydrogen abstraction may have considerable carbonium ion character[14] which would be stabilized by high electron density on the adjacent nitrogen lone pair. This suggests that the other tertiary > secondary > primary may also be followed by the hydrogen-abstraction mechanism, though the reactivity gradient may be somewhat smaller. This is corroborated by the observation that the α-hydrogen-abstraction rates of benzyl-*t*-

(10) (a) J. W. Linnett, *Am. Scientist*, **52**, 459 (1964); *J. Am. Chem. Soc.*, **83**, 2643 (1961). (b) A referee has requested clarification of the preference of a three-electron π bond over the classical carbon radical representation, >Ċ–N̈<. The chemical fact that attack occurs at the α position in preference to all other similarly accessible positions seems to require that the intermediate produced have added stability over any simple classical representation. Otherwise, there would seem to be no advantage to this chemical selectivity.

(11) A. Streitwieser, Jr., *J. Am. Chem. Soc.*, **82**, 4123 (1960).

(12) T. L. Cottrell, "The Strengths of Chemical Bonds," 2nd ed, Butterworth and Co., Ltd., London, 1958.

(13) *Cf.* G. Klopman, *J. Am. Chem. Soc.*, **86**, 1463 (1964); J. Hinze, M. A. Whitehead, and H. H. Jaffé, *ibid.*, **85**, 148, (1963).

(14) R. D. Gilliam and B. F. Ward, Jr., *ibid.*, **87**, 3944 (1965); A. Streitwieser, Jr., and C. Perrin, *ibid.*, **86**, 4938 (1964); G. A. Russell and R. C. Williamson, Jr., *ibid.*, **86**, 2357 (1964); J. A. Howard and K. U. Ingold, *Can. J. Chem.*, 41, 1744 (1963).

butylamine and dibenzylamine are about 1000 times greater than that of benzylamine and roughly parallel the relative rates of electron abstraction.

The magnitudes of the observed isotope effects substantiate the mechanistic assignments which have been made. It is true that the secondary isotope effects measured for benzyl *t*-butylamine and trimethylamine electron abstractions are high, but these results are not wholly unprecedented.[15] The effects can be closely likened to the β-deuterium isotope effects observed in SN1 reactions in which carbonium ion intermediates are produced. In this type of transition state, it appears that there is a considerable *decrease* in the force constant of the β-carbon–hydrogen bond on going from reactants to transition state. Since the force constants are the same for hydrogen and deuterium, the effect of the mass change is to lower the frequency for the carbon–deuterium bond and thus lower the zero-point energy relative to the carbon–hydrogen bond. The effect would be greater in the reactants (with the larger force constants) and least in the transition state (with the smaller force constants). Hence, a normal isotope effect results (the rate for the hydrogen analog is faster than the rate for the deuterium analog). The explanation described has been used to justify appreciable secondary isotope effects, based on transition states in which the bond reorganization is high (whether it be due to electronic, hyperconjugative, or steric influences[16]). Thus, the isotope effect which we have interpreted as a secondary isotope effect is evidence for extensive bond reorganization in the amine cation radical relative to the amine. This reorganization can be attributed to two causes, (a) the assumption of a planar configuration[9c] by the cation radical with rehybridization, and (b) strong electronic interactions with the α-carbon–hydrogen orbital by the nitrogen atom, resulting from acquisition of a positive charge and a "quasi-open" orbital[17] by the nitrogen atom. (It is also conceivable that the reaction component having the low isotope effect for secondary amines could have a mechanism involving hydrogen abstraction from the nitrogen atom. However, such a reaction should have *a much higher activation energy* than benzylic α-hydrogen abstraction. The bond dissociation energy for N–H (cited for ammonia) is approximately 110 kcal as compared with about 75 kcal for benzylic hydrogen.[12] Therefore hydrogen abstraction from the nitrogen atom should be a generally less favorable mode of attack.)

The primary deuterium isotope effects observed for the α-hydrogen-abstraction components for benzyl-*t*-butylamine are easily reconciled with known magnitudes[18] for primary effects.

