The Reaction of Chlorine Dioxide with Triethylamine in Aqueous Solution[1]

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Chlorine dioxide oxidizes triethylamine in aqueous solution with the production of diethylamine, acetaldehyde, hydrogen ion, and chlorite ion. The reaction is first order with respect to each reactant. The second-order rate constant, calculated with respect to concentrations of amine free base and chlorine dioxide, is approximately $2 \times 10^5\ M^{-1}$ sec.$^{-1}$ at ambient temperature (24.4–28.5°).

Chlorine dioxide is comparable to chlorine as a germicide for drinking water,[2] and has found extensive use[3] in the oxidative destruction of certain noxious chemical contaminants in water supplies, especially phenols. The desire to understand more fully the reactions of chlorine dioxide with other classes of organic compounds that might occur as water contaminants prompted the present investigation. For this purpose, triethylamine was chosen as a model tertiary amine.

Chlorine dioxide has been characterized[4] as unreactive towards aliphatic amines in aqueous solution, but this observation was made on mixtures of low pH, which, as may be inferred from the present study, would be expected to exhibit very low reaction rates.

The reaction which has been discovered and investigated in the present work, namely oxidation by chlorine dioxide of the α-carbon of an aliphatic tertiary amine followed by cleavage of the carbon–nitrogen bond, is analogous to reactions occurring between several other oxidants and a variety of tertiary amines.[5] Such reactions, in fact, are far more usual than amine oxide formation, which is brought about only by hydrogen peroxide, peroxy acids, and, under appropriate conditions, ozone.[6]

Experimental

Generation of Chlorine Dioxide.—The method of Granstrom and Lee was used to produce chlorine dioxide.[7,8] One hundred milliliters of 4% aqueous potassium persulfate (J. T. Baker, C.P.) and 50 ml. of 16% aqueous sodium chlorite (purified flake, Matheson Coleman and Bell) were poured simultaneously into a 250-ml. tall-form gas washing bottle provided with an inlet tube terminating in a fused-on fritted glass cylinder. Air passed through this solution carried the generated chlorine dioxide through a flake sodium chlorite-filled tube and a safety trap to the point of use. (The use of a sodium chlorite tube in the line is an added precaution, probably not necessary with this method of chlorine dioxide generation, to ensure conversion of any elemental chlorine in the gas stream to chlorine dioxide.) When a pure aqueous solution of chlorine dioxide was to be prepared, the gas stream was passed for about a half-hour through a tube terminating in a fused-on fritted glass cylinder, into a dark 500-ml. bottle about four-fifths full of distilled water, well chilled in an ice bath to minimize the loss of chlorine dioxide to the atmosphere. Protected from bright light and refrigerated, the solutions were relatively stable for as long as a month.

Analysis of Chlorine Dioxide Solution.—Concentrated chlorine dioxide solutions (*i.e.*, above $10^{-3}\ M$) were analyzed according to the method of Ingols and Ridenour,[9] using the reaction $2ClO_2 + 2I^- \rightarrow 2ClO_2^- + I_2$. Inasmuch as the oxidation of iodide by chlorite is acid catalyzed, it was considered desirable to use a buffer at about pH 7. Even so, the end point had a tendency to return slowly, so that the analysis had to be performed rapidly, with well chilled solutions. The following gave reproducible results. A 1–5-ml. aliquot of chlorine dioxide solution was released slowly, with the pipet tip submerged, into a well chilled mixture of 5 ml. of 0.04 N potassium iodide plus 10 ml. of 0.1 M phosphate buffer (pH 7). The mixture was immediately titrated with 0.05 N sodium thiosulfate from a 2-ml. microburet, with the buret tip submerged. When the yellow color of iodine became faint, a few drops of starch solution were added, and titration was continued until the solution just became colorless.

Dilute solutions of chlorine dioxide ($<10^{-3}\ M$) were analyzed spectrophotometrically at 355–360 mμ, with a molar absorbancy index[8] of 1230 being used to calculate the concentration.

