Dye-Sensitized Photochemical Autoxidation of Aliphatic Amines in Nonaqueous Media

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The reactions involved in photosensitized autoxidation of mono-, di-, and tributylamine in organic solvents have been identified by examination of the reaction products. The predominant initial oxidation process is dehydrogenation in each case. Subsequent major reactions include (1) hydrolysis of imines to lower alkylated amines and aldehyde, (2) β-oxidation of N-alkylidene groups to give hydroperoxides which lead to formamides or α-ketoaldehyde derivatives, and (3) addition of hydroperoxide to intermediate imines followed by base-catalyzed rearrangement to amides. Several other reactions have also been established. The reactions of hydrogen peroxide with these amines in the dark take similar courses to a minor extent, N-oxidation being the major result.

Dye-sensitized photochemical autoxidation is of great interest as a possible technique for chemical utilization of the energy of visible light. Our own attention has focussed on sensitized autoxidation of nitrogen compounds and particularly on alkylamines, substrates which have received considerable study since Gaffron's original work in 1927[1] and which in recent years have become of practical importance in amine-activated photopolymerization processes.[2]

The extensive literature on both anaerobic photoreduction of dyes by amines and dye-sensitized autoxidation of amines was very helpful in our approach to this field, but it was evident that the published work fails to provide a basic understanding of the processes involved or indeed a consistent description of the phenomena to be observed. The major part of the published experimental work on autoxidation consists of measurements of the rate of oxygen absorption under illumination. Such data show the relative reactivities of different substrates, and general agreement has been reached that in water or in ethanol amines obey the reactivity order, tertiary > secondary $\gg$ primary.[3,4] Surprisingly, there has been no comment on the observation of Gaffron that the order is primary, secondary $\gg$ tertiary in acetone or pyridine. Oxygen-uptake measurements have also led to conclusions regarding the ultimate oxygen–amine stoichiometry which, however, has commonly appeared to vary with the solvent and with the experimenter.[3-5] From such work have come two basic, but conflicting, oversimplifications which have long influenced thinking in this area: Weil's recovery of trimethylamine oxide in fair yield after autoxidation of trimethylamine in water[3] has been taken as evidence for a general mode of reaction, while Schenck has stated that aliphatic amines are attacked cleanly at α-methylene groups to introduce one hydroperoxide structure at each available position.[5] In work which we shall not report in detail,[6] we have also attempted to measure the rates of oxygen uptake by amines in various solvents while concurrently monitoring the composition of the reaction solution. This approach was abandoned for several reasons: (1) rates were meaningless because in no case did the concentration of the sensitizing dye remain even approximately constant, (2) dark, oxygen-absorbing reactions were obviously contributing to the observed rates, (3) in no case could oxygen absorption be brought to completion, and rarely were sharp rate changes evident, (4) product analyses showed no simple correlation with the amount of oxygen absorbed, and (5) the reaction product mixtures were extremely complex almost from the outset. Inasmuch as many of these experiments were carried out at concentrations close to those reported by others, we doubt that published data of this kind can have more than crude qualitative value at present.

We have attempted to reduce this very complex problem to practical dimensions by concentrating on identification of the autoxidation products derived from mono-, di-, and tri-*n*-butylamine and from this knowledge attempting to deduce the basic oxidation processes. In preliminary experiments, it was found that dye-sensitized autoxidation in aqueous solution caused stepwise dealkylation, $Bu_3N \rightarrow Bu_2NH \rightarrow BuNH_2$, and formation of butyraldehyde. We chose to avoid the occurrence of the hydrolytic steps which these results implied by conducting the autoxidation in organic solvents where, indeed, more interesting solvent interaction might be expected. These reactions have proven to be much more complex than anticipated and to proceed through initial stages not evident in earlier work. However, nearly all aspects find precedent in other amine-oxidation processes.

In most of this work, rose bengal has been used as the sensitizer with occasional recourse to ethyl eosin or hematoporphyrin base for greater solubility in methyl methacrylate. Our experience, partly described herein, together with the published literature has convinced us that the dyes which are effective sensitizers of amine autoxidation (*e.g.*, eosin, rose bengal, methylene blue, chlorophyll, riboflavin, etc.) act by a common mechanism although with different efficiencies. We are not concerned here with the details of the photoexcitation and dye-recycling processes or with a close analysis of the reaction rates.

Results and Discussion

Autoxidation of *n*-Butylamine.—Initial experiments disclosed that dye-sensitized autoxidation of *n*-butylamine (**1**) in acetonitrile, ethanol, or methyl methacrylate gave N-butylidenebutylamine (**2**) in high yield as the first observable product. Measured rates of disappearance of **1** and appearance of **2** are shown in

(1) H. Gaffron, *Chem. Ber.*, **60**, 2229 (1927).
(2) G. Oster and N.-L. Yang, *Chem. Rev.*, **68**, 125 (1968).
(3) L. Weil and J. Maher, *Arch. Biochem. Biophys.*, **29**, 241 (1950).
(4) W. R. Frissell, C. W. Chung, and C. G. Mackenzie, *J. Biol. Chem.*, **234**, 1297 (1959).
(5) G. O. Schenck, *Angew. Chem.*, **69**, 579 (1957).
(6) In collaboration with W. E. Mealmaker.

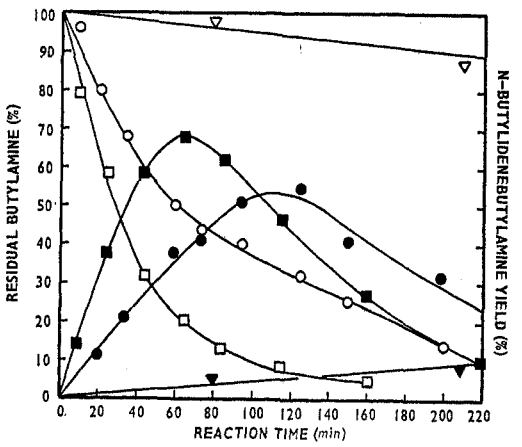


Figure 1.—Autoxidation of butylamine in various solvents (amine concn 0.02 *M*; sensitizer concn 1 × 10^{-4} *M*): ○ and ●, hematoporphyrin, methyl methacrylate; □ and ■, rose bengal, acetonitrile; ▽ and ▼, rose bengal, ethanol.

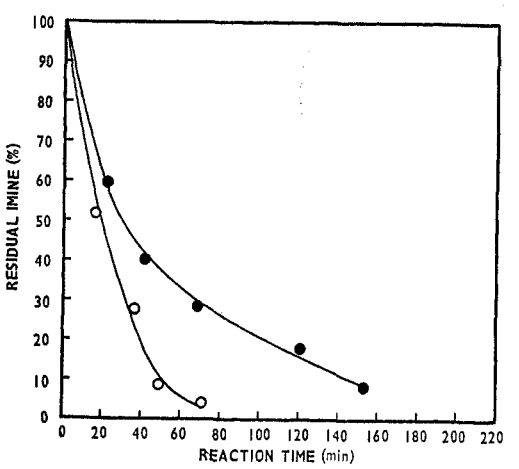


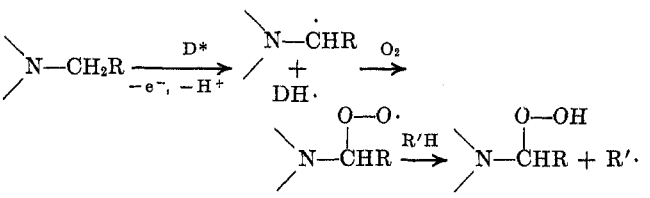
Figure 2.—Autoxidation of imines (imine concn 0.02 *M*; rose bengal concn 1.0 × 10^{-4} *M*): ○, N-butylidenebutylamine in acetonitrile; ●, N-isopropylidenebutylamine in acetone.

Figure 1. Further oxidation of **2** produced complex mixtures which presented difficult identification problems. When acetone was used as solvent, the primary amine was found to be nearly entirely present as N-isopropylidenebutylamine (**3**) from the outset.[7] This ketimine is closely analogous to **2**, and because the two alkyl moieties in **3** are distinguishable, we chose to examine its autoxidation products first. The rates of destruction of **2** and **3** are shown in Figure 2. The latter is slightly in error because of the presence of an unresolved minor amount of **2** formed by displacement of acetone from **3** by butyraldehyde, an observed oxidation product.

