A stock solution of lithium aluminum hydride in ether was prepared by heating the solid with anhydrous ether under nitrogen for several hours. The solution was clarified by settling and the clear supernatant solution was standardized by the iodometric procedure of Felkin.[28] Solutions of the desired concentration were prepared by dilution of the stock solution in a dry box under nitrogen.

Method A.—A silica ultraviolet cell having a ground glass top closure was filled in the drybox under nitrogen with a known volume of hydride solution. The cell was then capped with a serum stopple which was wired in place. If necessary the solution was clarified by centrifugation and then allowed to equilibrate thermally. A measured volume of a solution of the pyran of known concentration was added to the cell *via* a syringe. The solution was mixed by brief shaking, and the mixture was centrifuged and then placed in the thermostatted cell compartment of a Cary 15 spectrophotometer. The reaction was followed by monitoring the disappearance of the pyran absorption band. The temperature in an oil filled cell at thermal equilibrium in the cell compartment was measured just prior to each run.

Method B.—Measured volumes of solutions of pyran and lithium aluminum hydride of known concentration were brought to thermal equilibrium and then mixed in a vessel permitting withdrawal of aliquots. Aliquots were withdrawn at intervals and the reaction solution was immediately mixed with a measured volume of a solution of durene of known concentration. Reaction was quenched by careful addition of water, and the organic layer was separated from the precipitated salts. The salts were washed with ether, and the washings were combined with the main solution. The solution was carefully concentrated and the concentrations of durene, pyran, and alcohol were determined by glc. Analysis was carried out with a 7 ft × 0.125 in. 5% Carbowax 20M on 60/80 mesh firebrick using a Disc integrator to determine relative peak areas. A plot of log $A_p/(A_p + A_{al})$ *vs.* time gave a straight line (A_p = area of pyran peak; A_{al} = area of alcohol peak). Constancy of the ratio $A_D/(A_p + A_{al})$ (A_D = area of the durene peak) provided a check against loss of material or incursion of side reactions. The rate constants determined by this method were in good agreement with those ascertained by method A.

(28) H. Felkin, *Bull. Soc. Chim. Fr.*, 347 (1951).

Registry No.—**2**, 35031-06-2; **3**, 5552-30-7; **4**, 5526-16-9; **5**, 35031-09-5; **8**, 5631-86-7; **9**, 35031-10-8; **10**, 35031-11-9; **10** trans isomer, 472-80-0; **11**, 35031-13-1; **14**, 35031-14-2.

Ozonation of Amines. VI.[1] Primary Amines

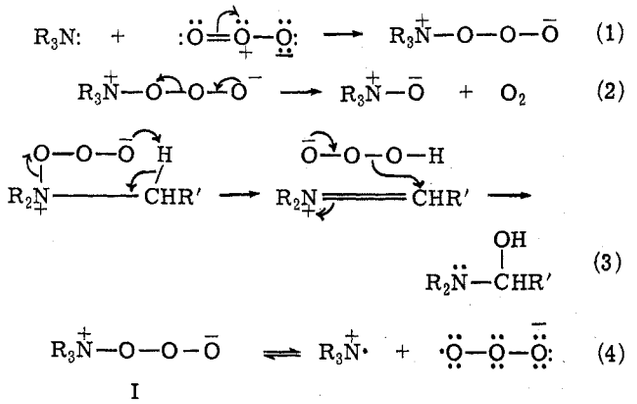
PHILIP S. BAILEY,* THOMAS P. CARTER, JR., AND LLOYD M. SOUTHWICK

Department of Chemistry, The University of Texas at Austin, Austin, Texas 78712

Received March 17, 1972

A detailed study of the ozonation of two primary amines, *n*-butylamine (having a primary alkyl group) and isopropylamine (having a secondary alkyl group), has been made and the results have been compared with those of *tert*-butylamine in regard to the three principal fates of the initial amine–ozone adduct.

In preceding papers in this series, the ozonations of *tert*-butylamine,[2,3] tri-*n*-butylamine,[2,4] di-*tert*-butylamine,[5] and di-*tert*-butyl nitroxide[1] were reported. The results of the ozonations of the amines were rationalized by means of an initial electrophilic ozone attack (eq 1) followed by four competing fates of the initial amine–ozone adduct.[2,5] Three of these fates, loss of oxygen to form an amine oxide product or intermediate, intramolecular side-chain oxidation, and dissociation to cation and anion radicals (followed by further reactions of these intermediates), are described by eq 2–4.



(1) For paper V of this series, see P. S. Bailey and J. E. Keller, *J. Org. Chem.* **35**, 2782 (1970).

(2) P. S. Bailey, J. E. Keller, D. A. Mitchard, and H. M. White, *Advan. Chem. Ser.*, **77**, 58–64 (1968).

(3) P. S. Bailey and J. E. Keller, *J. Org. Chem.*, **33**, 2680 (1968).

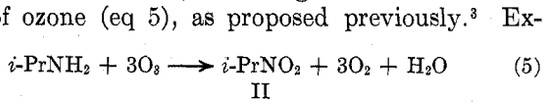
(4) P. S. Bailey, D. A. Mitchard, and A. Y. Khashab, *ibid.*, **33**, 2675 (1968).

(5) P. S. Bailey, J. E. Keller, and T. P. Carter, Jr., *ibid.*, **35**, 2777 (1970).

The purpose of the presently reported research was to study the ozonation of two additional primary amines with which a competition among all three of the pathways was possible, in order to gain information concerning the factors which affect this competition, as was done with the tertiary amine, tri-*n*-butylamine.[4] One of the primary amines chosen was *n*-butylamine, having a primary alkyl group, and the other was isopropylamine, which has a secondary alkyl group.

The ozonation of isopropylamine was studied in chloroform solution at three different temperatures (−65, −30, and 0°), in methylene chloride at −78°, and in pentane at −78°. The ozonations were carried out with a slight excess of ozone over a 1:1 amine–ozone ratio; on the average slightly less than 1 mol of ozone reacted per mole of amine. In addition, a less detailed study of the ozonation of isopropylhydroxylamine was made. All results are shown in Table I.

The production of 2-nitropropane (II) is analogous to the formation of 2-methyl-2-nitropropane from ozonation of *tert*-butylamine[3] and almost certainly occurs by the amine oxide route, involving a total of 3 molar equiv of ozone (eq 5), as proposed previously.[3] Ex-



pected intermediates in this reaction are isopropylhydroxylamine (IV) and 2-nitrosopropane (V). Evidence for the proposed reaction pathway is that the major product from ozonation of IV is 2-nitropropane (Table I, expt 10–13) and that the pale blue color of 2-nitrosopropane (V) was evident throughout the ozonations of both isopropylamine and the hydroxyl-

TABLE I

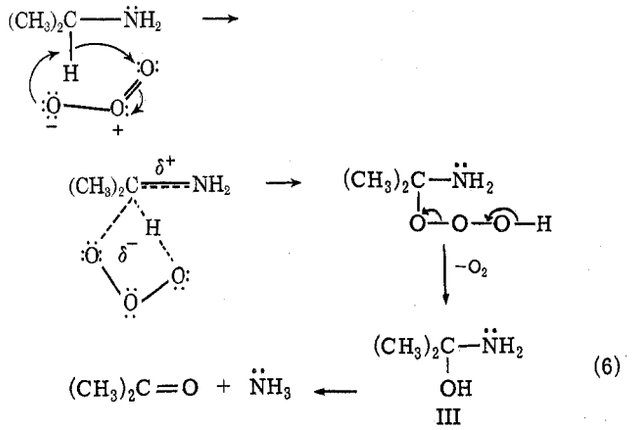
OZONATION OF ISOPROPYLAMINE AND ISOPROPYLHYDROXYLAMINE[a]