Identification of Acetaldehyde.—An air stream containing chlorine dioxide from the generation apparatus was slowly bubbled through 170 ml. of 0.125 M aqueous triethylamine. The pH, initially 12, dropped as the yellow chlorine dioxide was absorbed and decolorized. When the pH had reached 10.7, and until it reached 10.5, the effluent air stream, possessing an acetaldehyde odor, was bubbled through cold water; this water, on testing for aldehyde by the *p*-phenylphenol–sulfuric acid method,[10] exhibited a strong positive reaction not obtained with a triethylamine blank. While the triethylamine reaction mixture was in the pH range 10.5 to 9.5, the effluent air stream was bubbled through a 0.4% dimedone solution buffered to pH 4.7 with 0.2 M acetate; within a few minutes, a precipitate of the dimedone derivative of acetaldehyde formed. The gas bubbling was now discontinued overnight, then resumed (pH 9.2). Upon reaching pH 7.5, the reaction mixture appeared yellow, but slowly faded when introduction of chlorine dioxide stopped. The pH was raised periodically by addition of base while passage of chlorine dioxide continued. A point was soon reached where the pH continued to drop (*e.g.*, from 7 to 5.5) even after termination of the gas stream and disappearance of the yellow color of chlorine dioxide; at this time, along with the pH drop, the reappearance of the yellow color and the presence of the sharp odor of chlorine dioxide were noticed. During the course of this experiment, it was necessary to recharge the chlorine dioxide generator several times.

The identity of the acetaldehyde derivative precipitated in the dimedone solution was ascertained on the basis of its melting point (140–141.5°, lit.[11] 140°). This derivative was converted to the anhydride by boiling it (0.1 g.) for 3 hr. in a mixture of

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[1] This paper was presented at the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962.

[2] R. S. Ingols, *J. Inst. Water Engrs.*, **4**, 581 (1950).

[3] R. S. Ingols and G. M. Ridenour, *Water Sewage Works*, **95**, 187 (1948); F. Cardey, *Eau*, **40**, 75 (1953); H. Adamski and W. Hoffmann, *Gaz, Woda Tech. Sanit.*, **34**, 154 (1960); L. Haines, *J. Am. Water Works Assoc.*, **49**, 309 (1957).

[4] E. Schmidt and K. Braunsdorf, *Ber.*, **55B**, 1529 (1922).

[5] E. Müller, Ed., "Houben-Weyl's Methods of Organic Chemistry," Vol. XI/1, Georg Thieme Publishing Co., Stuttgart, 1957, pp. 976–984; N. J. Leonard M. A. Rebenstorf, *J. Am. Chem. Soc.*, **67**, 49 (1945); N. J. Leonard and D. F. Morrow, *ibid.*, **80**, 371 (1958); S. Dunstan and H. B. Henbest, *J. Chem. Soc.*, 4905 (1957); E. Boyland and D. Manson, *ibid.*, 4689 (1957); C. F. Cullis and D. J. Waddington, *Proc. Roy. Soc.* (London), **A244**, 110 (1958); **A246**, 91 (1958); H. E. de la Mare, *J. Org. Chem.*, **25**, 2114 (1960).

[6] E. Müller, Ed., "Houben-Weyl's Methods of Organic Chemistry," Vol. XI/2, George Thieme Publishing Co., Stuttgart, 1958, pp. 190–200; H. B. Henbest and M. J. W. Stratford, *Chem. Ind.*, 1170 (1961).

[7] M. L. Granstrom and G. F. Lee, *J. Am. Water Works Assoc.*, **50**, 1453 (1958).

[8] M. L. Granstrom and G. F. Lee, "The Disproportionation of Chlorine Dioxide," unpublished report, Department of Sanitary Engineering, School of Public Health, University of North Carolina, Chapel Hill, 1957.

[9] R. S. Ingols and G. M. Ridenour, *J. Am. Water Works Assoc.*, **40**, 1207 (1948).

[10] F. D. Snell and C. T. Snell, "Colorimetric Methods of Analysis," Vol. III, D. Van Nostrand Co., Inc., Princeton, N. J., 1953, p. 262.

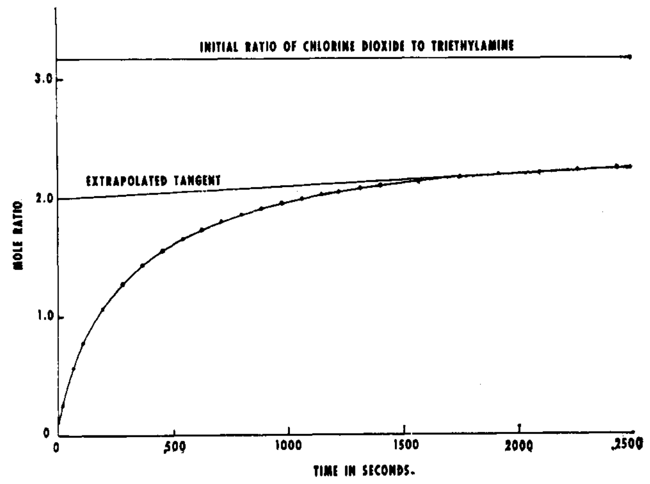

Fig. 1.—Determination of ratio of chlorine dioxide consumed to triethylamine initially present; $[(C_2H_5)_3N]_{\text{initial}}$ 9.43×10^{-6} *M*.

