ment with those calculated by using the partial molecular rotatory contributions given in Table I. Good correlations for the 1,6-anhydro-4-deoxy-β-hexopyranoses and their diacetates can be obtained[12] by taking into account the interaction of the C-4 substituent with C-6. The 2,7-anhydro-β-heptulopyranoses can be accommodated by inclusion of an additional term for the hydroxymethyl group. Details of these calculations, together with calculations on aminodeoxy derivatives of 1,6-anhydro-β-hexopyranoses, will be given in a separate report.

Registry No.—I (*allo*), 14059-68-8; I (*altro*), 10339-41-0; I (*gluco*), 498-07-7; I (*manno*), 14168-65-1; I (*gulo*), 14274-90-9; I (*ido*), 10339-42-1; I (*galacto*), 644-76-8; I (*talo*), 14059-73-5; II (*allo*), 14661-09-7; II (*altro*), 14661-10-0; II (*gluco*), 13242-55-2; II (*manno*), 13242-48-3; II (*gulo*), 14661-13-3; II (*ido*), 14661-14-4; II (*galacto*), 4132-24-5; II (*talo*), 14661-16-6.

Oxidations of Amines. IV. Oxidative Fragmentation[1]

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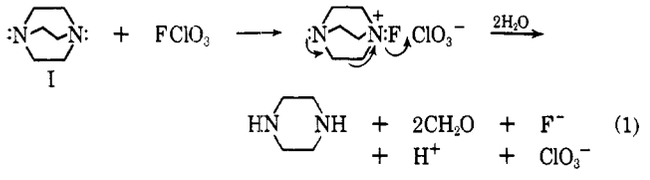
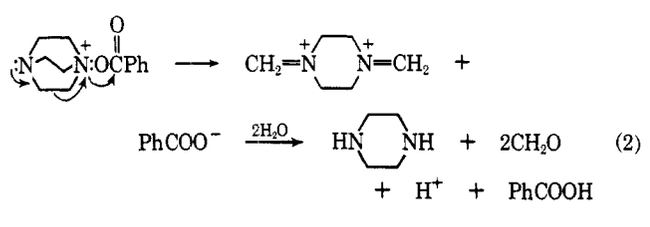
Received January 13, 1967

Oxidation of a representative group of β-amino and β-hydroxy amines with either chlorine dioxide or sodium hypochlorite resulted in carbon–carbon cleavage to give formaldehyde along with ammonia or the corresponding primary or secondary amine. The obvious relationship of this reaction to the fragmentation reactions described by Grob and co-workers[2] suggested the term "oxidative fragmentation."

The observation by Gardner and co-workers[3] of carbon–carbon scission in the perchloryl fluoride oxidation of triethylenediamine (I) (eq 1) led to speculation on the similarity of this phenomenon to the fragmentations reported by Grob, *et al.*[2] The comparison was strengthened by Huisgen and Kolbeck's report[4] of carbon–carbon bond breaking when the mono-N-oxide of I was treated with benzoyl chloride; here the oxidative step had been accomplished as a separate and discrete operation (eq 2). When Higuchi observed[5] that the oxidizing properties of hypochlorous acid disappeared in the presence of I, in contrast to the stability of hypochlorous acid toward quinuclidine,[6] it seemed likely to us that these differences might best be reconciled in terms of the above cited fragmentations; we have termed this "oxidative fragmentation." The objectives of this study were (a) to establish the products and probably nature of the reaction of I with hypochlorous acid, (b) to extend the comparison of reactions of I with oxidizing agents to chlorine dioxide, whose reactivity toward amines had been rather extensively studied by us,[1] and (c) to explore the scope of hypochlorous acid and chlorine dioxide mediated oxidative fragmentations to other vicinally substituted amines. These objectives have been realized to a considerable extent.



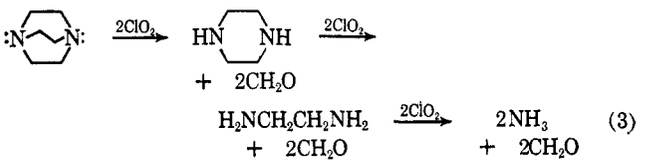
(1)



(2)

Results

The amines investigated as candidates for the oxidative fragmentation are compiled in Table I with their proposed oxidation products. The isolation of products from a number of these oxidations posed some difficulties. The formaldehyde formed in the oxidations of amines with chlorine dioxide was rapidly oxidized by chlorite ion to formic acid below pH 6, resulting in very low apparent yields of this aldehyde. Another difficulty encountered in isolation of formaldehyde from solutions occurred when ammonia as well as formaldehyde was an oxidation product. This difficulty was possibly due to the reaction between ammonia and formaldehyde to yield hexamethylenetetramine.[7] Isolation of the amine fragments from the chlorine dioxide oxidations was complicated in that the amine products underwent further degradation with excess chlorine dioxide. An example of such progressive degradation is that of the oxidation of I by chlorine dioxide; in the presence of a large excess of chlorine dioxide, I was observed to degrade to ammonia and formaldehyde (eq 3). In contrast to the extensive degradation of I