The isotope effects for the ratios, $R = k_2/k_{-1}$, were determined for benzyl-*t*-butylamine and trimethylamine, but the interpretations of these effects are less straightforward than interpretations of the other isotope effects. It may be assumed that the origin of the isotope effect on k_2 is the loss of the proton or deuterium ion as depicted in eq 1. It is thus a primary isotope effect. However, the nature of the isotope effect on k_{-1} is more obscure. Presumably, it is a secondary effect if it exists at all. If the cause would be a change in the force constant of the α-carbon–hydrogen (or deuterium) bond, this change would be expected to be more complete in the *intermediate* cation radical than in the transition state. The situation would be as schematically represented in Figure 7, where the zero-point energy changes are indicated. It is apparent from this diagram that a *reverse* isotope effect is expected for k_{-1}. If R_H/R_D now be considered to be simply a measure of $(k_2)_H/(k_2)_D$, any neglected effect of k_{-1} would tend to provide a high apparent measure of $(k_2)_H/(k_2)_D$. That the isotope effect on the reverse reaction should be smaller than the forward secondary isotope effect seems reasonable, since the force constant should undergo a much smaller change in the reverse direction (owing to the similarity of the transition state to the aminium cation intermediate) than in the forward reaction (where the reaction profile is highly endothermic, and bond reorganization is implied to be much greater).[19] Thus, it may be assumed, $(k_{-1})_D/(k_{-1})_H \leqq 1.8$ for benzyl-*t*-butylamine from the results of Table II. From $R_H/R_D = 2.5$ for benzyl-*t*-butylamine, it then appears that $1.4 \leqq (k_2)_H/(k_2)_D \leqq 2.5$. From $R_H/R_D = 5.43$ and the ratio $(k_1)_H/(k_1)_D = 1.3$ for trimethylamine is analogously obtained: $4.2 \leqq (k_2)_H/(k_2)_D \leqq 5.4$. This result implies that the assumption that k_2 involves loss of a proton is probably correct, and that this step is subject to a measurable primary isotope effect.

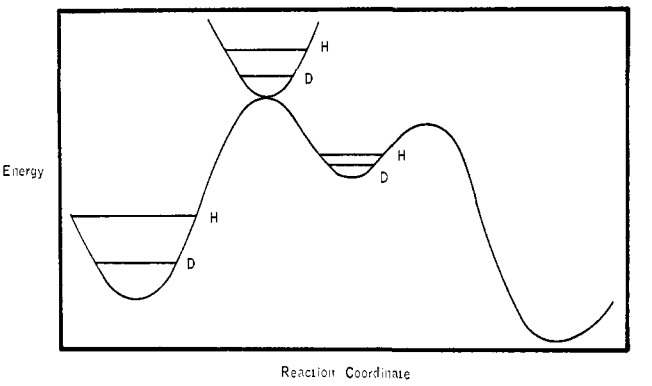

Figure 7. Schematic representation of secondary isotope effects. Zero-point energies are shown.

Experimental Section

Materials. Water triply distilled from basic permanganate[1b] or acid permanganate[20] was used throughout. Chlorine dioxide solutions were prepared, stored, and analyzed as previously described.[13] Trimethylamine-d_9 hydrochloride was obtained from Merck Sharp and Dohme of Canada, Ltd., and contained 99% α-deuterium labeling. (This material contained a trace of water-

(15) *Cf.* V. J. Shiner, Jr., *J. Am. Chem. Soc.*, **76**, 1603, (1954). Values up to about 28% per deuterium are reported; V. J. Shiner and J. G. Jewett, *ibid.*, **86**, 945 (1964), reported one example of 44% for a single deuterium atom in a conformationally regulated system.

(16) S. I. Miller, *J. Phys. Chem.*, **66**, 978 (1962); A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *J. Am. Chem. Soc.*, **80**, 2326 (1958).

(17) Use of this terminology is analogous to the "open sextet" principle, G. W. Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p 258 ff, which is used to describe the high tendency for aromatics to interact with reagents in substitution reactions to produce intermediates.

(18) K. B, Wiberg, *Chem. Rev.*, **55**, 713 (1955).