7 ml. of ethanol and 10 ml. of 1 *N* hydrochloric acid, and diluting afterward with 20 ml. of water; m.p. 175.5–177°, lit.[11] m.p. 175–176°.

Identification of Chlorite.—Equal volumes (25 ml. each) of 0.028 *M* aqueous triethylamine, 0.4 *M* phosphate buffer (pH 7.5), and 0.034 *M* chlorine dioxide were mixed; the yellow color was gone within a minute, and the final pH was 7.58. After 5 min., 35 ml. of 0.1 *N* sodium hydroxide was added (to stabilize the oxychloro anions), giving a pH of 10.88. The mixtures was spotted (15 and 50 μl.) on Whatman no. 1 filter paper strips and chromatographed[12] overnight in a "Chromatobox" apparatus (Research Specialties Co.) with an isopropyl alcohol–water–pyridine–29% ammonium hydroxide (15:2:2:2) developing solvent. After drying at room temperature, the filter paper strips were sprayed with 0.1 *N* silver nitrate, dried at room temperature, exposed to ultraviolet light for 10 min. and sprayed with diphenylamine reagent (a 1:1 mixture of 5% diphenylamine in ethanol with 1:1 acetone–3 *N* hydrochloric acid). No violet spots (chloride) appeared at R_f 0.25 after the ultraviolet treatment, and, after spraying with diphenylamine reagent, no green spots (chlorate) appeared at R_f 0.53, but light blue spots appeared at once at R_f 0.34, indicating the presence of significant amounts of chlorite ion (standard R_f 0.35 ± 0.03). The minimum amounts of the chlorine-containing ions detectable after chromatography are about 10 μg., or perhaps a little less for chlorate.

Identification of Diethylamine.—A concentrated aqueous solution containing 9×10^{-3} mole of chlorine dioxide was prepared from the polyhydrate which had been collected by passing the generator effluent through a freeze trap; the quantity of chlorine dioxide was estimated by titration. This was added to a concentrated aqueous solution of 3.7×10^{-3} mole of triethylamine, base being added concurrently to hold the pH between 7 and 10 until all the chlorine dioxide was decolorized. The pH was allowed to drop below 7, and a concentrated aqueous solution of 10^{-2} mole of silver nitrate was added to precipitate most of the chlorite, which was removed by filtration. The yellow-tinged solution was decolorized with 2×10^{-2} mole of sodium sulfite, which precipitated some silver ion as well; after filtration, the pH of the solution was 7.5. The filtrate was acidified with 2 ml. of 2 *N* hydrochloric acid, filtered away from silver chloride and evaporated at reduced pressure to a white solid, smelling faintly of acetaldehyde. The solid was distilled from 50% sodium hydroxide into ether, and the ether was treated with gaseous hydrogen chloride. The denser of the two layers which formed was evaporated at reduced pressure to a white solid residue, the amine hydrochloride. This solid had an infrared spectrum similar to, though not identical with, that of diethylamine hydrochloride (but quite different from the spectra of the triethylamine and ethylamine hydrochlorides). A 75-mg. portion of this hydrochloride was overlaid with 0.5 ml. of xylene, treated with 0.1 ml. of 50% sodium hydroxide, and shaken to ensure extraction. A 0.5-μl. aliquot of the xylene extract was analyzed in the Burrell Kromo-Tog K-2 vapor phase chromatograph (thermal conductivity detector) with a packing of 20% GE SF-96 silicone on Fluoropak-80 in a 0.5 × 250 cm. glass column at 179°. The emergence time of 2.7 min. corresponded to diethylamine, whereas the respective emergence times of authentic ethylamine and triethylamine are 1.8 and 4.1 min. under the same conditions.

Extent of Reduction of Chlorine Dioxide by Excess Triethylamine.—A solution was made up to contain 10^{-3} *M* chlorine dioxide, 10^{-3} *M* triethylamine, and 5×10^{-2} *M* phosphate buffer (pH 7.05), and permitted to stand for 5 min. before titration, by which time decolorization was complete. The mixture was then treated with potassium iodide and hydrochloric acid to bring the pH to 1 and titrated for all oxidant originally present as chlorite and chlorine dioxide (or hypochlorite). A decrease in titer of 23%, compared to a blank containing no triethylamine, was observed. A decrease of 20% in the titer would correspond to the stoichiometric transformation from chlorine dioxide to chlorite ion.