(3)

(1) Papers of this series: (a) I, D. H. Rosenblatt, A. J. Hayes, B. L. Harrison, R. A. Streaty, and K. A. Moore, *J. Org. Chem.*, **28**, 2790 (1963); (b) II, D. H. Rosenblatt, L. A. Hull, D. C. DeLuca, G. T. Davis, R. C. Weglein, and H. K. R. Williams, *J. Am. Chem. Soc.*, **89**, 1158 (1967); (c) III, L. A. Hull, G. T. Davis, D. H. Rosenblatt, H. K. R. Williams, and R. C. Weglein, *ibid.*, **89**, 1163 (1967).

(2) P. Brenneisen, C. A. Grob, R. A. Jackson, and M. Ohta, *Helv. Chim. Acta*, **48** (No. 1), 146 (1965), and papers cited therein.

(3) D. M. Gardner, R. Helitzer, and D. H. Rosenblatt, *J. Org. Chem.*, **32**, 1115 (1967).

(4) R. Huisgen and W. Kolbeck, *Tetrahedron Letters*, No. 12, 783 (1965).

(5) T. Higuchi, unpublished results.

(6) T. Higuchi and A. Hussain, submitted for publication.

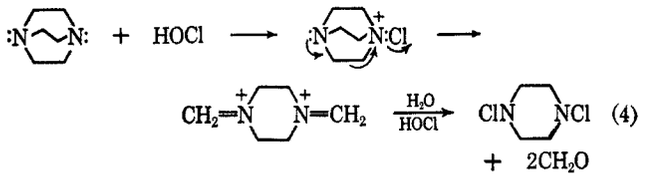
(7) J. F. Walker, "Formaldehyde," 2nd ed, Reinhold Publishing Corp., New York, N. Y., 1953, p 407.

TABLE I

FRAGMENTATION PRODUCTS

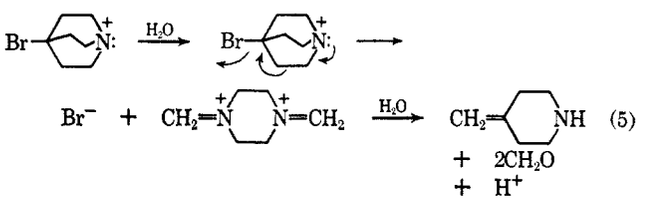
Amine	Oxidant	Predicted products	Found
Triethylenediamine	HOCl	1,4-Dichloropiperazine	53%
		Formaldehyde	40%
	ClO_2	Piperazine	By tlc
		Formaldehyde	40%
Piperazine	HOCl	Ethylenediamine	Not detected
		Formaldehyde	Easily detected
Ethylenediamine	ClO_2	Ammonia	Easily detected
		Formaldehyde	Small amount
	HOCl	Ammonia	Easily detected
		Formaldehyde	Small amount
3-Quinuclidinone	HOCl	N-Chloropiperidine-4-carboxylic acid	50%
		Formaldehyde	43%
	ClO_2	Piperidine-4-carboxylic acid	Not detected
		Formaldehyde	Trace amount
3-Quinuclidinol	HOCl	N-Chloro-4-formylpiperidine	Impure
		Formaldehyde	18%
	ClO_2	4-Formylpiperidine	Not detected
		Formaldehyde	Trace amount
3-Hydroxy-N-ethylpiperidine	HOCl	N-Chloropiperidine	Easily isolated
		Formaldehyde	Easily isolated
Triethanolamine	HOCl	Diethanolamine	Not isolated
		Formaldehyde	25%
	ClO_2	Diethanolamine	Not detected
		Formaldehyde	Easily detected
Diethanolamine	HOCl	Monoethanolamine	Not detected
		Formaldehyde	87%
Monoethanolamine	HOCl	Ammonia	Easily detected
		Formaldehyde	Trace amount
	ClO_2	Ammonia	Easily detected
		Formaldehyde	Small amount
2-Amino-2-methyl-1-propanol	ClO_2	Ammonia	Easily detected
		Acetone	Easily by vpc
		Formaldehyde	Easily detected
2-Hydroxy-2-amino-1,3-propanediol	ClO_2	Ammonia	Small amount
		Dihydroxyacetone	Indirectly
		Formaldehyde	Small amount
3-Hydroxypiperidine	HOCl	3-Aminopropionaldehyde	Not detected
		Formaldehyde	Easily detected
2-Hydroxy-2-amino-1,3-propanediol	HOCl	Ammonia	Easily detected
		Dihydroxyacetone	Not attempted
		Formaldehyde	Easily detected

by chlorine dioxide, the oxidation of I by hypochlorous acid proceeded to the easily isolated 1,4-dichloropiperazine, which was not readily susceptible to further attack (eq 4). However, it was observed that a pure sample