(19) G. S. Hammond, *J. Am. Chem. Soc.*, 77, 334 (1955).

(20) Acid permanganate distilled water was required for kinetics of benzylamine in order to eliminate interfering substances present in basic permanganate distilled water. Even after elimination of these interferences, the reaction of benzylamine was so slow that the slow disproportionation of chlorine dioxide at pH values employed constituted a major correction which had to be applied to the kinetics. The results for benzylamine and for deuteriobenzylamine are thus subject to greater errors than the results for the other amines.

insoluble impurity estimated at less than 1%.) Other amine hydrochlorides were prepared by the action of gaseous hydrogen chloride on ethereal solutions of amines. They were purified by repeated recrystallization from isopropyl alcohol to give purities greater than 99.8% as measured by vapor phase chromatography of the free bases. Their properties have been reported previously.[1b] Buffers employed were prepared from commercial cacodylic acid, sodium tetraborate, potassium dihydrogen phosphate, and sodium monohydrogen phosphate. Sodium chlorite was Matheson Coleman and Bell analytical grade.

α,α-d_2-Benzyl-*t*-butylamine Hydrochloride. α,α-d_2-Benzyl chloride[21] (3.15 g) and *t*-butylamine (6.00 g) were heated under reflux for 17 hr. After treatment with strong base, extraction with ether, drying over sodium hydroxide pellets, and distillation, 1.98 g of free amine, bp 82.5° (5.5 mm), was obtained. This was converted to 2.30 g of hydrochloride, mp 247–249 dec, raised to 247.5–249° dec by one recrystallization from isopropyl alcohol. The material contained 97% deuterium atoms in the benzylic position, as shown by mass spectra and nmr. The liberated amine was vpc pure.

α,α-d_2-Benzylamine. Weighings and transfers of solvents were made in a drybox. Reduction of 11.20 g of benzonitrile in 100 ml of ether with 5.0 g of lithium aluminum deuteride in 100 ml of ether by the inverse addition method described by Soffer and Katz[22] gave 11.93 g of the crude hydrochloride. Liberation of the free amine, bp 74–78° (20 mm), followed by conversion to the hydrochloride gave, after recrystallization from isopropyl alcohol, 5.04 g of hydrochloride, mp 264.5–265.5°, 99.9% pure by vpc. The material was labeled with 99.5% deuterium atoms in the α position as determined by nmr.

Kinetic Methods. A. "Slow Reactions." Reactions were followed at 400 mμ (this wavelength was employed instead of 357 mμ[1a] because of the interfering absorbance by chlorite ion) on a Cary Model 14 recording spectrophotometer. Stock solutions of reactants were thermostated prior to reaction. Sufficient sodium chloride was contained in the amine hydrochloride stock solution to give a final ionic strength of 0.200. The amine hydrochloride and stock buffer solutions were premixed. A 25-ml aliquot of chlorine dioxide solution was placed in a 10-cm cell with a capacity somewhat greater than 30 ml.

Then 5 ml of the amine–buffer solution was added to give a final chlorine dioxide concentration of about 2.5×10^{-4} *M*, the cell rapidly shaken, and the spectrophotometric tracking of reaction initiated. Readings of $A_\infty - A$ were plotted *vs.* time on semilogarithmic paper. Good straight line plots were obtained in all cases, usually through at least three half-lives, except for diisopropylamine kinetics, which showed slight negative curvature (slowing with time) according to the equation

$$2.303 \log (A_\infty - A) = k_0 t + \text{constant}$$

where A_∞ = absorbancy at infinite time, A = absorbancy at time t, and k_0 = pseudo-first-order constant. Second-order constants were obtained from first-order values by application of the equation

$$k_0 = \{K_a[B]/([H^+] + K_a)\}k_2$$

where [B] is the total amine hydrochloride concentration initially added, and the other symbols have the usual significance.