Expt[a]	Solvent[b]	Temp, °C	O_3/amine[c]	O_2 evolved/ O_3 reacting	Acetone[d]	2-Nitropropane[d]	Isopropyl isocyanate[d]	Isopropylammonium chloride[d]	Total yield,[e] %
1	$CHCl_3$	−65	1.1	*f*	4	25	18	48	95
2	$CHCl_3$	−65	1.0	*f*	5	27	15	51	98
3	$CHCl_3$	−65	0.9	0.7	6	28	15	49	97
4	$CHCl_3$	−30	0.8	0.7	10	23	5[g]	40	86
5	$CHCl_3$	−30	0.8	0.9	10	22	5[h]	47	89
6	$CHCl_3$	0	0.9	*f*	15	19	5[i]	42	90
7	$CHCl_3$	0	0.9	0.7	14	22	5[i]	46	97
8	CH_2Cl_2[j]	−78	1.1	0.8	12	36	5[k]	43	96
9	Pentane	−78	1.4	*f*	8	53	0	6[l]	67[m]
10[a]	$CHCl_3$	−65	2.0	*f*	15	51	*f*	*f*	*f*,[n]
11[a]	$CHCl_3$	0	1.2	*f*	11	44	*f*	*f*	*f*, *n*
12[a]	CH_2Cl_2[j]	−78	1.4	1.0	Trace	76	*f*	*f*	*f*, *n*
13[a]	CH_2Cl_2[j]	0	1.0	*f*	5	28	*f*	*f*	*f*, *n*

[a] In expt 1–9, the amine was isopropylamine, while in expt 10–13, isopropylhydroxylamine was employed. [b] Approximately 6–8 ml of solvent per 5 mmol of amine was employed. [c] Unless otherwise stated, each run employed 5 ± 1 mmol of amine and 6 ± 1 mmol of ozone from an ozone–nitrogen stream (see Experimental Section), which was an excess of ozone. The ratio shown is of ozone reacting to amine employed, all of which reacted. [d] Per cent yield based on amine employed, all of which reacted. [e] Total per cent yield. This equals the total amount of the isopropyl group of the amine accounted for. The total nitrogen accounted for is equal to this value minus the acetone yield. [f] Not determined. [g] In addition, an 8% yield of *N*,*N*-diisopropylurea was obtained. Yield is based on percentage of original amine ending up as urea. [h] Plus 5% diisopropylurea. See footnote *g*. [i] Plus 9–10% diisopropylurea. See footnote *g*. [j] The results constitute an average of 2–3 runs. [k] With CH_2Cl_2 solvent the product was *N*-isopropylformamide. In two of the three runs averaged in this experiment 18 ± 3 mmol of amine was employed. [l] The isopropylammonium salt cannot be the chloride, of course. It appears to be largely nitrate. [m] In addition, 2-pentanone and 3-pentanone were identified. These products are not obtained when ozone is passed into pure pentane under the same conditions. [n] No acetone oxime was detected.

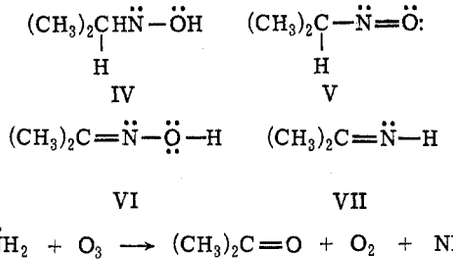
amine IV. Similar observations were made during the ozonation of *tert*-butylamine.[3] The fact that, unlike the nitrosoalkane, the alkylhydroxylamine has not been isolated or observed in the ozonations of primary amines does not cast doubt on its role as an intermediate. Because of the α effect[6] it would be expected to react with ozone faster than the parent amine.

The acetone obtained is a product expected from side-chain oxidation of the isopropylamine, whether it be by the mechanism of eq 3 (or a similar mechanism[4]) or by 1,3-dipolar insertion[7] (eq 6).



(6)

Another conceivable source of acetone is ozonation or hydrolysis of acetone oxime (VI) obtained by rearrangement of 2-nitrosopropane (V).[8] Ozonation of oximes has been found to yield the corresponding aldehyde or ketone as the major product.[9] This is thought not to be the source in the present case, however, because no indication of the presence of the oxime was observed from ozonation of either isopropylamine or isopropylhydroxylamine, even when less than 1 equiv of ozone was employed. In contrast, ozonation of *n*-butylamine did give a low yield of the corresponding oxime (Table II), but this was due to the fact that the ozonations were not carried out to completion and some nitrosobutane probably was present at the end of the ozonations. The oxime did not appear until the reaction mixture had stood overnight. Most likely, the acetone obtained from ozonation of isopropylhydroxylamine also arose from side-chain oxidation. The overall side-chain oxidation of isopropylamine to acetone, whether it be by the mechanism of eq 3 or 6, can be expressed by eq 7.



(7)

Alternatively, it is conceivable that decomposition of amino alcohol III to imine VII and water rather than to acetone and ammonia occurs. The acetone then would be derived from either ozonation or hydrolysis of VII. This route is probably minor in a protic solvent like chloroform, however, as will be discussed later in regard to ozonations of isopropylamine and *n*-butylamine in pentane.

Similar to the ozonation of *tert*-butylamine in chlorinated solvents,[3] a major product of the ozonation of isopropylamine in chloroform and methylene chloride was the corresponding ammonium chloride. Accompanying this in chloroform was isopropyl isocyanate (VIII) and (at −30 and 0°, but not at −65°) diiso-

(6) J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, **84**, 16 (1962).
(7) J. E. Batterbee and P. S. Bailey, *J. Org. Chem.*, **32**, 3899 (1967).
(8) G. B. Bachman and K. G. Strawn, *ibid.*, **33**, 313 (1968).
(9) R. E. Erickson, P. J. Andrulis, Jr., J. C. Collins, M. L. Lungle, and G. D. Mercer, *ibid.*, **34**, 2961 (1969).

propylurea (IX),[10] whereas the companion product in methylene chloride was *N*-isopropylformamide (X). These are exactly the results expected by the cation radical, ozonate anion radical pathway (initial steps expressed by eq 1 and 4, followed by eq 8–11 for the ozonation in chloroform and eq 12–14 for the ozonation in methylene chloride). Our interpretation of reactions 4 followed by 8 and 9 or 12 and 13 is that the dissociation of the amine–ozone adduct (eq 4) is reversible and goes to products only if the cation radical can readily abstract a hydrogen atom from its environment (eq 8 or 12). The ozonate anion radical and the solvent radicals of eq 9 and 13 are then in a solvent cage and react immediately at the reaction temperatures employed.

$$i\text{-PrN}\dot{\text{H}}_2^+ + \text{CHCl}_3 \longrightarrow i\text{-PrNH}_3^+ + \cdot\text{CCl}_3 \quad (8)$$

$$\dot{\text{O}}_3^- + \cdot\text{CCl}_3 \longrightarrow \text{O}\overset{\curvearrowright}{\text{O}}\text{O}\overset{\curvearrowright}{\text{O}}\text{C}(\text{Cl})(\text{Cl})\text{Cl} \longrightarrow$$

$$\text{O=CCl}_2 + \text{O}_2 + \text{Cl}^- \quad (9)$$

$$\text{O=CCl}_2 + 3\,i\text{-PrN}\ddot{\text{H}}_2 \longrightarrow i\text{-PrN=C=O} + 2\,i\text{-PrNH}_3\text{Cl}^- \quad (10)$$