(4)

of 1,4-dichloropiperazine underwent slow degradation in water to give formaldehyde and chloride. The proposed synchronous fragmentation of I by hypochlorous acid is identical with that which has been postulated for the perchloryl fluoride oxidation in eq I and is analogous to the solvolytic fragmentation of 4-bromoquinuclidine (eq 5) described by Grob.[2]



(5)

The kinetics of amine oxidations by chlorine dioxide were examined by measuring the disappearance of chlorine dioxide in a spectrophotometer. Although the measurements do not represent a detailed kinetic study, they indicate the order of magnitude of the oxidations. The second-order rate constants in M^{-1}/sec^{-1}, assuming amine free base as reactant in each case, were obtained in buffered aqueous solutions at ionic strength of 0.2: 3-quinuclidinol, 1.2×10^2; 2-hydroxymethyl-2-amino-1,3-propanediol, 6.7×10^{-2}; triethanolamine, 1.0×10^4; piperazine, 3.7×10^3; ethylenediamine, 1.84×10^{-1}.

An attempt was made to follow the kinetics of oxidative fragmentation with hypochlorous acid iodometrically. In an experiment using 0.1 M triethanolamine, 0.005 M hypochlorous acid, pH 7 phosphate buffer, and 0.3 ionic strength at 25°, there was a rapid initial decrease in chlorine, too fast to be measured by manual sample withdrawal, followed by a very slow decay with a first-order half-life of 10 hr. Monoethanolamine under similar conditions showed a slow decay with a first-order half-life of several hours. Other kinetic investigations of amine oxidations with hypochlorous acid have shown[8] that the tertiary amines react much faster than do secondary and primary amines.

From these observations one may suggest two mechanisms occuring in stepwise manner during the oxidation. The first step would be the rapid fragmentation of the chlorammonium ion (eq 6). The secondary amine product then reacts with excess hypochlorous acid present to form the chloramine (eq 7). The chloramine hydrolyzes by the same mechanism described by Grob[2] (eq 8). Primary amines may also form chloramines and hydrolyze in a manner similar to the secondary amines.

$$(HOCH_2CH_2)_3N: + HOCl \underset{}{\overset{\text{slow}}{\rightleftharpoons}} (HOCH_2CH_2)_3\overset{+}{N}Cl$$

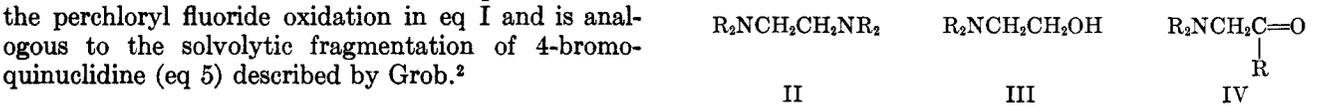
$$(HOCH_2CH_2)_3\overset{+}{N}Cl \xrightarrow{\text{fast}} (HOCH_2CH_2)_2 + 2CH_2O + Cl^- \quad (6)$$

$$(HOCH_2CH_2)_2NH + HOCl \xrightarrow{\text{fast}} (HOCH_2CH_2)_2NCl + H_2O \quad (7)$$

$$(HOCH_2CH_2)_2NCl \xrightarrow{\text{very slow}} HOCH_2CH_2NH_2 + 2CH_2O + Cl^- \quad (8)$$

Discussion

The present work defines oxidative fragmentation as the decomposition of β-substituted amines of general structures II, III, and IV by action of either hypochlorous acid or chlorine dioxide, resulting in cleavage between the α and β carbons. Although the natures of

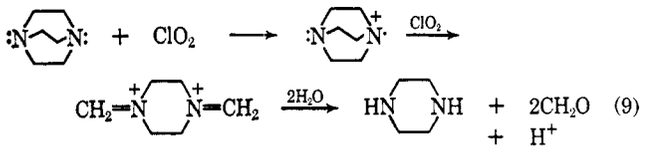


II III IV

the oxidative fragmentation reactions presented herein have not been established unequivocally, plausible mechanisms can be suggested upon the basis of earlier studies. Ellis and Soper reported kinetic and spectroscopic evidence showing that hypochlorous acid interacts with trimethylamine to form the trialkylchlorammonium cation,[9] R_3NCl^+. Loss of hydrogen chloride