Autoxidation of **3** in acetone produced an astonishing variety of low-molecular-weight products by the time the ketimine had been completely destroyed, although about 80% of the material was lost as nonvolatile, probably polymeric tars. All of the appreciable glpc-detectable products were identified, however, and gave a fair picture of the reactions involved as well as the nature of the missing material. These identified products were butyraldehyde (**4**, *ca.* 0.1 mol/mol of **1**), N-butylformamide (**5**, 0.1 mol), N-butylacetamide (**6**, 0.02–0.04 mol), N-butylbutyramide (**7**, 0.005–0.02 mol), N,N′-dibutyloxamide (**8**, 0.005 mol), 2,2-dimethyl-6-propyl-4-piperidone (**9**, 0.03 mol), and N,N′-dibutylacetamidine (**10**, 0.01 mol). Fugitive intermediates also identified were **2** (0.1–0.2 mol maximum) and N,N′-dibutyl-1,2-propanediimine (**11**, 0.05 mol maximum). The yields of **6** and **7** nearly doubled as the oxidation product solution aged. Approximately 10 other products were present in smaller concentrations. It was significant, however, that the potential products, butyramide, N-formylbutyramide, dibutyramide, N-isopropylformamide, and N-isopropylbutyramide, could not be detected.

The observed products can be rationalized as indicated in the overall view of Scheme I. The reacting system probably contains several oxidizing species: excited dye, oxygen (ground state and excited singlet),[9,10] hydrogen peroxide[3] (possibly as $HO_2\cdot$ or $O_2\cdot^-$)[11,12] from reoxidation of the reduced dye by oxygen, and a variety of peroxy radicals, hydroperoxides, and peroxides. In some oxidation processes several of these may be equivalent. In others the reactions require specific oxidant types. Five significantly different oxidation processes (a–e) are discernible.

a. "Type I Photosensitized Oxygenation."—This classification has been given by Schenck[13] to hydroperoxide-forming reactions which proceed by hydrogen abstraction from the substrate, addition of oxygen to the substrate radical, and transfer of a hydrogen atom to the peroxy radical. His view[5] that sensitized autoxidation of amines is such a reaction has been widely accepted.[14] The capacity of excited dyes to



abstract hydrogen from amines (more precisely, a process of electron abstraction followed by release of a proton[17]) is well known from many anaerobic photoreduction studies.[18a] In the presence of oxygen, radicals thus produced could be expected to yield hydroperoxides in a reaction analogous to benzophenone-sensitized autoxidation of isopropyl alcohol.[18b] The semireduced dye might react with oxygen,[3] producing the hydroperoxy radical or be reoxidized by the peroxyamine radical, in which case no hydrogen peroxide-related species would appear. The latter would be in accord

(7) This easy reaction seems unappreciated.[8] Ir spectra show that, at concentrations below 0.4 *M*, less than 5% free amine is present after 2 hr. 2-Butylamino-2-hydroxypropane is insignificant at equilibrium.

(8) R. W. Layer, *Chem. Rev.*, **63**, 487 (1967).

(9) C. S. Foote and S. Wexler, *J. Amer. Chem. Soc.*, **86**, 3879, 3880 (1964).

(10) E. J. Corey and W. C. Taylor, *ibid.*, **86**, 3381 (1964).

(11) J. Weiss, *Trans. Faraday Soc.*, **34**, 451 (1938).

(12) L. Lindqvist, *Ark. Kemi*, **16**, 79 (1960).

(13) G. O. Schenck, *Ind. Eng. Chem.*, **55**, No. 6, 40 (1963).

(14) Recent demonstration of the quenching effect of tertiary amines toward singlet oxygen, without chemical reaction,[15] should restrain invocation of this species as the reagent in dye-sensitized amine autoxidation.[16]

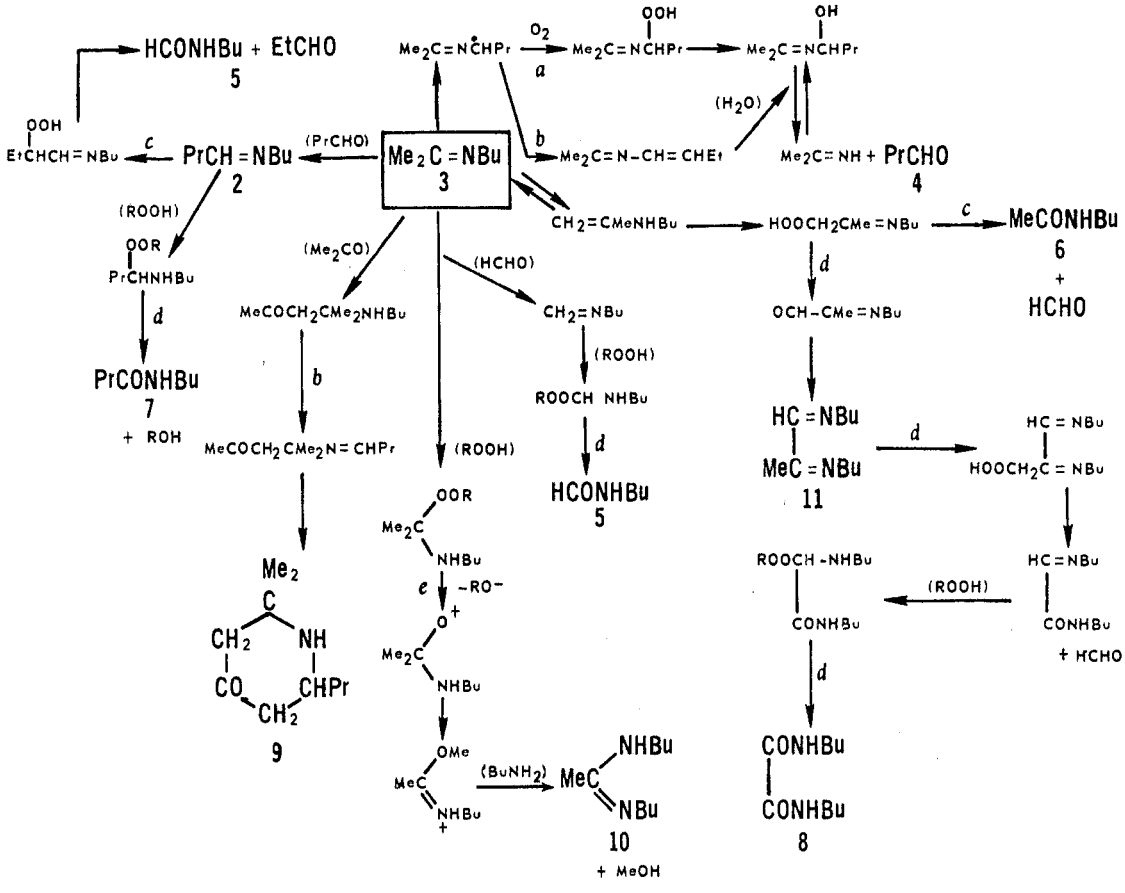
(15) C. Ouanès and T. Wilson, *J. Amer. Chem. Soc.*, **90**, 6527 (1968).

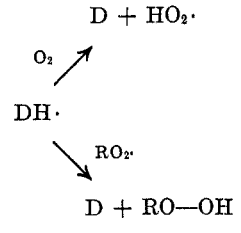
(16) K. Gollnick, *Advan. Photochem.*, **6**, 1 (1968).

(17) L. Horner in "Autoxidation and Antioxidants," Vol. I, W. O. Lundberg, Ed., Interscience Publishers, New York, N. Y., 1961, p 171.

(18) (a) H. Meier, "Die Photochemie der Organischen Farbstoffe," Springer Verlag, Berlin, 1963, p 91; (b) G. O. Schenck, H. D. Becker, K. H. Schulte-Elte, and C. H. Krauch, *Chem. Ber.*, **96**, 509 (1963).

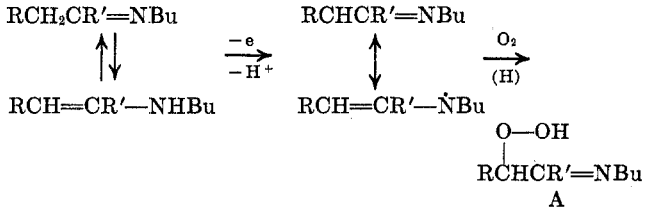
SCHEME I





with the fact that chain reactions have not been observed and also with our observation that dehalogenation of the sensitizers rose bengal and eosin does not occur, as could be expected if the semireduced dye had an appreciable lifetime.[19]

Radical attack on **3** may in this way give a hydroperoxide which might be degraded[20] to butyraldehyde (**4**) *via* a hemiaminal (Scheme I), although we are inclined to favor an alternate route (see b below). Abstraction of an electron from **3** or its tautomeric enamine[21] can also give a resonance-stabilized β radical



from which a β-hydroperoxide (A) will arise. As discussed below, an intermediate of type A is probably involved in the formation of **11**.

b. Dehydrogenation.—Oxidation of aliphatic amines by a variety of methods[22-26] has been shown to give imines and enamines. Such an oxidative process could be responsible for the conversion of **3** to **4**, an ambiguous case. Clear examples of dehydrogenation were later found with dibutylamine and tributylamine. Formation of **9** in the autoxidation of **3** is logically attributed to the steps shown in Scheme I. Dehydrogenation of the secondary amine formed by addition of acetone to **3**, followed by cyclization,[27] accounts for the formation of **9**.