VIII

$$i\text{-PrN=C=O} + i\text{-PrN}\ddot{\text{H}}_2 \longrightarrow i\text{-PrNHCNH-}i\text{-Pr} \quad (11)$$

IX

$$i\text{-PrN}\dot{\text{H}}_2^+ + \text{CH}_2\text{Cl}_2 \longrightarrow i\text{-PrNH}_3^+ + \cdot\text{CHCl}_2 \quad (12)$$

$$\dot{\text{O}}_3^- + \cdot\text{CHCl}_2 \longrightarrow \text{O}\overset{\curvearrowright}{\text{O}}\text{O}\overset{\curvearrowright}{\text{O}}\text{C}(\text{H})(\text{Cl})\text{Cl} \longrightarrow$$

$$\text{O=CCl(H)} + \text{O}_2 + \text{Cl}^- \quad (13)$$

$$\text{HCCl(=O)} + 2\,i\text{-PrNH}_2 \longrightarrow i\text{-PrN(H)CH(=O)} + i\text{-PrNH}_3\text{Cl}^- \quad (14)$$

X

As was also true with the *tert*-butylamine ozonations,[5] the ozonate anion radical ($\cdot O_3^-$) was observed both by its pink color and by epr during ozonation of isopropylamine in methylene chloride at −95° or pentane at −120°. In these cases an actual buildup of crystalline isopropylammonium ozonate occurs. This should deter reaction 13 from occurring. However, no 1,1,2,2-tetrachloroethane was found in the methylene chloride reaction mixture. Under these conditions the solvent radical is probably destroyed by interaction with molecular oxygen, which is a product of reaction pathways 5 and 7. Oxygen has been shown to be a powerful scavenger of these radicals in similar situations.[11] It is possible that even under ordinary conditions oxygen competes with the ozonate anion radical (eq 9 and 13) for the solvent radical, to give $\cdot\text{OOCCl}_3$. This radical then could decompose to phosgene and $\cdot$OCl. Additional data and arguments favoring the ion-radical mechanisms can be found elsewhere.[2,3,5]

A combination of eq 1, 4, 8, 9, and 10 gives eq 15, which expresses the ion-radical pathway for the isopropylamine ozonation in chloroform at −65°. The data of expt 1–3 (Table I) fit fairly well the ammonium chloride/isocyanate ratio predicted by eq 15, although on the average the experimental ratio is slightly high. This possibly is due to some loss of isocyanate through hydrolysis, or to minor side reactions which produce hydrogen chloride. A similar summation for the ozonation in methylene chloride predicts a higher formamide/ammonium salt ratio than found in expt 6 (Table I).

$$4\,i\text{-PrNH}_2 + \text{CHCl}_3 + \text{O}_3 \longrightarrow i\text{-PrN=C=O} + 3\,i\text{-PrNH}_3\text{Cl}^- + \text{O}_2 \quad (15)$$

This is undoubtedly due to considerable decomposition of formyl chloride to carbon monoxide and hydrogen chloride before interaction with isopropylamine. It is interesting to note that formamide was not observed at all as a product of the ozonation of *tert*-butylamine in methylene chloride;[3] the more hindered amine apparently has no chance at all of reacting with the formyl chloride before it decomposes. The reaction of isopropylamine with the decomposed formyl chloride is represented by eq 16. Summation of eq 1, 4, 12, 13, 14, and 16, giving twice as much weight to eq 16 as eq 14, results in eq 17 as a reasonable representation of the ion-radical pathway in methylene chloride at −78°.

$$\text{HCCl(=O)} + i\text{-PrNH}_2 \longrightarrow i\text{-PrNH}_3\text{Cl}^- + \text{CO} \quad (16)$$

$$7i\text{-PrNH}_2 + 3\text{O}_3 + 3\text{CH}_2\text{Cl}_2 \longrightarrow 6i\text{-PrNH}_3\text{Cl}^- + \text{HCNH-}i\text{-Pr(=O)} + 2\text{CO} + 3\text{O}_2 \quad (17)$$

Equation 18 is the summation of eq 5 (amine oxide pathway), 7 (side-chain oxidation), and 15 (ion-radical pathway) for the ozonation of isopropylamine in chloroform at −65°, assuming approximate weightings of 55, 10, and 35%, respectively, for the above pathways. Equation 19 is a similar summation of eq 5, 7, and 17, giving weights of 50, 20, and 30%, respectively, for the three pathways in the −78° methylene chloride ozonation. Below each product in these equations is the theoretical yield as dictated by the equation (below ozone is the ozone/amine ratio). It can be seen that the equations describe the data of expt 1–3 (chloroform) and 8 (methylene chloride) of Table I quite adequately, with the exceptions that the experimental O_3/amine ratios are slightly low and the oxygen yield is low, especially considering that the equations do not include any ozonation of ammonia. These discrepancies are perhaps caused by the fact that the oxygen evolved

(10) Isopropyl isocyanate was found to react very slowly with isopropylamine at −65° to give the urea. *tert*-Butyl isocyanate does not react at all with *tert*-butylamine at −65°.

(11) W. J. Lautenberger, E. N. Jones, and J. G. Miller, *J. Amer. Chem. Soc.*, **90**, 1110 (1968).

TABLE II

OZONATION OF *n*-BUTYLAMINE

Expt[a]	Solvent	Temp, °C	O_3/amine[b]	O_2/O_3[c]	Products[m] A[d,e]	B[d]	C[d,f]	D[d,e]	E[d,e]	F[d]	G[d,e]	H[d,e]	Total C[g,h]	Total N[g]
14	Pentane[i]	−60	1.5	0.7	11	14	18[e,f]	0	*j*	0	2.5	4	67	67
15	$CHCl_3$	−60	1.1	0.6	2	18	36	7.5[k]	5	4	0.5	3	94	84
16	$CHCl_3$	0	1.1	0.7	7.5	14	29	5.5[k]	2.5	0	*l*	*l*	74	65
17	CH_2Cl_2	−60	1.1	0.7	4	17	20	2.5[k]	0	6.5	*l*	*l*	56	52
18	CCl_4	−25	1.0	0.7	6	13	27	5[k]	0	0	*l*	*l*	62	56

[a] Reactions were run on a 5-, 10-, or 20-mmol scale employing approximately 2.5 ml of solvent per millimole of amine. The results shown were obtained from several different runs in each solvent, as described in the Experimental Section. [b] In each case 1 mmol of ozone (in a nitrogen stream) per millimole of starting amine was employed and reacted completely. Unreacted amine was determined and the ratio is that of ozone reacting to amine reacting. [c] Ratio of molecular oxygen evolved per mole of ozone reacting. [d] These values equal the number of moles of product (rounded off to the nearest half mole) obtained per 100 mol of *n*-butylamine (see footnote *e*). [e] In these cases the actual percentage yield is twice the value shown, since 2 mol of amine were required to produce 1 mol of product (see footnote *d*). [f] In expt 14 the salt is in the form of the nitrate and arose from 2 mol of amine, one to form the ammonium ion and one to form the nitrate. [g] The total C is the total percentage yield based on an accounting of the butyl group; the total N is the total percentage yield based on an accounting of nitrogen. [h] Small amounts of butyraldehyde and butyric acid also were detected in all cases. In expt 15, propionic acid also was detected. [i] Also detected among the products were 1–2% yields of a mixture of 2- and 3-pentanol and 8% yields of 2- and 3-pentanone. Yields are based on ozone reacting, since these are oxidation products of the solvent. [j] A trace was detected. [k] It is possible that these values are high by the amount of formamide and butyramide present, since the NH peak used in the nmr determination could have included all three amides through hydrogen exchange. [l] Not determined. [m] A is PrCH=NBu; B is $BuNO_2$; C is $BuNH_3^+$, Cl^-, or NO_3^-; D is BuNH(C=O)NHBu; E is $PrCH{=}N^+O^-Bu$; F is PrCH=NOH; G is Pr(C=O)NHBu; H is H(C=O)NHBu.