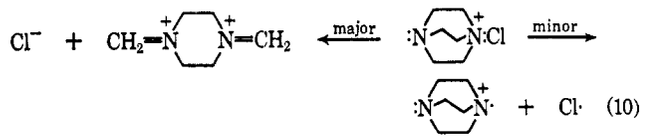
(8) W. H. Dennis, Jr., unpublished results.
(9) A. J. Ellis and F. G. Soper, *J. Chem. Soc.*, 1750 (1954).

from this cation could lead to the quaternary Schiff base, $R'CH^+{=}NR_2$, which appears as the intermediate in many of the equations presented herein. The existence of the quaternary Schiff base, $CH_2{}^+{=}NR_2$, has been demonstrated by Böhme and co-workers.[10] Previous investigations by Hull, *et al*,[1c] have shown that chlorine dioxide can generate the aminium radical by electron abstraction at the nitrogen electron pair. In the reactions considered in the present study, this aminium radical may initiate the fragmentation of the molecule. Indeed, such a mechanism must be postulated for the oxidation of triethylenediamine by chlorine dioxide (eq 9). Evidence for the presence of the tri-



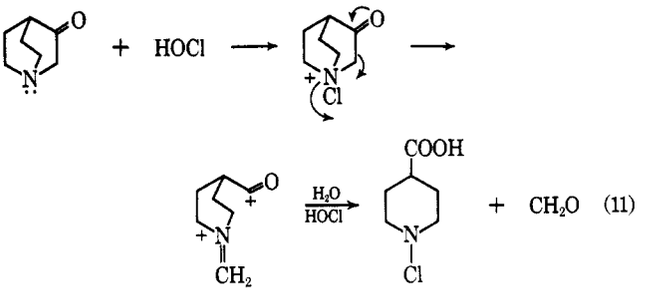
(9)

ethylenediamine cation radical, in solutions of triethylenediamine in the process of oxidation by hypochlorous acid or chlorine dioxide, has been found by observing the electron spin resonance spectra.[11] The spectra obtained were identical with the one reported earlier wherein the triethylenediamine cation radical was generated by electrochemical means.[12] A red transient color has been observed in the present oxidation of I with both hypochlorous acid and chlorine dioxide; however, the significance of this phenomenon as a possible indicator of the presence of a free radical species is still uncertain. Whereas chlorine dioxide, being a one-electron oxidant,[1] would be expected to produce the cation radical of I by electron abstraction at the nitrogen, hypochlorous acid, being a two-electron oxidant, passes through the chlorammonium ion to products and possibly generates the aminium cation radical by means of a side reaction (eq 10).



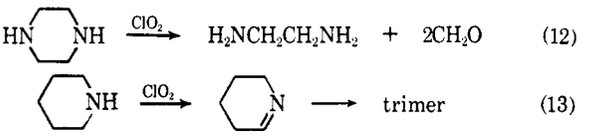
(10)

The requirement for an appropriate heteroatom at the β carbon of the amine is evident when the oxidations of those amines that undergo oxidative fragmentation are compared with oxidations of their analogs possessing no β substituent under similar conditions. Whereas I undergoes facile ring opening by hypochlorous acid or chlorine dioxide, quinuclidine, having but a single bridgehead nitrogen atom, is resistant to oxidative cleavage.[13] Instead, chlorine dioxide gives rise to quinuclidine N-oxide, possibly through interaction of oxygen with the quinuclidine aminium cation radical.[9] In contrast to the stability of the bicyclic system of quinuclidine toward hypochlorous acid, 3-quinuclidinone, a β-substituted amine, was found to decompose readily, for which the mechanism given in eq 11 is proposed. A further example showing the need for a β-substituted heteroatom is that of piperazine. Piper-



(11)

azine is oxidized by either hypochlorous acid or chlorine dioxide to formaldehyde (eq 12) whereas the analog, piperidine, gives N-chloropiperidine with hypochlorous acid and yields the enamine, Δ^2-piperideine, isolated as the trimer (tripiperideine), on treatment with chlorine dioxide (eq 13). Whereas triethanolamine in the



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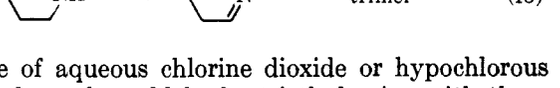
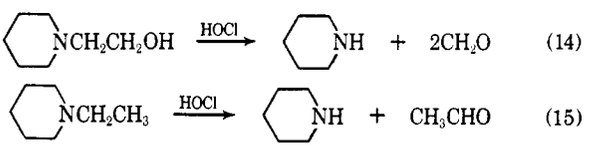