A plausible reaction of **3**, or of an imine produced by amine dehydrogenation, is base-catalyzed addition of hydrogen peroxide or a hydroperoxide.[28] We suggest that this is the probable source of the α-peroxides which others have reported and which we require as intermediates in the formation of various product amides (see d below).

c. α,β Cleavage of Imines.—This process has become well recognized as a pathway of autoxidation of

(19) G. Oster, G. K. Oster, and G. Karg, *J. Phys. Chem.*, **66**, 2514 (1962).

(20) R. Hofmann, H. Hübner, G. Just, L. Krätzsch, A. K. Litkowez, W. Pritzkow, W. Rolle, and M. Wahren, *J. Prakt. Chem.*, [4] **37**, 102 (1968), show easy homolytic decomposition of hydroperoxides in basic solution. Reduction by **3** is an alternative demonstrated in the present work.

(21) B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, **73**, 2196 (1951).

(22) D. H. Rosenblatt, G. T. Davis, L. A. Hull, and G. D. Forberg, *J. Org. Chem.*, **33**, 1649 (1968).

(23) D. Buckley, S. Dunstan, and H. B. Henbest, *J. Chem. Soc.*, 4880, 4901 (1957).

(24) H. E. De La Mare, *J. Org. Chem.*, **25**, 2114 (1960).

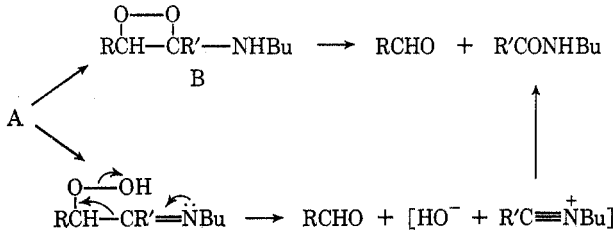
(25) M. Masui, H. Sayo, and Y. Tsuda, *J. Chem. Soc., B*, 973 (1968).

(26) (a) S. G. Cohen and R. J. Baumgarten, *J. Amer. Chem. Soc.*, **87**, 2996 (1965); (b) S. G. Cohen and R. J. Baumgarten, *ibid.*, **89**, 3471 (1967); (c) S. G. Cohen and H. M. Chao, *ibid.*, **90**, 165 (1968).

(27) (a) W. Heinz, *Justus Liebigs Ann. Chem.*, **189**, 214 (1877); (b) O. Antrick, *ibid.*, **227**, 365 (1885).

(28) E. Höft and A. Rieche, *Angew. Chem. Int. Ed. Engl.*, **4**, 524 (1965).

imines and enamines,[21,29a] although the details remain uncertain. Hydroperoxides of the type A might conceivably form transitory cyclic peroxides (B) which undergo carbonyl-forming scission, or a fragmentation process might be involved.[21,29b] In this way **3** gives rise to **6** and formaldehyde. Similarly, **2** will be



oxidized to **5** and propionaldehyde. The latter can reenter the degradation process, being converted to acetaldehyde and finally to formaldehyde as long as **3** remains. Recently singlet oxygen has been shown to be an excellent reagent for such enamine cleavage;[30] its involvement here provides a third possible mechanism.

d. Base-Catalyzed Peroxide-to-Carbonyl Elimination.—A well-documented mode of decomposition of hydroperoxides in alkaline media is the elimination reaction[31]

$$RR'CH{-}OOH \xrightarrow{-H^+} RR'\dot{C}{-}OOH \longrightarrow RR'C{=}O + OH^-$$

N-Butylbutyramide (**7**) must be formed by such a process, following addition of a hydroperoxide to **2**.[32]

An intermediate hydroperoxide of type A provides a plausible mechanism for the early formation of **11**.

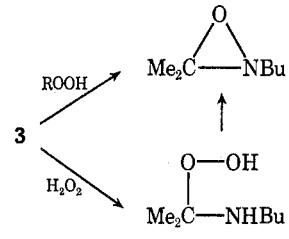
$$HO{-}OCH_2CMe{=}NBu \xrightarrow{(base)} O{=}CHCMe{=}NBu \xrightarrow{(3)} \mathbf{11} + Me_2CO$$

Such an oxidation product of an amine, imine, or enamine has not previously been reported to our knowledge. The bisimine **11** is, of course, susceptible to further oxidation. To some extent this could take the route shown in Scheme I which leads to the observed product **8**.

e. Heterolytic Peroxide Cleavage and Baeyer–Villiger Rearrangement.—The conversion of **3** to **10** depicted in Scheme I is analogous to a rearrangement observed as a side reaction in hydrogen peroxide oxidation of dibutylamine.[33]

Additional modes of oxidation of the ketimine could be postulated but were rejected as of no significance when the related potential products were shown not to be present in detectable amounts. (1) The ketimine apparently does not tautomerize significantly to the isomeric aldimine, since neither N-isopropylformamide nor N-isopropylbutyramide was found. (2) Further oxidation of the initial amide products to diacylamides cannot be appreciable;[34,35] neither N-formylbutyramide nor dibutyramide was detectable.

Other conceivable oxidation processes could be involved, but no conclusive evidence pro or con can be adduced. (1) 2-Butyl-3,3-dimethyloxazirane might be obtained by epoxidation of the ketimine.[28,36,37] This



product would probably not be stable in the basic reaction, mixture, however. Basic decomposition would give ammonia, acetone, and butyraldehyde; a radical oxidation process could lead to **6**.[37] The oxazirane was definitely not present in significant quantity in the final reaction mixture. (2) A nitrone might be a reasonable product to expect. Such compounds are prone to

$$(CH_3)_2C{=}N{-}C_4H_9 \xrightarrow{ROOH} (CH_3)_2C{=}\overset{\uparrow}{N}(O){-}C_4H_9$$

dimerize in alkaline media, however, which would lead to products of very low volatility.[38] In any case no glpc peak of substantial size was observed which could be attributed to this nitrone.

The formation of nonvolatile products from the bulk of the starting material is ascribed to base-catalyzed aldehyde and aldimine polymerization, aldehyde–amide condensation, oxidation of aldehyde to acid, and very possibly polymerization of oxazirane intermediates.[37]

Returning to the photosensitized autoxidation of butylamine itself, it is evident from the relationship in Figure 1 that this reaction must proceed predominantly by way of **2**. We see little doubt that this involves the dehydrogenation process (b above).[39] Conversion of

$$\underset{\mathbf{1}}{C_4H_9NH_2} \xrightarrow{-e} C_3H_7CH_2\dot{N}H_2^+ \xrightarrow{-H^+} C_3H_7\dot{C}H{-}NH_2 \longrightarrow C_3H_7CH{=}NH$$

$$C_3H_7CH{=}NH + \mathbf{1} \longrightarrow \underset{\mathbf{2}}{C_3H_7CH{=}NC_4H_9} + NH_3$$

the radical to the imine could be a disproportionation process[40] or proceed by a second electron and proton (or hydrogen atom) abstraction. The aldimine would be expected to react at once with starting amine.

Examination of the products from autoxidation of **2** in acetonitrile, ethanol, or methyl methacrylate[41] by glpc revealed no major differences, although only reactions in acetonitrile were studied in detail. In this

(29) (a) H. B. Henbest and P. Slade, *J. Chem. Soc.*, 1555 (1960); (b) E. Schmitz, A. Rieche, and A. Stark, *Chem. Ber.*, **101**, 1035 (1968).

(30) (a) C. S. Foote and J. W.-P. Lin, *Tetrahedron Lett.*, 3267 (1968); (b) J. E. Huber, *ibid.*, 3271 (1968).

(31) A. G. Davies, "Organic Peroxides," Butterworth and Co. (Publishers), Ltd., London, 1961, p 28.

(32) The influence of an α-amino group is uncertain. Decomposition by a radical process may compete, leading to an α-amino alcohol[20b] and to an aldehyde, or the base-catalyzed elimination may be slow as suggested by the gradual formation of **7**. [Compare W. H. Richardson and R. S. Smith, *J. Amer. Chem. Soc.*, **91**, 3610 (1969).] The enhanced acidity of a β proton in a β-peroxyimine such as A should favor elimination in competition with α,β cleavage.