B. "Fast Reactions." These kinetics were followed (for trimethylamine and trimethylamine-d_9) using the type of apparatus described in ref 4. This is a modified stopped-flow syringe injection system with fast oscillographic read-out. The syringe was precalibrated before use and delivered about 0.3 ml of 0.006 *M* chlorine dioxide into 6.00 ml of solution containing amine with buffer and electrolytes (chlorite and chloride) adjusted to give a final ionic strength of 0.200 and final amine concentration of 0.0099 *M*. The reaction was conducted in a thermostated, 2.00-cm cell. The fastest half-life studied was approximately 0.3 sec. Mixing times were less than 0.1 sec. Transmittancy readings were obtained from photographic records of oscillographic scans, and were converted to absorbancy prior to plotting. Plotting and data treatment were accomplished as described above for "Slow Reactions."

Noncomplexing of Chlorine Dioxide by Chlorite Ion. The concentration of chlorine dioxide was measured in the vapor phase in a 10-cm spectrophotometer cell flushed initially with nitrogen and containing 3 ml of an aqueous chlorine dioxide solution (initially 5×10^{-3} *M* in chlorine dioxide and 0.067 *M* in pH 6.7 phosphate buffer) both when the solution contained 0.33 *M* chlorite and when chlorite was absent. The vapor concentrations of chlorine dioxide reached in 4–6 min (as well as the shapes of the curves showing the rise to these concentrations) were very close in the two cases. Thus, any complex present was not formed in quantities which would explain the kinetic retardations by chlorite ion.

Noninteraction of Triethylamine with Chlorite Ion. Titrations of 0.2 *M* triethylamine hydrochloride with 0.9705 *M* sodium hydroxide in 0.2 *M* sodium chloride and in 0.2 *M* sodium chlorite were carried out. The titration curves were essentially identical and did not suggest the occurrence of complexation. (Note: A small amount of base was added with the amine hydrochloride in each titration before addition of the salt. This prevented generation of chlorine dioxide from the chlorite at the beginning of the titration.)

The distribution of triethylamine (initially 3×10^{-4} *M* in the aqueous phase) between phosphate buffer of pH 11.3 and ionic strength 0.12 and purified cyclohexane (volume ratio 20:1) was carried out in the presence of either 0.08 *M* sodium chloride or 0.08 *M* sodium chlorite. The details of the distribution method and analysis are not described here, as they will be published elsewhere.[23] The pK_a, 10.78 (Table I), was used to correct apparent distribution coefficients to those for the free base; this compensated for minor differences in pH. Ionic strengths in all cases were 0.2. The measured effect of chlorite was to change the distribution coefficient (concentration in organic phase/concentration in aqueous phase) from 24.9 ± 1.3 to 20.9 ± 1.3. This effect is far too small to explain the large kinetic effects of added chlorite ion on the reaction of chlorine dioxide with triethylamine.

Oxidation of Tris-(*p*-dimethylaminotriphenyl)amine by Chlorine Dioxide. Tris(*p*-dimethylaminophenyl)aminium perchlorate was prepared analogously to methods described by Walter.[9a] Quantitative electron spin resonance determinations showed one spin per molecule. The radical had a characteristic green color. Reaction of tris(*p*-dimethylaminophenyl)amine with chlorine dioxide in carbon tetrachloride–acetonitrile mixtures gave the green color and electron spin resonance spectrum of the above synthetic material. This shows the oxidation product to be the cationic aminium free radical.

Oxidation of N,N,N′,N′-Tetramethyl-*p*-phenylenediamine by Chlorine Dioxide. Reaction of an aqueous solution of N,N,N′,N′-tetramethyl-*p*-phenylenediamine with chlorine dioxide at pH 7 (phosphate buffer) gave the deep blue color characteristic of a Wurster's salt. The electron paramagnetic resonance spectrum gave fine structure distinct from the spectrum of chlorine dioxide. The color formation was not reversed at pH 7 by addition of excess chlorite ion.

(21) Prepared by the procedure of J. F. Bunnett, G. T. Davis, and H. Tanida, *J. Am. Chem. Soc.*, 84, 1606 (1962).

(22) L. M. Soffer and M. Katz, *ibid.*, 78, 1705 (1956).

(23) The authors wish to thank M. M. Demek and co-workers for these determinations. Details of the method will be published later.