(13)

presence of aqueous chlorine dioxide or hypochlorous acid produces formaldehyde, triethylamine with these oxidants undergoes carbon–nitrogen cleavage to yield acetaldehyde and diethylamine. Likewise, N-(2-hydroxyethyl)piperidine fragments in the presence of hypochlorous acid to give piperidine and formaldehyde (eq 14), whereas the analog N-ethylpiperidine is oxidized to piperidine and acetaldehyde (eq 15). In order to



(14)

(15)

compare the rate of cleavage of the N-ethyl group to the rate of fragmentation of the N-β-hydroxyethyl group, an excess of N,N-diethylethanolamine was allowed to react with HOCl and the ratio of acetaldehyde to formaldehyde determined. The reaction favored ethyl cleavage over fragmentation in a ratio of about 200:1.

The concurrency of reactions other than oxidative fragmentation, which involves the attack of the oxidant at the nitrogen, cannot be discounted in the case of the mono-, di-, and triethanolamines. There is the possibility that degradation also proceeds through the alkyl hypochlorite, which would readily form under the conditions of oxidation. Also, in the case of the primary and secondary amines of Table I, the chloramine rather than the chlorammonium ion may be the reactive species.

There are a number of reactions involving scission of the carbon–carbon bond that yield products similar to those predicted by the fragmentation mechanism presented in this paper; however, it is likely that the mechanisms involved are different. Secondary and primary vicinal amino alcohols are known to be oxidized by periodic acid. An example of this is the oxidation of 1 mole of diethanolamine to form 1 mole of ammonia and 4 moles of formaldehyde.[14] Although the reaction is formally similar to oxidative fragmentation, the

(10) H. Böhme, E. Mundlos, and O. Herboth, *Chem. Ber.*, **90**, 2003 (1957).
(11) W. Giordano, *et al.*, unpublished results from these laboratories.
(12) T. M. McKinney and D. H. Geske, *J. Am. Chem. Soc.*, **87**, 3013 (1965).
(13) L. A. Hull, unpublished results.
(14) E. L. Jackson, *Org. Reactions*, **2**, 343 (1949).

mechanism is different, as is borne out by the fact that vicinal amino alcohols with the tertiary amine function undergo only C–N fission with the reagent. Secondary and primary 1,2-amino alcohols react with lead tetraacetate giving the products of carbon–carbon scission.[14,15] However, 1,2-amino alcohols with the tertiary amine function react with lead tetraacetate to give products resulting from carbon–nitrogen cleavage.[16] Curragh, Henbest, and Thomas have described the oxidation of triethylenediamine with manganese dioxide to form 1,4-diformylpiperazine by an unspecified mechanism.[17] Henbest and Stratford have also reported that ozone reacts with tributylamine to give dibutylformamide.[18] Finally, amino acids are known to degrade in the presence of hypochlorous acid to form ammonia, carbon dioxide, and aldehyde[19] by an unspecified mechanism; we have found glycine, in fact, to degrade in this manner in the presence of chlorine dioxide.

The present study has shown that certain amines having the amino, the hydroxy, and in a single instance the oxo group as β substituents undergo similar fragmentations upon oxidation by hypochlorous acid or chlorine dioxide. This degradation is unlike the oxidation of monofunctional amines which undergo only carbon–nitrogen scission.

Experimental Section

Reagents.—Sodium hypochlorite was used in the form of commercial bleach. Chlorine dioxide was prepared as in previous studies.[15] Solutions of sodium chlorite and potassium persulfate were mixed in a gas washing bottle and a stream of nitrogen was introduced to sweep the chlorine dioxide from the wash bottle into a container of chilled water where the chlorine dioxide was reabsorbed. Nessler's reagent was prepared by the usual method.[20] Dimedone (5,5-dimethyl-1,3-cyclohexanedione) was used as a saturated aqueous solution. The liquid amines were distilled prior to use.

Oxidation Conditions.—Most of the oxidations were carried out in water at room temperature. However, some reactions were very exothermic and cooling with ice was necessary. The reaction solutions were buffered to pH 8; higher alkalinity would have caused some disproportionation of the chlorine dioxide to chlorite and chlorate ions.