Ratio of Chlorine Dioxide Used to Initial Triethylamine Concentration.—Three experiments at ambient temperature (initially about 25°, but with a final temperature of about 32°) were carried out at pH 7.8, with variations in the initial concentrations of reactants. The first reaction was run in 0.1 *M* borate buffer, the second and third in phosphate buffer, with the following general procedure. The transmittancy at 355 mμ of 25 ml. of a buffered chlorine dioxide solution in a cell of 10-cm. light path was measured in a Perkin-Elmer recording spectrophotometer. Then a 5-ml. aliquot of buffered triethylamine solution of known concentration was added with good mixing, and the transmittancy of the mixture measured over a period of 43 min. The transmittancies (ranging from 20 to 95%) were converted to absorbancies, and thence to chlorine dioxide concentrations. The initial chlorine dioxide concentrations were taken as five-sixths of the concentration before addition of triethylamine. The initial concentration minus the concentration at time *t* was equal to the concentration decrease due to reaction. The ratio of concentration decrease to initial concentration of triethylamine was plotted (*e.g.*, Fig. 1). It was observed that these plots never flattened out completely. This was undoubtedly due to secondary (slow) reactions of chlorine dioxide which continued after the triethylamine reaction was complete. A fair estimate of the stoichiometry was possible, however, by extrapolating the tangents to the curves at about 35–40 min., where the curves were nearly linear, to zero time (or more properly, perhaps, but with no important effect, to the time at which the initial reaction was half complete and the presence of reaction products began to be a factor). These experiments showed a stoichiometric ratio (chlorine dioxide to triethylamine) of 2.

An attempt was made to determine the stoichiometry titrimetrically, but for reasons covered in the Discussion, the ratio (of about 1.5) obtained is probably not valid. A mixture was made of the following prechilled (0–4°) solutions, and kept in an ice-water bath: 45 ml. of water, 5 ml. of 0.1 *N* sulfuric acid, 50 ml. of 0.4 *M* phosphate buffer (pH 6.23), 25 ml. of 0.0283 *M* triethylamine, and 75 ml. of 0.034 *M* chlorine dioxide. A blank with water in place of the sulfuric acid and amine was used to establish the zero-time reading. Ten-milliliter aliquots were withdrawn periodically and each titrated at once in the usual manner. The data, converted to ratio of chlorine dioxide consumed to initial triethylamine are shown in Table I.

Ratio of Acid Evolved to Chlorine Dioxide Used in Presence of Excess Triethylamine.—A Polarad AT-2A automatic titrator was used to maintain pH close to 7.18 at 25° during the reaction brought about by adding 0.976 ml. of 0.00600 *M* chlorine dioxide (generated the previous day) to 9 ml. of 0.00330 *M* triethylamine which had been adjusted to the desired pH. A total of 0.1963 ml. of 0.0296 *N* sodium hydroxide, delivered in 0.5 hr., was required. Following the addition of chlorine dioxide, the pH dropped to a minimum value of 6.86, but soon returned to 7.18. The ratio of acid produced to chlorine dioxide used was 0.99:1.

Kinetics of the Reaction of Triethylamine with Chlorine Dioxide.—The experiments were intended to show gross effects of variations in pH, reactant concentrations, and possibly buffer concentrations on the reaction between chlorine dioxide and triethylamine. The reactions took place within the range of 26.5

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[11] Staff of Hopkins and Williams Research Laboratory, "Organic Reagents for Organic Analysis," Chemical Publishing Co., Brooklyn, N. Y., 1946, p. 120; "Tables for Identification of Organic Compounds; Supplement to Handbook of Chemistry and Physics," C. D. Hodgman, Ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, p. 68.

[12] B. L. Harrison and D. H. Rosenblatt, to be published in *J. Chromatog.*

TABLE I

RATIO OF CHLORINE DIOXIDE CONSUMED TO INITIAL TRIETHYLAMINE

Time, sec.	Ratio
0	0.000
58	.237
285	.685
460	.772
655	.917
855	.996
1225	1.097
1729	1.213
2250	1.314
3110	1.408
4100	1.459
4475	1.473