is singlet oxygen,[12] and it may be reacting in place of ozone as an oxidant to some extent.

$$\underset{1.02}{41i\text{-PrNH}_2} + 42O_3 + 7CHCl_3 \longrightarrow$$

$$\underset{27\%}{11i\text{-PrNO}_2} + \underset{5\%}{2Me_2C{=}O} + \underset{51\%}{21i\text{-Pr}\overset{+}{N}H_3\bar{Cl}} +$$

$$\underset{17\%}{7i\text{-PrN}{=}C{=}O} + \underset{100\%}{42O_2} + 2NH_3 + 11H_2O \quad (18)$$

$$\underset{1.4}{14i\text{-PrNH}_2} + 20O_3 + 3CH_2Cl_2 \longrightarrow$$

$$\underset{36\%}{5i\text{-PrNO}_2} + \underset{14\%}{2Me_2C{=}O} + \underset{43\%}{6i\text{-Pr}\overset{+}{N}H_3\bar{Cl}} +$$

$$\underset{7\%}{i\text{-PrNHCH}\overset{\|}{O}} + \underset{100\%}{20O_2} + 5H_2O + 2NH_3 + 2CO \quad (19)$$

A comparison of expt 4 and 5 (ozonation at −30°) and 6 and 7 (ozonation at 0°) with expt 1–3 (ozonation at −65°) reveals that there is a temperature effect in the ozonation of isopropylamine similar to the one found earlier in the ozonation of tri-*n*-butylamine,[4] although not as great. If one does a similar summation with the −30 and 0° chloroform data as was done with the −65° data, it can be seen that the ratios of amine oxide to side-chain oxidation to ion-radical pathways are approximately 50:30:20 for the −30° reaction and 40:30:30 for the 0° ozonation, compared to 55:10:35 for the −65° reaction.

The data obtained from ozonation of isopropylamine in pentane is more difficult to interpret, since the total accounting of starting material in terms of products is not as great. The same is true with the ozonation of *n*-butylamine in pentane, and these reactions will be discussed together later.

The ozonation of *n*-butylamine required 1.6–1.9 molar equiv of ozone compared to less than 1.0 for isopropylamine. This difference is due to the greater reactivity of the primary ozonation products toward ozone in the case of butylamine. Table II contains the data obtained from the ozonation of *n*-butylamine in various solvents. In each case only 1 mol of ozone per mole of amine was employed. The amount of unreacted amine was determined and the product yields are based on unrecovered amine.

Since the only good accounting of reacting starting material in terms of determined products occurred with the ozonation in chloroform at −60°, only these data will be discussed in detail. The *n*-butylammonium chloride and *N*,*N*′-di-*n*-butylurea (XI) are products expected from the ion-radical pathway. In this case only the urea and no isocyanate was observed, due largely to the fact that amine was still present to react with any isocyanate when the reaction mixture was allowed to come to room temperature. When the ozonation of *n*-butylamine was carried out at −60° using 1.6–1.9 molar equiv of ozone, a small amount of isocyanate was observed in the reaction mixture. A summation of the *n*-butylamine equivalents of eq 1, 4, and 8–11 gives eq 20 for the ion-radical pathway in the ozonation of *n*-butylamine. As with the *tert*-butylamine[5] and isopropylamine ozonations, the ozonate

$$5BuNH_2 + O_3 + CHCl_3 \longrightarrow$$

$$3Bu\overset{+}{N}H_3\bar{Cl} + \underset{\text{XI}}{BuNHC(=O)NHBu} + O_2 \quad (20)$$

anion radical was identified by epr during low-temperature ozonations in pentane at −100°.

By analogy to the other primary amine ozonations, 1-nitrobutane (XII) is the expected major product of the amine oxide pathway, as expressed by eq 21.[3] The

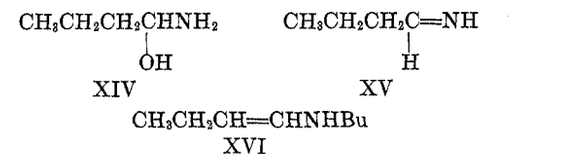
$$BuNH_2 + 3O_3 \longrightarrow \underset{\text{XII}}{BuNO_2} + 3O_2 + H_2O \quad (21)$$

butyraldoxime XIII, found in low yield, must also be a product of the amine oxide route, *via* isomerization of the nitrosobutane intermediate, as proposed previously by Bachman and Strawn.[8] The amine oxide route to the oxime can be expressed by eq 22.

$$BuNH_2 + 2O_3 \longrightarrow \underset{\text{XIII}}{PrCH{=}NOH} + HOH + 2O_2 \quad (22)$$

(12) R. W. Murray, W. C. Lumma, Jr., and J. W.-P. Lin, *J. Amer. Chem. Soc.*, **92**, 3205 (1970).

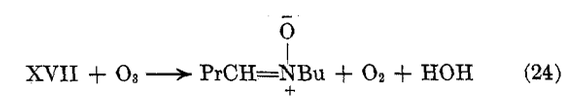
The other observed products are best explained by the side-chain oxidation pathway involving the formation of amino alcohol XIV as the primary product (*via* either the mechanism of eq 3 or of eq 6). Dehydration of XIV would give imine XV, whereas deamination would give butyraldehyde. In a protic solvent the latter would appear more likely, at least at low temperatures, as will be discussed later. This is thought to be the explanation for the better accounting of products in expt 15 (Table II) than in expt 14 or 16, where unstable XV was probably an important intermediate. Butyraldehyde was observed as a minor product, as was its oxidation product, butyric acid. Addition of butylamine to butyraldehyde yields amino alcohol XVII, which appears to be the key intermediate in the formation of at least three of the remaining determined products. Dehydration of XVII could occur in two ways, to give imine XX, a minor product, or



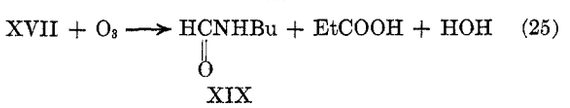
XIV XV

XVI

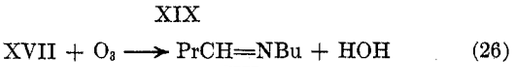
XVII (23)



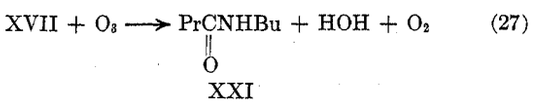
XVIII (24)



XIX (25)



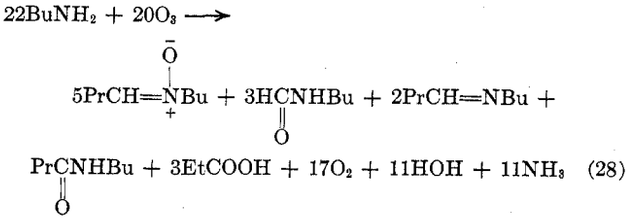
XX (26)