(33) A. A. A. R. Sayigh, and H. Ulrick, *J. Chem. Soc.*, 3144 (1963).

(34) M. V. Lock and B. F. Sagar, *ibid.*, B, 690 (1966); B. F. Sagar, *ibid.*, 428, 1047 (1967).

(35) G. M. Burnett and K. M. Riches, *ibid.*, *B*, 1229 (1966).

(36) H. Krimm, *Chem. Ber.*, **91**, 1057 (1958).

(37) W. D. Emmons, *J. Amer. Chem. Soc.*, **79**, 5739 (1957).

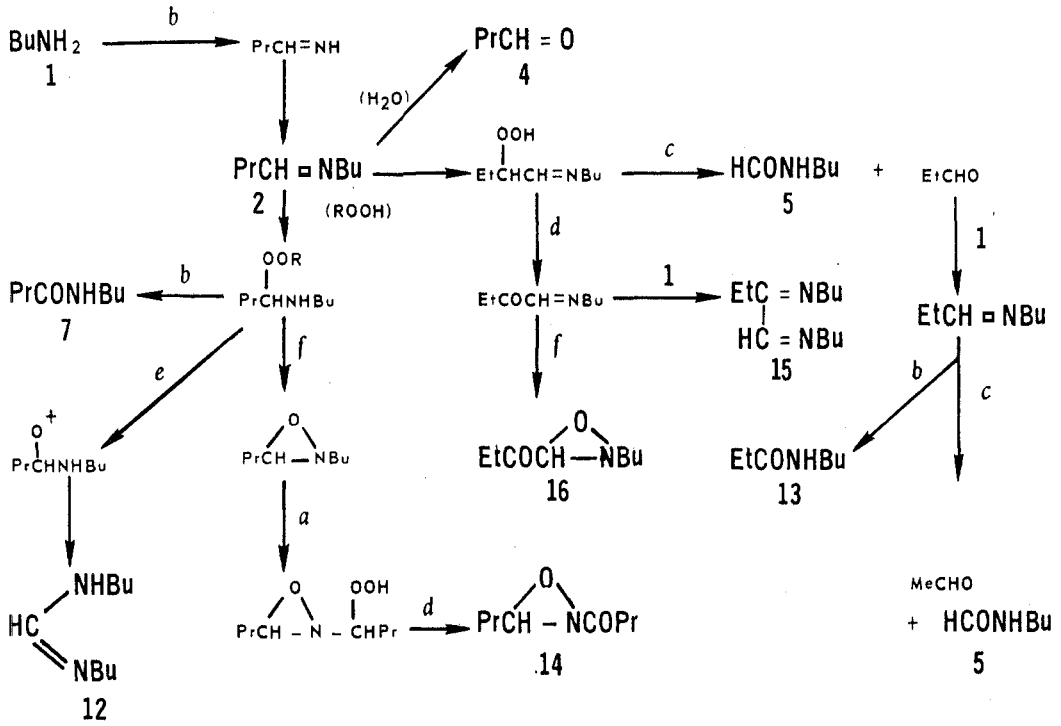
(38) R. Bonnett, R. F. C. Brown, V. M. Clark, I. O. Sutherland, and A. Todd, *J. Chem. Soc.*, 2094 (1959).

(39) Although dehydrogenation of **1** is not unequivocally demonstrated by the immediate appearance of **2**, this process is strongly indicated by the less debatable dehydrogenations seen with dibutylamine and tributylamine.

(40) D. Mackay and W. H. Waters, *J. Chem. Soc., C*, 813 (1966).

(41) Methyl methacrylate reacts with **1** to give methyl 3-butylamino-2-methylpropionate, but this reaction is too slow to interfere significantly.

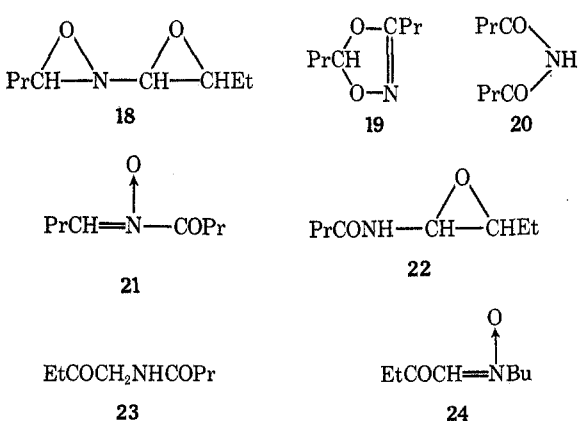
SCHEME II



solvent virtually identical product mixtures were obtained from **1**, distilled **2**, or **2** prepared *in situ* from equivalent amounts of **1** and **4**. The results were similar to those discussed above for **3** in acetone, and several of the same products were identified. However, in this case strong evidence of the involvement of oxazirane intermediates was found. Scheme II summarizes these results and indicates the occurrence of processes a–e as discussed above. The added oxazirane-forming oxidation is indicated as f. All of the oxidation processes of Scheme I have their counterparts here with the exception of the formation of **9**. However, this reaction, too, may have a parallel in the formation of a minor amount of 3,5-diethyl-4-propylpyridine (**17**) which was detected in the mass spectra of various partially resolved fractions (see below).

The major glpc-detectable products present after autoxidation of a 0.4 *M* solution of **1** in acetonitrile for 24 hr (essentially complete destruction of **1** and **2**) were **5**, a compound tentatively identified as 2-butyryl-3-propyloxazirane (**14**), and a mixture of N,N′-dibutylformamidine (**12**) and the acetamidine **10**. An intermediate product (**15**) was also observed to reach a maximum yield of about 15% when **1** was about half destroyed, but it was not detectable in the final mixture. Compound **15** was not isolated in sufficiently pure or stable form for satisfactory identification, but its glpc characteristics and other behavior were very similar to those of **11**, and it is eminently reasonable to identify it as N,N′-dibutyl-1,2-butanediimine.

In the course of experiments to identify **15**, a previously unseen compound (**16**) was discovered as a major component of the distilled concentrate containing **15**. Compound **16** was not a significant component of the autoxidation mixture and may have been formed in the distillation itself.[42] Its molecular weight was shown to be 157, most logically $C_8H_{15}NO_2$. The product **14**, which was more advantageously obtained as an autoxidation product of dibutylamine, proved to be isomeric with **16**. These compounds are believed to be oxazirane derivatives as indicated in Scheme II. Alternative formulations for the relatively volatile isomer **16** are **18** and **19**. Formation of **18** would require a dubious multistage oxidation, however. Rearrangement of **14**[43] might conceivably give **19** which cannot be ruled out with complete confidence. In any case, the formation of an oxazirane structure is required to explain the product, and this is the basic point to be made. Consequently, it is probable that 2-butyl-3-propyloxazirane (**25**) is also present. It may in fact account for an observed species, *m/e* 141, in the mass spectrum of crude **16**. (Loss of oxazirane oxygen, 157 → 141, might occur, but this is not a cleavage observed with 2-butyl-3,3-dimethyloxazirane.)



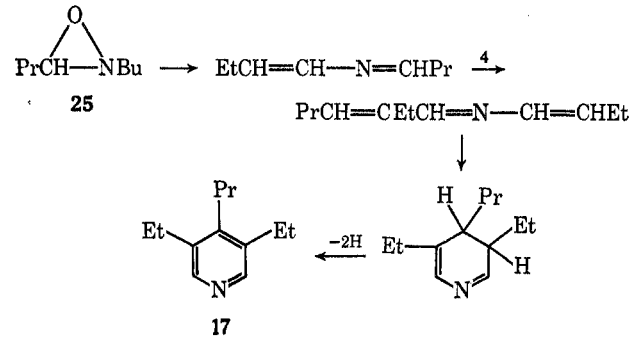
Assignment of the structure **14** to the less volatile $C_8H_{15}NO_2$ isomer rests on the following grounds. The glpc behavior is suggestive of an N,N-disubstituted

(42) A. Padwa, *J. Amer. Chem. Soc.*, **87**, 4365 (1965), has described a stable 3-acyloxazirane.

(43) E. Schmitz and S. Schramm, *Chem. Ber.*, **100**, 2593 (1967).

amide (**20**, **21**, **22**, and **23** would have much longer retention times). Such a product is a very likely one to be produced by autoxidation of **25** which is probably present during the reaction. The nitrone **24** remains a weak possibility.