± 2°. The general procedure was as follows. Working solutions containing approximately 10^{-4} M or 2×10^{-4} M chlorine dioxide in 0.02–0.08 M buffer were prepared from stock solutions. To 25 ml. of a working solution of chlorine dioxide contained in a cylindrical quartz spectrophotometer cell of 10-cm. light path, there was added 5 ml. of a solution containing the desired concentration of triethylamine which had been neutralized with a nearly equivalent amount of hydrochloric acid. The cell was rocked back and forth to mix its contents, and quickly put into the cell compartment of a Beckman Model DK-2 spectrophotometer. Absorbancy of chlorine dioxide was measured at intervals against a water blank at the 355-mμ maximum. Absorbancy readings were corrected, where practical, by subtracting the rather small and constant readings obtained after at least ten half-lives. The logarithms of the absorbancies (without conversion to concentrations) were plotted against time to obtain pseudo first-order rate constants; when corrected absorbancies were used, the plots were linear for up to five half-lives (*e.g.*, Fig. 2). Thus, the reaction was shown to be first order with respect to chlorine dioxide. The pseudo first-order rate constants were divided by the corresponding analytical concentrations of triethylamine to give apparent second-order rate constants. A plot of these apparent second-order rate constants against pH gave a straight line of slope 1.0 (Fig. 3). This result indicated that true second-order rate constants would be obtained by using the concentrations of free base rather than the analytical concentrations of triethylamine. The results are also shown in Table II, in which it can be seen that neither buffer concentration nor variation of the concentration of unprotonated triethylamine (by means of changes in pH or in the analytical concentration of triethylamine) had any significant effect on the value of the second-order rate constant, 2.1×10^{-5} M^{-1} sec.$^{-1}$. For calculation of the rate constant; the reaction was considered first order with respect to triethylamine free base and first order with respect to chlorine dioxide. Spontaneous decomposition of chlorine dioxide is slow enough[8,13] to be neglected over the pH range studied.

TABLE II

REACTION KINETICS OF TRIETHYLAMINE AT 26.5 ± 2° WITH CHLORINE DIOXIDE (10^{-4} M–2×10^{-4} M)

pH	Buffer	Molarity	Analytical concn. (M) of triethylamine $\times 10^4$	Concn. of free base[a] triethylamine = B $\times 10^7$, M	k_{obs}, sec.$^{-1}$	$k_2 \times 10^{-5} = k_{obs}/B \times 10^{-5}$, M^{-1} sec.$^{-1}$
4.70	Acetate	0.033	9.07	0.00868	0.000192	2.21
5.98	Cacodylate	.033	9.07	0.165	.00423	2.56
6.50	Phosphate	.067	30.2	1.82	.0305	1.67
6.50	Phosphate	.067	30.2	1.82	.0291	1.59
6.53	Phosphate	.033	30.2	1.95	.0385	1.97
6.53	Phosphate	.033	30.2	1.95	.0387	1.98
6.54	Phosphate	.017	30.2	2.00	.0408	2.04
6.54	Phosphate	.017	30.2	2.00	.0403	2.01
6.55	Phosphate	.033	18.1	1.23	.0259	2.11
6.55	Phosphate	.033	18.1	1.23	.0259	2.11
6.56	Phosphate	.033	9.07	0.629	.0154	2.45
6.56	Phosphate	.033	9.07	0.629	.0147	2.34
6.77	Phosphate	.067	9.07	1.02	.0220	2.14
6.77	Phosphate	.067	9.07	1.02	.0221	2.16
6.85	Phosphate	.017	9.07	1.23	.0325	2.65
6.85	Phosphate	.017	9.07	1.23	.0322	2.63
7.11	Phosphate	.033	9.07	2.23	.0465	2.08
7.11	Phosphate	.033	9.07	2.23	.0456	2.04
7.11	Phosphate	.033	9.07	2.23	.0471	2.11
					Average	2.15

[a] $K_a = 1.91 \times 10^{-11}$.

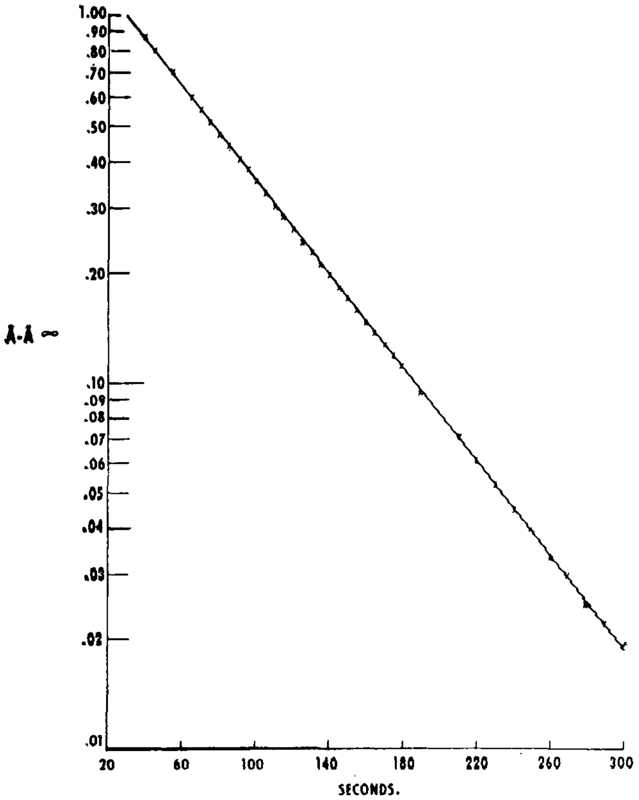

Fig. 2.—Decrease in chlorine dioxide absorbancy upon addition of triethylamine—showing first order; pH 6.56; [$(C_2H_5)_3N$], 9.07×10^{-4}; 0.037 M phosphate buffer.