XXI (27)

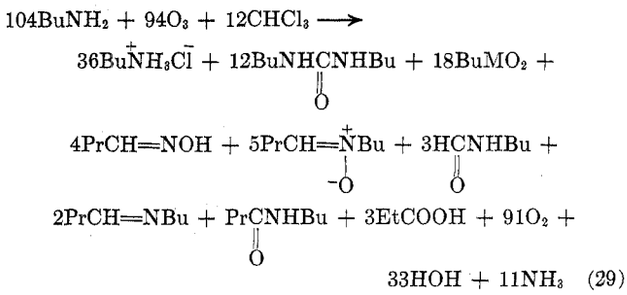
enamine XVI, which could undergo ozonolysis to formamide XIX, another minor product. Further side-chain oxidation of amino alcohol XVII (*via* a geminal diol) would produce *N*-butylbutyramide (XXI), also a minor product. The intermediacy of XVII in the formation of XIX and XXI finds analogy in the earlier reported results of ozonation of tri-*n*-butylamine.[4] The probable route to nitrone XVIII is *via* the amine oxide of XVII, followed by dehydration.

The reactions just discussed can be expressed by eq 23, followed by eq 24–27. If one sums these equations, multiplying eq 24, 25, 26, and 27 by 5, 3, 2, and 1, respectively (see Table II), and eq 23, consequently, by 11, eq 28 results as a representation of the side-chain oxidation pathway in the ozonation of *n*-butylamine.



(28)

By summation of eq 28 with 12 times eq 20 for the ion-radical pathway, 18 times eq 21 and 4 times eq 22, for the amine oxide pathways (see Table II), one arrives at eq 29 for the ozonation of *n*-butylamine. It can be seen that this fits the data of Table II quite well, except for the urea yield, the ozone to amine ratio, and



(29)

the oxygen to ozone ratio. The low urea yield most likely is due to some loss of phosgene during the ozonation and the low oxygen yield is perhaps due to some involvement of singlet oxygen in the amine oxidation, as was also suggested for the ozonation of isopropylamine. The fact that more ozone was actually used in the ozonation than implied by equation 29 most likely is due largely to the fact that the equation does not take into account any ozonation of ammonia. Undoubtedly, some of the ammonia escaped, but some was oxidized. The oxidation would require between 2 and 4 molar equiv of ozone.

If eq 29 is a reasonable representation of the *n*-butylamine ozonation, it and the equations leading up to it show that the ratio of moles of amine initially attacked by ozone *via* the amine oxide, the ion-radical, and the side-chain ozonation pathways is 22:12:11, respectively, or, on a percentage basis, 49, 27, and 24%.

As has already been mentioned, the accounting of both isopropylamine (Table I) and *n*-butylamine (Table II) in terms of products from the ozonations in pentane is poor. The identity and source of the missing products are uncertain, but it seems most likely that they are side-chain oxidation products. It is quite likely that major products of side-chain oxidation of both isopropylamine and *n*-butylamine in pentane are the corresponding imines VII and XV, from expulsion of water rather than ammonia from the corresponding amino alcohols III and XIV. In a nonprotic solvent hydroxyl should be a better leaving group than amino, whereas the opposite might be expected to be true in a protic solvent such as chloroform, at least at the temperature of expt 15 (Table II), due to the greater basicity of the amino group over that of the hydroxyl group. The chemistry expected of simple imines such as VII and XV is not clear. The most likely fate for VII or XV is polymerization.[13] Polymeric material was detected in the ozonation products of both isopropylamine and *n*-butylamine. Low yields of identified products from dye-sensitized photochemical autoxidation of butylamine are also thought to be due to polymerization of imine XV.[14]

The detection of pentanols and pentanones from ozonations of isopropylamine and of *n*-butylamine in

(13) E. M. Smolin and L. Rapoport in "The Chemistry of Heterocyclic Compounds," Vol. 13, A. Weissberger, Ed., Interscience, New York, N. Y., 1969, pp 505–509.

(14) F. C. Schaefer and W. D. Zimmermann, *J. Org. Chem.*, **35**, 2165 (1970).

pentane is analogous to similar findings with *tert*-butylamine.[3] Since the pentanones were not observed from ozonations of pentane in the absence of an amine, they are thought to evolve from the ion-radical pathway by mechanisms previously described.[3] These involve no overall loss of amine. It is noteworthy that the yield of isopropylammonium salt determined in the ozonation of isopropylamine in pentane is approximately equal to the acetone yield (Table I, expt 9) and that a similar correlation can be seen between the *n*-butylammonium salt yield and the sum of the yields of imine XX, *N*-butylbutyramide, and *N*-butylformamide from ozonation of *n*-butylamine in pentane (Table II, expt 14). These salts are thought to be nitrates and probably arise from oxidation of the ammonia expelled during formation of the stated products, followed by reaction of the resulting nitric acid with unreacted amine, rather than by an ion-radical pathway.

Thus, it appears that the products resulting from ozonation of isopropylamine and *n*-butylamine in pentane arise by the amine oxide and side-chain oxidation routes only. If the assumption is made that the products not accounted for in these ozonations are side-chain oxidation products, it can be shown, by calculations similar to those already made, that the proportions of amine oxide to side-chain oxidation occurring during attack of ozone on isopropylamine and *n*-butylamine in pentane are 56:44 and 22:78, respectively, as shown in Table III.

TABLE III

COMPETITIONS IN OZONATIONS OF PRIMARY AMINES HAVING TERTIARY, SECONDARY, AND PRIMARY ALKYL GROUPS

Amine	Solvent	Temp, °C	Amine oxide pathway[a]	Ion radical pathway[a]	Side-chain oxidation[a]
t-Bu	$CHCl_3$	−65, −60	50	50	*b*
i-Pr	$CHCl_3$	−65	55	35	10
n-Bu	$CHCl_3$	−60	49	27	24
i-Pr	$CHCl_3$	−30	50	20	30
i-Pr	$CHCl_3$	0	40	30	30
t-Bu	Isooctane	−78	100	*c*	*b*
i-Pr	Pentane	−78	56	*c*	44
n-Bu	Pentane	−60	22	*c*	78

[a] Approximate percentages by each pathway. [b] Not possible in this case. [c] Occurs to some extent, but does not show up in products derived from the amine.

Table III compares the results of ozonation of *tert*-butylamine,[3] isopropylamine, and *n*-butylamine in chloroform at −60 to −65° and in pentane at −60 to −78°. In the ozonations in chloroform solution the amine oxide pathway is the major pathway in all three cases. The ion-radical pathway decreases in importance in going from *tert*-butyl to isopropyl to *n*-butyl. This could simply reflect the increasing side-chain oxidation, but also may indicate a steric factor; the equilibrium between the adduct and the ion radicals may shift slightly in favor of the ion radicals as bulk around the nitrogen increases.