Thin Layer Chromatography.—The progress of amine oxidation could be followed easily by means of thin layer chromatography (tlc). Speedy analyses were accomplished by the use of silica gel coated microscope slides as chromatography plates. Methanol containing 1% concentrated ammonium hydroxide was employed for development and iodine vapor used to detect migrated materials. Iodine vapor detects chloramines and amines especially well. This technique was used primarily as a rapid method for monitoring the constituents of a reaction and as a rough qualitative tool. Silica gel plates (10 cm) were used for more refined qualitative determinations.

Product Isolation.—The oxidation of amines by hypochlorous acid posed little difficulty in product isolation. A general procedure was used to work up most of these reactions. The following will be referred to as procedure I. After the monitoring showed the disappearance of reacting amine, the solution was cooled in ice to precipitate the formed chloramine if insoluble. Remaining chloramine was extracted with dichloromethane after adjustment of the aqueous solution to pH 5. The aqueous solution, free of chloramine, was treated with sodium thiosulfate to destroy remaining active chlorine. An excess of saturated dimedone solution was added and the pH lowered to 4.5, whereupon formaldehyde would precipitate in the form of the dimedone derivative, mp 188–189°. The isolated chloramine could be identified by melting point (if solid) and through the infrared spectrum. The chloramine could be converted to the free amine by treatment with thiosulfate and the benzenesulfonamide was prepared by treating the alkaline amine solution with benzenesulfonyl chloride.

Hypochlorous Acid Oxidations. Triethylenediamine.—Triethylenediamine (1.12 g, 0.01 mole) in 20 ml of 2 *M* sodium hydrogen phosphate adjusted to pH 8 was mixed with 120 ml of 1.27 *M* hypochlorous acid solution. The red transient intermediate appeared upon mixing, lasting for a few seconds. Tlc showed almost instantaneous oxidation, the sole product being a chloramine. The solution was cooled in ice whereupon 0.54 g of a white crystalline solid precipitated. This substance melted at 70–72° and oxidized potassium iodide to iodine; it had the same melting point as 1,4-dichloropiperazine described by Leulier and Cohen[21] and showed no mixture melting point depression with an authentic sample.

3-Quinuclidinone.—A solution of 3-quinuclidinone (0.125 g, 0.001 mole) in 10 ml of water was added to 50 ml of 0.1 *M* sodium hydrogen phosphate solution containing hypochlorous acid (0.005 mole). At short intervals, small aliquots of the solution were removed for tlc analysis; the latter indicated the formation of a new material of higher R_f value than 3-quinuclidinone and possessing the ability to oxidize potassium iodide. After 5 min, no quinuclidinone remained in the solution and sodium thiosulfate was added to destroy all chlorine species present. The isolated dimedone derivative weighed 0.137 g and showed no melting point depression with an authentic sample of methylenebismethone.

A similar reaction was carried out using excess hypochlorous acid and 3 g of 3-quinuclidinone in order to isolate the chloramine. This was accomplished by cooling the reaction mixture in ice and lowering the pH to 3 after tlc analysis showed the reaction to be complete. A white crystalline chloramine (1.53 g) was isolated from the solution by filtration, mp 118–119°. The infrared spectrum showed carbonyl stretching at 1700 cm^{-1} as well as a broad band at 935 cm^{-1}, both corresponding to the carboxylic acid function. The sulfonamide (procedure I), soluble in alkali and insoluble in dilute acid, had the same melting point (154–157) as that of the product synthesized from an authentic sample of piperidine-4-carboxylic acid, and the same infrared spectrum.

3-Quinuclidinol.—Sodium hydrogen phosphate solution (0.1 *M*, 50 ml) at pH 8, containing hypochlorous acid (0.005 mole), was added to 3-quinuclidinol (0.002 mole) in 10 ml of water at 25°. After 5 min, tlc showed a number of newly formed materials, the major constituent being a chloramine. Formaldehyde was isolated as the dimedone derivative in 18% yield. The chloramine was extracted from the reaction solution with dichloromethane and found to be a liquid. The infrared spectrum of this chloramine showed aldehyde carbonyl absorption at 1720 cm^{-1} and a weak band at 2820 cm^{-1} which corresponds to the CH of the aldehyde function. There were no other distinguishing assignments. The benzenesulfonamide of this amine was difficult to purify and melted broadly at 90–105°. It was found that this material was being oxidized by air as indicated by the isolation of piperidine-4-carboxylic acid, mp 152–155°. It was therefore concluded that 3-quinuclidinol is oxidized by hypochlorous acid intially to 1-chloropiperidine-4-aldehyde, a product sensitive to air oxidation.