Reaction of Diethylamine and Trimethylamine with Chlorine Dioxide.—Experiments with diethylamine such as those described in the preceding paragraph were performed at pH 7.14 and 8.97 in phosphate and borate buffers, respectively. They gave a calculated true second-order rate constant for the free base (assuming $K_a = 10^{-11}$) of about 2×10^3 M^{-1} sec.$^{-1}$. This is roughly 10^{-2} times the rate constant for triethylamine. Hence, oxidation of diethylamine, formed by the initial reaction, cannot have interfered significantly with the kinetic experiments of the preceding section.

An experiment run similarly with trimethylamine (assuming $K_a = 1.59 \times 10^{-10}$) at pH 6.78 gave a value of 10^5 M^{-1} sec.$^{-1}$ for the "true" second-order rate constant. At pH 6.00, pseudo first-order plots were not obtained.

Attempt to Initiate Polymerization of Acrylonitrile.—To 90 ml. of an aqueous solution containing 5 ml. of acrylonitrile, 0.58 mmoles of chlorine dioxide and pH 7 phosphate buffer (0.028 M) there was added 10 ml. of aqueous triethylamine (1.07 meq.). The chlorine dioxide was completely decolorized without appearance of any turbidity, in about 5 min. A parallel experiment was carried out, in which 0.56 mequiv. of nearly neutral sodium hypochlorite was substituted for chlorine dioxide. Turbidity appeared the moment the triethylamine was added and seemed to increase for several minutes. This initiation of acrylonitrile polymerization was first demonstrated by Horner and Podschus.[14]

Results

The principal products of the reaction between chlorine dioxide and triethylamine were identified qualitatively as acetaldehyde, diethylamine, chlorite ion,

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[13] M. L. Granstrom and G. F. Lee, *Public Works*, **88**, 90 (December, 1957).

[14] L. Horner and G. Podschus, *Angew. Chem.*, **63**, 531 (1951).

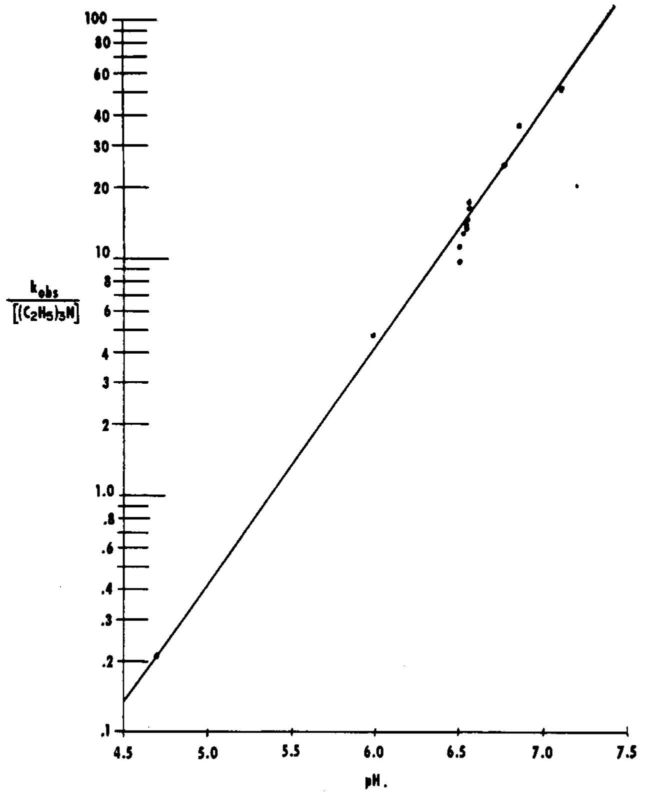

Fig. 3.—Plot of apparent second-order rate constant against pH for the reaction of chlorine dioxide with triethylamine at 26.5°.