Table III also shows that there is a much greater solvent effect with *n*-butylamine than with isopropylamine. With isopropylamine there is no change in the percentage of amine oxide pathway and only a 34% variation in the side-chain oxidation pathway in going from chloroform to pentane at −65 to −78°. In contrast, with *n*-butylamine there is a 27% decrease in the amine oxide pathway and a 54% increase in the side-chain oxidation pathway in going from chloroform to pentane. The *n*-butylamine solvent effect is similar to that of tri-*n*-butylamine.[4] This suggests that side-chain attack with isopropylamine may occur to a large extent by the 1,3-dipolar insertion mechanism (eq 6), whereas that with *n*-butylamine and tri-*n*-butylamine occurs predominantly by the mechanism of eq 3. A solvent effect is expected in the competition between reactions 2 and 3, but not between reactions 2 and 6.[4] There are also indications of this difference in the ozonation of triisopropylamine.[15] The increase in the side-chain oxidation pathway in going from isopropylamine to *n*-butylamine in chloroform appears to be largely a statistical factor, but also may reflect this difference in mechanism. The small temperature effect noted in the ozonation of isopropylamine is possibly due to a decreasing stability of the amine–ozone adduct with increasing temperature and a consequential increase in 1,3-dipolar insertion at the side chain. It is not possible to judge from Table II whether there is a temperature effect in the ozonation of *n*-butylamine or whether there is a solvent effect involving methylene chloride and carbon tetrachloride.

Experimental Section

Materials.—The isopropylamine and *n*-butylamine were J. T. Baker reagent grade. They were dried over potassium hydroxide and distilled before use. *N*,*N*′-Di-*n*-butylurea[16] and *N*,*N*′-diisopropylurea[17] were prepared by treatment of the corresponding primary amine with phosgene or the corresponding isocyanate in ether or chloroform solution. Formylation of *n*-butylamine with chloral afforded *N*-*n*-butylformamide.[18,19] Isopropylhydroxylamine,[20,21] *N*-isopropylformamide,[22,23] *N*-*n*-butylbutyramide,[24,25] and *N*-*n*-butylidene-*n*-butylamine[26,27] were prepared and purified by standard procedures. *C*-propyl-*N*-butyl nitrone was synthesized by the general method of Utzinger,[28] involving hydrogen peroxide oxidation of the corresponding hydroxylamine (di-*n*-butylhydroxylamine), which was, in turn, synthesized by the amine oxide pyrolysis method of Cope[29] starting with tributylamine.[3] The dibutylhydroxylamine melted at 51–52°.[29] The nitrone gave important ir absorptions (CCl_4) at 1587 (C=N) and 1178 cm^{-1} (N^+O^-) and nmr absorptions (CCl_4) at δ 6.52 (t, 1, J = 6 Hz, CH=N), 3.60 (t, 2, J = 7 Hz, CH_2N), 2.35 (m, 2, CH_2CH=N), 1.57 (m, 6, CH_2CH_2CH=$NCH_2CH_2CH_2$), 1.00 (t, 3, CH_3), and 0.98 ppm (t, 3, CH_3). The other materials used were obtained commercially and purified, when necessary, by standard procedures.

General Equipment and Procedures.—The ozonation setup and procedures, including the use of ozone–nitrogen and the determination of molecular oxygen yields, are described in

(15) P. S. Bailey, D. E. Lerdal, and T. P. Carter, Jr., results to be reported shortly.
(16) F. Cramer and M. Winter, *Chem. Ber.*, **92**, 2761 (1959).
(17) T. Curtius, *J. Prakt. Chem.*, **125**, 152 (1930).
(18) F. F. Blicke and C. J. Lu, *J. Amer. Chem. Soc.*, **74**, 3933 (1952).
(19) P. L. deBenneville, J. S. Strong, and V. T. Elkind, *J. Org. Chem.*, **21**, 772 (1956).
(20) W. R. Dunslan and E. Goulding, *J. Chem. Soc.*, **75**, 792 (1899).
(21) P. A. S. Smith, H. R. Alul, and R. L. Baumgarten, *J. Amer. Chem. Soc.*, **86**, 1139 (1964).
(22) H. Morawetz and P. S. Otaki, *ibid.*, **85**, 463 (1963).
(23) L. A. LaPlanche and M. T. Rogers, *ibid.*, **86**, 337 (1964).
(24) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 2nd ed, Longmans, Green and Co., London, 1951, pp 396–397.
(25) K. Heyns and W. von Bebenburg, *Justus Liebigs Ann. Chem.*, **595**, 55 (1955).
(26) K. N. Campbell, A. H. Sommers, and B. K. Campbell, *J. Amer. Chem. Soc.*, **66**, 82 (1944).
(27) W. S. Emerson, S. M. Hess, and F. C. Uhle, *ibid.*, **63**, 872 (1941).
(28) G. E. Utzinger, *Justus Liebigs Ann. Chem.*, **556**, 50 (1944);
(29) A. C. Cope and H.-H. Lee, *J. Amer. Chem. Soc.*, **79**, 964 (1957).

earlier papers.[30] Ir spectra were recorded with a Beckman IR-5A double-beam infrared spectrophotometer and mass spectra were obtained with a Consolidated Engineering Corp. 21-491 double-focusing medium-resolution mass spectrograph.

Epr Procedures.—All spectra were recorded with a Varian Associated V-4502 spectrometer equipped with a Varian field dial and a 9-in. magnet using a modulation frequency of 100 kcps.[31] Special techniques for recording spectra while ozonating were described earlier.[5]

Glpc determinations were made with either a Varian Aerograph 1520B dual-column chromatograph equipped with hydrogen flame ionization detectors and a Beckman recorder and disk integrator or with an F & M 500 gas chromatograph, equipped with a disk integrator. Yields were determined by the internal standard method with the Aerograph 1520B and by comparison with standard solutions of known compounds with the F & M 500. With the Aerograph 1520B the following columns were employed: (1) 20% Dowfax 9N9, 2.5% NaOH on Chromosorb W, $^1/_{16}$ in. × 10 ft; (2) 30% silicone gum rubber SE-30 on Chromosorb P, acid washed, $^1/_{16}$ in. × 10 ft; (3) 15% Carbowax 20M on Chromosorb W (AW), $^1/_{16}$ in. × 10 ft; (4) 5% DEGS, 2% H_3PO_4 on Chromosorb P, $^1/_{16}$ in. × 10 ft; (5) 5% Versamid 900 on Chromosorb G (AW), $^1/_{16}$ in. × 5 ft. With the F & M 500 the following columns were employed: (6) 20% Carbowax 20M on Chromosorb P, $^1/_4$ in. × 15 ft; (7) 10% Carbowax 20M–10% NaOH on Chromosorb P, $^1/_4$ in. × 20 ft; (8) 5% Celanese ester #9 on Haloport F, $^1/_4$ in. × 10 ft; (9) 30% silicone gum rubber SE-30 on Chromosorb P, $^1/_4$ in. × 10 ft.

A Varian Aerograph A-90-P3 gas chromatograph was used for preparative work.