In the course of a brief study of the properties of **25** prepared by an authentic procedure, it was found that heating at 150° caused the formation of **17**. This probably proceeds by way of an enimine.[37] The same



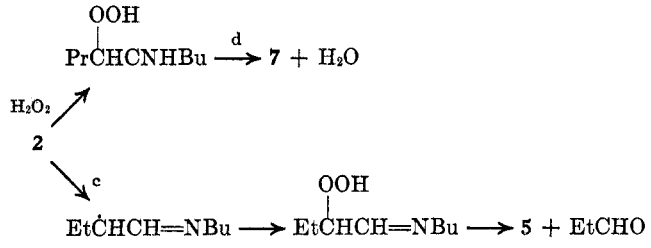
intermediates could well be formed in the autoxidation process[44] and are reflected in the occurrence of an *m/e* 177 species in the mass spectra of several product fractions having appropriate retention times.

The apparent absence of butyramide in the autoxidation product mixture from **1** provided further support for our persuasion that an α-hydroperoxy primary amine is not an important intermediate.

Oxidation of the Butylamines by Hydrogen Peroxide.—Hydrogen peroxide is probably produced during dye-sensitized autoxidation of amines in the cyclic regeneration of the dye from its semireduced form. Consequently it was significant to test its mode and rate of reaction with the usual substrates. Unsensitized reactions of **1**, dibutylamine (**26**), or tributylamine (**27**) with hydrogen peroxide in acetonitrile were found to occur readily at rates comparable to that of photosensitized autoxidation under our standard conditions. In each case the same oxidation products were formed as had been identified in the autoxidation studies. Product ratios were altered, however, and previously unobserved products of oxygenation at nitrogen reached substantial yields.

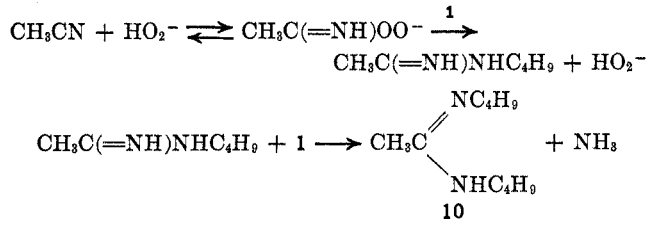
In acetonitrile the hydroperoxide anion tends to add to the nitrile group to give the peracetimidic acid anion, $CH_3C(=NH)OO^-$, which is recognized as a potent oxidant.[45] As the expected by-product of oxidations by this species or as the product of its reaction with additional hydrogen peroxide, acetamide was formed in substantial amount in each of these experiments.

The aldimine **2** was clearly the initial product obtained from **1**. It was found to react considerably faster than the primary amine with hydrogen peroxide, about $^1/_3$ being converted to **7** and **5** in a ratio of about 4:1. A smaller amount of **1** presumably was oxidized to N-butylhydroxylamine and this to butyraldoxime, an identified product. Oxygenation at the nitrogen atom is probably an appreciable reaction of peroxide in this system because of its high concentration. In autoxidation reactions, more reactive intermediate products may be efficient traps for the peroxide, as **2** proves to be. The dehydrogenation reaction leading to **2** demonstrates the capability of the peroxide to initiate concurrent dark free-radical reactions leading to the same products as observed in photosensitized autoxidation.[46] The ratio of **7** to **5** here is much higher than in autoxidation, reflecting the greater probability in this system of addition of peroxide to the imine structure compared to the radical process c.[47] The major part of



the substrate, as in autoxidation, was converted to nonvolatile products.

Interestingly, if the temperature was allowed to rise to about 60°, hydrogen peroxide reacted in a very different way with **1** in acetonitrile, producing **10** in about 80% yield. This seems best explained as hydroperoxide ion catalyzed addition of butylamine to the nitrile group.



It had been noted that in the autoxidation of **3** in acetone the reaction solution at no time contained an iodometrically detectable amount of peroxide, although autoxidations of the various substrates in other solvents commonly produced major amounts of titratable peroxide. Presumably the difference was owing to the ability of acetone to form hemiketal peroxides of much reduced oxidizing power. Hydrogen peroxide in acetone was sufficiently active to be measured satisfactorily by iodometry, but no reaction could be detected with **3** in the presence of a threefold excess of hydrogen peroxide in 24 hr. This system thus offered an excellent opportunity to test the possibility of dye-sensitized oxidation by peroxides, a type of process which may be involved in any of the sensitized autoxidation reactions. Such a reaction did occur under the usual photosensitization without added oxygen, and substantially the same product distribution as in autoxidation was obtained.

Reaction of **26** with hydrogen peroxide in acetonitrile gave a substantial yield of N,N-dibutylhydroxylamine (**28**) together with lesser amounts of **2** and its oxidation products. Oxidation at nitrogen was also an important reaction with **27**, giving tributylamine oxide in 43% yield. Accompanying dehydrogenation produced N-1-butenyldibutylamine (**29**) which in turn gave **4** and **26** in major amounts.

(44) A referee has pointed out that 1,4 cycloaddition of singlet oxygen to EtCH=CH—N=CHPr would provide an alternative source of the $C_8H_{15}NO_2$ compounds.

(45) G. B. Payne, *Tetrahedron*, **18**, 763 (1962).

(46) Weil[3] was able to show such participation of hydrogen peroxide during methylene blue-sensitized autoxidation of nicotine in water.

(47) C. Mentzer and Y. Burguer, *Bull. Soc. Chim. Fr.*, 218 (1952).

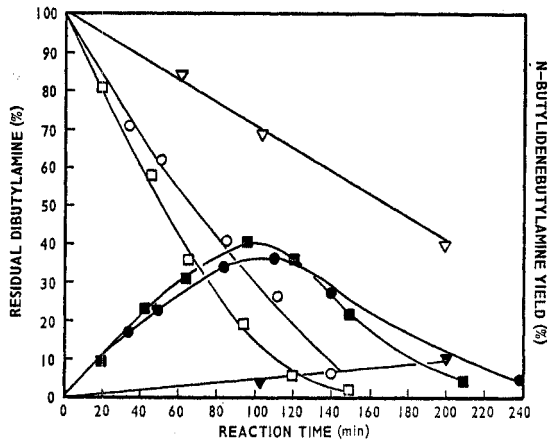


Figure 3.—Autoxidation of dibutylamine in various solvents (amine concn 0.02 *M*; sensitizer concn 1.0×10^{-4} *M*): ○ and ●, rose bengal, acetone; □ and ■, rose bengal, acetonitrile; ▽ and ▼, rose bengal acid, methyl methacrylate.

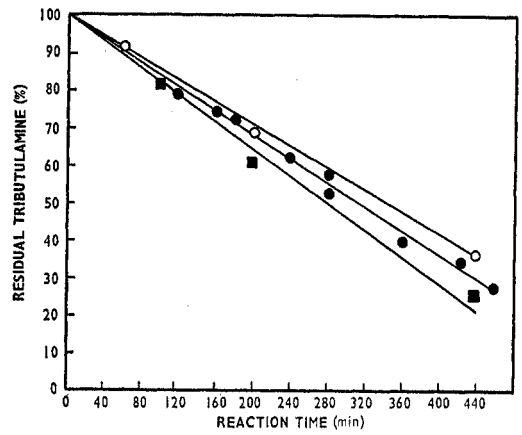


Figure 4.—Autoxidation of tributylamine in various solvents (amine concn 0.02 *M*; rose bengal concn 1.0×10^{-4} *M*): ○, acetone; ●, methyl methacrylate, absolute, ethanol, 95% ethanol; □, acetonitrile.

Autoxidation of Dibutylamine.—The rates of destruction of dibutylamine (**26**) by rose bengal-sensitized autoxidation in acetone, acetonitrile, and methyl methacrylate are shown in Figure 3 which also shows the concurrent formation of **2** as the predominant initial product. Examination of the oxidation product mixtures after substantial conversion disclosed the typical range and proportions of compounds obtained from **2** itself. In addition, N,N-dibutylformamide (**30**) was found in substantial amounts which depended on the solvent used. This amide must be an oxidation product of **29** which was never present at a detectable level, however. In principle, oxidation of **29** might

$$(C_4H_9)_2NH \underset{+2,\ -NH_3}{\overset{+C_3H_7CHO}{\rightleftharpoons}} (C_4H_9)_2NCH{=}CHC_2H_5 \xrightarrow{O_2} (C_4H_9)_2NCHO + C_2H_5CHO$$

26 **29** **30**

give rise to N,N-dibutylbutyramide as well, but this compound was not found.