Ethylenediamine.—An excess of ethylenediamine was mixed with a 0.15 *N* solution of sodium hypochlorite at pH 8 and 25°. Sodium thiosulfate was added to reduce any chloramine and nitrogen was bubbled through the solution to sweep out any ammonia formed. The sweep gas was led into Nessler's reagent where it gave a positive test for ammonia.[22]

1-(2-Hydroxyethyl)piperidine.—The amine (0.5 g, 0.0039 mole) in 10 ml of 1 *M* sodium hydrogen phosphate was treated with 50 ml of 0.078 *N* hypochlorous acid solution. Piperidine was isolated as the benzenesulfonamide, mp 88–89°.[23] This had

(15) R. Criegee, *Z. Angew. Chem.*, **50**, 153 (1937).

(16) N. J. Leonard and M. A. Rebenstorf, *J. Am. Chem. Soc.*, **67**, 49 (1945).

(17) E. F. Curragh, H. B. Henbest, and A. Thomas, *J. Chem. Soc.*, 3559 (1960).

(18) H. B. Henbest and M. J. W. Stratford, *Chem. Ind.* (London), 1170 (1961).

(19) H. Gilman, "Organic Chemistry," Vol. II, 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1948, p 1100.

(20) "Handbook of Chemistry and Physics," 41st ed, Chemical Rubber Publishing Co., Cleveland, Ohio, p 1653.

(21) A. Leulier and R. Cohen, *J. Pharm. Chim.*, **29**, 245 (1939); *Chem. Abstr.*, **34**, 784 (1940).

(22) F. Feigl, "Spot Tests in Inorganic Analysis," 5th ed, Elsevier Publishing Co., New York, N. Y., 1958, p 238.

(23) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed, John Wiley and Sons, Inc. New York, N. Y., 1956, p 288.

an infrared spectrum and melting point identical with those of an authentic sample of piperidine benzenesulfonamide.

N-Ethylpiperidine.—When N-ethylpiperidine (0.002 mole) was treated with sodium hypochlorite (0.005 mole) in aqueous solution, acetaldehyde was isolated as the dimedone derivative, mp 139°, and piperidine as the benzenesulfonamide, mp 88–89°. The sulfonamide was identical with an authentic sample of piperidine benzenesulfonamide.

3-Hydroxypiperidine.—Hypochlorous acid (10 ml, 0.08 *M*) in aqueous phosphate buffer was permitted to react with 3-hydroxypiperidine (0.2 g) in 10 ml of water. The formaldehyde was isolated as the dimedone, but no attempt was made to isolate the amine fragment.

Tri-, Di-, and Monoethanolamine.—Hypochlorous acid (12.8 ml, 0.078 *N*) was added to 0.02 mole of each amine dissolved in 20 ml of 1 *M* sodium hydrogen phosphate solution. After 15 min, procedure I was used to isolate the dimedone derivative of formaldehyde from each oxidation. Triethanolamine and diethanolamine were found to degrade to formaldehyde in yields of 25 and 87%, respectively, based on the concentration of hypochlorous acid. Monoethanolamine gave only a small amount of the dimedone derivative of formaldehyde. No attempt was made to isolate the amine fragments from these oxidations.

2-Amino-2-hydroxymethyl-1,3-propanediol.—An excess of amine was mixed with sodium hypochlorite solution. After 30 min, sodium thiosulfate was added and the pH adjusted to 4.5 immediately after addition of dimedone solution. Formaldehyde was precipitated as the dimedone derivative in low yield and ammonia was detected by Nessler's reagent.

Decomposition of 1,4-Dichloropiperazine.—1,4-Dichloropiperazine was prepared by slowly adding excess sodium hypochlorite solution to 1 g of piperazine in 50 ml of water at 0° containing 0.05 mole of sodium hydrogen phosphate. The white dichloramine which precipitated was filtered from the solution and washed with a large quantity of cold water, mp 70–71°. The fresh material was placed into 50 ml of distilled water at 25°. After 10 min, the formation of formaldehyde was confirmed through isolation of the dimedone derivative. The concentration of formaldehyde was observed to increase on standing. The expected ethylenediamine could not be isolated.

Chlorine Dioxide Oxidations. Triethylenediamine (0.01 mole) in 50 ml of 0.1 *M* sodium hydrogen phosphate solution adjusted to pH 8 was treated with chlorine dioxide solution (0.002 mole) to give a red transient color lasting for a few seconds. Tlc showed the presence of piperazine in the oxidized solution, but no attempt was made to isolate it. Formaldehyde was isolated as the dimedone derivative in 40% yield.

Ethylenediamine.—An excess of ethylenediamine was mixed with a solution of chlorine dioxide and buffered to pH 8 with sodium hydrogen phosphate. After the color of the chlorine dioxide had disappeared, the dimedone derivative was recovered from the solution and ammonia was identified by passing a stream of nitrogen through the alkaline solution and into Nessler's reagent.