and hydrogen ion. Chlorite ion and hydrogen ion were produced nearly quantitatively in experiments in which triethylamine was in excess. Furthermore, when chlorine dioxide was in excess (and the pH in the proper range) it reacted with triethylamine in the ratio of 2:1; the excess chlorine dioxide continued to be consumed, though rather slowly, through subsequent reactions. The dependence of the kinetics on pH (Fig. 3) almost certainly demonstrates that the amine reacts only as the free base. The dependence on free base concentration is first order, as is, likewise, the dependence on chlorine dioxide concentration (*e.g.*, Fig. 2), at least in the presence of excess triethylamine. The data summarized in Table I appear to indicate no striking effects due to changes in buffer concentration, and hence, no striking salt effects. The reaction products, especially at higher concentrations and low pH, can undergo further interactions to produce chlorine dioxide. The true second-order rate constant at 26.5 ± 2° is about $2 \times 10^5 M^{-1}$ sec.$^{-1}$.

Chlorine dioxide attacks diethylamine much more slowly than triethylamine under comparable conditions and attacks trimethylamine somewhat more rapidly in the pH range studied. According to a free base concentration comparison, however, triethylamine is actually more reactive than trimethylamine. Provided the pH is high enough, both the diethylamine and trimethylamine reactions are apparently first-order with respect to chlorine dioxide.

Discussion

Stoichiometric Formulation.—All evidence obtained points to the following over-all reaction.

$$H_2O + 2ClO_2 + (C_2H_5)_3N \longrightarrow CH_3CHO + (C_2H_5)_2NH + 2H^+ + 2ClO_2^-$$

This type of reaction of tertiary amines with oxidants is quite common. As in the permanganate reaction,[15] and probably in all those in which such a concentration is meaningful and measurable, it is evidently the concentration of the amine free base which determines the rate of reaction. The organic products were not measured quantitatively, so that the formation of intermediates and of polymeric products, such as those which might arise from the possible intermediate vinyldiethylamine or from acetaldehyde, is not to be excluded.

Side Reactions.—The acetaldehyde and chlorite produced in the initial reaction are capable of interacting with each other at low pH. Chlorine dioxide is

$$H^+ + CH_3CHO + 3ClO_2^- \longrightarrow CH_3CO_2^- + Cl^- + 2ClO_2 + H_2O$$

produced by this side reaction,[16] as well as by the decomposition of chlorous acid,[17] and accumulates under appropriate conditions, since it is evolved more rapidly than it can be used up. This is evidently what happened when the pH fell during the experiment on identification of acetaldehyde and also explains the low stoichiometric ratio obtained at pH 6.2. When chlorine dioxide is formed in this manner and then consumed by more triethylamine, the net effect is the following.

$$H_2O + 2ClO_2 + 3(C_2H_5)_3N \longrightarrow 3(C_2H_5)_2NH + CH_3CHO + 2CH_3CO_2H + 2HCl$$

The chlorine dioxide also can be used up by reaction with diethylamine and perhaps also with ethylamine, although rather slowly, presumably by reactions analogous to that of triethylamine. The rate relationship of the tertiary to the secondary amine reaction is the same as that observed for permanganate[18] with the two classes of amines.

Reaction Order.—The stoichiometric reaction as shown should require that the kinetics be first order with the amine (or, as is actually the case, with the amine free base) and second order with chlorine dioxide. Yet there is no doubt that the reaction is first order in chlorine dioxide concentration. A reasonable way in which this could arise is represented as follows.

$$ClO_2 + (C_2H_5)_3N \xrightarrow{\text{rate determining}} \text{intermediate}$$

$$ClO_2 + \text{intermediate} \xrightarrow{\text{fast}} \text{products}$$

Since chlorine dioxide does not appear to dimerize,[19-22] even at low temperatures,[21] it seems unlikely that the dimer is involved, despite the postulated existence of some type of transition-state chlorine dioxide dimer.[23] It is suggested, on the basis of this formulation, that the intermediate in question is a free radical, even though the reaction failed to initiate polymerization of acrylonitrile.

Choice of Experimental Conditions.—For most of the experiments, the chlorite–aldehyde side reaction and the spontaneous decomposition of chlorous acid were

[15] B. V. Tronov and L. S. Nikonova, *J. Russ. Phys. Chem. Soc.*, **61**, 541 (1929).

[16] H. F. Launer and Y. Tomimatsu, *Anal. Chem.*, **31**, 1385 (1959).

[17] J. F. White, M. C. Taylor, and G. P. Vincent, *Ind. Eng. Chem.*, **34**, 782 (1942).

[18] D. Vorländer, G. Blau, and T. Wallis, *Ann.*, **345**, 261 (1906).

[19] W. Bray, *Z. Phys. Chem.*, **54**, 569 (1906).