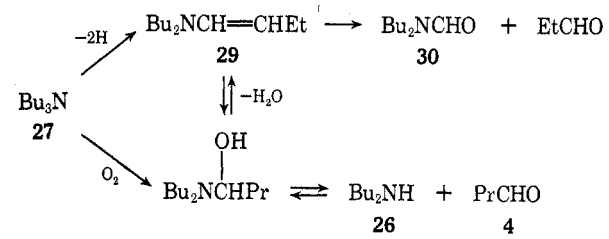
Autoxidation in acetonitrile gave **30** in about 5% yield. However, in acetone a selective interaction increased the yield of this product to 23% without other significant changes being apparent. Possibly formation of an adduct, $Me_2C(OH)NBu_2$, partially protects the amine from attack until displacement of the acetone by **2** or **4** gives the easily oxidized enamine **29**. Infrared spectra did not give conclusive evidence for such an acetone adduct but did show that dehydration to N-isopropenyldibutylamine was not a significant reaction. Nevertheless, oxidation of this enamine would give N,N-dibutylacetamide, which appeared to be present in small amount.

The sluggish reaction in methyl methacrylate was primarily owing to the abnormal condition of the dye in this nonpolar solvent. The usual products were obtained, but as the oxidized solution aged in the dark, the yield of **30** increased substantially and, especially interestingly, the compound **14** increased from a very small amount to a 10–12% yield. These products may be slow to form because of the low polarity of the solvent or because of stabilization of peroxy radicals or hydroperoxides by addition to the methacrylate double bond.

Although dibutylhydroxylamine is a major product of the reaction of dibutylamine with hydrogen peroxide, it was not found in any autoxidation experiment.

Autoxidation of Tributylamine.—Sensitized autoxidation of **27** in acetone, acetonitrile, ethanol, or methyl methacrylate under standard conditions resulted in substantially equal rates of disappearance of the starting amine (Figure 4). The reactions in acetone and in acetonitrile gave very similar products. When the starting amine was 65–85% destroyed, about $^2/_3$ could be accounted for as an exceptionally clean mixture of identifiable compounds. The predominant product was **30** accompanied by substantial amounts of **4** and **26**. N-Butylidenebutylamine (**2**) and its principal derivatives, **5** and **7**, were minor constituents. In neither case could tributylamine oxide be detected.

Evidently two degradation paths compete in these reactions. The key intermediate leading to **30** must be **29** which cannot actually be observed. This undergoes oxidative cleavage of the α,β double bond to give the formamide and propionaldehyde. Two routes to **29** are available: dehydrogenation of the starting amine seems most reasonable as the principal route, following established precedent; α-oxidation may give rise to an α-hydroxy amine which can both lose water to give **29** and dissociate to **4** and **26**. As long as **26** remains, it will be



in equilibrium with **29** and can be converted to **30**. However, it will also be oxidized irreversibly to **2** and its derivatives. When the reaction was run in absolute ethanol, the product ratio **26**:**30** was greater, and a further increase resulted when 5% water was present. Presumably either water or ethanol reduces the small equilibrium concentration of **29**.

In methyl methacrylate, although the measured rate of loss of **27** was substantially the same as in acetone or acetonitrile, the reaction must take a new course leading

predominantly to non-glpc-detectable products. The yield of **30** was especially low, suggesting that the enamine might have been intercepted by the reactive solvent, but we find that **29** remains essentially unchanged in methyl methacrylate for several days at room temperature.

Experimental Section

Materials Used.—Rose bengal (disodium 3,4,5,6-tetrachloro-2′,4′,5′,7′-tetraiodofluorescein) and ethyl eosin (ethyl ester of 2′,4′,5′,7′-tetrabromofluorescein) were stain-grade dyes obtained from Allied Chemical and Dye Corp. Rose bengal acid was obtained by acidification of an aqueous solution of the sodium salt with sulfuric acid. Hematoporphyrin base was precipitated from an aqueous solution of the hydrochloride (Nutritional Biochemicals Corp.) by addition of sodium hydroxide. The butylamines and benzaldehyde (Eastman Kodak Co.) were redistilled before use and were essentially pure by glpc.

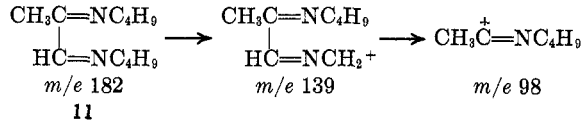
Glpc Techniques.—A flame ionization detector provided sufficient sensitivity for satisfactory observation of compounds at concentrations of 10^{-5} M. Usually the solvent was used as an internal standard with sufficient reproducibility. Chromatographic sensitivities were established for all of the principal components which could be identified. Otherwise it was assumed that the signal strength was proportional to the carbon content of the effluent gas stream. Identification of the reaction products was based on direct comparison by glpc with known materials when these were available or could be synthesized readily. Retention time agreement on two types of glpc columns was usually considered adequate proof of identity. A stationary phase of 4:1 polyethylene glycol–KOH was preferred for resolution of the amines as well as practically all products of reasonable volatility. For less volatile compounds and for comparison on a nonpolar column, silicone gum rubber was employed. Occasionally a column containing nonylphenoxypolyethoxyethanol–KOH was used; this had similar characteristics to the KOH–polyethylene glycol column. Similar $^1/_4$-in. columns were used with a thermal conductivity detector for analysis of product concentrates in a glpc–mass spectrometer combination.

We have found that the reaction products undergo further changes in dark storage after the photosensitized autoxidation reaction has stopped. Not only are unstable materials observed to disappear, but the concentrations of some products increase for a few days. This is presumably owing to slow breakdown of peroxides present. It might be considered that the compounds observed in glpc analysis are not present as such in the product mixture but are artifacts produced by pyrolysis in the gas chromatograph inlet from such peroxides and from polymeric material. Indeed, it is likely that such effects do occur and are responsible for some difficulties in using the glpc–mass spectrometer combination effectively. However, we are convinced that the reproducible retention times and clean peak shapes signify that our interpretation is proper; pyrolytic processes appear to have caused only high background signals.

Autoxidation Rate Measurements.—Appropriate solutions (50–70 ml) contained in 20 × 450 mm Pyrex glass tubes were irradiated with "Cool-White" fluorescent lamps while "breathing air" was continuously introduced at the bottom of the tubes through fritted disks at a rate ensuring active agitation and essential saturation of the solution (about 400 ml/min). A Dry Ice–acetone reflux condenser was used to minimize loss of solvent and reactants. The reaction mixtures were analyzed at appropriate intervals by glpc.

Autoxidation of N-Isopropylidenebutylamine (3) in Acetone.—Several runs were made at various concentrations and for various lengths of time without appreciable differences in the product distribution. Work-up varied for isolation of particular products. The overall results are summarized under Results and Discussion.

To recover a major but fugitive product, **11**, autoxidation of a 0.4 M solution of **3** was stopped after 4 hr when **11** was near its maximum concentration (5% yield). The solvent was evaporated and the residue extracted with petroleum ether, thus removing **11** from insoluble tar. Adsorption on a silica gel column and elution with ethyl ether gave an early fraction which appeared to be >90% **11** by glpc, and this material was moderately stable at −15°. Compound **11** had glpc characteristics suggestive of a strongly basic polyamine, and its ir spectrum exhibited a complex pattern in the 1500–1700-cm^{-1} region with very little –OH or –NH absorption. Mass spectrometric examination at low temperature and low voltage, with very short photoplate exposure to minimize fragmentation, failed to give a satisfactory spectrum. However, high resolution-peak matching under normal operating conditions identified two fragments as $C_8H_{15}N_2$ (calcd mass, 139.124; found, 139.125) and $C_6H_{12}N$ (calcd mass, 98.097; found, 98.097). These appeared to be derived from a parent compound of mass 182 (although this peak was very weak) formulated as **N,N′-dibutyl-1,2-propanediimine**. This identification of **11** was confirmed by glpc comparison with an authentic sample prepared by reaction of pyruvic aldehyde with excess butylamine.



11

To identify the products, 2,2-dimethyl-6-propyl-4-piperidone (**9**) and N,N′-dibutylacetamidine (**10**), a 0.4 M solution of **3** was autoxidized for 24 hr (about 90% destruction of **3** and **2**). Evaporation of the solvent left a gum which was extracted with petroleum ether. Nearly all **9** was found in the extract and **10** remained undissolved. Compound **9** was retained on a silica gel column after washing with petroleum ether which removed most of the other reaction products present in the extract. It was then eluted with ethyl ether and refined by further chromatography, yielding a product in which **9** was the only appreciable component (by glpc). Examination by ir suggested the presence of a propyl or butyl group and a carbonyl group (ν 1710 cm^{-1}, probably ketone). High resolution mass spectrometry at low temperature gave the empirical formula $C_{10}H_{19}NO$ (calcd mass, 169.147; found, 169.146). Fragments were also identified which helped suggest the 4-piperidone structure. This compound was synthesized as described later and proved to be identical with the autoxidation product **9**.