Piperidine (1 g) in 20 ml of 1 *M* sodium hydrogen phosphate was added to 100 ml of 0.12 *M* chlorine dioxide solution. The chlorine dioxide was rapidly decolorized. The solution was concentrated, made alkaline, and extracted with 100 ml of ether. Evaporation of the ether resulted in an orange viscous liquid having a musty odor. After pumping the material at low pressure to remove excess piperidine, the nonvolatile residue was removed and its infrared spectrum obtained. The spectrum was identical with that of tripiperidine hydrate obtained by Gardner and co-workers[3] from the hydrolysis of N-perchlorylpiperidine.

2-Amino-2-methylpropanol.—Chlorine dioxide (0.005 mole) in water was allowed to react with 1 g of amine in 50 ml of 0.1 *M* phosphate buffer at pH 8. The color of chlorine dioxide faded quickly. Saturated dimedone solution was added and the pH adjusted to 4.5, whereupon a small quantity of the formaldehyde derivative was obtained. Half the solution was distilled and the distillate analyzed by gas chromatography, utilizing a 6-ft column containing 5% silicone rubber SE-30 at 75°; acetone was found. The starting material was checked for acetone, but none was found. The second half of the solution was made alkaline and swept with a nitrogen stream. The sweep gas was found to contain ammonia by means of Nessler's reagent.

2-Amino-2-hydroxymethyl-1,3-propanediol.—Amine (5 g) and 50 ml of chlorine dioxide solution (0.07 *M*) were mixed. After 30 min the color of chlorine dioxide faded. Part of the solution was treated with dimedone and a small quantity of the formaldehyde derivative obtained. Another part of the reaction solution was made alkaline and swept with nitrogen. Ammonia was detected in the sweep gas by means of Nessler's reagent. The expected dihydroxyacetone could not be isolated but was detected in a indirect manner as follows. The remainder of the solution was treated with saturated dimedone solution and left to stand 12 hr at pH 7 to react completely with the formaldehyde present. The dimedone derivative was removed by filtration after lowering the pH to 4.5. The clear solution was then treated with 0.25 g of periodic acid and, on standing for only a few minutes, gave a precipitate of the dimedone derivative of formaldehyde, mp 188–189°. This formaldehyde most probably arose through the cleavage of dihydroxyacetone present in the solution to glycolic acid and formaldehyde. It may therefore be concluded that the formaldehyde obtained in this manner came from the cleavage of the dihydroxyacetone present in the solution.

3-Quinuclidinol.—An excess of 3-quinuclidinol was mixed with chlorine dioxide solution at pH 8. The disappearance of chlorine dioxide was very slow. After 12 hr, sodium sulfite was added to destroy the chlorite ion. The solution was adjusted to pH 6.3 and the vapors from the solution were examined with the mass spectrophotometer; formaldehyde was detected.

Ratio of Ethyl Cleavage to Fragmentation.—N,N-Diethylethanolamine (0.05 mole) in 100 ml of water containing 0.05 mole of sodium bicarbonate was treated with 2 mequiv of hypochlorous acid. After 20 min (no active chlorine remained), the solution was treated with dimedone solution (0.01 mole), and acetic acid was added to adjust the pH to 4.5. Twenty-four hours were given for complete precipitation of the aldehydes. The dried derivative weighed 300 mg and melted at 133–138°. The derivative was refluxed 5 min in ethanol containing 1 drop of HCl in order to cyclize the ethylidenebismethone to the octahydroxanthene,[24] mp 175–176°. The unreactive methylenebismethone could be separated from the cylized material by extraction with dilute aqueous alkali. Upon acidification of the aqueous extract, the methylenebismethone precipitated (3 mg, mp 186–189°).

Registry No.—Triethylenediamine, 280-57-9; piperazine, 110-85-0; ethylenediamine, 107-15-0; 3-quinuclidinone, 3731-38-2; 3-quinuclidinol, 1619-34-7; 3-hydroxy-N-ethylpiperidine, 13444-24-1; triethanolamine, 102-71-6; diethanolamine, 111-42-2; monoethanolamine, 141-43-5; 2-amino-2-methyl-1-propanol, 124-68-5; 2-hydroxy-2-amino-1,3-propanediol, 13444-25-2; 3-hydroxypiperidine, 6859-99-0; 1-(2-hydroxyethyl)piperidine, 3040-44-6; N-ethylpiperidine, 766-09-6; 2-amino-2-hydroxymethyl-1,3-propanediol, 77-86-1; piperidine, 110-89-4.

(24) See ref 23, p 220.