Nmr Spectra and Procedures.—A Varian A-60 spectrometer was used for ordinary spectra, whereas a Varian HA-100 instrument was used for most quantitative analyses using, usually, 1-nitropropane as an internal standard. Chemical shifts are reported on the δ scale, with TMS internal standard. Important spectra observed follow: *n*-butylamine (CCl_4), 2.64 (t, 2, J = 6 Hz, CH_2N), 1.52 (s, 2, NH_2), 1.40 (m, 4, $CH_2CH_2CH_2N$), 0.92 (t, 2, CH_3); *N*-*n*-butyl-*n*-butyramide ($CDCl_3$), 6.49 (1, NH), 3.24 (m, 2, CH_2N), 2.18 (t, 2, J = 7 Hz, CH_2CO), 1.48 (m, 6, $CH_2CH_2CH_2NCOCH_2CH_2$), 0.94 (t, 3, CH_3), 0.91 (t, 3, CH_3); *N*-*n*-butylformamide ($CDCl_3$), 8.16 (s, 1, CHO), 3.30 (m, 2, CH_2N), 1.42 (m, 4, $CH_2CH_2CH_2N$), 0.94 (t, 3, CH_3); *N*,*n*-butylidene-*n*-butylamine (CCl_4), 7.57 (t, 1, J = 4 Hz, CH=N), 3.29 (t, 2, J = 6 Hz, CH_2N), 2.17 (m, 2, CH_2CH=N), 1.43 (m, 6, CH_2CH_2CH=$NCH_2CH_2CH_2$), 0.94 (t, 3, CH_3), 0.92 (t, 3, CH_3); *n*-butyraldoxime (CCl_4), 9.91 (broad s, 1, OH), 7.34 (t, 0.5, J = 6 Hz, CH=N), 6.65 (t, 0.5, J = 6 Hz, CH=N), 2.27 (m, 2, CH_2CH=N), 1.52 (m, 2, CH_2CH_2CH=N), 0.96 (t, 1.5, CH_3), 0.94 (t, 1.5, CH_3); *N*,*N*′-di-*n*-butylurea ($CDCl_3$), 5.67 (2, NH), 3.16 (m, 4, CH_2N), 1.39 (m, 8, $CH_2CH_2CH_2N$), 0.92 (t, 6, CH_3); 1-nitrobutane (CCl_4), 4.37 (t, 2, J = 7 Hz, CH_2NO_2), 2.00 (m, 2, $CH_2CH_2NO_2$), 1.42 (m, 2, $CH_2CH_2CH_2NO_2$), 0.98 (t, 3, CH_3); *N*-isopropylformamide (CCl_4), 1.16 (d, CH_3), 4.00 (heptet, CHN), 7.93 (s, CHO).

Ozonation of Isopropylamine and Isopropylhydroxylamine.—Ozonations were generally run on a 5 ± 1 mmol scale in 6–8 ml of solvent[32] and using 6 ± 1 mmol of ozone (a slight excess), from an ozone–nitrogen stream, at the designated (Table I) temperature. A pale blue color (of 2-nitrosopropane) developed immediately and persisted until the ozonation was nearly complete and, in the methylene chloride and chloroform runs with isopropylamine, a white solid (the ammonium chloride) precipitated. An excess of ozone was employed because of difficulty in determining unreacted isopropylamine by glpc, due to tailing with some columns and conversion of isopropylammonium chloride to free amine by others. The amount of excess ozone was determined by titration of the iodine produced in the iodide trap. The reaction mixture was brought to room temperature and diluted to a known volume of solvent, and the liquid components were determined by glpc, using the F & M 500. Column 6 (above) was used for the determinations of acetone, 2-nitropropane, and isopropylformamide (at column temperatures of 75, 125, and 200°, respectively), and column 8 was used for the isopropyl isocyanate determination at a column temperature of 50°. The isopropylammonium chloride was determined by evaporating the reaction mixture, drying the residue for 24 hr in a vacuum desiccator, and weighing it. It was completely water soluble and was shown to be the salt by comparing its ir spectrum with that of an authentic sample and by conversion to isopropylamine with base. The isopropylamine was determined by glpc using column 7. In one instance a chloride determination was made. Results are shown in Table I.

Infrared spectra of the reaction mixture confirmed the presence of the above substances, showing peaks at 1720 (acetone carbonyl), 1675 (isopropylformamide carbonyl), 1543 and 1357 (nitro group), and 2275 cm^{-1} (isocyanate). A qualitative test for ammonia in the effluent from one reaction mixture was made by using an ethereal hydrogen chloride trap at −78° and evaporating the ether to give a white solid, which gave a positive test.[33]

In ozonations of isopropylamine in chloroform at −30 and 0°, *N*,*N*′-diisopropylurea was a product. It was determined by weighing the residue from evaporation of the reaction material after the isopropylammonium chloride had been extracted with water. It melted at 186–188°[17] and absorbed at 1661 cm^{-1} (urea carbonyl) in the ir.

From isopropylamine ozonations in pentane, 2- and 3-pentanone was qualitatively identified by glpc using column 6 at a column temperature of 145°. These were not produced when pentane alone was ozonized. Evaporation of the pentane ozonation solution to dryness gave a residue which was shown by mass spectroscopy to contain some polymeric material (m/e over wide range, continuing in excess of 200), perhaps from polymerization of imine VII. Part of the residue, however, was soluble in water and gave a positive nitrate ion test.[34] Treatment with base converted it to isopropylamine, which was determined by glpc on column 7. On this basis the residue was listed in Table I as isopropylammonium nitrate.

Ozonation of isopropylamine in methylene chloride at −95° gave a reddish solution which became colorless when the temperature was allowed to rise. The reaction mixture was analyzed for 1,1,2,2-tetrachloroethane by glpc, using column 9, but none was found. By epr the red solution was shown to contain the ozonate anion radical.[5] The anion radical also was shown to be strongly present from ozonation of isopropylamine in pentane at −120°. In this case, a red precipitate formed.

Ozonation of *n*-butylamine in chlorinated solvents afforded a pale yellow solution containing a white solid. The data shown in Table II resulted from numerous runs employing 5, 10, or 20 mmol of amine in 2.5 ml of solvent per millimole of amine and utilizing 1 mol of ozone (in a nitrogen stream) per mole of amine. Product determinations were performed as follows. Determinations by glpc were carried out with 1-nitrobutane (column 2 at a column temperature of 90° and toluene as an internal standard), butyraldehyde (column 3, column temperature 90°, ethylbenzene as internal standard), and *N*-*n*-butylbutyramide and *N*-*n*-butylformamide (column 5, 170°, phenyl propyl ketone internal standard). It was impossible to determine unreacted butylamine by glpc with chloroform as solvent because the two came off together. After these determinations were made, the reaction mixture was extracted with aqueous potassium hydroxide. The extract was acidified and carefully extracted with ether. Butyric acid was determined on the ether extract, using column 4 at a temperature of 120° with phenyl propyl ketone as internal standard. A small propionic acid peak was also detected, but not determined quantitatively. With 1-nitrobutane as the internal standard (peak at δ 4.38 ppm) the following substances were then determined by nmr from a $CDCl_3$ ozonation solution and using the HA-100 spectrometer: unreacted *n*-butylamine (δ 2.89, CH_2N), *N*-*n*-butylidene-*n*-butylamine (δ 7.72, CH=N), *C*-*n*-propyl-*N*-*n*-butylnitrone (δ 6.67, CH=N), and *n*-butyraldoxime (δ 7.39, CH=N); the butyraldoxime peak did not show up until the reaction mixture had been kept in the refrigerator overnight. The *n*-butylammonium chloride was determined in a 10-mmol run by partially evaporating the solvent, extracting the salt with water, and determining chloride ion in the aqueous extract by standard methods. A D_2O extract of the residue was shown to contain largely the butylammonium salt, by comparison with an authentic sample (nmr). The organic layer was then

(30) A. M. Reader, P. S. Bailey, and H. M. White, *J. Org. Chem.*, **30**, 784 (1965), and references cited therein.

(31) This instrument was made available to the Chemistry Department through NSF Grant GP-2090.

(32) During ozonations carried out in nonpolar solvents (pentane, isooctane, and carbon tetrachloride) a black, particulate material appeared in the iodide trap.

(33) N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," 2nd ed, Interscience, New York, N. Y., 1960, Chapter 5.