Compound **10** was extracted from the petroleum ether–insoluble gum with 0.5 N HCl under ethyl ether. The aqueous phase was then made strongly basic and extracted with ethyl ether. The solute recovered contained **10** with much larger amounts of **5** and **6**. Column chromatography on silica gel with ethyl ether elution removed much of the amide material leaving **10** on the column. Subsequent elution with methanol yielded a small amount of material in which the largest component was **10** with smaller, roughly equal amounts of **5**, **6**, and **9** present. It was suspected that **10** was either N,N′-dibutylformamidine or N,N′-dibutylacetamidine, and these compounds were prepared for glpc comparison by reaction of formamidine and acetamidine hydrochlorides, respectively, with butylamine in boiling ethanol followed by liberation of the free bases with aqueous KOH. The two amidines were not distinguishable on the KOH–polyethylene glycol column, but on the silicone column identity of the product **10** with the acetamidine was clear. For additional proof, the crude sample was hydrolyzed with aqueous methanolic KOH at 70° resulting in a substantial increase of the ratio of **6** to **5** in the solution.

At one point it appeared that autoxidation of **3** might be giving a product which was not resolvable from solvent acetone. This doubt was eliminated by carrying out a comparable autoxidation of *n*-octylamine in acetone. As with **1**, the ketimine was formed very quickly and was destroyed at about the same rate as **3**. Octanal and N-octylideneoctylamine were formed as expected, and as with **3** at least 75% of the octylamine was converted to nonvolatile, presumably polymeric material.

Autoxidation of Butylamine (1) in Acetonitrile.—The rate of destruction of **1** under standardized conditions is shown in Figure 1. When an identical run was interrupted after 85 min and the solution stored overnight in the dark, further 26% and 33% losses of residual **1** and **2** occurred during the dark period.

Autoxidation of **1** (0.4 M) in acetonitrile required 24–30 hr for essentially complete destruction of **1** and **2**. Glpc analysis showed the presence of compounds having the characteristics of **N,N′-dibutylformamidine** (**12**, approximately 0.06 mol per mol of **1**), **5** (0.05–0.06 mol), **4** (0.05 mol), **7** (0.025 mol), **13** (0.015 mol), **6** (0.01 mol), and **8** (0.005 mol). An additional major product (**14**, 6–8%) was unknown. An intermediate product (**15**) was also observed which reached a maximum yield of about 15% when **1** was half destroyed but was not detectable in the final

mixture. Several additional compounds were detectable in trace amounts. The product distribution did not change appreciably when the starting concentration of **1** was varied or if **2** was used either as freshly distilled material[48] or prepared *in situ* from **1** and **4**. In one run, exit gases were shown to contain ammonia trapped as NH_4Cl.

By interrupting the autoxidation of **2** (0.1 *M*) after 5 hr, when **15** was near maximum concentration, and evaporating the solvent, a product concentrate was obtained which contained **15** and a second substantial unknown product **16**, which seemed identical with 2-butyl-3-propyloxazirane (**25**) in glpc comparison on the silicone column. Both **15** and **16** were lost within 24-hr storage of the concentrate at −15°. Attempts to obtain their mass spectra through use of the glpc–mass spectrometer technique were unsuccessful with respect to **15**, but **16** was resolved sucessfully, and a satisfactory spectrum was obtained distinguishing this compound from **25**. The apparent molecular ion had *m/e* 157 and other masses observed were 141, 98, 84, 70, 60, 57, 41, 30, 29. The combined fresh product solutions from several concurrent runs were distilled rapidly through a short-path still at high vacuum. About 1/3 was collected below 150° (0.1 mm) and contained **15** (fraction 1); another third distilled at 150–200° (0.1–0.05 mm) and proved to be rich in **12** (fraction 2). Compound **16** was lost in the distillation, and **15** was still unstable in fraction 1. Attempts to resolve **15** from the fresh distillate by the glpc-mass spectrometer technique were unsuccessful, as were attempts at isolation by preparative glpc. Its properties were strikingly similar to those of **9**.

Experiments with **10** and **12** showed that, although these compounds are not resolvable on the KOH–polyethylene glycol column, the silicone column distinguishes between them when high concentrations are present. However, at low levels in autoxidation product mixtures their retention times are unreliable. Mass spectrometric examination of the distilled fraction 2 (above) gave no indication of the presence of either **10** or **12** although glpc had shown a high content of one or both. By mild hydrolysis of a sample of fraction 2 with aqueous KOH, the content of **5** was greatly increased while the amidine content decreased relative to other components, thus providing positive evidence for the presence of **12**.

Reaction of Amines with Hydrogen Peroxide in Acetonitrile. A. N-Butylidenebutylamine (**2**).—Hydrogen peroxide (98%) was dissolved in acetonitrile to give an 0.20 *M* solution. To this an equimolar amount of **2** was added at 25°. Analysis of the solution at intervals by glpc showed 39% loss of **2** in 2 hr and 50% loss in 8 hr, the reaction approaching a halt due to exhaustion of the peroxide. Residual **2** continued to decrease owing to slow disproportionation.[48] Glpc showed the major detectable product to be **7** (approximately 11% yield) with **5** about 3%. Butyraldehyde was also found in about 15% yield early in the reaction.

B. Butylamine (**1**).—Under the same conditions **1** was 30% destroyed in 24 hr, and no titratable peroxide remained. In another experiment the peroxide concentration was tripled (cooling required to hold the solution at 25°), resulting in 40% loss of **1**. A 13% yield of **2** was present after 12 hr when reaction had essentially stopped. The other principal detectable products were **5** (2.2%), **7** (1.8%), butyraldoxime[49] (1.9%), and PrCH=CEtCH=NBu (1.3%). Acetamide was also present in somewhat larger amount, but no amidine (**10** or **12**) was detected.

This experiment was repeated, but the temperature was allowed to rise to 50–60° during the initial mixing, leading to very different results. The predominant product was **N,N'-dibutylacetamidine** (**10**) (80% yield by peak area). Its identity was established by glpc isolation and high-resolution mass spectrometry which unequivocally gave the composition $C_{10}H_{22}N_2$ (calcd mass, 170.178; found, 170.178). It was then shown to be identical with an authentic sample by glpc and mass spectrometric comparison.

C. Dibutylamine (**26**).—Reaction of **26** (0.02 *M*) with hydrogen peroxide (98%, 0.62 *M*) in acetonitrile at room temperature essentially stopped at about 45% conversion in 90 min, when 2–3% yields of both **2** and **4** were present. The major detectable product proved to be N,N-dibutylhydroxylamine (**28**), approximately 12% yield. An unstable compound was also present (3% yield) in the fresh reaction mixture but was gone after 3 days. This had the glpc characteristics of **11**. Small amounts of N,N-dibutylformamide (**30**), **7**, and possibly **13** were present as well as considerable acetamide.

Identification of **28** was based on isolation by preparative glpc and comparison with an authentic sample by ir and mass spectrometry. The comparison sample was prepared by addition of an equivalent amount of 6% aqueous hydrogen peroxide to an equal volume of methanol containing **26**.[50] A distilled fraction boiling at 78–80° at 1.5 mm contained about 60% **28** plus substantial amounts of **30** and **7**. Mass spectrometric identification of **28** caused some problems because, instead of the molecular ion (*m/e* 145), the highst mass found was 143. This behavior was identical with both the experimental product and the comparison sample, for which the ir spectrum was adequate identification. Possibly the mass 143 represents the nitrone, PrCH=N(O)Bu, produced by dehydrogenation in the mass spectrometer.

D. Tributylamine (**27**).—An acetonitrile solution containing **27** (0.02 *M*) and hydrogen peroxide (98%, 0.62 *M*) was stored at room temperature for 4 days. Glpc analysis then showed 81% loss of **27**, and **4** and **26** were present in yields of 33% and 30%, respectively, based on converted **27**. Small amounts (3–5% yields) were also found of **7** and N-butenyldibutylamine (**29**). The crude reaction mixture was evaporated to remove most of the acetonitrile and the residue was dissolved in ether. Mixing with water then extracted the tributylamine oxide present, and addition of aqueous picric acid to the water solution precipitated the amine oxide picrate, mp 108–110° (lit.[51] 100°), 43% yield.