[20] N. W. Taylor, *J. Am. Chem. Soc.*, **48**, 854 (1926).

[21] F. E. King and J. R. Partington, *J. Chem. Soc.*, 925 (1926).

[22] M. Green and J. W. Linnett, *ibid.*, 4959 (1960).

[23] J. Halperin and H. Taube, *J. Am. Chem. Soc.*, **74**, 375 (1952).

to be avoided. Since these reactions are probably of a relatively high kinetic order,[24] the pH below which their interference would be important must depend on the concentrations of aldehyde and chlorite, and hence on the initial concentrations of amine and chlorine dioxide; the higher the reactant concentrations, the higher this pH. For example, the spectrophotometric kinetic experiments with 10^{-4} M chlorine dioxide were carried out successfully even at pH 4.7. By contrast, the attempt to measure the stoichiometry of the reaction titrimetrically at pH 6.2, with initial concentrations of 0.013 M chlorine dioxide and 0.0035 M triethylamine, gave a final ratio of chlorine dioxide used to triethylamine taken of only about 1.5 instead of 2. High concentrations of reactants were required by the titrimetric procedure, which also required that each sample be titrated immediately. The low pH and temperature were necessary to slow the reaction to a rate at which a sufficient number of samples could be withdrawn and titrated.

The reaction of chlorine dioxide with triethylamine was so rapid that there was no need to go to very high pH levels for the purpose of reaching convenient reaction times. With diethylamine, or more especially with even less reactive amines, the pH levels needed for sufficiently fast reaction (*i.e.*, above 10) might require consideration of the chlorine dioxide disproportionation to form chlorite and chlorate.[7,8]

Acknowledgment.—The authors are indebted to Mr. Raymond C. Roy for technical assistance in measuring acid production and to Mr. Joseph Epstein and Dr. George T. Davis for their stimulating discussion and encouragement of this investigation.

[24] H. F. Launer and Y. Tomimatsu, *J. Am. Chem. Soc.*, **76**, 2591 (1954).

Reactions of Indole. IV.[1] The Synthesis of Some Aminoindoles

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A procedure for the convenient preparation of 5-aminoindole-3-acetic acid in practical yield is described. This method, employing indoline intermediates, also was used to prepare 5-aminoindole-3-propionic acid as well as 5-amino-, 6-amino-, and 7-aminoindole.

Although investigation of the chemistry of indole is one of the oldest and most intriguing of chemical problems, the preparation of benzene-substituted indole derivatives still remains, by and large, a formidable synthetic effort. Acid-catalyzed substitution reactions on indole derivatives containing only 3-substituents in the pyrrole ring, in general, are prohibited by the acid lability of the indole nucleus, and in those cases where these reactions are possible (*i.e.*, with gramine,[2] 3-carbethoxyindole,[3,4] and indole-3-aldehyde[3-5]), the substituent orientation and the remaining functionality are not always the most desired. Ready access to 3-indoleacetic[6] and propionic acids[1,7] as well as other 3-indolealkanoic acids[8] has provided the impetus to investigate synthetic schemes that might be expected to provide various benzene-substituted derivatives of these acids. Additionally, the carboxyl group would allow for a considerable variety of other transformations. This communication describes general procedures by which 5-, 6-, and 7-aminoindole derivatives may be conveniently prepared.

Indoline and its derivatives may be considered as substituted anilines and, accordingly, aromatic substitution reactions that are applicable to aniline systems should also be useful for the derivatization of indolines. Thus, it is possible to postulate a synthetic sequence whereby: (1) a given indole is hydrogenated to the corresponding indoline; (2) the desired aromatic substitution reaction is performed; and, finally, (3) the indole derivative is recovered by dehydrogenation of the substituted indoline.[9] Chart I illustrates the preparation of 5- and 7-aminoindole derivatives *via* this route and in this manner it was possible to prepare 5-aminoindole-3-acetic acid in *ca.* 50% over-all yield.

A number of aminoindole derivatives have been prepared.[10] The preparations, in general, were made using the classic Fischer indole synthesis on the corresponding nitrophenylhydrazones followed by a reduction to the amine. Low yields invariably were experienced and the desired product was only one of several encountered in the reaction mixture. Of the simple aminoindoles, the preparation of the 6-isomer was reported in 1930,[11] although its identification was not confirmed until 1953 when Brown and Nelson[12] obtained it as a crystalline substance. Both the 4-[13] and 5-[14] isomers were prepared soon after; 7-aminoindole apparently has not been reported. 6-Aminoindole-3-acetic acid is known[15] and derivatives of 5-aminoindole-3-acetic and propionic acids recently have been synthesized.[16]

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