(34) P. Arthur and O. M. Smith, "Semimicro Qualitative Analysis," 3rd ed, McGraw-Hill, New York, N. Y., 1952, p 263.

evaporated to a thick oil, $CDCl_3$ was added, and the *N,N'*-di-*n*-butylurea was determined by nmr (δ 5.55, NH), using 1,4-dioxane (δ 3.69) as an internal standard. Although the urea peak employed appears to be distinctive in comparison to those of the other amides, it is possible that a mixture of all three amides would have a common NH peak due to hydrogen exchange, thereby causing the urea value to be high. Molecular oxygen analyses were carried out by standard procedures already referenced.

In a few instances the amine was ozonized in chloroform at −60° with an excess (2–3 molar equiv) of ozone, resulting in the reaction of 1.6–1.9 molar equiv of ozone. The major products were the nitrobutane and the *tert*-butylammonium chloride. Small amounts of *n*-butyric acid, *N*-*n*-butyl-*n*-butyramide, and *n*-butyl isocyanate (column 2, 90°) were detected by glpc. Quantitative determinations were made, however, only in the case of the *n*-butylammonium chloride (36% yield).

Ozonation of *n*-butylamine (20 mmol) in pentane at −60° with 1 molar equiv of ozone resulted in the formation of a white solid which melted and settled to the bottom as a small yellow aqueous layer when the reaction mixture was allowed to warm to room temperature. The two layers were separated and analyzed independently. The *pentane layer* was analyzed for 1-nitrobutane, *N*-*n*-butyl-*n*-butyramide, and *N*-*n*-butylformamide by glpc in the same manner as described for ozonations in chlorinated solvents. Glpc determinations were also employed for unreacted butylamine and *N*-*n*-butylidene-*n*-butylamine (column 1, 75° for 4 min and 75–175° at 6°/min, propylbenzene as internal standard), and the pentanones and pentanols (column 3, 90°, ethylbenzene as internal standard); the 2- and 3-pentanones were not separable from each other and are reported together in Table II. A trace of *C*-*n*-propyl-*N*-*n*-butylnitrone was shown to be present by nmr (see details under chlorinated solvent experiments).

A portion of the *aqueous phase* was dissolved in acetone and traces of pentanones and pentanols were determined by glpc using the procedure already described. The aqueous phase was concentrated at room temperature under reduced pressure (6 mm) for 40 min and the volatile material was trapped at −70° and weighed. This was shown to be composed of water and unreacted amine; the amounts were obtained by integration. The residue from the aqueous phase was extracted with chloroform and analyzed by glpc for *N*-*n*-butyl-*n*-butyramide and *N*-*n*-butylformamide, using the procedure already described. The *n*-butylammonium cation was determined by nmr ($BuNH_3^+$ peak at δ 7.09) on a portion of the original residue, using the butyramide as an internal standard ($EtCH_2CONHBu$ at δ 2.17). Since the residue gave a positive nitrate anion test,[3a] the salt is reported in Table II as the nitrate. In a separate experiment, a trace of butyric acid was identified in the aqueous phase by acidification, extraction with ether, and glpc analysis of the ether extract, using the procedure already described. The values for unreacted amine, the butyramide, and the formamide reported in Table II are the sums of the determinations in the pentane and aqueous phases.

Ozonation of *n*-butylamine in pentane at −100° gave a colorless solution which, however, gave a strong epr signal for the ozonate anion radical.

Registry No.—Isopropylamine, 75-31-0; isopropylhydroxylamine, 5080-22-8; *n*-butylamine, 109-73-9.

Acknowledgment.—This work was supported by grants from the Robert A. Welch Foundation (F-042) and the National Science Foundation (GP-7351), for which the authors are grateful. Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of the research.

Addition of Pseudohalogens to 1,5-Cyclooctadiene[1]

JOHN N. LABOWS, JR., AND DANIEL SWERN*

Fels Research Institute and Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122

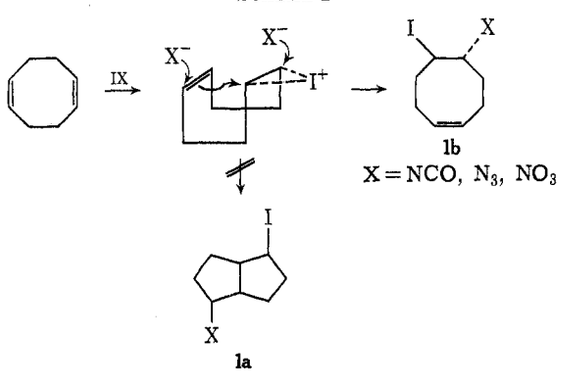
Received March 15, 1972

The addition of pseudohalogens IX, where X = NCO, N_3, NO_3, to 1,5-cyclooctadiene (mole ratio 1:1) yields 1,2-monocyclic adducts. In contrast, addition of iodine in methanol activates the second double bond, resulting in the direct formation of *endo,endo*-2,6-diiodo-9-oxabicyclo[3.3.1]nonane (**2**). The complete analysis of the nmr spectrum of **2** with the help of chemical shift reagents confirms the chair conformation for this fused ring system Similarly, the reaction of 5-methoxycyclooctene (**5**) with iodine in methanol gives *endo*-2-iodo 9-oxabicyclo[3.3.1]-nonane (**7**), whereas cyclooct-1-en-5-ol (**6**) gives only *endo*-2-iodo-9-oxabicyclo[4.2.1]nonane (**8**).

The addition of various reagents to 1,5-cyclooctadiene (COD) can lead to either monocyclic or bicyclic products. The monocyclic products arise by simple addition of the reagent to one of the double bonds, while the formation of bicyclic products involves transannular π participation, a well-documented pathway.[2] Recently, a detailed study of ionic additions to COD outlined some of the requirements for formation of bicyclic *vs.* monocyclic products and also presented information on the stereochemistry of the substituents on the bicyclic ring skeleton.[3]

We were interested in the preparation of 2-amino-6-iodobicyclo[3.3.0]octanes (**1a**) (Scheme I) and felt that

SCHEME I



1b
X = NCO, N_3, NO_3

1a

these could be obtained by the addition of pseudohalogens of type IX to COD.[4] It was visualized that the initial formation of an iodonium ion might be followed by transannular π participation to form a bicyclo[3.3.0]octane. However in all cases, where X^- =

(1) (a) This work was supported in part by U. S. Public Health Service Grants CA-05222, 07803, and 07174 of the National Cancer Institute. Pseudohalogens. XVIII. Paper XVII: *Amer. Chem. Soc., Div. Petrol. Chem., Prepr.*, **15**, E39 (1970). (b) Presented at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971, Paper 169, Organic Chemistry Division.

(2) R. Dowbenko, *Tetrahedron*, **20**, 1843 (1964); L. Friedman, *J. Amer. Chem. Soc.*, **86**, 1885 (1964); G. Pregaglia and G. Gregorio, *Chim. Ind. (Milan)*, **45**, 1065 (1963); M. Julia and E. Colomer, *An. Quim.*, **67**, 199 (1971); T. Cantrell and B. L. Strasser, *J. Org. Chem.*, **36**, 670 (1971).

(3) I. Tabushi, K. Fujita, and R. Oda, *J. Org. Chem.*, **35**, 2376 (1970).

(4) (a) S. Rosen and D. Swern, *Anal. Chem.*, **38**, 1392 (1966); (b) F. W. Fowler, A. Hassner, and L. A. Levy, *J. Amer. Chem. Soc.*, **89**, 2077 (1967).