For the comparison above and other purposes, **29** was prepared by gradual addition of **4** to a small excess of **26** in cold ether in the presence of anhydrous potassium carbonate.[52] After 3 hr anhydrous magnesium sulfate was added, and the solution was later distilled. A fraction boiling at 72° at 3 mm was at least 90% pure by glpc.

Autoxidation of Dibutylamine. A. In Acetonitrile.—Autoxidation of a 0.2 *M* acetonitrile solution of **26** under the usual conditions destroyed 35% of the amine in 11 hr. Approximately 20% of the amine lost was present as **2** at this point. The solution was evaporated and the residue was examined as follows. Glpc analysis showed **5** to be the major detectable product, with N,N-dibutylformamide (**30**), **7**, **13**, and **6** present in lesser amounts, decreasing in that order. Compounds **12** and **14** also appeared at low levels. The compound **14** was isolated satisfactorily in the glpc–mass spectrometer and found to have *m/e* 157 with fragment ions of masses 142, 129, 115, 100, 84, 72, 57 (doublet), 46, and 41. High resolution mass spectrometry of the total reaction product concentrate revealed the presence of two compounds with mass 157. One of these was **30** ($C_9H_{19}NO$: calcd mass, 157.147; found, 157.146); the other (**14**) had the composition $C_8H_{15}NO_2$ (calcd mass, 157.110; found, 157.111) and is believed to be **2-butyryl-3-propyloxazirane**.

The plausible oxidation product **28** would, if present, not be resolvable from **5** by the KOH–polyethylene glycol column nor from **30** by the silicone column. However, by isolation of the **5** peak using a KOH–polyethylene glycol column in the glpc–mass spectrometer combination it was shown that the characteristic *m/e* 143 fragment of **28** was absent.

As the product concentrate aged, a group of eight glpc peaks appeared which were shown by comparison with standards to be owing to the four possible aldehyde "dimers" from a mixture of **4** and propionaldehyde, together with the four aldimines derived by condensation of these dimers with **1**.

When the autoxidation was carried out in acetonitrile containing 5% water, there was very little difference in the reaction rate or the products. The yields of **2** and **4** were somewhat higher, however, 53 and 74%, respectively, at their maximum values.

B. In Acetone.—Changes in the concentrations of **26** and **2** during autoxidation under standard conditions are shown in Figure 3. The possibility that the glpc peak for **2** included appreciable **3** was rejected because of the presence of **4** throughout the run. Examination of the final solution (4-hr reaction) showed the predominant glpc observable product to be **30** (about 23% yield). Other amides present were **5** (8%

(48) The aldimine **2** disproportionates spontaneously to **1** and PrCH=CEtCH=NBu to the extent of 13% in 21 hr in 0.2 *M* solution. This is too slow to cause appreciable complication. In longer time, higher condensation products are formed, but only this "dimer" is observed in the autoxidation reactions.

(49) Butyraldoxime, when freshly prepared, gives two glpc peaks on the KOH–Carbowax column, but in the presence of amines it is rapidly converted to a single isomer

(50) W. R. Dunstan and E. Golding, *J. Chem. Soc.*, 1004 (1899).

(51) H. B. Henbest and M. J. W. Stratford, *ibid.*, 711 (1964).

(52) C. Mannich and H. Davidsen, *Chem. Ber.*, **69**, 2106 (1936).

yield), **6** (3%), **7** (1%), and **13** (1%). The presumed oxazirane derivative **14** amounted to about 3%, and other minor products normally derived from **2** were observed. The enamine **29** was not present in detectable amount. (A standard sample of **29** was easily resolved from the autoxidation products by the KOH–polyethylene glycol column.) A minor peak corresponding to N,N-dibutylacetamide could be seen when the silicone column was used, but this identification could not be confirmed because of inadequate resolution from **30** on the KOH–polyethylene glycol column.

The mass spectrum of the **30** peak after resolution on a silicone column contained no component of mass 143. This established the absence of **28** and of N-butyl-N-propylformamide which could conceivably have been an unresolvable product.

C. In Methyl Methacrylate.—For this reaction, rose bengal was used in the "acid" form (lactonized). In the presence of the amine (0.02 *M*) 63% of the normal dye absorbance developed. As reaction proceeded, partial dye precipitation occurred. Autoxidation products appeared much the same as in acetonitrile. When 60% of the starting amine was destroyed, **5**, **7**, and **30** were each present in about 6–7% yield. The yield of **16** was very low at this time but increased to 10–12% as the solution was held at 5° for 24 hr; **30** increased substantially, also.

Reaction of **26** with methyl methacrylate is too slow to interfere with the autoxidation process.

2,2-Dimethyl-6-propyl-4-piperidone (**9**).—A solution of 10.0 g of 2-amino-2-methyl-4-oxopentane acid oxalate,[53] 5.0 ml of butyraldehyde, and 20 ml of ethanol was heated at reflux for 20 hr.[54] After cooling, the mixture was filtered, and the salt was treated with excess KOH in ether–water. The ether phase was evaporated and the residue was examined by glpc. The predominant component was identical with **9** obtained in autoxidation of **3**.

Reaction of 2-amino-2-methyl-4-oxopentane with butyraldehyde yielded a crude sample of **N-butylidene(2-amino-2-methyl-4-oxopentane)** which had glpc characteristics that would have made its resolution impossible in the autoxidation mixtures. It could have accompanied **11** as a fugitive intermediate. This aldimine was unstable at 25°, apparently "dimerizing" somewhat faster than **2**.

Examination of 2-Butyl-3,3-dimethyloxazirane.—This oxazirane was prepared by the general method of Krimm.[36] It distilled cleanly at 43–45° at 10 mm and was essentially pure by nmr examination: nmr (CCl_4) δ 1.30 (s, 3, CH_3), 1.46 (s, 3, CH_3), 2.63 (m, 2, NCH_2Pr), 1.50 (m, 4, $CH_2CH_2CH_2CH_3$), 0.93 (t, 3, CH_2CH_3); mass spectrum *m/e* (relative intensity) 129 (1), 114 (2), 100 (1), 86 (5), 84 (2), 73 (2), 70 (2), 58 (8), 57 (4), 56 (6), 55 (2), 44 (100), 43 (38), 42 (10), 41 (9). The oxazirane gave a clean peak on the silicone column at 30–100° at the same retention time as **2**, but it was shown by mass spectrometry that the oxazirane was not present in this peak after autoxidation of **3**. On the KOH–polyethylene glycol column the oxazirane decomposes to several products, probably[37] including N-butyl-N-methylacetamide and **6**; this behavior contraindicates its presence in autoxidation product mixtures.

The oxazirane was destroyed completely in an acetone solution containing an equivalent amount of **3** within 24 hr at 25°, but no products were formed which were detectable by glpc in the usual range of retention times. Presumably only polymeric imines and ammonia were formed.[37]

2-Butyl-3-propyloxazirane (**25**).—The product prepared by reaction of peracetic acid with **2** in CH_2Cl_2 according to the general procedure of Emmons[37] (bp 56° at 6 mm) was only about 50% pure by glpc and nmr analysis, containing a roughly equal amount of PrCH=CEtCHO. The somewhat different procedure of Krimm[36] gave essentially the same result. This low purity did not hamper establishment of the glpc characteristics of **25**. Drastic decomposition occurred on the KOH–polyethylene glycol column at 65°, but on the silicone column **25** was stable to at least 150°.

Decomposition of crude **25** at 120° was >90% complete in 50 min and produced two unknown compounds, X and Y, as well as a small amount of **7**. Subsequent heating for 45 min at 150° caused conversion of Y to another new substance, Z, and marked reduction of the butyraldehyde dimer. Distillation of the mixture yielded a fraction rich in X and Z from which both were isolated by preparative glpc using the Millipore Filter technique. The ir spectrum of X was consistent with a nitrone structure[55] PrCH=N(O)Bu: ir 1645 and 1632, strong doublet (C=N), 1085 and 1062 cm^{-1}, medium weak (possibly N→O). The only spectroscopically plausible alternative has appeared to be a disubstituted amide (*i.e.*, HCONBuPr), which would not be consistent with the glpc characteristics of X.

Spectroscopic evidence supported the postulated structure, **3,5-diethyl-4-propylpyridine** (**17**) for the product Z: ir 1602 (w), 1564 (m), 1417 (m, substituted pyridine nucleus), 902 cm^{-1} (m, isolated aromatic hydrogen);[56] mass spectrum *m/e* 177 (M^+), 176, 162, 149, 148, 134, 121, 106, 91, 77, 65, 53, 51, 44, 41.

Registry No.—**1**, 109-73-9; **2**, 4853-56-9; **3**, 6700-95-4; **26**, 111-92-2; **27**, 102-82-9.

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